The Ethically Required Level of Mental Capacity Needed for Consent to Participate in Clinical Research on the Terminally Ill

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Abstract

While medical informed consent documents have received much attention in literature and throughout varying North American legal jurisdictions, the competence needed to be able to provide informed consent is often overlooked. This is especially apparent in the medical research field where clinical trials are done with terminally ill human subjects. However, analyzing competence is crucial for the protection of subjects' autonomy. If informed consent is to be truly considered an expression of autonomous action, then it is necessary that the decision-maker be sufficiently competent to provide that informed consent. Given the vital role that competence plays in proper autonomous decision-making, the following will first engage in an examination of the concept of competence and second the requisite competence needed for terminally ill subjects to be able to provide informed consent to research participation. Since there is still some disagreement regarding the components of competence, first a proper description of competence will be provided. This will involve depicting competence as being comprised of four sub-abilities, specifically understanding, appreciation, reasoning, and voluntariness. With the proper depiction of competence, the remainder of this work will contend that current approaches to determine competency requirements are flawed, that the medical research context ought to require more stringent competency requirements than the medical practice context for the terminally ill, and that a Subject Rights Advocate (SRA), unaffiliated with the research study, should be employed to bolster/enhance and evaluate the competence of terminally ill potential subjects, as well as solicit the final informed consent. It will additionally be argued that the method the SRA ought to use in achieving such aims should be based on a conversational approach.

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everything they have done for me and for their continued love. It is to them that I dedicate this work.

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Chapter 1: Introduction to Competence, Consent, Autonomy and the Medical Research Context

We, often without any conscious recognition, make determinations of others' competence on a daily basis. Every time we respect the decision of a friend or co-worker we have implicitly assumed that he/she possesses a certain level of competence. Our reactive behaviours and attitudes towards others are determined by these types of assumptions. We may accept and endorse the decision or behaviour of another, or reject it outright based on what level of mental capacity we think he possesses. While some might suggest that this is an overstatement of the extent to which we make competence assumptions regarding others and the extent to which such assumptions influence our behaviour, we may posit various hypothetical, yet not uncommon scenarios, to see that it is indeed not an exaggeration.

Imagine a friend, we may call him Bob, informs you that he is about to go purchase a ring and propose to his girlfriend of one year. Your immediate reaction might be one of jubilation for him, and you will likely even congratulate him. It is possible that you may even offer your assistance, by perhaps accompanying him to the jewelers in order to provide advice regarding which ring to purchase.

However, if we modify the scenario slightly, a different reaction might seem more plausible. Instead imagine that you find yourself in the exact same situation, except in this second scenario, you know that Bob is fairly inebriated. You realize that his mental abilities are likely far too impaired to make such a decision, and instead of congratulating and encouraging him, you reject his idea to propose and perhaps even attempt to prevent him from carrying out his plan to fruition.

What has changed? In one instance you respect your friend's decision, accept it as a legitimate one and even endorse it. However, in the second scenario, your knowledge of Bob's level of intoxication, which may prevent him from deliberating properly, had you second-guessing his decision. In scenario 2, you second-guessed whether he was sufficiently competent to decide for himself.

This example demonstrates that even in common situations, assumptions of competence are being made. This remains true for many other serious decisions that you see others make from day to day, whether that involves moving to a different location, changing careers, or embarking on certain investment opportunities. Our reactions to a myriad of decisions made by others are in part determined by a presumption of their competence, for if we thought otherwise and had reason to think that they had a diminished mental capacity, there is a good chance that we would behave differently, and as with the proposal example, perhaps second-guess their decision.

Determinations of mental incompetence are crucially important, in both day to day interactions and particularly in the law. Depending on a person's mental capacity, she may or may not have certain decision making rights. An individual in an advanced stage of Alzheimer's or dementia for example, will likely lack the competence needed to be permitted to purchase or operate a vehicle. The implications of competence assessments are extensive and have particular importance for our laws. Many of our legal rights can be usurped due to a finding of incompetence. Even our ability to stand trial for example, is something that requires a certain level of competence; an issue that has received more attention in American and Canadian societies in recent decades. "Earlier estimates place the number of competence-to-stand-trial evaluations performed each year in the United

States at around 20,000, with more recent statistics citing 60,000, making such evaluations a significant focus of mental health inquiry in the criminal justice system."[1]

While the claim that a person's mental capacity is directly correlated with the acts or decisions she may or may not be permitted to perform should not be considered contentious or unethical, the topic of competence remains shrouded in controversy and ethical quandaries. What should the threshold level of competence be for a particular action? By what process should we determine another's mental capacity? How much evidence of a person's competence is required before making a competency determination? Given the importance of autonomy,[2] being able to navigate through these types of questions is a necessity. Mistakenly assessing one as incompetent when she actually has a great level of mental capacity may constitute a serious infringement on the rights of a citizen as this person would have her autonomy undermined. Thus, discovering solutions to these types of questions is paramount, especially in western cultures where autonomy is treasured as a foundational value.[3]

While it may prove difficult to actually solve some of these issues, it can furthermore become especially controversial in the realm of medicine. In the medical field, patients considering certain treatments and subjects of research are often faced with complicated, risky, and in many cases life altering decisions. We generally assume that before a patient makes a decision to accept or reject a particular treatment, or before a

[1] Debra A. Pinals, Chad E. Tillbrook, and Denise L. Mumley. "Practical Application of the MacArthur Competence Assessment Tool-Criminal Adjudication (MacCAT-CA) in a Public Sector Forensic Setting" *J Am Acad Psychiatry Law*, Vol. 34(2), pp. 179-188, June 2006, p.179.

[2] The concepts of autonomy and competence are related and will be further clarified later in this chapter, but for now a brief pragmatic definition should suffice. Autonomy refers to the state of being self-determining or self-governing, while competence may be thought of as "the ability to be autonomous" (Stephen Wear. "Patient Autonomy, Paternalism, and the Conscientious Physician" *Theoretical Medicine*, Vol. 4, pp. 253-274, 1983, p. 266).

[3] Many, for example, have suggested that autonomy constitutes a necessary element of human dignity. See: James Griffin. *On Human Rights* (New York: Oxford University Press, 2008) pp.149-158.

subject consents to participate in a medical research trial, that this person is competent enough to make these autonomous decisions. However this is not always the case. While much scholarship has been dedicated to the issue of the mental capacity of patients,[4] the matter that requires more attention and will be explored presently will involve the level of mental capacity which can enable an autonomous and ethical informed consent to medical research participation. More specifically, further consideration and analysis must be given to the matter of competence regarding terminally ill[5] individuals who find themselves considering participation as subjects in medical research. The decision to participate in research for these patients is often incredibly complex and difficult to make, as can be highlighted by the following case: A patient has recently been diagnosed with advanced pancreatic cancer and told he has at most six months to live. Surgery is not an option and the benefits of radiation therapy are marginal. Chemotherapy with Mitomycin is thought to offer him the best chance of living out the year. The patient is frightened and

[4] See, for example: Paul Appelbaum. "Assessment of Patients' Competence to Consent to Treatment" *The New England Journal of Medicine*, Vol. 357, pp. 1834-1840, 2007; Thomas Grisso, and Paul S. Appelbaum. *Assessing Competence to Consent to Treatment: A Guide for Physicians and Other Health Care Professionals* (New York: Oxford University Press, 1998); Paul S. Appelbaum, and Thomas Grisso. "Capacities of Hospitalized, Medically Ill Patients to Consent to Treatment" *Psychosomatics*, Vol. 38(2), pp. 119-125, 1997; Irwin Kleinman. "The Right to Refuse Treatment: ethical considerations for the competent patient" *Can Med ASSOC J*, Vol. 144(10), pp. 1219-1222, 1991; Paul S. Appelbaum and Thomas Grisso. "The MacArthur Treatment Competence Study. I: Mental Illness and Competence to Consent to Treatment" *Law and Human Behavior*, Vol. 19(2), pp. 105-126, 1995; Lainie Friedman Ross. "Health Care Decisionmaking by Children: Is it in their best interest?" In *Health Care Ethics in Canada*, Francoise Baylis, Jocelyn Downie, Barry Hoffmaster, & Susan Sherwin, eds. (Toronto: Nelson Ltd., 2004); and Alec Buchanan. "Mental Capacity, Legal Competence and Consent to Treatment" *Journal of the Royal Society of Medicine*, Vol. 97, pp. 415-420, 2004.

[5] What specifically constitutes a terminal illness may be a question that elicits some disagreement. Generally though, a terminal illness is thought to be a disease that cannot be cured or sufficiently treated and is likely to result in a patient's death. Certain types of cancer have become paradigmatic examples of terminal illness. We may proceed forward applying an often used definition in many North American jurisdictions. More specifically, a terminal illness refers to "an incurable and irreversible disease that has been medically confirmed and will, within reasonable medical judgment, produce death within six months" (Oregon Health Authority, The Oregon Death With Dignity Act: Oregon Revised Statutes, 1994, last accessed Jan. 2015: <http://public.health.oregon.gov/ProviderPartnerResources/EvaluationResearch/DeathwithDignityAct/Pages/ors.aspx>). It should be noted however, that some diagnosed with a terminal illness live long past the six month life expectancy time period.

desperate to beat the odds. He has heard of a high risk clinical trial that is testing a new anti-cancer drug. At this stage, the experimental drug is not a validated medical treatment and its therapeutic potential is still uncertain. If the patient is enrolled in the experimental arm of the trial he will forego the limited benefits of the best available validated treatment for pancreatic cancer. Even so, the patient wishes to enroll in the trial and is hopeful that this may be the miraculous cure he needs.

This case highlights some of the ethical concerns that should prompt investigation into the nature and level of competence needed for terminally ill persons to consent to participate in medical research. Does for example the patient understand the difference between the aims of research and standard medical practice? Does the patient's state of desperation constitute duress, and if not does it make him more vulnerable to other undue pressures? Is the level of mental capacity needed for this patient to consent to treatment adequate for him to consent to participate in research? These types of questions require some examination. In what follows, it will firstly be contended that a greater level of mental capacity is needed for terminally ill individuals to provide consent for research participation, than would be needed to consent to treatment for the condition under study. Exactly how great a level of competence, and how best to evaluate whether an individual possesses that level of competence, are two other issues that will also be addressed.

It should be noted though that an assumption has been made that there exists a real and morally relevant distinction between medical therapeutic practice and medical research. The distinction is of vital importance. Whether a particular intervention constitutes therapy or research, will determine to what types of moral standards and ethical guidelines it will be subjected, and this distinction will further have serious legal

implications since the two activities are governed by different laws. "Should a proposed course of conduct fit under the rubric of treatment [for example], an IRB[6] has no mandate or authority to review or comment upon its provisions."[7] The Belmont Report provides a concise description of the distinction between therapeutic practice and medical research, asserting that:

> 'practice' refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment, or therapy to particular individuals. By contrast, the term 'research' designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.[8]

While the difference between the two may seem intuitive, this distinction is not without its own controversy. For even with a seemingly unambiguous definition as the one provided by The Belmont Report, certain scenarios tend to blur this distinction. Two of these types of cases are often referred to as therapeutic research and experimental treatment. The term "therapeutic research" refers to research that is carried out where the research offers some potential for therapeutic benefit and may actually be performed in

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[6] An IRB is an institutional review board, whose function, according to the U.S. Food and Drug Administration (hereafter FDA), is to review and "approve every clinical trial taking place within their jurisdiction--usually a hospital. [More specifically] the purpose of an IRB review is to ensure that appropriate steps are taken to protect the rights and welfare of participants as subjects of research. If the risks to participants are found to be too great, the IRB will not approve the research, or it will specify changes that must be made before the research can be done" (U.S. Department of Health And Human Services, U.S. Food and Drug Administration, "Inside Clinical Trials: Testing Medical Products in People" Last Updated: June 2014, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143531.htm>). In Canada, the term research ethics board (REB) is used as opposed to IRB for the particular body responsible for reviewing and approving clinical trials with human subjects.

[7] Ezekiel J. Emanuel, Robert A. Crouch, John D. Arras, Jonathan D. Moreno, and Christine Grady. *Ethical and Regulatory Aspects of Clinical Research* (Baltimore: The Johns Hopkins University Press, 2003) p. 95.

[8] The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Washington, D.C.: Department of Health, Education, and Welfare, 1979), Section A *Boundaries Between Practice and Research*.

combination with standard medical care. The term "experimental treatment" describes a situation wherein a physician may attempt an uncertain non-validated procedure because he believes that it is the only recourse left in order to benefit the patient.[9] It should be noted that the use of these terms has elicited some controversy, especially the term "therapeutic research".[10] Nonetheless, despite the potential controversy surrounding the use of this term, it does denote a distinct type of research scenario where an individual might be receiving an already validated therapeutic treatment that he would otherwise be receiving for his particular ailment and the physician is also documenting the results for the purposes of research and contributing to generalizable knowledge in the field. Thus while the term used to define such a case might be controversial, this and the experimental treatment case are both scenarios that may represent some difficulty for the therapy/research distinction, and will thus be given further attention in Chapter Three.

Setting these blurry cases momentarily aside, it still appears that even if a strong distinction between research and therapy is maintained, determining the ethical level of mental capacity required for a terminally ill research subject to be able to provide informed consent for research participation remains a very broad and lofty order, and will thus require further narrowing. For example, prior to embarking on this endeavor, it is imperative that the different stages of clinical research trials be explicated.

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[9] "For example, consider the case of Baby Fae, an infant born with a defective heart who received a baboon heart when no human hearts were available… Or consider the birth of Louise Brown, the world's first test tube baby, in 1978. No one had performed in vitro fertilization in human beings before she was conceived. An obstetrician, Patrick Steptoe, performed this procedure in order to benefit his patient, Lesley Brown, who was suffering from fertility problems" (Adil E. Shamoo and David B. Resnik. *Responsible Conduct of Research* (New York: Oxford University Press, 2009) p. 250).

[10] See Robert J. Levine. *Ethics and Regulation of Clinical Research 2nd edition* (Baltimore: Urban & Schwarzenberg, Inc., 1986) pp. 8-10; and Robert J. Levine. "Clarifying the Concepts of Research Ethics" *Hastings Center Report,* Vol. 9(3), pp. 21-26, 1979. Some of the controversial issues surrounding such terminology usage will be explored subsequently in Chapter Three.

Health Canada and the FDA have a four category classification scheme for the different phases of clinical studies. We shall proceed by briefly examining each one in turn.

Phases of Clinical Trials[11]

Phase I trials, representing "the earliest-stage clinical trials for studying an experimental intervention in humans, are small (typically fewer than 100 participants) and aim to determine the toxicity and maximum safe dose of a new drug."[12] More specifically "in phase I drug studies, investigators are measuring the pharmacological and toxicological effects of a drug to estimate a maximum tolerable dose."[13] While many Phase I clinical trials often involve paid healthy subjects who receive no therapeutic benefits from participation, some are conducted on severely and/or terminally ill patients.[14] Terminally ill cancer patients, for example, might be used in Phase I cancer trials. "The reason for this is that most anticancer agents, whether cytotoxic chemotherapies or other more targeted non-cytotoxic agents, commonly have toxic

[11] It should also be noted that prior to Phase I trials, preclinical studies are conducted in a laboratory setting and often on animals. The preliminary data obtained through these trials is used to support a request to the appropriate body (Health Canada or the FDA for example) to begin testing the non-validated procedure on humans.

[12] National Bioethics Advisory Commission (NBAC), *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries Vol. I*: *Report and Recommendations of the National Bioethics Advisory Commission*, (Bethesda, Maryland: 2001) p. 21.

[13] Shamoo and Resnik, 2009, p. 248.

[14] See, for example: Robin Fretwell Wilson. "The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research" *American Journal of Law & Medicine,* Vol. 36, pp. 295-325, 2010. The Jesse Gelsinger case is a fairly recent example that ended in scandal. "Jesse had a rare disease, a liver deficiency called ornithine transcarbamylase deficiency ("OTCD") that made it difficult for his liver to process proteins" (Wilson, 2010, p. 298). He participated in a Phase I gene- therapy trial, and due to various unethical practices, including a lack of proper disclosure, being exposed to a considerably higher dosage of the treatment than was considered appropriate, being given the non-validated treatment despite the fact that "his ammonia levels fell outside the protocol's safety limit" (Wilson, 2010, p. 300), and an overarching conflict of interest, he subsequently died.

effects in normal tissues at doses that are likely to be effective."[15] Since Phase I trials are the first time that the non-validated procedure is tested on humans, there are a myriad of observations that researchers can record. However, though there are certain secondary observations made in a Phase I trial, which may include determining the pharmacokinetics (PK)[16] of the experimental drug, assessing the pharmacodynamics (PD),[17] and sometimes even documenting any obvious potentially therapeutic activity of the experimental drug, such as recording anti-tumor effects, it is crucial to realize that the primary aim of a Phase I trial is "to determine [the] recommended dose of the new agent for further study,"[18] which is often the maximum tolerable dose (MTD).[19] Insofar as determining the PK and PD are necessary for recommending further dose scheduling of the experimental drug, they may be considered primary observations necessary in a Phase I trial, however any possible observations concerning the therapeutic potential of the non-validated drug/intervention may be properly considered secondary observations, and are often left to later trial phases.

[15] Elizabeth A Eisenhauer, Chris Twelves, and Marc Buyse. *Phase I Cancer Clinical Trials: a practical guide* (New York: Oxford University Press, 2006) p. 42.
[16] Pharmacokinetics involves studying the bodily absorption, distribution, metabolism, and excretion of the experimental agent.
[17] These are the "pharmacologic effects of the drug on the body (eg, nadir neutrophil or platelet count, nonhematologic toxicity, molecular correlates, imaging endpoints)" (Christophe Le Tourneau, J. Jack Lee, and Lillian L. Siu. "Dose Escalation Methods in Phase I Cancer Clinical Trials" *J Natl Cancer Inst,* Vol. 101(10), pp. 708-720, 2009, p. 709).
[18] Eisenhauer et al., 2006, p. 41, table 3.1.
[19] More specifically Phase I trials involve an escalation of the administration of the drug until the MTD is discovered. The trial design functions by applying the concept of dose-limiting toxicity (DLT) which is defined as the "toxic effects that are presumably related to the drugs that are considered unacceptable (because of their severity and/or irreversibility) and that limit further dose escalation" (Tourneau et al., 2009, p. 709). "Generally two patients out of a minimum of three or six must experience DLT for escalation to cease. The dose level at which DLT is seen in the minimum number of patients required to halt further escalation is termed the maximum tolerated dose (MTD)" (Eisenhauer et al., 2006, p. 54).

Phase II studies are conducted on a slightly larger group of subjects (typically between 100 and 300). This is the first instance where controlled clinical trials[20] are used to determine the effectiveness of the non-validated drug/intervention. While determining the relative safety continues to be an important goal in this phase, at this stage the main emphasis is placed on beginning initial therapeutic exploration. "Additional objectives of clinical trials conducted in Phase II may include evaluation of potential study endpoints, therapeutic regimens (including concomitant medication) and target populations (e.g. mild versus severe disease) for further study in Phase II or III."[21] The subjects of these studies are often chosen by fairly narrow criteria, are those who are afflicted with the disease or condition for which the experimental drug or procedure was produced, and are monitored very closely.

Provided that adequate results from the Phase II study are obtained, a Phase III trial may commence with the non-validated drug/procedure. "Phase III trials are large, frequently multi-institution studies, and typically involve from a hundred to thousands of participants. Approximately 25 percent of all drugs tested in clinical trials successfully complete Phase III testing."[22] A Phase III trial's main aim is to acquire additional evidence regarding the effectiveness of the non-validated intervention. While Phase II trials are sometimes labeled therapeutic exploratory, Phase III trials are sometimes

[20] A controlled clinical trial is designed in order to establish a standard against which a non-validated drug/procedure may be properly evaluated. This often involves two groups of subjects whereby one group receives the non-validated drug/procedure, while the other group receives either standard validated treatment or in some cases a placebo. One common type of controlled clinical trial is the randomized controlled trial (RCT) wherein the subjects of the clinical study are randomly placed in the different arms of the trial. The often cited benefit of RCTs is the reduction in the bias associated with allocating certain subjects to one particular arm of the trial over the other.

[21] Health Canada, *Guidance for Industry: General Considerations for Clinical Trials ICH Topic E8*, (Ottawa, Ontario: Minister of Public Works and Government Services Canada, 1997), p. 9.

[22] National Bioethics Advisory Commission (NBAC), *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries Vol. I*: *Report and Recommendations of the National Bioethics Advisory Commission*, (Bethesda, Maryland: 2001) p. 21.

referred to as therapeutic confirmatory trials. Often, the non-validated drug/intervention is tested against a placebo or current validated treatments for the disease/ailment under study in order to confirm its efficacy as therapeutically beneficial. "These studies carried out in Phase III complete the information needed to support adequate instructions for use of the drug (official product information)."[23]

Phase IV studies are conducted after the drug/intervention has been approved. Though these studies are typically not deemed necessary for approval, they may still prove to be quite significant as they can contribute to optimizing the use of the drug/intervention. These post-marketing studies can come in a multitude of forms and for a variety of purposes. Some common examples include studies investigating: drug-drug interactions, indications "for which it is presumed that the drug, once available, will be used,"[24] the long term effects that a drug may have on morbidity and mortality, and additional information regarding the use of the drug "in a patient population not adequately studied in the premarketing phase, e.g., children."[25]

Given these differences between different trial phases, we may now narrow the focus of this work as being applicable to only certain phases of clinical trials. More specifically the following will undertake to investigate and determine the level of mental capacity which can enable an autonomous and ethical informed consent to participate in phase I, II, and III medical research trials. One of the main primary aims in what follows will be to demonstrate that greater mental capacity is required for terminally ill

[23] Health Canada, *Guidance for Industry: General Considerations for Clinical Trials ICH Topic E8*, (Ottawa, Ontario: Minister of Public Works and Government Services Canada, 1997), p. 10.
[24] Levine, 1986, p. 7.
[25] Levine, 1986, p. 6. It may additionally be noted that sometimes Phase IV trials are also done for the purposes of introducing a drug to a physician and getting her to prescribe it in the hopes that the prescribing will continue. These types of trials, often known as "seeding trials", are for marketing purposes and have no scientific value.

individuals to consent to participate in phase I, II and III research trials than to consent to treatment for the condition under study. Ensuring that an appropriate level of competence is possessed by potential research subjects is one of the best safeguards that can be offered in order to protect subjects' interests.

Corruption in Research

The idea that the health and wellbeing of patients should reign as a supreme value in medicine, even more importantly than the advancement of medical knowledge, is not a new concept at all, stemming back to the time of Hippocrates (460-377 B.C.). For "although Hippocratic physicians sought to improve medical knowledge, their code of ethics and their philosophy of medicine implied that medical advances would occur slowly and would not sacrifice the welfare of the individual patient for scientific progress."[26] Unfortunately at times throughout our recent history it appears as though we have forgotten this basic precept as medical research has been plagued with horrible abuses through numerous scandals. This can be seen by some of our most infamous examples such as the medical experimentation done under the Nazi regime in WWII, and the Tuskegee Syphilis study.

The medical research done in Nazi Germany provides various examples of particularly horrific experimentation.

> These "experiments" included deliberate infection with poisons or pathogens, such as typhus, malaria, smallpox, cholera, yellow fever, and diphtheria, to study the course of the illnesses and possible vaccinations and treatments; studies in which victims were locked in low pressure chambers that duplicated conditions such as falling great distances through space without oxygen; experiments in which victims were exposed for hours to freezing temperatures or freezing water; infliction of simulated battle-caused wounds and infections to test various treatments; sexual sterilization experiments using surgery, high-dose x-rays, and pharmacological

[26] Shamoo & Resnik, 2009, p. 237.

> techniques; and the deliberate "induction" of the death of selected Jewish inmates to provide skulls and skeletons for research purposes.[27]

It was from the Military Tribunals following this atrocity that the Nuremberg Code, an internationally recognized document regarding the ethics of research, was developed.

However, despite recognizing this code and some of the core ethical values it advocated, the United States was not without its own infamous cases of reprehensible medical experimentation. For example, the U.S. has been widely criticized for its implementation of the Tuskegee Syphilis Study. This research study began in 1932 and was initiated in

> Macon County, Alabama, to determine the natural course of untreated, latent syphilis in black males. The test comprised 400 syphilitic men, as well as 200 uninfected men who served as controls. … When Penicillin became widely available by the early 1950s as the preferred treatment for syphilis, the men did not receive therapy. In fact on several occasions, the USPHS [U.S. Public Health Service] actually sought to prevent treatment. Moreover, a committee at the federally operated Center for Disease Control decided in 1969 that the study should be continued. Only in 1972, when accounts of the study first appeared in the national press, did the Department of Health, Education and Welfare halt the experiment. … At that time seventy-four of the test subjects were still alive; at least twenty-eight, but perhaps more than 100, had died directly from advanced syphilitic lesions.[28]

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[27] Jocelyn Downie, Timothy Caulfield, and Colleen M. Flood. *Canadian Health Law and Policy 2nd edition* (Ontario: Butterworths Canada Ltd., 2002) p. 464. (This information was derived from T. Taylor. "Opening Statement of the Prosecution December 9, 1946" In *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation,* Annas and Grodin, eds. (New York: Oxford University Press, 1992). It should further be noted that despite the focus historians and ethicists have placed on the Nazi experiments during World War II, Japan was guilty of performing equally atrocious medical experiments during the same time. "From 1932-1945, Japanese medical researchers killed thousands of human subjects in medical experiments… The experiments included intentionally wounding and operating on human beings for surgical training, vivisection of live humans, infecting humans with pathogens, exposing subjects to extremes of temperature, and biological and chemical warfare research… At the end of the war, the U.S. government made a deal with Japan to gain access to the data from chemical and biological warfare experiments. In exchange for this data, the U.S. government agreed to not prosecute Japanese physicians and scientists for war crimes. As a result of this cover-up, the Japanese atrocities were not widely known until the 1990s, and Japanese political leaders have been reluctant to acknowledge that these crimes against humanity occurred" (Shamoo and Resnik, 2009, pp. 241-242). For more on this see: T. Tsuchiya. "Imperial Japanese Medical Atrocities and Their Enduring Legacy in Japanese Research Ethics" In *Contemporary Issues in Bioethics*, Beauchamp, Walters, Kahn, and Mastroianni, eds. (Wadsworth, Belmont, CA, pp. 56-64, 2008).

[28] Allan M. Brandt. "Racism and Research: The Case of the Tuskegee Syphilis Study" *The Hastings Center Report*, Vol. 8(6), pp. 21-29, 1978, p. 21. What perhaps further adds to the degree to which ethics was ignored in this case was the fact that the subjects who participated were not informed of their particular

Of course these are not the only two cases of misconduct in medical research involving human subjects,[29] and as the numerous cases have been brought to the public's eye, so too has the desire for proper oversight. In fact, regulatory changes including research ethics codes, laws, and international guidelines regarding medical trials, have often come as a response to these disgraceful cases of ethical indiscretions in medical research. For example:

> Vaccination trials conducted without consent on poor and vulnerable people, mainly abandoned children and prostitutes, led to research regulations in Prussia as early as 1900 and, remarkably, to rather detailed regulations in pre-Nazi Germany in 1931. [As previously mentioned] the horrific experiments conducted by German doctors under the Nazi regime led to the first internationally influential declaration of standards for medical research, commonly known as the *Nuremberg Code*."[30]

It would thus seem to be no exaggeration to assert that "research ethics-as a discipline that informs and responds to clinical and regulatory practice- was 'born in scandal and reared in protectionism,' to use Carol Levine's apt phrase."[31] While governments have often responded to these dark moments by releasing codes and guidelines for medical research, the problem of ethical misconduct on human subjects in medical research still persists.

Though the situation may look bleak, it should be noted that much work and progress has been done in order to try to afford better protections from abuse and unethical conduct for subjects of clinical research, especially for certain vulnerable

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illness, or that they were even participating in a research study. Rather they were told that their blood was bad and could receive free treatment and lunches.

[29] See: J. Kats. *Experimentation with Human Beings* (New York: Russell Sage Foundation, 1972); H. Beecher. "Ethics and Clinical Research" *N Eng J Med*, Vol. 274, pp. 1354- 1360, 1966; M. Pappworth. *Human Guinea Pigs* (London: Routledge & Kegan Paul, 1967); and Hyman v. Jewish Chronic Disease Hospital, 248 N.Y.S.2d 2455 (1964). Canada has also not been immune to medical research scandals, engaging in its own share of unethical research practices. "One of the most notorious research scandals involved the scientifically flawed mind-altering experiments by then world-renowned psychiatrist Dr. Cameron at McGill University's Allan Memorial Hospital in the 1950s. Another instance of abuse of research subjects in psychiatric research came to light only recently, with an investigation into the administration of lysergic acid diethylamide ("LSD") and electroconvulsive therapy ("ECT") in Kingston's federal prison for women" **(**Downie et al., 2002, p. 466).

[30] Downie et al., 2002, p. 464.

[31] Emanuel et al., 2003, p. 2.

populations, including children, prisoners and pregnant women. Various guidelines, such as Title 45 (Public Welfare), Code of Federal Regulations, Part 46 (Protection of Human Subjects)[32] and The International Ethical Guidelines for Biomedical Research Involving Human Subjects[33] have focused on ensuring that these and other vulnerable populations do not have their vulnerability exploited.[34] However it seems that one particular vulnerable group requires far more attention. More specifically, it must be recognized that terminally ill persons also constitute a vulnerable population and require similar consideration.

Many of the ethical controversies surrounding terminally ill subjects often revolve around a disrespect for the requirement of informed consent. While informed consent has proven to be a great safeguard against abuse, it alone is insufficient. A crucial issue often neglected is determining the competency of a potential research subject. However, this is a vital step, for it should be clear that if autonomy is to truly be respected, then for an informed consent to be considered ethically legitimate it must be the case that the person is substantially competent to provide the informed consent. Unfortunately, this realization raises more questions than it answers. How great does one's level of mental capacity need to be in order to consent to participate in a medical research trial? Does the level of risk associated with participation play any type of significant role in determining one's

[32] U.S. Department of Health and Human Services, National Institutes of Health, and Office for Protection from Research Risks, Title 45 (Public Welfare), Code of Federal Regulations, Part 46 (Protection of Human Subjects) Washington, D.C.: Revised January 15, 2009 (Effective July 14, 2009).
[33] Council for the International Organizations of Medical Sciences (CIOMS) in Collaboration with the World Health Organization (WHO): International Ethical Guidelines for Biomedical Research Involving Human Subjects, (Geneva: August, 2002).
[34] It should be noted that despite the various advances and attention on correcting potential ethical misconduct with vulnerable populations, the situation is still far from being resolved. However, the regulatory guidelines, laws, and the fact that ethics has become a prominent matter in this field, certainly demonstrate progress and suggest a step in the right direction.

competency? Assuming evaluations of others' competence can be mistaken, what level of evidence is necessary to show that an individual is competent to participate?

However, prior to engaging in any analysis regarding the requisite level of competence, or evidence of competence, needed for participation in medical research, it is imperative that first a precise definition of competence be adopted, second that an account of informed consent be provided, and third that the concept and value of autonomy be explicated. Thus, we shall proceed by examining each in turn.

Competence/Mental Capacity

Throughout this chapter it may be noted that the terms "mental capacity" and "competence" have been used interchangeably, and while this is not entirely accurate, it has served a practical purpose. In actuality competence is often thought of as a legal requirement, and the term "mental capacity" is instead frequently employed to refer to a person's capability to perform a decisional task when the law itself is not being discussed. Despite this dissimilarity though, the two terms are thought to have similar, if not the exact same, criteria and conditions. The only real difference is that competence, being a legal term, functions as a threshold. This implies that a person is either considered legally competent or not for the specific decisional task at hand. Whereas, mental capacity is often recognized as being a matter of degree, and thus though two persons might both be legally competent to perform some decisional task, providing an informed consent for example, the mental capacity of one might be greater than that of the other. However, since much of the literature, laws, and ethical guidelines tend to

oscillate between the two terms, this distinction need not trouble us any further as we shall proceed using both terms interchangeably in order to avoid confusion.[35]

No longer concerning ourselves with this distinction, we may appropriately ask: how is competence/mental capacity to be defined? Competence is often considered to be 'the ability to perform a task', and thus competence for the medical research context will refer to the ability to perform the task of decision making regarding participation in medical research trials. However, this definition alone is incomplete as it does not provide a satisfactory explanation of all of the elements that comprise competence.

Though establishing criteria for competence is a fairly controversial topic, and the legal standards for competence appear to vary slightly between jurisdictions, both the law and leading contributions to this topic seem to have converged somewhat and agreed that some form of the following four conditions are at least necessary for competence.[36] These conditions include (1) Understanding, (2) Appreciation, (3) Reasoning, and (4) Intentional/Voluntary Choice.[37] Though some have also argued that a value criterion

[35] It should be mentioned that this will not affect any of the arguments made below since both competence and mental capacity are thought to consist of very similar if not the exact same elements. Furthermore, "although incompetence denotes a legal status that in principle should be determined by a court, resorting to judicial review in every case of suspected impairment of capacity would probably bring both the medical and legal systems to a halt" (Appelbaum, 2007, p.1834). Recognizing that many evaluations of capacity will thus occur on the fly by medical practitioners and researchers, all recommendations made herein regarding the appropriate standards of competence for terminally ill medical research subjects, should be applied by courts and the relevant medical personal alike. However, it should be noted that in the following Chapters, recommendations will be provided as to who ought to be the competency evaluator for terminally ill subjects of medical research.

[36] Some of the controversy revolves around whether or not a value criterion should be included.

[37] These criteria are derived primarily from: Louis Charland, "Decision-Making Capacity", *The Stanford Encyclopedia of Philosophy (Fall 2008 Edition)*, Edward N. Zalta (ed.), URL = <http://plato.stanford.edu/archives/fall2008/entries/decision-capacity/>. However, the criteria along with the accompanying analysis of each condition have also been heavily influenced by Appelbaum 2007; Thomas Grisso, and Paul Appelbaum. *Assessing Competence to Consent to Treatment: A Guide for Physicians and Other Health Care Professionals* (New York: Oxford University Press, 1998); Tom Beauchamp & James Childress. *Principles of Biomedical Ethics* (New York: Oxford University Press, 2009); and Jessica Berg, Paul Appelbaum and Thomas Grisso. "Constructing Competence: Formulating Standards of Legal Competence to Make Medical Decisions" *Rutgers L. Rev.* Vol. 48, pp.345-396, 1995-1996.

should be added, the acceptance or denial of this fifth condition is irrelevant for our present purpose.[38]

The understanding component is perhaps the most evident condition of competence. It involves both being in possession of and having the ability to grasp the salient information in a particular decision making context. In the medical practice or medical research context, understanding can be compromised not only if the person cannot adequately comprehend certain facts, but also if the physician or researcher respectively does not disclose relevant or correct information to the patient or subject. Since a full or complete understanding of all aspects of a decision is unlikely if not impossible, an appropriate level of understanding will likely refer only to some substantial level of comprehension regarding relevant information. However, what may properly constitute relevant information is not always clear. This ambiguity has allowed for an abundance of controversies and legal disputes.[39]

There is an additional manner in which understanding can be compromised that is specific to the medical research context. Namely, sufficient understanding is lacking if the research subject does not grasp the nature and purpose of the research study. More specifically, the subject may misconstrue the research trial for therapeutic practice. This

[38] Though not vital for our purposes, a brief explanation of the contentious value criterion may be instructive. The value condition can be said to require that a person be able to make a judgment about the relevant information in light of her values. "Since a subject's values can be expected to change over time, what is required is not an immutable, fixed, set of values, but a minimally consistent and stable set of values (Buchanan & Brock, 1987, 24). Another way of expressing this point is to say that capacity requires 'a conception of what is good' (*Ibid*). The reason for this last requirement should be obvious. Weighing the risks and benefits of various alternative choices requires values (Charland 1998a). So does selecting one option over others" (Charland, 2008).

[39] See, for example: Reibl v. Hughes, (1980) 2 S.C.R. 880. The facts of this case are discussed below in note 45.

phenomenon has become a prevalent dilemma in medical research trials and has been referred to as the therapeutic misconception.[40]

Furthermore, as will be the case with all four conditions of competence, it should be recognized that ensuring that the criterion is satisfied at one particular occasion may not be sufficient. Since, as time passes, new information may become available, the understanding criterion is only met if any new relevant material is made known to the decision-maker. This can become especially pertinent in the medical research context, where it is likely that new salient information may become available. The *International Conference on Harmonisation, Guideline for Good Clinical Practice* (hereafter ICH-GCP) corroborates this sentiment, asserting that the "subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial."[41] For this reason, the understanding criterion of competence, and the three remaining criteria discussed below, can be viewed as requiring a continual fulfillment, as opposed to simply being satisfied at the onset of the clinical trial.

The appreciation condition, being slightly more complex than understanding, requires that a subject be able

> 'to appreciate the nature and meaning of potential alternatives — what it would be like and "feel" like to be in possible future states and to undergo various

[40] The therapeutic misconception and how it affects competence will be elaborated upon in Chapter Three.
[41] International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonised Tripartite Guideline- Guideline for Good Clinical Practice (Geneva: 1996), p.15. This international document forms the basis for much of the ethical regulations in clinical trials. In fact "certain member states of the European Union, Japan, Russia, Hungary, and Poland have adopted ICH-GCP as national law; the United States, Canada, India and the Philippines have adopted ICH-GCP as official guidance" (National Bioethics Advisory Commission (NBAC), *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries Vol. II*, "Comparative analysis of international documents addressing the protection of research participants" (staff analysis), Bethesda, Maryland, 2001, p. D-60). It should be noted that since this publication Hungary and Poland have in fact become member states of the European Union.

> experiences — and to integrate this appreciation into one's decision making' (Buchanan & Brock, 1989, 24). This element of capacity is sometimes held to derive from the legal requirement that each subject must have 'insight' into the circumstances of a given decision (Glass 1997).[42]

Appreciation, for example, in regards to medical treatment decisions would thus refer to "the ability to relate diagnostic and treatment information and related consequences to one's own personal situation"[43] as opposed to merely understanding that information in an abstract and detached sense. Thus, for example, "patients who accept that their physicians believe they are ill, but deny that there is a problem in the face of objective evidence to the contrary, would fail this component."[44]

This criterion of competence emphasizes the significance of grasping the relevance of certain information and decisions for one's own personal circumstances. What is required for appreciation may thus be different from person to person. This denotes a slight departure from the understanding criterion. An example may be helpful in demonstrating the difference. We can imagine two patients, both being brought to the hospital and as a result of both being diagnosed with a gangrenous leg, each patient will require amputation. These individuals are further informed that after the surgery they will then be provided with prosthetic replacements.

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[42] Louis Charland, "Decision-Making Capacity", *The Stanford Encyclopedia of Philosophy (Fall 2008 Edition)*, Edward N. Zalta (ed.), URL = <http://plato.stanford.edu/archives/fall2008/entries/decision-capacity/>.

[43] Jennifer Moye and Daniel Marson. "Assessment of Decision-Making Capacity in Older Adults: An Emerging Area of Practice and Research" *The Journal of Lifelong Learning in Psychiatry,* Vol. 7(1), 2009, p. 91.

[44] Berg et al., 1995-1996, p.355. See for example: Roe, 583 N.E.2d 1282, 1286 (Mass. 1992); and Lane v. Fiasconaro, 1995 WL 584522 (Mass. App. Div.); and also Alaska Statutes 2011, Title 47, Welfare, Social Services and Institutions, Sec. 47.30.837(d)(1)(B) (2011) which asserts that competence includes that a patient "appreciates that the patient has a mental disorder or impairment, if the evidence so indicates; denial of a significantly disabling disorder or impairment, when faced with substantial evidence of its existence, constitutes evidence that the patient lacks the capability to make mental health treatment decisions."

It may seem clear that the understanding component for both patients will require some level of comprehension regarding their diagnosis of gangrene, the treatment of amputation, and how prosthetics function. This does not represent an exhaustive list of everything that these patients ought to understand, but it does suggest that the information that must be understood will be similar for both of them. However, what the patients must appreciate might be different. Expanding on this hypothetical case, we may further imagine that one of these patients was a professional basketball player, while the other was an author. Appreciation for the basketball player may require some comprehension of how this procedure will affect his career and perhaps even the manner in which he views himself. However, appreciation for the author may be quite different. For the manner in which she conceives of what it would be like to be in the possible future state post amputation, and how she integrates that in her decision making, may vary greatly from that of the basketball player since her career and identity do not have their foundation in her ability to run or perform well in athletics.

Thus, while some may misguidedly conflate the understanding and appreciation criteria and view them as one in the same, the stark differences between the two should now be apparent, and any true assessment of another's competence will require an evaluation of both.[45]

[45] To see how understanding and appreciation both play a significant role in legal matters, consult: Reibl v. Hughes, [1980] 2 S.C.R. 880. Mr. Reibl "elected to undergo an internal carotid endarterectomy to remove an occlusion in an artery near his brain… The operation was performed competently by Dr. Hughes, a fully qualified neurosurgeon. However, following the procedure, Reibl suffered a massive stroke, resulting in the paralysis of his entire right side…The risk of stroke, in the absence of surgery, had not been imminent… The trial judge found that the precise purpose for the operation was not sufficiently explained, and that Mr. Reibl was left only with the impression that his headaches and hypertension would decrease… The only risks Mr. Reibl was cognizant of were those inherent in any surgical procedure, such as infection. Had he known of the more serious risks, Mr. Reibl claimed he would not have gone ahead with the operation, especially in light of the fact that he was only one and a half years away from being eligible for pension benefits from his employer" (Francoise Baylis, Jocelyn Downie, Barry Hoffmaster, & Susan Sherwin.

The third condition, categorized as reasoning, involves the ability to "engage in a rational[46] process of manipulating the relevant information."[47] This includes some level of consistency in choices, actions and deliberation, as well as the ability to derive the appropriate conclusions from premises. This is not to suggest that choices must be consistent with past character and values, for that would be an element of a value condition, but rather merely that a person should not exhibit obscenely frequent reversals of choice, which may show a defect in cognitive functioning. "Reasoning is also usually said to include the ability to weigh risks and benefits and evaluate putative consequences,"[48] an ability that is crucial in the medical research decision making context.

There might be some concern that including the ability to rationally manipulate information in order to derive a conclusion could "lead to incompetence adjudications based simply on the unconventionality of a patient's decisions."[49] The issue being that any decisions made contrary to a physician's professional opinion might be deemed irrational. Any criteria of competence which could lead to this consequence would

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Health Care Ethics in Canada 2nd edition (Toronto: Nelson Ltd., 2004) p. 245. In this case it was thus determined that the material risks that must be disclosed to a patient considering a treatment cannot be determined solely by an objective standard or subjective standard, but rather should be based on some combination of both. Ultimately, it was decided that Dr. Hughes in this case behaved negligently as a result of not adequately disclosing certain risks that would not only be considered relevant by any reasonable person, but were also particularly relevant given the specific circumstances of the patient, Mr. Reibl. This thus left Mr. Reibl unable to satisfy the appreciation criterion needed for the capacity to be able to consent to treatment.

[46] While the concept of rationality is quite complex, a rough and ready definition will suffice here. Thus rationality can be understood simply as the ability to formulate proper interests and ends, pursue one's interests and ends, and effectively employ proper means/ends reasoning. More concisely, rational means the ability to further one's interests in an effective way. For a more specific depiction of rationality see: John Rawls. "Justice as Reciprocity" In *Collected Papers: John Rawls*, Freeman, eds. (Cambridge: Harvard University Press, 1999) p. 199.

[47] Appelbaum, 2007, p. 1836. Appelbaum also correctly elucidates the point that this condition "focuses on the process by which a decision is reached, not the outcome of the patient's choice" (Appelbaum, 2007, p. 1836).

[48] Charland, 2008.

[49] Berg et al., 1995-1996, p. 358. Similar to the position adopted here, these authors also do not view this fear as warranted.

certainly be flawed. However, an appropriate application of this reasoning criterion of competence must recognize that what is sought is not some absolute, objective rational decision, but rather that whatever the decision, it can be demonstrated as following logically from relevant premises. Thus this reasoning criterion may be satisfied even if the decision made is not in accordance with that of a medical professional. While the medical professional may be a reasonable person himself, his preferences "are neither exhaustive or definitive of the repertoire of the reasonable man."[50] We may therefore dismiss this concern as something that would only follow from a misguided and inappropriate use of the reasoning criterion of competence.

The fourth condition, frequently referred to as the choice criterion, is often thought of as merely "expressing a choice, referring to the patient's ability to state a preference."[51] However, it is crucial that this criterion be revised such that the notion of voluntariness be incorporated. Though voluntariness is often considered a condition of informed consent,

> it can also be thought of as an important aspect of the choice element of decision-making capacity. The ability to express a choice is morally irrelevant if the choice itself cannot be made voluntarily. Even if a person is expressing a choice but is unable to mentally overcome a coercive environment, as would be the case if the person made a choice while being deceived or manipulated, then the expression of the choice was certainly not a true satisfaction of this fourth requirement of decision-making capacity. Other scholars have alluded to something similar; for example, Beauchamp & Childress (2009) state that "patients or prospective subjects are competent to make a decision if they have the capacity to…communicate freely their wishes to caregivers or investigators" (p. 113). The term "freely" implies what is being argued here, namely, that voluntariness is a feature of the choice condition of decisional capacity. While

[50] Benjamin Freedman. "Competence, Marginal and Otherwise: Concepts and Ethics" *International Journal of Law and Psychiatry*, Vol. 4 (1-2), pp.53-72, 1981, p. 60.
[51] Grisso & Appelbaum, 1998, p. 58.

> this voluntariness feature can be considered to be an implicit part of the choice element of competence, it is certainly worth emphasizing.[52]

The addition of this voluntariness aspect is crucial. For it must be noted that an individual who possesses the requisite understanding, appreciation and reasoning, but who lacks confidence in himself to such an extent that his opinion can be swayed by the mere suggestion of another, may be unable to make competent decisions, even if he was physically capable of expressing a choice. This is not just an unlikely hypothetical, but may be particularly true in the medical decision making context where decisions may be of a complex and emotionally taxing nature and may require a certain confidence and strength of will. Jessica Berg et al. express a similar sentiment in a discussion of autonomy claiming that:

> People who feel they are too ignorant or too weak to make choices, or who cannot find the emotional strength to do so, are not capable of acting autonomously. As a result, they may become overly susceptible to external influences that would otherwise not be considered undue. They may, for example, be overawed by the prestige of medical professionals or defer to an authority figure in their family. Some people may suffer from phobias or other internal constraints that overwhelm their wills so they cannot freely choose an option they would otherwise desire. A patient who has been sexually abused, for example, might feel incapable of having a physical exam despite intellectually recognizing the health-related benefits it may afford.[53]

The connection between voluntary choice making and competent decision making should thus seem clear. It is not merely sufficient that people be able to understand, appreciate and reason substantially, but must furthermore make their final decision freely based on that understanding, appreciation, and reasoning. In judging one's ability to make competent decisions, if there is a disconnect between the first three conditions of

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[52] Alessandro Manduca-Barone. "Including Appreciation and Voluntariness: The other two elements of decision-making capacity" *American Journal of Bioethics Neuroscience*, Vol. 2(1), pp. 43-45, 2011, p. 43.
[53] Jessica Berg, Paul Appelbaum, Charles Lids and Lisa Parker. *Informed Consent: Legal Theory and Clinical Practice 2nd edition* (New York: Oxford University Press, 2001) p. 25.

competence, and the choice made at the end of the day, then the fact that one is capable of understanding, appreciation, and reasoning, becomes almost irrelevant, as the decision made would be an incompetent one. Thus this fourth condition of competence may properly be referred to as the intentional/voluntary choice criterion.[54]

Apart from adding a voluntariness aspect to the choice criterion, it is further important to realize that mere expression of choice should not form a necessary part of this fourth criterion of competence, for it would fail to account for a person who possesses a full and healthy level of mental capacity, but has a muscular ailment that impedes him from using his facial muscles to speak. Of course, as some have noted, the mere inability to speak does not mean that one cannot satisfy this condition, for "some patients may be able to express a choice in nonverbal ways, for example, in writing or by giving signals with their hands or eyes in response to questions."[55] However, we may adjust our example and assume even further that the patient was incapable of any muscular movement. This is not an implausible scenario "since some patients — for example, stroke victims — can have an active mental life and satisfy our first three conditions for capacity, but are unable to express anything verbally or through gestures

[54] The type of voluntariness being discussed here may differ from common conceptions of voluntariness. For it is often the case that a physical coercion is considered to render an action involuntary. However, while a physical coercion does indeed make an action involuntary, it would not be able to render a decision incompetent. It would be conceptually false to claim that a perfectly competent individual with respect to certain decisions is rendered mentally incompetent in the presence of physical coercion despite the fact that his mental faculties are the exact same as they were prior to the physical coercion. This amounts to the recognition that the deliberative process, and not the actual decision made or action taken, is the true object of assessment in competency determinations. Thus, for the above claim, specifically that for a decision to be competent it must be made voluntarily, it must be acknowledged that this only applies to a particular subsection of voluntariness, specifically mental voluntariness. Thus while a physical coercion would not count against one in a competency evaluation, falling prey to manipulation, being influenced by verbal bullying, or being in a state of mind of desperation, phobia, or addiction, that would have one make a decision that did not properly follow from the requisite level of reasoning, understanding, and appreciation, would fall in the category of failing to satisfy this fourth and final condition, namely the voluntariness needed for competence.

[55] Grisso and Appelbaum, 1998, p. 37.

(e.g. blinking the eyes, lifting a finger etc.)."[56] Would this render competence an impossibility for this individual? Certainly not, for all of his cognitive faculties may still prove to be substantially intact.

The fact that a person cannot physically express a choice does not speak in any way to her level of competence, for she may still have great understanding, appreciation, and reasoning abilities and may also be able to freely formulate choices. That is why this fourth condition of competence must not only include a voluntariness aspect, but also exclude the previously accepted, ability to express a choice, feature. The ability to express the preference is irrelevant to competence, though it should be recognized that for practical purposes, a person who cannot communicate in any manner may justifiably be provided a surrogate to make decisions on her behalf, but from a conceptual standpoint, this is not equivalent to a determination of incompetence. To suggest otherwise would not accord with our long-standing common usage of the term competence which relates to mental abilities (the deliberative process for example), not physical ones. In fact it appears evident that any expression of choice criterion would be "the least mental of the sub-capacities that constitute capacity, which may explain why it is not considered an element of capacity by some authors."[57] Mental processes are the correct object of evaluation here and thus this fourth element of capacity must be considered to be the ability to intentionally and voluntarily formulate preferences. [58]

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[56] Louis Charland. "Decision-Making Capacity", *The Stanford Encyclopedia of Philosophy (Summer 2011 Edition)*, Edward N. Zalta (ed.), URL = <http://plato.stanford.edu/archives/sum2011/entries/decision-capacity/>.

[57] Charland, 2011.

[58] It is likely that courts and scholars have considered the, "expression of choice", condition to be a necessary part of competence in order to be able to easily manage situations where patients are comatose or in a persistent vegetative state. It is often said that these patients can be deemed incompetent since they cannot express a choice (Berg et al., 1995-1996, p.353 and specifically footnote 24). However, this is the very conceptual flaw that must be dispelled. What makes the comatose or persistent vegetative state patient

Competence will be considered to be a combination of these four sub-abilities, namely understanding, appreciation, reasoning, and the ability to intentionally and voluntarily formulate preferences. As will become evident in the proceeding chapters, only through an analysis of each of these four elements can one attempt to ascertain the appropriate degree of competence needed by terminally ill individuals for an ethical consent to medical research participation. It is interesting to note that "legislatures often do not specify the degree of incapacity (except, perhaps, in broad terms such as 'substantial' or 'minimal') required for a finding of incompetence and instead leave the decision to the courts or to clinicians."[59] It should thus then come as no surprise that medical and legal systems lack a uniform standard for competence. However, there is great value in establishing a uniform concept of the requisite degree of capacity required in certain situations, since otherwise, individual clinicians or researchers at one hospital may apply very different standards from those at another hospital, and competency assessments will lack consistency, and may at times be flawed and unethical.[60]

Informed Consent

Given that in the following chapters an appropriate standard of competence required for terminally ill individuals to provide an ethical informed consent to research participation will be established, it is imperative that the concept of informed consent be

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incompetent is that he lacks the ability to understand, appreciate, reason, and freely formulate a preference, and not that he cannot physically express a choice.

[59] Berg et al., 1995-1996, p. 349, footnote 15.

[60] Since there is no single perfect approach to ascertaining competence, it may be noted that even with an established standard of competence needed for consent, there is still no guarantee that the standard will be applied consistently by different people at different institutions. Therefore, in addition to establishing the necessary standards of competence for terminally ill research subjects, it will be similarly important to establish some sort of procedure by which such a standard can be applied in order to best ensure consistency between different research institutions. Such an issue will be revisited in Chapters Five and Six.

explored in some depth. "Although usually viewed as a legal concept informed consent is essentially an ethical imperative to promote personal well-being and self-determination."[61] In the medical context, it accomplishes this goal through attempting to ensure that a patient or research subject is provided with the relevant information necessary for him to make an autonomous decision.

It should come as no surprise that one of the main questions surrounding informed consent concerns the particular items that must be disclosed in order for consent to be considered informed. Precisely what an informed consent must entail has elicited its own controversy in the medical research context as guidelines and academic literature sometimes present varied opinions. However, some features of the informed consent process in medical research that are generally agreed upon in codes and guidelines involve the disclosure of the procedure and purpose of the research, and the risks and benefits associated with participation. Robert Levine presents a more detailed analysis of the features that should comprise informed consent for research participation, providing the following eleven elements:[62]

1. A clear statement of the overall purpose of the research…
2. A clear invitation (not a request or a demand) to the individual to become a research subject…
3. The prospective subject should be informed as to why he has been selected for participation in the research…[63]
4. A fair explanation of the procedures to be followed, and their purposes…
5. A description of any attendant discomforts and risks reasonably to be expected…[64]

[61] Irwin Kleinman. "The Right to Refuse Treatment: ethical considerations for the competent patient" *Can Med Assoc J*, Vol. 144(10), 1991, p.1219.
[62] Robert Levine. "The Nature and Definition of Informed Consent in Various Research Settings" In National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *Appendix to the Belmont Report*, Vol. I. U.S. Government Printing Office, DHEW publication no. (OS)78-0013, pp. 3-1 to 3-91. For a discussion of the elements that should comprise informed consent in the medical practice context, see: Downie et al., 2002, p.141.
[63] The reason may often be because the prospective subject is afflicted with the specific disease under study, or the prospective subject is part of the key demographic being studied.

6. A description of any benefits reasonably to be expected…
7. A disclosure of any appropriate alternative procedures that might be advantageous for the (prospective) subject…
8. An offer to answer any inquiries concerning the procedures…
9. When appropriate there should be a suggestion to the prospective subject that he might wish to discuss the proposed research with another before consenting…
10. It should be stated that the prospective subject is free to refuse to participate in the research [without incurring any form of penalty][65] and further, that he is free to withdraw from the research at any time…[66]
11. In some studies it is necessary to inform the prospective subject that some information is being withheld deliberately.[67]

Though this list is not universally accepted, and should not be assumed to be definitive or exhaustive, many of these eleven elements will be found in some form in most laws, codes, and guidelines. Robert Veatch would also "include the need for a specific disclosure of the presence of a control group within the research design and an explanation of who is to be held responsible should the subject be harmed in the course of the research (in anticipated

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[64] As Levine notes this should include physical and psychological discomforts as well as personal inconveniences. It should be noted that there is controversy over which risks must be disclosed, and to what extent they must be disclosed. While the ethical dilemma with under-disclosure should seem apparent, since not disclosing pertinent risks would undermine the very well-being and autonomy we seek to protect, over-disclosure may have its own problems. For example, some have suggested that if every risk is disclosed and explained in great detail, then many potential subjects may feel confused or intimidated. For example, in a study that described various risks of a drug in great detail it was noticed that there was "a remarkably high incidence of refusal to take an experimental drug based upon its apparent danger. At the conclusion of the study [the researchers]…informed the individuals who refused that the drug they were describing… was aspirin; many of those who refused were regular users of aspirin. Almost all of them reported that although they had declined participation in the "study", they intended to continue to use aspirin essentially as they had before" (Levine. DHEW publication no. (OS) 78-0013, p. 3-18). This demonstrates the dilemma with an over-disclosure and reveals the arduous predicament in attempting to delineate the type of and extent to which risks ought to be disclosed. We shall revisit this issue in Chapter Four.

[65] This caveat is especially important where a potential subject's physician is also the investigator for the research study, and the subject may thus be concerned with incurring some form of reprisal from his physician in their ongoing relationship as a result of the refusal to participate in the research trial.

[66] The fact that consent must be voluntary further implies that it must be free from undue influence which may take the form of inducement, threats, excessive exercise of authority, insistent pressure, or manipulation.

[67] For instance some behavioral research or patient compliance studies may require that the potential subjects remain ignorant of the purpose of the study until the study has been completed. A specific example may involve some research in psychology which "seeks to learn about human responses to situations that have been created experimentally. Such research can only be carried out if the subjects do not know in advance the true purpose of the research" (Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, 1998; with 2000, 2002, 2005 amendments) p. 2.3.

and unanticipated ways)."[68] Of course, these additional elements, particularly the latter, are far more controversial, but demonstrate the potential for disputes in determining the ethically appropriate elements of disclosure for informed consent.[69]

Apart from disclosing various facts to potential subjects, as some guidelines explain, it is also imperative that all "the information that is given to the subject or the [subject's legally authorized] representative shall be in language understandable to the subject or the representative. [Additionally] no informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence."[70]

Given the above explanation and elements of informed consent, its value should seem evident. The aim of an informed consent process is to protect a subject's well-being and respect her autonomy. In order to truly respect peoples' autonomy and allow persons to make decisions freely in a manner that they see as beneficial for themselves, it is imperative that any consent acquired be a competent consent. As discussed previously, understanding is a vital component of competence, and since the informed consent process aims at ensuring that the relevant information is provided to the decision maker, it can be viewed as a

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[68] Benjamin Freedman. "The Validity of Ignorant Consent to Medical Research" *The Hastings Center: Ethics and Human Research*, Vol. 4 (2), pp. 1-5, Feb., 1982. pp. 1-2.

[69] The *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* mentions a few other possible items of disclosure. Some notable ones include: the identity of the researcher, the presence of any conflict of interest, the potential for the publication and commercialization of the research findings, an explanation of how confidentiality will be maintained, and information on who to contact regarding possible ethical concerns in the research (*Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, 1998, pp. 2.5-2.7). Other items that some may additionally wish to add to the disclosure may include whether or not the researcher is being specifically paid to recruit patients, who will control the decision to publish, and whether the sponsor may elect to terminate the trial for commercial reasons.

[70] U.S. Department of Health and Human Services, National Institutes of Health, and Office for Protection from Research Risks, Title 45 (Public Welfare), Code of Federal Regulations, Part 46 (Protection of Human Subjects) Washington, D.C.: Revised January 15, 2009 (Effective July 14, 2009) Section 46.116. The "readability" of consent forms has been an ongoing concern for some time. See: Levine, 1986, pp. 138-139.

necessary step in ensuring that the consenter is indeed competent to consent. However, informed consent "is justified not only out of respect for patient [and subject] autonomy but also because of positive consequences anticipated in its pursuit. These include: protection of patients and subjects, avoidance of fraud and duress, encouragement of self-scrutiny by medical professionals, promotion of rational decisions, and involvement of the public in health care."[71] Despite these advantages though, the informed consent process has come under scrutiny and has been criticized by scholars and medical researchers alike, with some suggesting moderate adjustments to the process, while others seemingly preferring its abolition. Before proceeding, it would be prudent to briefly examine some of the criticisms launched against informed consent.

A recent objection voiced by Ian Roberts and collegues relates specifically to the process of informed consent in emergency care research.[72] Their argument asserts that since various trials attempt to assess experimental non-validated time-critical treatments for life-threatening ailments, such as traumatic brain injury, then any consent process that increases the wait time to receiving treatment, increases mortality rates and should be viewed as unethical. They assert that "the CRASH-2 trial showed that giving tranexamic acid to trauma patients with bleeds results in a significant and clinically important reduction in overall mortality (relative risk 0·91, 95% CI 0·85—0·97)… [and] further analyses have shown that these beneficial effects depend importantly on the promptness with which treatment with tranexamic acid is started."[73] The authors continue to argue that the delay from the informed consent process thus diminishes these beneficial effects, increases the

[71] Berg et al., 2001, p.26.
[72] Ian Roberts, David Prieto-Merino, Haleema Shakur, Iain Chalmers, Jon Nichol. "Effect of consent rituals on mortality in emergency care research" *The Lancet*, Vol. 377(9771), pp. 1071 - 1072, March 2011.
[73] Roberts et al., 2011, pp. 1071 – 1072.

mortality rate among the patients/subjects, and that therefore the informed consent process in emergency care research should be eliminated.

One glaring problem with this argument relates to the overall lack of evidence. The conclusion only follows from their example because in the one particular case described, the non-validated experimental treatment turned out to be effective. It is important to remember though that in research, before a trial is completed there will be some genuine uncertainty about the efficacy of the medical intervention being tested. The argument presented by Roberts et al. relies heavily on "hindsight and only has the appearance of validity because in [this case]… the drug was efficacious; had the drug lacked efficacy (or worse) the conclusion would have been very different."[74] Since there is no certainty regarding the efficacy of the non-validated treatment, to eliminate a consent process may subject patients to possibly dangerous and harmful medical research that the patient may have refused. Roberts and collegues' argument must therefore not be accepted since despite the example provided, "there is [still] no evidence that not acquiring patients' consent confers net aggregate benefit [and any] post-hoc counterfactual arguments should not influence ethical debate."[75]

Furthermore, even despite this tremendous flaw, a complete elimination of the consent process in emergency research leaves open the possibility for increased abuse by researchers and sponsors. This should not be viewed as an unwarranted fear with no basis, for as mentioned earlier the medical research sector is rife with scandals. It would seem that

[74] TL Zutlevics. "Consent in emergency care research" *The Lancet*, Vol. 378(9785), pp. 25-26, July 2011. We may recall, as discussed above that in fact only about 25 percent of all drugs tested in clinical trials successfully complete Phase III testing and thus it would be inappropriate to assume that non-validated experimental treatments will in fact become validated effective treatments.
[75] JF Boylan, NP Conlon, and MJ Jaigirdar. "Consent in emergency care research" *The Lancet*, Vol. 378(9785), p. 25, July 2011.

"the research enterprise has the onus of proving its trustworthiness before we embrace any further deregulatory measures, however reasonable they seem."[76]

Another, less recent, but far more common objection insists that informed consent may be too stringent of a requirement in all circumstances as it may lead to poor recruitment into some trials. This concern has led to some precarious arguments that seem to minimize the importance of ensuring the patient/subject's welfare in favour of expediting medical research.[77] Jeffrey Tobias, however, presents a slightly more palatable solution to the problem of under-recruitment by proposing an alternative approach to informed consent, whereby a patient is asked for a "blanket" approval, at the start of treatment, to be included in studies that might be in progress while the patient is ill, and to accept that the physician would always act in good faith.[78]

While Tobias' main concern appears to be a noble one, hoping to accelerate the research process through which new medical knowledge can be attained and thus potentially provide substantial benefits for future patients, it is not thus free from ethical

[76] Miran Epstein and Mark Wilson. "Consent in emergency care research" *The Lancet*, Vol. 378(9785), p.26, July 2011.

[77] Some strong versions of this objection, for example, claim that participation in medical research is an obligation and not an option. This obligation argument is often justified by the suggestion that each one of us takes part in, and advantage of, belonging to a society with certain medical innovations, and thus it is in each one of our interests to commit ourselves to the continuation of this enterprise through clinical research participation. The argument can also be construed such that one's obligation to participate in research constitutes a repayment for the benefits bestowed on him from the participation in research trials from others in the past and thus the individual has a duty to repay this deed and ensure that future generations will be able to reap the benefits of further advancements in medicine. These two similar arguments can be referred to as the social contract and reciprocity argument respectively. However, this type of approach to solidifying some obligation to participate in medical research has been sufficiently refuted. See for example: David Heyd. "Experimentation on Trial: Why Should One Take Part in Medical Research?" *Jahrbuch fur Recht und Ethik* [Annual Review of Law and Ethics] Vol.4, pp. 189-204, 1996. Heyd argues that "because medical research is often an intergenerational enterprise and… there can be no coherent intergenerational social contract, the use of social contract views to ground an obligation to participate in medical research fails. He concludes that participation in research is best thought of as an act of supererogation" (Emanuel et al., 2003, p. 152).

[78] Jeffrey S. Tobias. "BMJ's present policy (sometimes approving research in which patients have not given fully informed consent) is wholly correct" *British Medical Journal*, Vol. 314, p. 1111, 1997.

scrutiny. Though advancements in the field of medicine are vital, we cannot decide in pursuit of a healthier disease free tomorrow to shed the shackles of morality today. As appealing as Tobias' proposal might be, it is based on an unrealistic expectation that the physician would always act in good faith, and on an implicit supposition that is ethically flawed, namely that sometimes a person's well-being can be made secondary to the achievement of the goals of medical research.

First, the suggestion that one should accept that the physician will always act in good faith, gives a misrepresentation of the situation. If a medical practitioner is attempting to recruit a patient into a research trial, then he is acting as a researcher or investigator who plays a significantly different role in medicine than one's physician.[79] This indicates that a patient must then put faith, not simply in the medical practitioner whom she has known, perhaps even for some time, as her physician, but in the physician who is also assuming the role of a researcher/recruiter, a role that brings with it different duties and responsibilities than that of a physician. Given the various scandals that medical research has faced, and the numerous cases where a subject's wellbeing was ignored in favour of the goals and aims of the research, the suggestion that one should trust that the medical practitioner attempting to recruit him into a clinical trial will always act in good faith, appears to be more of a fantasy than a reality.

Second, it should be recognized that at the root of most suggestions to reduce the restrictions that informed consent places on research, lies the extremely dangerous notion

[79] This tends to get confusing since both roles can be played by the same medical practitioner; something that Jay Katz has called being a double agent. In fact Katz "encourages physician-investigators to see themselves 'as scientists only and not as doctors'. Only by adopting this univocal self-image, he suggests, will investigators be able to avoid unwittingly becoming 'double agents' with conflicting loyalties" (Emanuel et al., 2003, p.193). The differences between the two roles of physician and researcher and their ethical significance will be elaborated on in Chapter Three. For more on Jay Katz's argument see: Jay Katz. "Human Experimentation and Human Rights" *St. Louis University Law Journal*, Vol. 38, pp.7-54, 1993.

that sometimes the infringement of a particular individual's rights is permissible in order to achieve a greater public good. Accepting a "blanket" approval at the onset of treatment to be included in medical research, avoids informing the potential subject of pertinent information needed in order to make competent decisions. This thus not only allows a person to enter into an environment with an increased possibility that he will incur physical harm, but may do so without the person even knowing of such a possibility, and thus also disrespects his autonomy, something that is often viewed as harmful in itself.[80]

Justifying the sacrificing of one's good for the general good of society represents a disrespect for the dignity and autonomy of persons and sets a dangerous precedent. "One need only recall the horrors of medical experimentation during World War II to appreciate the brutal extension of the utilitarian philosophy of the sacrifice of the individual for a societal purpose."[81] Abandoning the informed consent process in order to increase recruitment numbers and thus benefit society, while certainly not in itself equivalent to some of the horrors that plague our medical research history such as the WWII experiments, does still employ the same type of unethical and dangerous reasoning. It should be noted that "accepting the unconscionability of inflicting such harm in the public interest may well mean that some potentially fruitful medical research cannot be done because of the problem of under-recruitment. So be it; this is the price we pay for living in a society which is morally worth preserving, one where we treat each other with respect and where we take human rights seriously."[82]

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[80] The type of harm that is created by a disrespect to autonomy will be further discussed later in this chapter.

[81] Mortimer B. Lipsett. "On the Nature and Ethics of Phase I Clinical Trials of Cancer Chemotherapies" *JAMA*, Vol. 248, pp. 941-942, 1982.

[82] Len Doyal. "Journals Should Not Publish Research To Which Patients Have Not Given Fully Informed Consent: With Three Exceptions" *British Medical Journal*, Vol. 314(7087), pp. 1107-1111, April 1997, p. 1109.

Furthermore, despite the alleged social good[83] produced by improving recruitment in medical research trials, it is interesting to note that we generally do not even allow an exception to the informed consent process in the medical practice context for the possibly more noble reason of attaining good for the particular patient involved. In the medical practice context there are two main exceptions to the rule of informed consent. A physician is permitted to bypass the informed consent process with a patient in the case of an emergency[84] or therapeutic privilege.[85]

Therapeutic privilege allows for an exception to the informed consent requirement where the information that a physician is withholding would be harmful to the patient. Harmful in this sense is often taken to mean a psychological harm so severe that it would impede the patient's rational decision-making ability anyway. Though a full analysis of this concept cannot presently be undertaken, it must be noted that the scope of this exception has often been and must continue to be very limited, since if harm is defined too broadly it would allow physicians to avoid disclosure in every instance where it was thought that the disclosure of information would have the patient render a decision which was contrary to the

[83] Some have questioned the social good that is actually produced by recent clinical trials. See: Marcia Angell. *The Truth About the Drug Companies* (New York: Random House Inc., 2005). The argument is not that medical innovations have not or will not be beneficial, but rather, Marcia Angell puts forth an indictment of pharmaceutical companies, demonstrating that the motives and goals behind the development of new drugs through clinical trials may not always be the advancement of the social health and welfare, but rather an increase in profits.

[84] While the exact definition of an emergency is not fully straightforward, though often it will involve a situation where a patient's condition is such that he may suffer death or serious bodily harm if the informed consent process is not circumvented and action is not immediately taken, the reasoning behind this emergency exception to informed consent is fairly self-explanatory. "The rationale for this rule is that since reasonable persons would consent to treatment in an emergency if they were able to do so, it is presumed that any particular patient would consent under the same circumstance" (Berg et al., 2001, p. 76). Thus it is often assumed that there is at least an implied consent.

[85] There are two other often noted circumstances in which physicians may be exempted from the requirement of informed consent in the medical practice context. These would be in cases of compulsory treatment, where there might be a legal requirement to treat, such as is the case where treatment is "ordered for the dangerous mentally ill patients with infectious diseases" (Berg et al., 2001, p. 90) and waivers where patients in some situations may waive their right to informed consent. The issue of waiving such a right will be discussed further in Chapter Three. For an in depth explanation of all four exceptions to informed consent, see: Berg et al., 2001, pp. 75-91.

physician's judgment. In fact in the landmark case of *Canterbury v. Spence*, it was ruled that "the physician's privilege to withhold information for therapeutic reasons must be carefully circumscribed,… for otherwise it might devour the disclosure rule itself. The privilege does not accept the paternalistic notion that the physician may remain silent simply because divulgence might prompt the patient to forego therapy the physician feels the patient really needs."[86]

Relating this back to our medical research context, it can be said that if indeed there is good ethical reasoning to not allow an exception to informed consent even when a physician thinks the welfare of the patient may be better served by employing the exception, then certainly an exception to informed consent cannot be permitted in order to increase the number of subjects in a research trial, an objective that is unrelated to the particular patient's interest. The issue in the *Canterbury v. Spence* case may have proved to be a difficult ethical quandary because of the fact that it required consideration between two conflicting fundamentally important operating principles in medicine, namely: (1) ensuring the well-being of the patient and (2) respecting the patient's autonomy. However, this conflict is not present in the research case, and thus the decision to not infringe upon one's right to autonomous decision making should be that much clearer.

Thus, permitting an exception to informed consent in order to improve recruitment in clinical trials would prove to be inconsistent with current ethical views regarding informed consent and autonomy, and represents a dangerous rational. The claim that one can assume that the physician involved in the recruitment will be acting in

[86] *Canterbury v. Spence*, 464 F.2d 772 (D.C. Cir. 1972). For a more recent example and discussion of therapeutic privilege consult: Matthew Wynia. "Invoking Therapeutic Privilege" *Virtual Mentor: American Medical Association Journal of Ethics*, Vol. 6(2), Feb. 2004.

good faith does little to assuage these fears. "The suffering and indignity which some medical research has visited upon unsuspecting and vulnerable patients must never be allowed to happen again. To ignore the lessons of the past through not taking the right of informed consent seriously is to insult the memory of those who paid such an unacceptably high price in the name of medical progress."[87]

While the informed consent process may not be perfect, for the reasons outlined above it is imperative that it not be eliminated despite some objections.[88] Its value cannot be underestimated as it proves to be one of the greatest protections for potential subjects of medical research as it ensures respect for their autonomy and dignity. It furthermore is a key protection for physicians and researchers from having to bear the burden of the blame and responsibility should one of the risks of research occur. In many legal cases, properly obtaining an informed consent from the potential subjects would have provided the researchers necessary legal protection.[89] Informed consent thus not only empowers the potential subject, and ensures respect for his/her autonomy, but also allows physicians and researchers to not bear full moral or legal responsibility for any damages suffered by the subjects. Therefore it remains the case that informed consent is a process that is vital to the proper continuation of medical research. It is thus not surprising that every document and guideline concerning medical research with human subjects reviewed by the National

[87] Doyal, 1997, p.1110.
[88] While two main objections to informed consent have been discussed and ultimately dismissed, Benjamin Freedman raises a slightly different form of opposition against informed consent that warrants some attention. He provides some arguments as to the ethical permissibility of an ignorant consent. Much of his argument relates to the differences, or as he argues lack thereof, between the medical practice and medical research contexts and will thus be further examined in Chapter Three.
[89] See the cases of: *Halushka v. University of Saskatchewan* [1965], 53 D.L.R. (2d) 436; and *Weiss v. Solomon*. 1989, 48 C.C.L.T. 280 (Que. S.C.).

Bioethics Advisory Commission[90] "has specified a need for the informed consent process."[91]

Autonomy

As Len Doyal contends, in regards to the objections to informed consent:

> "it is unlikely that any of these arguments against informed consent would be taken seriously unless they were linked to the further belief that it is acceptable to compromise individual rights if the public interest demands it. Such arguments amount to justifying exploitation of individuals and ignore the objective harm which is inflicted upon them by disrespect for their autonomy. Harm of this kind should not be equated with physical damage or emotional distress and is therefore not affected by the level of risk of either. Rather it is an attack on human dignity: the harm is to the moral integrity of the uninformed volunteer."[92]

Doyal's sentiment rightly suggests that what is of concern is not solely physical or psychological harm, but something else as well, namely disrespect for an individual's autonomy. While many ethical discussions in law, politics, and medicine presume the value of autonomy, its definition and importance require some elaboration.

Though autonomy and competence differ in meaning, where autonomy refers to self-determination or self-government, and competence refers to the ability to perform a task, the two are inextricably linked. A right to self-determine, that is one's right to autonomy, presupposes the capacity for self-determination. Competence/mental capacity

[90] The review compared 25 separate documents concerned with the protection of research subjects and included both, various guidelines developed by international organizations such as: The Nuremberg Code, The Declaration of Helsinki, The Council for International Organizations of Medical Sciences (CIOMS)-International Ethical Guidelines for Biomedical Research Involving Human Subjects, and the ICH-GCP, as well as documents developed by specific countries such as: Australia's National Statement on Ethical Conduct in Research Involving Humans, Canada's Tri-Council Policy Statement- Ethical Conduct for Research Involving Humans, and Denmark's Act on a Scientific Ethical Committee System and the Handling of Biomedical Research Subjects.

[91] National Bioethics Advisory Commission (NBAC), *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries Vol. II*, "Comparative analysis of international documents addressing the protection of research participants" (staff analysis), (Bethesda, Maryland: 2001) p. D-4.

[92] Doyal, 1997, p. 1109.

can thus appropriately be thought of as the ability to be autonomous.[93] This relationship between the two concepts is further solidified by the fact that the criteria of autonomous action share many similarities with the criteria of competence discussed earlier. Though somewhat contentious "it is widely agreed that, for an action to qualify as autonomous, it must be (1) intentional, (2) based on sufficient understanding, (3) sufficiently free of external constraints, and (4) sufficiently free of internal constraints."[94] Most of these conditions were explicated in the earlier discussion of competence, however it should be noted that as a result of the similar criteria between competence and autonomy, many of the hindrances to one are similarly hindrances to the other.

Obvious examples of factors that can hinder or in some cases eliminate autonomy, include some form of external or internal constraint,[95] where the former may be understood "as including physical barriers deliberately imposed by other individuals and different forms of coercion…, [while the latter involves] internal phenomena that, to some degree, constrain our actions and choices,"[96] such as alcoholism, drug addiction and intense fears. An extensive, but by no means exhaustive list of potentially autonomy hindering factors includes: external constraints such as physical force or imprisonment and internal constraints such as depression, intense fear, alcoholism, drug addiction, pain,

[93] Stephen Wear echoes a similar conceptualization of competence as noted above in footnote 2. See: Wear, 1983, p.266.
[94] Mappes and Degrazia, 2001, p 39. One of the controversies revolves around whether truly "autonomous action involves the exercise of the capacity to form higher order values or desires about the desires (to do certain things) that are involved in intentional action" (Mappes and Degrazia, p. 52, note 37). See, for example, Harry G. Frankfurt. "Freedom of the Will and the Concept of a Person" *Journal of Philosophy*, Vol. 68, 1971.
[95] The existence of social constraints should also be noted. This may include, for instance, a lack of health insurance which may render an individual as only being able to receive health care through clinical trials. This type of social constraint and its impact on autonomous decision making will be explored in more detail in Chapter Three.
[96] Mappes & Degrazia, 2001, pp. 41-42.

strong emotions, stress, ignorance,[97] limited capacities, certain commitments, limited self-control, and limited rationality.[98] Though, it would be odd to speak of external constraints such as physical force or imprisonment as diminishing one's competence,[99] internal constraints can function as impediments to both autonomy and competence. In fact, it is by hindering one's competence, that these internal constraints prevent truly autonomous action.

Given what autonomy is, it remains necessary to inquire about its value. Autonomy has often been recognized as the moral cornerstone of the Western World's democratic system. While autonomy is not necessarily considered a supreme value by every culture,[100] its importance for morality cannot be understated.

> Put most simply, to be autonomous is to be one's own person, to be directed by considerations, desires, conditions, and characteristics that are not simply imposed externally upon one, but are part of what can somehow be considered one's authentic self. Autonomy in this sense seems an irrefutable value, especially since its opposite — being guided by forces external to the self and which one cannot authentically embrace — seems to mark the height of oppression.[101]

Autonomy thus places limits on what others can do to us. In the context of medicine it has limited what physicians can do to patients. In fact, the "principle of respect for

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[97] Many cases can be concocted in order to demonstrate that ignorance can hinder one's competence and autonomy. "To use Mill's famous example of the person about to walk across a damaged bridge, if we could not communicate the danger (he speaks only Japanese) [even] a soft paternalist would justify forcibly preventing him from crossing the bridge in order to determine whether he knows about its condition," because it is assumed that his ignorance of the bridge's condition renders him incapable of substantially competent choices and actions regarding whether or not to use the bridge (Gerald Dworkin, "Paternalism", *The Stanford Encyclopedia of Philosophy (Summer 2009 Edition)*, Edward N. Zalta (ed.), URL = <http://plato.stanford.edu/archives/sum2009/entries/paternalism/>).

[98] We should recall, as mentioned earlier, that rationality entails both the ability to formulate proper ends and the ability to pursue those ends while applying appropriate means-ends reasoning.

[99] See previous footnote 54 where this is discussed.

[100] For example, some studies have demonstrated that certain cultures prefer a family-centered model over a patient-centered autonomy model in making certain medical decisions. See: Leslie J. Blackhall, Sheila T. Murphy, Gelya Frank, et al., "Ethnicity and Attitudes Toward Patient Autonomy" *Journal of the American Medical Association*, Vol. 274, pp. 820-825, Sept. 1995.

[101] John Christman, "Autonomy in Moral and Political Philosophy", *The Stanford Encyclopedia of Philosophy (Spring 2011 Edition)*, Edward N. Zalta (ed.), URL = <http://plato.stanford.edu/archives/spr2011/entries/autonomy-moral/>.

autonomy has grounded several rights for patients, including rights to receive information, to consent to and refuse procedures, and to have confidentiality and privacy maintained."[102]

However, autonomy's moral significance is also very relevant in the medical research context, as it places limits on what investigators may do to subjects. While the immorality of researchers behaving negligently and imposing physical and psychological harms that could have been avoided seems self-evident, a researcher should also not be permitted to disrespect the autonomy of a subject, something that is harmful in itself. This is supported by the fact that while "it is sometimes argued that minimal risks might justify the randomisation of patient volunteers without their consent (for example, in studies where one group is unknowingly used as a control)….some patients have been outraged to discover that they were used in a trial without their knowledge. The fact that they faced small risks in the process was not the point."[103] The concern here is deontological. From a Kantian perspective "autonomy is the ground of the dignity of human nature and of every rational nature."[104] While Kantian ethics was mainly concerned with moral autonomy, one of Kant's oft cited formulations of his categorical imperative seems to relate quite closely to our present concern. This formulation states that "one should always act in such a way that humanity either in oneself or in others is always treated as an end in itself and never merely as a means. [For] if a person is treated as a mere means, then he is treated as nothing more than a thing without purposes of his

[102] Beauchamp & Childress, 2009, p. 207.
[103] Doyal, 1997, p. 1109.
[104] Immanuel Kant. *Grounding for the Metaphysics of Morals* 1785, James Ellington, ed. (Indianapolis: Hackett Publishing Company, Inc., 1993) p. 41.

own rather than as a self-determining rational agent."[105] Morality thus requires us to always respect other persons as self-determining autonomous agents. This becomes especially relevant in the medical research context where it may sometimes be difficult to view the subjects as anything more than the means to achieving scientific progress. However, any form of deception, manipulation, coercion, or even failing to disclose relevant information, constitutes this moral failing. To accord subjects of research their due respect as autonomous agents, they must never be solely treated as the mere means to scientific progress and thus never prevented, either explicitly or implicitly, from decision making regarding their participation in the medical trial.[106]

It is this type of moral reasoning that had led some to view an abandonment of the informed consent process in medical research as ethically perilous. As Len Doyal argues:

> To deny volunteers such information is a clear breach of their moral rights. Our abilities to deliberate, to choose, and to plan for the future are the focus of the dignity and respect which we associate with being an autonomous person capable of participation in civic life. Such respect is now widely regarded as essential for good medical care and should dominate the practice of medical research.[107]

[105] Kant, (1785/1993), p. vii. It should be noted that although Kantian ethics relates closely with the issue at hand, Kant was not alone in attributing moral value to autonomy. One of the prominent proponents of Utilitarianism, John Stuart Mill, similarly espoused the importance of autonomy, though for different reasons. "For a utilitarian such as Mill, respect for individual autonomy has utility value. A society that fosters respect for persons as autonomous agents will be more progressive and, on balance, a happier society because its citizens will have the opportunities to develop their capacities to act as rational, responsible moral agents" (Mappes and Degrazia, 2001, p. 44). For more see: John Stuart Mill. *Utilitarianism* 1863, George Sher, ed. (Indianapolis: Hackett Publishing Company, Inc., 2001).

[106] It should be noted that this obligation to respect the autonomy of others takes the form of both a negative and positive duty. In our medical research context, this moral principle's formulation as a negative duty should seem apparent, for it would merely require that researchers not interfere in the competent decision making of the prospective subject. As a positive duty however, respecting autonomy may further involve an effort to ensure understanding and an ongoing disclosure of the relevant information needed for subjects to be able to make autonomous decisions. "As some contemporary Kantians declare, the demand that we treat others as ends requires that we assist them in achieving their ends and foster their capacities as agents, not merely that we avoid treating them solely as means to our ends" (Beauchamp and Childress, 2009, p.104).

[107] Doyal, 1997, p.1108.

It is important to realize that the claim here is not that autonomy is important since respect for a person's autonomy may diminish the probability of a harm befalling him that he would have otherwise not permitted, though this is indeed true, but rather that "autonomy is in fact a constituent of a person's well-being, and that therefore any violation of a person's autonomy is a harm to that person."[108] We may thus posit a scenario where a researcher fails to notify a subject of a particular risk associated with participation in a research trial, and though the risk itself never materializes, given the above claim about autonomy, it is still appropriate to maintain that a harm has in fact been done; specifically a harm to the dignity associated with being an autonomous agent. Thus, in the discussion that follows regarding the use of terminally ill persons as subjects for medical research, it is crucial to recognize that judgments and evaluations concerning the level to which medical research may be inappropriate and unethical, are not to be limited to an analysis of bodily and/or psychological harm, but must also include an assessment of harms to autonomy. This is an issue that may become particularly relevant in the case of minimal risk research trials.

We may conclude with a brief discussion of the relation between the three main concepts explicated above. While the three terms that have been expounded in some detail -- autonomy, informed consent, and competence/mental capacity -- may have at first seemed to be quite different concepts, they are clearly intimately intertwined with one another. The relation between the three can be described as follows: a certain level of mental capacity/competence is required in order to enable the autonomous decision

[108] Roger Crisp. "Medical Negligence, Assault, Informed Consent, and Autonomy" *Journal of Law and Society*, Vol. 17(1), pp.77-89, 1990, p. 81. Crisp goes on to correctly point out that "one's well-being is constituted partly by the very living of one's life oneself, as opposed to having it led for one by others. The fear we have of paternalism does not arise merely from the thought that we know our own interests better than others, but from the high value we put on running our own lives" (Crisp, 1990, p. 82).

making of an individual, which in our clinical research context is performed through the process of informed consent. The importance of determining the necessary level of mental capacity for a decision thus becomes apparent, since our ability to truly act autonomously is ultimately what is at stake. It is this close relationship between these terms that have led some to suggest that "consent capacity is a fundamental aspect of personal autonomy."[109]

Given the relation between these three terms, the central aim in what follows can properly be described as attempting to establish the appropriate degree of competence needed for the informed consent that enables and protects the autonomous rights of terminally ill subjects of research. However, prior to establishing this minimum standard, it will be necessary to first engage with a common risk based approach to determining appropriate degrees of competence needed for particular contexts. This method suggests that competence to consent should vary in accordance with risk. According to this approach, as the risks of a particular decision increase, so too must the level of mental capacity needed to consent. It is thus often referred to as the risk based sliding scale approach to competence. In Chapter Two the merits of such a proposal will be examined, and ultimately it will be concluded that such an approach is not only conceptually flawed, but also fails at providing the type of protection being sought for the terminally ill potential research subject.

Apart from the flaws of this type of approach, it must also be recognized that it would be ethically perilous to assume that the appropriate standard of competence for making treatment decisions translates into an appropriate standard of competence for

[109] Moye and Marson, 2009, p. 91. It should be noted that this quote was in reference to one's consent to treatment decisions. However, the same relationship holds in other decision making contexts as well, including the medical research decision making context.

medical research decision making. This is especially true since generally when one consents to treatment, "the law presumes patient competence."[110] However, often, research participation decisions require greater mental capacity than consenting to treatment[111] and thus merely presuming competence would fail to provide any type of adequate respect or protection for research subjects. Chapter Three will then demonstrate that the medical research and medical practice contexts are fundamentally different, and thus one cannot extrapolate an appropriate level of competence for research decision making from the appropriate level needed for decision making in a therapeutic setting. This chapter will conclude that for terminally ill persons, a greater mental capacity is required for research participation decisions than for consent to treatment for the condition under study.[112] The differences between the two contexts expressed in Chapter Three will influence the minimum standard of competence that will ultimately be shown to be necessary for terminally ill subjects of research. The establishment of this standard will comprise Chapter Four. Chapters Five and Six will provide a basis for understanding what type of and how much evidence is needed to determine that one is sufficiently competent to ethically consent to research participation. Appendix A will then provide cases that will illustrate how these recommendations regarding standards of competence and types of evidence of competence can be applied in practice.

While numerous guidelines, and much academic scholarship has been dedicated to protecting the rights of vulnerable populations in medical research, ensuring that one is

[110] Kleinman, 1991, pp. 1219-1220.
[111] The reasons for this will be fully expressed in Chapter Three.
[112] Limiting my argument to "the condition under study" rules out examples involving unrelated conditions. I am not, for instance, arguing that greater capacity is required to consent to research participation in a simple antibiotic trial than would be required to consent to a quality-of-life-reducing treatment for pancreatic cancer. It should also be noted that this dissertation will exclude: studies with healthy volunteers, pure treatment studies and minimal risk studies on minor conditions for which persons often refuse treatment, e.g. an antibiotic for acne.

sufficiently competent to provide an autonomous consent in the first place might prove to be the greatest and most empowering protection of all.

Chapter 2: What Role Should Risk Play in the Determination of Competence?

Some of the current bioethical literature expresses the idea that one's required level of competence to be able to consent to medical decisions will vary in accordance with risk.[113] Thus, greater levels of mental capacity are required to consent to medical decisions when the amount of risk present is greater. A person may then be found sufficiently competent to consent in one scenario, but may lack the necessary competence for consent in a scenario where the decision is riskier. This strategy is often referred to as the sliding-scale approach, for it dictates that as the "risks of a medical intervention increase for patients, we should raise the level of ability required for a judgment of competence to elect or refuse the intervention. [Conversely] as the consequences for well-being become less substantial, we should lower the level of capacity required for competence."[114] Thus, the required mental capacity needed for an ethical consent slides up (more demanding) and down (less demanding) in accordance with risk. This is often accepted in medicine as a necessary way for physicians to ensure the right balance between respecting autonomy and concern for the patient's welfare.

This position however, has some intriguing implications for medical research participation. It may suggest, assuming that participation in a medical research trial will often involve additional risks than standard therapy,[115] that by applying this sliding-scale

[113] We may recall from Chapter One that the terms competence and mental capacity will be used interchangeably.
[114] Tom Beauchamp & James Childress. *Principles of Biomedical Ethics* (New York: Oxford University Press, 2009) p.116.
[115] This assumption will be explored further in what follows. More specifically, it will be noted that such an assumption may not always be correct. The most obvious counter example would be cases of minimal risk research, such as research regarding best treatment for a sprained ankle. However, as will be discussed further in this chapter, even in cases of research on terminal illnesses, where the non-validated drugs or medical interventions are likely to be more dangerous and thus where this assumption is most likely to hold, there may still remain serious reasons to question it.

strategy of competence, it would be justifiable to require greater levels of competence for consent to participate in research than for consent to medical treatment. While this may certainly seem prima facie intuitive, in what follows I shall demonstrate that this is a mistaken way in which to construe competence requirements.[116]

Grounding a requirement for a higher level of competence for medical research participation decisions in risk proves to be a conceptually and morally flawed analysis of competence determinations. It is dubious to suggest that the actual capacity required for a particular decision is relative to the possible harmful consequences of that decision. Some proponents of such a strategy seem to confuse the complexity or difficulty of a decision with the risk associated with that decision. It may be appropriate to suggest that the required capacity to decide depends upon the complexity of a decision, and that often more complex decisions tend to also be riskier ones, but this is conceptually quite different from the assertion that required capacity to decide ought to vary with risk.

Still, various arguments have been put forth in favour of the sliding scale strategy. As shall be demonstrated, these arguments not only contain various fallacies, they are also ethically problematic, and furthermore fail to accord with the long-standing interpretation of competence assessments as being process-oriented and not results oriented.

However, even setting aside the conceptual errors to such an approach, it would still lack in practical applicability. For, apart from questioning the appropriateness of using risk in the first place to determine competence requirements, it will furthermore be demonstrated that this sliding-scale strategy of competence is ineffective in determining

[116] Though an increased standard of competence for the medical research context may be appealing, as it may aid in protecting potential subjects of research, it will be argued that a risk based sliding scale approach to competence only appears to provide such protection but ultimately fails to do so.

the adequate level of competence that ought to be required for consent to medical research participation. The basis of this argument will revolve around the notion that once risk has been clearly demarcated between treatment and research, and once the condition of clinical equipoise[117] has been met, our risk based sliding-scale strategy accomplishes very little, if anything at all. Thus, any notion that a risk related sliding scale approach to competence entails that research participation decisions ought to require higher levels of competence on the part of potential subjects for their consent to be ethical, is mistaken.[118] This has the further implication that any protection that advocates of the sliding scale approach thought was being provided to potential subjects of research by this strategy, is illusory.

However, prior to highlighting the flaws with such an approach to competence, it is necessary to first better explicate the sliding scale strategy and describe the arguments its advocates have put forth in support of it.

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[117] The concept of clinical equipoise will be further elaborated below. For now it suffices to state that this condition dictates that medical research is ethical as long as there exists a genuine uncertainty within the expert medical community regarding the relative merit between the various arms of the clinical trial. It should be noted that the requirement of clinical equipoise has come under some recent scrutiny. Some, for instance, have argued that such a requirement would prohibit what many would consider to be vital research. See for instance: Franklin G. Miller and Howard Brody. "A Critique of Clinical Equipoise: Therapeutic Misconception in the Ethics of Clinical Trials" *The Hastings Report*, Vol. 33(3), pp.19-28, 2003. For more on current criticisms of clinical equipoise, also see: James Fries and Eswar Krishnan. "Equipoise, Design Bias, and Randomized Controlled Trials: The Elusive Ethics of New Drug Development" *Arthritis Research & Therapy*, Vol.6(3), pp. R250–R255, 2004. One criticism of clinical equipoise suggests that it may pose serious problems when it comes to treatments that are widely accepted but that have never actually been properly tested. For instance, it was very difficult to mount a trial testing the value of using the Swan-Ganz catheter in ICU patients because of the belief that it provided highly valuable information. However when the trial was actually done it was shown that the use of the catheter was not beneficial (G. Guyatt. "A Randomized Control Trial of Right Heart Catheterization in Critically Ill Patients: Ontario Intensive Care Study Group" *Journal of Intensive Care Medicine*, Vol.6(2), pp. 91-95, 1991). However, despite some criticisms, the clinical equipoise requirement is still held by many to be an important safeguard in clinical research. I am indebted to Professor Joel Lexchin at York University for bringing this criticism to my attention.

[118] It should be recognized that the position I will be advancing does not commit me to the claim that medical research participation decisions do not require greater levels of mental capacity for consent compared to medical treatment decisions, but rather that if indeed it is the case that research decisions require this greater level of competence, the reason cannot be risk related, but instead must be due to some other factors.

The Sliding-Scale Strategy

Some recent literature has already begun to question this sliding scale approach to competence. Tom Beauchamp and James Childress claim that:

> This account is conceptually and morally perilous… [For] it is confusing to blend a decision's complexity or difficulty with the risk at stake. No basis exists for believing that risky decisions require more ability at decision making than less risky decisions.[119]

Contrary to this line of argument, many maintain that there exists a very real correlation between risk and the amount of decisional capacity needed to consent. As Paul Appelbaum reminds, "Although some commentators object to this "sliding scale" approach, it makes sense from a policy perspective, it was endorsed by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research,[120] and in the judgment of many experts, it reflects how courts actually deal with these cases."[121]

As is often argued by its proponents, applying this risk based sliding scale strategy is the best way in which to balance two vital medical values; respecting the patient's, or subject's, in the case of medical research, autonomy, and protecting that individual's wellbeing. Thomas Grisso and Paul Appelbaum suggest that it may be useful to think of this process as involving a "competence balance scale". The

[119] Beauchamp & Childress, 2009, p. 117.
[120] Specifically this report states that in determining competence, "since the assessment must balance possibly competing considerations of well-being and self-determination, the prudent course is to take into account the potential consequences of the patient's decision… When little turns on the decision, the level of decisionmaking capacity required may be appropriately reduced" (President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *Making Health Care Decisions: a report on the ethical and legal implications of informed consent in the patient-practitioner relationship.* Vol. 1. Washington, DC: Government Printing Office, 1982, p. 60).
[121] Paul Appelbaum. "Assessment of Patients' Competence to Consent to Treatment" *The New England Journal of Medicine*, Vol. 357, pp. 1834-1840, 2007, p. 1836-1837.

> competence balance scale has cups suspended at the ends of each arm, with a fulcrum between them. One cup is labeled "autonomy," the other "protection." It is in this balance that the judgment [of competence] will be made, as elements for consideration are deposited in each cup. The judgment will be for competence, if the interest in respecting the patient's autonomy finally outweighs the interest in protecting the patient from the potentially harmful consequences of his or her decision-making incapacities. It will be for incompetence, if the interest in protection outweighs autonomy.[122]

Given this depiction, the appeal of such a strategy becomes apparent. Since the principles of respecting autonomy, and beneficence[123] can often conflict, especially in the field of medicine,[124] medical professionals are often put in difficult, seemingly intractable situations attempting to determine which ethical norm should outweigh the other. The risk based sliding scale strategy seems to offer a method to make such decisions easier.[125] Specifically, this strategy suggests that the riskier a decision appears to be, the less likely a patient will be competent to decide and thus the more justifiable it is to behave beneficently as opposed to respecting the patient's decision.

Apart from this seemingly appealing upshot, this risk based sliding scale position is one that is also supported by various scholars in the field as it has been entrenched in a great variety of bioethics literature, perhaps most notably by Allen Buchanan and Dan Brock.[126]

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[122] Thomas Grisso and Paul S. Appelbaum. *Assessing Competence to Consent to Treatment: A Guide for Physicians and Other Health Professionals* (New York: Oxford University Press, 1998), p. 130.

[123] A "principle of beneficence refers to a statement of moral obligation to act for the benefit of others" (Beauchamp & Childress, 2009, p. 197). In medicine, such a principle would refer to the physician's or other health care professional's obligation to act in such a way so as to serve the welfare of patients. This can be contrasted with the principle of nonmaleficence which imposes an obligation to not inflict any harm on patients.

[124] An often citied example of this involves the case of the Jehovah's Witness who refused a life-saving blood transfusion. See: Re T [1992] 4 All E.R. 649. This case will be described in further detail below.

[125] This attractive upshot will be questioned later in this chapter as it appears fraught with ethical pitfalls. Most notably, as will be argued below, such rationale may open the door for a hidden and objectionable form of paternalism.

[126] Allen Buchanan & Dan Brock. "Deciding for Others" *The Milbank Quarterly,* Vol. 64, Supplement 2, pp. 17-94, 1986; and Dan Brock. "Decisionmaking Competence and Risk" *Bioethics,* Vol. 5 (2), pp. 105-112, 1991.

They endorse this risk related view of competence as a way in which to contest what they refer to as the "fixed minimal capacity" view where competence is not decision relative. "The simplest version of this view holds that a person is competent if he or she possesses the relevant decision-making capacities at some specified level, regardless of whether the decision to be made is risky or nonrisky, and regardless of whether the information to be understood or the consequences to be reasoned through are simple or complex."[127]

Buchanan and Brock appear correct in objecting to this view, for this position would possibly create too strong a required level of competence for some cases and too weak a required level in others since the mental capacity required for any decision would remain fixed regardless of any external factors related to the particular decision itself. Given though that competence is the ability to perform a task, then it seems clear that the level of competence required may vary between different tasks and different contexts within which the task must be performed.[128]

According to Buchanan and Brock, the risk related sliding scale strategy is not only superior to the fixed minimal capacity view in this respect, but there are various other points favouring such an approach. We shall proceed by examining each in turn.

First, as they suggest, this risk based sliding scale approach to competence is consistent with how people already intuitively make informal competency

[127] Buchanan and Brock, 1986, p. 38.

[128] However, it is important to realize that rejecting this "fixed minimal capacity" view does not necessarily entail adopting a risk based sliding scale strategy. A rejection of the "fixed minimal capacity" view simply requires an acknowledgement that competence is decision relative and that the factors that determine competence will not be completely internal, but will require some analysis of the external factors related to the decisional context itself. This issue will be further elaborated upon in the subsequent section. For a more detailed analysis of decision relative conceptions of competence and how they compare to a fixed minimal capacity view, see: Tom Buller. "Competence and Risk-Relativity" *Bioethics*, Vol. 15 (2), pp. 93-109, 2001.

determinations. "For example, you may decide that your 5-year-old child is competent to choose between a hamburger and a hotdog for lunch, but you would not think the child competent to make a decision about how to invest a large sum of money. This is because the risk in the latter case is greater, and the information required for reasoning about the relevant consequences of the options is much more complex."[129] There are various other common everyday examples where it appears as though we routinely require a greater level of competence for riskier decisions, such as is the case with Alzheimer's patients, who many think may be competent enough to choose their meals, but not their medicine.

Second, it seems this approach better coheres with our current legal framework since the courts have accepted that a fixed minimal capacity view is inappropriate. It is now widely accepted throughout our legal institutions that competence "is not an all-or-nothing status"[130] and that for example children might be competent to make certain decisions, but not others.[131] The judgment made in the now well-known Jehovah's Witness blood transfusion case lends further support to Buchanan and Brock's risk based sliding scale strategy. In this case the Court of Appeal had to consider the situation of

> an adult Jehovah's Witness who refused treatment. [More specifically] A pregnant woman was involved in a car accident and, after speaking with her mother, signed a form of refusal of blood transfusion. After the delivery of a stillborn baby, her condition deteriorated, therefore a Court order was obtained in order to legalise a blood transfusion…[132]

[129] Buchanan and Brock, 1986, p. 39.
[130] Buchanan and Brock, 1986, p. 40.
[131] For a more detailed discussion on the legal shift from a fixed conception of competence to a variable one for children, see: Willard Gaylin. "The Competence of Children: no longer all or none" *The Hastings Center Report*, Vol. 12(2), pp.33-38, 1982. Since it is easy to tell when an individual is eighteen, Gaylin noted that at that time "society preferred a fixed definition of competence based on age…Increasingly, however, [he added] the reliance on a fixed age of competence is being undermined. For one thing, case law is operating on an ad hoc basis to destroy that position. Moreover, the new bio-medical technologies (such as safe abortion techniques) are demanding a variability in the assignment of autonomous rights" (Gaylin, 1982, p. 33).
[132] Margherita Tanzarella & Salvatore Marco Mura. "Is the assessed capacity increased with the seriousness of what is at stake?" *The Psychiatrist: Correspondence*, Vol. 34, 2010, p. 499.

Regarding the matter of the role risk plays in determining competence, the court declared that, "what matters is that the doctors should consider whether at that time he had a capacity which was commensurate with the gravity of the decision. The more serious the decision, the greater the capacity required."[133]

The third argument offered is related to the notion of paternalism.[134] In addition to the fact that legal cases have sometimes applied a risk-based sliding scale strategy, Brock and Buchanan further point out that this approach remains consistent with the law's general refusal to allow interference with a competent patient's voluntary choices. While related to their previous point, since if true, this would demonstrate further coherence with our current legal framework, we shall treat this as a separate and third argument.[135] The main idea is that since generally "the law makes a finding of incompetence a necessary condition for justified paternalism,"[136] then the sliding scale strategy garners further support by increasing the chances of finding an individual incompetent in precisely those circumstances where paternalistic behaviour will most likely occur, namely in high risk decision making contexts. Therefore, this sliding scale approach to

[133] *Re T* [1992] 4 All E.R. 649.

[134] Paternalism may be defined as "the intentional overriding of one person's preferences or actions by another person, where the person who overrides justifies this action by appeal to the goal of benefiting or of preventing or mitigating harm to the person whose preferences or actions are overridden" (Beauchamp & Childress, 2009, p. 208). While paternalism is thought to involve the usurping of the person's decision making power for that person's own benefit, a distinction is often made between soft and hard paternalism. These terms distinguish between cases where the individual whose decision making power is usurped, is or is not considered substantially competent. Soft paternalism thus involves the interference with a person who is less than substantially competent while hard paternalism involves interference with a person who is considered substantially competent. The terms weak and strong are sometimes used to create the same distinction. This was first introduced in: Joel Feinberg. "Legal Paternalism" *Canadian Journal of Philosophy*, Vol. 1, pp.105-124, 1971. Certain clear cases of soft paternalism are frequently accepted by society such as when parents make decisions for their children, or family members make decisions for a mentally impaired loved one. In these cases the individuals who are subjected to paternalism lack the necessary competence for truly autonomous self-determination.

[135] The reason for this stems from the fact that in the following section, where each of these arguments will be scrutinized, this particular argument will require its own critical assessment as it appears to be perhaps the most problematic and morally dangerous.

[136] Buchanan and Brock, 1986, p. 40.

competence "allows paternalism in situations in which the case for paternalism seems strongest, while at the same time preserving the law's fundamental tenet that, in general, people may be treated paternalistically only when they are incompetent to make their own decisions."[137]

As a fourth point, Brock and Buchanan point out that the sliding scale strategy allows "a finding of incompetence for a particular decision to be limited to that decision, and so it is not equivalent to a change in the person's overall status as a decision maker."[138] In their view, this limitation acts as a safeguard, ensuring that one finding of incompetence does not compromise an individual's autonomy over other aspects of her life.

The fifth and final argument, which may be referred to as the balance argument, maintains that the sliding scale technique is far superior to a fixed minimal capacity view in its ability to balance the competing values of self-determination and well-being. As already discussed above, this alluring feature appears to be one of the most popular reasons many adopt the risk based sliding scale strategy and is succinctly explicated by Grisso and Appelbaum's "competence balance scale". Recalling their explanation of the balance scale, it would appear that the crucial feature of such an argument is that when a risky decision is made, this type of scale would place less weight on respecting the wishes of the decision maker. Put conversely, a decision with a poor risk/benefit ratio would add "substantial weight to the cup representing protection."[139] Brock and Buchanan corroborate such sentiments and perhaps go a step further suggesting that the

[137] Buchanan and Brock, 1986, p. 40. This reasoning appears almost circular, and as shall be demonstrated in the following section, represents a potentially dangerous rationale.
[138] Buchanan and Brock, 1986, p. 40.
[139] Grisso & Appelbaum, 1998, p. 139.

level of "importance or value to the patient of self-determination can vary depending on the choice being made."[140]

Given a proper understanding of competence as outlined in chapter one, we may now submit such arguments in favour of the sliding scale strategy to ethical scrutiny. Ultimately it will be demonstrated that each reason supporting such a strategy is either fallacious or has unforeseen ethical pitfalls, and that there remains no good reason to accept that the level of risk present in a decision determines the required level of capacity for one to be declared sufficiently competent to decide.

However, before proceeding to an evaluation of the various arguments given in favour of the sliding scale, it is important to note that proponents of this approach are committed to an asymmetrical conception of competency in medical decision making. That is to state that consents and refusals for the exact same decision will not necessarily have the same competence requirements attached to them. "Because the consequences of consenting to a procedure are different from those of refusing to undergo it, a person can be competent to refuse to participate in research but not to agree, and to consent to a treatment but not to refuse."[141] This asymmetrical conception of competence in medical decision making will be questioned in the following sections which will be dedicated to assessing each argument put forth in support of the sliding scale. However, the implication for the medical research context specifically, namely that an application of the risk based sliding scale will create a greater level of competence requirement when

[140] Allen Buchanan and Dan Brock. "Standards of Competence" In *Biomedical Ethics fifth edition*, Mappes and Degrazia, eds. (New York: McGraw-Hill Companies, Inc., pp. 109-114, 2001) p.111. Article reprinted from: Allen Buchanan and Dan Brock. *Deciding for Others: The Ethics of Surrogate Decision Making* (Cambridge: Cambridge University Press, 1989).

[141] Alec Buchanan. "Mental Capacity, Legal Competence and Consent to Treatment" *Journal of the Royal Society of Medicine*, Vol. 97, pp. 415-420, 2004, p. 416.

agreeing to participate in research but a lower one when refusing participation, a consequence of the sliding scale strategy that some may find favourable as it seems to provide greater protection for potential subjects of research, will merit its own analysis later in this chapter.

Flaws with the Sliding Scale Strategy and the Arguments in Support of it

Before critiquing each of the five arguments presented, it is important to first make note of a general dilemma with two of the arguments. Arguments 2 and 4 suggest that the risk based sliding scale approach better coheres with our current legal framework since the courts have rejected the fixed minimal capacity view and unlike the fixed minimal capacity view, the risk based sliding scale ensures that one isolated finding of incompetence for one particular decisional context does not qualify that individual as incompetent in all aspects of life, respectively. While these points are certainly true, Buchanan and Brock seem to create a false dichotomy suggesting that if indeed we are not to subscribe to this fixed minimal capacity view, then we must embrace a risk based sliding scale strategy. However, these are not the only two options. For example, we may instead accept a sliding scale approach that turns solely on the complexity or difficulty of the decision, and not the risk. The idea here being that as the difficulty of either possessing or performing any of the four elements of competence, as described in Chapter One,[142] increase, it may be appropriate to suggest that the level of competence required would increase as well. Buchanan and Brock ignore this and other possible solutions to avoiding the fixed minimal capacity view and as such, while the two arguments they present demonstrate that a decision relative conception of competence is

[142] These were understanding, appreciation, reasoning, and intentional/voluntary choice.

preferable, they do not truly justify embracing specifically a risk based sliding scale. Despite this general flaw, the five arguments are also fraught with other errors and fallacious reasoning. We may proceed by examining each in turn.

Two problems arise with the first argument, that the risk based sliding scale strategy is actually how people already intuitively make informal competence judgments. First, such an argument appears to fall prey to the is/ought fallacy. It is an error in reasoning to derive an "ought", a statement regarding what should be done, from an "is", a statement describing a current state of affairs. To do so would involve a jump from a descriptive claim, in this case that we already make competency determinations based on risk, to the normative claim that we should make competency determinations based on risk and thereby adopt the risk based sliding scale approach. The fallacy here lies in the idea that the mere fact that a practice is commonly accepted does not in itself make that practice justifiable.[143] It should be noted however, that Brock and Buchanan do not explicitly commit such a fallacy, for that would require a jump to the normative claim without any other justification other than the descriptive claim. Instead, Brock and Buchanan seem to have provided various justifications for adopting the sliding scale. However, as shall be demonstrated in what follows, each justification will not withstand scrutiny, and as such, if all that remains is the mere fact that we generally already make informal competency determinations based on risk, then any conclusion that we therefore

[143] Mark Wicclair raises a similar point against Brock and Buchanan asserting that "even if there are high risk decisions that do not require complex decision-making skills and abilities, and even if it is accepted practice to utilize a strong criterion of decision-making capacity in such cases, the mere fact that the use of a strong criterion is accepted practice under such circumstances does not show that it is warranted…" (Mark R. Wicclair. "Patient Decision-Making Capacity and Risk" *Bioethics*, Vol.5(2), pp.91-104, 1991, p.97).

ought to accept the risk based sliding scale strategy will indeed commit the is/ought fallacy.

While this fallacy presents a problem for their first argument, there is a second concern as well, namely that this is not even an accurate descriptive claim in the first place. For even if in an attempt to be charitable we overlook the looming is/ought fallacy, and focus solely on the descriptive claim that indeed the risk based sliding scale is intuitively already applied by people, there is still a dilemma, particularly that this is factually incorrect. The example used by Buchanan and Brock, as discussed above, was that of a child who may be competent to choose between a hotdog and hamburger for lunch, but who would not be thought competent to decide how to invest a large sum of money. According to Buchanan and Brock we would not assume the child competent to decide in the latter situation because the risks associated with the consequences of the decision are far greater.

Though we may agree that the child may be competent to decide between a hot dog and hamburger, but not competent to invest a large sum of money, it can be questioned whether the reason that drives this intuition is really risk related. It seems clear that deciding about an investment, which may typically require an understanding of economics, an appreciation of one's current financial situation, some basic mathematical reasoning skills, among other things, is of a more complex nature than deciding between a hot dog and hamburger for lunch, which is commonly accepted as merely a matter of one's taste preferences. Therefore, a greater level of ability is indeed required in the decision making process in the investment case, specifically a level of competence that

the child will lack.[144] The conclusion then, that the child will be competent to choose between a hamburger and a hotdog, but not competent to invest a large sum of money, is primarily based on the fact that the complexity and difficulty of the decision is far greater. Since this fact alone appears to justify our competency assumptions regarding the child, it therefore seems unnecessary and arbitrary to posit that the additional risk also plays a significant role in those assumptions.[145]

In order to further demonstrate that risk is not the motivating factor behind the intuition that the child is not competent to decide in the investment case, but might be in deciding what to have for lunch, a slightly modified version of the example may be construed. Posit the exact same 5 year old child, faced with an investment decision involving a large sum of money, for example $100,000. However, suppose that this child's family were billionaires and actually gave their child a $200,000 a week allowance simply to see how she would spend it. Though this may seem implausible, it

[144] The suggestion here is that the real reason why the child should not be deemed competent to decide about investments is as a result of the greater level of ability required in the decision making process. We may recall the four elements of competence, and note that given the complexity of the information related to investments, and the type of reasoning needed when deciding about investments, it should be clear that at least the understanding, appreciation, and reasoning conditions of competence become more difficult to satisfy in the investment as opposed to the lunch decision.

[145] We need only recall Occam's razor that suggests that it is poor reasoning to assume a plurality of explanations for a particular phenomenon without necessity, that is, when the additionally posited explanations do not contribute any explanatory power. This principle is often described as asserting that when all else is equal, a simpler explanation is preferable. The mistake of attributing a greater competence required in some decisional contexts to the risk that is present in those decisions, is exacerbated by the fact that in some cases it appears that "there may be a correlation between greater risk and increased complexity of requisite decision-making skills and abilities" (Mark R. Wicclair. "The Continuing Debate Over Risk-Related Standards of Competence" *Bioethics,* Vol. 13(2), pp.149-153, 1999, p.151). That is to suggest that the sliding scale's intuitive appeal may be as a result of the fact that in many of the cases where it seems that a greater level of capacity should be required, situations where decision-making is of a complex/difficult nature, there also happens to be a greater level of risk involved, and thus it seems that the sliding scale strategy accurately portrays some intuition we commonly feel about competency evaluations. Many life and death decisions are clear examples of such situations. However, this need not be the case, as the risk of a decision and its complexity are not necessarily intertwined. Indeed, a decision might be simple and risky, or complex and fairly harmless. An example of the latter will be presented in what follows by constructing a modified version of the 5 year old child example.

should be noted that this reconstructed version of the example is such that there is little to no risk involved in the child's decision. For if the 5 year old were to invest poorly and lose all the money, it would not affect her well-being, or her family's. The loss would be shrugged off as many of us might do with the loss of a penny. But note, even with the risk being minimized, if not completely eliminated from this example, it would still be inappropriate to consider the 5 year old, in any way sufficiently competent to decide how to invest the money. Thus, it must actually be something else that drives this intuition that the child does not have the capacity to decide about investments; something separate from risk. I have already argued that what actually prompts the intuition is the degree of complexity present in the decision, and more specifically the level of difficulty involved in performing or possessing the particular elements of competence themselves.

Brock and Buchanan's second line of argument, alleging that the risk based sliding scale approach better coheres with our current legal framework also suffers from some fallacious reasoning and inaccuracy. First, it must be acknowledged that whether or not something is legal does not necessarily indicate whether it is morally or ethically correct. This is not to suggest that there is no overlap between morality and law, for that would be plainly false. However, one need look only to the days of slavery in the American South to notice an example of where what was legal did not correspond with what many of us now take to be an obvious ethical precept, namely that all persons have a right to freedom and equal treatment. In fact, as is acknowledged in jurisprudence, "moral criticism is often used to support a change in the law"[146]; a fact that necessitates that what is law and what is moral might diverge. Thus, it would be improper to conclude

[146] Bernard Gert. "The Definition of Morality", *The Stanford Encyclopedia of Philosophy (Fall 2012 Edition)*, Edward N. Zalta (ed.), URL = <http://plato.stanford.edu/archives/fall2012/entries/morality-definition/>.

that we ought to accept the risk based sliding scale approach merely because it cohered with current law and policy.

However, putting this issue aside, there still remains a factual problem with Brock and Buchanan's second line of argument. They correctly suggest that the courts seem to have rejected a fixed minimal capacity view and instead embraced, for the most part, a decision relative conception of competence. They are further correct in asserting that in regards to children, courts have seemed to accept that "features of the decision itself (including risk) are relevant factors in determining whether the child is competent to make that decision."[147] However, despite this, the claim that the risk based sliding scale accords with current law appears to be too strong a statement. The reason for this is that much case law also exists where judgments were made that are contrary to the risk based sliding scale approach.

The case of *Lane v. Candura*[148] functions as such an example. In "*Lane v. Candura*, a Massachusetts Appellate Court upheld the right of a woman to refuse amputation of a gangrenous leg. The court found that Ms. Candura appreciated the nature and consequences of her act because she accurately believed that she was suffering from gangrene and would likely die without surgery."[149] Initially the woman's "daughter, Grace R. Lane of Medford, filed a petition in the Probate Court for Middlesex County seeking appointment of herself as temporary guardian with authority to consent to the operation on behalf of her mother. An order and a judgment were entered in the Probate Court to that effect, from which the guardian ad litem appointed to represent Mrs.

[147] Buchanan and Brock, 1986, p. 40.
[148] *Lane v. Candura*, 376 NE 2d 1232 – Mass : Appeals Court 1978.
[149] Jessica Berg, Paul Appelbaum and Thomas Grisso. "Constructing Competence: Formulating Standards of Legal Competence to Make Medical Decisions" *Rutgers L. Rev*, Vol. 48, pp.345-396, 1995-1996, p.356.

Candura has appealed."[150] The court considered that in the proceeding for the appointment of a guardian,

> Dr. Kelley, one of two psychiatrists who testified, did state that in his opinion Mrs. Candura was incompetent to make a rational choice whether to consent to the operation… [However this court ruled that] the decision of the judge, as well as the opinion of Dr. Kelley, predicates the necessity for the appointment of a guardian chiefly on the irrationality (in medical terms) of Mrs. Candura's decision to reject the amputation… But the irrationality of her decision, does not justify a conclusion that Mrs. Candura is incompetent in the legal sense. The law protects her right to make her own decision to accept or reject treatment, whether that decision is wise or unwise.[151]

The court thus seemed to suggest that Mrs. Candura's competence was not to be assessed in reference to the risky nature of her decision, even when a risk as severe as death was present. Instead her competence was evaluated based on her ability to appreciate and reason. This judgment further reinforces the idea that the decision made, regardless of how risky or how much others may disagree, is not the appropriate object of evaluation in competence assessments. Instead, a judgment of incompetence must be based on cognitive capabilities and more specifically the four criteria of competence as set out in Chapter One.

It must furthermore be noticed, that the ruling in this case and in most case law, seems fairly consistently committed to the notion that competence assessments are not to be made by the application of a best interest standard. That is to state that what is in a person's best interest is irrelevant when evaluations of competency are being conducted. However, this runs contrary with one of the underlying features of the risk based sliding scale, specifically that competence assessments should be closely connected with one's

[150] *Lane v. Candura,* 1978, p.379.
[151] *Lane v. Candura,* 1978, p.383-384.

welfare.[152] Instead, the law in most North American jurisdictions seems to recognize that determining what is best for a person's well-being should not be considered an appropriate element in competency determinations. This was reinforced more recently in *Starson v. Swayze*[153] where "both the six-judge majority and three-judge dissent in this Supreme Court judgment agreed that under Ontario's test for capacity to make treatment decisions, persons are not held to a 'best interests' standard and so may make decisions that are contrary to physicians' advice,"[154] even if such a decision is considered to be riskier. Furthermore, despite the fact that Starson in this case was considered to be making the riskier decision by refusing certain medical treatments for his psychiatric condition, Justice Major made his ruling based on whether Starson appreciated the potential risks of the decision in question. It was found that Starson indeed did appreciate the

> primary intended effects of these medications, and rejected them. These included the dulling of his perception and slowing or "normalizing" of his thought, to produce in him a condition he deemed "so boring it would be like death." The evidence did not disprove Starson's assertion that the proposed drug treatments would prevent him from engaging with theoretical physics, which was what gave his life meaning. Thus he appreciated the intended benefits, but valued these differently than his doctors did.[155]

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[152] This feature of the risk based sliding scale is made explicit by Grisso and Appelbaum's "competence balance scale" and also by any suggestion by proponents of the sliding scale that evaluations of competence must consider both a respect for an individual's autonomy as well as his well-being.

[153] *Starson v. Swayze*, 2003 SCC 32, [2003] 1 S.C.R. 722. This case involved the Supreme Court of Canada affirming "the rulings of both courts below to overturn a decision of Ontario's Consent and Capacity Board that Starson was incapable of deciding whether to accept or refuse certain medical treatments proposed by his psychiatrists. Those treatments included neuroleptic medication, mood stabilizers, anti-anxiety medication, and anti-Parkinsonian medication (the last was proposed for relief of certain side effects of the neuroleptics). Starson, an unusually gifted thinker in the area of theoretical physics, was involuntarily committed to [a] psychiatric hospital in 1999 by disposition of the Ontario Review Board following a criminal court finding that he was not criminally responsible for two counts of uttering death threats. He had a history of psychiatric admissions reaching back to 1985. His most consistent diagnosis was bipolar disorder. Once in hospital, Starson refused the above medications, consenting to psychotherapy only" (Shelia Wildeman. "Case Description: *Starson v. Swayze*" In *Health Care Ethics in Canada second edition*, Baylis, Downie, Hoffmaster, and Sherwin, eds. (Toronto: Nelson Ltd., 2004) p.299).

[154] Wildeman, 2004, p. 299.

[155] Wildeman, 2004, p. 300.

This legal reasoning supports the idea that the inherent riskiness of the decision itself is not relevant in an evaluation of competence, but rather the ability to appreciate and reason are the appropriate objects of assessment.[156] The judgment explicitly maintained that "the legislative mandate of the Consent and Capacity Board is to adjudicate solely upon a patient's capacity and the Board's conception of the patient's best interests is irrelevant to that determination."[157]

Both of the cases presented here demonstrate that the risk based sliding scale in fact does not cohere with current legal framework as Brock and Buchanan suggest. Instead, in both cases it is clear that the level of risk of the decision itself did not play any significant role in the competency evaluation. Furthermore, as is exemplified by the above two cases, the principle that the best interest of a patient is irrelevant to competency assessments, is one that is endorsed by our current legal framework, and such a principle appears to be in direct opposition to the risk based sliding scale strategy.

Momentarily setting aside Brock and Buchanan's third argument, we may notice that not much can be disputed regarding their fourth point. This suggested that an upshot of the risk based sliding scale was that it ensures that one isolated finding of incompetence for one particular decisional context would not label an individual as incompetent in all other aspects of life. This was praised as being a safeguard that is built into the risk based sliding scale. However, as noted previously, this, while certainly true,

[156] It must be recognized that this does not imply that risks play no role in competency determinations, for as Chapter One elucidated, both the appreciation and reasoning components of competence require some grappling with the potential risks of a decision. The judgment discussed above concerning Starson further demonstrated this by ensuring that he reasoned through the risks and benefits of the decision and appreciated what those meant for him. However, acknowledging that one must appreciate risks and be able to include those risks in one's deliberation does not amount to the claim that the level of risk present in a decision is itself a factor in competence evaluations or standards. It is disagreement on precisely this that appears to most separate supporters of the risk based sliding scale from its critics.

[157] *Starson v. Swayze*, 2003, p.724.

will only provide reason and support for a decision relative conception of competence and not necessarily the risk based sliding scale. This is true since all decision relative conceptions of competence would have a similar built-in safeguard.

With that, Buchanan and Brock's arguments 1,2 and 4 in support of the risk based sliding scale have all been undermined, and only 3 and 5 remain. These were the paternalistic and balance arguments respectively. These are perhaps the most troubling of the five arguments and warrant their own separate analysis. For as the following section will demonstrate, the implications of both ultimately fall prey to serious ethical pitfalls.

The Problem of Disguised Paternalism

Buchanan and Brock admit and agree with the law in most North American jurisdictions that "has in general steadfastly refused to recognize a right to interfere with a *competent* patient's voluntary choice on purely paternalistic grounds - that is, solely to prevent harms or to secure benefits for the competent patient him or herself. Instead, the law makes a finding of incompetence a necessary condition for justified paternalistic interference with the patient's choice."[158] We may refer to this as the patient paternalism principle.[159] However, while they may be in agreement with this principle, they have endorsed a strategy that runs contrary to the spirit of this legal precept. This is exemplified by Brock and Buchanan's third and fifth arguments. Both of these arguments appear to suffer from the same dilemma, namely that they demonstrate that the risk based sliding scale strategy would allow for a disguised hard paternalism and thus render this

[158] Brock, 1991, p. 106.
[159] Other endorsers of the risk based sliding scale have similarly maintained such a principle. As Loane Skene asserts, for example, "in law, autonomy prevails over beneficence" (Loane Skene. "Risk-Related Standard Inevitable in Assessing Competence" *Bioethics*, Vol. 5(2), p. 113-117, 1991, p.115).

approach to competence as being in contravention with the patient paternalism principle. In order to demonstrate this we must briefly recall both arguments.

The third argument suggested that the risk based sliding scale remains in accordance with our current legal framework by following the generally accepted principle that justified paternalism requires a finding of incompetence. As previously discussed, this is often referred to as soft paternalism, while paternalistic action against a competent individual is referred to as hard paternalism, and is generally considered unjustifiable. Brock and Buchanan suggest that the risk based sliding scale remains in accordance with this principle by increasing the chances of finding an individual incompetent in precisely those circumstances where paternalistic behaviour will most likely occur, namely in high risk decision making contexts. The fifth argument, specifically the balance argument, suggested that a proper assessment of competence requires considerations of beneficence as well as autonomy, and that the sliding scale achieves a balance between these two values by accounting for the well being of the individual in the competence evaluation itself.[160]

Through an analysis of both of these arguments, it will become apparent that implementing a risk based sliding scale approach will have the dangerous consequence of allowing a disguised hard paternalism. This dilemma, more specifically, is that there is a potential danger that patients, and subjects of research alike, may have themselves unjustly deemed incompetent so that a physician may behave paternalistically. Buchanan and Brock assert that according to their risk based sliding scale approach,

[160] We may recall Grisso and Appelbaum's version of this argument and their balance scale. This suggested that when the risk to a patient is low, the balance will tip in favour of respecting the patient's autonomy and thus a weak standard of competence would be appropriate. Whereas when the risks to a patient are high, the balance will tip in favour of protecting the wellbeing of the individual and thus a stronger standard of competence would be appropriate.

> the greater the potential harm to the individual, the higher the standard of competence. From this it follows that a finding of incompetence is more likely in precisely those instances in which the case for paternalism is strongest - cases in which great harm can be easily avoided by taking the decision out of the individual's hands. Thus, the concept of competence favored here allows paternalism in situations in which the case for paternalism seems strongest, while at the same time preserving the law's fundamental tenet that, in general, people may be treated paternalistically only when they are incompetent to make their own decisions.[161]

Without realizing it, Buchanan and Brock have expressed a very dangerous consequence of their view. In order to circumvent hard paternalistic behaviour, which is often condemned, physicians may apply this risk based sliding scale strategy, and set the criteria for competence impossibly high when the perceived risks to the patient are great enough to convince the physician that paternalistic action is appropriate. Thus, a competent person may be inappropriately judged incompetent and have her autonomy usurped based solely on the fact that her decision did not coincide with her physician's recommendation and was therefore considered too risky.[162]

This dilemma is further exacerbated by the balance argument that acknowledges and encourages competency evaluators to account for the well-being of the individual whose competence is being assessed. Thus, even for a competency evaluator who claims

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[161] Buchanan and Brock, 1986, p. 40. This, they seem to argue is a positive upshot of the risk based sliding scale. As shall be argued presently, this is mistaken, and in fact this conception of competence is ethically perilous. However, apart from this it should also be recognized that a correct conception of competence will not necessarily be one that gives society license to behave paternalistically when it feels it should. Questions concerning when it is appropriate to behave paternalistically are conceptually separate from questions concerning proper assessments of competence.

[162] In Chapter One we examined a similar concern that determinations of incompetence would be made based solely on the unconventionality of a patient's decisions. The concern more specifically was that including a reasoning component in competence assessments could allow some physicians or other health care professionals to find a patient incompetent when that patient's decision did not coincide with the health professional's medical opinion. This concern was dismissed as only following from an inappropriate and perverse application of the reasoning criterion since proper reasoning would not require that the decision-maker arrive at some fixed, absolute, objective decision, but rather only that it can be demonstrated that whatever the decision made, it had been arrived at logically and as following from relevant premises. However, while this concern was dismissed, it would seem to reemerge here, and apply quite aptly if this risk based sliding scale strategy were implemented.

to value and respect the autonomous choices of competent patients, an acceptance and implementation of this sliding scale would still allow for a patient to "be *classified as incompetent* when setting aside their treatment choices is thought to be justified by a concern for their well being."[163] Brock and Buchanan's assurance that the risk based sliding scale approach only allows for paternalistic behaviour when one is incompetent proves to be completely meaningless if the sliding scale is designed to allow for a finding of incompetence in precisely those situations where paternalism is most likely to occur. This is truly troublesome, because it appears that a tactic is made available by this sliding scale strategy whereby patients can simply be deemed incompetent when a physician may not agree with their choices, and thus any paternalistic action would prima facie appear to be a justifiable soft paternalism, when in fact it may be a hard paternalism masquerading as soft.[164]

We generally view such hard paternalism as unconscionable due to the high value we place on respecting and protecting the autonomy of individuals.[165] Despite this though, the sliding scale strategy manages to allow for this type of disguised hard

[163] Wicclair, 1991, p. 96.

[164] This is not to suggest that soft paternalism is always justifiable and permissible or that hard paternalism is never permissible, for that would be plainly false. We often accept as permissible certain laws that force particular courses of action upon individuals without their voluntary consent. For example the law that forces persons to wear seat belts in cars may be considered a permissible form of hard paternalism. Furthermore, even some forms of soft paternalism have come under criticism. For example, some have argued that "soft paternalistic governmental policies or health care practices may be susceptible to abuse if they lack public scrutiny" (Beauchamp & Childress, 2009, p. 212). Thus the idea that soft paternalism is always permissible while hard paternalism is never permissible is not being advanced here. However, these are exceptions caused by overriding or extenuating factors and present a departure from the typical acceptance of soft paternalism and condemnation of hard paternalism. We must realize that the conceptual difference between the two types of paternalism, namely that hard involves a disrespect or devaluing of a person's autonomy while soft paternalism does not, makes the former highly controversial and condemnable while the latter generally acceptable. Thus, we may assume that in cases of hard paternalism the onus would be on the person behaving paternalistically to produce an adequate justification for his/her action, while in cases of soft paternalism the onus would be on critics to demonstrate why the paternalistic act might not be justifiable.

[165] Recall the discussion of autonomy and its value from Chapter One.

paternalism precisely in those instances in which society or medical professionals would most want to behave paternalistically by raising the standards of competence in those cases. However, without any good reason to require a raised standard of competence in higher risk cases,[166] then to raise the standard for this reason alone would be to completely undermine the legal spirit of the patient paternalism principle. It appears on the surface to satisfy such a principle since paternalist measures will still only be forced on those deemed incompetent, but it creates a situation where a finding of incompetence can occur much more easily where paternalism seems most desirable. As a result it fails to truly respect autonomy and thus runs contrary to the spirit of the patient paternalism principle, while deviously managing to appear as if it has satisfied it. If a model of competence is adopted "whereby striking a proper balance between autonomy and beneficence is part of the process of assessing the competency of patients, then the statement that the treatment preferences of competent patients cannot be set aside for paternalistic reasons is an empty tautology, and *not* a strong affirmation of patient self-determination."[167]

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[166] As was already established in the previous section some of the main arguments supporting the risk based sliding scale are fraught with flaws and fail to be any good reason to accept such a strategy.

[167] Mark Wicclair. "A Response to Brock and Skene" *Bioethics*, Vol. 5(2), pp. 118-122, 1991, p.122. It is possible that Brock and Buchanan began to notice the hard paternalistic consequence of their view. For in describing the difference between a low and high risk choice, in an earlier work they state that the "presumed net balance of expected benefits and risks of patient choice in comparison with other alternatives refers to the physician's assessment of the expected effects in achieving the goals of prolonging life, preventing injury and disability, and relieving suffering from a particular treatment option as against its risks of harm" (Buchanan and Brock, 1986, p. 34). This places the final decision regarding risk and thus competence with the physician. For, given this, a physician would have the sole power in determining when risks were sufficiently high so as to warrant a raised level of competence, and thus the concern of a disguised hard paternalism would be quite warranted. However, in a later work, Buchanan and Brock suggest that a risk and benefit assessment "should focus on the expected effects of a particular treatment option in forwarding the patient's underlying and enduring aims and values, to the extent that these are known" (Allen Buchanan and Dan Brock. *Deciding for Others: The Ethics of Surrogate Decision Making* (Cambridge: Cambridge University Press, 1989) p.52. This seemingly slight shift allows for a patient's autonomous desires to play a significant role in risk assessments, and since according to the risk based sliding scale, competence adjudications are contingent on determinations of risk, then this shift may return some decision-making power to the individual patient. However, while accepting this latter interpretation

It should also be noted that the patient paternalism principle "appears to require that assessments of decision-making capacity focus on the decision-making process and not its outcome. [We may call this the process-oriented rule.] Specifically, the principle appears to express the idea that if there are no relevant deficits in a patient's understanding, reasoning, and so forth, then even if a treatment refusal appears to be a bad decision from the perspective of a patient's well being, such refusals generally should be respected."[168]

However, the process-oriented rule, like the patient paternalism principle, is similarly not satisfied by the risk related sliding scale which endorses an asymmetrical conception of competence. As mentioned earlier, supporters of a risk based sliding scale are committed to the idea that a choice to accept treatment or refuse participation in medical research will likely have a lower standard of competence required than a refusal of treatment or consent to participate in medical research. This is as a result of the fact that the risks will change depending on the decision made, and decisions to reject treatment or to participate in medical research are generally considered riskier than their

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of risk assessment that Brock and Buchanan provide may certainly demonstrate a step in the right direction, a risk based sliding scale approach will always leave open the possibility of a disguised hard paternalism since it will inevitably be the physician who will be viewed as having the more reputable, and ultimately final say regarding the risks and benefits between the various possible choices that a patient could make.

[168] Wicclair, "A Response to Brock and Skene" 1991, p.119-120. Such a principle has been deeply entrenched in a variety of governmental reports and scholarly literature on the topic. For example The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research rejected "as the standard of capacity any test that looks solely to the content of the patient's decision" (U.S. Government Printing Office, *Making Health Care Decisions: a Report on the Ethical and Legal Implications of Informed Consent in the Patient-Practitioner Relationship*, Vol. 1, President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, Washington, D.C., 1982, p.61). In fact even proponents of the sliding scale strategy have endorsed this process-oriented rule. For example, as mentioned in Chapter One in a discussion regarding the reasoning component of competence, Paul Appelbaum asserted that this condition "focuses on the process by which a decision is reached, not the outcome of the patient's choice" (Paul Appelbaum. "Assessment of Patients' Competence to Consent to Treatment" *The New England Journal of Medicine*, Vol. 357, pp. 1834-1840, 2007, p. 1836). Buchanan and Brock also assert that an "adequate standard of competence will focus primarily not on the content of the patient's decision, but on the *process* of reasoning that leads up to that decision" (Buchanan and Brock, 1986, p. 33). As shall be discussed below however, the endorsement of a risk based sliding scale is inconsistent with any true acceptance of the process-oriented rule.

decisional counterpart. This asymmetrical feature of the risk based sliding scale may itself already alarm some. For it appears to follow from the four elements of competence as described in Chapter One that the "choice between having treatment x and not having treatment x requires an ability to comprehend and weigh the consequences of *both* options."[169] If true, this would then suggest that regardless of the decision made, the same level of deliberative processes should be required.[170]

Apart from this however, an asymmetrical conception of competence which is inextricably bound to the risk based sliding scale "appears to be incompatible with the principle that assessments of decision-making capacity should utilize a standard that is *process*-oriented, and not result-oriented."[171] This is evident by the fact that the asymmetry here entails that competence assessments can be determined by the result of the deliberative process (i.e. the choice made) and not the deliberative process itself.[172]

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[169] Wicclair, "A Response to Brock and Skene" 1991, p.119.

[170] This view of competence is shared by other scholars. For example, Charles Culver and Bernard Gert suggest that "two decisions are of the same kind with regard to competence when a person who understands and appreciates the pertinent information relevant to deciding in one way - for example, consenting to a treatment - also understands and appreciates the pertinent information relevant to deciding in the other - refusing the very same treatment. It should not be surprising, when we are discussing a person's competence to make a decision about his medical treatment, that if we regard him as competent to consent to a given medical treatment, then we must regard him as competent to refuse that very same treatment" (Charles Culver and Bernard Gert. "The Inadequacy of Incompetence" *The Milbank Quarterly*, Vol. 68(4), pp.619-643, 1990, p.620).

[171] Wicclair, "A Response to Brock and Skene" 1991, p. 118.

[172] We should note that this criticism applies generally to the risk related sliding scale strategy and not just to Brock and Buchanan's version of it. We may recall Grisso and Appelbaum's claim that a judgment "will be for incompetence, if the interest in protection outweighs autonomy" (Grisso & Appelbaum, 1998, p. 130), that is, if the interest in protecting the wellbeing of the patient outweighs the value placed on respecting autonomy. However, this falls prey to the same line of criticism. It enables a hidden hard paternalism to occur by making a finding of competence contingent upon the actual decision made and not the mental process by which it was made. A closer examination of Grisso and Appelbaum's statement reveals the dilemma with their reasoning. The assertion that the interest in protecting wellbeing may override respecting one's autonomy does not in any way speak to the issue of mental capacity. Instead the acceptance that respecting one's autonomy may be overridden by the value in protecting wellbeing presumes that a patient may indeed be capable of being autonomous and thus have the mental capacity/competence required for a truly autonomous decision, but that this can be overridden in certain situations by what would be a clear case of hard paternalistic action. It must be recognized that a concern for wellbeing cannot in itself provide any type of justification for deeming one incompetent. To confuse the two would be to create the dangerous scenario described above, whereby hard paternalistic action can be

This is truly problematic for the sliding scale approach since it is the decision-making process that is the appropriate object of assessment, and not whether the person's decision is judged by others to be in his best interest.[173]

Brock attempts to defend the asymmetry stating that "one reason a patient might be competent to consent but not to refuse a treatment, and vice versa, is that the two choices to consent or refuse will be based on different processes of reasoning or desisionmaking; the overall processes of reasoning must be different if for no other reason than that they result in different choices."[174] If indeed a consent to or refusal of treatment or research participation would entail two different processes of reasoning, then applying different standards of competence might remain perfectly consistent with a process-oriented approach to competence.

However, such a position would actually rob the process-oriented rule of any meaning. For if a difference in the result of a deliberation is sufficient to require a different standard of competence, then in what sense is a process oriented model being utilized? It seems that if "one holds that different choices (outcomes) warrant the

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performed under the guise of soft paternalism by unjustly deeming persons incompetent. It seems that proponents of the risk based sliding scale inevitably conflate two distinct questions, precisely: "(a) Does a patient have decision-making capacity with respect to a particular choice or set of choices? (b) Is it justified to override the patient's decision for paternalistic reasons?" (Wicclair, 1999, p.149-150).

[173] It should be noted that the concern here regarding the process-oriented principle is also intimately intertwined with the previous matter concerning hard paternalism. For imagine that we accept such an asymmetrical approach to competence and, for example accept that, as Brock suggests: "when clearly beneficial life-saving treatment is accepted, minimal understanding may be sufficient to warrant respecting the patient's self-determination since doing so has no cost for, but on the contrary furthers, his well-being. If the treatment is refused, on the other hand, the price for the patient's well-being of respecting his self-determination may now, by his own standards, be too high" (Brock, 1991, p. 112). Then it seems that we have further facilitated an environment where physicians are able to disguise hard paternalistic action under the guise of a more ethically permissible soft paternalism. This is true since it would seem that such an asymmetry would provide justification for findings of incompetence by raising the required level of competence too high when the decision made conflicts with the recommendation of the treating physician. However, as has already been argued, it is conceptually flawed to suggest that that the level of competence required when making a decision changes depending on the actual choice made by the decider.

[174] Brock, 1991, p.112.

conclusion that the processes of reasoning are sufficiently different to call for different criteria of decision-making capacity, it is implausible to maintain that a process-oriented standard is being used to assess decision-making capacity."[175] Thus Brock's defense of the asymmetry ultimately fails and it becomes clear that a risk based sliding scale approach cannot be considered consistent with the process-oriented rule.

It should be noted that an asymmetry may be acceptable in regards to standards of evidence of competence. That is, it may be appropriate to suggest that indeed there is reason to apply a stricter standard of evidence for determining competence when the risk is great, as it is when life-saving treatment is refused. Accordingly, when risks are high, the evidence of competence that must be obtained might be greater, and the methods for acquiring that evidence might be stricter, but this is conceptually quite different from suggesting that the actual level of competence required by the patient ought to be greater. It seems that advocates of this risk based sliding scale approach may also be conflating precisely these two issues: (1) the required mental capacity needed in order to consent and (2) the required evidence needed by a physician or research investigator in order to

[175] Wicclair, "A Response to Brock and Skene" 1991, p.119. In order to make explicit the conceptual flaw present in Brock's assumption that different choices must be the result of different processes of reasoning, we may posit the following thought experiment: Imagine a patient with a fairly low level of decision making capacity. His physician informs him that he has a respiratory infection and will require antibiotics that should clear up the problem within a week, but without which, more serious complications could result such as pneumonia. The patient decides to flip a coin in order to determine whether he will take the antibiotics. Now, in one version of this scenario, the coin flip results in the patient choosing to take the antibiotics, and according to the risk based sliding scale strategy, since such a choice is associated with very low risks, he would be deemed competent. However, if the coin flip was such that the patient chooses not to take the antibiotics, then this strategy may justify a finding of incompetence since such a decision would be quite risky. However notice, even though two different choices could have been made, the decision making process, as absurd as it was, was the same. The same identical decision-making abilities were present regardless of which choice was made. Thus, Brock's assertion that different choices are necessarily associated with different processes of reasoning is untrue. It should also be noted that for an example such as this, a proper process oriented analysis utilizing the four elements of competence, would likely declare that this patient's decision, whichever way he did choose, was not competent. This aligns with where our intuitions might already fall in this case.

deem a patient or subject competent, whereby risk may only significantly influence the latter and not the former.

This mistake seems to occur since we generally do not question the competence of a patient who makes a choice that is commonly viewed as non-risky and as being in her best interest. However, this is done for pragmatic reasons and not because we take our approval of the patient's decision as somehow being evidence that the patient is indeed competent. It is clear that merely being in agreement with another's choice fails to demonstrate that the decision-maker possesses the necessary decision-making capacity. "If [for example] a two year old child does not want to play in the street or pet a strange dog, it does not follow that she has the capacity to decide whether to play in the street or to pet strange dogs. Assent to the correct option from the perspective of one's welfare no more suffices to establish decision-making capacity than a lucky guess suffices to establish knowledge."[176] Lowering the required capacity for a decision simply because the choice actually made is the less risky one commits this very mistake of attempting to classify one as competent simply because her decision is one with which we would agree.

However, it is still appropriate to suggest that in such a case, the required level of evidence necessary to determine that the patient is competent is quite low since any mistake in competency assessment would not result in any harm. Whereas greater evidence of competence might be necessary when the risk of harm is greater since the stakes in making a correct competence evaluation are higher. This is to suggest that when a riskier decision is made, health care professionals must be that much more certain that the decision was made competently, lest they allow for an individual to make a decision that brings him harm despite not having the requisite decision making capacity.

[176] Wicclair. "Patient Decision-Making Capacity and Risk" 1991, p.100-101.

The idea here is that the level of risk may in fact be relevant, but only in determining how certain we ought to be that a patient is competent before proceeding with his decision.

> When the consent is to a lifesaving and benign procedure [for example], it doesn't matter whether we are wrong to judge the patient competent; we will treat the patient in any case. When, however, that patient changes his or her mind and refuses the procedure, it matters a great deal whether we're wrong in judging the patient to be competent and, in the name of self-determination, we permit the refusal to stand. In this circumstance, we rightly demand a much higher degree of evidence for that person's competence, not because the capacities necessary for a competent decision about this treatment have changed, but because our need to be sure about the patient's possession of those capacities has escalated dramatically.[177]

It seems that without realizing it, this variable standard of evidence that turns on risk is actually what the supporters of the sliding scale are seeking. For example Brock and Buchanan assert the following:

> When the expected effects of the patient's choice for his or her well-being appear to be substantially worse than available alternatives, as in the refusal of a simple appendectomy, the requirement of a high/maximal level of competence provides grounds for relying on the patient's decision as itself establishing that the choice best fits the patient's good (his or her own underlying and enduring aims and values). The highest level of competence should assure that no significant mistakes in the patient's reasoning and decision making are present."[178]

This demonstrates that what is truly sought is an assurance that the patient, or subject as in the case of medical research, is actually competent to decide and was not mistakenly deemed competent and allowed to consent to high risk procedures or interventions while actually being incompetent to do so. Thus risk may actually increase the evidence we require that someone is in fact competent, but this is not to suggest that it increases the

[177] Tom Tomlinson. "Who Decides, and What?" In *Biomedical Ethics fifth edition*, Mappes and Degrazia, eds. (New York: McGraw-Hill Companies, Inc., pp. 114-116, 2001) p. 116. Similar suggestions have been made by others as well. For instance see: Joseph Demarco. "Competence and Paternalism" *Bioethics*, Vol. 16(3), 2002.

[178] Brock and Buchanan. "Standards of Competence" In *Biomedical Ethics fifth edition*, Mappes and Degrazia, eds. (New York: McGraw-Hill Companies, Inc., pp. 109-114, 2001) p. 112.

required level of competence itself for that decision. This is the conceptual flaw that appears to exist throughout the literature that supports the risk based sliding scale.[179]

It has now been demonstrated that the various reasoning and arguments in favour of the sliding scale approach are all lacking. The previous section made clear that it is not, as Brock and Buchanan had claimed, the case that informal competency determinations are already being intuitively made in accordance with the risk based sliding scale or that this approach coheres with our current legal framework. Additionally, to accept such a competence strategy allows for a dangerous asymmetrical approach to competence evaluations, which as has been argued, can lead to a disguised hard paternalism that egregiously undermines the value of autonomy; a value that is often considered paramount in medicine. More specifically the risk based sliding scale will inevitably present the danger "that standards of understanding, reasoning, and so forth will be set arbitrarily and unattainably high by those who believe that paternalism is

[179] Ian Wilks, an avid supporter of the risk based sliding scale discusses a case regarding a pneumonia patient who in one scenario acquiesces to treatment with antibiotics, but in another scenario refuses that same treatment. He then suggests that in such cases there is no difference between a greater standard of evidence and a greater standard of competence, ultimately concluding that such a distinction "is not a real one" (Ian Wilks. "Asymmetrical Competence" *Bioethics*, Vol. 13(2), pp. 154- 159, 1999, p155). He continues to assert that "if we do not assess very closely how people meet a standard it becomes much easier for them to get by without actually meeting that standard - which is in effect exactly the same as holding them to a lower standard" (Wilks, 1999, p.155). While Wilks might be correct in pointing out that both methods would similarly accomplish the goal of preventing some persons from "getting by" and being incorrectly deemed competent, the two approaches are certainly not the same. The difference is not only conceptually apparent, but will have ramifications in reality as well. If standards of competence are themselves greater, then the patient will need to demonstrate greater levels of the four sub abilities that comprise competence, that is, understanding, appreciation, reasoning, and voluntariness. However, if greater evidence of competence is all that is sought, then higher abilities on the part of the patient need not be demonstrated. Instead, only further inquires and assurances that the patient is indeed competent might be undertaken. Thus the main difference would be specifically the different tools, methods, and instruments that would be applied in order to test the patient. Methods for determining or assessing the presence of greater levels of competence would only be appropriate if the standards of competence change. This difference further implies that the same person who might be deemed incompetent under a higher standard of competence, might be deemed competent under only a higher standard of evidence of competence. Wilks' objection fails to account for this crucial difference. A more detailed discussion regarding the different tools and instruments used in order to assess competence will be provided in Chapters Five and Six.

justified when perceived risks are great."[180] Furthermore, such an approach runs contrary to the often accepted principle that competency assessments must embrace a method that is process oriented and not result oriented. Given these various objections, it becomes difficult to maintain that this risk based sliding scale strategy is one that is ethically defensible and should be implemented. Any continued suggestion to this effect, as has been argued, is likely a mistake in categorization, where one is conflating a greater standard of competence with a greater level of evidence necessary for a competence determination. "While the risks related to a decision might be grounds for taking more care in assessing a person's competence, they should not provide grounds for increasing the standards by which a person's competence is assessed."[181]

Sliding Scale and the Research Context

Given the various dilemmas with the arguments supporting a risk based sliding scale approach to competence, it seems clear that such an approach stands on fairly unstable conceptual and ethical grounds. However, before entirely dismissing it as a method for consideration in our current effort to derive an appropriate standard of competence for the medical research context for terminally ill subjects, it would be prudent to note how such an approach would function specifically in that context. Apart from the criticisms put forth above against the risk based sliding scale approach, its use and application in the medical research context might still be urged by some who may view it as an appropriate safeguard since it would seem to entail that greater competence

[180] Wicclair, "Patient Decision-Making Capacity and Risk" 1991, p.99.
[181] Gita Cale. "Continuing the Debate Over Risk-Related Standards of Competence" *Bioethics*, Vol. 13(2), 1999, p. 148.

would be required to consent to participate in a clinical trial as opposed to consenting to treatment.

This may indeed appear to be an appealing possible safeguard for potential subjects of research, and perhaps especially so for terminally ill subjects. However, it must be questioned whether this risk based sliding scale strategy can actually justify requiring a greater level of competence for medical research participation decisions than for decisions regarding treatment. It may seem fairly intuitive that the answer should be in the affirmative, for having experimental medical interventions tested on one seems inherently riskier than standard therapy, and thus the sliding scale strategy would seem to require a greater level of competence for consent to medical research participation. However, I shall demonstrate that with a proper understanding of research risks and the ethical condition of clinical equipoise, this assumption should be viewed as specious.

It is crucial to be careful when discussing the risks associated with medical research trials. In assessing the risk[182] associated with a research trial, it is imperative that the risks related to the research itself are demarcated from the risks related to the standard therapeutic intervention that the patient would otherwise confront. Rather than viewing all the risks related to the interventions in the research trial as risks of research, one must determine which of the interventions are purely grounded in research and accept the risks related to only these interventions as research risks. In a discussion regarding minimal risk, Benjamin Freeman and Charles Weijer articulate this view well, asserting that minimal risk should be understood as "risks commensurate to the experiences of the group being studied, that is, as relative to the experiences and associated risks inherent in

[182] Risk is often understood as encompassing both the magnitude of harm and the probability of its occurrence.

the daily lives of the relevant population."[183] Research risks therefore do not include risks that would otherwise be present if the subject of the research were instead receiving standard therapy. Thus, for example, a patient with cancer who is enrolling in a research trial that is testing a new form of chemotherapy that has many severe side effects, should not be considered to be accepting substantially additional risks, if the risks related to the medical intervention in the trial arm for which he is a subject, are the same as the risks related to the chemotherapy treatment that this patient would otherwise be receiving if he had not enrolled in the research trial.

> That therapeutic and research interventions need to be demarcated in the ethical analysis of clinical studies underlies several comments made by the Belmont Commission and the interpreters of the United States' regulations adopted following that Commission's recommendations. These speak of the need to distinguish which procedures are "purely investigational," [and] which parts of the activities "are research and which are practice".[184]

[183] Benjamin Freedman & Charles Weijer. "Demarcating Research and Treatment Interventions: A Case Illustration" *IRB: A Review of Human Subjects Research*, Vol. 14(4), pp. 5-8, 1992, p.7.

[184] Benjamin Freedman, Abraham Fuks, and Charles Weijer. "Demarcating Research and Treatment: A Systematic Approach for the Analysis of the Ethics of Clinical Research" *Clin Res*, Vol. 40, pp. 653-660, 1992, p. 654. It should be noted that the process of separating research risks from therapeutic practice risks involves a difficult conceptual problem, namely, being able to distinguish research from therapy. How "therapy" or "research" is defined will affect which interventions are to count as therapeutic practice or research and thus which risks ultimately constitute risks of research. Without fully exploring this issue, for a full analysis of this matter is beyond our current scope, we might recall as mentioned in Chapter One that *The Belmont Report* provides the criteria for a fairly instructive distinction. As *The Belmont Report* elucidates: "the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment, or therapy to particular individuals. By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective" (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Washington, D.C.: Department of Health, Education, and Welfare, 1979). Section A *Boundaries Between Practice and Research*).

Given that the risks of research are to be separated from therapeutic risks, it would seem "that relatively few clinical research studies [should] pose a high incremental risk associated with fully demarcated interventions."[185]

This analysis already begins to place pressure on the notion that a risk related sliding scale strategy would necessitate that a greater level of competence is required to decide about medical research participation, by demonstrating that much of the risk in many research trials can actually be classified as therapeutic risk. However, the ethical requirement of clinical equipoise further pushes the point. As the *Tri-Council Policy Statement* suggests: "at the start of the [research] trial, there must be a state of clinical equipoise regarding the merits of the regimens to be tested,"[186] which requires that there exist a "genuine uncertainty within the expert medical community... about the preferred treatment."[187] More specifically there must not be a "consensus within the expert clinical community about the comparative merits of the alternatives to be tested"[188] and furthermore the research trial should be designed such that it is reasonable to expect that the successful completion of the trial will disturb clinical equipoise. Thus, for example, if there is a potentially new treatment X, which can be tested on a population P that has a

[185] Freedman, Fuks, & Weijer, 1992, p. 660.
[186] Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.* 1998 (with 2000, 2002 and 2005 amendments) p. 7.1.
[187] Benjamin Freedman. "Equipoise and the Ethics of Clinical Research" *New England Journal of Medicine*, Vol. 317(3), pp. 141-145, 1987, p. 141.
[188] Freedman, 1987, p. 144. This is contrasted with the outdated requirement of what Benjamin Freedman referred to as "theoretical equipoise" which requires a "state of genuine uncertainty on the part of the clinical investigator regarding the comparative therapeutic merits of each arm in a trial" (Freedman, 1987, p. 141). This notion has often been summed up by asserting that the investigator of a clinical trial must have no treatment preference between the arms in the trial. Though the difference between clinical and theoretical equipoise may seem slight, the implications of the difference are quite substantial. The theoretical version of equipoise was deemed unsatisfactory for a multitude of reasons, perhaps most notably because of its fragility. For it seems that theoretical equipoise is disturbed by not only personal hunches and biases of investigators, but it is also jeopardized by the earliest results of a trial which may lend support to one arm over the other, and thus the trial would need to be halted.

specific disease for which there is a current accepted treatment A, then clinical equipoise would require that "there exists (or, in the case of a novel therapy, there may soon exist) an honest, professional disagreement among expert clinicians about the preferred treatment"[189] between X and A and that the completion of the trial can be expected to resolve this disagreement.

The condition of clinical equipoise therefore necessitates that the risk/benefit ratio between the arms of a trial be roughly equivalent, or at least that one arm of the trial is not thought by the expert clinical community to have a substantially worse risk/benefit ratio. If, experimental treatment X, was known to have a significantly worse risk/benefit ratio than standard treatment A, or visa versa, then clinical equipoise would already be disturbed and the medical research trial would be ethically impermissible. Given this we may begin to notice the dilemma with applying a risk based sliding scale strategy to the medical research scenario.

If research and treatment risks are properly differentiated, and if the clinical equipoise requirement is satisfied, then these two conditions together would entail that research risks are appropriately determined by examining the risks of the medical interventions specific to research, and that the risk/benefit ratio of these research specific interventions be approximately equivalent to the risk/benefit ratio of standard treatment. It can then be concluded that therefore research that satisfies the clinical equipoise requirement does not force the subject of the research to bear substantially greater incremental risks. Thus, requiring a greater level of competence when risk is greater would become a meaningless condition in medical research; for if indeed the medical research trial satisfied clinical equipoise, then taking part in the research should not be

[189] Freedman, 1987, p. 144.

considered to knowingly have any substantial risk/benefit differences from standard treatment. It seems that applying the risk based sliding-scale approach would therefore not accomplish anything useful in the medical research context, and certainly would not afford potential subjects any additional protections by justifying a higher standard of competence.[190] If we expect a sliding-scale strategy of competence to have any significance in the medical research decision-making setting, it seems apparent that it must be grounded in something other than risk.[191]

Before proceeding with this argument it would be prudent to discuss a potential objection. Specifically, the objection involves the recognition that having the arms of the trial in a state of clinical equipoise does not entail that there are no added risks to participating in a medical research trial. The risk related to added uncertainty is always present regarding the more novel or experimental arm of the research trial.[192] This is because even though the trial arms may be in a state of clinical equipoise, the knowledge regarding the experimental/novel procedure is often less than what is known regarding the current standard treatment. The standard therapy may have numerous years of use in

[190] I am indebted to Professor Duff Waring at York University for bringing this argument to my attention.
[191] One may suggest that I have mistakenly assumed that the risks associated with participating in research are roughly the same regardless of the type of research. However, the objector may claim that this is not true, and that a research study on a new cancer chemotherapy intervention, for example, compared to a research study on Advil would certainly seem to have very different risks associated with them, with the former study appearing far riskier than the latter. Thus it would seem that different research trials can have different levels of risk associated between them and that therefore a risk based sliding scale strategy of competence may still prove beneficial. However, this line of criticism crumbles as soon as it is examined. For, if one properly demarcated research and treatment risks, it would become clear that this objection is fallacious. The subject population enrolling in the chemotherapy research trial are those for whom the risks of the chemotherapy intervention, given that the trial is in clinical equipoise, are not incrementally greater than the risks associated with the treatment that these subjects would otherwise be receiving if they had not enrolled in the research, but instead had received standard cancer chemotherapy treatment. Thus, though it may seem that one research trial appears far riskier than the other, a proper separation of treatment related risks from research related risks, demonstrates that in fact once the treatment risks have been accounted for, the remaining risks associated with the research should be minimal and roughly similar between different research trials.
[192] I am indebted to Professor Trudo Lemmens at The University of Toronto for bringing this objection to my attention.

which the evidence accumulated regarding its safety and efficacy far outweigh any knowledge regarding the experimental procedure. It is this added uncertainty that can be considered to be an additional risk associated with participating in research.

Though it must be conceded that in fact uncertainty remains as a potential additional risk, two points must be made regarding this issue.

First of all, it should be recognized that the level of uncertainty present cannot be thought to pose too great of a risk. For it seems that properly satisfying clinical equipoise would require that enough preliminary data on the experimental intervention exists such that there is a genuine uncertainty among the expert clinical community between the comparative risk/benefit ratios of this experimental intervention and standard treatment. More precisely, "for a nonvalidated intervention to be in equipoise with a standard treatment arm, its associated expectations of risk and benefit must be roughly equivalent to those of treatments commonly used in clinical practice."[193] Thus, even though the standard treatment may have potentially many more years of knowledge accumulated regarding its safety and efficacy, the added uncertainty with the experimental intervention cannot be considered to be too great of a risk if clinical equipoise has been satisfied. I would then contend that this additional risk is not sufficient to justify requiring a greater level of competence for consent.

Second, it must be questioned whether the risk of uncertainty is the type of risk that could even warrant a change in the level of competence required to make a decision. We may consider the following thought experiment. Peter is attempting to decide between two potential investment opportunities that his investment broker has discussed with him. Both types of investments are actually quite similar. The amount that Peter

[193] Freedman, Fuks, Weijer, 1992, p. 656.

would have to invest is the same, the level of active involvement required of Peter would be the same, and the type and length of the forms that Peter would have to fill out is also the same. Furthermore, the level of complexity associated with each type of investment, the mathematical calculations for example, and the economic jargon used, is also the same. The only difference between the two investments is that investment A has a 99.9% chance of providing Peter with a 2.5% return on his investment, whereas the exact return on investment B is unknown. Investment B could provide Peter with a return anywhere between the range of 0 and 5%. Thus, the only real difference between these two investments is the level of uncertainty.

Does this uncertainty increase the level of competence that should be required of Peter in order to consent to investment B? It would certainly seem odd, given the similarities between the two investment opportunities, to consider investing in B as requiring a greater level of competence than investing in A. Uncertainty does not seem to necessarily raise the complexity or difficulty of the material that needs to be understood, appreciated, reasoned or voluntarily decided about in order for a decision to be considered competent. This investment case clearly demonstrates this fact as the level of complexity of the information involved in each investment was the same. It may be appropriate to suggest that as the level of uncertainty of the consequences of a decision increases so too should the level of certainty that the competence judger must have in order to conclude that the individual deciding is competent to do so. However, this is akin to raising the standards of evidence required for one to be declared competent, but it is not to raise the level of competence itself required to decide.

With the recognition that the level of uncertainty in medical research trials cannot be so great so as to disturb clinical equipoise, and that uncertainty is not likely to be the type of risk that could justify an increase in the level of competence required in order for one to make a decision, the earlier assertion that a risk based sliding scale approach to competence is useless in the medical research setting, can be maintained.[194]

Concluding Remarks

It may have been noticed that when I have referred to the sliding scale strategy, I have qualified it by placing the term "risk based" in front. This was to allude to the idea that there may be other ways in which to ground a sliding scale approach. While it was argued that risk may only appropriately affect the level of evidence of competence that ought to be required, for example by investigators who are recruiting potential subjects for research, we do not have to completely abandon a sliding scale strategy for competence. Rather than discard this approach entirely, it may be appropriate to instead ground it in something other than risk. The suggestion offered earlier was that a sliding scale strategy can be grounded in the complexity of the decision. For it appears "correct to say that the level of demonstrated skill to decide will rise as the complexity or difficulty of a task increases (deciding about spinal fusion, say, as contrasted with

[194] It should be noted that what has been argued here does not amount to the assertion that indeed all clinical trials always maintain a reasonably equivalent risk/benefit ratio between standard therapy and the non-validated experimental intervention and that clinical equipoise is always satisfied. Indeed, many clinical trials often involve procedures that are too risky. We need only recall the Jesse Gelsinger case, discussed in Chapter One footnote 14, in order to recount an example where the risk was incredibly high and various ethical principles such as clinical equipoise were ignored. However, the immorality and sometimes illegality of such research is not currently being discussed. It is quite clear that corrupt or negligent medical research does occur, and is indeed ethically and sometimes legally condemnable. However, the crucial aspect for what is being argued here, is that even in cases where our ethical precepts such as clinical equipoise are followed, and even where blatant levels of corruption and negligence are absent in a clinical trial, then it is still necessary to ensure the protection of research subjects' autonomy by ensuring an appropriate degree of competence. And given this aim, it is clear that applying the risk based sliding scale approach proves futile.

deciding whether to take a minor tranquilizer)."[195] More specifically, as a decisional context is such that it is more difficult to satisfy the four conditions of competence, namely understanding, appreciation, reasoning, and voluntariness, then it would be appropriate to raise the required standard of competence.

This may be precisely the situation for our medical research context where the potential subjects are terminally ill persons. This research scenario, as compared to the decision making in a standard therapeutic context, seems to represent a situation where numerous factors are present that would make it more difficult to satisfy the four criteria of competence. For example, research trials that facilitate a therapeutic misconception,[196] provide undue payments, or that exploit the desperation of terminally ill patients,[197] might all increase the level of difficulty for the potential subject in possessing or performing the four criteria involved in competence.

The assertion that the medical research context might be substantially different from the context of therapeutic practice so as to warrant requiring a different level of competence for consent is a fairly controversial claim, but it is this claim that will be the focus of the following chapter. More specifically, Chapter Three will examine relevant differences between the therapeutic and research contexts that will influence the level of competence that ought to be required in the latter. It will be these differences that will ultimately fuel the discussion in Chapter Four that will be dedicated to specifically

[195] Beauchamp and Childress, 2009, p. 117.
[196] As we may recall from Chapter One, this is the phenomenon where a subject of research misconstrues the research trial for therapeutic practice.
[197] As Mark Hochhauser has recently pointed out, many research trials have a "brand name" which can often exploit the desperate and hopeful mindset of severely and terminally ill patients and may also contribute to a subject's therapeutic misconception. See: Mark Hochhauser. "Therapeutic Misconception and Recruiting Doublespeak in the Informed Consent Process" In *Ethical and Regulatory Aspects of Clinical Research*, Emanuel et al., eds. (Baltimore: The Johns Hopkins University Press, 2003) p. 222. This issue will be discussed in more detail in the following chapter.

determining how high the required level of competence ought to be for medical research participation with terminally ill subjects.

As Jocelyn Downie et al. state: "in the interest of the protection of research participants, both ethics and law have placed a central focus on the promotion of autonomy or self-determination. Informed consent as an expression of autonomous choice is seen as a crucial component of research participation."[198] However, in order to truly respect autonomous choice, it is imperative that we properly judge competence, so that those whose autonomy is being respected are in fact those who possess the necessary mental capacity for truly autonomous choice. To that end, it has been argued that a risk based sliding scale approach to competence is a misguided position, for it not only proved to be questionable conceptually and ethically, but it failed to be any type of safeguard in our medical research context. While this approach must be abandoned, it is still necessary to look elsewhere for the appropriate safeguards for terminally ill potential subjects of medical research. However, while establishing the proper safeguards that will regulate terminally ill persons' participation in medical research is of vital ethical importance, we must remember that succeeding in this endeavour will first require establishing the appropriate competence requirement suited to such a context. It is only by determining and applying the appropriate competency requirement for this context that people's autonomy will truly be respected and their wellbeing protected. It is to this task that we now turn.

[198] Jocelyn Downie, Timothy Caulfield, & Colleen Flood. *Canadian Health Law and Policy* (Canada: Butterworths Canada Ltd., 2002) p. 479.

Chapter 3: The Requirement of Competence: A Comparative Analysis Between the Medical Practice and Medical Research Context

Understanding the context within which an action is preformed is critical for its ethical evaluation. "A kiss may be just a kiss; but, depending upon the context in which bestowed it may also be a mark of affection, the fulfillment of a contract for services, or as in the Godfather saga, the pronouncement of the death penalty."[199] It should thus seem clear that context matters when determining the ethicality of an action. However, the same can be said regarding standards of competence. An ethically appropriate standard of competence in one context may be wholly inappropriate in another. Though the notion that different contexts and different tasks will require different levels of competence has been generally assumed in the prior chapters, a brief elaboration will prove instructive.[200]

Since, as discussed in previous chapters, the generic meaning of competence is *the ability to perform a task*, then the level, or standard of competence required, will vary from context to context depending on the specific task. The required standard "for someone's competence to stand trial, to raise dachshunds, to write checks, or to lecture to medical students are radically different. The competence to decide is therefore relative to the particular decision to be made. Rarely should we judge a person incompetent with respect to every sphere of life."[201]

Assuming then, that different decisional tasks require different levels of competence, our question thus becomes: what level or standard of competence is required

[199] Benjamin Freedman, Abraham Fuks, Charles Weijer. "Demarcating Research and Treatment: A Systematic Approach for the Analysis of the Ethics of Clinical Research" *Clin Res*, Vol. 40(4), pp.653-660, 1992, p.653.
[200] It should be noted that in what follows, one who possesses adequate competence in a particular context will be referred to as being substantially or sufficiently competent for that context.
[201] Tom Beauchamp & James Childress. *Principles of Biomedical Ethics* (New York: Oxford University Press, 2009) p.112.

in the medical research context with terminally ill subjects or, put differently, what degree of competence constitutes substantial competence in the medical research context?[202] While the level of competence needed to make some decisions may seem clear, such as where one should eat, or how one should invest her money, some contexts are more elusive on this matter. Deciding where to eat will likely require a relatively low level of competence since a person would simply require knowledge regarding her personal taste preferences.[203] Deciding how to invest money however, will likely require a comparatively higher level of competence since an understanding of some basic economic principles along with mathematical reasoning skills may be required. However, determining the requisite level of competence becomes a quite complex matter with medical decisions, and an especially controversial issue in the context of medical research participation decisions for the terminally ill specifically.

We must be cautious and not depict the standard of competence needed in medical research as too great by requiring something resembling full or complete competence. This would render decision making in the medical research context

[202] Some have objected to this type of analysis of competence, contending that it creates a false dichotomy "i.e., that competence is an all-or-nothing phenomenon… [the idea being that this analysis of competence will] lump all sorts of patients, with quite different degrees of mental impairment, into the same class, *vis.* those for whom an active paternalistic stance is always appropriate" (Stephen Wear. "Patient Autonomy, Paternalism, and the Conscientious Physician" *Theoretical Medicine*, Vol. 4, pp. 253-274, 1983, p. 259). It must be admitted that this objection raises a good point, for the degree of competence may in fact vary greatly from person to person, where the range runs from complete competence to partial proficiency to total mental ineptness, and the objection is further correct in asserting that with the above analysis persons with different degrees of competency or incompetence may be all lumped into one category. "Nonetheless, [in the medical context] it is confusing to view this *continuum* in terms of degrees of *competency.* For practical and policy reasons, we need *threshold levels* below which a person with a certain level of abilities for a particular task is incompetent. Not all competent persons are equally able, and not all incompetent persons are equally unable, but competence determinations sort persons into these two basic classes, and thus treat persons as either competent or incompetent for specific purposes" (Beauchamp and Childress, 2009, pp. 113-114).

[203] Of course the level of competence required for such a situation may appropriately increase if the context changes, for example if the person deciding where to eat has a particular food allergy or is on a specific diet.

impossible, and clearly misconstrues our endeavour in a problematic way. For as Beauchamp and Childress elucidate: "to restrict adequate decision making by patients and research subjects to the ideal of fully or completely autonomous decision making strips their acts of any meaningful place in the practical world, where people's actions are rarely, if ever, fully autonomous."[204] Asserting that full or complete competence is required for decision making in the medical research context certainly sets the standard too high, however, assuming the threshold so low that the only persons who fail to have substantial competence are children and the mentally handicapped seems similarly inappropriate.

Though currently participating as a subject in medical research entails that the subject first review and freely sign an informed consent document, the question of how competent a potential subject must be in order to be able to provide informed consent remains largely unanswered. There appears to be a common implicit assumption that the standard of competence needed to consent to medical research should be akin to the standard applied in ordinary therapeutic medical practice decision making.[205] In fact

[204] Beauchamp and Childress, 2009, p. 101.

[205] See: Robert Levine. "Consent Issues in Human Research" In *Ethical and Regulatory Aspects of Clinical Research*, Emanuel, Crouch, Arras, Moreno, & Grady, eds. (Baltimore: The Johns Hopkins University Press, 2003), who in a discussion regarding standards of informed consent, "proposes that both patients and clinical research participants should be afforded the same rigorous degree of protection in this regard" (Ezekiel J. Emanuel, Robert A. Crouch, John D. Arras, Jonathan D. Moreno, and Christine Grady. *Ethical and Regulatory Aspects of Clinical Research* (Baltimore: The Johns Hopkins University Press, 2003) p. 189). It should be noted that the discussion of standards of informed consent is intimately tied to our discussion here regarding standards of competence, in that a certain level of competence is required for an ethical informed consent. However, the issue of determining informed consent standards has become more of a legal matter, with arguments suggesting that the law should afford greater protections through thoroughly detailed and properly structured informed consent documents. Whereas the issue being explored here, regarding the appropriate standard of competence required, relates more to a person's decisional capacity, and thus a higher standard of competence requirement would imply, not that a more elaborate and better detailed informed consent document should be required, but that many individuals simply may not have the requisite capacity needed to provide informed consent for medical research participation. This controversial assertion along with possible remedies will be explored in greater detail in this chapter. However it is important to recognize that a specific standard of competence for the medical research context is not being suggested here, but rather it will be argued that the level of competence needed of a

"there is virtually no case law on the basis of which legal standards for consent to research, as distinguished from practice, might be defined."[206] However in what follows it will be demonstrated that this is an ethically flawed approach. While patients are generally assumed to be competent when consenting to therapy, unless there is reason to suspect otherwise, the medical research context with terminally ill subjects is markedly different such that the same assumption is not warranted or ethically appropriate.

The proceeding discussion will be dedicated to presenting a tripartite argument in favour of a higher standard of competence for the medical research context compared to the therapeutic medical practice context with terminally ill persons. This argument will demonstrate that there exist three significant differences between the medical practice and the medical research contexts such that the latter requires a higher level of competence for decision making. These differences include the difference in the nature of the researcher/subject relationship as opposed to the physician/patient relationship, the higher potential for exploitation of the situation or mental state of terminally ill subjects, and the presence of the therapeutic misconception.[207]

The claim that participating in medical research must require a greater level of competence than consenting to medical therapy for terminally ill persons may warrant some immediate doubt and concern. How can a government or a researcher justify the

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terminally ill person in order to be able to provide an ethically appropriate informed consent for participation in medical research is comparatively higher than the level of competence required for that person to make decisions in the context of ordinary medical practice.

[206] Levine, pp. 197-198. One notable exception occurs in the case of Halushka v. University of Saskatchewan, where the Court determined that the level of disclosure required for a proper informed consent for medical research participation should be "at least as great as, if not greater than, the duty owed by the ordinary physician or surgeon to his patient. [Furthermore] there can be no exceptions to the ordinary requirements of disclosure in the case of research as there may well be in ordinary medical practice" (Halushka v. University of Saskatchewan [1965], 53 D.L.R. (2d) 436.)

[207] Recall from Chapter One that the therapeutic misconception is the phenomenon where a subject of research may misconstrue the research trial for therapeutic practice.

scenario where a person's desire to be admitted into a medical research trial is overridden? Is this type of paternalism[208] ever permissible in a state that values autonomy? To highlight the issue, we may consider the following case:

Sandy, a 45 year old woman who has always displayed the utmost rationality has recently discovered that she has terminal cancer. Her physician has made her aware of a new clinical trial that is testing new cancer therapies. The clinical trial is a Phase I trial which has at its primary aim, to test toxicity levels of the new treatment so that an appropriate dosage can be recommended for further trials.[209] Since this is a trial that tests toxicity levels, it has a fairly poor risk/benefit ratio. Sandy, feeling hopeful and optimistic that this could be a miracle cure for her, begins to misconstrue this research trial as therapeutic practice. However, she is alarmed when she is told that she will not be permitted into the medical trial as a result of her misconception of the trial as a potentially miraculous life saving therapy. She is especially shocked because at no point in her life, while making decisions regarding medical procedures, has her competence ever been questioned. Now suddenly her ability to make her own medical choices has been deemed insufficient.

It appears that Sandy may seem justified in feeling frustrated by this paternalistic interference. Sandy, and many others, would argue that her level of competence, which has always been substantial enough so as to be capable of making medical decisions, is similarly sufficient in this context to decide whether to enter the medical research trial.

[208] Refer back to Chapter Two for a full explanation of paternalism and the distinction between soft and hard paternalism. Briefly, soft paternalism involves interference with a person who is less than substantially competent while hard paternalism involves interference with a person who is considered substantially competent.
[209] Refer back to Chapter One for a full explanation of Phase I trials.

However, though this may seem intuitive, the significant differences between the medical practice context and the medical research context must give us pause.[210]

While full competence cannot be an accurate depiction of the level of competence required of terminally ill individuals in order to be able to provide an ethical informed consent for participation in medical research, it shall be argued that the level of competence required must be greater than that required of them in medical practice decision making.[211] This will be demonstrated with a threefold argument analyzing the previously mentioned three significant differences between medical practice and medical research and their relation to the claim that a higher level of competence requirement is needed in the medical research as opposed to the medical practice context. We shall proceed by examining each difference in turn.

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[210] It should be noted that my position may seem to conflict with certain studies that suggest that the competence of medically ill patients is not markedly different from the competence possessed by their healthy counterparts. For example Paul Appelbaum and Thomas Grisso produced a study that demonstrated that hospitalized patients do "not differ from the non-ill comparison subjects on three instruments developed to assess abilities related to decision-making competence... [Furthermore they concluded that] there is no reason to believe that hospitalized patients... -even if being treated for potentially life-threatening conditions- are at increased risk of inability to engage in a meaningful informed consent process" (Paul Appelbaum and Thomas Grisso. "Capacities of Hospitalized, Medically Ill Patients to Consent to Treatment" *Psychosomatics*, Vol. 38(2), pp.119-125, 1997, p. 119). However, it is important to recognize that studies such as this are in regards to the ill patient's competence regarding medical treatment. The situation is fundamentally different for the medical research setting due to the three differences that will be discussed in this chapter. Therefore, it is not my claim that ill persons are necessarily or even more likely to be incompetent by virtue of their illness, but rather that a greater level of competence is required for the medical research decision making context. As the ensuing argument will establish, what justifies requiring a greater level of competence for medical research participation decisions with terminally ill persons will mostly stem from the context within which the decision is made. This suggests that the type of decision in deciding whether to participate in research relating to one's terminal illness is fundamentally different from the type of decision regarding whether to accept or refuse treatment for that same illness. As shall be demonstrated, it is this shift in decisional context that will justify a greater standard of competence for the research as opposed to treatment setting.

[211] It is crucial to realize that the argument being advanced here is not the controversial and previously refuted idea that a higher degree of competence is required when the risks associated with the decision are greater, as would be suggested by the risk based sliding strategy. Refer back to Chapter Two for a full explanation and refutation of such a theory. Instead the claim here will involve a demonstration that satisfying the sub-abilities that constitute competence, namely understanding, appreciation, reasoning, and voluntariness, becomes more difficult in the medical research as opposed to the medical practice context for terminally ill persons. If true, then the claim that the medical research decision-making context requires a greater level of competence for ethical informed consent follows logically and becomes a mere tautology rather than a controversial claim.

Difference 1: Relationship between Researcher and Subject versus Physician and Patient

It must firstly be recognized that the nature of the relationship between a researcher and subject fundamentally differs from that between a physician and patient. Specifically, the loyalty that a physician is thought to have toward a patient is not present between a researcher and subject. Though fidelity is not as often cited, as autonomy or beneficence is, as one of the fundamental moral principles in health care and research, its value in medical ethics cannot be ignored.[212] "Professional fidelity, or loyalty, has been traditionally conceived as giving the patient's interests priority in two respects: (1) the professional effaces self-interest in any situation that may conflict with the patient's interests, and (2) the professional favors the patient's interests over others' interests."[213] This formulation of a physician's obligation of fidelity to the patient can be seen as more of an ideal, and often in practice the obligation is not as strict. For example, "caring for patients in epidemics has often been considered praiseworthy and virtuous rather than an obligatory instance of fidelity."[214] However, despite this, the distinction between the physician/patient relationship and the researcher/subject relationship should become apparent. For the researcher is not thought to have even a non-idealistic version of such an obligation.[215]

[212] In fact some have argued that a moral norm of fidelity in medical ethics arises as a specific application of one or more of the commonly assumed four fundamental principles in medicine, namely: respect for autonomy, nonmaleficence, beneficence, and justice. For example respecting the autonomy of a patient may involve disclosing certain facts or potential conflicts of interest that would not only enable a patient to make an autonomous decision, but would also demonstrate a loyalty to the patient by placing her interests above other interests.

[213] Beauchamp and Childress, 2009, p. 311.

[214] Beauchamp and Childress, 2009, p. 311.

[215] It should be realized that the researcher does have some obligation to the subject insofar as the subject is a person with inviolable human rights, but this is far from establishing anything akin to the obligation of fidelity that exists in the physician/patient relationship.

The reason for this difference in relationship relates to the differing goals between the physician and the researcher. The primary goal and aim of medical practice is intended to benefit the patient, whereas the primary aim of medical research is not intended to benefit the subject. More specifically, recalling our distinction from Chapter One:

> 'practice' refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment, or therapy to particular individuals. By contrast, the term 'research' designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships)…[216]

Thus while the physician's and patient's interests are thought to align, the same cannot be said regarding the researcher's and subject's interests.[217] As a result, the method and administration of medical interventions in research differs significantly from that performed in medical practice. Certain methodologies in research such as randomization,

[216] The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Washington, D.C.: Department of Health, Education, and Welfare, 1979). Section A *Boundaries Between Practice and Research.*

[217] It should be noted that some current medical practices represent a departure from this notion of alignment between the physician's and patient's interests. Such examples would typically involve the physician acquiring patients through a third party arrangement, such as might be the case with a physician working in a prison, the military, or even a scenario where a physician is required to assist in determining "whether applicants for insurance policies are safe risks. In some circumstances the health care professional may rightly not regard the person examined as his or her patient, but, even so, the professional still has certain responsibilities of due care" (Beauchamp and Childress, 2009, p. 312). These cases demonstrate scenarios where a physician's duty to a patient may conflict with an obligation to a third party institution. It can be said that therefore even physicians in the therapeutic medical practice context face conflicts of interest that prevent them from having their interests perfectly align with the patient's. However, it must be recognized that these cases represent a departure from typical therapeutic medical practice. Thus, even though some currently accepted practices place the physician in such a conflict, they are not paradigmatic of the more trusting and often closer type of relationship that most individuals have, or are thought to have, with their physician.

placebo controls, and double blinding, all demonstrate that in research as opposed to medical practice, the subject's wellbeing and interests are not primary.[218]

"In randomized clinical trials, for instance, research subjects are randomly assigned to one of two (or more) treatments that are being compared (or, when treatment is compared to placebo, to either treatment or placebo). In clinical care, by contrast, treatment is most often geared towards the particular treatment needs of individual patients, as determined in consultation with an individual physician."[219] Furthermore, the requirement that clinical trials be double blind entails that neither the subject nor investigating physician knows what medical intervention the subject is receiving. These approaches have become a necessary way to guarantee the integrity of the research by ensuring that the conclusions drawn from the trials are without bias. However, the use of the randomization and double blinding methodologies demonstrate that indeed the interests of the research are placed above the interests of the subjects, representing a clear departure from ordinary medical practice.[220] It may additionally be noted that in many cases, participating in a research trial may preclude a subject from taking other

[218] Some researchers may contend that their primary interest is in the research, which may help future generations of patients, and that thus their interest is in the welfare of patients. Though this may be the case for some researchers, such an explanation is still very far from having the interest of the current subject as the primary interest. Indeed, this is a further demonstration that the welfare and interests of the current subject is being made secondary to some other interest, either that of the research or future patients, or both.
[219] Jocelyn Downie, Timothy Caulfield, and Colleen M. Flood. *Canadian Health Law and Policy 2nd edition* (Ontario: Butterworths Canada Ltd., 2002) p. 462.
[220] For more on the ethics of randomized clinical trials (RCTs) consult: Samuel Hellman and Deborah Hellman. "Of Mice but Not Men: Problems of the Randomized Clinical Trial" *New England Journal of Medicine,* Vol. 324, pp.1585-1589, 1991; and Robert Truog. "Randomized Controlled Trials: Lessons from ECMO" *Clinical Research,* Vol. 40, pp. 519-527, 1992. Samuel and Deborah argue that the requirement of randomization amounts to the claim that the interests of individual patients are secondary to the interests of general society, which would appear to violate the Kantian principle that the individual should never be made into solely a mean for the benefit of others and appears to set a dangerous precedent. Robert Truog instead, accepts RCTs for most types of medical research, but argues that they become seriously unethical in the case of life-threatening conditions.

potentially beneficial medicines and drugs external to the research trial as that may interfere with the results of the research.[221]

It should thus be clear that research trials employ "several methodological requirements that threaten to undermine the traditional medical ethic of undivided physician loyalty to the individual patient."[222] Some ethical guidelines have attempted to combat this problem by proposing certain principles that would require researchers to treat subjects' individual interests as primary. For example the American Medical Association asserts that "in conducting clinical investigation, the investigator should demonstrate the same concern and caution for the welfare, safety, and comfort of the person involved as is required of a physician who is furnishing medical care to a patient independent of any clinical investigation."[223] However, this type of guideline and ethical principle is impractical and infeasible as the very structure of the medical research enterprise rests on methods which by their very nature conflict with any obligation to treat a subject's interest as primary and certainly diverges from a physician's duty to be loyal to patients and provide best care for their wellbeing.

Based on the methods used in clinical research, it becomes clear that the interests of investigators in the research context differ significantly from those of physicians in the medical practice context and thus the relationship between a physician and patient is

[221] Furthermore, in some medical research situations, even if a subject is experiencing therapeutic benefit from the experimental non-validated intervention in the medical trial, the medical intervention may be taken away from that subject upon completion of the trial, further exemplifying that the interests of the research investigators cannot be thought to align with those of the subjects (See: Kolata and Eichenwald. "Stopgap Medicine: For the Uninsured, Experiments may Provide the Only Treatment" *New York Times*, June 22, 1999). This type of issue may be particularly problematic in Phase I trials, explained in Chapter One, where even in the rare occurrence where a subject is noticeably benefiting from the particular drug being tested, the dosage will continue to shift to more toxic and possibly less effective amounts. This would again further demonstrate that in medical research the subject's interests are subordinated by the interests of the research itself.

[222] Emanuel et al., 2003, p. 193.

[223] American Medical Association, *AMA's Code of Medical Ethics*: *section 2.07 — Clinical Investigation*. Issued prior to April 1977; Updated June 1994 and June 1998.

significantly different from that between a researcher and subject. However some further elaboration regarding the specific interests present in research may further demonstrate how drastically the physician/patient relationship differs from the researcher/subject relationship.

Within medical research, the primary interest is often one or both of the following: I) to benefit the financial interests of the company who funds the research[224] or II) to benefit society as a whole.[225] Each of these interests may conflict with the interests of the subject. Though this may seem clear in the case of financial interests, the conflict similarly arises when the primary interest of the researcher is to benefit society by contributing to scientific knowledge. Where research is done in the name of providing benefit to society then accordingly, these "responsibilities to future generations may conflict with due care for current patients who become research subjects."[226] This leads to a crucial distinction, being that "the prospective subject should be informed that in research, in contrast with practice, the subject will be at least in part a means and perhaps primarily a means to an end identified by someone else."[227]

[224] Commercial interests have become the paradigm case for conflict of interest dilemmas that occur in medical research. "Pharmaceutical companies and contract research organizations ("CROs") now play a leading role in research, and they often solicit participation among private practitioners outside of academic centres" (Downie et al., 2002, 467). The pressures and influence that commercial interests exert on researchers have constituted some of our more current examples of unethical conduct in medical research where subjects' interests are seen as either secondary or nonexistent. For a recent example see the controversy that surrounded Dr. Nancy Olivieri, the University of Toronto, the Toronto Hospital for Sick Children and the pharmaceutical company Apotex. In this case, Apotex insisted that Dr. Olivieri not inform the research subjects of her concerns regarding the toxicity of the experimental drug being administered (J. Thompson, P. Baird & J. Downie. *The Olivieri Report: The Complete Text of the Report of the Independent Inquiry Commissioned by the Canadian Association of University Teachers,* (Toronto: James Lorimer & Company Ltd., 2001)).

[225] Although most of the discussion regarding conflicts of interest in medical research will revolve around financial and societal interests, "other interests, such as professional advancement or standing and friendships, are no less important" (Beauchamp and Childress, 2009, p. 314).

[226] Beauchamp & Childress, 2009, p. 317.

[227] Levine, p. 198.

Furthermore, that the researcher's and subject's interests do not align, and that thus the subject will be at least in part treated as a means, increases the possibility of corruption, misuse, and abuse in the research case. Since achieving the goals of research may conflict with the subject's own interest, there is an added incentive for researchers, which is not present in medical practice, to tend to ignore or diminish a subject's rights or interests in favour of the aims of the research. In fact, "there is ample historical evidence to suggest that researchers' interests in the results of research may at times lead to the neglect of the rights and interests of research participants… [Apart from the often cited medical experimentation that occurred during the Nazi regime, and the Apotex case cited previously], the names 'Brooklyn Jewish Chronic Disease Hospital,' 'Tuskeegee' [*sic*] and 'Willowbrook' are enshrined in medical history as examples"[228] of the kind of unethical conduct that may transpire in research when a gross neglect of the research subject's rights and interests occurs. This neglect of a research subject's interests occurs in order to advance the conflicting interests of the research. It must be recognized that this type of conflict of interest is not present in standard medical practice.[229] Thus, a significantly different relationship exists between researcher and subject as opposed to physician and patient, specifically a relationship where interests are not thought to align versus a relationship where the interests do align, respectively.

[228] Downie et al., 2002, pp. 463-465.

[229] However, it should be noted that controversies do exist whereby physicians have serious and potentially unethical conflicts of interest. Certain relationships with pharmaceutical companies and referral arrangements have been noted as generating conflicts of interest for physicians. However, these are cases whereby a physician has broken the ethical principles, and in some cases the laws, of his/her profession. Thus, the claim made above remains legitimate. For, it is still the case, despite examples of corruption, that the nature of the physician is such that his/her interests are to align with those of the patient, whereas this is not so with researchers, who by nature have interests, either financial or societal or other, that conflict with the interests of research subjects.

This difference in relationship suggests that a greater level of competence is needed in medical research decision making. For since the researcher and subject may have conflicting interests, the subject must be that much more competent in order to be able to receive what the researcher tells her with a healthy skepticism, be able to effectively evaluate the situation on her own, and be confident enough with her knowledge of the situation to be able to challenge the researcher's advice or opinion if the situation should warrant it. Thus it would seem that at least a higher level of the appreciation and reasoning elements of competence would be necessary in the medical research as opposed to the therapeutic medical practice context.

Difference 2: The Potential for Exploitation of the Situation or Mental State of Terminally Ill Subjects

"Some persons report feeling heavily pressured to enroll in clinical trials"[230] by the situation they are faced with. Thus, though some would argue that many of these enrollments may still technically classify as voluntary, since the person involved may have still made the choice without being under the direct control of another's influence,[231] the degree to which the choice is voluntary seems greatly diminished by heavy pressures. For the terminally ill individual seeking a miracle cure, this may seem obvious. It should be noted that being in such a situation in and of itself is not sufficient to characterize the medical research context as making voluntary choice more difficult than in medical practice, especially since even in medical practice, one's particular illness may pressure him to choose surgery or medicine that he would not otherwise have considered. Benjamin Freedman correctly distinguishes between choices forced by man

[230] Beauchamp & Childress, 2009, p. 255.
[231] See: Beauchamp & Childress, 2009, p. 255.

and choices forced by nature, where only the former necessarily undermine voluntariness in a morally significant way. For it ought to be:

> granted that natural contingencies ('acts of God,' things which come to pass naturally, those contingencies which we cannot hold anyone responsible for) do not render a person unfree, nor do they render unfree the choices which a person makes in light of those contingencies…I am not - in the morally relevant sense – lacking in freedom because I cannot, unaided, fly through the air, or live on grass. Nor am I unfree because my heart is about to give out. Nor am I unfree when, recognizing that my heart may give out, I choose to undergo surgery.[232]

However, though "the situation may not necessarily render choices less voluntary… it suggests that seriously ill patients may be particularly vulnerable to unrealistic enticements and manipulation of hope."[233] This may be especially true for the terminally ill individual. It appears that the unfortunate situation that confronts this person is such that he may feel that the research trial is the only choice available. This may be as a result of financial constraints that make such a patient view participation in the research trial as the only way to gain access to medical resources,[234] or due to viewing his situation as so hopeless that out of desperation he inappropriately views the research trial as a miracle cure.

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[232] Benjamin Freedman. "A Moral Theory of Informed Consent" *The Hastings Center Report*, Vol. 5(4), pp. 32-39, 1975, p.36. It should be pointed out however, that though natural contingencies themselves, such as terminal illness, do not necessarily detract from the voluntariness with which a decision is made; it may do so in the situation where the illness leads to depression or some other type of internal constraint that can in turn seriously undermine competence and specifically voluntariness.

[233] Robert Nelson & Jon Merz. "Voluntariness of Consent for Research: An Empirical and Conceptual Review" *Medical Care*, Vol. 40(9), pp. V69-V80, Sept., 2002. p. V-72.

[234] Such a scenario is more likely in countries, such as the United States, that lack a universal insurance system. However, countries that have universal health care, such as Canada, are not completely immune to such a dilemma. There may for instance be certain treatments not covered by government health care. This may leave one in a similarly financially constrained situation which may lead him to look to research trials as a way to gain access to certain medical resources. This situation unfortunately can affect many Canadians. Recently, the family of a 12 year old girl, Madi Vanstone, negotiated for over a year with the province of Ontario to cover the drug Kalydeco. The drug was needed to treat "a rare form of cystic fibrosis, a genetic disease that creates a sticky, thick mucus which builds up in the lungs and affects other organs" (CBC News, "Madi Vanstone, 12, asks Ontario to fund pricey drug" March 2014, <http://www.cbc.ca/news/canada/toronto/madi-vanstone-12-asks-ontario-to-fund-pricey-drug-1.2557905>). Such a scenario demonstrates the possibility for financial concerns to affect even those who live in countries with universal health care.

The second significant difference between the medical research and therapeutic medical practice context which will demonstrate that for the terminally ill a greater level of competence is required in making decisions about the former, therefore relates to the possibly exploitable situation or mental state of the terminally ill person. The lack of access to necessary medical resources due to a poor financial situation or the possible desperate mental state of the terminally ill person can facilitate an environment where decisions are made without an adequate level of voluntariness and where the potential for exploitation arises. We may proceed by examining each issue in turn.

"The problem of exploitation centers on whether solicited persons are situationally disadvantaged and without viable alternatives, feel forced or compelled to accept attractive offers that they otherwise would not accept, and assume increased risk in their lives."[235] This appears to pertain quite aptly to the terminally ill subject who is unable to afford medical care.

Some subjects of research interviewed as part of the President's Advisory Committee on Human Radiation Experiments (ACHRE) alluded to being motivated to participate in research for financial reasons. One "respondent with breast cancer stated plainly that she, as someone without health insurance, had enrolled in research to get treatment and 'didn't have to worry about trying to pay something back later on'."[236] While few respondents in this study were as specific in citing monetary reasons for consenting to participate in the research, many insinuated it by alleging that they were motivated to participate in order to acquire care that would have otherwise been

[235] Beauchamp & Childress, 2009, p. 256.
[236] The President's Advisory Committee on Human Radiation Experiments, "Chapter 16: Subject Interview Study," Endnote 47, in Final Report of the Advisory Committee on Human Radiation Experiments (Washington, D.C.: U.S. Government Printing Office, 1995)

unaffordable. Another respondent, for example "commented that since doctors at the military hospital where he received his care were very busy, he could receive closer attention and obtain appointments more easily by enrolling in research."[237] This type of "inducement that may arise from a monetary incentive is commonly acknowledged as a threat to an individual's ability to freely volunteer and to act on behalf of his or her best interest."[238]

Unfortunately this motivation for entering into a clinical trial is not limited to only a few examples, but as an article in the New York Times reported, has become fairly pervasive in the United States. The article spoke of Ms. Danforth, a:

> chronically ill [woman] with limited or no health insurance, relying on clinical trials by private doctors as their primary source of medical care. For these people, experiments have become treatments; clinical investigators are their specialists. … Even people with insurance plans that impose significant restrictions -- like managed care programs that require pre-approval to visit a specialist -- are circumventing the gatekeepers by seeking out clinical trials, researchers said. "A lot of patients tell me that they feel frustrated with the care that they receive from the H.M.O.," said Dr. Norman Zinner, a Los Angeles doctor who heads Affiliated Research Centers, an organization of private-practice urologists who do drug studies.[239]

This issue is further exacerbated for the terminally ill who may have unusually high health care costs associated with their remaining days, and who may further feel

[237] The President's Advisory Committee on Human Radiation Experiments, "Chapter 16: Subject Interview Study" in Final Report of the Advisory Committee on Human Radiation Experiments (Washington, D.C.: U.S. Government Printing Office, 1995)

[238] C. Tishler and S. Bartholomae. "The Recruitment of Normal Healthy Volunteers: a review of the literature on the use of financial incentives" *The Journal of Clinical Pharmacology*, Vol. 42, pp.365-375, 2002, p.369.

[239] Kolata and Eichenwald, 1999. It is important to note that current changes in policy aimed at insuring more citizens in the United States may help alleviate only some of this problem since as pointed out by Kolata and Eichenwald, "the financial difficulties that lead patients to choose experiments for their health care are not limited to people with little or no insurance" (Kolata and Eichenwald, 1999). Numerous examples exist whereby a patient feels compelled to enter into a clinical trial because their health insurance failed to provide sufficient health care.

compelled to enter into a clinical trial in order to avoid being a financial burden on their family.[240]

It would be a mistake to assume that countries such as Canada, where health care is publicly funded, are immune to such a problem. Even where health care costs are covered, patients may still mistakenly view the clinical trial as the best or only way to obtain the most current and optimal health care. Thus, though the possible exploitation of the economic situation and need for medical care of the terminally ill subject is of concern, the potential desperate mental state of such individuals may further be a factor in undermining the voluntariness and thus competence with which a decision is made.

As the ACHRE demonstrated, "most patients reported that they had joined a research project to get better treatment… and because being in research gave them hope."[241] Desperation and feelings of hope often form the primary motivation of terminally ill individuals upon joining a clinical trial. Many such subjects of research have:

> remarked that they had joined because they believed that they had "no choice," meaning they had no medical alternatives. [One subject remarked] "my doctor

[240] The concern of an exploited economically disadvantaged subject of research is not confined to the terminally ill. Healthy volunteers for medical research "may be vulnerable to inappropriate influence or coercion by others because of social or economic status. For this reason, research with prisoners, students, and the poor … raises special concerns" (Nelson & Merz, 2002, p. V-71) with regards to voluntariness. While prisoners may be enticed to participate if there is a possibility of a reduction in their prison sentence, individuals who are in need of money, may also feel that medical research participation is the only option available. In fact studies have shown that the primary motivation for healthy volunteers to participate in research is monetary. See: Tishler & Bartholomae, 2002. Though these authors admit that "investigation regarding the impact of monetary incentives is limited" (Tishler & Bartholomae, 2002, p. 366), in seven studies examined by the authors, the results demonstrated that at least 50% of research subjects in each medical research trial investigated, cited financial reasons as the most important reason for volunteering. Some studies even found that over 90% of the research subjects had volunteered for monetary reasons. Also, the authors note that "financial reward was found to be the most important motive for younger healthy volunteers" (Tishler & Bartholomae, 2002, p. 368). While the matter of exploitation may indeed apply to any research subject, the continued discussion here will involve considering only the situation faced by terminally ill subjects of research.

[241] The President's Advisory Committee on Human Radiation Experiments, "Chapter 16: Subject Interview Study" in Final Report of the Advisory Committee on Human Radiation Experiments (Washington, D.C.: U.S. Government Printing Office, 1995).

> told me if I do not take the drug, in a couple of months I ... [will] ... die. So, I had no choice. Who wants to die? Nobody." Another respondent said, "I had one more option as he [the doctor] put it." Hope and desperation pervaded the remarks of many terminally ill patients. Patients said they wanted to "try anything" or that this was their "last resort." One man explained, "Well, what was driving me to say 'yes' was the hope that this drug would work. ... When you reach that stage ... and somebody offered that something that could probably save you, you sort of make a grab of it, and that's what I did."[242]

A painful terminal illness may render an individual as feeling particularly desperate. As some studies have shown, pain has an "indirect effect on trial participation, as it leads to a higher perceived severity of illness, which in turn affects the feeling of urgency, which subsequently increases the probability that a patient will participate"[243] in the clinical trial.

Some may object that such desperation and hopefulness does not undermine voluntary and thus competent decision making in any type of morally relevant manner. Such a critic may further point out that apart from the medical research context, we often make, what are deemed as competent decisions, based on our emotions including desperation. This may be particularly true of a terminally ill patient who consents to a risky therapeutic procedure. However, the main problem in the medical research context is that this type of desperate or hopeful mental state may render one especially vulnerable to manipulations of hope, and that such manipulations or deceptions would themselves undermine voluntary and thus competent decision making. Unfortunately some tactics used by investigators do exploit such a state of mind.

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[242] The President's Advisory Committee on Human Radiation Experiments, "Chapter 16: Subject Interview Study" in Final Report of the Advisory Committee on Human Radiation Experiments (Washington, D.C.: U.S. Government Printing Office, 1995).

[243] Frank Verheggen, Fred Nieman, Ruud Jonkers. "Determinants of Patient Participation in Clinical Studies Requiring Informed Consent: Why Patients Enter a Clinical Trial" *Patient Education and Counseling*, Vol. 35, pp.111-125, 1998, p. 122.

Sometimes the hopeful and desperate thinking of terminally ill participants allows them to construe research as merely a new and possibly revolutionary therapy.[244] Researchers can and have exploited this in their recruitment process. As Mark Hochhauser has pointed out, many research trials now have a 'brand name' which often serves to manipulate potential subjects of research. Examples include names such as 'MIRACL' or 'SAVED' which are actually acronyms.[245] However, it is clear from these types of brand names that "the clinical trial's 'brand' is not just a convenient but meaningless acronym, but often an acronym that may subliminally suggest a particular perspective on the trial."[246]

A simpler tactic often employed by researchers relates to the manner in which they discuss the research trial with potential subjects. One subject of research described the recruitment strategy "in these words: It was almost as if they were courting me… everything was presented in the best possible light."[247] It has also been noted that sometimes "professional pressure can lead researchers to underestimate inconvenience and hazard, misleading volunteers in the process."[248]

These types of tactics, coupled with the possibly desperate state of mind of a terminally ill potential subject creates a dangerously competence undermining cocktail. It must be recognized that researchers presenting the information in such a way so as to

[244] This is often known as the therapeutic misconception and will be further elaborated upon in the following section.
[245] MIRACL actually stands for: Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering.
[246] Mark Hochhauser. "Therapeutic Misconception and Recruiting Doublespeak in the Informed Consent Process" *IRB: Ethics and Human Research*, Vol. 24(1), pp. 11-12, 2002, p.11. For more on the brand naming of clinical trials see: Michael Berkwits. "CAPTURE! SHOCK! EXCITE! Clinical Trial Acronyms and the "Branding" of Clinical Research" *Annals of Internal Medicine*, Vol. 133(9), pp. 755-759, 2000.
[247] Paul Appelbaum, Loren Roth, Charles Lidz, Paul Benson, & William Winslade. "False Hopes and Best Data: consent to research and the therapeutic misconception" *The Hastings Center Report*, Vol. 17(2), pp. 20-24, Apr., 1987, p. 23.
[248] Len Doyal. "Journals Should Not Publish Research To Which Patients Have Not Given Fully Informed Consent: With Three Exceptions" *British Medical Journal*, Vol. 314(7087), pp. 1107-1111, April 1997.

downplay the negatives and emphasize the positives constitutes a manipulative tactic that desperate and hopeful terminally ill persons may be susceptible to, and may undermine the level of voluntariness regarding the decision to participate.

Thus, it seems apparent, given these concerns of possible exploitation, that voluntariness becomes a more difficult condition of competence for some to satisfy in the medical research as opposed to medical practice context.[249] This is especially true if researchers employ deceptive and manipulative tactics. The misconceptions about research that these tactics seem to promote are the subject of the third salient difference between the medical practice and medical research context.

Difference 3: The Therapeutic Misconception

As previously mentioned the phenomenon whereby subjects of medical research misconstrue the research trial as therapeutic practice is known as the therapeutic misconception. Recalling the distinction between the two and specifically how divergent the goals between medical research and medical practice are, it seems clear that such a misconception is seriously problematic.[250] For it may not only demonstrate a lack of the

[249] This is not to suggest that it is impossible for terminally ill individuals to partake in medical research with a sufficient level of voluntariness. For that would deny the possibility that altruism alone, as opposed to desperation or a lack of access to medical care, sometimes motivates one to partake in such endeavours. However, despite the possibility of altruism, the presence of an easily exploitable desperate state of mind and financial situation creates an environment where the voluntariness condition of competence may prove to be more difficult to satisfy in the medical research as opposed to medical practice context where this potential for exploitation is not thought to arise.

[250] Without recounting all the differences between medical research and practice we may recall that many of the approaches and methods used in research such as randomization, the use of placebos, the double blind methodology, the fact that most research prevents the use of other medicine by subjects…etc., may all conflict with a patient's medical interests. Refer back to earlier in this chapter for a full explanation of these methods used in research and how they may conflict with a prospective subject's best interests. Given this, it becomes apparent why the therapeutic misconception is so troublesome. Potential subjects ignore some or all of these features of the research and fill in "assumptions that decisions would be made in their best interests" (Appelbaum et al., 1987, p. 21). Thus, their consent to participate in such research is provided under false assumptions and therefore lacks the requisite understanding for competence.

requisite understanding needed by the subject in order for him to possess the substantial competence required for ethical informed consent, but this misconception may also significantly influence and unreasonably sway a person's decision to partake in the research in the first place.

Unfortunately this misconception is a widespread problem. Many research subjects incorrectly see:

> No conflict between the goals of research and treatment, especially when the researcher is also their treating physician. They expect the research to help them, not harm them. Some may even think that they're getting state-of-the-art treatment, a drug that's so new (and so effective) that other people don't yet have access to it.[251]

A study conducted on research participants carried out by the ACHRE provides empirical support for this claim. In an in depth subject interview study it was found that subjects':

> research experiences…were inextricably interwoven with their medical care experiences. One respondent described her research experience "as a means of treating what I have"…Most patients reported that they had joined a research project to get better treatment… [In fact] when asked to describe the research project they were in, most of the patient-subjects we talked with described the project as part of their therapy.[252]

Other research has demonstrated that cancer patients consenting to participate in clinical trials have expectations of therapeutic benefit that exceed those of their physicians.[253] In fact some studies have further shown that:

> "Cancer patients who participate in phase I trials are strongly motivated by the hope of therapeutic benefit.[254] Altruistic feelings appear to have a limited and

[251] Hochhauser, 2002, p. 11.
[252] The President's Advisory Committee on Human Radiation Experiments, "Chapter 16: Subject Interview Study" in Final Report of the Advisory Committee on Human Radiation Experiments (Washington, D.C.: U.S. Government Printing Office, 1995).
[253] Neal Meropol, Kevin Weinfurt, Caroline Burnett et al. "Perceptions of Patients and Physicians Regarding Phase I Cancer Clinical Trials: Implications for Physician-Patient Communication" *Journal of Clinical Oncology*, Vol. 21(13), 2003, pp. 2589-2596.
[254] More specifically one study revealed that "eighty-five percent of patients decided to participate in a phase I trial for reasons of possible therapeutic benefit" (C. Daugherty, M.J. Ratain, E. Grochowski, C. Stocking, E. Kodish, R. Mick, M. Siegler. "Perceptions of Cancer Patients and Their Physicians Involved

> inconsequential role in motivating patients to participate in these trials. Cancer patients who participate in phase I trials appear to have an adequate self-perceived knowledge of the risks of investigational agents. However, only a minority of patients appear to have an adequate understanding of the purpose of phase I trials as dose-escalation/dose-determination studies."[255]

The presence of the therapeutic misconception among research subjects becomes even more worrisome with the recognition that it affects not just persons who are easily susceptible to suggestions or that generally lack understanding in most contexts, but it also affects persons who may have exhibited high levels of competence throughout their medical history. For example, in a separate study a:

> Subject was a twenty-five-year-old woman with three years of college. At the time of the interview, she had minimal psychiatric symptoms and her understanding of the research was generally excellent. She recognized that the purpose of the project was to find out which treatment worked best for her group of patients. She spontaneously described the three groups, including the placebo group, and indicated that assignment would be at random. She understood that dosages would be adjusted according to blood levels and that a double blind would be used. When asked directly, however, how *her* medicine would be

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in Phase I Trials" *Journal of Clinical Oncology*, Vol. 13(5), pp. 1062-72, 1995, p.1062). Manish Agrawal and Ezekiel Emanuel have recently contended however, that such a motivation, or even the belief that one may get therapeutic benefit from phase I trials, despite typically low response rates and poor risk/benefit ratios in such studies, does not actually represent a misunderstanding. They claim that "the fact that patients participate primarily for the chance of benefit is often seen as indicative of a deficiency in comprehension. Yet [they argue], this interpretation fails to recognize that patients could very well comprehend their limited chance for personal benefit and still hope that they may actually benefit" (Manish Agrawal and Ezekiel Emanuel. "Phase 1 Oncology Research" In *The Oxford Textbook of Clinical Research Ethics*, Ezekiel J. Emanuel, Christine Grady, Robert A. Crouch, Reidar K. Lie, Franklin G. Miller, and David Wendler, eds. (Oxford: Oxford University Press, pp. 356-367, 2008) p. 365). Indeed, the authors go on to contend that current evidence shows that despite the majority of subjects enrolling for therapeutic benefit, many can sometimes recognize that the chances might be low but believe that "they might be in the lucky group" (Agrawal and Emanuel, p. 366). The authors then argue that phase I studies may be defended by arguing that current data may not necessarily show that phase I research participants have a misunderstanding, but instead may "have a form of adaptive denial" (Agrawal and Emanuel, p. 366). However, even if this assessment is correct, it does little to quell the overall concerns regarding competence or more specifically the issue of the therapeutic misconception. Indeed, we are still left with a good reason to question the competence of these subjects to provide consent, though now for a slightly differently labeled reason. This may instead suggest that subjects might understand, but still fail to adequately appreciate what the information actually means for them. Furthermore, as will be contended in the remainder of this section, even possessing some understanding regarding the research, the therapeutic misconception may still persist, as potential subjects may continue to view the research as their personal therapy. It should be noted that Agrawal and Emanuel also further contend that the risk/benefit ratio of phase I oncology trials is actually not as poor as typically assumed. However, more details regarding their argument and the actual response rates of phase I oncology trials will be provided in Chapter Four.

[255] Daugherty et al., 1995, p. 1062. Refer back to Chapter One for a full explanation of Phase I trials.

> selected, she said she had no idea. She then added, "I hope it isn't by chance," and suggested that each subject would probably receive the medication she needed.[256]

This case shows that despite even high levels of understanding about research, and a high level of cognitive ability, "the subject's conviction that the investigators would be acting in her best interests led to a distortion of an important element of the experimental procedure and therefore of the risk-benefit analysis."[257] This demonstrates that the therapeutic misconception can affect all persons, not just those who appear gullible or often demonstrate low levels of intelligence and understanding. In fact, the Advisory Committee on Human Radiation Experiments found that, despite the fact that when asked, "patients appeared to clearly understand which interventions were associated specifically with the research, they also conceived of the research as their medical treatment."[258]

There are various reasons for why the therapeutic misconception exists, and how it became so prevalent. A complete overview of these reasons would require an examination beyond the scope of our current discussion; however a brief overview might prove instructive.

Firstly, manipulative tactics employed by researchers may contribute to the therapeutic misconception. As previously mentioned, the brand names of clinical trials often inappropriately suggest that a trial will have therapeutic benefit. For example, some of the names used such as MIRACL, SAVED, RESCUE, and ALIVE,[259] all seem to be designed in order to influence the prospective subject's assessment of the non validated

[256] Appelbaum et al., 1987, p.22.
[257] Appelbaum et al., 1987, p.22.
[258] The President's Advisory Committee on Human Radiation Experiments, "Chapter 16: Subject Interview Study" in Final Report of the Advisory Committee on Human Radiation Experiments (Washington, D.C.: U.S. Government Printing Office, 1995).
[259] Hochhauser, 2002, pp. 11-12.

drug or procedure. The goal behind such a brand naming technique seems specifically to be to bolster and reinforce the therapeutic misconception.

The use of language by researchers and by authors can also contribute to the therapeutic misconception. "The term 'therapeutic research' should be avoided, because it can draw attention away from the fact that *research* is being conducted… Attaching the positive term 'therapeutic' to research suggests 'justified intervention' in the care of particular patients"[260] and only facilitates the environment where research can be confused with therapeutic practice. It must be recognized that not only researchers need to avoid this terminology, but similarly authors ought to do the same. Publishing literature that attempts to disguise research as therapy only serves to further exacerbate this problem.[261] Apart from misusing the term 'therapy' or 'therapeutic', it is equally important to not refer to research participants as patients.[262] Though some may be hesitant to refer to them as subjects, since that term may seem to belittle and make participants feel like 'guinea pigs', it is sometimes important to do so in order to draw a

[260] Beauchamp & Childress, 2009, p. 318.

[261] See, for example: Mortimer Lipsett. "On the Nature and Ethics of Phase I Clinical Trials of Cancer Chemotherapies" *Journal of the American Medical Association* Vol. 248, pp. 941-942, 1982. In this article, Lipsett claims in reference to Phase I research trials that "first, there is always therapeutic intent." This is not only misleading but represents a clear example of how terminology usage can play a role in contributing to the therapeutic misconception. As previously mentioned, "personalized attention characteristic of medical therapy is lacking in clinical trials that provide treatment according to a scientific protocol. This makes it misleading to characterize such treatment as therapeutic in intent" (Franklin Miller and Howard Brody. "What Makes Placebo-Controlled Trials Unethical?" *The American Journal of Bioethics*, Vol. 2(2), 2002, p. 6).

[262] Again, it is imperative that authors as well as researchers refrain from this misleading terminology usage. See for example: Miller and Brody, 2002, p. 4. In this article Miller and Brody suggest that researchers "seek to answer clinically relevant scientific questions by conducting experiments that test the safety and efficacy of treatments in *groups* of patients" (Miller and Brody, 2002, p.4). This mischaracterization further obfuscates the distinction between medical research and therapeutic practice and allows the therapeutic misconception to flourish.

clear distinction between those undergoing medical practice and those taking part in research.[263]

Another reason that shall be highlighted for why the therapeutic misconception exists, is the confusion between physicians and researchers. For:

> Much of contemporary medicine takes place in health care institutions, which makes it difficult to distinguish clearly the roles and responsibilities of physicians from those of investigators. …Research and treatment are often carried out simultaneously, as, for example, when research is designed to evaluate a particular therapeutic intervention and involves persons who suffer from an illness the intervention is designed to treat. [As mentioned previously] the task of distinguishing research from treatment is further complicated by the frequent usage of the term 'therapeutic research' which obfuscates the fact that research, unlike therapy, has as an aim the production of generalizable knowledge. Blurring of the distinction between research and therapy is also due in part to some notable departures from standard practice that have often been referred to as 'experimental' interventions, particularly by the courts,"[264]

as for example when a physician attempts an uncertain experimental procedure because he believes that it is the only recourse left in order to aid the patient. For individuals to be able to distinguish between medical practice and research, it is crucial that they be able to distinguish between physicians and researchers. Of course this can be highly problematic especially when the researcher is also a subject's treating physician. Referring to the dual nature of the physician/investigator, Trudo Lemmens and Paul Miller ask: "can one really expect the research subjects to be aware of such subtle and continuous transformations? Jekyll and Hyde wear the same white coat, speak the same language, and handle the same instruments. They seem the mirror image of one another to the unsuspecting patient."[265] Jay Katz "encourages physician investigators to see themselves as scientists only and not

[263] For more on unacceptable terminology usages regarding medical research see: Robert J. Levine. *Ethics and Regulation of Clinical Research 2nd edition* (Baltimore: Urban & Schwarzenberg, Inc., 1986) pp. 3-10; and Robert J. Levine. "Clarifying the Concepts of Research Ethics" *Hastings Center Report,* Vol. 9(3), pp. 21-26, 1979.
[264] Downie et al., 2002, pp. 459-460.
[265] Trudo Lemmens & Paul Miller. "Avoiding a Jekyll-and-Hyde Approach to the Ethics of Clinical Research and Practice" *The American Journal of Bioethics*, Vol.2(2), pp.14-17, 2002, pp.15-16.

as doctors. Only by adopting this univocal self-image, he suggests, will investigators be able to avoid unwittingly becoming 'double agents'."[266]

Though this is by no means an exhaustive list of why the therapeutic misconception exists, it begins to demonstrate why it is so prevalent in our society. As Rebecca Dresser asserts, "in this environment, it would be shocking if patients were *not* affected by the therapeutic misconception."[267] The above discussion also begins to illustrate how undermined a potential subject's understanding and appreciation of research might be. It should thus seem clear that satisfying these criteria of competence is more difficult in the medical research as opposed to the medical practice context for the terminally ill. More specifically, understanding and appreciation should at least be great enough in order to be able to overcome the high potential for the therapeutic misconception.[268]

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[266] Emanuel et al., 2003, p.193. See: Jay Katz. "Human Experimentation and Human Rights" *St. Louis University Law Journal*, Vol. 38, pp. 7-54, 1993. The Tri-Council Policy Statement corroborates this sentiment asserting that in order "to preserve and not abuse the trust on which many professional relations reside, researchers should separate their role as researcher from their roles as therapists, caregivers, teachers, advisors, consultants, supervisors, students, employers and the like. ... Researchers should disassociate their role as researcher from other roles, in the recruitment process and throughout the project" (Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.* 1998 (with 2000, 2002 and 2005 amendments) p. 2.8).

[267] Rebecca Dresser. "The Ubiquity and Utility of the Therapeutic Misconception" *Social Philosophy & Policy*, Vol.19(2), pp.271-294, 2002, p. 285. In her article Dresser provides various examples as to how "researchers, physicians, government officials, corporate sponsors, patient advocates, and the popular media collaborate in perpetuating the therapeutic misconception" (Dresser, 2002, p. 284).

[268] Some may point out that a version of the therapeutic misconception occurs at times in standard medical practice, whereby a patient may view treatment as having a greater therapeutic benefit than is actually warranted. Thus, it may seem that such a misconception affects both the medical research and medical practice context similarly and therefore ceases to be, as I have classified it, a fundamental difference between the two contexts. However, though some version of this misconception may occur in medical practice, the therapeutic misconception in research is radically different and more impactful on one's competence and thus more ethically perilous. As previously mentioned, the therapeutic misconception in research, unlike in medical practice, is often promoted by literature, tactics employed in research, and the already blurry distinction between research and therapy and researchers and physicians, making it unnecessarily potent and thus persuasive. The immensity of this misconception in the research context has "led commentators and expert panels, including the National Bioethics Advisory Commission, to suggest that TM [therapeutic misconception] may constitute a major obstacle to meaningful decisionmaking" (Paul Appelbaum, Charles Lidz, and Thomas Grisso. "Therapeutic Misconception in Clinical Research:

It is thus quite clear, based on all three salient differences between the medical research and the medical practice context, namely the difference in relationship between the physician/patient and the researcher/subject, the exploitable situation and mental state of the terminally ill, and the presence of the therapeutic misconception, that the conditions of competence each become more difficult to satisfy in the medical research context. As has been demonstrated, each difference relates to a greater need for one or more of the elements of competence, specifically understanding, appreciation, reasoning and voluntariness, in order for a terminally ill person to be sufficiently competent to provide informed consent to participate in medical research. Thus, since a greater level of each of these elements of competence is required, it thus follows that a greater level of competence as a whole is necessary for a terminally ill person to be able to consent to medical research participation. Specifically a potential subject must be that much more competent in order to be able to steer clear of all the influences and potential for misconceptions that would render her competence less than substantial and thus unsuitable for providing consent.

Given that a greater level of competence is needed for the terminally ill to provide consent to participate in medical research trials, the question now becomes, how great a level of competence is required, and how should we test for this competence. These

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Frequency and Risk Factors" *IRB: Ethics and Human Research*, Vol. 26 (2), pp.1-8, 2004, p.2). The therapeutic misconception in medical practice, on the other hand, does not appear as powerful, as little to no evidence exists demonstrating that it poses the same threat to one's competence or that it is influential enough to persuade a patient to make a choice that he would not have otherwise made. Therefore, despite the existence of a therapeutic misconception in standard medical practice, the misconception in research is of a fundamentally different kind, and thus the assertion that it represents a serious difference between the medical research and medical practice context, remains intact. The misconception present in medical practice might be better labeled as therapeutic optimism, so as to distinguish it from the type of severely competence hindering therapeutic misconception present in the medical research context. (I am grateful to Professor Joel Lexchin for bringing to my attention the presence of the therapeutic misconception in standard medical practice).

questions will be addressed in Chapters Four and Five respectively. However, prior to engaging with these issues, three objections to the above argument need to be addressed. These three objections include the concern that this greater competence requirement amounts to an unjustifiable hard paternalism, that the proposal for a greater level of competence in research accomplishes nothing more than the already rejected risk based sliding scale approach that was criticized in Chapter Two, and that, as Benjamin Freedman has written, an ignorant consent to participate in medical research might be ethically justifiable. We shall proceed by addressing each challenge in turn.

The Paternalism Objection

If the above assessment is correct, and the medical research context indeed requires a greater level of competence for consent than the medical practice context for terminally ill individuals, then it appears that the implication of this is that some of the research subjects who are currently being permitted to enter into a research trial should not be so permitted, as their consent may not be competent.[269]

Do governments or individual medical researchers ever have the right to override a potential subject's decision to enroll in a medical research trial? This was one of the

[269] Though the immediate issue appears to be that this would lead to there being too few subjects for research and that this would therefore slow medical research to a standstill, various suggestions and proposals exist which if implemented would better enable competence amongst research subjects. Thus the concern that medical research trials would grind to a halt is one that can be largely mitigated with the implementation of certain competence enhancing approaches to acquiring consent. One suggestion for example may involve the use of a third party, unaffiliated with the research, to solicit the consent from any terminally ill prospective research subject. This third party individual would be trained to be able to adequately explain the therapeutic misconception, clearly demonstrate the differences between research and therapy and what those differences mean for the potential research subject, and also assess whether the potential subject possesses the adequate levels of understanding, appreciation, reasoning, and voluntariness to be able to provide informed consent. While this is only one brief suggestion, it demonstrates the possibility of being able to find ways to improve the competency environment currently surrounding terminally ill research subjects and thus maintain substantial enrollment numbers for medical research. These types of proposals will be looked at in more depth in the following chapters.

issues that arose in a 2007 U.S. court case[270] where it was determined that there is no constitutional right to access experimental drugs or participate in experimental medical research. The issue of paternalism re-emerges here. For if indeed governments and perhaps even medical researchers are permitted to usurp the decision making authority from an individual in the research context, then either a form of hard paternalism that disrespects individual autonomy is being advocated, or this usurping of decision making authority is actually a form of soft paternalism.[271]

In the 2007 court case Abigail Alliance v. Eschenbach, it was decided that there does not exist any constitutional right for even competent persons to accept any level of risk to access experimental drugs or procedures. In a popular dissent, Judge Judith Rogers claimed that:

> In the end, it is startling that the oft-limited rights to marry, to fornicate, to have children, to control the education and upbringing of children, to perform varied sexual acts in private, and to control one's own body even if it results in one's own death or the death of a fetus have all been deemed fundamental rights ... but the right to try to save one's life is left out in the cold despite its textual anchor in the right to life. This alone is reason the court should pause…[272]

Though a very powerful dissenting opinion, it must be recognized that nothing that has been argued here falls prey to this type of argument. This dissenting opinion which has garnered much support, attacks the hard paternalistic decision made by the courts which prevents even competent persons from entering into certain medical research.

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[270] Abigail Alliance v. Eschenbach (2007) U.S. Court of Appeals for the District of Columbia Circuit. N0.04-5350.

[271] It should be noted that the 2007 court case did not distinguish between the two forms of paternalism, and since the court's ruling was not made specific to those who lacked substantial competence, dissenters were able to characterize the decision as a hard and "dangerous brand of paternalism" (Abigail Alliance v. Eschenbach, p. 28 of the dissenting opinion). However, what has been argued here does not follow the same pitfall. For as shall be demonstrated the arguments here are at most only committed to a soft paternalism.

[272] Abigail Alliance v. Eschenbach, pp. 2-3 of the dissenting opinion.

Alternatively, the arguments presented here in no way suggest that competent persons should be prevented from enrolling in medical research, but rather only that the amount of competence required to make such a decision and to be able to provide informed consent may be greater than previously thought, and specifically greater than the amount of competence required to make decisions in the medical practice context for terminally ill persons. As a result of this, it does become the case that some individuals who may have previously been thought of as substantially competent, might now, in light of the higher standard, be seen as falling below the minimum required level of competence needed to consent. However, preventing these individuals from enrolling in medical research trials only amounts to a soft and justifiable paternalism since these individuals fall short of satisfying the required level competence necessary for participating in medical research. It is important to stress that therefore any paternalism that may result from the argument here only amounts to a justifiable soft paternalism. For if indeed one lacks sufficient competence in a particular context, then allowing that individual to make decisions on such a matter cannot be viewed as any respect for autonomy and rights, but instead as a lack of regard for the well-being of that person. Thus, despite the fact that as a result of what has been argued here, some persons will no longer be admitted into medical research, since there will be persons that fall below the new higher threshold of competence required in the medical research context, only soft paternalism is being employed. Therefore, objections against hard paternalism do not affect the present argument.

Is this Different than the Risk Based Sliding Scale?

The risk based sliding scale approach to competence, discussed in Chapter Two, suggested that the required competence for a decision should shift depending on the risk present in the decision. The riskier a decision is, the greater the amount of competence ought to be for making such a decision. It would therefore seem that both my proposal here and the sliding scale strategy that was rejected in Chapter Two, might be seen as accomplishing the same goal, namely raising the level of competence required in certain medical research decision making contexts for terminally ill persons. Thus one may wonder if there is any difference between the two approaches, and why the sliding scale should be rejected while this proposal accepted. To this there appear two clear retorts. First, as we may recall the sliding scale strategy may not be as successful as one may intuitively think at necessitating a higher level of competence in the medical research context. It gives the illusion of requiring a raised level of competence for medical research participation decisions since many assume those decisions to be especially risky, but as demonstrated in Chapter Two, this assumption is false. As argued previously, given a proper demarcation of therapeutic risks from research risks and combining that with the principle of clinical equipoise,[273] it is clear that the sliding scale strategy provides little ground for raising the level of competence needed in the medical research context.

Second, it was also demonstrated that there were numerous issues and possible ethical pitfalls with the sliding scale approach that are not present with the proposal here. While the sliding scale approach allowed for a raising of the required standard of

[273] This principle requires that there exist genuine uncertainty among the clinical community regarding the relative merits of the arms being tested in the trial. For a full explanation of clinical equipoise or the proper demarcation between therapeutic and research risks, refer back to Chapter Two.

competence by medical professionals to a possibly unachievable level, and thus enabled an unjustifiable hard paternalism,[274] the proposal outlined here in Chapter Three does nothing of the sort. In fact what is being suggested here merely asserts that given the definition of competence as being context relative, and given the differences between the medical practice and medical research context, it is clear that the latter context requires a higher level of competence for decision making than the former, for terminally ill persons. It is a logically derived conclusion, a mere tautology true simply by virtue of the definition of competence and the nature of medical research compared to the nature of the medical practice. This makes what is being argued here less likely to be subjected to the abuses that were discussed as being related to the sliding scale. Furthermore, as previously argued, using risk to determine competency is arbitrary, and proper competency determinations must be based on a consideration of the elements that comprise competence. Only in this manner can we expect evaluations of competence to be consistent and accurately reflect the decision making capacity of individuals. The proposal here thus provides protection for terminally ill subjects of research by ensuring that they possess the necessary competence for an ethical and autonomy preserving consent, while managing to avoid the conceptual and ethical pitfalls associated with the sliding scale strategy.

What about an Ignorant Consent?

The final potential objection that shall be considered involves considering a proposal initially put forth by Benjamin Freedman which suggests, contrary to what has

[274] Recall for example that one of the concerns with the risk based sliding scale was that some persons may be denied the right to act as they wish based simply on the physician's subjective interpretation of how much risk one should be permitted to accept.

been argued here, the legitimacy of an ignorant consent to participate in medical research.[275]

Ignorant consent involves a person who waives the informational component associated with consent. Thus, "an ignorant consent is offered when an individual consents in violation of the common informational components required by reasonable people."[276] Freedman offers the following thought experiment:

> Consider an individual, Brown, undergoing invasive electrophysiological studies for clinical reasons. He is a candidate for concurrent noninvasive research; e.g., his body-surface will be 'mapped' electrocardiographically… Upon being invited to participate in a study described to him as posing some discomfort but no intrinsic risk… the subject consents. The investigator indicates that further information is generally provided before the subject makes up his mind: the nature of the experiment, its potential benefits, and so on; but the subject declines to be further informed… [As Freedman elucidates] Brown has clearly consented under conditions of ignorance. Far from being cognizant of such esoterica as the presence of a control group, or the names of the members of the institutional

[275] Benjamin Freedman. "A Moral Theory of Informed Consent" *Hastings Center Report*, Vol.5(4), pp.32-39, 1975; and Benjamin Freedman. "The Validity of Ignorant Consent to Medical Research" *The Hastings Center: Ethics and Human Research*, Vol. 4(2), pp. 1-5, Feb., 1982. Variations of Freedman's argument have also been made by others more recently. See, for example: Gopal Sreenivasan. "Does Informed Consent to Research Require Comprehension?" *The Lancet*, Vol. 362, pp. 2016-2018, 2003. While Freedman's proposal will require some further consideration, Sreenivasan's argument can be briefly addressed immediately. Sreenivasan argues that physicians and investigators are asked to shoulder too much of the burden in achieving comprehension in the subject. He further argues that "in a shared relationship, successful communication is normally a shared responsibility. Why should the physician-patient relationship be an exception?" (Sreenivasan, 2003, p.2016). More specifically he suggests that it is mistaken to burden "researchers with a commitment not to enrol anyone with a therapeutic misconception" (Sreenivasan 2003, p.2016) in a research trial. This notion that investigators should not be overly concerned with disabusing potential subjects of the therapeutic misconception fails to acknowledge that researchers are to a large extent responsible for the existence and continued prevalence of such a misconception. As previously argued, researchers accidentally or in some instances purposefully, engage in tactics that bolster the misconception, whether by inadvertently acting as both physician and investigator, by using misleading terminology, by overemphasizing the therapeutic benefit of certain clinical trials, or by brand naming trials in order to manipulate subjects' expectations. Thus, given the large role that researchers have played in generating the therapeutic misconception, it is ethically appalling to suggest that they need not be overly concerned with it. Sreenivasan also mistakenly argues that subjects are still protected by the fact that they "always retain the right not to enrol in a trial or to withdraw from it, even if it has been passed by an institutional review board. Even without comprehension, [he adds] individuals are always free to choose not to participate in research" (Sreenivasan, 2003, p.2017). However, Sreenivasan fails to realize that this protection of being able to refuse to enrol in a trial is at stake when one lacks adequate comprehension and is afflicted with the therapeutic misconception. If one is plagued by such misconceptions, it may influence him to participate in a trial that he otherwise would not have. Thus it is precisely this protection that is threatened by the therapeutic misconception.

[276] Freedman, 1982, p. 2.

> review board (IRB) that had approved the protocol, he does not even know the nature and purpose of the research. The only element of which he is aware is that of risk, and even here he is not fully informed[277].[278]

Is this ignorant consent a legitimate ethical consent? In attempting to demonstrate that it could be, Freedman offers three types of argument. We shall engage with each in turn and through an analysis notice that each argument has significant shortcomings that prevent one from concluding that an ignorant consent could be appropriate in the medical research context.

The first argument involves the recognition that we already allow for somewhat of an ignorant consent in the medical practice setting, and that there are no salient differences between the medical practice and research setting that would suggest that the same cannot apply in the latter. As Freedman elucidates, in the therapeutic setting it is "not unusual for a patient to give his doctor *carte blanche* to perform any medical procedure which the physician deems proper in order to effect a cure. He, [the patient], is telling the doctor to act as his agent in choosing which procedure to follow."[279] Given

[277] It should be noted that the term fully informed implies possessing a complete set of information, and is often thought of as more of an ideal, but not something that could ever truly be accomplished. Thus Freedman perhaps misused the term. Freedman, in attempting to express that even in regards to the one element of the research that Brown was somewhat aware of, namely risk, he still knew very little, most likely meant to suggest that Brown was not well informed, as opposed to fully informed which instead represents a standard that can never be satisfied. Though this may appear as mere semantics, the issue is crucial, for if all that is meant by an ignorant consent is one that falls short of full information, then there should be very little opposition to Freedman's proposal. However, Freedman does in fact have something far more radical in mind, specifically the idea that an ignorant consent involves one whereby the level of information obtained by the consenter falls far below the generally assumed level required by a reasonable person prior to providing consent.

[278] Freedman, 1982, p. 1-2.

[279] Freedman, 1975, p. 34. The notion of an uninformed consent to medical treatment is not new and many have maintained its ethical permissibility. Jessica Berg, Paul Appelbaum, Charles Lids and Lisa Parker for example have argued that "informed consent is a right of patients (and subjects) and that as part of that right, patients may seek advice from and even share decision making with those whom they trust" (Jessica Berg, Paul Appelbaum, Charles Lids and Lisa Parker. *Informed Consent: Legal Theory and Clinical Practice 2nd edition* (New York: Oxford University Press, 2001) p. 31). Others have suggested that we ought to ensure that patients make their own decisions in matters of health care. See for example: E. Haavi Morreim. *Balancing Act: The New Medical Ethics of Medicine's New Economics.* (Washington, D.C.: Georgetown University Press, 1995) pp. 134-139. However, regardless of what one concludes on the matter

this, Freedman considers potential differences between the two contexts that would justify allowing an ignorant consent for one, but not the other. However, he only adequately discusses one difference, namely that "in the therapeutic context it is supposed that the physician knows what the sequelae to treatment will be, which information, by definition, is not available in the experimental situation."[280] Freedman then demonstrates that this distinction is not relevant since an ignorant consent might be ethical in the *therapeutic-experimental* "situation, where a new drug or procedure is being attempted to aid the patient"[281] and where, similar to the research setting, the sequelae are not known.

Freedman is certainly correct in asserting that this, knowing the sequelae difference, cannot justify allowing an ignorant consent in medical practice, but not in research, since as he explains, an ignorant consent might still be valid in the therapeutic-experimental context where the sequelae are similarly not known. However, it is unfortunate that this is the only difference between medical practice and research that Freedman discusses. He ignores the three very relevant differences discussed earlier. These differences included the relationship difference between the physician/patient and the researcher/subject, the potentially exploitable situation or mental state of the prospective subject, and the presence of the therapeutic misconception. Each difference lends support to the idea that the research context differs significantly from the medical practice context with respect to consent and, more specifically as I have argued, with respect to the required level of competence needed.

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of the ethical permissibility of an uninformed or ignorant consent in medical practice, in what follows it shall be contended that the medical research context differs fundamentally such that an uninformed or ignorant consent cannot be appropriate, even if it is deemed so in the medical practice context.

[280] Freedman, 1975, p. 34.

[281] Freedman, 1975, p. 34.

The first difference is especially relevant in responding to this line of argument from Freedman. For it seems that persons are able to give their physicians the authority to make their decisions precisely because of the trusting relationship that they have built with the physician; a relationship whose foundation is based on the fact that both patient and physician have the same goal, specifically the wellness of the patient. However, as previously discussed, this type of relationship does not exist between the researcher and subject, whose aims differ and often can conflict. Thus, in this context it would seem wildly inappropriate to allow for a person to give authority to the researcher to make her decisions. It is also for this reason that therapeutic privilege[282] is deemed appropriate for medical practice but "invoking the doctrine of therapeutic privilege to assure a subject's cooperation in a research project is almost never appropriate"[283]

Freedman's second line of argument suggests that we in fact already allow for ignorant consent in the research context. He mentions the cases of placebo administration, and blind or double-blind experiments; both of which he claims are based on an ignorant consent from subjects. He also provides the example of psychological research whereby subjects agree to be deceived in the research.[284]

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[282] Therapeutic privilege is an exception to informed consent that "permits the doctor to withhold information when, in his or her judgment, disclosure would be detrimental to the patient's interests or well-being" Robert Levine. "Consent Issues in Human Research" In *Ethical and Regulatory Aspects of Clinical Research*, Emanuel, Crouch, Arras, Moreno, & Grady, eds. (Baltimore: The Johns Hopkins University Press, 2003) p. 201.

[283] Levine, p. 201. It should noted that even Berg et al. who as previously mentioned support the ethicality of an uninformed consent to therapeutic decisions notice a relevant difference between the two contexts. They assert that "with respect to enrolling in a research study that does not have his individual benefit as its primary goal, a patient may be quite reluctant to entrust decisional authority to someone else, especially to the physician-researcher; however, in an individualized therapeutic context, the same patient may be most comfortable relying on his doctor to employ medical expertise and benevolent intentions to decide on his behalf" (Berg et al., 2001, pp. 27-28).

[284] In these types of psychological research cases, Freedman points out that the potential subjects "could be told that any experiment of which they would be the subject will pose no (physical) risk, and will have been approved by an IRB, which is concerned to safeguard their rights; but they would not be told when, or whether, or how they will be studied" (Freedman, 1982, p. 2).

Though Freedman has provided examples that demonstrate cases whereby a subject's consent is somewhat ignorant, they fall short of being what may appropriately be called "ignorant consent". That is to suggest that merely because a potential subject is ignorant with respect to some element of the research; it is not necessarily the case that the consent itself must be deemed ignorant in any morally relevant sense. For if that were the case, then all consent to research would be deemed ignorant since no subject will ever have full information, and will always be ignorant in some respect or another. The concept of informed consent would thus become meaningless. The question that must be asked is not, whether there was something that the subject did not know, but whether what the subject did not know was relevant enough to deem the consent as one that falls short of an informed consent (i.e., an ignorant consent). Again it must be stressed that any ignorance is not sufficient to deem a consent as not informed, for then all consent would be uninformed or ignorant since none can live up to the ideal of fully informed consent.

Thus a brief review of some of the elements of an informed consent would prove instructive.

> As Levine notes, current U.S. federal regulations require that researchers disclose specific information bearing on (1) the purpose of a study, (2) its foreseeable risks and benefits, (3) the various alternatives to participation in research, (4) protections of confidentiality, (5) the availability (if any) of compensation for research-related injury, and (6) conditions of participation, including reassurances that participants can leave a study at any time without penalty or forfeiture of their medical entitlements.[285]

[285] Emanuel et al., p. 190. Refer back to the section on informed consent in Chapter One for further detail regarding the elements of informed consent. Also see: R.J. Levine. "The nature and definition of informed consent in various research settings" In *The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Appendix to the Belmont Report,* Vol. I. U.S. Government Printing Office, DHEW publications no. (OS) 78-0013; and R.M. Veatch. "Three theories of informed consent: philosophical foundations and policy implications" In *The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Appendix to the Belmont Report,* Vol. II, DHEW publication no. (OS) 78-0014.

Given that these are the generally accepted elements of an informed consent, and given that Freedman defines an ignorant consent as one where some or all informational components of informed consent are waived, then for Freedman's examples to truly constitute ignorant consent they would have to have at least one of the six components listed above missing. However, the placebo example, double-blind example, and the psychological research example do not inherently cause a lacking in any of the six informational components.[286]

In all three cases, a potential subject may still be sufficiently informed of the study's purpose, its risks and benefits, alternatives to research,…etc. Thus, it is difficult to see why Freedman would classify these cases as examples of ignorant consent. Freedman's best example is perhaps the use of a placebo, which seems to add uncertainty regarding the risks that may befall a subject, but this is not to say that the subject is ignorant of the potential risks. Certainly the fact that one may not know whether or not she has received a placebo will have some bearing on what risks she may be exposed to, but the subject, though ignorant of whether she has received the placebo, can still be informed about what the risks are either way, whether she receives the placebo or the

[286] As discussed further in Chapter One, some may argue that a few additional elements of informed consent ought to be included as well. For instance, some have argued that informed consent should also require knowledge regarding such matters as "the reason for selecting this individual as a subject, the procedures to be followed and the discomforts that the subject will suffer as a result of them… Robert Veatch would include the need for 'a specific disclosure of the presence of a control group within the research design' and an explanation of who is to be held responsible should the subject be harmed in the course of the research" (Freedman, 1982, p. 1-2). As Levine has suggested, other elements that might be required in informed consent include: an offer to answer any inquiries concerning the procedures, a suggestion to the prospective subject that he might wish to discuss the proposed research with another before consenting and where appropriate it may be necessary to inform the prospective subject that some information is deliberately being withheld. However, even including all of these additional elements of informed consent it must still be noted that the placebo example, double-blind example, and the psychological research example do not inherently cause a lacking in any of these informational components.

active agent. Thus, even in the placebo case, it seems that all elements of informed consent, even the knowledge of risk element, are known.[287]

It must therefore be concluded that Freedman has not demonstrated anything useful with his examples. Though his attempt was to demonstrate that we already allow for an ignorant consent in research, all he has demonstrated are cases whereby a subject is ignorant in some respect, but has the relevant information necessary for his consent to be deemed an informed and not an ignorant consent.

Freedman's third and final attempt at demonstrating the validity of an ignorant consent to research fails as well. His final argument is in the form of a response to the idea that informed consent is a right that cannot be waived.[288] He provides examples of other rights that cannot be waived and demonstrates that these other rights are significantly dissimilar from the right to informed consent such that the justification behind not allowing them to be waived cannot apply for the right to informed consent.

Freedman's main example is that of public education. "There is a right to be educated, one possessed by the resident and enforceable against the government. But education… is not an option. Put another way, there is a right to education but no right to

[287] The fact that certain methods used in research such as double-blinding do not necessarily render consent uninformed or ignorant has even been acknowledged in some ethical guidelines. In regards to randomization and blinding in clinical trials, the *Tri-Council Policy Statement* for instance, states that "such research is not regarded as a waiver or alteration of the requirements for consent if subjects are informed of the probability of being randomly assigned to one arm of the study or another" (Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.* 1998 (with 2000, 2002 and 2005 amendments) p. 2.1). The idea being that methods such as double-blinding do not necessarily require a subject to be lacking in any of the informational components of informed consent, and thus a subject of research may indeed be able to provide informed consent when entering into a clinical trial that makes use of these types of approaches.

[288] It should be understood that I do not intend to argue whether the right to informed consent is indeed a right that cannot be waived. Such an argument would require a philosophical and legal analysis that cannot be presently undertaken. Instead, I merely wish to demonstrate that Freedman's argument as to why the right to informed consent can be waived, fails.

truancy."[289] Thus it seems that the right to be educated is one that cannot be waived, at least by minors. However, Freedman then argues that this is not comparable to the right to informed consent. For it is the case that the children involved in the right to be educated, lack competence, whereas we assume that the potential research subjects are competent. As Freedman elucidates, "if we did not believe the subject to be competent, informed consent would not be required"[290].

However, this is not a correct view of informed consent. The information component of informed consent is not provided to persons because they are already competent to consent to research, but because they have the potential to be competent.[291] To be competent for a context requires that a person satisfy the conditions of competence as discussed above.

Ignorance, by definition, implies a lack of knowledge and understanding. If a person is ignorant of a certain topic, it can be said that he lacks a sufficient level of knowledge and understanding about that topic. This is where Freedman's dilemma begins; for it seems highly problematic to claim that a person is substantially competent for a particular situation if that person lacks the requisite understanding needed for competence. Furthermore, since the reasoning condition of competence involves the ability to weigh risks and benefits, then the ignorant person may lack the necessary reasoning condition as well, as he may be ignorant of the risks and benefits. Also, depending on how ignorant the person is, it may also be argued that ignorance impedes

[289] Freedman, 1982, p. 3.
[290] Freedman, 1982, p. 3.
[291] We must recall that competency is not all or none, and is context relative. Thus one may be competent in most respects in life, but may be incompetent in others. Thus a potential subject of research may be generally competent in various aspects of life, but without the relevant information regarding the research trial cannot be said to be competent to decide whether or not to participate in the research.

the appreciation component of competence since the person lacking information regarding the clinical trial will be unable to see what participation may mean for him. Thus ignorance renders one incompetent for that context, and a willful ignorance is no different.

In what sense then, can Freedman claim that the person who gives an ignorant consent is competent? Perhaps by competence Freedman means that the person has displayed competence with respect to most other aspects in life, or that the subject has the cognitive capacity to be competent, that is that the subject has the potential for competence.[292] However, neither of these is sufficient. Demonstrating competence in other facets of life does not imply that one will necessarily be competent in the medical research context, and having the potential for competence is certainly not in itself sufficient for a legitimate informed consent. Thus it seems that Freedman's account of an ignorant, yet competent consent, cannot be maintained.[293]

Given that each of Freedman's three arguments in favour of an ignorant yet valid consent in medical research fails, it must be concluded that an ignorant consent to

[292] We shall return to this issue in Chapter Four, as a further depiction of Freedman's account will be provided. Ultimately, Freedman concludes that an ignorant consent is ethically permissible as long as the decision maker's choice can be deemed responsible. In addition to the issues already raised with Freedman's arguments, Chapter Four will further demonstrate that such a proposal is problematic.

[293] One may attempt a response by suggesting that this analysis commits me to the view that an ignorant consent in ordinary medical practice also lacks competence and is therefore similarly invalid. According to this view, consent from a patient who trusts her physician enough such that when it comes to minor procedures, such as undergoing a routine surgery, she consents to the physician's recommendations without requiring much information, would be inappropriate. However, while some may be inclined to argue in this manner, for example Veatch reminds that "it can be seriously questioned at the ethical level whether one is justified in waiving information necessary to make a consent informed" (Freedman, 1982, p. 4), I am not necessarily committed to this view. We must recall the first distinction between the medical practice and medical research contexts, namely the difference in relationship between the physician/patient and the researcher/subject. Since the former relationship is based on a trust that exists because both parties have the same goal, namely the welfare of the patient, then allowing one's physician to be somewhat of a proxy decision maker, may be appropriate at times. However, since this relationship does not exist between the researcher and a subject, the same justification cannot be employed in order to allow for a researcher to decide on behalf of subjects. Thus, while I have argued that ignorance will render one incompetent to consent to research and thus an ignorant consent to research should be viewed as inappropriate, particularly for terminally ill persons, I am not committed to the same position in the medical practice context.

medical research cannot be permitted. Thus, this proposal poses no significant objection to what has been proposed here, namely that for the terminally ill, consent to medical research will require a level of competence greater than that required in the medical practice context. If consent is not provided competently then the notion of informed consent is a mere illusion; a device used only as a protection for researchers from legal ramifications, instead of a protection for those whom it was initially intended to protect, namely research subjects.

Before proceeding, it would be prudent to briefly recap. In Chapter One, the connection between autonomy, consent and competence was highlighted, and ultimately it was shown that an autonomous and ethical consent must be a competent one. Chapter Two then examined the commonly applied risk-based sliding scale approach to competence, whereby the requisite competence is determined by the riskiness of the decision. This approach to competence was shown to not only be conceptually and morally flawed, but also inappropriate for the medical research context. Instead, it was argued that only when the difficultly in achieving one or more of the elements of competence increases, should a greater level of competence be required. Chapter Three then demonstrated that in the clinical research as opposed to the medical practice context for the terminally ill, all four elements of competence, namely understanding, appreciation, reasoning, and voluntariness, are more difficult to satisfy and that thus a greater level of competence is required for ethical consent to participate in medical research. It still remains to be seen however, what specific level of competence should be required in this research context for the terminally ill individual. It is to this query that we now turn.

Chapter 4: Elements of Competence: How Great of an Ability to Understand, Appreciate, Reason, and Decide Voluntarily is Necessary for Competence in the Medical Research Context with Terminally Ill Subjects

Moving from Informed Consent Forms to Competency

In an effort to protect potential subjects of research, much effort has been expended on analyzing and restructuring informed consent forms. Due to the complexity and length of these consent forms, much research has been dedicated specifically toward analyzing the readability of forms by potential subjects.[294] If subjects are unable to read the forms, or at least cannot adequately retain information from the forms, then informed consent is not truly possible. Some of the more recent suggestions aimed at resolving this issue involve ensuring consistency in consent forms between institutions and allowing only minimal modification of such forms by local IRBs,[295] including more direct verbal communication in the informed consent process,[296] and altering consent forms into a social networking format that facilitates

[294] See for instance: Stuart Grossman, Steven Piantadosi and Charles Covahey. "Are Informed Consent Forms that Describe Clinical Oncology Research Protocols Readable by Most Patients and their Families?" *Journal of Clinical Oncology*, Vol. 12, pp. 2211-2215, 1994; Nigel Buller, Claire Campbell, David Denison, Kim Priestly and Christopher Valentine. "Are Patient Consent Forms for Research Protocols Easy to Read?" *British Medical Journal* Vol. 305, p.1263, 1992; Kenneth Tarnowski, Denise Allen, Christine Mayhall, and Patricia Kelly. "Readability of Pediatric Biomedical Research Informed Consent Forms" *Pediatrics*, Vol. 85(1), pp. 58-62, 1990; Lynn White, Jeffrey Jones, Christopher Felton, and Linda Pool. "Informed Consent for Medical Research: common discrepancies and readability" *Academic Emergency Medicine*, Vol. 3(8), pp. 745-750, 1996; and Michael Sharp. "The Problem of Readability of Informed Consent Documents for Clinical Trials of Investigational Drugs and Devices: United States Considerations" *Drug Information Journal*, Vol. 38(4), pp. 353-359, 2004.

[295] Koyfman et al. "Consent Form Heterogeneity in Cancer Trials: the cooperative group and institutional review gap" *Journal of the National Cancer Institute,* Vol. 105, pp. 947-953, 2013.

[296] James Flory and Ezekiel Emanuel. "Interventions to Improve Research Participants' Understanding in Informed Consent for Research: A Systematic Review" *Journal of the American Medical Association,* Vol. 292(13), pp.1593-1601, 2004. This type of proposal has been similarly echoed by many others. For example, concerned over the accessibility of some consent forms to those possessing only low levels of education, Hammerschmidt and Keane suggest that complex research studies ought to be presented to subjects by "someone knowledgeable about the study, knowledgeable about informed consent, and skilled at the presentation of technical information to a lay audience of limited education" (Dale Hammerschmidt and Moira Keane. "Institutional Review Board (IRB) Review Lacks Impact on the Readability of Consent Forms for Research" *American Journal of the Medical Sciences,* Vol. 304(6), pp. 348-351, 1992, p. 351).

better online communication.[297] However, throughout the continued development of informed consent forms, most of the effort has been dedicated to ensuring an appropriate level of language and technical jargon,[298] with some recommendations suggesting that such forms "be written at or below an eighth-grade reading level in order to accommodate the diverse reading skills and competencies of most research participants."[299] Though the importance of devising a suitable language for informed consent forms should not be understated, the correlative to ensuring that the language in informed consent forms is accessible to the varying competencies research subjects may possess would be to also attempt to ensure that prospective subjects possess a sufficiently high level of competence. Merely lowering the language and technical jargon in order to accommodate the diverse reading skills and competencies of potential research participants seems contrary to the main goal of the informed consent process, which is to ensure autonomous and thus competent informed consent.[300] Therefore, to this end, added attention must be dedicated toward

[297] Holland et al. "Protecting Human Research Participants: reading vs understanding the consent form" *Journal of the National Cancer Institute*, Vol. 105, pp.927-928, 2013.

[298] A large amount of medical terminology in informed consent forms can unfortunately make the document too complex for many patients and research subjects alike. This issue can lead to lawsuits over whether patients or research subjects were ever adequately informed prior to providing consent to a particular medical intervention or research trial. For example, in a 1996 Florida case, "plaintiffs (the class of pregnant women enrolled in a study) sought damages due to lack of informed consent, claiming both that the forms were written in language too technical for the women to understand and that the subjects were coerced into signing the forms" (Jessica Berg, Paul Appelbaum, Charles Lidz, and Lisa Parker. *Informed Consent: Legal Theory and Clinical Practice 2nd edition* (New York: Oxford University Press, 2001) p. 203). See: Diaz v. Hillsborough County Hospital Authority, 165 F.R.D.689 (M.D. Fl 1996).

[299] Ezekiel J. Emanuel, Robert A. Crouch, John D. Arras, Jonathan D. Moreno, and Christine Grady. *Ethical and Regulatory Aspects of Clinical Research* (Baltimore: The Johns Hopkins University Press, 2003) p. 445.

[300] It is important to note that this is not meant to suggest that only those with higher reading levels are capable of competent decision-making. Rather, it is meant to suggest that if indeed the main goal behind much of the focus on the readability of consent forms has been and continues to be the preservation of the autonomy of prospective research subjects, then such a goal requires more than *only* adjusting the language of reading forms. Indeed, such a goal might be better achieved by also attempting to enhance/bolster the competence of potential subjects. Though such an idea will be explored in greater detail in the following chapter, it can be noted that others have echoed a similar sentiment. Tom Beauchamp & James Childress, for instance, have stated that a respect for autonomy may include "in some contexts, building up or

ensuring a higher level of competence, as opposed to only attempting to accommodate lower levels of competence.[301]

The shortcomings of informed consent forms further support such a change in strategy. Apart from the issue of the complexity of medical language in informed consent forms, additional concerns have arisen regarding their length and use. Firstly, there appears to be an inherent tension between the goal of including all relevant information related to a clinical trial that may factor in a potential subject's decision to participate, with the goal of not overwhelming or overburdening the potential subject with information. It has long been known that "evidence exists that patient understanding of information on consent forms is inversely related to their length.[302] Overly inclusive consent forms may have the paradoxical effect of decreasing the level of patient understanding, perhaps even increasing the chance that a patient will feel misled, aggrieved, and inclined to sue."[303] The same holds true of consent forms in the research setting. However, despite this, over the years many consent forms in research have actually increased in length.[304]

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maintaining others' capacities for autonomous choice" (Tom Beauchamp & James Childress. *Principles of Biomedical Ethics* (New York: Oxford University Press, 2009) p.103).

[301] This is not to suggest that potential subjects will need to be capable of comprehending the various scientific intricacies of the experimental procedure at the level of the experts, but rather, as shall be argued in what follows, it should be required that subjects have the ability to comprehend the relevant facts sufficiently enough such that they are able to deliberate about participation on their own.

[302] See for example: Lynn Chaikin Epstein and Louis Lasagna. "Obtaining Informed Consent: Form or Substance" *JAMA Internal Medicine*, Vol. 123(6), pp. 682-688, 1969.

[303] Berg et al., 2001, p.195.

[304] In a study conducted on the use of consent forms for research in a Veterans Administration medical center, Baker and Taub found that "the mean number of lines in 1982 was almost twice the number used in 1975" (Marilyn Baker and Harvey Taub. "Readability of Informed Consent Forms for Research in a Veterans Administration Medical Center" *JAMA*, Vol. 250(19), pp. 2646-2648, 1983, p. 2647). In a more recent study it was found that "the mean length of the ICDs [informed consent documents] increased from 338 (range 276–464) words in 1987–1990 to 1087 words (range 399–2345) in 2005–2007" (O. Berger, B.H. Gronberg, K. Sand, S. Kaasa, and J.H. Loge. "The Length of Consent Documents in Oncological Trials is Doubled in Twenty Years" *Annals of Oncology*, Vol. 20(2), pp. 379-385, 2009, p. 379). The issue of length has ironically been exacerbated by an effort to reduce the complexity of consent forms. The problem seems to lie in the fact that "polysyllabic medical jargon is often shorthand for longer descriptions using simpler words, [and thus] efforts to reduce the complexity of consent forms almost inevitably increase their length. [For instance] to simplify the sentence, 'We are conducting an investigation of the

Furthermore, overtime the informed consent document has transformed into a tool used to protect certain parties from legal ramifications. That is, "in an effort to avoid liability, consent forms have increasingly included legalistic language about participants' rights, confidentiality, and compensation for injury, among other things."[305] The byproduct of such a change has been an increase in technical jargon, though of a legal variety, despite the concern over complicated and burdensome language in informed consent forms. The inclusion of legal jargon in informed consent forms also further adds to their tedious length, decreasing the likelihood that potential subjects will fully and carefully read them. Additionally, such an alteration signals that a change in focus has occurred with informed consent forms, where they previously were thought of as an informative and necessary safeguard for potential subjects, are now an instrument of protection for the investigators and institutions conducting the research. This reality has not been lost on patients and subjects alike, who, as studies have shown, generally do not view these consent forms as being for their interests or well-being. In a study involving 200 cancer patients who had signed consent forms for chemotherapy, radiation therapy, or surgery, it was concluded that "most believed that consent forms were meant to 'protect the physician's rights.' Although most thought that consent forms were necessary and comprehensible and that they contained worthwhile information, the legalistic connotations of the forms appeared to lead to cursory

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pathogenesis and pathophysiology of hyperlipidemia,' which consists of twelve words, we would have to resort to something like: 'We are trying to find out more about persons who have unusually high levels of fats in their blood. In particular, we are studying what leads to the development of this condition and related changes in the way the body works.' Although eminently clear, the more colloquial version more than triples the number of words used in the more technical version" (Berg et al., 2001, pp. 197-198).

[305] Emanuel et al., 2003, p.445. That the use of informed consent forms has shifted in this fashion is a sentiment corroborated by many other scholars as well. For example, in regards to consent forms, Berg et al. note that "there is a fundamental tension with respect to whose interests are being protected - those of the patient/subject or of the physician/researcher" (Berg et al., 2001, p. 190).

reading and inadequate recall."[306] Such results have been reaffirmed more recently in the medical research setting. In a study on 100 individuals who had provided informed consent for participation in medical oncology clinical trials, Olver et al. stated that "both this study and a parallel study that we performed with patients receiving chemotherapy outside of a clinical trial confirmed Cassileth's finding that most patients did not realise that the information and consent form was primarily meant to benefit them."[307] The perception that the role of informed consent forms is to serve the physicians or research investigators undermines what ought to be the main goal of such forms, namely securing the well-being of patients or subjects by ensuring the preservation of their autonomy in the decision-making process.[308]

This indictment of informed consent forms should not be taken as undermining the efforts put forth by those interested in ensuring the ethicality of such forms. Rather, such criticism is meant to serve as an indication that what is required is a shift in focus. While it is imperative that informed consent forms be constructed such that they do not deceive potential subjects and disclose all relevant information necessary in order to make an informed choice, as the preceding discussion from Chapter Three on the therapeutic

[306] Barrie R. Cassileth, Robert V. Zupkis, Katherine Sutton-Smith, and Vicki March. "Informed Consent — Why Are Its Goals Imperfectly Realized?" *New England Journal of Medicine,* Vol. 302, pp.896-900, 1980, p. 896.

[307] N. Olver, L. Buchanan, C. Laidlaw, and G. Poulton. "The Adequacy of Consent Forms for Informing Patients Entering Oncological Clinical Trials" *Annals of Oncology,* Vol. 6, pp. 867-870, 1995, p. 869.

[308] That the perception of informed consent forms as legal protection for physicians or researchers could lead to the undermining of the very goals of informed consent is a concern that has been voiced by many others. Bottrell et al. for example argue that "aspects of many forms, such as the requirement of a witness countersignature, add to their legal appearance and further distance patients. Combined with concerns about legal jargon, these format issues help to explain why patients believe forms were created to protect hospitals or physicians. Anything that contributes to such appearances or perceptions is likely to hinder, if not counteract, the goals of informed consent. Inadequately or legalistically crafted forms also have risks for patients. Forms with a solely legalistic appearance may lead to either cursory or suspicious reading of forms, and therefore, an inadequate or distorted understanding" (Melissa Bottrell, Hillell Alpert, Ruth Fischbach, Linda Emanuel. "Hospital Informed Consent for Procedure Forms: facilitating quality patient-physician interaction" *Journal of the American Medical Association Surgery,* Vol. 135(1), pp.26-33, 2000, p. 30).

misconception revealed, much of the confusion, misunderstandings, and false beliefs that subjects often have, actually stem from sources other than the informed consent form itself.[309] In fact, in an examination of phase I oncology trial consent forms, Horng et al. concluded that while the consent forms they analyzed:

> could do more to counteract misunderstandings that subjects may bring to a trial,... their substance does convey the purpose, risks, and benefits of the trials. [Furthermore they state that] much of the attention currently devoted to consent forms by researchers, institutional review boards, and regulators could be directed more usefully to the enhancement of other aspects of the informed-consent process.[310]

Concurring with such a sentiment, the approach suggested here has been to redirect efforts toward ensuring the *competence* of terminally ill potential research subjects. As Paul Appelbaum reminds, "one way of protecting people's rights and interests is to help them make decisions for themselves."[311] It is precisely this thought that fuels our current endeavour. While informed consent forms can be overly wordy and possibly further convolute the matter, ensuring the competence of potential subjects places them in a situation where they are better able to protect themselves. If indeed research subjects are sufficiently competent to make research participation decisions, then some of the ethical concerns surrounding clinical trials with terminally ill subjects, such as misconceptions, deceitful tactics employed by some researchers, neglect of the interests of subjects, and

[309] Revisit Chapter Three for a full description of causes of the therapeutic misconception. Additionally, given some of the previously mentioned issues regarding informed consent forms, namely readability, length, retention, complexity, and inclusion of legalistic jargon, it has been questioned whether informed consent documents can actually ever be proof of informed consent. As one court noted, a "form signed by the patient does not always indicate that the patient's consent was in fact informed consent" (Barner v. Gorman, 605 So.2d 805 (Miss. 1992)). This further signals the need for a shift in focus away from informed consent documents toward competence bolstering and assessment.

[310] Sam Horng, Ezekiel Emanuel et al. "Descriptions of Benefits and Risks in Consent Forms for Phase I Oncology Trials" *The New England Journal of Medicine*, Vol. 347(26), pp. 2134-2140, 2002, p.2140.

[311] Paul Appelbaum. "Missing the Boat: Competence and Consent in Psychiatric Research" *The American Journal of Psychiatry*, Vol. 155(11), pp. 1486-1488, 1998, p. 1488.

the possible undermining and disrespect of an individual's autonomy that is often associated with cases of corruption in medical research, are all greatly mitigated if not completed eliminated in some instances.[312]

In proceeding then, it is imperative to recognize that our endeavour is not to determine what particular information must be conveyed during the informed consent process so that the subject can possess the adequate facts needed to provide consent.[313] Nor is our task to determine what specific information must be appreciated or reasoned about for ethical informed consent. Rather, we must proceed by examining how much of an ability to understand, appreciate, reason, and decide voluntarily a terminally ill person is required to have for a competent and thus ethical and autonomous consent to research participation. It is only by viewing each element of competence as a separate sub-ability, that we may proceed and determine to what extent one must be capable of each of the four elements of competence, and thus to what extent one must be competent overall to be able to ethically consent to medical research for terminally ill subjects.

The Competency Continuum

Current regulations tend to be fairly vague on the requisite competence for consent to medical research. In the U.S. for instance, the Department of Health and Human Services Title 45 C.F.R. Part 46, barely even acknowledges competence, opting

[312] For instance, any deception or manipulative tactics that contribute to a potential research subject's therapeutic misconception would become largely ineffective if the subject was competent enough to understand the existence of the therapeutic misconception, appreciate what it may mean for her, and be able to reason with that information. Thus, a higher level of competence would enable the subject to protect herself from some of the potential harms, especially those to her autonomy, which may exist in certain research trials.

[313] For such a matter refer back to Chapter One where the various elements of disclosure in the medical research context were discussed, along with some of the possible controversies surrounding them.

instead to focus on the criteria for informed consent documents. In describing the general requirements for informed consent, Title 45 C.F.R. 46 does state that:

> An investigator shall seek such consent only under circumstances that provide the prospective subject or the [legally authorized] representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative.[314]

Though this appears to touch upon both the understanding and voluntariness elements of competence, it fails to discuss either of these in a meaningful way, and falls far short of identifying the criteria necessary for a sufficient understanding or voluntariness needed for competent consent. Unfortunately, apart from this issue, rarely do regulations such as this even mention the other two elements of competence, namely appreciation and reasoning.

Other regulations do not fare much better. Similar to Title 45 C.F.R. 46, the ICH-GCP,[315] dictates that voluntariness is imperative regarding subject participation, stating that "neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial."[316] Understanding is addressed almost as cursorily, with statements not suggesting much more than the importance of providing information in a language that is non-technical and easily understandable by subjects, or that at times a witness may be required to help ensure

[314] U.S. Department of Health and Human Services, National Institutes of Health, and Office for Protection from Research Risks, Title 45 (Public Welfare), Code of Federal Regulations, Part 46 (Protection of Human Subjects) Washington, D.C.: Revised January 15, 2009 (Effective July 14, 2009), Section 46.116.
[315] International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonised Tripartite Guideline- Guideline for Good Clinical Practice (Geneva: 1996).
[316] ICH-GCP, Section 4.8.3, p. 15.

understanding when a potential subject is unable to read the informed consent document.[317]

The Declaration of Helsinki[318] makes some advancement, specifically identifying necessary elements of disclosure needed for adequate understanding as well as detailing certain issues surrounding voluntariness. For instance, regarding voluntariness, it states that "when seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship."[319] However, despite some improvements recognizing certain issues related to understanding and voluntariness, The Declaration of Helsinki ultimately still falls short of acknowledging a requisite level of either understanding or voluntariness, or of competence overall, necessary for consent to research. This is especially true given that, as with most other guidelines, both appreciation and reasoning are not addressed.

As a refreshing change of pace, the Tri-Council Policy Statement[320] does acknowledge the requirement of competence and even mentions some of its components as it states that competence "involves the ability to understand the information presented, to appreciate the potential consequences of a decision, and to provide free and informed consent."[321] It further correctly recognizes that competence is decision relative and that

[317] ICH-GCP, Section 4.8.9, p. 16.
[318] World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *The Journal of the American Medical Association*, Vol. 310(20), 2013.
[319] World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *The Journal of the American Medical Association*, Vol. 310(20), 2013, Section 27.
[320] Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.* 1998 (with 2000, 2002 and 2005 amendments).
[321] *Tri-Council Policy Statement*, p. 2.9.

therefore competence does not require that potential subjects be able to make every type of decision, but instead that they "be competent to make an informed decision about participation in particular research."[322] While these assertions are certainly an important step forward in addressing the competency requirement for medical research subjects, the Tri-Council Policy Statement similarly falls short of fully dealing with the issue. For instance, it still remains unclear as to what would constitute substantial competence for the research context. Instead the document suggests that since competency laws vary between jurisdictions, "researchers must comply with all applicable legislative requirements."[323] However, as previously mentioned, the law does not help clarify this issue. "There are few cases or statutes that speak to this issue in the treatment setting, and none that address competence to consent to research."[324]

It should be noted that often guidelines and regulations, including the four just mentioned, do attempt to address the proper course of action with incompetent potential subjects.[325] However, "the regulations… [ultimately remain] silent on the question of what constitutes incompetence in a research setting"[326] in the first place. It is to this difficult task that we will turn in the following sections.

However, prior to this, it is crucial to note that the constituent parts of competence, just as with competency overall, are not all or nothing phenomena. That is to state that it would be a false dichotomy to assume that, for example, an individual either has understanding or lacks it. In fact the understanding a person may possess falls

[322] *Tri-Council Policy Statement*, p. 2.9.
[323] *Tri-Council Policy Statement*, p. 2.9.
[324] Berg et al., 2001, p. 266.
[325] Some examples include requiring a legally authorized representative for the consent process, or requiring that the research will not expose the incompetent subjects to anything more than minimal risk unless there is the potential for benefit as well.
[326] Berg et al., 2001, p. 266.

somewhere along a continuum that ranges from full understanding to complete ignorance. While a person might fall anywhere along this continuum and thus all individuals may possess quite different levels of understanding pertaining to a certain context, for pragmatic purposes it will be imperative that we separate those who possess a sufficient amount of any of the particular elements of competence, for example understanding needed to participate in a medical trial, from those who do not.

The recognition that the constituent parts of competence, namely understanding, appreciation, reasoning, and voluntariness, all exist on a continuum would seem to entail that there are a possible infinite amounts or levels of each that one may possess. For example, it would seem conceptually impossible to set out three different levels of understanding, such as very high, moderate, and low, and expect that each and every person will fall neatly within one of those three categories. Indeed many individuals may fall somewhere between such categories. However, despite this we shall proceed by highlighting six different levels along the spectrum for each element of competence. Though individuals may not fall neatly into any one of these six categories, such a detailed overview of the spectrums of the elements of competence will enable us to note a threshold level, below which a person can be said to be lacking that necessary component of competence needed to be substantially competent to consent to the medical research trial.[327] We shall proceed by analyzing each element of competence in turn, beginning with appreciation.[328]

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[327] While it has been acknowledged that three levels, nor six, nor any other number could completely outline every potential level of a sub-ability of competence that a person may possess, in what follows, using six separate levels to map out the spectrum for each sub-ability will prove to strike an appropriate balance between practicality and comprehensiveness.

[328] It should be noted that the following spectrums of the four elements of competence and more importantly the determination of the minimum level of each that is required for competent consent to research, will only apply to terminally ill subjects of research. As previously noted, the context and factors

The Spectrums of the Four Elements of Competence

In what follows, six different levels of ability will be identified for each of the elements or sub-abilities that comprise competence, namely understanding, appreciation, reasoning, and voluntariness. See figure 1 below for a chart outlining the six levels of each sub-ability. Though the levels discussed will fail to identify every possible level of ability, for such would be impossible, it will provide the basis needed to attempt to ascertain to what degree a terminally ill person must be capable of the sub-abilities in order to be considered competent for consent to medical research. This will be compared and contrasted with the level often thought necessary for the therapeutic context. The establishment of a minimum level necessary of each of the four sub-abilities will be influenced by the three relevant differences between the research and medical practice context that warrant a greater level of competence for consent in the former, as was argued in Chapter Three.[329] We may recall that these three differences were the difference in the nature of the researcher/subject relationship as opposed to the physician/patient relationship, the higher potential for exploitation of the situation or mental state of terminally ill subjects, and the presence of the therapeutic misconception. Each of these differences will play a vital role in determining how much understanding, appreciation, reasoning, and voluntariness ought to be necessary for competent consent to medical research for terminally ill persons.

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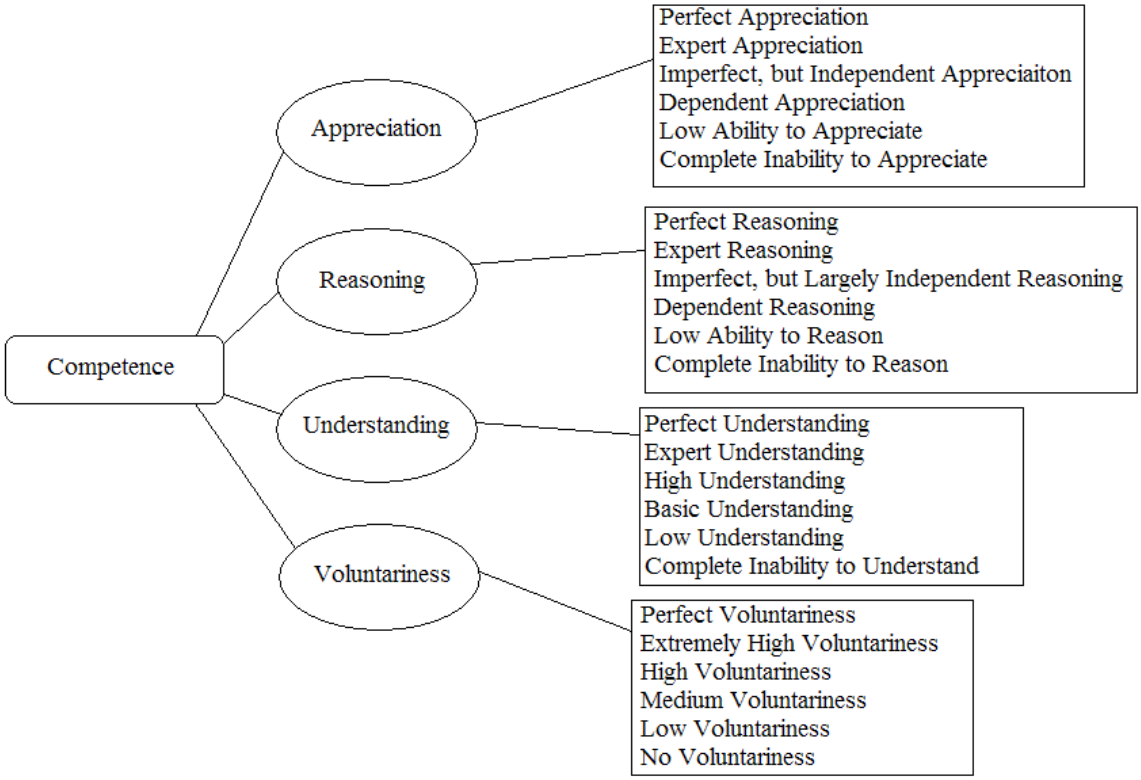
surrounding terminally ill persons participating in research are such that the appropriate level of competence that they ought to possess for research participation may be radically different than the level of competence that ought to be required for consent in other research contexts with other populations, and as argued in Chapter Three, quite different from the level of competence required to consent to treatment.

[329] It is important to reaffirm that current law, the courts, and existing literature on the topic, fails to detail the extent to which each of the abilities that comprise competence is necessary for the research context, especially with terminally ill subjects. Even literature that acknowledges the different elements of competence and explains their importance for medical treatment decision making with patients, often ignores the task of determining how great an ability to appreciate, or reason…etc. is needed for ethical consent. This fact coupled with the inconsistencies that exist between jurisdictions in dealing with competence overall, forces us to wade through some uncharted territory as we proceed.

Fig. 1 Different Levels of Competence Sub-Abilities[330]



Only by establishing such sub-ability requirements can we ensure the ethicality of medical research trials by ensuring that the terminally ill potential subjects possess a sufficient level of competence necessary for truly autonomous consent.

Recalling the first difference specifically, between the research and medical practice context, namely that the nature of the relationship between the research investigator and subject is fundamentally different than that between a physician and patient, it becomes clear that both the appreciation and reasoning elements of competence may become more

[330] Each of the levels pertaining to their respective sub-ability of competence will be explained in detail in the following sections.

difficult to satisfy in the research context. As such, we shall proceed by dealing with these elements first.[331]

Appreciation

We may recall that appreciation involves the ability to realize the significance and implications of different potential alternatives for one's own life. More specifically, this criterion of competence requires that one be able to somewhat foresee and grasp what it might be like to be in possible future states and to incorporate that into one's decision making. Furthermore, as previously stated, "this criterion of competence emphasizes the significance of grasping the relevance of certain information and decisions for one's own personal circumstances."[332] Given this definition, the highest level of appreciation on our spectrum would be the ability to foresee every direct and indirect consequence of every possible decision a person may make, and to know how those consequences will affect one's self. Conversely, the lowest level of appreciation on our spectrum would involve a complete inability to have any insight into the consequences of a decision. See Spec. 1 below for the full six level spectrum of appreciation.

[331] In what follows, it will be imperative to first establish the spectrums for appreciation and reasoning, and then demonstrate where along those spectrums lies the minimum threshold necessary for competence in the research setting with terminally ill subjects.
[332] See Chapter One, p.19. For a more detailed explanation of appreciation, refer back to Chapter One.

Spec. 1 Appreciation Spectrum[333]

1. Perfect Appreciation – The ability to foresee every direct and indirect consequence of every possible decision. This level of appreciation would further enable one to know how those consequences will affect her, given her own unique situation and individual needs, and be able to include that in her decision making in such a way so as to make the decision that brings about the most desirable future state of affairs possible. Such perfect appreciation is impossible and thus shall only serve as the upper limit on the appreciation spectrum.

2. Expert Appreciation – Often capable of foreseeing most consequences, and especially the most likely consequences, of one's decisions, with consistent accuracy. Moreover, this level of appreciation would entail that a person would in most cases be able to know how she would feel in the various possible future states where those consequences were actualized. Such appreciation may not be as conceptually impossible as perfect appreciation, but is still likely to be unattainable by most persons in most situations. Therefore, this level of ability to appreciate might only be possible by certain experts making decisions within the field in which they are experts, for example a researcher deciding to test a new experimental intervention on herself.

3. Imperfect, but Independent Appreciation – This level of appreciation involves being able to foresee the more likely consequences of one's decision and to be able to ascertain how one might feel in the possible future states where those consequences are actualized. Such a level of appreciation might be imperfect, as one might not be able to fully grasp exactly how she will feel in certain future states, especially those with which she has had no prior experiences, but is still often effective in assisting one in making good choices. Most importantly, someone who is capable of this level of appreciation is able to arrive at her insights on her own without assistance from others.

4. Dependent Appreciation – Capable of grasping the consequences of a decision and what those consequences may mean for one's self, but usually only once someone else has described them. Such a person may be able to realize the significance, for one's own personal circumstances, of a decision, and even will be able to effectively incorporate that into the decision making process, but usually only once it is pointed out by another. An example of this may involve an athlete who consents to surgery to repair a torn ACL (Anterior Cruciate Ligament), and only begins to question such a decision once someone else points out that the lengthy recovery from such a procedure would keep the athlete out of sports for the remainder of the year. It should be noted that it is likely this level of appreciation that is considered adequate in the medical practice setting where physicians often presume the competence of their patients. A patient is probably capable of this level

[333] It should be noted that all four of the spectrums will be designed in an ordinal fashion as opposed to interval. That is to state that the relative degree of difference between each of the levels should not be assumed to be the exact same as the relative difference between any other levels on the spectrum. It is important to note that the ordinal ranking will be sufficient to accomplish our current purpose, namely to establish qualitative descriptions of various levels within each sub-ability of competence such that arguments regarding minimum threshold levels required for a competent consent to research may be presented.

of appreciation so long as she can acknowledge her condition and grasp the consequences of it and available treatment options as explained by the physician. A patient might only fail to demonstrate this level of appreciation if she holds beliefs that are "substantially irrational, unrealistic, or a considerable distortion of reality."[334]

5. Low Ability to Appreciate – Often incapable or unwilling to attempt to foresee even the more likely consequences of one's decision. Even once the potential consequences of a decision are realized by the person, she will still likely not engage in the process of attempting to determine how she might feel in the possible future states where those consequences are actualized. This level of appreciation may apply to many young children, as it is often thought that their ability to appreciate is hindered "by the lack of sufficient life experience."[335] Such a low level of appreciation is sometimes assumed of juvenile criminals who perhaps did not attempt to grasp the significance for themselves of the longer term consequences of committing the crime.

6. Complete Inability to Appreciate – Lacks any insight into the consequences of one's actions. A person with such little ability to appreciate would likely be unable to engage in any meaningful decision making. Such a level of inability is unlikely in most adults, as typically only infants will lack the ability to appreciate to this extent. However, this level of appreciation may be present in some patients with severe mental cognitive impairments, who cannot recognize how their mental illness affects them, rendering them unable to competently make treatment decisions. As the courts have recognized, if a "patient's condition results in him being unable to recognize that he is affected by its manifestations, he will be unable to apply the relevant information to his circumstances, and unable to appreciate the consequences of his decision."[336] In such cases surrogate decision makers or the practice of involuntary commitment are sometimes utilized. [337]

As already demonstrated, the requisite level of competence, and more specifically of each of the four sub-abilities of competence, is greater in the research context with terminally ill subjects than in the medical practice context. However, given this six leveled spectrum of appreciation, it now becomes possible to ascertain how great a level specifically is necessary for terminally ill subjects for competent consent to medical research. It might be noted that typically the medical practice context seems to require

[334] Thomas Grisso and Paul Appelbaum. *Assessing Competence to Consent to Treatment: A Guide for Physicians and Other Health Professionals* (New York: Oxford University Press, 1998) p. 45.
[335] Allen Buchanan and Dan Brock. "Deciding for Others" *The Milbank Quarterly*, Vol. 64, Supplement 2: Medical Decision Making for the Demented and Dying, pp. 17-94, 1986, p. 25.
[336] *Starson v. Swayze*, 2003 SCC 32, [2003] 1 S.C.R. 722.
[337] It is important to note that the above spectrum is not meant to be comprehensive or exhaustive of all possible levels of appreciation, nor is it meant to add any profound details as to the definition of appreciation. Rather, it is only meant to serve as a general outline that will be sufficient for constructing a minimum threshold that ought to be required for competence for terminally ill research subjects.

only, what I have referred to as *Dependent Appreciation*, that is, the ability to grasp the consequences for one's self, even if only once explained by the healthcare professional.[338] However, by applying our three relevant differences between the research and medical practice context, and most specifically in the case of appreciation, the first difference regarding the nature of the relationship between the researcher and subject, it will be argued that we ought to require at least what I have referred to as *Imperfect, but Independent Appreciation* for the research context with terminally ill subjects.

We may recall from Chapter Three that the first fundamental difference between the medical practice and medical research context that was discussed revolved around the nature of the relationship between a physician and patient compared to that between a researcher and subject. Whereas the former is generally viewed, though with some exceptions, as a relationship involving a certain degree of loyalty and obligation of fidelity,[339] the same could not be said regarding the researcher and subject relationship. As previously discussed, as a result of the diverging goals between research and therapy, the interests of physicians and researchers are radically different, and thus, while the physician's and patient's interests are thought to align, a researcher's and subject's may actually conflict. The type of methodologies and approaches used in conducting research are indicative of such a lack of alignment between the interests of the researcher and

[338] For a more detailed depiction of the requisite level of appreciation, or of the other sub-abilities of competence required in the medical practice context, see: Grisso and Appelbaum, 1998. Unfortunately apart from this text and some similar works by these authors, there is little to no established guidelines or laws on exactly how much appreciation, or competence overall, should be required of a patient. Instead, it is often generally accepted practice that determinations of incompetence are made by individual physicians if they notice something amiss with their patient. The problem with such idiosyncratic clinical competency evaluations will be explored in the following chapter. However, it should be noted, that as a result of the current lack of literature, it is impossible to refer to precise laws or guidelines that would assist in noting the exact place on the appreciation or other spectrums that is currently required of patients in the medical practice setting.

[339] Consult Chapter Three for a discussion of some exceptions.

subject.[340] Such methodologies that do not appear to be in the subject's interest, but are used in order to ensure the integrity of the research, include randomization, placebo controls, and double blinding, which all demonstrate that in research as opposed to medical practice, the subject's wellbeing and interests are not primary, but are made secondary to the goals of the research trial. This appears especially true with terminally ill subjects of research who may be seeking a last hope miracle cure when participating in research, but where the research trial design is not created or carried out in such a manner so as to make such a hope realistic.[341]

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[340] For a full discussion regarding the methodologies applied in research that demonstrate that the interests of research and the researcher can in fact conflict with the subject's interests, refer back to Chapter Three.

[341] This is particularly apparent in phase I oncology trials, which as previously mentioned, are designed to test the toxicity and highest tolerable doses of the anticancer drugs or interventions under clinical investigation. In fact in an examination of 272 consent forms Horng et al. found that "only 1 of the 272 consent forms stated that subjects were 'expected' to benefit" (Horng et al., 2002, p. 2136). Furthermore, there is only "an overall complete response rate of 0.5 per cent and a partial response rate of 1.5 per cent (total response rate two per cent) in phase I oncology trials" (W. Glannon. "Phase I Oncology Trials: Why the Therapeutic Misconception Will Not Go Away" *Journal of Medical Ethics*, Vol. 32(5), pp. 252-255, 2006, p. 252). Others have placed the potential chance of therapeutic benefit as being less than 5% (Christopher K. Daugherty, Donald M. Banik, Linda Janish and Mark J. Ratain. "Quantitative Analysis of Ethical Issues in Phase I Trials: A Survey Interview Study of 144 Advanced Cancer Patients" *IRB: Ethics and Human Research,* Vol. 22(3), pp. 6-14, 2000, p.11). Nonetheless, it is clear that these types of trials are designed with the subject's interest being placed second to the goals of the research. Some have recently argued that despite the various studies that claim such low response rates for phase I oncology trials, a more critical analysis may reveal otherwise. Manish Agrawal and Ezekiel Emanuel claim that many phase I oncology research trials involve "vaccines, immune modulators, antiangiogenesis factors, and signal transduction agents [and that] these agents are widely perceived to be less toxic than chemotherapeutic agents" (Manish Agrawal and Ezekiel Emanuel. "Phase 1 Oncology Research" In *The Oxford Textbook of Clinical Research Ethics*, Ezekial J. Emanuel, Christine Grady, Robert A. Crouch, Reidar K. Lie, Franklin G. Miller, and David Wendler, eds. (Oxford: Oxford University Press, pp. 356-366, 2008) p. 358). Additionally, they claim their benefits "may not be appropriately measured by evaluating tumor response [since] these agents usually control cancer growth rather than kill cancer cells" (Agrawal and Emanuel, p.358). Once this is accounted for, the authors contend that the overall response rate becomes 10.6%, which includes both complete and partial responses, and that 34.1% of subjects had some form of disease stabilization, although they admit that "the significance of stable disease as a response to an investigational intervention is controversial" (Agrawal and Emanuel, p. 359). However, despite even these more optimistic figures, the authors still admit death from toxicity in phase I trials still occurs. They cite a few studies that seem to all place the overall toxicity death rate around 0.5% with some studies suggesting the number is as high as 0.57% (Agrawal and Emanuel, p. 357). Furthermore, the authors also admit that phase I oncology trials have "a rate of 10.3% for serious, that is grade 3 or 4, nonfatal, toxic events... Of these toxic events, 85% were reported as partially or completely reversible… [with some data showing that] for single investigational chemotherapy agents, 15% of patients had a grade 4-life-threatening-toxic event" (Agrawal and Emanuel, p. 357). However, more importantly, it must be recognized that even accepting a slightly better risk/benefit ratio does not negate or undermine the need for the heightened competence standards.

Without rehashing this issue, it is important that we recall the implications of such a realization, namely that as a result of this difference in relationship, a greater level of competence is needed for the medical research as opposed to the medical practice context. More specifically, this difference significantly impacts the appreciation and reasoning elements of competence, though we shall discuss only the former presently. While the consequences that one may experience when undergoing medical treatment are typically accounted for by the attending physician with the patient's best interests being paramount, the consequences that may ensue to a subject of research will typically not be accounted for in the same way.[342] Thus, while the extent to which a patient must appreciate a particular medical procedure for his consent to be competent and ethical might be mitigated by the fact that his physician and the therapeutic clinical community have accounted for the patient's best interests prior to making available or proposing a certain medical procedure, the same does not hold true in the research context. Instead, it is of far greater importance in the research context that a subject be capable of appreciating the potential consequences of participation and the various manners in which such a decision may impact one's life since no medical professional may exist in this context who attempts to account for that on behalf of the subject. Thus, it should not be surprising that the medical practice context may only warrant requiring, what I have

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This is especially true since the underlying reasons for the greater competence standards, namely the three main differences between the medical practice and research context, persist regardless of an improved interpretation of the response rate in phase I oncology trials. Furthermore, and more specifically, the above claim that these types of trials are designed with the subject's interest being placed second to the goals of the research also remains intact as it too is unaffected by a slightly improved interpretation of response rates.

[342] Although sometimes ignored, the laws and ethical guidelines in most countries do require that a subject's interest be accounted for at least minimally insofar as that subject is a person and has a certain moral standing and inviolable rights. Such standards may require, for example, that a subject cannot be subjected to unnecessary or excessive harm. However, such guidelines fall far short of amounting to a precept that requires that researchers account for the best interests of a subject.

referred to as *Dependent Appreciation*, since a patient can reasonably trust that any proposed medical procedures are recommended with his best interests in mind. However, the higher *Imperfect, but Independent Appreciation* standard, is needed for the research context, where subjects are more so left on their own to determine which decision would be in their best interest.

Secondly, the lack of alignment of interests between researchers and subjects may also increase the chance of abuse, corruption and an overall disrespect of one's autonomy in research. Such abuses often occur in research in an attempt to better achieve the goals and aims of research.[343] It is necessary, that such a possibility also be included in one's appreciation. It is important that we not think that only the consequences of the non-validated medical interventions need to be appreciated, but also a subject must somewhat foresee how it will feel to be treated at least in part as a means to someone else's end, and the potential risks that may go along with that. This further demonstrates that *Imperfect, but Independent Appreciation* is needed for the medical research context since it is unlikely that anyone else will assist the prospective subject in appreciating such a fact.[344]

Thus it can be concluded that the difference in relationship between a researcher and subject compared to a physician and patient leads to two reasons for supporting this higher standard of appreciation in the medical research setting. First, as was argued, the need for a patient to appreciate, for example, a recommended therapeutic procedure, is lessened by the fact that in the medical practice context a patient can reasonably trust that the methodologies applied by, and recommendations of, her physician are in her best

[343] Refer back to Chapter Three and Chapter One for examples and further discussion of some such cases of abuse in research.

[344] Such a problem will be somewhat mitigated by the proposal that will ultimately be presented in what follows. More specifically a proposal will be outlined which suggests that a subject rights advocate be employed to assist potential subjects in appreciating certain features of participating in medical research.

interests, but in medical research, such an assumption would be untenable and unrealistic. Instead, it seems appropriate to require that subjects be able to appreciate the methodologies applied in research and what being a participant in such methods may mean for them. For instance, in a Phase I trial it would be crucial for a research subject to appreciate the consequence to her of the fact that the clinical trial is designed to "end just at that point where the drug becomes too toxic to administer"[345] regardless of whether any beneficial effects were beginning to present themselves. Second, the greater appreciation recommended for the medical research context is made necessary by the fact that unlike in medical practice, the subject must appreciate the significance for herself, of being treated, at least in part, as a means to another's end.

Additionally, though related to the third relevant difference between medical practice and research, which will be discussed in more detail in the following sections regarding understanding and voluntariness, the presence of the therapeutic misconception also affects the standard of appreciation required. As Chapter Three noted, the various factors that can contribute to the therapeutic misconception all make it more difficult for a prospective subject to possess adequate appreciation. It is next to impossible to have a substantial appreciation for the consequences of the decision to participate in research, if one is confused and considers the research trial their medical therapy instead. Obviously if subjects fail to understand that they are participating in research, they will fail to appreciate the consequences of such a decision.[346] Thus, given the various factors that contribute to such a misconception, it is further imperative that we require the higher *Imperfect, but*

[345] Emanuel et al., 2003, p. 101. Also see: Benjamin Freedman. "Cohort-Specific Consent: An Honest Approach to Phase 1 Clinical Cancer Studies" *IRB: Ethics and Human Research*, Vol.12(1), pp. 5-7, 1990.
[346] This may be a particularly difficult problem in cases where individuals lack medical insurance, thus rendering them unable to afford treatment, and therefore seek research trials as their only way of getting access to medical therapy.

Independent Appreciation standard, since it will be necessary that a subject be capable of not allowing such factors to hinder his appreciation of the fact that he is indeed participating in research.

Reasoning

We may recall from Chapter One that reasoning involves the ability to "engage in a rational process of manipulating the relevant information."[347] This includes the ability to formulate proper interests and ends, effectively employ proper means/ends reasoning in pursuing those interests and ends, demonstrate some level of consistency in choices, actions and deliberation, as well as the ability to derive the appropriate conclusions from premises, and weigh risks and benefits of possible choices. It is through this ability to reason that the information we understand and appreciate is able to factor into our final decision. That is to say that "without the mental ability to engage in *reasoning* and manipulate information rationally, it is impossible for understanding and appreciation to issue in a decision."[348] We may also recall from Chapter One that any analysis of one's reasoning ought to focus on the process by which a decision is made, and not on the particular outcome of the decision-making process.[349]

Given this characterization of reasoning, the highest level on our spectrum would involve the ability to determine one's best interests in every situation and also know the

[347] Paul Appelbaum. "Assessment of Patients' Competence to Consent to Treatment" *The New England Journal of Medicine*, Vol. 357, pp. 1834-1840, 2007, p.1836.
[348] Louis Charland, "Decision-Making Capacity", *The Stanford Encyclopedia of Philosophy (Fall 2008 Edition)*, Edward N. Zalta (ed.),
URL = <http://plato.stanford.edu/archives/fall2008/entries/decision-capacity/>.
[349] We may recall that it is by this principle that disagreements can exist between reasonable people. Therefore, as previously discussed, reasonable patients or subjects may indeed disagree with their respective physicians and reach different conclusion from them. However, reaching such a conclusion is not in itself cause to suspect a flaw in their reasoning since a particular physician or medical personnel's opinion is not exhaustive of the possible opinions of the reasonable individual.

most effective means by which to achieve such ends. By contrast, the lowest level of reasoning will involve the complete inability to figure out one's best interests, and to be incapable of any means/ends reasoning. See Spec. 2 below for the full six level spectrum of reasoning.

Spec. 2 Reasoning Spectrum

1. Perfect Reasoning – Capable of determining one's absolute best interests, and further determining the most effective means by which to achieve those interests. Perfect reasoning would also include wholly correct risk/benefit analysis. Put differently, one who possesses this level of reasoning would be able to establish that among various possibilities, end x would be in his best interest, and that means y would be the most effective and efficient manner in which to achieve that end. Such perfect reasoning is not only impossible since the reasoning of individuals can never be without flaw, but is further impossible since such reasoning would require a complete understanding of all the relevant facts and almost infallible foresight. This unattainable level of reasoning shall only serve as the upper limit on the spectrum of reasoning.

2. Expert Reasoning – Often capable of determining one's best interests and the most appropriate means of achieving it. Such reasoning may not require an unachievable perfect level of knowledge and foresight as was the case with perfect reasoning, but will still require an incredibly high amount of both. Therefore, this level of reasoning will likely only be possible by certain experts in the field in which they are making a decision. Experts will likely possess the amount of knowledge and amount of practice reasoning with such knowledge necessary to reason in this manner.[350] Though not completely unattainable, as was perfect reasoning, it is doubtful whether most of us can perform this level of reasoning in much of our daily decisions. This is not only due to the fact that we may often lack the knowledge necessary in many situations to reason in this manner, but also due to the fact that we often fail to engage in the decision making process in a purely rational way. As Grisso and Appelbaum point out, "much attention has been devoted in recent psychological research to documenting the many ways in which people deviate from a purely 'rational' model of decision making. The role of emotions in decisional processes has been a particular focus of concern."[351]

[350] It is important to recall that competence and its elements are decision and context relative. Thus, one who possesses an expert level of reasoning in one context, may find his ability to reason diminished in a radically different context. We may for example envision a biologist attempting to reason through the best way to verify a hypothesis regarding cellular structure, as compared to that same biologist attempting to reason through the best way to win a formula one race. It should be clear that such an individual may be capable of an expert level of reasoning in the first situation, but might be utterly lacking in his ability to reason in the second situation.

[351] Grisso and Appelbaum, 1998, p.55.

3. Imperfect, but Largely Independent Reasoning – While reasoning in the medical research context by terminally ill possible subjects will to some extent depend on material and information provided by the medical professionals involved either in the recruitment process, or in the ongoing trial itself, a person capable of this level of reasoning will also be capable of researching, and learning on his own, and more importantly using any learned facts in his assessment of the situation. Such a reasoner will be able to take the advice from medical personnel, and family or friends, as not being definitive or absolute, but as requiring one's own independent analysis. Such an evaluation may involve the ability to ascertain whether the reasons and advice of others are questionable. A person who has the ability to reason at this level may not know what action will be in his absolute best interest with certainty, but is fairly assured that his independent analysis can provide him with a high probability of success in his decision making.

4. Dependent Reasoning – Capable of following the reasoning as set out by others, but often lacking the ability to produce such reasoning on one's own. An example may involve being able to follow the explanations of a medical professional regarding the risks and benefits of various treatment options, and following the reasoning behind the risk/benefit analysis that would lead the medical professional to select one option over the others. Such a reasoner may also be able to recreate the reasoned analysis on his own, but will ultimately lack the ability to have produced the analysis, provided by the medical professional, on his own in the first place.

5. Low Ability to Reason – Seems to at times lack basic knowledge regarding one's best interests, and struggles to follow means/ends analysis. Such a reasoner may further demonstrate an inability or unwillingness to engage with the risks and benefits of possible options and evaluate them. As a result, such a person may demonstrate frequent reversals of choice, often without basis.

6. Complete Inability to Reason – Unable to grasp one's best interests, and unable to engage in any means/ends reasoning. Individuals with such an inability will likely be infants or those with severe mental cognitive impairments.

While what I have referred to as *Dependent Reasoning,* is often seen as acceptable in the medical practice context,[352] our first difference between medical research and

[352] Again, as was already mentioned with appreciation, there are little to no established guidelines or laws on exactly how much reasoning or competence overall, should be required of a patient in the medical practice context. However, we may appropriately assume that all that is typically required is a level of reasoning akin to what I have referred to as *dependent reasoning*, since one's ability to reason, and indeed overall competence, is generally assumed to be intact by physicians in the medical practice context so long as the patient appears to follow and agree with the physician's assessment. As Thomas Grisso and Paul Appelbaum elucidate, it seems only when certain indicators are present that a physician may question the reasoning, or overall competence of a potential patient. Such indicators may include: abrupt changes in a patient's mental state, a refusal of treatment, and other contextual or situational factors such as a patient's age (Grisso and Appelbaum, 1998, pp. 61-76).

practice shall again serve to demonstrate that this would be an inappropriate standard for the medical research context with terminally ill subjects. Just as with appreciation, the difference in the nature of the relationship between a physician and patient as compared to a researcher and subject will similarly impact the reasoning component of competence.

As already discussed, in the medical practice context, physicians and patients "are presumed to share the same goal: promoting patients' health. They may disagree over the means, but a general coincidence of interests is ordinarily the rule."[353] Thus, since it is reasonable for a patient to trust that a physician's analysis of treatment options is conducted with her best interests in mind, being able to follow and ultimately accept the analysis of the physician might be wholly appropriate in the medical practice setting, and a greater level of reasoning may not be required to provide consent to treatment. However, as already discussed, unlike the physician and patient whose interests will likely align, the researcher and subject can be expected to have interests that may conflict. The researcher's interest is in the research, while the subject's interests will likely be her own wellbeing. As previously noted, the procedures applied in research reveal the issue with such a conflict since the methods used to conduct research, such as randomization, double blinding, phase I trial designs…etc., conflict with best care standards that a patient would ordinarily receive.

Though this conflict is one that seems to occur inherently given the nature of research as contrasted with medical practice, the problem of conflict of interest in research is further exacerbated by the presence of corruption.[354] Apart from the

[353] Berg et al., 2001, p. 279.
[354] It is important to note that corruption and abuse, often of a financial nature, is certainly also possible in the medical practice context. (See: Dennis Thompson. "Understanding Financial Conflicts of Interest" *The New England Journal of Medicine,* Vol. 329(8), pp. 573-576, 1993). However, as previously stated the

seemingly naturally occurring conflict issue in research that has already been discussed, as was previously briefly mentioned in Chapter Three there is unfortunately the potential for more sinister types of conflicts of interest,[355] often of a financial nature. This difference between the two types of conflict is sometimes referred to as the distinction between conflicts of commitment and conflicts of interest,[356] whereby the former only refers to the type of naturally occurring conflict that has been the main focus of much of the discussion thus far. However, with the commercialization of scientific discoveries there "has been a growing link between researchers and industry, leading to a profusion of reports about researchers' conflicts of interest and the potential adverse consequences for research participants."[357]

A previously mentioned example from Chapter Three included the case of Dr. Nancy Olivieri, the University of Toronto, the Toronto Hospital for Sick Children and the

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medical research context has inbuilt conflicts stemming from its very nature. This makes it easier for financial conflicts and corruption to appear, sometimes inconspicuously, in medical research than in medical practice since we already expect research to be conducted without an alignment of interests between the researchers and subjects.

[355] See Chapter Three.

[356] Emanuel et al., 2003, p. 370.

[357] Emanuel et al., 2003, p. 369. Though for our current purposes the focus on these conflicts of interest will deal with their impact on subjects, it should also be noted that substantial studies have demonstrated that the sources of funding for research can greatly influence the outcome of the research. For instance, in a study of 349 cardiovascular clinical trials, Ridker and Torres found that "Among not-for profit trials, 51 (49%) of 104 reported evidence significantly favoring newer treatments...By contrast, among for-profit trials, 92 (67.2%) of 137 reported evidence significantly favoring newer treatments...The proportion of trials significantly favoring new treatments for studies jointly funded by for-profit and not-for-profit organizations was approximately midway between these 2 values (56.5%)…[Additionally] for randomized trials evaluating drugs, the proportions favoring newer agents were 39.5% for not-for-profit, 54.4% for jointly sponsored, and 65.5% for for-profit trials" (Paul Ridker and Jose Torres. "Reported Outcomes in Major Cardiovascular Clinical Trials Funded by For-Profit and Not-for-Profit Organizations: 2000-2005" *Journal of the American Medical Association*, Vol. 295(19), pp. 2270-2274, 2006, p. 2272). This report also went on to show that device trials showed the largest discrepancy between not-for-profit and for profit trials in terms of outcome. For more on the manner in which research results can be biased see: Marcia Angell. *The Truth About the Drug Companies* (New York: Random House Inc., 2004). Also for a more current and detailed analysis of the consequences of industry funding on the results of clinical trials, see: Andreas Lundh, Sergio Sismondo, Joel Lexchin, Octavian Busuioc, and Lisa Bero. "Industry Sponsorship and Research Outcome" *Cochrane Database of Systematic Reviews,* Issue 12, Dec. 2012. This analysis provides an examination of a variety of factors including, efficacy results, risk ratio, and harm results, in order to demonstrate the disparity in results and conclusions between industry sponsored studies and those sponsored by other means.

pharmaceutical company Apotex, where Apotex insisted that Dr. Olivieri not inform research subjects of her concerns regarding the toxicity of the experimental drug being administered.[358] Another example previously discussed involved the death of Jesse Gelsinger who was a subject of a Phase I gene therapy trial. Jesse was subjected to various unethical practices including being exposed to inappropriately high doses of the non-validated treatment and being included as a subject to the non-validated treatment despite the fact that "his ammonia levels fell outside the protocol's safety limit."[359] Additionally, it was discovered that an overarching financial conflict of interest likely played a role in such unethical conduct. Specifically, "after Jesse's death, the media reported that one researcher, Dr. James Wilson, held shares in a biotech company, Genovo, which stood to gain from the research's outcome."[360] Apart from these two cases, there exist many more instances of financial conflicts of interests present in medical research. However, it should be noted that these types of harmful conflicts of interest need not necessarily be driven by personal financial gain. For instance other conflicts of interests in research may emerge as a result of a "preference for family and friends or the desire for prestige and power...[as well as the possible] interest in obtaining provocative results or pressure to favor previously published findings of colleagues, friends, or researchers in collaborating groups."[361]

Given the conflicting interests that naturally occur due to the nature in which research is conducted, as well as the potential for these more sinister, often financial,

[358] J. Thompson, P. Baird & J. Downie. *The Olivieri Report: The Complete Text of the Report of the Independent Inquiry Commissioned by the Canadian Association of University Teachers* (Toronto: James Lorimer & Company Ltd., 2001).
[359] Robin Fretwell Wilson. "The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research" *American Journal of Law & Medicine*, Vol. 36, pp. 295-325, 2010, p 300.
[360] Wilson, 2010, pp. 295-296.
[361] Thompson, 1993, p.573.

conflicts of interests that may arise, it becomes apparent that a terminally ill research subject should require at least *Imperfect, but Largely Independent Reasoning*, for competent consent. Such an individual need not be able to research and analyze their predicament and choices at the level of a scholar or expert, but should be capable of largely independent analysis, which will include the ability to receive what a researcher tells her with a healthy skepticism, to effectively evaluate the situation on her own, and be sufficiently confident with her knowledge of the situation to be able to challenge a researcher's advice or opinion should the situation warrant it.[362]

Though as already mentioned, the therapeutic misconception will be discussed more fully in the proceeding conversation regarding understanding and voluntariness, it is important to realize that any factors that contribute to such a misconception, will also present themselves as obstacles to proper reasoning. It thus remains imperative that this higher level of independent reasoning be required, since one who is capable of such reasoning, will also be far more likely to steer clear of the therapeutic misconception and will have her reasoning less impacted by those factors that contribute to such a misconception.

[362] Others have hinted at a similar notion. For example, in a discussion regarding the conflicting interests between researchers and subjects, Berg et al. state that "the need to take this conflict into account in the decisionmaking process is largely responsible for the differences between consent to research and consent to treatment" (Berg et al., 2001, p. 280). As has been suggested here, the best way in which to account for this difference between the research context and the treatment context and possibly remedy the potential damage that may occur to prospective subjects as a result of conflicting interests, is to require what I have referred to as *Imperfect, but Largely Independent Reasoning* in the research context, while only requiring what I have referred to as *Dependent Reasoning* in the therapeutic context. It is important to note that in the research context, the conflicting interests between researcher and subject must not only be appreciated by the potential subject as previously argued, but since what this means for the subject is that she may not be able to fully trust everything the researcher tells her as being in her best interest, must now also be prepared to reason through the advice of the researchers on her own without their assistance or interference, and question anything that appears dubious.

Understanding

Thus far we have mainly only dealt with our first difference between medical research and medical practice, namely the difference in relationship between a researcher and subject as compared to that between a physician and patient. This difference assisted in determining how much higher a standard of appreciation and reasoning ought to be required for the medical research context as opposed to the medical practice context with terminally ill individuals. However, the other two differences, namely the presence of the therapeutic misconception, along with the potential for exploitation of the mental state and situation of the terminally ill subject will be shown to similarly impact the understanding and voluntariness components of competence respectively.

We may recall that the understanding component of competence requires both being in possession of and comprehending the salient information needed for a particular decision. We shall presently only be concerned with the latter. In the medical context, being in possession of the relevant information is largely a function of the medical professionals' willingness to share and impart the information. However, as mentioned at the onset of this chapter, our goal is not to determine what particular information ought to be considered material information and thus a necessary part of disclosure; such an issue has been debated in the literature and by the courts on numerous occasions.[363] Instead, as was the case with appreciation and reasoning, we shall seek the appropriate level of understanding that a terminally ill person ought to be capable of in order to be considered competent to consent to medical research.

[363] Refer back to Chapter One for a discussion on the elements of disclosure and some of the controversies surrounding it.

Though the concept of understanding may seem basic, an analysis regarding the ability to comprehend and

> the psychological processes related to it are not easily defined. A person's accurate assimilation of information involves a complex series of events. First the information must be received as presented, a process that is influenced not only by sensory integrity, but also by perceptual functions such as attention and selective awareness. Whatever is received then undergoes cognitive processing and is encoded in a manner consistent with the person's existing fund of information and concepts, which in turn influences how, and how well, the message is recorded and stored in memory.[364]

However, given that some of these more intricate details surrounding our ability to understand are not vital to the present issue, it may be prudent to leave them aside and construct our understanding spectrum using only general terms such as high, basic and low understanding. While this terminological issue may appear to render the various standards of understanding that will be laid out in our spectrum as somewhat vague, such an issue will be remedied by providing a specific example for each level of understanding. The example will involve a newly diagnosed type II diabetic patient attempting to decide whether to take a particular medication for his ailment as suggested by his physician. Through such an example, the various differences and distinctions between the levels of understanding in our spectrum will be highlighted. See Spec. 3 below for the full six level spectrum of understanding.

Spec. 3 Understanding Spectrum

1. Perfect Understanding – Capable of comprehending everything regarding the particular issue that may factor into one's decision. Such an individual would be able to grasp all possible information and would not be lacking in any knowledge on the matter before him and thus such a level of understanding is impossible to achieve.

> Diabetic Example Case:
> With perfect understanding our diabetic patient would be capable of knowing everything related to his illness as well as the various treatment options. This would

[364] Grisso and Appelbaum, 1998, p.38.

include being able to fully grasp all knowledge related to: i) the nature or causes of his illness, ii) the illness' effects on him both in terms of physically evident symptoms as well as the internal biological and chemical effects on his body, and iii) how the various treatment options work, including the pharmacokinetics and pharmacodynamics[365] of any drug and the likelihood of success related to the various treatment options.[366]

2. Expert Understanding – Capable of comprehending most of the current information regarding a particular issue that may factor into one's decision. This would include the ability to grasp even the more obscure and esoteric information often only assumed comprehensible to scholars, specialists and experts on the matter.

Diabetic Example Case:

With expert understanding abilities, our diabetic patient would be capable of availing herself of all current knowledge on the topic. This would not require perfect understanding, as some matters in the medical sciences remain beyond even the experts, but would require an ability to understand at the level of a medical specialist in the field of diabetes. Such a person for example would need to be able to understand not only that diabetes is a disease related to sugar, but more specifically that it involves the body's inability to either produce insulin or properly use insulin, and the relation of this to the resulting high levels of glucose in the blood. Similarly, such a person would be able to understand not only that this is dangerous, but also why and how it is dangerous at an expert level. For instance, such a person would be able to comprehend specifically *how* this ailment relates to a decrease in quality of life by decreasing mobility, increasing the chance for other health complications such as stroke, heart disease, kidney disease, blindness, amputation…etc. as well as increase the chance of mortality.[367] Similarly an expert understander would be able to comprehend, not only that some treatment options might be helpful for him, but more specifically the effects and risks of varying options and how they compare. For example, this may include understanding that "as compared with standard therapy, the use of intensive therapy to target normal glycated hemoglobin levels ... increased mortality and did not significantly reduce major cardiovascular events."[368] Obviously such a level of understanding is generally lacking in daily decision making and should not be deemed necessary for competence in most cases.

[365] We may recall from Chapter One that pharmacokinetics involves studying the bodily absorption, distribution, metabolism, and excretion of an agent, whereas pharmacodynamics are the "pharmacologic effects of the drug on the body (eg, nadir neutrophil or platelet count, nonhematologic toxicity, molecular correlates, imaging endpoints)" (Christophe Le Tourneau, J. Jack Lee, and Lillian L. Siu. "Dose Escalation Methods in Phase I Cancer Clinical Trials" *J Natl Cancer Inst*, Vol. 101(10), pp. 708-720, 2009, p. 709).

[366] As we proceed through the understanding spectrum it will be precisely the ability to understand matters regarding these three types of issues that will aid in demonstrating the different levels of understanding with our diabetic case example.

[367] Canadian Diabetes Association, Last accessed: 2014. <http://www.diabetes.ca/diabetes-and-you/what/prevalence/>.

[368] Brillon, Cordero, Richardson, Ganz et al. "Effects of Intensive Glucose Lowering in Type 2 Diabetes" *The New England Journal of Medicine*, Vol. 358(24), pp. 2545-2559, 2008, p. 2545.

3. High Understanding – Capable of comprehending much of the current and common information regarding a particular issue that may factor into one's decision. This would include the ability to grasp some of the complicated information surrounding a decision, but would not involve the ability to comprehend some of the more obscure and esoteric information that was the case with the expert level of understanding.

> Diabetic Example Case:
>
> For our diabetic patient, a high level of understanding would not involve being able to grasp the pharmacokinetics and pharmacodynamics of possible drug treatments, as was the case with both higher levels of understanding. Such a person may not even be able to fully comprehend the internal biological and chemical effects of the disease. However, the patient will be capable of a high level of understanding if they can understand the likely causes, symptoms, implications and possible treatment options of the disease beyond a merely superficial level. Such a person for instance should be able to grasp not only that a sedentary lifestyle and high sugar and high fat diet contribute to the disease but would also be able to understand how this occurs. This may include, for instance, being able to understand some of the more intricate details such as which types of fats are particularly harmful and which can be helpful in a proper diet.[369]

4. Basic Understanding - Capable of comprehending some of the current and common information regarding a particular issue that may factor into one's decision. Such a person may lack the ability to understand some of the complexities surrounding the decision as a high level understander might, but would nevertheless be capable of grasping the rudimentary facts necessary to still be able to engage in a meaningful discussion on the topic.

> Diabetic Example Case:
>
> For example a person with diabetes may possess basic understanding if he can only grasp the more commonly known causes, symptoms, and treatment options. This individual may be able to comprehend that poor diet and lack of exercise can contribute to obesity which is related to the disease, that the disease can impact one's quality of life, and that certain medications and lifestyle changes can better the situation, but not understand much more than that. Such a person may also only understand that the medication may help decrease the probability of further harmful effects associated with the disease, even if the person cannot fully grasp what those effects might be.[370]

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[369] For instance it has been demonstrated that saturated fat may be a key contributor to type II diabetes, while unsaturated fat is not (Haitao Wen, Denis Gris, Yu Lei, Sushmita Jha, Lu Zhang, Max Tze-Han Huang, Willie June Brickey and Jenny P-Y Ting. "Fatty acid–induced NLRP3-ASC inflammasome activation interferes with insulin signaling" *Nature Immunology*, Vol. 12, 2011, pp.408–415).

[370] It should be noted that one of the main differences between the high level and basic level of understanding is that while a person who possesses the latter may understand *that* a disease will have x effects or *that* treatment option z will likely result in y consequences, a person with a high level of understanding will further be able to comprehend *how* the disease and treatment options function. For a patient dealing with a disease, understanding how the disease impacts one's life can better assist him in making life choices and preparing accordingly. For instance understanding how diabetes develops may allow one to make better diet decisions. Although, as will be argued in what follows, this may be especially crucial for terminally ill subjects of research, since *how* research is conducted and not just *that* research is being conducted will be imperative to avoiding the therapeutic misconception.

5. Low Understanding - Barely capable of comprehending the current and common information regarding a particular issue that one may reasonably expect to factor into one's decision. For such an individual, even rudimentary facts surrounding a particular decision may be beyond one's abilities.

Diabetic Example Case:

For our diabetic patient, such a level of understanding may entail that he only be able to grasp that his disease is related to unhealthiness, that it is bad for him and that medicine is thought to help, though he may perhaps even struggle to fully acknowledge those facts. Such an individual may be convinced for instance that medicine or any medical intervention cannot aid him and that his disease was obtained by purely random chance and cannot be alleviated or cured.

6. Complete Inability to Understand - Incapable of comprehending any of the information regarding a particular decision. Individuals with such an inability will likely be infants or those with severe mental cognitive impairments.

Diabetic Example Case:

A person with a complete inability to understand will likely not even be able to grasp that he has a disease.

In medical practice "patients are expected to be able to understand that information which must be disclosed under the law of informed consent."[371] Often, though there may sometimes be slight variations between jurisdictions, disclosure requires at least that the health professional "describe the disorder, potential ways to treat it, and their benefits and disadvantages..."[372] Thus it can be stated that in medical practice, possessing sufficient competence for making treatment decisions requires being able to understand the nature of one's ailment, sometimes including its cause, symptoms and long term consequences, if known, as well as some details surrounding the particular treatment options such as their risks and benefits and the associated likelihood of each. However, the extent to which such information must be comprehended is usually at a fairly basic level scientifically. That is to state that we do not require that patients have the ability to understand the cellular or molecular behaviour of their disease, nor the biological and chemical ways that their body

[371] Grisso and Appelbaum, 1998, p. 38.
[372] Grisso and Appelbaum, 1998, pp. 37-38.

will react to various treatment options. However, patients should be aware of the more apparent outward manifestations of their disease and treatment options. For example, we would not demand that a patient diagnosed with a sinus infection understand that the bacteria that often causes acute sinusitis includes Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis, but we would require that they comprehend that this ailment has symptoms that may include headache, facial tenderness and pain in the sinuses, fever, feeling stuffy, sore throat…etc and that antibiotics may help cure it. Thus, the level of understanding needed of patients is certainly not that at the level of an expert, but will often be at best what I have referred to as a basic level of understanding.[373]

Furthermore, in the medical practice setting "understanding choice can also be reconciled with a decision to let a trusted physician decide what is the best treatment. Such a choice... may be made for good reasons and represent a decision in favor of one set of values (safety or anxiety reduction) over another (independence and personal initiative)."[374] However, it must be clear that this would not be appropriate in the medical research setting with research investigators. As previously argued, decisions to place one's trust in one's physician may be well grounded and based on the foundations of fidelity and an alignment of interests that physicians are often thought to have with their patients. However, as already discussed, this is not present in the researcher/subject relationship and thus any similar

[373] In some cases of routine procedures even a low level of understanding has generally been accepted. For example in consenting to a routine blood test in order to determine one's cholesterol, a procedure that a patient may already be quite familure and comfortable with, current standards seem to allow for a patient to consent knowing only that there are little to no risks from a blood test, and that 1-2 weeks from giving blood they will have the data they seek. In such a case an ability to understand more complex information such as how the cholesterol numbers are determined using the blood sample as well as the existence and consequences of varying treatment options should the cholesterol be deemed too high, may not be necessary for a competent consent to a blood test, and as such, a low ability to understand has often been deemed appropriate. It should be pointed out though that despite the fact that such low levels of understanding may have become commonplace for many patients consenting to routine procedures, an argument may be made as to whether or not such low levels of understanding *should* be appropriate for even routine diagnostic procedures such as blood tests.

[374] James Drane. "The Many Faces of Competency" *The Hastings Center Report,* Vol. 15(2), pp.17-21, 1985, p.20.

relinquishing of decisional control to an investigator in a medical research trial may not be deemed competent or be ethically permissible. Thus while basic understanding and allowing a family physician to determine the best course of action, might often be seen as appropriate in the medical practice setting, its supporting reasons cannot similarly be applied in the medical research context with terminally ill subjects.

Instead, what is referred to in the understanding spectrum as a high level of understanding appears ethically necessary in the research context with terminally ill subjects, especially given the presence of the therapeutic misconception. As previously mentioned the main difference between the high level and basic level of understanding is that the former involves grasping *how* something occurs, while the latter may simply involve recognizing *that* something is occurring. For our diabetic example case, high understanding involved the patient being able to grasp not only *that* a sedentary lifestyle and high sugar and high fat diet contribute to the disease but also *how*. Understanding how, for example, his diet relates to the disease better enables him to make certain decisions such as deciding which types of fats should be avoided and which are more permissible. This distinction between the high and basic levels of understanding might be particularly important to terminally ill medical research subjects.

Though basic or in some cases even a low level of understanding may be generally appropriate in the medical practice setting, in the medical research context with terminally ill individuals the presence of the therapeutic misconception creates a need for a greater level of understanding. We may recall that the presence of the therapeutic misconception can severely hinder one's understanding in a way that would render it insufficient for competent

decision making.[375] Thus, if we hope for potential research subjects to be able to steer clear of such a misconception, it is imperative that we require *high understanding*, which would thus involve being able to grasp *how* research is conducted and not just *that* research is being conducted. This seemingly small distinction is imperative in avoiding the therapeutic misconception. For instance, being able to grasp how a Phase I trial functions; that it, for example, ends once the MTD (maximum tolerable dose) is discovered despite any possible benefits from receiving the non-validated drug, can greatly aid a potential subject in combating the therapeutic misconception, thus enabling her to make a competent decision. Similarly it will be imperative for competent decision making that potential subjects understand the other aspects surrounding how research functions. This will include grasping some of the methods applied in research such as randomization, double-blinding, and placebo controls, the grasping of which will aid a potential subject in avoiding the therapeutic misconception since understanding such methods will enable one to see the significant departure from standard therapy that medical research represents.

In addition it will be crucial that subjects also have a high level of understanding regarding the therapeutic misconception itself, and thus be able to grasp not just *that* a phenomenon such as the therapeutic misconception exists, but more specifically *how*. Most notably this will involve grasping at least some of the more common factors that contribute

[375] We must recall that the presence of the therapeutic misconception is not a rare occurrence that arises only with unintelligent individuals, for as studies have demonstrated this has become a pervasive problem in how, many subjects including those with high levels of education and intelligence understand their research trials. As has been documented, "when not given information about how treatment decisions would be made, subjects fabricated reasonable-sounding explanations that placed their therapeutic interests first. Even when information was offered about the procedures that would be employed (e.g., randomization, double-blind, placebos), many subjects failed to acknowledge what they had heard, to apply it to their own circumstances, or to admit that the procedures served any interests other than their personal care" (Berg et al., 2001, p.288). For further examples regarding the pervasiveness of the therapeutic misconception and to what extent it afflicts subjects, refer back to Chapter Three.

to the misconception, including: manipulative tactics employed by researchers, for example by brand naming clinical trials with names such as MIRACL, or SAVED, improper use of language in literature and by researchers, for example terms such as "therapeutic research", or suggesting that clinical trials all have "therapeutic intent", as well as the confusion that seems to exist in distinguishing between a physician and a researcher.[376]

Given this, it is imperative that subjects be capable of comprehending something in addition to what is required of them in the medical practice setting, namely these factors that may potentially hinder understanding. This may be quite difficult to grasp in light of all the opportunities for misconceptions in the research setting. However, how the therapeutic misconception functions and thus the presence of these types of factors should be understood by prospective subjects if we hope for them to make a competent decision based on a comprehension of the correct information. This means that unlike in the routine blood test case, or even in the sinus infection case, there exists a body of knowledge, some of which will be new and complex for terminally ill individuals, which must be understood in order to possess a level of understanding needed for competent consent to medical research.

It is crucial that we recognize that this requirement involves far more than a basic understanding that research is being conducted or that the therapeutic misconception exists, but also how research is conducted and how the therapeutic misconception exists and can impact one's ability to correctly understand the nature of the research trial. The ability to understand must be great enough so as to have a reasonable expectation that potential subjects will not be making decisions based upon a therapeutic misconception. Thus, a high

[376] Refer back to Chapter Three for a more detailed analysis regarding the factors that contribute to the therapeutic misconception.

level of understanding should be necessary for competent decision making in the medical research context with terminally ill subjects.[377]

Voluntariness

We may recall that unlike some current literature, Chapter One demonstrated the need to reformulate the voluntary choice criterion of competence as requiring something other than merely being able to express a choice.[378] Instead the voluntariness necessary for competent decision making refers to an individual's ability to make a decision that follows freely from her understanding, appreciation and reasoning.[379] This is crucial since even if a person is capable of sufficient levels of understanding, appreciation and reasoning, but fails to make her final decision based on those considerations, then such a decision may be a severely incompetent one. As previously expressed, the ability to understand, appreciate, and reason are futile if they do not factor into the final decision being made. Unfortunately such a situation may very well present itself in cases whereby individuals feel weak, insecure, lack emotional strength, lack confidence in themselves or

[377] It should further be noted that requiring a high level of understanding from prospective subjects increases the likelihood that the subject will be able to grasp any new relevant information that arises as the clinical trial proceeds. Continued understanding, as previously mentioned, is necessary for true competence, since competence to consent is best thought of as an ongoing process and thus the need for a high level of understanding requirement appears all the more necessary.

[378] See Chapter One.

[379] It is important to note that a voluntary decision need not proceed from only adequate levels of understanding, appreciation, or reasoning. That is, the voluntariness condition only requires that the decision made stems from one's *own* understanding, appreciation, and reasoning, and that influences not hinder one's ability to make such a free decision. We can imagine for instance an individual who is convinced that vaccinations are a conspiracy by the government to inject mind control devices into the population. Such an individual may choose to avoid receiving vaccinations, and does so freely and voluntarily since his decision stemmed from his own understanding, appreciation and reasoning, as mistaken as they may be. Such a decision would still qualify as incompetent for failing the first three criteria of competence, but not voluntariness. Therefore, a satisfaction of the first three elements of competence is not necessary for the voluntariness criterion to be satisfied.

their knowledge.[380] "As a result, they may become overly susceptible to external influences that would otherwise not be considered undue. They may, for example, be overawed by the prestige of medical professionals or defer to an authority figure in their family."[381] This may be particularly important in the medical, and specifically the medical research, context with terminally ill individuals where decisions may be of an emotionally taxing nature and may require a certain confidence and strength of will.[382]

Prior to constructing a spectrum for voluntariness and determining the level appropriate for the research context with terminally ill subjects, it must be acknowledged that true voluntary action cannot be construed as an action done without any influencing factors.[383] For instance, we would be remiss if we were to consider certain parental

[380] It should be recognized that the characterization of voluntariness as a certain type of ability represents a striking divergence from some current literature on the matter which attempts to identify voluntariness as more of a legal condition fulfilled by the absence of certain types of coercive forces. As Appelbaum, Lidz, and Klitzman state, "for legal purposes, a decision is presumed voluntary if no evidence exists that someone else has unduly influenced it or coerced the person deciding" (Paul Appelbaum, Charles Lidz, and Robert Klitzman. "Voluntariness of Consent to Research: a conceptual model" *The Hastings Center Report*, Vol. 39(1), pp. 30-39, 2009, p. 32). The authors then continue on to explain the types of influences that may constrain voluntariness. Beauchamp and Childress similarly focus on attempting to identify undue forms of influence that would inappropriately control one's decision (Beauchamp and Childress, 2009, p.133-134). However, while a large focus here will indeed be on the types of influence that can be exerted on terminally ill prospective subjects, and determining which ones are inappropriate and how best to protect against them, there is also the added depiction of voluntariness as an ability, namely the ability to freely make a choice that follows from one's own understanding, appreciation and reasoning, which will likely require a certain level of confidence in one's self, emotional stability, and courage. Though approached slightly differently, Laura Weiss Roberts has suggested a similar approach to the conceptualization of voluntariness. She argues that volutariness should be defined "as ideally encompassing the individual's ability to act in accordance with one's authentic sense of what is good, right, and best in light of one's situation, values, and prior history. Voluntarism involves the capacity to make this choice freely and in the absence of coercion" (Laura Weiss Roberts. "Informed Consent and the Capacity for Voluntarism" *The American Journal of Psychiatry*, Vol. 159(5), pp.705-712, 2002, p.707). The recognition of voluntariness as an ability similar to the other elements of competence is vital since it better enables researchers and any competence assessors to pinpoint those who may be particularly vulnerable to making an involuntary decision. Identifying those who may be particularly at risk of making involuntary decisions and further knowing the specific qualities that contribute to making one prone to involuntary decision making is a key step in both being able to assess the voluntariness needed for competence, and creating an environment that is more likely to facilitate voluntary decision-making.

[381] Berg et al., 2001, p. 25.

[382] Again, refer back to Chapter One for a more detailed depiction of voluntariness.

[383] It should be recognized that the conversation here regarding voluntariness will not delve into the deeper metaphysical questions surrounding the freewill/determinism controversy. Instead, for pragmatic purposes,

decisions, such as those that pose financial burdens as lacking in voluntariness because such decisions were influenced by concern for those parents' children. Similarly we would not necessarily wish to consider a spouse's decision to refuse a career opportunity abroad in order to remain with her husband as lacking voluntariness. It seems that we often allow for, and rightly so, certain influences to factor into voluntary decision-making. It would be practically absurd to demand that voluntariness require a complete absence of any and all influences, for that would render it meaningless in the real world where often proper moral and prudential decision-making appears to warrant consideration of those with whom we have certain relationships.

Conversely, it is clear that not all influences are appropriate as some may indeed undermine the voluntariness of the decision. The following discussion will identify some specific examples of such undue influences, but for now, it suffices to state that some of the more commonly acknowledged ones include intimidation/bullying, deceit, manipulation, or any actions and behaviours that place excessive duress on the decision-maker with the intent to coerce or control him. Others have noted this distinction between influences that hinder voluntariness and those that leave voluntariness intact. As Appelbaum, Lidz, and Klitzman note, "the presence of influences does not mean that a decision is not voluntary. A decision is involuntary only if it is subject to a particular type of influence that is external, intentional, illegitimate, and causally linked to the choice of the research subject."[384]

Thus voluntariness proves to be difficult conceptually as it requires that a certain degree of controlling influences not be present while at the same time accepting that a

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the same metaphysical capacity for voluntary choice and action that is assumed in our laws will similarly be assumed as possible here and in what follows.

[384] Appelbaum, Lidz, and Klitzman, 2009, p. 33.

certain degree of influences ranging from considerations of other persons to contextual factors may all legitimately figure into a voluntary decision. Therefore, voluntary decision making depends on one's ability to take only appropriate influences into account and to account for them only up to a reasonable extent. Most importantly, the final decision made must be one that follows from the decision-maker's own understanding, appreciation and reasoning.[385] Given this understanding of voluntariness, see Spec. 4 below for the full voluntariness spectrum.

[385] Some instances of pressure and coercion may clearly constitute undue influence. Extreme intimidation may represent such an example. However, there exist many situations whereby it will be difficult to determine whether or not an influence qualifies as undue. One often suggested way to characterize the distinction between influences that are undue and those that are appropriate in competent decision making is to determine whether or not the influence controls the decision-maker. For instance, "if a physician orders a reluctant patient to undergo cardiac catheterization and coerces the patient into compliance through a threat of abandonment, then the physician's influence controls the patient. If, by contrast, a physician persuades the patient to undergo the procedure when the patient is at first reluctant to do so [by using convincing well reasoned arguments], then the physician's actions influence, but do not control, the patient" (Beauchamp and Childress, 2009, p.133). One upshot of the explanation of voluntariness offered here is that it provides a method to assist in making these determinations. That is, it can be said that once it becomes clear that the influence in question has compromised the decision-maker's ability to make a decision based on his understanding, appreciation and reasoning of the situation, then it is likely that the influence has become undue. In the above example, the threat of abandonment by the physician would clearly count as an undue influence since the patient's decision would no longer be made based on his own understanding, appreciation, or reasoning of cardiac catheterization, but instead on fear. Whereas, appropriate persuasion through well reasoned arguments may enable the patient to better develop his own understanding and appreciation and ultimately still make a voluntary decision based on those considerations. Chapters Five and Six will delve more deeply into how to best test for an adequate level of volutariness and the other elements of competence.

Spec. 4 Voluntariness Spectrum[386]

1. Perfect Voluntariness- This may be difficult to envision, but would essentially involve an individual who was completely impervious to any forms of undue influences or coercion.[387] Such a person would be able to perfectly balance the extent to which any external influences should factor into her final decision and thus could never be controlled by others.

2. Extremely High Voluntariness- Very often capable of reaching a decision for one's self based upon his own understanding, appreciation and reasoning regarding the situation. Such an individual should not be characterized as being insensitive to other's interests or as never taking others into account, but rather as never being controlled by influences such that any decision made would fail to follow from his own understanding, appreciation or reasoning. Thus such a person can be persuaded with reason, and is willing to take the advice and interests of others into consideration, but only up to an appropriate extent and will ultimately possess the confidence needed to make the decision for himself. This person would likely be secure and confident enough in his own decision making so as to be able to resist even strong pressures and coercive attempts from others such as excessive appeals to emotion, or exploitative and manipulative tactics.

3. High Voluntariness- Often able to reach a decision for one's self based upon her own understanding, appreciation and reasoning regarding the situation. Such a person may still at times be susceptible to emotional pleas,[388] and manipulative or exploitative tactics,

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[386] It should be noted that "until recently, there has been a remarkable paucity of empirical research on the capacity for voluntary choice in the context of consent, and the means to assess it" (Charland Louis. "Decision-Making Capacity", *The Stanford Encyclopedia of Philosophy* (Spring 2014 Edition), Edward N. Zalta (ed.), URL = <http://plato.stanford.edu/archives/spr2014/entries/decision-capacity/>). Though this situation is beginning to shift as more scholars in the field recognize the complexities surrounding voluntariness and its significance for competence and informed consent, we are far from a general consensus on the appropriate characterization of it, as well as the best way to test for and protect it.

[387] It is important to note that coercion as it is used within this context applies only to situations whereby another human agent attempts to gain control of the decision maker. This contrasts with the broader and sometimes common usage of the term "coercion" as referring to any scenario where the decision maker has her options limited, which could then include cases where a person's choices are limited though chance and states of affairs unrelated to any other person. However, coercion in any morally significant sense should be defined more narrowly and can be properly characterized by the "following definition: A person is coerced when her choices are unfavorably narrowed by someone who is trying to get her to do something she would not otherwise do" (Jennifer Hawkins and Ezekiel Emanuel. "Clarifying Confusions about Coercion" *The Hastings Center Report*, Vol. 35(5), pp.16-19, 2005, p.17). Refer back to Chapter Three for a further explanation of the difference between a morally significant coercion and choice constraining natural states of affairs.

[388] This is not to suggest that emotions can never factor reasonably into a decision. Indeed given that often to be human may involve possession of moral sentiments and feelings of compassion and generosity, it is clear that competent and voluntary decisions may often in daily lives be persuaded by emotions. Person A's decision to skip a concert she had be looking forward to for months to tend to a grieving friend who recently lost a loved one would and should certainly count as a voluntary decision. However, it is important to note that emotional dispositions may only form a part of a voluntary decision, as the moment a decision is made purely on emotional grounds with little to no application of the understanding, appreciation, and reasoning that comprise competent and thus autonomous decision making, it can be seriously questioned whether or not such a decision flowed voluntarily from the person making it. We can imagine person B,

but will often likely have the confidence in her own decision making abilities that she can filter out most voluntariness hindering influences.

4. Medium Voluntariness- Sometimes able to reach a decision for one's self based upon his own understanding, appreciation, and reasoning. Such a person may be capable of making decisions, but may sometimes lack the confidence in himself to do so without the support of others. Such an individual may not always trust his own knowledge or judgments and may thus rely too heavily on the advice of others, or may find it difficult to resist pressure from others as well.

5. Low Voluntariness- A person who possessed this level of voluntariness may be unlikely to reach a decision that stemmed from her own understanding, appreciation and reasoning. Often individuals who are afflicted with extreme fears, phobias, addictions, or anxiety may be more susceptible to exploitative tactics that use those fears or anxieties in order to gain controlling influence over the person. Persons may also qualify as possessing only a low level of voluntariness if they see themselves as too ignorant or too emotionally weak to make certain decisions and may thus excessively appeal to authority figures, or may at times even be easily swayed by the mere suggestion of another.

6. No Voluntariness- Similar to perfect voluntariness, it is difficult to imagine what this may look like in an adult. Those who are completely incapable of making any voluntary decisions will likely only represent newborns, very young children,[389] and the extremely mentally disabled.

The recognition of the significance of voluntariness in medical research participation decision making is fairly ubiquitous. In fact the first line of The Nuremberg Code states: "the voluntary consent of the human subject is absolutely essential."[390] Sometimes it is assumed that voluntariness merely requires that a person not be

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who though capable of high levels of understanding, appreciation and reasoning, lacks confidence in himself, and is often fearful of confrontation or disappointing others. As a result person B may make decisions that may not follow from his ability to understand, appreciate or reason; instead he may be easily persuaded to do things out of fear of disappointing others, or he may feel pressured by others and fearing confrontation may make decisions that are not really his. Peer pressure may indeed be the most apt example to describe this phenomenon, since adolescents may often make decisions due to feelings of pressure and fears of not "fitting in", that they otherwise would not make. Depending on the circumstances, it may be appropriate to consider some such decisions as lacking in voluntariness.

[389] Some have suggested that "an individual's capacity for voluntarism is affected by the person's development in terms of cognitive abilities, emotional maturity, and moral character" (Roberts, 2002, p.707) which may all be fairly minimal at young ages. A greater capacity to make voluntary choices "accompanies the older adolescent's emerging abilities to think abstractly, to recognize personal values in relation to those of others, to reflect on one's place in the world, and to begin to consider the repercussions of a decision based on some accumulated personal life experience" (Roberts, 2002, pp.707-708).

[390] U.S.A. vs. Karl Brandt et al. In *Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law*, Vol. 2, No. 10, Washington, D.C.: U.S. Government Printing Office, 1949.

physically forced into any decision or action. However, the nature of voluntariness and its fulfillment as a criterion of competence are far more complicated. The Nuremberg Code briefly elucidates this point by stating that subjects "should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion…"[391] Unfortunately, we may recall that our second significant difference from Chapter Three between the medical practice and medical research context significantly impacts voluntariness. This second significant difference between the two contexts, and the only one that has yet to be discussed presently, namely the potential for exploitation of the situation or mental state of terminally ill subjects, demonstrates the increased concern regarding voluntariness in the medical research context.

As elucidated in Chapter Three, terminally ill subjects may often be in pain, desperate, unrealistically hopeful, and anxious about financial concerns related to the cost of treatment, along with dealing with other possible stresses as well. While unfortunate situations alone are not sufficient to deem decision making involuntary, it does suggest that these individuals may be additionally susceptible to enticements of hope, possible deceit, manipulation or pressures.[392] Terminally ill potential subjects are vulnerable to having their situation exploited by those interested in admitting research subjects into clinical trials. Thus while situations and states of affairs do not in themselves diminish voluntariness, they can make it more likely that something else will.

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[391] U.S.A. vs. Karl Brandt et al. In *Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law*, Vol. 2, No. 10, Washington, D.C.: U.S. Government Printing Office, 1949.

[392] Appelbaum, Lidz and Klitzman offer a similar point suggesting that "situational constraints may set the stage for intentional efforts to influence decisions (including intentional manipulation of the situation created by the constraints) and may make intentional efforts both easier to engage in and harder to detect" (Appelbaum, Lidz and Klitzman, 2009, p. 33).

As Chapter Three highlighted, various methods and approaches are often employed by researchers that would seem to exploit the situation and mental state[393] of the terminally ill prospective subject and thus undermine voluntariness. This included tactics such as brand naming clinical trials with names that suggest miraculous cures, employing recruitment strategies that use the hopeful and desperate mindset of individuals in order to make the clinical trial appear in an unrealistically positive light, or even applying pressure on potential subjects who may not have the confidence to resist.[394] Even power relationships and feelings of trust and dependency can be exploited in this context.[395] As the *Tri-Council Policy Statement* notes, IRBs and REBs should "pay particular attention to the elements of trust and dependency - for example, within doctor/patient… relationships - because these can constitute undue influence on the patient to participate in research projects, especially those involving residents in long-term care facilities or psychiatric institutions."[396] This may be especially problematic

[393] It should be noted that the mental state of some terminally ill individuals may render them, at least at certain times, with a very low ability for voluntariness and thus extremely susceptible to influence that may have otherwise not necessarily been excessive or undue. Physical illnesses, for instance, may sometimes be accompanied by depression and since "ambivalence and indecisiveness, poor energy, and negative thoughts are among the elements that define depression and physical disorders" (Roberts, 2002, p.708), it becomes clear that illness may severely impact one's ability for voluntariness. As previously noted, pain may also affect the mental state of terminally ill individuals as it may create a greater sense of desperation further making one vulnerable to influences that may lead to making an involuntary choice. Refer back to Chapter Three for further detail regarding pain's potential role in the mental state of individuals considering medical research participation.

[394] As previously discussed, some of these tactics also contribute to the therapeutic misconception and thus may also undermine other elements of competence.

[395] See: Nancy Kass, Jeremy Sugarman, Ruth Faden, and Monica Schoch-Spana. "Trust: The Fragile Foundation of Contemporary Biomedical Research" *The Hastings Center Report*, Vol. 26(5), pp.25-29, 1996, for more on how trust relationships specifically with one's physician can impact the decision-making process.

[396] Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.* 1998 (with 2000, 2002 and 2005 amendments) p.2.4.

with a terminally ill patient whose physician also recruits subjects for certain research trials.[397]

Apart from the actions and behaviours of physician recruiters and of research investigators, Chapter Three had further mentioned the potential for certain familial pressure which can create undue influence. Many ill subjects' struggle to afford the costs of their health care leads them to enroll in clinical trials.[398] Again, though such a situation may not necessarily deem a choice as lacking voluntariness, it may if the ill individual feels unduly pressured by his family into participating in a clinical trial in order to unburden them with the financial costs.

Thus it appears that the situation and mental state of terminally ill individuals can be such that they are susceptible to controlling influences that will have them make decisions that did not freely follow from their own understanding, appreciation, or reasoning of the situation. If a terminally ill individual adequately understands, appreciates and reasons about whether or not to participate in a medical trial, but ultimately makes her decision to participate during a period of desperation that was unfairly exploited by research recruiters, due to pressure from trusted physicians or family members, or even during a phase where the individual lacked the emotional strength or confidence needed to resist certain influences, then such a decision may lack the voluntariness necessary for competence.

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[397] As previously mentioned this situation can also add to the confusion that already exists when distinguishing between researcher and doctor and the differing roles of each and thus may contribute to the therapeutic misconception. Refer back to Chapter Three for more on this issue.

[398] See: The President's Advisory Committee on Human Radiation Experiments, "Chapter 16: Subject Interview Study," Endnote 47, in Final Report of the Advisory Committee on Human Radiation Experiments (Washington, D.C.: U.S. Government Printing Office, 1995); and Kolata and Eichenwald. "Stopgap Medicine: For the Uninsured, Experiments may Provide the Only Treatment" *New York Times*, June 22, 1999. Also refer back to Chapter Three for further details relating to the significance of monetary issues in clinical trial participation decisions.

Though the previous sections employed the differences between medical practice and medical research in order to demonstrate that a specifically higher level of appreciation, reasoning, and understanding respectively are necessary in the medical research context with terminally ill individuals, the same approach would seem odd with voluntariness. As previously argued, a terminally ill subject should require what I have referred to as imperfect but independent appreciation, imperfect but independent reasoning, and a high level of understanding in order to make a competent decision regarding medical research participation. Possessing lesser abilities in any of those categories would render one's decision incompetent. However, requiring a specific level of ability related to voluntariness from our spectrum would be inappropriate since being susceptible to manipulation, deceit, exploitation, or lacking in confidence in one's self or one's knowledge does not itself necessitate that someone will be manipulated, deceived, exploited, or pressured and thus make an involuntary choice; it rather just increases the probability of such events. We would rightly hesitate to consider voluntary the decision of a terminally ill person to participate in research if she possessed anything less than what I have referred to as medium voluntariness, but otherwise the differences between the other levels of voluntariness seem only to affect the likelihood that someone's decision will be involuntary.

Thus we should always hope for the utmost ability to make a voluntary decision from our decision makers, in this case terminally ill potential subjects of research, while at the same time realizing that a lesser ability to do this does not automatically disqualify one from competent decision making. Therefore, instead of recommending a specific level of voluntariness that is appropriate for the medical research context with terminally

ill subjects, we shall instead employ Hans Jonas' descending order of permissibility concept, along with a recognition that the recruitment process of terminally ill subjects should be conducted in such as way so as to prevent involuntary choices from being made.

Hans Jonas was fairly skeptical regarding allowing the ill to participate in clinical trials, for as he states, their "physical state, psychic preoccupation, dependent relation to the doctor, the submissive attitude induced by treatment- everything connected with his condition and situation makes the sick person inherently less of a sovereign person than the healthy one."[399] However, what has been presented thus far here is far less pessimistic. Indeed, the arguments advanced presume that the terminally ill may still make competent and autonomous choices, it may just be more difficult to do so given the context. However, despite Jonas' pessimism, he offers a useful concept for the recruitment of subjects. He suggests that recruitment be done by applying his rule of the descending order of permissibility, whereby "those patients who most identify with and are cognizant of the cause of research-members of the medical profession (who after all are sometimes patients themselves)-come first; the highly motivated and educated, also least dependent, among the lay patients come next; and so on down the line."[400] The idea here being to attempt to admit only those subjects into research for whom it would seem the least unethical to recruit. Though as a whole such an approach may seem problematic since it may appear to restrict recruitment too far[401] or lack specified categories along the

[399] Hans Jonas. "Philosophical Reflections on Experimenting with Human Subjects" *Daedalus*, Vol. 98(2), pp.219-247, 1969, p.239.
[400] Jonas, 1969, p.239-240.
[401] Though Jonas suggests that such a problem can be alleviated by continuing down the order of permissibility, he appears to recognize that such a procedure may indeed lead to slower recruitment. However, he does not allow this to deter his ethical outlook as he states that we must "remember that a slower progress in the conquest of disease would not threaten society, grievous as it is to those who have to

order of permissibility such that it could be practically applied, it may be reconstructed and applied to our voluntariness spectrum.

Obviously we desire that potential subjects be the type of individuals who possess what I have labeled as an extremely high ability for voluntariness. This would entail that they be confident in their own decision making and so cannot be easily swayed by undue appeals to emotion, authority figures, or manipulative, deceitful and exploitative tactics. We would further hope that a potential subject of research be secure enough in her own abilities and emotionally stable enough such that she would feel comfortable stating and defending her position/decision against undue pressure and furthermore be able to resist any coercive tactics. However, since voluntary choice is still possible for those who possess lesser abilities in this regard, we may appropriately accept that they too can competently decide to participate in a trial and move down the voluntariness spectrum via the decreasing order of permissibility concept until the clinical trial has been filled. However, given that this approach might still ultimately permit some individuals who possess only a medium ability for voluntary decision making to enroll in clinical trials, it becomes incumbent upon us to ensure that the environment in which they make the decision to participate fosters a voluntary decision making process. As the final section of this chapter will elucidate, this is likely best achieved through the employment of a subject's rights/competency advocate whose role it will be to both assess and bolster the elements of competence with prospective terminally ill subjects.

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deplore that their particular disease be not yet conquered, but that society would indeed be threatened by the erosion of those moral values whose loss, possibly caused by too ruthless a pursuit of scientific progress, would make its most dazzling triumphs not worth having" (Jonas, 1969, p. 245).

Freedman Revisited

Before proceeding with an explanation of such a strategy, it would be prudent to note a departure from some current thought. As previously mentioned in Chapter Three, Benjamin Freedman maintained that an ignorant consent to research participation may be ethically permissible. It was then argued that the three arguments Freedman presented in favour of such an account were each flawed for a variety of reasons.[402]

However, here again, we may note a strict departure from Freedman's approach. While it has presently been argued that a terminally ill potential subject of research ought to possess certain required levels of the sub-abilities of competence in order to be able to ethically consent to participate in the research, Freedman instead offers his requirement of responsibility condition.[403] This suggestion states that we ought to only require that a potential subject make a responsible, even if uninformed and ignorant, choice. More specifically, Freedman asserts that the responsibility:

> which we require is to be predicated not on the nature of the particular choice, but on the nature of the patient/subject. What we need to know is whether *he* is a responsible man ('in general,' so to speak), not whether the choice which has been made is responsible... In this sense, responsibility is a dispositional characteristic. To say that someone is a responsible individual means that he makes choices, typically, on the basis of reasons, arguments, or beliefs-and that he remains open to the claims of reason, so that further rational argument might lead him to change his mind.[404]

[402] More specifically it was argued that the differences between the research and medical practice context, especially the difference relating to the nature of the relationship between a physician and patient as compared to that between a researcher and subject, the fact that Freedman's examples failed to be actual examples of ignorant consent, and the fact that at least in this particular context, ignorance, even if willful, renders one incompetent to make a decision, all demonstrated that Freedman's proposal and its underlying arguments were untenable. Refer back to Chapter Three for the entire objection to Freedman's proposal.
[403] It should be noted that Freedman additionally includes a voluntarism condition for proper consent. However, we shall presently only be concerned with Freedman's argument regarding permitting an ignorant but responsible consent. Freedman's account of voluntarism and more specifically the manner in which it may differ from our account of voluntariness will be discussed in Chapter Six.
[404] Benjamin Freedman. "A Moral Theory of Informed Consent" *Hastings Center Report,* Vol.5(4), pp.32-39, 1975, p. 35.

It is important to recognize that Freedman characterizes his responsible choice condition in this manner in order to avoid permitting overly paternalistic actions toward potential subjects. By suggesting that we only consider whether the person is typically responsible, and not consider whether the particular choice itself is a responsible one, Freedman hopes that we have prevented those inclined to behave paternalistically from being able to refuse another's choice merely because they deemed it to be a bad or irresponsible choice. However, despite this alleged upshot, permitting ignorant consent to research and applying this responsible choice condition, instead of requiring a more typical informed consent procedure, or the more rigorous competence requirements that have been argued for in this chapter, proves to be a flawed proposal.

First, a proper understanding of competence and the medical research context reveals that it is ethically irrelevant whether or not a potential subject of research has previously demonstrated responsible decision making in other aspects of his life and may therefore be assumed to be a responsible person. As has already been argued, competence to consent is task and context relative. Similarly, it may be argued that one's ability to make a responsible choice is relative to the demands of the particular context. A person may possess a great level of understanding, appreciation, reasoning, and voluntariness and thus be able to engage in a meaningful and responsible decision making process in one context, but be utterly lacking in some or all of those abilities in another context. Contexts that are overly emotional, stressful, or complicated, for instance, may make responsible decision making more difficult. Thus, in assessing whether one's consent to participate in research is competent or responsible, it would be prudent to examine the choice being made within the actual context within which it is being made, as opposed to

determining whether the decision-maker has made responsible choices in the past in other contexts. This is to state that past decision-making performance, in separate unrelated decision-making contexts, fails to be a good indicator of performance in new contexts. Even Freedman admits that "all responsible people are at times pigheaded, at times short-sighted, at times flighty. That is to say, all responsible men at times act irresponsibly."[405]

The difficulty in extrapolating from past decision-making performances might be especially true for the medical research context with terminally ill subjects, since as has been demonstrated, this context allows for many otherwise previously competent and responsible individuals to make less than competent and responsible decisions. This, as previously explained, is due to the myriad of factors, including possible desperation, the presence of pain, the potential for exploitation, and the therapeutic misconception along with all of its possible contributing factors, which make this context a particularly difficult one for decision-makers.

A second issue with Freedman's proposal is that it remains unclear how one is ever able to determine that a person is by nature a "responsible person". The problem is that the term "responsibility" is ambiguous and Freedman fails to provide any concrete criteria for who may qualify as being responsible.[406] It may be reasonable to suggest that responsible decision-making requires that one be able to make a choice having understood the relevant facts related to the decision, been able to somewhat foresee what it may be like to live with the consequences of the decision, and to be able to compare

[405] Freedman, 1975, p. 35.

[406] It should also be acknowledged that even if Freedman provided some criteria for responsibility, it would still remain unclear who would decide whether the decision-maker is a responsible person. Certainly researchers would typically not have the type of longstanding relationship with prospective subjects that would be needed in order to note a past pattern of responsible decision-making. In fact, in many instances the informed consent process is delegated to someone on the clinical team who is a stranger to the prospective subject, and who will likely not even be the primary investigating physician. (I am grateful to Professor Duff Waring at York University for bringing this point to my attention).

and contrast possible choices through a risk/benefit analysis. However, this would entail that responsible decision-making may require some level of understanding, appreciation, reasoning, and thus competence, and if so, then Freedman would be left with the same question which began this current project, namely determining how much competence ought to be required for subjects to be able to consent to participate in research. Though Freedman may not wish to construe responsibility in this fashion, it remains unclear how else to define it,[407] and given this ambiguity, it thus further remains uncertain how one will be able to determine whether or not a person satisfies this responsibility condition.

Given these two issues, it becomes clear that such an approach is not practically tenable, nor would it aid in improving the ethicality of research. We ought thus to proceed acknowledging that the competence sub-ability requirements previously set out, are likely to be a better way forward in order to ensure that prospective terminally ill subjects of research can ethically provide consent to participate, and that their autonomy is protected.

The Strategy going Forward

Given that we have now established a minimum level of ability for all four elements of competence, it can be stated that thus the minimum level of competence required for a terminally ill subject to consent to participate in research would be the amalgamation of these four minimum standards. That is, only by satisfying the minimum

[407] It would be difficult to argue that a responsible decision can be made if a decision-maker is unable to understand any of the relevant facts, appreciate the consequences of the decision, or be able to reason through the pros and cons of possible choices. Indeed, without at least some minimum level of ability to do this, it becomes difficult to imagine what responsible decision-making would look like.

levels of each of these four sub-abilities can one be said to truly be substantially competent in order to be able to provide consent in this medical research context.[408]

How ought policy to proceed then with terminally ill research subjects? It should be apparent by now that merely requiring that an informed consent form be signed without an adequate determination of competence represents too lax and ethically perilous a standard.[409] Ensuring a sufficient level of competence is paramount in informed consent, since any informed consent without competence fails to be any real expression of a person's autonomy. This chapter has already demonstrated how much competence one should possess in order to be able to provide consent to medical research for terminally ill subjects. However, the question remains regarding the specific policies that ought to be enacted in order to best protect terminally ill potential subjects of

[408] It must be realized that two separate recommendations have actually been proposed by the preceding arguments. The explicit recommendation is precisely what has been stated, namely that the four elements of competence should be required at the levels I have specified, and that a descending order of permissibility should be utilized for voluntariness. However, there is an implicit recommendation here as well, namely that there must be an overall shift in mentality and approach when addressing competence in this setting. In a discussion regarding competence to consent to treatment, Grisso and Appelbaum point out that we tend to "all assume, appropriately, that the people with whom we deal are competent to make decisions about their own lives- indeed, the law makes a similar assumption- only when our unconscious monitoring detects something unexpected do we attend to it directly" (Grisso and Appelbaum, 1998, p.61). This statement refers to the fact that in medicine, as in most other facets of life, we assume others to be competent, unless we are given a particular reason to suspect otherwise. However, though the proposal here stops well short of assuming incompetence for potential subjects, it does suggest that in the medical research setting with terminally ill persons, it would be inappropriate to simply assume competence. Thus, some measures and assessments ought to be implemented that may assist in bolstering the competence of prospective subjects as well as ultimately testing for the required levels of the four sub-abilities in order to ensure sufficient competence to consent to the research trial. Specifics regarding such measures and assessments will be explored in the following chapters.

[409] This further represents a departure from current practice in the therapeutic setting since in typical medical practice a patient is presumed to be competent unless there are good reasons to suspect otherwise and thus actual determinations of competence are not generally thought necessary. For example, the Health Care Consent Act of Ontario states that "a person is entitled to rely on the presumption of capacity with respect to another person unless he or she has reasonable grounds to believe that the other person is incapable with respect to the treatment…" (Health Care Consent Act, S.O. 1996, CHAPTER 2 Schedule A, S. 4 (3)). However, peoples' competence "will depend in part on the demands of the specific task that they face" (Grisso and Appelbaum, 1998, p. 21) and as previously argued the task of consent and the context within which that task must be performed for terminally ill research subjects is radically different from the task of consent in the medical practice setting for patients, such that automatic presumptions of competence in the medical research context with terminally ill individuals would be ethically inappropriate.

research. In a discussion regarding phase I trials on the terminally ill, George Annas suggests a threefold approach. He asserts that:

> In addition to all other legal and ethical requirements for the approval of a research protocol by national and local scientific and ethical review boards (including IRBs), research in which terminally ill patients participate as research subjects shall be approved only if the review board specifically finds that:
> (a) The research, if it carries any risk, has the intent and *reasonable probability* (based on scientific data) of improving the health or well-being of the subject, or of significantly increasing the subject's length of life without significantly decreasing its quality;
> (b) There is no *a priori* reason to believe that the research intervention will significantly decrease the subject's quality of life because of suffering, pain, or indignity attributable to the research; and,
> (c) Written informed consent…may be solicited only by a physician acting as a *patient rights advocate* who is appointed by the review committee, is independent of the researcher, and whose duty it is to fully and objectively inform the potential subject of all reasonably foreseeable risks and benefits inherent in the research protocol.[410]

Though such a proposal might indeed protect terminally ill research subjects, it is important to note that it is not overly realistic. Both conditions (a) and (b) may seem not only too difficult to satisfy, but condition (a) specifically might prove to be impossible.

Condition (a) which requires that the research must have the intent and reasonable probability of improving the health or well-being of the subject is somewhat ambiguous. It could imply that the primary intent of the research must be the health interest of the subject. However, as was previously argued, given the methodologies employed in medical research, namely randomization, placebo controls, and double blinding,[411] research cannot be viewed as having the primary intent of achieving the well-being and health interests of its subjects. We may instead though interpret this condition to imply merely that some intent, and not necessarily the primary intent, must be the improvement

[410] George Annas. "The Changing Landscape of Human Experimentation: Nuremberg, Helsinki, and Beyond" *Health Matrix*, Vol. 2, pp. 119-140, 1992, p. 138.
[411] As previously argued these methods applied in research demonstrate a strict departure from best care standards for patients.

of the health or well-being of the subject. However, this interpretation would similarly not suffice as it would render phase I trials impossible.[412] Phase I trials are designed specifically to test toxicity and cannot be misconstrued as having any type of therapeutic intent. Furthermore, given the incredibly low response rate[413] and the fact that the trial will end once the maximum tolerable dose is determined regardless of any therapeutic benefit, phase I trials cannot have any reasonable probability of improving one's health. Annas' policy would thus essentially prohibit phase I trials on the terminally ill. It is then unclear how the data obtained from these trials would ever be obtained and how the other phases of the clinical trial could ever proceed.

Though critics may point to the flaws in Annas' overall proposal, we would be remiss if we abandoned all three of his conditions as a result of some difficulties we see in the first. Indeed, his condition (c) may prove particularly useful as the starting point to the type of policy that can protect terminally ill subjects by ensuring their competence. Annas' condition (c) can be reformulated as requiring that a third party patient/subject rights advocate, who is completely unrelated with the research, be charged with the task of attempting to bolster some of the sub-abilities of competence with potential subjects and ultimately be able to test those abilities to ensure that subjects are sufficiently competent to consent. This third party individual should be the sole party soliciting the consent from terminally ill potential research subjects. As a result of the various tasks and obligations this competence assessor and consent solicitor will undertake, such a position

[412] Annas admits this as a consequence of his recommendations, but fails to provide a method by which research could then continue without the information derived from phase I trials.
[413] Refer back to earlier in this chapter where the response rate in phase I trials was discussed.

should only be filled by one qualified in competency assessment and knowledgeable in the specific issues revolving around terminally ill subjects of research.[414]

Prior to a discussion of the more specific duties of such an individual, it should be noted that this process appears to suggest that the competency assessment be done verbally through communication instead of being written. Though assessing competency, especially the understanding or comprehension portion of it, could be attempted through the use of written questionnaires, and for certain medical contexts such a tactic has been suggested for decades,[415] it would seem that communication based approaches may better achieve the desired aim. Firstly, as was already mentioned earlier in this chapter, verbal communication better facilitates comprehension and information retention than do written documents.[416] Secondly, it has also been argued that "the use of a questionnaire may embarrass those who feel they are being 'tested' and could miss barriers to understanding that are not included on the form…In like manner, patients who 'pass the test' may feel falsely reassured of their understanding and be reluctant to raise additional

[414] It should be noted that such a strategy may have the added upshot of quelling one of the concerns that might be associated with requiring an increased level of competence for research participation. Namely, even though the approach advocated for here has not been to engage in any hard paternalism by prohibiting research on the terminally ill, as was previously noted in Chapter Three, the revelation that a greater level of competence should be required in the medical research context has the consequence that many of the subjects who may have previously been thought of as competent to consent to medical research would now fall below the new minimum threshold. Thus, enrollment may decrease in certain medical trials. Though this may be the unfortunate result of conducting ethical research on the terminally ill, employing the reformulated version of Annas' condition (c) may mitigate such consequences by bolstering the competence of potential subjects of research.

[415] See for instance: R. Miller and H.S. Wilner. "The Two-Part Consent Form: a suggestion for promoting free and informed consent" *New England Journal of Medicine*, Vol. 290(17), pp.964-966, 1974. Miller and Wilner suggest replacing the typical consent form with a two part version. The first part consists of the typical informational disclosure, while the second part consists of a questionnaire that attempts to assess patient's comprehension.

[416] Refer back to the onset of this chapter for further information regarding the superiority of verbal communication compared to a written format.

questions."[417] Thus, it would seem wise to pursue oral competency testing procedures as opposed to the more typical written methods.[418]

Though the next chapter will delve into the issue of how to specifically test for our newly defined minimum level of competence, it would be prudent to discuss generally some of the tactics and approaches the third party competence bolsterer/assessor should employ.

This patient/subject rights advocate would likely be more effective in bolstering competency if she began by discussing those areas in medical research that are often the hindrances to adequate competency. To such an end, the first task would be to adequately explain the therapeutic misconception, and be prepared to attempt to dispel it if the individual indeed has the misconception. This may involve a discussion regarding some of the misleading terminology and brand naming used by researchers and research companies, or it may involve an explicit statement that the primary purpose of medical research is non-therapeutic. Some of the specifics of the conversation would of course be dependent on the research trial itself.

The second task, related to the first, would involve explaining the difference between medical research and medical practice, specifically the difference in the goals and aims of a research trial and the researcher himself compared to the aims of a physician in ordinary medical practice. With the goals and aims of research being not only explicitly stated, but contrasted with the goals and aims of medical practice, the

[417] Berg et al., 2001, p.198.

[418] Additionally it would likely be difficult to devise a questionnaire that could appropriately evaluate the voluntariness of one's decision. The conversational method would fare far better in this endeavour as "an assessment of voluntariness might [best] begin with a general inquiry into the motivations for a person's decision" (Appelbaum, Lidz and Klitzman, 2009, p. 35). Such a simple approach might serve the assessor well in attempting to determine the presence of any undue and controlling influences.

potential subject will be put in a position to be more competent going forward since she will be less likely to confuse the researcher with her physician throughout the research trial. Thus, the subject is given a warning that will allow her to be more cautious and approach any advice from researchers, during the medical research trial, with the healthy skepticism quintessential of the competent research subject.

Through a discussion of the therapeutic misconception and an explicit statement regarding the differences between research and therapy as well as the differences between a researcher and one's physician, potential subjects may have a better understanding, might better be able to reason through their situation, and will more likely be able to make a voluntary choice. However, the consent solicitor must also attempt to bolster the appreciation of the potential research subject. Such an endeavor may prove quite difficult and will likely vary, sometimes greatly from subject to subject. The reason for this is that, as previously stated, appreciation is mainly centered on the particulars of a person's life, and specifically the way in which participation in research will affect those particulars. Thus, since such particulars will vary from person to person, the approach and discussion the consent solicitor engages in will have to vary as well in order to meet the specific needs of the subject.[419] The general aim of such a discussion would be to attempt to facilitate a conversation that enables potential subjects to engage with the ways in which participation in the research trial could impact their lives and the various ways in which those impacts would affect them personally.

Finally after the initial consultation and any subsequent conversations that may be requested by the potential subject, at a separate time and date the subject may request to

[419] Something similar can be said in regards to voluntariness as well since the potential mental states that may reduce one's ability to make a voluntary choice will likely vary, sometimes to a great extent, between individuals.

sign the informed consent form.[420] Prior to this though, the consent solicitor shall have one last task, which will be to verbally test the overall competence of the subject. This shall be done through one final conversation where the consent solicitor will ask a variety of questions and through a qualitative analysis will determine whether the subject is sufficiently competent to consent to the research trial. The specifics and details of such a competency assessment is the issue to which we may now turn.

[420] The time in between the initial consultation and the actual signing of the consent forms does not need to be a lengthy one, for even a day or two may suffice. Such a requirement is deemed necessary in order to enable the prospective subject to digest the information that has been provided, reflect on the conversation had with the patient/subject rights advocate, read through any of the literature that may have been provided, and discuss the situation with friends and family as the person sees fit. In a discussion regarding competency for treatment decisions, Grisso and Appelbaum also suggest that a delay in assessing competence may be helpful in "distinguishing between time-limited and permanent impairments… [This may be especially appropriate for subjects] who have just learned that they have a life-threatening illness" (Grisso and Appelbaum, 1998, p. 92) or even for those who may simply become over stressed and overly anxious when presented with the details of the research trial. In these types of cases, delaying the competence assessment may give the potential subject some time to adapt to their situation and to the information provided to them regarding the research trial.

Chapter Five: Assessing the Competence of Terminally Ill Subjects of Research

Though a minimum requirement for each sub-ability of competence and thus competence overall has been established for the medical research context with terminally ill subjects, it still remains necessary to determine how to best test for such a level of competence. It is insufficient to merely provide a standard, but with no possible way of knowing whether a subject satisfies such a standard since then such a standard would be rendered meaningless and have little to no real effect. Hence, we must consider the issue of evidence of competence.

As previously stated, it is ethically inappropriate to merely assume that prospective subjects will possess sufficient competence to consent to participate in research, especially in this particular context fraught with numerous competence hindering factors such as the therapeutic misconception and its various causes. Without an appropriate testing method, a minimum standard of competence for a particular task becomes futile since we will never properly determine whether or not a person meets the necessary criteria and is thus capable of competent decision making. Failing in this manner would ultimately undermine the principle of respecting autonomy. The reason for this is twofold. First, it must be recognized that without testing for competence from our potential subjects, we may inadvertently permit incompetent participation decisions and as Chapter One discussed, incompetent decision making fails to be an exercise of real autonomous decision making. Second, without competence testing, we never give ourselves the opportunity to see when and how competence might be lacking and thus deprive ourselves of the opportunity to make attempts to enhance and bolster it where necessary. However, any true respect for autonomy compels us to do more than merely

avoid intentionally violating the autonomy of others, but to also make attempts to promote autonomous decision making.[421] To that end, it is imperative that we not only uphold an appropriate competence standard, but devise a testing method for it as well and attempt to enhance competence[422] where possible.

Developing a competence assessment method for our medical research context with terminally ill individuals is also necessary so that there can be consistency between institutions such that any determinations of competence or incompetence do not appear arbitrary. Allowing medical professionals to make subjective competence assessments leads to a lack of uniformity between institutions and the appearance that competence determinations are random. This is not merely fearful speculation, since as studies and reports have demonstrated, "clinical assessments of decisional capacity have shown poor interrater reliability."[423] Such a lack of uniformity may further lead to a lack of trust in those institutions.

While interrater consistency is likely more easily achieved in cases where the subjects of the competence assessment are healthy and well, typical medical contexts and specifically our medical research context with terminally ill subjects will only further hinder interrater agreement. As Marson et al. demonstrated in a study of physicians' competency evaluations, competency judgments of physicians showed low agreement

[421] Such a sentiment regarding autonomy has been expressed by others as well. For instance Beauchamp and Childress argue that a respect for autonomous agents "requires more than noninterference in others' personal affairs. It includes, in some contexts, building up or maintaining others' capacities for autonomous choice while helping to allay fears and other conditions that destroy or disrupt autonomous action. Respect,… [thus] involves acknowledging the value and decision-making rights of persons and enabling them to act autonomously…" (Tom Beauchamp & James Childress. *Principles of Biomedical Ethics* (New York: Oxford University Press, 2009) p.103). Refer back to Chapter One for a full discussion of autonomy.
[422] The techniques to enhance or bolster competence will be discussed in the final chapter.
[423] Dilip V. Jeste, Barton W. Palmer et al. "A New Brief Instrument for Assessing Decisional Capacity for Clinical Research" *Archives of General Psychiatry*, Vol.64(8), pp.966-974, 2007, p.966. Others have echoed similar findings suggesting that "informal assessments performed by physicians are idiosyncratic and unreliable" (Edward D. Sturman. "The Capacity to Consent to Treatment and Research: A Review of Standardized Assessment Tools" *Clinical Psychology Review*, Vol. 25, pp.954-974, 2005, p. 954).

when assessing patients with mild Alzheimer's disease. More specifically physicians achieved only 56% competency judgment agreement with such patients.[424] Such findings make the need for some type of structured instrument to test competence more apparent.[425]

Unfortunately while a commonly recognized instrument and method to test competence would prove helpful in both the treatment and research setting, "one universally accepted assessment does not currently exist."[426] This should not come as a surprise since there is still dispute on how to best define competency, though as previously mentioned most current analyses assume some form of the four elements that have been identified here as being necessary for competence.

Devising an entirely new competence assessment instrument would prove to be a lengthy and rigorous process, likely requiring its own entirely separate study and analysis apart from the one undertaken presently. This is partly due to the fact that such a creation

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[424] D.C. Marson, B. McInturff, L. Hawkins, A. Bartolucci, and L.E. Harrell. "Consistency of Physician Judgments of Capacity to Consent in Mild Alzheimer's Disease" *Journal of the American Geriatrics, Society*, Vol. 45(4), pp. 453-457, 1997. In addition to the percentage agreement, this study also evaluated the agreement of physicians' competency judgments using kappa scores and logistic regression. Both methods similarly revealed low interrater agreement. For instance, physician judgment agreement on the competency of patients with mild Alzheimer's disease received a kappa score of 0.14 (Marson et al., 1997, pp. 453-457).

[425] Various other publications demonstrate the problems of leaving competence assessment solely up to a medical professional's discretion. Rutman and Silberfeld found that large discrepancies can occur between clinical and test evaluations of competence. More specifically in a comparison between competence evaluations made by a multidisciplinary competency panel and the evaluations made by employing certain structured competency assessment instruments, it was found that "the multidisciplinary competency panel will more often find subjects competent than indicated by their psychometric test scores" (D. Rutman and M. Silberfeld. "A Preliminary Report on the Discrepancy Between Clinical and Test Evaluations of Competency" *Canadian Journal of Psychiatry*, Vol. 37(9), pp. 634-639, 1992, p. 634). Additionally, in a study evaluating the ability of internists, surgeons, and psychiatrists to assess patient competence, it was found that though physicians may know the standard for competence, they may still "apply it incorrectly. [The authors go on to claim that] this suggests that the common clinical practice of relying on expert medical opinion may introduce bias and produce inaccurate results that undermine patient autonomy" (L.J. Markson, D.C. Kern, G.J. Annas, and L.H. Glantz. "Physician Assessment of Patient Competence" *Journal of the American Geriatrics Society*, Vol. 42(10), pp.1074-1080, 1994, p. 1074).

[426] U.S. Department of Health & Human Services. Office of Extramural Research, National Institutes of Health, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider*, November 2009, <http://grants.nih.gov/grants/policy/questionablecapacity.htm#_ftn26>.

would require not only a comprehensive review of current standardized assessment tools, but also mainly because it would involve implementing and testing the assessment tool in actual practice, then reassessing and modifying where necessary. While such an endeavour cannot currently be undertaken, it will be imperative to acknowledge that a few testing methods have been developed and used, some with moderate success, and examine a couple of the more current seemingly successful ones. This will be followed with suggestions regarding how to improve upon such instruments in a manner that respects the necessary standards of competence for the research context with the terminally ill as discussed in Chapter Four.

Thus, in what follows, first, some general remarks will be necessary as to where most competence assessment methods and instruments err. Second, a closer and more detailed analysis of one of the most current, complete, and successful attempts at competence assessment will be undertaken, namely the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR). However, it will ultimately be demonstrated that while this instrument certainly represents a step in the right direction, it too suffers from some fundamental flaws that render it inadequate for our current purpose. More specifically, such an instrument falls prey to some of the common objections leveled against competence assessment instruments generally, inadequately assesses voluntariness, is unable to provide cut-off scores or standards that would aid a competence assessor in her competency determination, and also fails to adequately account for and combat the therapeutic misconception. Third, while developing a full competence assessment instrument remains beyond the scope of this work, ultimately, in Chapter Six, a methodological approach on how to conduct a competency assessment

procedure that builds on the foundations of the minimum requirements of the four sub-abilities of competence from Chapter Four shall be proposed. Such an approach will be labeled as the Subject Rights Advocate (SRA) Conversational approach, since it will involve both the employment of a particular type of patient/subject rights advocate, along with a conversational procedure for the competency evaluation. The approach will be tailored specifically for the research context with terminally ill subjects, though some of its features may be appropriately extrapolated to other contexts as well. The main feature of this proposal will involve embracing a fully conversational qualitative approach to competency assessment, which separately tests for the four sub-abilities of competence and has the potential to reveal possible unexpected competency hindering factors, while also attempting to bolster and enhance certain aspects of a potential research subject's competence. After such an approach is described, it will then be compared and contrasted with the MacCAT-CR and ultimately shown to succeed precisely where the MacCAT-CR has failed. Finally a couple of hypothetical case studies will be provided to demonstrate how the implementation of the SRA Conversational approach would function in the research context with terminally ill subjects.

Existing Competency Assessment Instruments

While there have been a variety of proposed competency assessment tools and approaches, with varied success, many of these prove to be inadequate given the account of competence provided in the preceding chapters. It is not merely that many of the competency assessment tools fail to recognize minimum standards for each element of competence needed for a particular context, such as those developed in Chapter Four, but

that many assessment tools fail to even acknowledge the existence of one or more of the elements of competence. That is to state that many past competency evaluations frequently ignored and thus did not test for one or more of the components of competence. It was most often the case that some combination of appreciation, reasoning, or voluntariness would be disregarded, while the understanding element of competence was given full attention. In some cases competency assessment tools and questionnaires appeared to only attempt to test for patient or subject understanding, and even then a number of which did so only superficially. For the sake of brevity, we shall only take a brief look at two instruments, namely The Evaluation to Sign Consent (ESC) and Aid to Capacity Evaluation (ACE), which while possessing certain advantages, reveal such inadequacies in previously developed competence assessments.

The ESC "was developed by Love in 1988 (unpublished; as cited in Deronzo, Conley, & Love, 1998[427])… and assesses the factual understanding of subjects and is composed of only five items."[428] It is likely its two greatest assets make it attractive as a tool for research investigators, namely, that it is quite short and quick to administer, consisting of only five items, and second that it is easily adjustable to fit with any research trial. This second feature is a function of the wording of the items found within the evaluation tool, including, "Items 1 (describing two risks to participation in the study) and 2 (knowing what is associated with participation)."[429] Such items easily lend

[427] E.G. DeRenzo, R.R. Conley, and R. Love. "Assessment of Capacity to Give Consent to Research Participation: State of the Art and Beyond" *Journal of Health Care Law and Policy*, Vol. 1, pp.66-87, 1998.
[428] Sturman, 2005, p. 963.
[429] B. Resnick, A.L. Gruber-Baldini, I. Pretzer-Aboff, E. Galik,V.C. Buie, K. Russ, S. Zimmerman. "Reliability and Validity of the Evaluation to Sign Consent Measure" *The Gerontologist*, Vol. 47(1), 2007, pp.69-77, p. 69.

themselves to be appropriate for a wide variety of different research trials and subject populations.

However, as admitted by the author, the "ESC may not be sufficiently rigorous... [and] it is highly likely that the ESC will be deemed too easy to pass."[430] More importantly and for our purposes, the ESC could never provide a proper competence assessment as it is only constructed to test for understanding. In a study examining the competence of subjects with schizophrenia and HIV, Moser et al. noted that the ESC disregards the other elements of competence and only "assesses understanding of consent form information."[431] Thus, even if this instrument proved to have great interrater reliability, it fails to test for appreciation, reasoning or voluntariness. It thus may be a useful tool in testing for understanding, but ultimately cannot be employed as a competence assessment tool, at least not on its own.

Many other assessment instruments do not fare much better, several of which similarly focus on understanding while ignoring the other elements of competence.[432] Some assessment methods and tools attempted to improve on this and were constructed to account for some form of the other elements, but in many cases did so only cursorily,

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[430] DeRenzo et al., 1998, p. 85.

[431] David Moser, Susan Schultz, Stephan Arndt et al. "Capacity to Provide Informed Consent for Participation in Schizophrenia and HIV Research" *American Journal of Psychiatry*, Vol.159, pp.1201-1207, 2002, p.1205.

[432] Some other competence assessment instruments that similarly focus on understanding while ignoring some or all of the other elements of competence and thus fall prey to this same line of criticism include: The Brief Informed Consent Test, the Quality of Informed Consent Questionnaire, the Deaconess Informed Consent Comprehension Test, the Two-Part Consent Form, the Competency Assessment Interview, the Informed Consent Survey, and the Hopkins Competence Assessment Tool. In some of these cases the authors of the instrument allege that the tool examines other components of competence, but further inspection and analysis of the tools have demonstrated otherwise. For more on these tools and in specific the elements of competence that they are capable of testing, see: Laura Dunn, Milap Nowrangi, Barton Palmer, Dilip Jeste, and Elyn Saks. "Assessing Decisional Capacity for Clinical Research or Treatment: A Review of Instruments" *American Journal of Psychiatry*, Vol. 163(8), pp. 1323-1334, 2006; and Edward D. Sturman. "The Capacity to Consent to Treatment and Research: A Review of Standardized Assessment Tools" *Clinical Psychology Review*, Vol. 25, pp.954-974, 2005.

still maintaining focus on the understanding component. One of the better developed and more current tools that attempted to improve on this issue was the Aid to Capacity Evaluation (ACE) which redirected its focus on the appreciation criterion of competence. This assessment tool is a bit more in depth than the ESC, involving an approximately 15 minute "semi-structured test that enables clinicians to rate patients as: definitely incapable, probably incapable, probably capable, and definitely capable."[433] Though this tool was constructed specifically for assessing a patient's capacity to consent to treatment, with some moderate adjustment it may be equally appropriate for ill subjects of research. The largest advantage of this assessment tool is that it can be tailored to account for the particular patient's, or subject's disorder. It does so by inquiring into a patient's or subject's "ability to appreciate the reasonably foreseeable consequences of accepting treatment... [and] ability to appreciate the reasonably foreseeable consequences of refusing proposed treatment,"[434] with questions forcing the patient to explain what consequences he thinks may occur if he consents to the treatment in question and what consequences may occur should he refuse the treatment. This tool further attempts to ascertain whether the patient or subject is making decisions based on delusions or depression, something which is often overlooked by assessment tools that focus solely on understanding. However, despite such improvements, as well as the high interrater reliability that the ACE has demonstrated,[435] this tool as well ignores elements of competence, focusing primarily on appreciation. Even if modified to test research

[433] Sturman, 2005, p. 964.
[434] E. Etchells, P. Darzins, M. Silberfeld et al. "Assessment of Patient Capacity to Consent to Treatment" *Journal of General Internal Medicine*, Vol. 14, pp.27-34, 1999, p. 28. It should be noted that the ACE is also a common test used in the emergency department to determine if patients should be stopped from leaving the department; for instance someone who is intoxicated.
[435] Sturman, 2005, p. 959.

subjects,[436] such an instrument would still leave out a proper evaluation for one's ability to reason or make choices voluntarily.

Given the full conceptualization of competence and its constituent parts, such testing methods can be deemed insufficient at determining a patient or subject's competence. Any adequate competence assessment method or instrument must recognize and test for all the elements of competence. In addition, though not entirely unrelated to this, many of the past competence assessment tools tend to fall prey to four general criticisms.

> First, in terms of the understanding component, patients may repeat or paraphrase details about their treatment even though they have little real understanding.[437] If they lack scientific or medical knowledge, [or if they have been misled,] then misunderstandings or mistaken beliefs are possible. Second, the reasoning component requires patients to recall the mental processes they used in arriving at a decision but these types of self-reports have been found to be inaccurate and patients will not really be able to perform this task (although it may provide other valuable information such as knowledge of important details that should go into a decision). Third, patients who perform poorly in terms of the abilities measured do not necessarily lack these same abilities. Performance could be affected by numerous factors such as lack of motivation, inattention, mistrust, [desperation, depression, anxiety, insecurity,] or a misunderstanding of expectations. Finally, a savvy patient can tell investigators what he/she wants to hear, despite having a markedly different reasoning process (e.g., anorexic patients).[438]

We may refer to these issues as: the problem with repetition, the difficulty of self-reporting, the multi-factor hindrances to competence, and the problem of patient/subject deception, respectively. Further in this chapter we shall return to these four criticisms in order to ensure that the SRA Conversational approach that will ultimately be suggested here, steers clear of such issues. It should be noted that a proper competence assessment

[436] Such a modification could be achieved by replacing questions and inquiries regarding how consenting to or refusing a particular treatment would affect a patient with questions regarding how consenting to or refusing to participate in a particular research trial would affect a subject.
[437] It should be noted that repetition, even of some complex material may come easily to those with good memories, but does not necessarily indicate any real understanding of that material.
[438] Sturman, 2005, pp. 965-966.

method that accounts for, and attempts to test for all four elements of competence may potentially mitigate if not completely eliminate some of these issues.

MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR)

The importance of implementing a competence assessment tool that accounts for all four elements of competence cannot be understated. This is due to the fact that often, a person who may appear to excel in one area of competence may still have a significant deficiency in the others. We may recall from Chapter Three the story of the twenty-five-year-old women entering a research trial who demonstrated excellent understanding of the research aims and methods.

> She recognized that the purpose of the project was to find out which treatment worked best for her group of patients. She spontaneously described the three groups, including the placebo group, and indicated that assignment would be at random. She understood that dosages would be adjusted according to blood levels and that a double blind would be used. When asked directly, however, how *her* medicine would be selected, she said she had no idea. She then added, "I hope it isn't by chance," and suggested that each subject would probably receive the medication she needed.[439]

This person clearly exhibited a very high level of understanding in regards to the research trial, but was unable to appreciate what that information meant for her. Thus, such a case demonstrates that a person may possess, even to a high degree, one of the sub-abilities of competence, in this case understanding, but may still significantly lack one or more of the other sub-abilities, in this case appreciation. Thus, it is crucial that a competence assessment tool only declare a person competent if that person has demonstrated a sufficient level of ability relating to all four sub-abilities of competence.

[439] Paul Appelbaum, Loren Roth, Charles Lidz, Paul Benson, & William Winslade. "False Hopes and Best Data: consent to research and the therapeutic misconception" *The Hastings Center Report*, Vol. 17(2), pp. 20-24, Apr., 1987, p.22.

In light of this fact, one of the better, if not the best, competence assessment instruments thus far is the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR). Developed by Paul S. Appelbaum and Thomas Grisso, this instrument is actually a modified version of their earlier MacArthur Competence Assessment Tool for Treatment (MacCAT-T), initially "developed to assist clinicians in making"[440] competency evaluations with patients. The advantages of the MacCAT-CR instrument over its predecessors have not gone unnoticed. In comparison with other competence assessment instruments, Dunn et al. asserted that:

> the best choices for measuring capacity to consent to research and treatment, given their comprehensiveness and supporting psychometric data, will frequently be the MacArthur Competence Assessment Tools for Clinical Research and for Treatment, respectively. Of the instruments we examined that focus on research, the MacArthur Competency Assessment Tool for Clinical Research has been the most widely adopted, and, as a result, numerous lines of evidence supporting its reliability and construct validity have accumulated."[441]

The MacCAT-CR is provided in a semi-structured interview format that allows itself to be "customized to reflect the details of the particular research project to which subjects are being asked to consent."[442] It does so by establishing various general categories of questions under each of the four elements of competence and allowing the interviewer to fill in the specific details related to the actual clinical trial. For instance, the understanding section has 5 different subsections within it, each dedicated to assessing a different portion of what ought to be understood. As the MacCAT-CR specifies, the first subsection relates to assessing the:

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[440] Thomas Grisso and Paul S. Appelbaum. *Assessing Competence to Consent to Treatment: A Guide for Physicians and Other Health Professionals* (New York: Oxford University Press, 1998) p.101.
[441] Dunn et al., 2006, p.1331.
[442] Paul S. Appelbaum and Thomas Grisso. *MacCAT-CR: MacArthur Competence Assessment Tool for Clinical Research* (Sarasota, FL: Professional Resource Exchange, Inc., 2001) p. 5.

> understanding of disclosed information about the nature of the research project. This includes the objective of the project and three of its most important procedural elements, that is, those procedures experienced by subjects who participate in the study (e.g., duration, daily doses of medication, every-other-day interviews, and weekly blood drawing).[443]

Such a subsection is specific enough to inform a competence assessor specifically of what information a prospective subject must demonstrate to have an adequate understanding, while still maintaining the necessary flexibility to allow itself to adapt to varying clinical trials which may have very different procedural elements.

The remaining subsections of understanding are listed in the MacCAT-CR manual in a similar fashion and the assessment interview procedures for the other three elements of competence the MacCAT-CR tests for, namely appreciation, reasoning, and expression of choice, are conducted similarly as well. Without providing, in full, each category of inquiry with each element of competence that the MacCAT-CR tests for, a brief overview may prove helpful. Once the interview is completed the potential subject will allegedly have been assessed with regard to her:

> understanding of:
> i) the nature and procedures in the trial,
> ii) the primary purpose of the project,
> iii) the effect of research methods on personal care,
> iv) the potential benefits and risks/discomforts associated with participation in the research,
> v) matters relating to refusal to participate as well as withdrawing during the trial;
>
> appreciation of:
> i) the purpose of her being recruited,
> ii) the methods actually involved in the study and their use over typical methods applied in the individualized care setting,
> iii) the ability to decline participation or to withdraw at a later date without penalty,
>
> reasoning relating to:
> i) the consequences of potential choices,

[443] Appelbaum and Grisso, 2001, pp. 9-10.

ii) comparisons between various advantages and disadvantages of choices,
iii) anticipating consequences to everyday life,[444]
iv) the logical consistency of the choice,[445]

and the ability to express a clear choice.[446]

In addition to making these various inquiries, the interviewer is given space on the forms provided by the MacCAT-CR to record answers to the varying questions asked of the potential subject. Then, the interviewer is to rate each response between 0 and 2 for each of the subparts of each of the elements of competence. The MacCAT-CR provides guidelines that enable an interviewer to provide such ratings. For instance the guideline for the portion of the appreciation section that inquires into one's ability to appreciate why she has been recruited for the study suggests the following:

Rating	Guidelines
2	Subject acknowledges that he or she is being recruited for a valid reason unrelated to potential personal benefit from being in the study (e.g., because he or she has a condition of relevance to the study; because he or she has previously indicated a willingness to help with studies of this sort, etc.).
1	Subject acknowledges being recruited for reasons both related to and unrelated to potential personal benefit. OR

[444] This differs from the first subsection under reasoning that is concerned more so with the direct consequences of participating/not participating in the research as often identified by the disclosure information. Instead, this deals more specifically with consequences that relate to the specifics of one's life and typically go beyond the consequences listed during the disclosure. For instance, this may include the acknowledgement that and reasoning about a certain research related activity such as venipuncture which may cause arm pain, and how that may prevent one from partaking in their weekly bowling league (Appelbaum and Grisso, 2001, p. 24).
[445] This involves demonstrating the ability to make a choice that follows logically from a potential subject's own reasoning.
[446] While many of these categories may be self-explanatory, for a full depiction of each, see: Appelbaum and Grisso, 2001, pp. 9-25.

	Subject maintains he or she is being recruited for a reason related only to potential personal benefit, but has a plausible explanation for why this is the case.
0	Subject maintains he or she is being recruited for a reason related only to potential personal benefit, but does not have a plausible explanation for why this is the case. OR Subject offers response that is unrelated to the question or unintelligible.[447]

Given all of this, it is clear that the MacCAT-CR certainly represents one of the more rigorous and comprehensive competence assessment instruments available. Its recognition of the various elements of competence, and attempt to assess them in light of the specific factors revolving around the research context, allows it to correct for many of the issues related to past competence assessment instruments. Thus, this assessment tool represents significant progress in the field which can be highlighted by four of its main attractive features.

Advantages of the MacCAT-CR

First, it is important to note that a crucially important step in competence assessment made by Appelbaum and Grisso in both the MacCAT-T and MacCAT-CR, is to test for the sub-abilities of competence separately.[448] As they note, "how well patients performed in any one of these areas tended not to be a very good indicator of their

[447] Appelbaum and Grisso, 2001, pp. 19-20.
[448] This is especially important given that in the past there has sometimes been a conceptual conflation of understanding and appreciation. Refer back to Chapter One for a full account of each of the elements of competence and how they differ.

performance on the other abilities."[449] Indeed, as previously mentioned, a person may possess a very high level of understanding, but lack appreciation, or other elements of competence. Thus for our purposes, it must be stressed that understanding, appreciation, reasoning and voluntariness should be each evaluated separately from one another, and that a demonstration of a high level of ability in any one category of competence should not be taken as evidence of ability in any other category.

A second advantage of the MacCAT-CR, not unrelated to the first, is the fact that it does not provide an overall score of competence. While this may seem like a defect of the competence instrument, it is actually designed specifically in this manner because the authors recognize that to sum up the rating or scores of the varying elements of competence into one overall score would be inappropriate. This is due to the fact that "in some cases, a serious deficit in ability in any one of the four areas may translate to a clinical opinion of incompetence, even if the subject's capacities in the other three areas are quite adequate."[450] The SRA Conversational proposal that will ultimately be presented here will similarly take this into account and thus it will be the case that sufficiently lacking in any one of the elements of competence, below the minimum requirements as set out in Chapter Four, may render one's decision incompetent.

Third, the MacCAT-CR attempts to identify and assess one's ability to understand the difference between research and treatment, thus making some effort to account for and possibly combat the therapeutic misconception. It accomplishes this goal by going beyond the mere disclosure that the purpose of research is primarily the acquisition of generalizable knowledge as opposed to patient treatment. Instead, the MacCAT-CR goes

[449] Grisso and Appelbaum, 1998, p.102.
[450] Appelbaum and Grisso, 2001, p. 3.

into some detail assessing a potential subject's competence concerning the "effect of research methods on individualized care, that is, *how* the research project differs from ordinary treatment."[451] This involves asking potential subjects to explain particular methods of the research protocol that represent a contrast to ordinary best care standards, including the use of placebos, randomization, and double-blinding. As argued in previous chapters, the identification of specific research methods that differ from ordinary therapeutic methods is a necessary step in combating the potential for prospective subjects to consent to a clinical trial under the assumption that it will be, or at least be like, therapy. In addition to identifying the use of placebos, randomized assignments, and double-blinding, I have previously also suggested that Phase I trial protocols be identified and accounted for in a competence assessment for much the same reason. Given the flexible nature of the MacCAT-CR, this is something that could easily be included when the instrument is being used for a Phase I trial.

One final improvement made by the MacCAT-CR relates to one of the more general problems with competency assessment tools, namely that they fail to account for the differing standards of competence that may be needed given the context. As previously argued, since competence is task and therefore context dependent, a person may be competent to make a decision in one context, but given certain factors in another context may be appropriately deemed incompetent to make a decision. Any assessment or evaluation tool or method must be sufficiently versatile so as to be able to account for the context dependent nature of competence. Thus any adequate:

> determination of competency requires a proper assessment that incorporates many factors relevant to the unique circumstances of the patient [or subject] and cannot be ascertained on the basis of test scores alone… In addition to functional

[451] Appelbaum and Grisso, 2001, p. 10.

> abilities, a determination of competence or incompetence must take into account the decision-making demands placed on a patient [or subject], which include different situational and social factors, as well as the consequences of a judgement in terms of beneficence and autonomy.[452]

While one might claim that the MacCAT-CR does not go far enough in this endeavour, it must be noted that it certainly represents a step forward from past competency evaluations by attempting to account for various situational factors that may relate to the decision-making ability of the prospective subject. It does so through its appreciation and reasoning assessment methods, specifically by inquiring into such matters as one's ability to appreciate what participation in a particular research project may mean for her, and to relate that to her reasoning about whether or not to participate. This somewhat involves identifying certain particulars related both to the decision making context and the individual person. Such an approach thus enables, at least some of, the context and individual dependent factors in this type of scenario to properly factor into the competence assessment.

Given these various advantages, it can be stated that the MacCAT-CR certainly represents progress in the field of competence assessment with prospective research subjects.

Issues with the MacCAT-CR

Despite these undeniable upshots of the MacCAT-CR, it must still be noted that it too suffers some significant shortfalls. First, it does not fully address all four of the previously mentioned Sturman criticisms adequately. These were: i) the problem with repetition, ii) the difficulty of self-reporting, iii) the multi-factor hindrances to

[452] Sturman, 2005, p. 956.

competence, and iv) the problem of patient/subject deception, respectively. Though, as will be argued, the MacCAT-CR is able to solve the second and third issues, it still struggles with the first and fourth. In addition to these general criticisms often levied against competence assessment instruments, there are three additional objections specific to the MacCAT-CR that will be raised. These will include that the MacCAT-CR fails to take voluntariness into account, is unable to provide cut-offs or standards that would aid a competence assessor in her competency determination, and that a greater attempt at combating the therapeutic misconception is needed specifically for terminally ill subjects of research.

We may proceed by first examining each of the four Sturman criticisms. As already mentioned, the second and third criticisms do not cause any real dilemma for the MacCAT-CR. These were the difficulty of self-reporting, and the multi-factor hindrances to competence issues. The first of these states that when assessing a patient's or subject's reasoning by asking them to recollect the mental processes used in their decision-making process, the answers given are often inaccurate. This is not likely due to any purposeful deception by the patient or subject, but rather relates to the difficulty of the task of identifying and recalling one's past mental processes when making a decision. However, the MacCAT-CR ameliorates this issue, that is to the extent to which it can be ameliorated, by engaging in a series of questions, none of which directly ask the potential subject to merely remember her reasoning, but rather which will have her engage in the reasoning process right there, in front of and with the interviewer. Thus, the issue that arises with the inaccuracy of self-reporting is to a large extent alleviated.

Similarly, the MacCAT-CR is also able to handle the third of the Sturman criticisms quite well. This criticism suggested that given the many possible factors in a certain context that may hinder competence, one who fails to demonstrate an adequate level of any of the sub-abilities of competence is not necessarily a person who may generally lack that sub-ability, or competence overall, in life. However, the MacCAT-CR acknowledges this and is meant to assess competence only in the specific context for which its line of questioning is geared. It is not meant to provide blanket determinations of competence for a person. Furthermore, as already discussed, it attempts to account for at least some of the factors specific to the research context that may pose a hindrance to competence by attempting to identify them and test a person's competence in light of them.

Though the MacCAT-CR adequately overcomes these two of the four Sturman issues, it fails to do so with the remaining two. These were the problem of repetition and the problem of patient/subject deception.

The problem of repetition is concerned primarily with the understanding component of competence, though it may also indirectly relate to appreciation and reasoning as well. This issue is related to the fact that patients or subjects may be capable of merely repeating the consent-related information without any actual understanding of it.[453] This may lead to improper determinations of competence, especially for those who

[453] Though the concern here will be related to the research context, such an issue is also quite problematic with patient populations in the therapeutic context. In order to combat the issue in the therapeutic context some have suggested that physicians should be required to "ask questions that compel the patient to demonstrate a deeper understanding of the treatment proposals, not merely prompt the patient to parrot information back" (Jorie Epstein. "How Reliable is the Competency Assessment Process?" *Virtual Mentor: American Medical Association Journal of Ethics*, Vol. 10(8), pp. 511-515, 2008, p.513). However, it should be noted that there is currently little research on how to best accomplish this goal.

are able to memorize information well without ever comprehending it. Unfortunately the MacCAT-CR does little to rectify this issue.

The format of the semi-structured interview may pose as a particular problem given this type of criticism. The interview is conducted such that the interviewer asks direct questions pertaining to a specific element of competence immediately following the disclosure of the information necessary for that element of competence. This process increases the chance that a prospective subject will be able to memorize and only repeat back the information without adequate understanding. In fact the MacCAT-CR process states that a:

> Subject should be given a card containing the disclosure for each section and asked to read along as the disclosure is read to him or her… [Following this, the interviewer is instructed to] take the card from the subject. Tell the subject that you want to make sure he or she has understood what you have described. Ask the subject to describe to you his or her understanding of the information…[454]

This very process enables pure memorization of the disclosed information, and then tests for that information immediately after the subject was given the chance to memorize it. While the MacCAT-CR is right to include a verbal response procedure as opposed to merely a written one in an attempt to improve understanding and be better able to detect and combat issues such as this, the process of the interview, specifically having the inquiry follow immediately after the disclosure, enables this problem. It is odd that the MacCAT-CR would be conducted in this manner given that as mentioned in Chapter Four, in a discussion regarding competency for treatment decisions, Grisso and Appelbaum suggest that a delay in assessing competence may be helpful in "distinguishing between time-limited and permanent impairments… [which may be especially appropriate for those] who have just learned that they have a life-threatening

[454] Appelbaum and Grisso, 2001, p. 14.

illness"[455] or even for those who may simply become over stressed and overly anxious when presented with the details of their suggested treatment. Such reasoning not only similarly applies to the research context, but the delay in assessing competence may also greatly prevent this restating/memorization problem.[456]

The MacCAT-CR does not fare much better against the fourth Sturman criticism, namely that a patient or subject may deceive the assessor affecting his ability to accurately judge competence. More specifically, patients or subjects may say what they think a competence assessor will want to hear, despite possessing beliefs to the contrary. As Edward Sturman states, "what seems to be at issue are 'patently false beliefs,' held by patients who are motivated to hide these from health care professionals and have the presence of mind to do so. Thus, it is [likely] the appreciation component that is problematic."[457]

Some empirical evidence already exists demonstrating such a flaw with the MacCAT-T and the treatment decisions of certain types of patients. In one study examining the competence results of anorexic patients, it was found that "the participants performed on the MacCAT-T to a high standard, which was comparable to the healthy population control group in a previous study using the MacCAT-T."[458] However, the study argued that three potentially competence hindering factors were present with this population, namely the "impact of anorexia nervosa on attitudes to death and disability;

[455] Grisso and Appelbaum, 1998, p. 92.
[456] The concern of restating disclosed information as opposed to actually understanding it will reemerge later on when ultimately a proposal will be given as to how to best structure a competence assessment approach with terminally ill prospective subjects of research.
[457] Sturman, 2005, p. 966.
[458] Jacinta Tan, Tony Hope, and Anne Stewart. "Competence to Refuse Treatment in Anorexia Nervosa" *International Journal of Law and Psychiatry*, Vol. 26, pp. 697-707, 2003, p.704. For the most part this population was already quite knowledgeable about anorexia and the information relating to treatment options, and thus was capable of scoring well especially in the understanding portion.

impact of anorexia nervosa on values and personal identity; and ambivalence to treatment and recovery.... [the authors concluded that] all these factors are relevant to the participants' decisions about treatment and raise questions about their competence to refuse treatment"[459] despite being deemed competent by the MacCAT-T.

In addition, due to the nature of anorexia, these patients have patently false beliefs, but do not have any significant mental impairment such that they would be unable to understand the information and answer questions in such a manner so as to tell the interviewer what she wants to hear.

> It would therefore be possible for a grossly underweight anorexic patient to be fully capable [according to the MacCAT-T] of refusing treatment, despite having distorted or false beliefs about their self-image and the necessity of treatment. It should be noted that this patient would likely have adequate capacity on every component, save for appreciation, but this one deficit could be hidden and have a profound impact on the choice of the patient. This is a limitation that holds little promise of being solved because self-report measures, even diagnostic interviews, are easily manipulated by clever and motivated individuals.[460]

This issue may similarly apply with certain terminally ill individuals in the research context who are either desperate for a cure, or depressed due to their situation. Neither desperation nor depression would necessarily cognitively impair persons to the extent that they would be incapable of understanding the disclosed material, or of detecting what the interviewer may wish to hear during the MacCAT-CR interview. The ability for persons suffering from depression to have high cognitive abilities and have a high potential for understanding, is nothing surprising. In a study utilizing the MacCAT-CR to assess the competence of depressed persons for consenting to research, it was found that "the great majority of subjects performed very well on the measures of all three

[459] Tan et al., 2003, p.706.
[460] Sturman, 2005, p. 966.

abilities"[461] tested, namely understanding, appreciation and reasoning. Thus, similar to the anorexic patients, these individuals might have a high capacity for understanding, and might be able to figure out exactly what the interviewer will need to hear in order for them to score well on the MacCAT-CR. This combined with a potentially desperate mental state,[462] which may contribute to one's desire to view research as therapy, may cause one to attempt to deceive the interviewer in order to ensure admittance into the trial.

Such a problem is exacerbated by the style of questioning in the MacCAT-CR, which asks questions that are transparent enough so as to allow subjects to potentially decipher optimal answers. For instance the MacCAT-CR manual suggests the following questions for an interviewer assessing appreciation in a hypothetical double-blind, placebo-controlled study of a new medication for schizophrenia: "Do you believe that you have been asked to be in this study primarily for your personal benefit? [and] "Do you believe that you could get the sugar pill?"[463] This line of questioning, while correct in attempting to ascertain answers to questions that significantly relate to one's competence to consent to research, somewhat makes the correct answers obvious to the potential subject. The first question specifies personal benefit in a way that may make it clear to a clever interviewee that it is not the correct answer. The second question suffers a similar

[461] Paul Appelbaum, Thomas Grisso, Ellen Frank, Sandra O'Donnell, and David Kupfer. "Competence of Depressed Patients for Consent to Research" *The American Journal of Psychiatry*, Vol. 156, pp. 1380-1384, 1999, p. 1381-1382. Additionally, the study showed that subjects maintained this high level of performance over an extended period of time and that "there was no correlation between performance and degree of depressive symptoms" (Appelbaum et al., 1999, p. 1380).

[462] Refer back to Chapter Three for a discussion of the role that desperation and even pain can play in a potential subject's decision-making process. We may recall that The President's Advisory Committee on Human Radiation Experiments, "Chapter 16: Subject Interview Study" in Final Report of the Advisory Committee on Human Radiation Experiments (Washington, D.C.: U.S. Government Printing Office, 1995) provided ample examples of desperation in terminally ill subjects consenting to research. Furthermore, we may recall that desperation may make a person vulnerable to manipulations of hope and the therapeutic misconception.

[463] Appelbaum and Grisso, 2001, p. 36.

flaw, specifically pointing out the placebo to the prospective subject and possibly tipping him off that a good answer will involve admitting that receiving the placebo is always a possibility.[464] It thus may be better to, for instance, reword the question as: "What treatment or medications might you receive in this trial?" In this manner, the potential subject is not guided toward any answer by the question itself.

Thus, given the problem of subject deception that may occur with this population, the fact that the MacCAT-T has proven to be capable of falling prey to it, and that the MacCAT-CR interview questions somewhat enable it, depressed and desperate terminally ill prospective subjects might be able to score well on the MacCAT-CR despite holding onto unrealistic expectations and ultimately false beliefs regarding the curative potential of the clinical trial.

In addition to being unable to rectify the first and fourth of the Sturman criticisms, the MacCAT-CR suffers three additional flaws. This includes the MacCAT-CR's failure to take voluntariness into account, its inability to provide cut-off scores or standards that would aid a competence assessor in her competency determination, and that a greater

[464] Though it may seem somewhat self-contradictory, it is possible for the potential subject to state that receiving the placebo is a possibility to the interviewer all the while believing that he will not receive it. Such a distinction partially highlights the difference between understanding and appreciation and the difficultly that may exist in applying understood knowledge to one's self. We previously noted such an example with the story of the twenty-five-year-old women entering a research trial who demonstrated excellent understanding of the research aims and methods, but when asked how her treatment would be selected, she claimed that she hoped it would be based on need. (Refer back to the beginning of the *MacCAT-CR* section in this chapter for more on this case). Similar issues have been noticed in other populations as well. For instance, as the previously mentioned study on anorexic patients discusses, anorexic patients, may score well on the MacCAT-T, may fully understand the nature of the disease, perhaps even believe that they have it, but fail to truly appreciate the consequences as applying to them, even if they claim otherwise. The study showed for example, that when asked about death and disability related to the disease, some participants said "I didn't think it applied to me at all"…[and another replied that] although logic tells me I'm underweight, but I don't feel it" (Jacinta Tan, Anne Stewart, Ray Fitzpatrick, and R.A. Hope. "Competence to Make Treatment Decisions in Anorexia Nervosa: Thinking Processes and Values" *Philosophy, Psychiatry, & Psychology*, Vol. 13(4), pp.267-282, 2006, pp.271-272).

attempt at combating the therapeutic misconception is needed specifically for terminally ill subjects of research. We may consider each in turn.

First, while the account of competence provided by Appelbaum and Grisso proves to be one of the more comprehensive accounts of competence in current literature, and indeed much of the account of competence presented in Chapter One relied to some extent on such literature, one crucial dissimilarity exists. The most strikingly different feature between our account of competence and theirs, relates to the fourth criterion of competence. The MacCAT-CR and indeed much literature on competence includes: "expressing a choice, referring to the patient's ability to state a preference"[465] as a criterion. However, as argued in chapter one, this is an inappropriate and incomplete condition of competence. We may recall that it was previously argued that:

> The ability to express a choice is morally irrelevant if the choice itself cannot be made voluntarily. Even if a person is expressing a choice but is unable to mentally overcome a coercive environment, as would be the case if the person made a choice while being deceived or manipulated, then the expression of the choice was certainly not a true satisfaction of this fourth requirement of decision-making capacity.[466]

It was additionally further argued that an individual who possesses the requisite understanding, appreciation and reasoning, but who lacks confidence in himself to such an extent that his opinion can be swayed by the mere suggestion of another, may also be unable to make competent decisions, even if he was physically capable of expressing a choice.[467]

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[465] Grisso & Appelbaum, 1998, p. 58.
[466] Alessandro Manduca-Barone. "Including Appreciation and Voluntariness: The other two elements of decision-making capacity" *American Journal of Bioethics Neuroscience*, Vol. 2(1), pp. 43-45, 2011, p. 43.
[467] We should recall that this was not merely an unlikely hypothetical, but may be particularly true in the medical decision making context where decisions may be of a complex and emotionally taxing nature and may require a certain confidence and strength of will. As previously quoted, Jessica Berg et al. express a similar sentiment in a discussion of autonomy claiming that "people who feel they are too ignorant or too weak to make choices, or who cannot find the emotional strength to do so, are not capable of acting

The MacCAT-CR tests for this fourth criterion of competence by merely asking the interviewee to state their choice and then rates that decision according to the following:

Rating	Guidelines
2	Subject states a choice
1	Subject states more than one choice, seems ambivalent.
0	Subject does not state a choice.[468]

Such a condition and rating system fails to truly relate to competence, and the condition is far too easily satisfied. Likely only the "presence of certain psychiatric conditions may make it more difficult (e.g., mutism due to catatonia or severe depression, mania, thought disorder stemming from psychosis, etc...)."[469] The need to include voluntariness as one of the mental sub-abilities in competence has already been demonstrated, but is further revealed in the context of clinical research. As chapter 4 explained, the ability to understand, appreciate, and reason through a decision, would still not be sufficient for competence to make that decision if the person was unable to make a decision that stemmed from such understanding, appreciation, and reasoning. This additional ability, labeled voluntariness throughout this work, is necessary, especially in this context given that some individuals may lack the confidence in themselves to make the right decision,

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autonomously. As a result, they may become overly susceptible to external influences that would otherwise not be considered undue. They may, for example, be overawed by the prestige of medical professionals or defer to an authority figure in their family. Some people may suffer from phobias or other internal constraints that overwhelm their wills so they cannot freely choose an option they would otherwise desire. A patient who has been sexually abused, for example, might feel incapable of having a physical exam despite intellectually recognizing the health- related benefits it may afford" (Jessica Berg, Paul Appelbaum, Charles Lids and Lisa Parker. *Informed Consent: Legal Theory and Clinical Practice 2nd edition* (New York: Oxford University Press, 2001) p. 25). Refer back to Chapter One and Chapter Four for more on the voluntariness component of competence as well as the inadequacy of the expressing a choice component.

[468] Appelbaum and Grisso, 2001, p.25.

[469] Sturman, 2005, p. 955.

may be in an overly emotional state, may be desperate, and may thus be easily and unduly swayed by the suggestions of others, including recruiters for the trial or even close family members. Therefore the MacCAT-CR can be deemed inadequate as it fails to account for this crucial component of competence.

Second, as admitted by the authors, "the MacCAT-CR does not provide 'cut-off scores' that represent 'competence' or 'incompetence' on the four abilities. This is because the MacCAT-CR was designed to be consistent with a basic maxim in the legal definition of competence: No particular level of ability is always determinative of competence or incompetence across all subjects, all disorders, and all medical or research situations."[470] While the authors are correct in such an assertion, and indeed the account of competence put forth here has acknowledged that competence is task relative and thus no specific level of competence would be appropriate for all contexts, since we are presently only concerned with one specific context, namely the participation decisions of terminally ill subjects of research, we are in a position to provide cut-offs, and thus further aid those making the final determination of competence.[471] This was done previously in Chapter Four, when the minimum required levels of each of the four sub-abilities of competence were established. Though Appelbaum and Grisso are correct, and in fact these minimum requirements for competence may not be applicable in other

[470] Appelbaum and Grisso, 2001, p. 3.

[471] It should be acknowledged that while I have referred to the participation of terminally ill persons in research as one specific context for the sake of simplicity, there may still exist a large variety of contextual and situational differences even between different types of terminally ill subjects and different types of clinical trials. However, the proposal that will ultimately be suggested in what follows will be designed so as to accommodate the wide variety of potential situational differences that may arise with different terminally ill research subjects. Nonetheless, despite the possibility of some situational differences, as previously noted, the participation of terminally ill research subjects in clinical trials represents a distinct context that contains certain factors that may compromise competence, such as a high potential for the therapeutic misconception. Thus it remains appropriate to speak of research participation by the terminally ill as a certain type of context, while also acknowledging that any competence assessment or enhancement techniques should also account for possible situational differences that may exist between such individuals.

contexts, they represent a step forward in being able to approach both competence assessment and competence bolstering for this specific population. Indeed it may be the case that past work and research on this topic has struggled due to the fact that many attempted to view and subsequently assess competence broadly, without accounting for context and task specific factors that would enable the type of comprehensive approach and minimum requirements established here that will ultimately fuel the SRA Conversational competence assessment method that will be explained in the following section. Thus though the MacCAT-CR's lack of cut-offs or minimum standards is not entirely inappropriate, it does demonstrate some room for improvement, particularly when dealing with certain populations.

The third issue with the MacCAT-CR relates to the need for a greater attempt at combating the therapeutic misconception, specifically in the context of clinical trials with terminally ill research subjects. As already stated, the MacCAT-CR does make significant strides in this goal by being one of the only competence assessment instruments that attempts to both ensure understanding of the difference between research and treatment, but also attempts to ensure and test for a subject's understanding of the particular methods of the research protocol that represent a contrast to ordinary best care standards, including the use of placebos, randomization, and double-blinding. Inclusion of such criteria better enables a prospective subject to steer clear of the therapeutic misconception. However, as previously argued, the pervasiveness of such a misconception still requires even more than this step. While attempting to have subjects understand certain research methods represents an improvement, it does not go far enough in accomplishing the goal of combating the therapeutic misconception. Any

attempt to do so must also include ensuring that a subject appreciates what the difference between research and treatment means for her case specifically.[472] Unfortunately the MacCAT-CR still falls short in this endeavor. This was confirmed by a study that used the MacCAT-CR in order to test the competence of depressed individuals to consent to research.[473] According to the study:

> the great majority of subjects performed very well on the measures of all three abilities related to capacity to decide... The mean score on the understanding scale was 23.33 (SD=2.84) out of a maximum of 26, with no subject scoring below 20... Similarly, the mean score on the appreciation scale was 4.89 (SD=1.21) out of a maximum of 6, and the mean score on the reasoning scale was 6.50 (SD=1.75) out of a maximum of 8. Approximately 65%-75% of the subjects received full credit on most of the appreciation and reasoning items; scores of 0 were rare."[474]

However, despite scoring this well on the MacCAT-CR, further investigation revealed that there remained issues regarding subjects' actual appreciation of the research protocol. For instance, "some subjects appeared confused about the extent to which decisions about assignment to treatment groups would be made on the basis of their clinical condition rather than randomly."[475] There was additional concern regarding the adequacy of the:

> appreciation questions for assessing subjects' grasp of the implications of research involvement. When asked why others would participate in the research, one-third to one-half of the subjects mentioned one or more of three reasons: financial advantages (i.e., the therapy was free), higher anticipated quality of treatment at this well-known center, and obtaining help. Only one subject mentioned altruistic reasons (i.e., to help other depressed women by contributing to the advancement of knowledge about treatment of the disorder). When asked why they themselves had decided to participate, in contrast, 80% of the subjects mentioned the desire to obtain help for their depression, and roughly one-third of the subjects offered only

[472] This may include having insight into the impacts of research participation on matters such as one's health, ability to function, romantic relationships, career, passions/hobbies, family or any activities that may give one's life meaning or joy.
[473] Appelbaum et al., 1999, pp. 1380-1384.
[474] Appelbaum et al., 1999, pp. 1381-1382.
[475] Appelbaum et al., 1999, p. 1380.

> this reason. [The report goes on to state that such results raise concern over the] subjects' abilities to distinguish between reasons for seeking ordinary clinical care... and for participation in research studies.[476]

This further demonstrates that the MacCAT-CR is inadequate to properly deal with combating the therapeutic misconception in subjects, particularly in regards to the appreciation component of competence. Despite the fact that a large portion of the subjects in this study clearly remained confused over the difference between research and treatment, and more specifically did not seem to appreciate what the difference meant for them personally, they were able to score quite high on the MacCAT-CR. However, the therapeutic misconception poses a serious problem to the potential competence of subjects, and the inability of any competence assessment tool to adequately account for it renders such an instrument insufficient. Given the pervasiveness of this misconception, and the myriad of factors associated with it,[477] much more must be done to remedy the issue. It would for instance be prudent, not only to discuss the difference between therapy and research, but actually explain the existence of the therapeutic misconception itself, how ubiquitous it is, and some of the factors that may contribute to it, including possible deceptive tactics by researchers,[478] overly hopeful/optimistic recruitment procedures, general confusion between one's doctor and a research investigator, especially if they are one and the same, as well as a general confusion between a treatment facility and research facility, again especially if they are one and the same.[479] It is only in this manner that we may actually hope that potential research subjects will be able to understand the

[476] Appelbaum et al., 1999, pp. 1382-1383.
[477] Refer back to Chapter Three for a full account of the various contributing factors to the misconception.
[478] We may recall from Chapter Three the brand naming of pharmaceutical trials was an example of this type of problem.
[479] Refer back to Chapter Three for a more full account of the therapeutic misconception.

differences between research and therapy, apply that knowledge to their own situation, and ultimately ward off the therapeutic misconception.

Introducing the Subject Rights Advocate Conversational Approach

While much research has been dedicated to determining a proper method with which to test people's competence, it should be noted that the necessary ethical work in this field lies in developing an appropriate and comprehensive account of competence, as well as determining how much competence should be required of a person for a particular context. Many of the flaws and issues with past proposals, suggestions and research on this topic may stem from the fact that these two steps were either ignored, or at least dealt with only superficially. However, both of these objectives were met in the previous chapters, with Chapter 4 specifically outlining to what degree each element of competence should be required of terminally ill subjects of research prior to consenting to participate in a clinical trial.

Unfortunately, as previously mentioned, the task of developing a brand new assessment tool cannot presently be undertaken. Any adequate attempt would require research and analysis above and beyond the scope of this present work. For instance, such an attempt would require that whatever assessment procedure was developed, be tested and rated for its internal consistency,[480] interrater reliability,[481] concurrent validity,[482]

[480] Internal consistency typically measures the consistency between different items on the same test that are all directed at measuring the same phenomenon. Given that, as already previously mentioned, one's ability in one of the elements of competence do not necessarily correlate with ability in any of the other elements, internal consistency may best be used only to evaluate the items/questions within each element of competence. That is to suggest that it would be inappropriate to rate the internal consistency between the items related to understanding and those related to any other element of competence. Instead only the internal consistency between items related to the same element of competence should be rated for internal consistency.

sensitivity[483] and specificity.[484] Some may suggest that test-retest reliability should also be examined.[485] Then, the assessment procedure or instrument may require adjustments and modifications as may be warranted based upon the results of such testing. Such an undertaking would alone comprise an entire work, and thus will not be attempted here. However, given what has already been argued, a path forward may presently be suggested and a general methodological approach to competence assessment and consent solicitation for terminally ill prospective subjects of research that can account for the four requirements as set out in Chapter Four will be proposed.[486]

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[481] Interrater reliability is sometimes also referred to as interrater agreement or interrater consistency. It refers to the ability of a test or procedure to provide consistent results between different evaluators. In the case of a competence assessment instrument, strong interrater reliability would involve a competence instrument producing similar results regardless of who administers the instrument.

[482] Concurrent validity measures "the degree to which scores on a scale are associated with an accepted concurrent standard" (Dunn et al., 2006, p. 1328). This is a particularly difficult measure for competence assessment tools for two reasons. As one study suggests, though "several reports attempted to establish concurrent validity by showing the association with general functional or cognitive measures... because decisional capacity is context-and decision-specific, such correlations are not fully germane" (Dunn et al., 2006, p. 1329). Secondly, given the lack of a gold standard for competence assessment, "most commonly, validity has been established by comparing the various instruments with expert psychiatric opinion... However, psychiatrists' assessments may be idiosyncratic and pose a problem for the reliability of findings" (Sturman, 2005, p. 966). Indeed as previously mentioned clinical assessments of capacity have often lacked interrater consistency.

[483] Sensitivity refers to the proportion of positive findings that are correctly identified by the test in question. This is often referred to as a true positive. Since a competence assessment tool is testing for incompetence, a true positive would refer to a competence instrument's finding of incompetence with a subject who is indeed incompetent.

[484] Specificity refers to the proportion of negative findings that are correctly identified by the test in question. This is often referred to as a true negative. Since a competence assessment tool is testing for incompetence, a true negative would refer to an instrument's finding of competence with a subject who is indeed competent. Both sensitivity and specificity reflect the ability of a test to make accurate predictions.

[485] This is due to the fact that "to the degree that a person's decisional capacity is stable over brief spans of time, scores [of competence assessment instruments] should be consistent over brief follow-up intervals" (Dunn et al., 2006, p. 1325).

[486] "IRBs generally do not regulate the day-to-day practice of how consent information is actually delivered. This can, therefore, vary from handing the potential participant the form and asking for a signature to much more thorough procedures…" (Lisa Eyler and Dilip Jeste. "Enhancing the Informed Consent Process: A Conceptual Overview" *Behavioral Sciences and the Law*, Vol. 24, pp.553-568, 2006, p. 559). However, while much research and IRB review has been and continues to be spent on the structure of the consent form documents, as discussed in Chapter Four, such a document's real contribution to aiding subjects in making informed and competent decisions is questionable. Indeed as was previously suggested, it may be wise to refocus our attention on other aspects of the informed consent process which may themselves significantly impact competent decision making, including the delivery of the consent information, the assessment of competency, and the final solicitation of consent. The authors of the

Chapter Six: The Subject Rights Advocate Conversational Approach

The approach to competence assessment will involve two distinct features. First, that the administration of the competency evaluation and consent solicitation be conducted by a third party terminally ill subject's rights advocate (SRA), and second, that the competency evaluation take on a conversational approach as opposed to a structured interview, written test or questionnaire method. Before examining how this approach may rectify the previously mentioned issues with prior competence assessment methods, we may first briefly describe these two features of this proposal in turn.

The need for expert opinion within this field should be apparent. In a discussion regarding how well IRB's are equipped to analyze studies involving vulnerable persons, the NIH has suggested that a proper course of action:

> might be to involve the following individuals:
>
> - professionals with the appropriate background, knowledge and experience in working with individuals with impaired consent capacity;
> - representatives of patient advocacy groups;[487]
> - experts in the assessment of consent capacity; and/or
> - experts on the scientific and ethical issues relevant to studies involving vulnerable populations.[488]

Though lacking in more specific details, the 45 CFR 46 recognizes something similar stating that "if an IRB regularly reviews research that involves a vulnerable category of

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MacCAT-CR similarly acknowledge "the possibility that subjects' performances can be improved by modifying informational procedures" (Paul S. Appelbaum and Thomas Grisso. *MacCAT-CR: MacArthur Competence Assessment Tool for Clinical Research* (Sarasota, FL: Professional Resource Exchange, Inc., 2001) p.2). Thus though a general methodological approach will be suggested in what follows as opposed to a formal assessment tool, it is worth noting that a proper approach to such aspects of the subject recruitment process may themselves prove to be quite helpful in ensuring the preservation of autonomy among the potential subjects.

[487] This may also include individuals who had previously been part of a vulnerable category, such as ex-prisoners.

[488] U.S. Department of Health & Human Services. Office of Extramural Research, National Institutes of Health, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider*, November 2009, <http://grants.nih.gov/grants/policy/questionablecapacity.htm#_ftn26>.

subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion [into the IRB] of one or more individuals who are knowledgeable about and experienced in working with these subjects."[489]

These types of suggestions correctly point to the fact that the use of some vulnerable populations in research will likely present certain ethical challenges and obstacles, specifically regarding competence to consent, that may require oversight by persons with certain expertise. This is due to the fact that certain issues may arise that are specific to the vulnerable population in question, and that would not otherwise arise with other subject populations. An expert in the field may be better equipped to anticipate and deal with these types of issues specific to a vulnerable population. Though not acknowledged by many ethical guidelines and laws concerning clinical trials, in prior chapters I have established that the terminally ill constitute such a vulnerable population. Their use in research brings with it a variety of ethical challenges related to their ability to consent to participation. Without rehashing the arguments from prior chapters, factors such as depression, desperation, the therapeutic misconception (both naturally occurring as well as misconceptions created through manipulation and deception) all uniquely target a terminally ill prospective subject's ability to consent competently. Given this, the creation of a new position, a terminally ill subject rights advocate (SRA), is ethically necessary. This person will be a third-party individual, independent of the research trial, employed by the IRB or REB, who must possess the background knowledge in these issues with terminally ill subjects, and thus will be well equipped to be able to anticipate

[489] U.S. Department of Health and Human Services, National Institutes of Health, and Office for Protection from Research Risks, Title 45 (Public Welfare), Code of Federal Regulations, Part 46 (Protection of Human Subjects) Washington, D.C.: Revised January 15, 2009 (Effective July 14, 2009) Section 46.107.

and combat these and other competence hindering factors. Perhaps the most important part of this proposal is that this person not only be the competence assessor, but will be charged with two other tasks as well. This will include acting as both a competence enhancer, delivering necessary information to the potential subject as well as attempting to correct for any competence hindering factors, and as the consent solicitor. It is often typical that someone associated with the research trial solicits the consent from potential subjects. This may involve either the primary investigator, the nurse coordinator, or even a person hired by the research facility specifically for this purpose. However, who solicits consent can play a large role in the competence of the possible subject. First, the fact that those individuals, including physicians and nurses, working for the research institution will have their own interests in recruiting subjects that may conflict with a subject's best interest, could lead to unethical recruitment tactics.[490] Second, it is also the case that a potential subject will be less likely to confuse the setting of talking with a subject's rights advocate with a therapeutic medical practice setting, than if a medical professional solicited the consent.[491] Thus, the tactic of employing an SRA diminishes the potential for the therapeutic misconception from the onset.

The second feature of the proposal being suggested here relates specifically to how this SRA goes about enhancing/assessing competence and obtaining consent. The manner in which this is accomplished will utilize a conversational method and must

[490] As previously argued, two examples of this include manipulative brand naming of clinical trials, and having recruiters and consent solicitors present consent related information in the best possible light while downplaying any of the negatives associated with research participation. Refer back to Chapter Three for a more detailed discussion regarding ethical issues with recruitment practices.

[491] We may recall from Chapter Three the discussion regarding the difficulty for subjects to realize the difference between one's physician in the therapeutic setting, and the physician investigator conducting the research trial, especially in cases where they are one in the same. As was previously pointed out, physicians often, though sometimes unwittingly, become "double agents" and the distinction between research and therapy may become even further obfuscated.

relate specifically to the minimum requirements of the four sub-abilities of competence established in Chapter Four.

It should be noted that this conversational method is at least a two stage approach. The initial conversation will be based on competence bolstering which itself will involve delivering consent related information regarding the research trial, as well as having the prospective subject consider personal issues that would appropriately factor into the final decision. Then, as mentioned at the end of Chapter Four, after some brief time has passed, the SRA will engage in another conversation that will be more so dedicated to assessing competence and supervising the consent signing. This conversation will require the SRA to evaluate the potential subject with respect to all four sub-abilities of competence. This will involve a dialogue whereby the SRA may have to probe, with the use of various questions, into the mental processes of the subject upon making the decision to participate in the clinical trial.

Though a structured competence assessment instrument will not be provided, it would be prudent to discuss, in general terms, how this approach may be executed in light of the four elements of competence as well as the minimum standards established in Chapter Four. We may briefly examine the application of this approach with each element of competence in turn.

Understanding

The understanding element of competence will likely be the easiest one for the SRA to enhance and then subsequently test. Having an SRA as opposed to medical personnel, such as a physician investigator, provide an accurate disclosure of the consent related material within the context of a back and forth conversation will likely better

enable the potential subject to feel comfortable in asking questions. This is crucial as the type of questions asked by a potential candidate will likely signal the SRA as to which aspects of the clinical trial a particular individual may be struggling to understand. Given the SRA's already existing expertise with this type of population and context, she will be able to then focus any additional needed time and attention on addressing those specific aspects of the trial that may be most problematic.

Though the approach may be different, for the most part, the important components for adequate understanding during this process will not deviate substantially from other disclosure processes such as those found in the MacCAT-CR. More specifically, the conversation should revolve around a discussion regarding the difference between research and treatment, any actual specific procedural elements of the trial that the subject will have to undergo, the possible effects (both benefits and harms) associated with the various elements of the trial, the likelihood of both the risks and benefits of participation, the existence of the therapeutic misconception, the means by which such a misconception is able to spread, and that subjects of research are free to leave during the trial at any time without reprisal. However, the nature and focus of the conversation will likely differ depending on the potential subject and the SRA's ongoing analysis. For instance, if the SRA detects that the subject seems to understand the risks associated with the actual drug or agent being administered in the trial, but seems to be confused over the extent to which the research specific procedures such as randomization may affect her, then the SRA should steer the conversation towards addressing that feature.

Apart from the necessary disclosure that will occur, ultimately the SRA will have to test for an adequate level of understanding. We may recall from Chapter Four that an

appropriate level of understanding for terminally ill subjects of research is, what was previously labeled, a high level of understanding on the spectrum of understanding formerly outlined. This level of understanding required that subjects understand not merely *that* research differed from treatment, or *that* the therapeutic misconception exists, but also *how*. For instance, as previously argued it is imperative that certain clinical trial procedures that demonstrate how the research context differs from the therapeutic context be understood. This may, for example, involve ensuring that a potential subject grasp *how* a Phase I trial functions; that it, for example, ends once the MTD (maximum tolerable dose) is discovered despite any possible benefits from receiving the non-validated drug. This would also apply to the other features of research trials, including randomization, double-blinding, and the use of placebos.

Similarly, during the conversation, the SRA should ask questions regarding the existence of the therapeutic misconception. Given the high level of understanding standard, it will be imperative that the SRA determine whether the potential subject is able to grasp not only *that* such a misconception exists, but also *how* it exists. As Chapter Four elucidated, this will require comprehending some of the manipulative tactics that often fuel the misconception[492] as well as some of the naturally occurring ambiguities between physicians and investigators or between research facilities and medical practice facilities that seem to exist.[493]

[492] Refer back to Chapter Three for details regarding the factors that contribute to the therapeutic misconception, including misleading brand naming, deceptive language use, as well as overly optimistic rhetoric by recruiters.
[493] For a more full discussion regarding the importance of understanding *how* research is conducted and *how* the therapeutic misconception exists, refer back to Chapter Four.

Once this portion of the conversation is completed, the SRA should begin to steer the exchange towards a discussion related more so to the appreciation element of competence.[494]

Appreciation

We should recall that as argued in Chapter Four, the minimum standard of appreciation for a terminally ill subject of research will be what was referred to as *Imperfect, but Independent Appreciation.* This will involve the SRA ensuring that the potential subject be able to foresee at least some of the ways in which research participation will affect her and have the insight into how she may feel in those future states where those effects might be occurring.

The conversations related to appreciation will thus largely revolve around ensuring that potential subjects appreciate the purpose/methods of research and how its differences from ordinary treatment will affect them. Additionally, and the aspect of appreciation that is often neglected, the discussion will also require engagement with the various ways in which research participation may impact one's life specifically. As previously mentioned this may include wading through how participation will affect one's health, ability to function, romantic relationships, career, passions/hobbies, goals, family, or any activities that may give one's life meaning or joy. We may recall both the athlete example[495] and the Reibl v. Hughes case[496] provided in prior chapters, where

[494] It is important to recognize however, that in many cases the conversation will not be neatly divided into the four separate elements of competence. That is to suggest that while the SRA is probing into the understanding of the potential subject, the subject may make statements that will alert the SRA to possible issues with other elements of competence such as appreciation. Similarly the subject may make statements that already begin to demonstrate adequate levels of the other elements of competence without the SRA having to probe or steer the conversation. Either way, the SRA will have to recognize and account for this throughout the course of the conversational evaluation.

[495] This was the hypothetical case described in Chapter One regarding two separate patients who were both diagnosed with a gangrenous leg and each told that amputation would be required. We may further recall

appreciation was discussed in regards to treatment decisions. These types of cases demonstrate the unique nature of the conversation that the SRA will need to have with different individuals. Therefore a true assessment of appreciation in our terminally ill research context will involve much more than merely acknowledging the relevance of one's illness, and the possible medical/health effects of research, but also further how those matters may affect one's personal life. To what extent mobility, or eyesight, or hearing …etc is important in one's life may be radically different from person to person depending on the particulars of their life. Any adequate competency evaluation must account for appreciation in this manner. It is only through this type of conversation that somewhat forces potential subjects to consider their choices with respect to the various particulars of their lives that we can truly hope for potential subjects to make competent participation decisions.

Probing into one's ability to appreciate may be more difficult than probing into one's ability to understand. The SRA should remember some standard questions that may aid in his evaluation such as:

1. How do you think this medical research trial will affect you?

2. How will the procedure employed in a Phase I trial impact you? (Similar types of questions may be required in relation to other procedural aspects of the trial)

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that one patient was a professional basketball player, while the other was an author. Though their disease and treatment would be identical, it was previously recognized that what they needed to appreciate would be vastly different due to the different lives they led and how amputation would impact those lives.

[496] Reibl v. Hughes, [1980] 2 S.C.R. 880. As explained in Chapter One, this case described Mr. Reibl who "elected to undergo an internal carotid endarterectomy to remove an occlusion in an artery near his brain… However, following the procedure, Reibl suffered a massive stroke, resulting in the paralysis of his entire right side…The risk of stroke, in the absence of surgery, had not been imminent… The only risks Mr. Reibl was cognizant of were those inherent in any surgical procedure, such as infection. Had he known of the more serious risks, Mr. Reibl claimed he would not have gone ahead with the operation, especially in light of the fact that he was only one and a half years away from being eligible for pension benefits from his employer" (Francoise Baylis, Jocelyn Downie, Barry Hoffmaster, & Susan Sherwin. *Health Care Ethics in Canada 2nd edition* (Toronto: Nelson Ltd., 2004) p. 245). Ultimately, it was decided that risks that are particularly relevant given the specific circumstances of a patient needed to be disclosed, in this case that would have included any possible occurrences that may threaten Mr. Reibl's pension benefits.

3. How will this medical research trial affect any personal circumstance you are in (e.g. age, retirement…etc)?

4. How may this medical research trial affect personal or career goals (e.g. travel goals, completion of long term work projects, or athletic goals)?

5. How may this medical research trial affect others close to you (e.g. spouse, children, parents, close friends…etc)?

Reasoning

Given that some conversation related to understanding and appreciation has already taken place, the reasoning element of competence can be bolstered by attempting to engage the prospective subject in a conversation about the relative utility she might assign to her various options, which may include a comparison between entering the research study, pursuing other treatment options, or doing neither. Such conversations may "force individuals to examine trade-offs, which tend to improve the quality of decisions made. They also may be particularly useful in situations with high levels of emotion."[497]

We may recall that our minimum standard of reasoning established in Chapter Four was *Imperfect, but Largely Independent Reasoning.* This required that subjects be able to engage in effective means/ends reasoning, which includes being able to formulate appropriate ends for one's self as well as being able to compare and contrast different means to such an end. Furthermore, such reasoning requires that a person be able to pursue knowledge that would likely factor into such reasoning. This may involve a potential subject asking certain questions, reading the consent related material carefully, or even doing some independent research. Attempts to test for reasoning may involve the

[497] Lisa Eyler and Dilip Jeste. "Enhancing the Informed Consent Process: A Conceptual Overview" *Behavioral Sciences and the Law*, Vol. 24, pp.553-568, 2006, p.563.

SRA directing the conversation in such a way that enables her to ask for the main goals or aims of the potential subject, for a comparison between possible options, including an assessment of the risks/benefits of each, and which feature(s) of the option ultimately chosen made the subject choose that way.

Though there may be no strict guidelines and quantitative rating system, by the end of the conversation, the SRA should have taken "stock of the degree to which… [subjects] appear to consider the range of options, how they have weighted or evaluated the desirability of various consequences of these options, and whether their final choices appear to flow logically from their views of the consequences."[498]

Voluntariness

Bolstering and assessing voluntariness may be the most difficult tasks for the SRA. We may recall from Chapter Four that voluntariness requires that the final decision made be one that freely stems from one's own understanding, appreciation and reasoning. However, as argued, this should not exclude any and all influences from factoring into one's decision. Indeed, including some influences into competent decision making may be wholly appropriate, such a spouse's opinion on how a decision may affect one's family.[499] Nonetheless, as the previous chapters noted, various types of influences may

[498] Thomas Grisso and Paul S. Appelbaum. *Assessing Competence to Consent to Treatment: A Guide for Physicians and Other Health Professionals* (New York: Oxford University Press, 1998), p.58.

[499] As previously noted, many others have made a similar point suggesting that "the presence of influences does not mean that a decision is not voluntary. A decision is involuntary only if it is subject to a particular type of influence…" (Paul Appelbaum, Charles Lidz, and Robert Klitzman. "Voluntariness of Consent to Research: a conceptual model" *The Hastings Center Report*, Vol. 39(1), pp. 30-39, 2009, p. 33). Robert Nelson et al. have actually differentiated between certain types of influences that would undermine voluntariness from those that may be wholly appropriate stating that while coercion and manipulation may eradicate voluntariness, persuasion instead may not threaten it at all. They explain that "persuasion means rational persuasion, which is consistent with voluntariness. When persuaded, a person believes something through the merit of reasons proposed by another person. This is the paradigm of an influence that is both noncontrolling and warranted" (Robert Nelson, Tom Beauchamp, Victoria Miller, William Reynolds, Richard Ittenbach and Mary Frances Luce. "The Concept of Voluntary Consent" *The American Journal of Bioethics*, Vol. 11(8), pp. 6-16, 2011, p. 7).

indeed render a decision involuntary. These include intimidation/bullying, deceit, manipulation, or any actions and behaviours that place excessive duress on the decision-maker with the intent to coerce or control him. An SRA must walk the fine line when determining and distinguishing those influences that do and do not appropriately factor into one's decision. Additionally, an SRA should attempt to detect mental states that may make one excessively susceptible to influences. This may include noticing if individuals feel weak, insecure, lack emotional strength, lack confidence in themselves or in their own knowledge.[500]

We may recall that unlike with the other elements of competence, Chapter Four did not specify a strict standard for voluntariness, instead opting to employ a descending order of permissibility method. This suggested that those possessing *extremely high voluntariness,* as labeled on the voluntariness spectrum, be first to be admitted into research, and then gradually descending down the voluntariness spectrum, lower levels are permitted down to what was labeled *a medium level of voluntariness*. The reasoning for this was that requiring a specific level of ability related to voluntariness from our spectrum would be inappropriate since being susceptible to manipulation, deceit, exploitation, or lacking in confidence in one's self or one's knowledge does not itself necessitate that someone will be manipulated, deceived, exploited, or pressured and thus make an involuntary choice; it rather just increases the probability of such events.

Such a situation further complicates matters for the SRA who will have to determine through a conversation with potential subjects, whether the final decision to participate freely flowed from one's own understanding, appreciation and reasoning.

[500] Refer back to Chapter Four for a more detailed discussion regarding how these may affect one's ability to make decisions voluntarily.

Though such a task may be difficult, the conversational nature of the interaction with an SRA should better facilitate an environment where personal information is revealed by the subject that may alert the SRA to possible obstacles to voluntary decision making, than with other competence assessment approaches. Though there is currently very little literature on how to evaluate voluntariness, as Appelbaum et al. note, assessment

> might begin with a general inquiry into the motivations for a person's decision about enrolling in research...From the list of motives that most people will offer, the evaluator will want to pay particular attention to external and intentional influences that are most likely to impair the voluntariness of consent [as well as attempting to detect certain internal mental states, such as extremely low confidence or insecurity, which as previously mentioned, may make one especially vulnerable to external influences].[501]

Once the presence of any of these potentially problematic factors have been identified, the SRA will next have to determine to what extent these factors actually affected the potential subject and undermined voluntariness. The best manner in which the SRA will be able to determine this is to see if there is any discrepancy between the potential subject's understanding, appreciation, and reasoning, and the final decision

[501] Appelbaum et al., 2009, p. 37. It should be noted that the authors here seem to focus substantially on which external influences may qualify as "illegitimate influence," stating that the impact of influence "on voluntariness is not of concern unless these influences are also illegitimate-that is, the person exerting the influence does not have the right to act in this way according to generally accepted moral norms" (Appelbaum et al., 2009, p. 33). Such a sentiment is not new and represents a common approach to the concept of voluntariness. Benjamin Freedman, for instance, similarly provides a "distinction between choices forced by man, and choices forced by nature" where only the former are to be considered relevant, and where those choices forced by man are furthermore only relevant if they constitute a certain type of immoral/inappropriate pressure (Benjamin Freedman. "A Moral Theory of Informed Consent" *Hastings Center Report,* Vol.5(4), pp.32-39, 1975, p. 36). However, the account of voluntariness presented here differs from such accounts since it is admitted that what may undermine voluntariness is not necessarily only external and inappropriate influences, but rather influences that exert an excessive amount of control over a person's decision. Such a recognition, as previously discussed in Chapter Four, notes that sometimes certain mental states may render one unduly susceptible to influences that may have otherwise not been undue. Since an evaluation of competence is concerned with whether or not the actual person is making a voluntary choice, and not whether or not moral or legal condemnation is appropriate for those exerting influence on the individual, such matters should be accounted for in an account of voluntariness. Nelson et al. suggest something similar maintaining that "it is not the condition of being *unduly influenced* that renders an action involuntary; rather, involuntariness is caused by the *controlling effect* exerted in the circumstance of undue influence… Whether an external influence is morally legitimate is conceptually and morally distinct from whether the action taken in response to that influence is voluntary or involuntary" (Nelson et al., 2011, p. 13).

being made. If indeed it appears as though the decision being made is inconsistent with these other elements of competence, then the SRA will have to consider if one of the potentially problematic factors overly influenced this final decision and undermined voluntariness.[502]

Advantages of the SRA Conversational Approach

As already argued, the goal of the competence assessment process cannot only be to see if a potential subject meets some broad criteria for competence, but must also be to "provide information, assess the degree to which it is being adequately processed, and then to maximize this ability through further discussion and other remedial efforts on the basis of a given subject's particular areas of difficulty."[503] It is in part to this end that the conversational tactic should be utilized by the SRA, who through a conversational approach attempts to bolster as well as test a potential subject's competence. As previously admitted, it is beyond the scope of this current work to fully develop a new competence assessment tool, however, the implementation of this methodological approach will assist in rectifying many of the past problems and flaws with competency assessment, specifically with terminally ill subjects of research. In fact, this approach has many advantages and can mitigate if not completely correct for the issues and flaws

[502] It should be noted that while no current accepted empirical measurement of voluntariness exists, there have been instruments developed to test for perceived voluntariness. Both the Decision Making Control Instrument (DMCI) and The MacArthur Perceived Coercion Scale (PCS) test a person to see their perceived level of voluntariness (See: Victoria Miller et al., "The Decision Making Control Instrument to Assess Voluntary Consent" *Medical Decision Making*, Vol. 31(5), pp.730-741, 2011; and Appelbaum et al., 2009, p. 36, respectively). However, one's perceived voluntariness may not always be the greatest indicator of actual voluntary decision making. Indeed, that "which is voluntary *in fact* is to be distinguished from that which is *perceived* as voluntary by the person who decides or acts. Controlling influences are sometimes unobservable to a decision maker, and voluntariness is sometimes perceived as present when it is not" (Nelson et al., 2011, p. 13). This may be the case when a potential subject is deceived or manipulated, or even unable to withstand pressure from others due to a fragile mental state.

[503] Moser et al., 2002, p. 1205.

previously discussed with prior competence assessment methods including the MacCAT-CR. We may proceed by first looking at some general advantages of the SRA conversational approach, and then examine how such an approach also rectifies the specific criticisms previously leveled against the MacCAT-CR.

First, as studies have demonstrated, "oral consent in combination with written consent rather than written consent only has been shown to lead to greater understanding."[504] More specifically, some reviews and studies have found that certain interventions can greatly improve consent-related information delivery such as requiring oral responses by potential subjects, and providing corrective feedback,[505] both of which can be found within the SRA conversational approach.

Another feature of the SRA conversational approach worth mentioning is the highly interactive framework throughout the process. The delivery of consent related information, the competence assessment, and the final act of consent are all done with consistent interaction with the SRA. "Interactive questioning during the consent process has been shown to increase post-consent subject understanding, and has the added benefits of highlighting important elements for the subject to focus on, ensuring understanding of earlier material to allow understanding of subsequent information, and assessing subject understanding during the process to allow for appropriate explanation throughout the process."[506]

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[504] U.S. Department of Health & Human Services. Office of Extramural Research, National Institutes of Health, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider.* November 2009, <http://grants.nih.gov/grants/policy/questionablecapacity.htm#_ftn26>.
[505] Eyler and Jeste, 2006, p.561.
[506] U.S. Department of Health & Human Services. Office of Extramural Research, National Institutes of Health, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider.* November 2009, <http://grants.nih.gov/grants/policy/questionablecapacity.htm#_ftn26>.

A third upshot embedded within this method is that such an approach encourages questions from potential subjects. A lack of confidence, overly emotional state, or even being overly awed by medical professionals may often lead subjects to avoid asking questions. However, the SRA conversational approach should provide a setting that empowers potential subjects and invites them to ask any questions, thus enabling them to contribute to their own competence bolstering since subjects would best know which areas of the research study are most confusing to them and thus most in need of explanation.

Somewhat related to this previous point, another one of the advantages to the conversational approach is that it allows for a malleable environment that can be varied as necessary in order to meet the needs of particular potential subjects. In a discussion regarding competence to consent to treatment, Thomas Grisso and Paul Appelbaum argue that "patients' difficulties in the consent process can sometimes be ameliorated by altering the social context to provide them with additional support. The presence of family members, friends, a trusted personal physician, a member of the clergy of the patient's faith, or even just a staff member of the same ethnic group can reduce the level of anxiety that patients feel in unfamiliar and threatening medical environments."[507] This is similarly true in the research context with potential subjects. Should the situation warrant such a change in the social context, the additional person in the conversation, be it a spouse, other family member, close friend, or whoever, may assist in bolstering the competence of the potential subject in a myriad of ways. The additional person may for example assist the prospective subject in processing any information given. This may be accomplished simply with the presence of that additional individual since their presence

[507] Grisso and Appelbaum, 1998, p.97.

may be of comfort to the potential subject and may thus reduce any anxiety that the potential subject might be experiencing, which would then better enable him to receive any consent related information. Often the additional person may prove valuable by being able to reinterpret information in a language to which the potential subject is more accustomed. Furthermore, the more comfortable setting facilitated by the presence of this additional person may enable potential subjects to feel more confident in asking any questions they may have, further facilitating a better overall understanding.[508]

Finally, this approach employs a qualitative as opposed to quantitative analysis. Some critics may actually raise this point as an objection to the SRA conversational approach. Such a critic may object stating that a qualitative as opposed to quantitative approach opens up the possibility for the subjective biases of the evaluator to factor into the final determination of competence or incompetence. However, there are two problems with such an objection.

First, it must be noted, that despite the use of a quantitative competence assessment instrument, the manner in which it is administered and by whom, may still enable subjective biases. Even the MacCAT-CR, which asks evaluators to score subject responses on a scale between 0 and 2 may allow for the evaluator's subjective biases to rate responses too highly or too low.

However, the real dilemma with such an objection is not merely that subjective bias may still exist with quantitative approaches, but rather that it fails to recognize the

[508] It should be noted that while the presence of an additional person may be helpful in the initial conversation with the SRA, when it becomes time to assess the potential subject's competence, it remains imperative that such a conversation occur without the presence of others. The reason for this should be clear since the assessment is intended to ensure the competence of the potential subject only, and the presence of others, especially if they are involved in the conversation, may hinder the SRA's ability to evaluate the potential subject's own responses.

significant deficiency of quantitative approaches in the first place. Indeed, a quantitative method to competence assessment is unlikely to ever be optimally accurate in determining one's competence. The myriad of possible states of mind, influencing factors, and reasons for making certain decisions that different potential subjects may have, cannot all be accounted for quantitatively. Thus while it may give us a feeling of assurance to know that determinations of competence are reducible to seemingly easy mathematical computations, it is not realistic. Some studies have already demonstrated that qualitative approaches yield more accurate results when testing the competence of certain patient populations. "Recall that anorexic patients scored highly on all aspects of the MacCAT-T despite the fact that a qualitative analysis revealed ambivalence over treatment [among other issues.]"[509] One study showed that anorexia nervosa patients who were judged competent by the MacCAT-T actually had severe difficulties and defects in their thinking processes that are relevant to competence.[510] Thus, even this feature of the SRA conversational approach, namely that it utilizes a qualitative as opposed to quantitative method, should be seen as an advantage.[511]

We would be remiss though, if we did not recognize the appeal of quantitative competence assessments, namely that such approaches are more easily and quickly administered. However, we must not allow our desire for speed or ease to jeopardize the

[509] Edward D. Sturman. "The Capacity to Consent to Treatment and Research: A Review of Standardized Assessment Tools" *Clinical Psychology Review*, Vol. 25, pp.954-974, 2005, p. 966.
[510] Tan et al. "Competence to Make Treatment Decisions in Anorexia Nervosa: Thinking Processes and Values" *Philosophy, Psychiatry, Psychology*, Vol. 13(4), pp. 268–282, 2006, p. 279.
[511] Apart from the fact that qualitative approaches might be more accurate than quantitative ones, the concern of subject evaluator bias is largely ameliorated by the employment of a particular kind of expert to the SRA position. The SRA's expertise in dealing with terminally ill patients and subjects, as well as training with the four standards described in Chapter Four, should ensure that competency assessments are unaffected by any personal biases. It may further be noted that though the SRA conversational approach is qualitative in nature, it may still be tested and evaluated using similar empirical measures used to test other quantitative competence assessment instruments. For instance the interrater reliability, concurrent validity sensitivity, specificity, and test-retest reliability may all be appropriately used in order to evaluate the SRA conversational approach.

accuracy of competency assessments. It may indeed be noted that the minimum requirements of the four sub-abilities and thus cut-offs established in Chapter Four and used by the SRA conversational approach are not as clear as purely quantitative cut-offs would be with a competence assessment tool that numerically scored a subject's performance. Thus a person utilizing such a qualitative approach may have more difficulty evaluating the competency of potential subjects than would be the case with a quantitative method. This though only reinforces the need for the SRA to be a particular type of expert in such matters. Furthermore, as already argued, the advantages of such an approach outweigh the numerical cleanliness and ease of purely quantitative approaches.[512]

The SRA Conversational Approach Remedies the Criticisms of the MacCAT-CR

We may recall the 4 Sturman criticisms. These were i) the problem with repetition, ii) the difficulty of self-reporting, iii) the multi-factor hindrances to competence, and iv) the problem of patient/subject deception, respectively. Like the MacCAT-CR, the SRA conversational approach easily deals with the second and third criticisms in much the same manner as the MacCAT-CR.[513] However, unlike the

[512] In fact aside from what has already been argued, such a qualitative approach directly responds to one of Paul Appelbaum's criticisms of cutoff scores in general. "As Appelbaum notes, 'no single cutoff score yields both high sensitivity and high specificity'" (Epstein, 2008, p. 513). Though such an issue may never be fully rectified, it should be acknowledged that it applies more so to quantitative cut-offs which are problematically rigid such that they may either allow incompetent persons to qualify as competent, or competent persons to be deemed incompetent, that is false negatives and false positives respectively. However, such a dilemma is mitigated by the qualitative cut-offs offered here, which are flexible enough so as to allow the expert SRA to account for the unique factors of every case and make appropriate competency evaluations.

[513] The difficulty of self-reporting issue relates to the fact that when a patient's or subject's reasoning is assessed by asking them to recollect the mental processes used in their decision-making process, the answers given are often inaccurate. However, similar to what was previously argued regarding the MacCAT-CR, the SRA conversational approach avoids this dilemma. The tactic employed by the MacCAT-CR, namely engaging in a series of questions, none of which directly ask the potential subject to

MacCAT-CR, the SRA conversational approach is also able to remedy the first and fourth criticisms as well.

The first criticism, namely the problem with repetition, involved the potential for a subject to be deemed competent while only possessing the ability to repeat information, without having an adequate understanding of that information. This issue of mere repetition without actual understanding has at times been overlooked. In fact in studies examining past competence assessment methods, it was found that the methods used "sometimes examined recall of information rather than true understanding,"[514] making this issue one that was able to persist virtually undetected. However, the SRA conversational approach does not suffer this defect as did the MacCAT-CR. The very nature of this approach relies on an ability to converse, which itself will often require persons speaking on matters in their own words. The ability to vocalize concepts in one's own words itself requires a certain amount of comprehension regarding those concepts. This approach would thus eliminate the potential for a prospective subject to merely

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merely remember her reasoning, but rather which will have her engage in the reasoning process right there, in front of and with the interviewer, resolved this issue to a great extent. The SRA approach which utilizes a conversational method similarly, if not even more so, compels potential subjects to engage in the reasoning process right there with the SRA thus minimizing this self-reporting dilemma. The third Sturman criticism, specifically, the multi-factor hindrances to competence, is likewise avoided by the SRA conversational approach in much the same way as was previously discussed with the MacCAT-CR. This criticism suggested that given the many possible factors in a certain context that may hinder competence, one who fails to demonstrate an adequate level of any of the sub-abilities of competence is not necessarily a person who may generally lack that sub-ability, or competence overall, in life. However, just as was the case with the MacCAT-CR, the SRA conversational approach acknowledges this and is meant to assess competence only in the specific context for which its line of questioning is geared. It is not meant to provide blanket determinations of competence for a person. Refer back to Chapter Five for a more detailed discussion regarding these two criticisms and the MacCAT-CR.

[514] Eyler and Jeste, 2006, p.561. Part of this problem may stem from inaccurate or incomplete definitions and accounts of understanding which may lead to "a confusing between understanding and recall" (Laura Dunn and Dilip Jeste. "Enhancing Informed Consent for Research and Treatment" *Neuropsychopharmacology*, Vol. 24(6), pp.595-607, 2001, p. 604). One may refer back to Chapter Four for some detail regarding an appropriate depiction of understanding. However presently we may briefly note that "to understand a treatment or research protocol, a patient must receive, encode, retain, and process the information. This necessarily involves sensory modalities, attention, memory, and cognition... Recall alone does not imply understanding [and] furthermore, long-term recall is not always necessary, for example, in immediate treatment decisions" (Dunn and Jeste, 2001, p. 596).

regurgitate information that was only memorized, but not adequately understood. In fact any attempt to merely repeat purely memorized information would likely become apparent within the context of a back and forth conversation, alerting the SRA to a possible deficiency in the person's competence.[515]

Additionally, the built in waiting period after the disclosure conversation, but before the competence assessment conversation, greatly alleviates this issue in a way that the MacCAT-CR falls short. As already discussed the MacCAT-CR asks direct questions pertaining to a specific element of competence immediately following the disclosure of the information necessary for that element of competence. This increases the potential for a potential subject to simply repeat back the information he heard seconds before without any actual understanding. The waiting period thus not only accomplishes various goals explained beforehand,[516] but now also aids in preventing this obstacle to competency evaluations as well. The SRA conversational approach thus does not fall prey to this first line of criticism.[517]

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[515] Apart from testing for real understanding and not just memorization of information, an "assessment should also take into account an apparent lack of motivation, inattention, [or] mistrust" (Sturman, 2005, p.966), which can themselves lead to a subject processing information only cursorily, and perhaps may even cause a subject to not even attempt to do much more than just memorize information. The conversational format suggested here facilitates an exchange between the SRA and the potential subject that will enable the detection of these underlying issues as well, and thus better prevent dilemmas related to understanding than with previous competence assessment methods including the MacCAT-CR.

[516] These included, enabling the prospective subject to digest and read any information that has been provided, reflect on the initial conversation she had with the SRA, discuss the situation with friends and family, as well as allow the SRA to better distinguish between time-limited and permanent impairments, which may be particularly necessary for prospective subjects who have only recently learned that they have a terminal illness and may be over stressed or overly anxious.

[517] The idea of incorporating this type of waiting period before the final consent is one that has been corroborated by the National Institutes of Health, which has asserted that "it may be helpful to provide information incrementally and to build in a waiting period after the initial screening interview, before seeking the subject's formal written consent. A two-step informed consent process would facilitate family conferencing and consultation, and allow more time to weigh the pros and cons of study participation" (U.S. Department of Health & Human Services. Office of Extramural Research, National Institutes of Health, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider.* November 2009, <http://grants.nih.gov/grants/policy/questionablecapacity.htm#_ftn26>).

The fourth Sturman criticism, which the MacCAT-CR was unable to properly remedy, was the problem of patient/subject deception. This dilemma was concerned with patients or subjects being able to say what they think a competence assessor will want to hear, despite possessing beliefs to the contrary, thus enabling them to deceive the assessor affecting his ability to accurately judge competence. This may be especially problematic in research with terminally ill individuals who may be desperate to enter into a clinical trial. We may recall that the MacCAT-CR did not fare well against this line of criticism as was previously established with the anorexia example and the transparent style of questioning employed by the MacCAT-CR argument.[518] It should be recognized that such a problem may never be fully prevented, for there will always be some persons clever and motivated enough so as to deceive even the most proficient competence assessors. However, the type of thorough conversation in which the SRA will engage the potential subject, will go a long way in preventing possible deception. Given that a conversation revolving around the appreciation component of competence will allow the SRA to delve a little into the personal circumstances surrounding a potential subject, that subject will be less likely able to deceive the evaluator by lying about his or her beliefs. In fact any purposeful deceit may become more apparent and obvious to the SRA due to the nature and length of the conversation.[519] It may thus be concluded that the SRA conversational approach is able to rectify all four of the Sturman criticisms.

[518] Refer back to Chapter Five for a discussion of these arguments.

[519] For instance, we may envision a potential subject who possesses overly hopeful and unrealistic beliefs regarding the therapeutic potential of a trial, but decides to hide these from the competence assessor. Hiding such information might be easy during the course of a verbal questionnaire. However, successfully accomplishing such a task may become more difficult during the course of an in depth back and forth conversation where one's true beliefs are given various opportunities to surface, even if unintentionally. However, it should be noted that detecting deception is a highly difficult task. In fact "detecting deception often stumps the most experienced police officers, judges, customs officials and other forensic professionals. Research has shown that even agents from the FBI, CIA and Drug Enforcement Agency

In addition to these issues though, we may also investigate how well the SRA conversational approach fares with some of the criticisms specific to the MacCAT-CR. We may recall that there were three such criticisms previously discussed. These were the MacCAT-CR's failure to take voluntariness into account, its inability to provide cut-off scores or standards that would aid a competence assessor in her competency determination, and that a greater attempt at combating the therapeutic misconception was needed.

We may recall that the MacCAT-CR lacked an adequate assessment of one's voluntariness in decision making, opting instead to only determine whether an individual is able to express a choice, but ignoring whether such a choice ought to be considered voluntary. Competence assessment tools, including the MacCAT-CR fail to account for this voluntariness element of competent decision making largely due to the fact that such tools are established on accounts of competence that fail to acknowledge this component of competence. Without rehashing the various arguments previously made, it was established that voluntariness is an essential component to competent decision making. Possessing adequate understanding, appreciation, and reasoning is ultimately meaningless if the final decision made does not stem from one's understanding, appreciation and reasoning. Given that other accounts of competence fail to include this element, the SRA

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don't do much better than chance in telling liars from truth-tellers" (Rachel Adelson. "Detecting Deception" *American Psychological Association Monitor on Psychology*, Vol. 35(7), 2004, p.70). Thus, it is an unfortunate fact that even our SRA may be deceived by potential subjects clever and motivated enough to deceive. However, lying has been shown to have various verbal and bodily cues, such as pressing one's lips together, taking longer to begin answering questions, attempting to talk only minimally, and providing stories that are implausible (Adelson, 2004, p. 70). Though not an exact science, these types of cues, as well as other possible abnormalities in communication, may become obvious to an SRA over the course of a lengthy and personal conversation, thus potentially tipping off the SRA to possible deception.

conversational approach is able to succeed in an area that most, if not all, other competence assessment instruments and literature on this topic has overlooked.[520]

We may also recall, that the MacCAT-CR had no cut-offs or standards for assessors to use in order to make determinations of competency or incompetence. This was largely due to adherence to the principle that no one competency cut-off or standard could be applicable in all cases. Indeed, others, such as Dunn et al. have also acknowledged that "the lack of a predetermined cutoff separating capacity and incapacity is less a limitation than an intended feature of the MacArthur instruments; … [Further adding that] in any case, factors unique to certain contexts or populations will make other instruments preferable in some situations."[521] It is this last sentiment that drives our current endeavour, since as has been argued, the research context with terminally ill subjects represents a particular context and population that can be better served with a more specific competence bolstering/assessment procedure and instrument geared toward accounting for the factors unique to such a context. Thus, though Appelbaum and Grisso are correct in their assertion that no single standard could apply to the broad range of possible cases, such an issue is not presently relevant since the cut-offs/standards created in Chapter Four and employed here are specific only to one particular context with one type of population, namely terminally ill subjects of research.[522]

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[520] As previously discussed the nature of the conversation between the potential subject and the SRA will involve a discussion regarding the motivations and influences that may have been present in the decision-making process. In addition to accounting for and examining these, the SRA must also look for possible mental states that may undermine voluntariness, including extreme insecurity, a lack of confidence, an overly emotional or anxious state as well as others. Ultimately the SRA will have to determine whether or not the final decision made follows from a potential subject's own understanding, appreciation and reasoning. Refer back to earlier in this chapter for a more detailed account regarding the manner in which the SRA ought to analyze one's voluntariness.

[521] Dunn et al., 2006, p.1331.

[522] It should be noted the part of the problem identified by Appelbaum and Grisso, as well as others regarding the inability for a cut-off to apply in all cases, applies more so to quantitative cut-offs or

The ability to use cut-offs/standards, even qualitative ones, will be useful to competence assessors in making determinations of competence and incompetence in an accurate and efficient manner.[523] It will further enable them to make such determinations in a more uniform way, creating consistency between different research trials and between different jurisdictions.[524] Thus the SRA conversational method again proves able to improve upon past competence assessment approaches/instruments.

The final criticism of the MacCAT-CR involved the recognition that it does not go far enough in combating the therapeutic misconception and improving potential subjects' appreciation. However, it is here that the SRA conversational approach might best shine. Given the personal nature and structure of the conversation, the SRA should be able to facilitate a conversation that encourages the potential subject to engage with and consider how research participation may affect one's life. This will include not only

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standards and less to our qualitative standards. The reason being that quantitative cut-offs are rigid, whereas the qualitative standards employed here are more flexible and are more likely to accommodate the variety of unique factors or personal circumstances that different potential subjects may bring.

[523] One may note that though the MacCAT-CR has a rating system, without anything close to a set of standards or cut-offs, such numerical ratings are not overly helpful for the competence assessor in making competence evaluations. Indeed, as Appelbaum admits in regards to the competence assessment of patients, evaluators using the MacCAT-T should "integrate the results with other data in order to reach a judgment about competence" (Paul Appelbaum. "Assessment of Patients' Competence to Consent to Treatment" *The New England Journal of Medicine*, Vol. 357, pp.1834-1840, 2007, p.1837). However, "exactly what 'other data' should be collected and included in the assessment is not specified" (Jorie Epstein. "How Reliable is the Competency Assessment Process?" *Virtual Mentor: American Medical Association Journal of Ethics*, Vol. 10(8), pp. 511-515, 2008, p.513). This approach therefore, may further lead to inconsistent competency evaluations between research institutions and jurisdictions, thus demonstrating the need for some form of standards or cut-offs.

[524] The issue of consistency has also been raised in regards to competency assessment in the treatment setting with patients. In a criticism of standardized competence assessment instruments, Jorie Epstein touches on the importance of having a uniform procedure for competence evaluations stating that "one can see that the tests, while potentially helpful, are plagued by limitations, not the least of which is how to administer them more consistently. In order to achieve greater uniformity, a physician must know how to execute the exams properly. But do physicians receive specialized training for the specific assessment they will give? If the test itself is standardized, what are the procedures for administering it? Appelbaum states that 'there are currently no formal practice guidelines from professional societies for the assessment of a patient's capacity to consent to treatment', forcing one to ask, how useful are these assessment tools?" (Epstein, 2008, p. 513). Though this is in regards to the treatment setting, similar concerns can be raised about competence assessment tools utilized in the research setting with potential subjects. However, developing a standardized approach that employs a specific type of trained expert and qualitative cut-offs, both of which the SRA conversational approach accomplishes, such concerns are largely resolved.

some disclosure and conversation regarding the various methods in research that deviate from standard best care practices that would be typical in the therapeutic setting, but also a discussion over the existence of the therapeutic misconception itself, as well as some of its contributing factors. Such a discussion will better enable a potential subject as well as the SRA to recognize whether or not such factors are currently present and hindering the potential subject's competence. Additionally, as previously mentioned the conversation with the SRA will also force the subject to engage with the ways in which research participation may impact the various aspects of one's life, including health (quality and longevity), career, hobbies, family, other goals, and one's values, thus making this approach to enhancing and testing for appreciation more rigorous than other existing competence assessment instruments and methods.

It should be acknowledged that the SRA conversational approach may be lengthier than other competence assessment methods and instruments. This is largely due to two factors. First, there are two separate conversations built in to this approach, namely the disclosure/competence bolstering conversation, and the evaluation conversation. This alone increases the time it may take to enroll subjects in research trials. Additionally, the SRA conversational approach will likely involve discussions that are by their nature lengthier than what other instruments and methods require. This is as a result of the particular attention afforded to both appreciation and voluntariness, which due to their complexity and intricacies require uniquely personal conversations with potential subjects. It seems to be unfortunately the case that proper assessments of appreciation and voluntariness conflict with the simplicity and brevity of competence assessment methods. However, we cannot merely forget these two crucial pillars of

competence, but instead hope to strike the right balance between administrative practicality and the comprehensiveness of the competence evaluation procedure.

Concluding Remarks

The preceding Chapters have provided a crucial first step in improving the ethicality of research conducted on terminally ill individuals. More specifically, Chapter One explained the connection between competence, autonomy, and informed consent, whereby competence was shown as a requirement necessary if informed consent is to be truly considered an expression of one's autonomy. Put another way, incompetence precludes one from acting autonomously. Thus, it was concluded that respecting the autonomy of potential research subjects requires a serious focus on competence itself. Given this, a comprehensive depiction of competence was provided, where competence included four separate sub-abilities, including understanding, appreciation, reasoning and voluntariness.

Chapter Two examined a current common method for dealing with competence. This was the risk based sliding scale approach which dictated that the required competence for decision-making ought to vary with the riskiness of the decision. Therefore, as the risks of a decision increase so too should the required level of competence. Similarly, such an approach dictated that the less risky a decision, the lower the competency requirements ought to be. However, such a strategy to competency requirements was proven flawed for a myriad of reasons. More specifically, it was shown that the various underlying arguments in favour of the risk based sliding scale were fraught with fallacies, that competence assessments should not be affected by an

application of a best interest standard, that the risk based sliding scale would permit a disguised hard paternalism, that such a strategy conflicts with the vital precept that competency assessments should be process-oriented and not result-oriented, and also that it is dubious whether the risk based sliding scale is helpful in the medical research setting. Ultimately it was argued instead that the stringency of competency requirements should be related with the demands of the decisional task at hand. That is to state that as a decisional task is more complex, the greater the level of competence that ought to be required.

Given this, Chapter Three then demonstrated the need for a greater competency requirement in the research context with terminally ill subjects as compared to the medical practice context. Three significant differences between the two contexts were discussed and proved to cause decision making in the research context to be far more difficult than decision making in medical practice. These differences included the difference in the nature of the researcher/subject relationship as opposed to the physician/patient relationship, the higher potential for exploitation of the situation or mental state of terminally ill subjects, and the presence of the therapeutic misconception. Thus it was argued that the research context with terminally ill subjects represents a more difficult decision making context than the medical practice decision making context, and therefore such a context warrants greater competency requirements.

Chapter Four then provided such competency requirements. By establishing various possible levels within each sub-ability of competence, it became possible to note where it might be appropriate to set our standards for the research context with terminally ill individuals. The determination of such sub-ability requirements relied heavily on the

already previously established significant differences between the medical practice and medical research context. Ultimately, four separate standards, one for each sub-ability of competence, were generated, and the amalgamation of these was deemed to be the new competency requirement for the medical research context with terminally ill subjects.

However, since providing a competency requirement for the medical research context with terminally ill individuals requires more than merely establishing the requirement itself, Chapter Five began to lay the groundwork for the implementation of such requirements. More specifically, it remained to be determined how best to attempt to test for such a new competence requirement. Chapter Five thus examined some current competency assessment tools and methods, ultimately demonstrating their flaws. Most of the effort was directed towards examining the MacCAT-CR since it is often lauded as the superior competence assessment tool. However, it too proved to have some flaws, including its failure to take voluntariness into account, its inability to provide cut-offs or standards that would aid a competence assessor in her competency determination, that a greater attempt at combating the therapeutic misconception is needed specifically for terminally ill subjects, and that it does not attempt to correct for some common issues often levied against competence assessment tools such as the problem of repetition and the problem of subject deception.

Chapter Six was then tasked with providing a way forward to competence assessment that can attempt to correct for common criticisms often directed at competence assessment methods, as well as for the issues that plagued the MacCAT-CR, and be geared toward the medical research context with terminally ill subjects. Thus, the SRA conversational approach was provided. This approach involves the employment of a

subject rights advocate who is not related to the organization conducting the research, and who is charged with the task of both enhancing the competence of potential subjects, as well as ultimately testing for the necessary level of competence needed to consent to participate in the research trial. Both tasks are accomplished through a conversational method.

Though, as the final chapter demonstrated, such a strategy should correct for many of the past issues with competence assessments, as well as better serve to protect the autonomy of prospective subjects and hopefully diminish the potential for abuse and corruption, such a strategy too may have some limitations going forward.

It must, for example, be acknowledged that such an approach was designed specifically for use with terminally ill subjects. While some of the recommendations throughout this work may apply to other populations participating in research, many of the considerations applied in both the creation of the competence requirements, as well as the SRA conversational approach, would not pertain to other populations. For instance, the concern regarding the therapeutic misconception would not be as appropriate for healthy volunteer subjects of research.[525]

Additionally, the SRA conversational approach fell short of being a fully structured competence assessment tool. This was however in part by design. It was for instance argued that despite the ease of use with structured quantitative assessment tools, a qualitative approach will likely lead to more accurate results. As previously discussed, structured quantitative tools will render the competence assessment process as too ridged

[525] Despite this though, it should still be acknowledged that misconceptions are still common amongst healthy subjects as well. For example a healthy subject of research may not think of his participation as being akin to therapeutic treatment since he is not looking to have an ailment alleviated or cured, but he too may still be confused between the intent of researchers and research itself, as compared to that of typical medical practice.

to accommodate the various potential factors that may be present with prospective subjects of research. Nonetheless, it must be acknowledged that despite the underlying reasons for preferring a non-structured qualitative approach, the implementation of such an approach will be trickier and more time consuming. As a result, the integration of such a strategy into current research practices may prove to be a difficult and lengthy transition, but one that is nonetheless a necessary ethical step forward.

Finally, it ought to be acknowledged that some work still remains to be completed. The full implementation of a competence assessment method lay beyond the scope of this current project. As previously discussed, such a task would require testing and rating the SRA conversational approach for its internal consistency, interrater reliability, concurrent validity, sensitivity and specificity, and then making adjustments where necessary. Such tasks remain to be completed going forward. Additionally it still remains to be determined how best to structure the training and education for SRAs. Since the competence bolstering and assessment depends on the expertise of the SRAs, ensuring both that only qualified candidates are chosen, and second that the necessary training with the competency requirements is provided to those selected, similarly remains as the next steps essential to improve the ethicality of research conducted on terminally ill individuals.[526] Nonetheless, despite some of the remaining work, a crucial first step has been taken here, as the framework for both the necessary competence

[526] The importance of qualified and properly trained SRAs cannot be understated. Since the competence assessment/enhancement approach proposed is of a qualitative variety, some of the decisions regarding how to conduct portions of the conversation with prospective subjects will at times be left to the subjective interpretations of the SRA and thus, ensuring that the SRA is well educated on the four elements of competence, the competence requirements for terminally ill research subjects, as well as the types of factors that may arise with this population that may pose a hindrance to adequate competence, is paramount.

requirements, and competence assessment/enhancement approach, have been established for medical research on the terminally ill.

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Appendix A: Case Studies

There will likely be many instances where, through the conversational assessment approach, an SRA will be able to easily detect issues with one's competence. This may occur in cases where a potential subject consistently seems to confuse the research trial with his own personal therapy, even after the therapeutic misconception and its causative factors have been explained. This may also occur when it becomes clear to an SRA that the final decision made by a potential subject was not actually her own, but was controlled by another person, for instance a physician or family member. As previously argued, voluntariness may be affected in this manner when an individual is either too emotionally distraught or even insecure to reason through a decision on her own, and instead excessively relies on the opinions of others. Similar hindrances to voluntariness may also occur when a potential subject has been deceived or manipulated by another.

However, despite there being a body of possible cases where the SRA will be able to use the conversational approach as well as the standards for each element of competence established in Chapter Four to reach her competency determinations easily, the SRA will also encounter a handful of borderline cases where it may be more difficult to make a competency determination. Two such cases are presented below, with evaluations for each of the four separate sub-abilities of competence.

CASE 1: Colon Cancer Patient/ Phase I Trial

Case Details

Posit the following scenario:

George, a 22 year old senior college basketball player at the University of Kentucky, is currently leading his team in an important tournament, and has been diagnosed with colon cancer. His physician has informed him that current possible treatment involves a potential mixture of a chemotherapy regimen over the course of 8 weeks, surgery and radiation therapy. However, given the advanced stages of the illness, the likelihood of complete remission using standard therapy is only at best 50% and George is told that without complete remission, he may only have 2-4 years to live. He is further informed that such a process, especially during the chemotherapy regimen, may significantly impact his quality of life and at times render him so ill that he will be bedridden. Symptoms such as severe pains, increased chances of infections, nausea, extreme fatigue, and muscle weakness are most common, but there are many other possible adverse effects that may also occur.

However, the physician further informs him that he is the recruiter for a new clinical trial that is testing the efficacy of a new targeted cancer therapy that is designed to target specific molecular targets associated with the cancer as opposed to current standard chemotherapy regimens that affect all active bodily cells. Thus, George is further informed, such a potential therapy may come with far fewer and less severe side effects, and some studies in animals have shown that there is a chance that one may still be able to live a normal life while undergoing such a treatment. In its current stage of development, the non-validated drug has also shown the potential to be as effective as

current standard therapy in combating late stage cancers such as the one that currently afflicts George, though no accurate remission rates are currently known. The drug is currently about to commence testing in a Phase I study. More specifically, the study will escalate the dosages of the drug in various stages in an attempt to note its toxicity and determine a maximum tolerable dose (MTD). However, his physician further informs him that he thinks that for the majority of the trial, the side effects will be far fewer than with current standard chemotherapy treatment, and further adds that this is likely George's best chance to combat the disease. The physician continues on to tell George that after the trial, George will still be able to access current standard therapies. The physician then provides him with a promotional brochure for the trial.

George, who is distraught at the news, becomes visibly terrified and seems very uncertain as to what decision he should make. He is afraid of death and wants the best chance to live as long as possible. He also considers how such news will affect his basketball career, and more specifically the tournament in which he is thought to be currently leading his team to a potential championship. He knows that he will be unable to play if he decides to go with standard chemotherapy treatment, but that there is a chance that he will be well enough to play if he opts instead to enter the clinical trial. Though he is indeed concerned about the risks to his quality of life regardless of which option he chooses, his main priority is to attempt to overcome the disease as best as possible and live as long as possible. George is incredibly unsure what to do and decides to speak with his basketball coach, his family, and his doctor again in order to determine the best course of action for him. After such consultations, George decides to enroll in the trial. After an initial informational disclosure with the SRA, George decides that he will

participate in the trial, but must first have one more evaluative conversation with the SRA.

SRA Conversation[527]

In this conversation, George explains that he understands the nature of his disease and that it is likely to kill him within 4 years if he is not responsive to current standard treatment or to the non-validated targeted treatment administered in the clinical study. He claims that he would attempt anything to avoid death including attempting experimental interventions and further states that he is hopeful that this clinical trial will cure him. He appears incredibly saddened at the idea of not living a long enough life.

With some prompting by the SRA, George explains that he understands that this research trial differs from standard treatment, and that he for instance will not be getting the kind of personalized attention that he would otherwise receive with ordinary treatment. He acknowledges that this is a toxicity study and seems to realize that that makes it differ from standardized treatment. He furthermore seems to recognize the existence of the therapeutic misconception and that it may sway people to participate in research, thinking that it is standard therapy. George further explains that such a misconception may be especially problematic with desperate terminally ill individuals who may be inappropriately swayed into thinking that the research will provide some miracle cure.

When asked how research participation will impact his life, he claims that it will likely have less adverse effects, particularly in the early and middle stages of the trial,

[527] The following should not be taken as a full depiction of the conversation with the SRA. Such a conversation is likely to be much lengthier in nature, and may require several different types of inquiry by the SRA. Instead, the following should only be taken as some of the fundamental takeaways from the conversation that are relevant to the SRA's competency evaluation.

than standard chemotherapy, and that he may even possibly avoid the common side effects associated with current chemotherapy, and thus may have a chance to still play basketball this year and finish his tournament. It was for this reason that he claimed that his coach and team thought that this would be a good idea. He further voiced his contentment with the idea that he might be able to play in the tournament because it had been rumored that NBA scouts would be present. Potentially making it into the NBA was something that he and his parents had been working towards for his entire life. George claimed that this was one of the deciding factors that made his parents also agree that he should enroll in the trial. When further questioned about the role his coach, team, and parent's played in the final decision, George claimed that they all seemed in agreement that the trial would be able to help him combat the disease at least as well as standard therapy, while at the same time minimizing severe side effects and thus possibly enabling him to play in the current tournament. He further added that since he was unsure as to what he should do, and everyone around him seemed in such agreement, the choice became obvious for him.

When questioned by the SRA as to what the most important factor for George was when considering his options, George claimed that it was to ensure the best chance to increase his longevity. Avoiding an early death was paramount to George. However, when asked which option made such an outcome more likely, George replied that current standard treatment might work best since it has been established to cause complete remission for cases like his 50% of the time. However, he added that he hoped that participation in this trial would give him at least as good a chance to extend his life, though remission rates for the non-validated intervention are not as well known. After

avoiding death, George claimed that playing basketball was the most important factor in the decision making process.

When prompted by the SRA to explain his final choice to participate instead of opting for current standard treatment, George asserted that his main goals were to live as long as possible and still be able to currently play basketball. He again admitted that current chemotherapies gave him a good chance to survive and go on to live a long life, and probably represented the option that gave a more realistic chance to cause the cancer to go into remission. However, after speaking with his coach, team and parents, they all thought that the trial might work better since it may also cause the cancer to go into remission while at the same time minimizing possible side effects. George further claimed that this was also the opinion of his physician, and that everyone he consulted seemed to agree, and so he opted to enroll in the trial.

Considerations for the Final Competency Assessment

George appeared to demonstrate an understanding of his disease, the purpose of the trial, and the presence of the therapeutic misconception. He understood the potential for his disease to be terminal within 4 years, as well as what current standardized treatment would offer. He further seemed to understand not only *that* research differed from standard treatment, or *that* the therapeutic misconception exists, but also *how*, citing that the clinical trial would not afford him the type of personalized attention thought quintessential of ordinary best care standards, and that misconceptions that research was actually treatment are possible among certain individuals who may be desperate and thus

easily swayed. Thus it appears that George satisfies the high level of understanding criterion for competence.

George further seemed capable of appropriately appreciating the facts surrounding the clinical trial. He seemed to understand that it is a toxicity trial, and even alluded to the fact that with such a study the chance of success for him was unclear. He also seemed able to foresee how the possible side effects of both options might impact his life, specifically discussing how the potentially less severe side effects at least in the early stages of the trial would enable him to finish his tournament.

Though it required some prompting, George further seemed able to appreciate the relative affect on longevity of each option, citing that current standard treatment might be most beneficial to his longevity since it was known to have a 50% complete remission rate. However, he also claimed that he hoped that the trial would be at least as helpful, though he acknowledged that no similar statistics were known with the non-validated intervention. It was not completely clear though, whether George was aware that the actual procedures employed in a Phase I trial would diminish his personal chance of success with the non-validated drug, and thus may make the 50% remission success rate of the current standard treatments more likely to contribute to his longevity. Nonetheless, when prompted he seemed to foresee that his longevity would be better served with current chemotherapy treatments. As a result of this, it seems that indeed George sufficiently satisfies the *Imperfect, but Independent Appreciation* standard.

George furthermore, seemed capable of engaging in reasoning. He appears to have formulated a desired goal for himself, namely to live as long as possible, and secondly to play basketball. He further appears to be able to engage in appropriate

means/ends reasoning and seems to acknowledge that the current standard treatment option is more likely to achieve the former, while the clinical trial is more likely to accomplish the latter. Thus George seems to satisfy the *Imperfect, but Largely Independent Reasoning* standard.

However, it did not appear that George's final decision to participate in the clinical trial follows from his own understanding, appreciation, and reasoning. If his main goal is in fact to ensure his longevity, and he is able to understand and appreciate that the Phase I trial does not provide as good a chance at accomplishing a complete remission, then in conjunction with a reasoned analysis, the type of which George appears capable of, one may expect George to select current standard chemotherapy over the Phase I clinical trial. Instead, it appeared George was incredibly unsure what he should do, and relied excessively on his doctor's opinion, who as a recruiter for the clinical trial may perhaps unknowingly be biased, on his parent's opinions, which seemed to be based on a different main goal than George's, namely to have George be seen by NBA scouts, and finally on his coach's opinion, who also had a vested interest in having George play in the current tournament. Conversations with these three groups appeared to exert influence over George and excessively sway him towards participation, preventing him from voluntarily selecting the option which would follow from his own understanding, appreciation, and reasoning. George thus appears to have made his decision without an appropriate level of voluntariness.

SRA's Assessment: Incompetent

Though the prospective subject possesses a high level of understanding regarding the relevant trial related information, likely meets the appreciation criterion as well, and demonstrated an ability to reason with such understandings and insights, he ultimately appeared to fail to make a decision that stemmed from such understanding, appreciation, and reasoning. Instead it seemed clear that he did not make his choice with a sufficient level of voluntariness, but was instead swayed to select this option given the influences exerted upon him by varying other individuals.

CASE 2: ALS Patient/ Phase II trial

Case Details

Posit the following scenario:

A 60 year old retiree, Audrey, has recently been diagnosed with Amyotrophic Lateral Sclerosis (ALS). Her physician has informed her that though some ALS patients go on to live many years, she likely has between two and five years of life remaining. She is further told that this is a progressive neurodegenerative disease that will affect the cells in one's brain and spinal cord. The progressive degeneration of the cells will lead to a loss of muscular control, and some in later stages of the disease become completely paralyzed.[528] Though Audrey in not employed, she is a mother and grandmother of two and has a busy and rich family life, which will be greatly impacted by such a diagnosis. Audrey is further informed that there is currently no existing cure. However, her doctor provides her details of a Phase II trial that is currently testing a new drug that may mitigate the effects of ALS. This drug has shown some small chances of success in

[528] The ALS Association, Washington, D.C. Last accessed: 2014, <http://www.alsa.org>.

animals, however previous Phase I trials have demonstrated that the drug has some adverse effects that may impact one's quality of life. Some of these effects include inability to sleep, extreme muscle weakness and atrophy, small chances of possible hearing loss as well as the potential to reduce one's longevity. Convinced that this might be her best chance to combat the disease, Audrey decides to look into the clinical trial. After consulting with her family, and having the initial informational disclosure conversation with the SRA, she decides to enroll, but is first informed that she will need to have a second evaluative conversation with the SRA.

SRA Conversation[529]

In her conversation with the SRA, Audrey explains that she understands the nature of the disease, that it is a terminal degenerative disease that will likely cause her to lose motor function rendering her in a state of paralysis. She further states that she is aware of the side effects of the experimental drug administered in the trial. She also acknowledges that the trial is not the same as standard therapy and cites the use of randomized assignment and double blinding as examples. Additionally, given the initial conversation with the SRA, she is able to recognize the existence of the therapeutic misconception, and how it may affect especially desperate individuals in dire situations such as herself. She further states that she can see how easy it might be to confuse research and treatment given the primary investigator in the clinical trial is a physician and given the visual similarities in the settings in which treatment and research take

[529] Again, as previously mentioned, the following should not be taken as a full depiction of the conversation with the SRA. Such a conversation is likely to be much lengthier in nature, and may require several different types of inquiry by the SRA. Instead, the following should only be taken as some of the salient points from the conversation that are relevant to the SRA's competency evaluation.

place. However, despite all of this, she claims that she is very hopeful that the drug will work for her and potentially be, if not a cure, then at least a way to postpone the more severe symptoms of ALS. She further states that her family and doctor shared similar opinions, and that given the lack of available treatments for ALS, this was likely the only chance she might have.

Further in the conversation she states that a reduction in quality of life due to extreme paralysis would be an incredibly difficult life for her and her family. She claims that she can imagine such an existence and would do anything to attempt to avoid that outcome. Given her role in her family as well as the joy she receives from it, she further claimed that both she and the members of her family were desperate to try to avoid such an outcome.

When prompted to discuss how her life would be if she were in the trial, she claimed that she did not know for sure and that it would depend on how severe the side effects of the non-validated drug turned out to be, but that such side effects did not overly concern her. When further prompted to envision how such side effects and overall trial participation would impact her life, she claimed that while she acknowledges that some of the side effects of trial participation could severely impact some of her life's greatest joys such as spending time with her family, that her disease would likely do that anyways. She again stated that she hoped that the Phase II trial would help improve her quality of life and that this was likely the only chance she would have to be able to spend more quality time with her family.

When prompted to answer why she would want to take part in a study that may cause an earlier death than might have otherwise occurred with the disease alone, Audrey

responded that since her main motive is to spend as much quality time with her family, that even if the disease allowed her to live longer, but with paralyzing symptoms, that such an outcome would prevent her from doing what she loves anyways. Indeed she appeared to consider such an outcome as good as, if not worse than, death and that the clinical trial was her only good chance to live the way she would want.

Considerations for the Final Competency Assessment

The potential subject appeared to demonstrate a very good understanding of her ailment, medical research and of the trial procedures. She was able to grasp the likely symptoms associated with her disease, specifically mentioning paralysis throughout various points in the conversation. Though at times she seemed to downplay or at least not be overly concerned with some of the adverse effects of trial participation, she was able to acknowledge and understand such risks of the non-validated intervention. It thus seemed clear that she satisfies the *high level* of understanding standard since she additionally was able to not only state *that* research differs from treatment, and *that* the therapeutic misconception exists, but also *how*, citing specifically trial procedures such as randomization, as well as existing confusion between physicians and investigators, respectively.

Audrey also appeared to appreciate the differences between research and treatment and seemed to engage somewhat in how both her disease and trial participation would affect her personally, specifically mentioning the effects of both on her ability to live a rich and fulfilling family life. However, though capable of engaging in these considerations, she generally seemed to be disinterested in the adverse effects of the non-

validated drug and of trial participation overall. Instead this portion of the conversation seemed to involve a disproportionate amount of hopefulness and desperation. She seemed to consider this her last best chance despite there being a low chance of success and despite her having fully acknowledged both the adverse quality of life impacting side effects of the drug as well as the risks to her longevity.

Nonetheless it seemed that this was as a result of her reasoning that given the nature of ALS, and the lack of available treatment alternatives, the likely effects of her disease would be just as impactful on her quality of life and specifically how it would affect her ability to spend time with her family. She seemed to reason that since there was no current available treatment, the clinical trial at least provided a chance for some improvement despite also having similarly high risks to her quality of life.

When further prompted by the SRA to consider the impact of trial participation on her longevity, the prospective subject stated that she did not allow such a consideration to play a significant role in her decision making process because she viewed the symptoms of her disease, such as paralysis, as being a worse state of affairs than dying sooner, especially given the degree to which she desired to continue engaging in an active family life for her remaining days.

Thus, it seemed that Audrey had indeed, though perhaps not explicitly, acknowledged the possible impact on her life of the trial, but had merely not deemed it worse than the impact that her disease would have. Thus, she appeared to satisfy both the *Imperfect, but Independent Appreciation* and *Imperfect, but Largely Independent Reasoning* standards.

The former appears satisfied by the fact that she had some insight into what her life would be like if she accepted or refused to participate in the trial. She considered both states of affairs in light of her particular circumstances of wishing to engage in an active family life. The latter appears satisfied by the fact that she used this insight in conjunction with what she has deemed to be her main goal, namely spending high quality time with her family regardless of her longevity. This demonstrated that Audrey was able to identify her own best ends, as well as engage in appropriate means/ends reasoning, and conduct her own risk/benefit analysis considering and comparing the utility she may receive from both trial participation, and refusing to participate. Thus, despite some hopeful and desperate comments, and despite what may appear to be a lack of concern over the clinical trial's side effects, Audrey appears to be sufficiently capable of both appreciation and reasoning.

Finally, though she admitted to discussing the matter with her physician and family, neither seemed to control her decision in a way that would be relevant to voluntariness. In fact, her final decision flows logically from her understanding about the severity of her disease, information about the trial, as well as her appreciation and reasoning regarding her goals. Furthermore, it seems that her emphatic desire to attempt to maintain a high level of active family life was indeed her own, and that she has the confidence and emotional strength to make her own decisions in this tumultuous situation. Thus there was no reason to question whether she is capable of a high level of voluntariness.

SRA's Assessment: Competent

The prospective subject appears to satisfy all four criteria of competence at the required levels necessary in order to consent to participate in the clinical trial.