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True Protection for Persons with Severe Mental Disabilities, Such as Schizophrenia, Involved as Subjects in Research - A Look and Consideration of the Protection of Human Subjects

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TRUE PROTECTION FOR PERSONS WITH SEVERE MENTAL DISABILITIES, SUCH AS SCHIZOPHRENIA, INVOLVED AS SUBJECTS IN RESEARCH? A LOOK AND CONSIDERATION OF THE "PROTECTION OF HUMAN SUBJECTS"1

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I. INTRODUCTION

Recent accounts of human suffering by persons who are subjects of medical research projects have ignited discussion and debate over the possible need to

revise or update current protections given to such subjects. Of particular interest in this article are the federal regulations, promulgated by the Department of Health and Human Services (DHHS), provided to protect research participants, especially as they apply to mentally disabled subjects in medical research activities. It is the contention of this writer that the regulations are insufficient to adequately protect this group.

The concern of insufficient regulations, and their sloppy implementation, is illustrated by the real-life experience of research participant Gregory Aller, the first witness to testify in a congressional subcommittee hearing on May 23, 1994. Mr. Aller, then a junior at the University of California at Los Angeles (UCLA) and diagnosed with paranoid schizophrenia, spoke to Congress of his negative and harmful experience as a subject in a schizophrenia research study at UCLA. Mr. Aller’s plight had previously been disclosed in newspapers, and in at least one magazine and one law journal.

Mr. Aller’s testimony revealed that the consent forms he signed in order to participate in the UCLA research were later deemed invalid because UCLA had omitted two basic elements of informed consent: foreseeable risks and alternative treatments. Obtaining legally effective informed consent from research subjects is one form of protection offered by the DHHS regulations. Testimony also revealed that the informed consent process was performed

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4 This writer will focus on persons with schizophrenia serving as research subjects although the term "mentally disabled" includes many more than just those with schizophrenia. This was done to allow a more detailed analysis of the subject matter considered while retaining a reasonable length for an article of this type. Also, this writer will not discuss the special situation of those persons deemed mentally incompetent.

5 Problems in Securing Informed Consent of Subjects, supra note 2, at 4-9 (statement of Gregory Aller, Junior, UCLA).

6 Id.


10 Problems in Securing Informed Consent of Subjects, supra note 2, at 5 (statement of Gregory Aller).

between the subject and investigator without any special safeguards such as having a subject educator or advocate present. The current regulations do not require this form of protection for the mentally disabled but they should. Monitoring of the subjects by the UCLA investigators during the course of the research was also minimal.

The obvious problem is that UCLA did not follow the DHHS regulations on informed consent or monitor subjects adequately. Furthermore, an examination of the DHHS regulations designed to protect research subjects shows that the regulations are inadequate in providing protection to the mentally disabled. The regulations refer to the mentally disabled as a "vulnerable category of subjects," together with pregnant women, prisoners, and children. The regulations proceed to give additional protections to pregnant women, prisoners, and children, devoting a subpart to each, while providing only three additional safeguards for the mentally disabled, of which two of the three are vague. However, no subpart is devoted to the protection of the mentally disabled. This article will demonstrate that a subpart devoted to the protection of the mentally disabled, such as those with schizophrenia, is necessary to avoid potential future harms such as those suffered by Mr. Aller and his fellow subjects. Extra protection is particularly warranted in the areas of obtaining informed consent and monitoring research subjects.

This article begins with an in-depth discussion of the UCLA incident, followed by the history of protecting human research subjects and a review of the current law intended to protect research participants. Next, it explains the nature of schizophrenia and discusses the topic of schizophrenia and the informed consent process, explaining why persons with schizophrenia warrant more protection than is currently given, especially in the areas of monitoring and informed consent. This article also examines proposed ideas, from various sources, for better protection of the mentally disabled as research subjects. This article concludes with this writer's proposal as to how the DHHS regulations could provide true protection to the mentally disabled, such as those with schizophrenia, who serve as research subjects, by devising a separate subpart.
to the regulations. A rationale for each proposed section of the subpart is provided.

II. The UCLA Schizophrenia Study and the Concern It Created

In the early 1980's, UCLA began a research study, on an outpatient basis, involving persons with schizophrenia. Gregory Aller became a part of this study in the late 1980's. The study was divided into two phases. It began with the researchers placing the subjects on a standardized dose of Prolixin, an antipsychotic medication, in hopes of achieving mental stability. In the second phase of the study the stabilized subjects were taken off Prolixin so that the researchers could study "the development of the disease [of schizophrenia] and factors which may help predict its course in individuals." As part of the study, there was an agreement that medication would resume should a subject show "significant symptoms" of their illness from lack of medication and if they agreed to resume the medication.

As a subject in this research, Mr. Aller was stabilized on Prolixin, while working, and attending college. He was then asked to stop his medication, after which time his psychotic symptoms returned in full force. Due to this relapse, Mr. Aller's parents contacted the researchers numerous times, first concerned, and then increasingly angry over their son's deteriorated state. When an investigator finally consulted with Mr. Aller to see if he needed medication, Mr. Aller, in a paranoid frame of mind, responded "no." Months passed before Mr. Aller's medication was reinstated, and only after his father personally took him in to receive it.

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19 *Id.* at 4-9 (statement of Gregory Aller).
20 *Id.* at 5.
21 *Id.* at 45 (statement of Donald Rockwell, M.D.).
22 *Problems in Securing Informed Consent of Subjects*, supra note 2, at 44.
23 *Id.* at 45-46.
24 *Id.* at 5 (statement of Gregory Aller).
25 For instance, Mr. Aller had paranoid delusions that government agents were chasing him; he woke up one night thinking that he was sprouting another leg; he attempted to hitchhike to Washington, D.C. with the thought of assassinating the President; he threatened to kill his father; and he threatened his mother with a butcher knife. *Id.* at 6.
26 *Problems in Securing Informed Consent of Subjects*, supra note 2, at 6 (statement of Gregory Aller).
27 *Id.*
28 *Id.*
Other subjects, according to Mr. Aller's congressional testimony, suffered similar or worse fates. For example, one subject whose medication was withdrawn told the UCLA staff repeatedly that he was suicidal. He was subsequently "expelled" by the researchers from the program and eventually committed suicide by jumping from the roof of a UCLA building.29 Another subject, who lived in the community, experienced a severe relapse from the discontinuation of her medication, required hospitalization, and has remained institutionalized since 1985.30

In spite of these horrors, the Director of the Neuro-Psychiatric Hospital at UCLA's Medical Center stood behind the Center's research and informed consent process, although the Director admitted that it may be time to revisit the topic of ethical guidelines in research.31 Although Mr. Aller signed informed consent forms prior to participating in this research, the Office for Protection from Research Risks later declared the consent invalid because UCLA had omitted foreseeable risks and alternative treatments.32 Thus, UCLA violated federal regulations by disregarding elements of informed consent, one of the protections offered to human research subjects.

The congressional hearing of May 23, 1994 brought up the issue that no special regulations exist to guide research involving the mentally ill,33 and that such subjects are inadequately protected. Mr. Aller remarked, "I believe that the researchers view people with schizophrenia as subhuman" and "[t]he system does not protect human subjects; it protects the researchers."34

Mr. Aller's testimony reveals that special regulations to protect this group of research participants are necessary. What would have happened to Mr. Aller if his parents were not such strong advocates, or if they were not present at all? If Mr. Aller had received extra assistance during the consent process, would he have agreed to participate in the research or at least been more aware of the consequences of participating? If the investigator's monitoring of subjects was improved, would Mr. Aller's paranoia, a symptom of his schizophrenia that impaired his ability to inform the researchers that he needed help, have been detected earlier? Of course, we will never know the answers to these questions, but the system of protection can be improved in hopes of ensuring that future research participants like Mr. Aller are better protected.

29Id. at 6-7.
30Problems in Securing Informed Consent of Subjects, supra note 2, at 7-8.
31Id. at 43-47 (statement of Donald Rockwell, M.D.).
32Id. at 5 (statement of Gregory Aller).
33Id. at 32 (statement of Arthur Caplan, Ph.D., Center for Bioethics, University of Pennsylvania, Philadelphia).
34Problems in Securing Informed Consent of Subjects, supra note 2, at 8-9 (statement of Gregory Aller).
III. THE PROTECTION OF HUMAN RESEARCH SUBJECTS

A. The History of Protecting Research Subjects

Modern history shows the need to protect research participants from harm. This need was especially apparent following World War II when horrendous and deadly "experiments" on concentration camp prisoners by Nazi physician-experimenters were revealed. Various forms of atrocious experiments were performed, leading to the death or great physical harm of each subject. United States judges sat in judgment of these physician-experimenters and, after seeing evidence of such "horrendous non-therapeutic, nonconsensual prison research," created the Nuremberg Code. The Nuremberg Code has been declared "the most authoritative legal and ethical document governing international research standards, and one of the premier human rights documents in world history." The Nuremberg Code contains ten provisions, the first of which speaks directly of consent. This provision reads:

1. *The voluntary consent of the human subject is absolutely essential.*

This means that the person involved should have legal capacity to give consent; 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; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in

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36One such experiment included the "Experiments with Poison" in which prisoners were secretly given poison in their food so that the researchers could "investigate the effect of various poisons upon human beings." If the victims did not die from the poison, they were then killed so that the experimenters could perform autopsies on them. This is just one example of many different experiments that were performed. *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation* 100 (George J. Annas & Michael A. Grodin eds., 1992).


38Id.
the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.39

Other provisions of the Nuremberg Code relate particularly to the health and welfare of the subjects. For instance, random or unnecessary experiments may not be performed,40 all unnecessary suffering and injury, physical or mental, must be avoided,41 and the highest degree of skill and care should be provided during the experiment by scientifically qualified persons.42

The United States also saw its own horror stories of unethical research. For instance, in the 1970's it was discovered that 400 Black males involved in the Tuskegee Syphilis Study, sponsored by the Public Health Service, were intentionally left untreated with the disease for years so that researchers could study the natural progression of syphilis.43

The next big step in the area of protecting human research subjects occurred when the World Medical Association issued the Declaration of Helsinki in 1964, with amendments in 1975, 1983, and 1989.44 The Declaration contains twelve basic principles with recommendations from physicians to physicians regarding research.45 This document is ethical in nature, and is considered more permissive or lenient than the Nuremberg Code.46

In the United States, regulations protecting human research subjects, promulgated by the Department of Health, Education, and Welfare (now the Department of Health and Human Services), became effective on May 30, 1974.47 In 1981 the regulations were significantly revised and codified at Title 45 Part 46 of the Code of Federal Regulations.48 The regulations have been revised twice since 1981: in 1983 and 1991.49 Additional protections for some,
but not all, of the so-called vulnerable populations were adopted as follows: in 1975 for pregnant women, in 1978 for prisoners, and in 1983 for children.\textsuperscript{50}

Several reports and recommendations issued by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research have played a vital part in identifying and recommending basic ethical principles in research with human subjects. The Commission issued the influential \textit{Belmont Report} in 1978.\textsuperscript{51} The \textit{Belmont Report} delineated three basic ethical principles relevant to research involving human subjects: 1) respect for persons, which means that individuals should be treated as autonomous agents and that persons with diminished autonomy are entitled to protection; 2) beneficence, which is an obligation to do no harm by maximizing possible benefits and minimizing possible harms; and 3) justice, which means that the burdens and benefits of research are distributed fairly.\textsuperscript{52}

The \textit{Belmont Report} also spoke of informed consent.\textsuperscript{53} The three elements of informed consent are information, comprehension, and voluntariness. Information includes various items a reasonable volunteer would want to know before participating as a research subject.\textsuperscript{54} Comprehension involves "the subject's ability to understand [which] is a function of intelligence, rationality, maturity and language, [and] it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information."\textsuperscript{55} Finally, a true voluntary subject requires participation, void of any coercion or undue influence.\textsuperscript{56}

The Commission also issued reports and recommendations on research involving children,\textsuperscript{57} prisoners,\textsuperscript{58} fetuses,\textsuperscript{59} and those institutionalized as

\textsuperscript{50} Id. at xix.


\textsuperscript{52} Id. at 4-10 (emphasis added).

\textsuperscript{53} Id. at 10-14.

\textsuperscript{54} Id. at 11-12.

\textsuperscript{55} The Belmont Report, supra note 51, at 12 (emphasis added).

\textsuperscript{56} Id. at 14.


\textsuperscript{59} \textsc{National Comm'n for the Protection of Human Subjects of Biomedical and Behavioral Research, U.S. Dept Of Health, Educ., and Welfare, Pub. No. (OS)
"mentally infirm" which included mentally ill, mentally retarded, emotionally disturbed, and senile individuals. It is interesting to note that each of these subgroups, with the exception of the "mentally infirm," would subsequently receive additional regulatory protections when involved in research. It is suggested that the recommended protections for the "mentally infirm" did not evolve into regulations because they were excessively elaborate, and "to avoid stigmatization of the mentally infirm." Unfortunately, vulnerable subjects, not commissions, were left with minimal protections.

B. A General Overview of the Current Law

Federal regulations required by the Department of Health and Human Services, appearing at 45 C.F.R. §§ 46.101-46.409 (1994), provide for the protection of human subjects in "all research . . . conducted, supported or otherwise subject to regulation by any federal department or agency." Research is defined as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge." A similar set of protections also exists at 21 C.F.R. §§ 50.1-50.48 (1994), and is applicable to all "clinical investigations regulated by the Food and Drug Administration." Since the regulations are so similar, and in order to avoid confusion, this article will focus exclusively on the regulations issued by the Department of Health and Human Services (DHHS).

The DHHS regulations provide a number of protections for research subjects including requiring the investigators to obtain informed consent from a research subject prior to participating in research. The regulations enumerate eight basic elements of informed consent. The eight elements are:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's
participation, a description of the procedures to be followed, and identification of any procedures which are experimental; 68

(2) A description of any reasonably foreseeable risks or discomforts to the subject; 69

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research; 70

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject; 71

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained; 72

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained; 73

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; 74 and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. 75

Based on the DHHS regulations, informed consent is to be documented in one of two ways. 76 First, documentation can consist of a "written consent document that embodies the elements of informed consent required by § 46.116" which the subject is to sign following an "adequate opportunity" to read it. 77 The second form allows the elements of § 46.116 to be presented orally to the subject. However, a witness must be present and both subject and witness

76 45 C.F.R. § 46.117 (1994).
must sign to verify that an oral presentation has taken place. The requirement of a signed consent form can be waived if signing would result in a breach of confidentiality and the subject, not the researcher, opts to have no documentation, or, if the "research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context." The DHHS regulations also protect research subjects by requiring institutions involved in research to initially review and approve research projects through their Institutional Review Boards (IRBs). The IRBs are also required to review approved research projects at least once a year, and are to ensure investigators' compliance with § 46.116.

Each institution is given the authority to designate its own IRB, but must follow certain regulations in doing so. For instance, each IRB must have at least five members with varying backgrounds, at least one member's primary concern must be in a scientific area and at least one member's primary concern must be in a nonscientific area. Furthermore, each IRB must have at least one member who has no affiliation with the institution.

C. Providing Additional Protections to Those Deemed "Vulnerable"

The DHHS regulations also provide additional provisions for the protection of research participants belonging to "vulnerable populations." "Vulnerable populations" include "children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons." An examination of the regulations shows that pregnant women, prisoners, and children are given additional protections, clearly delineated in a subpart
devoted to each of these groups.\textsuperscript{91} However, there are no subparts devoted to the mentally disabled or economically or educationally disadvantaged.

1. Additional Protections for the "Mentally Disabled" Involved as Subjects in Research

The DHHS regulations refer to the mentally disabled in two sections. First, under "IRB membership" the DHHS regulations dictate that "if an IRB regularly reviews research that involves a vulnerable category of subjects, such as . . . mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects."\textsuperscript{92} Second, under "Criteria for IRB approval of research," the regulations state that IRBs are required to make certain that the selection of research subjects is equitable.\textsuperscript{93} The IRB is to consider the purpose and setting of the research, and "should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons."\textsuperscript{94} In the same section, the regulations mandate the inclusion of "additional safeguards" in research studies "when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as . . . mentally disabled persons," in order to "protect the rights and welfare of these subjects."\textsuperscript{95} However, such "additional safeguards" are not defined. It is interesting to note that these two sections apply to all "vulnerable" subjects, so again the regulations do not devote a section exclusively to the mentally disabled, despite declaring them a "vulnerable" group like pregnant women, prisoners, and children.

The DHHS regulations do not provide any requirements or guidance as to informed consent involving those individuals with severe psychiatric disabilities such as schizophrenia. The regulations give the IRBs the discretionary authority to require researchers to give additional information, beyond the eight elements of informed consent outlined in § 46.116, "when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects."\textsuperscript{96} This is not specifically addressed to any particular group of subjects, including the mentally disabled. The regulations also require IRBs to observe the consent process and research as part of their

\textsuperscript{91} 45 C.F.R. § 46 (1994), Subpart B (§§ 46.201-46.211) (provides additional protections for pregnant women), Subpart C (§§ 46.301-46.306) (provides additional protections for prisoners), Subpart D (§§ 46.401-46.409) (provides additional protections for children). There are no subparts E, F, or G.

\textsuperscript{92} 45 C.F.R. § 46.107(a) (1994).

\textsuperscript{93} 45 C.F.R. § 46.111(a)(3) (1994).

\textsuperscript{94} 45 C.F.R. § 46.111(a)(3) (1994).

\textsuperscript{95} 45 C.F.R. § 46.111(b) (1994).

\textsuperscript{96} 45 C.F.R. § 46.109(b) (1994).
duty to review research at their facility.\(^\text{97}\) Again, this general rule is not specifically addressed to any particular group of subjects.

The Institutional Review Board Guidebook (the Guidebook), which is written to provide guidance to IRBs, states, "[t]he predominant ethical concern in research involving individuals with psychiatric, cognitive, or developmental disorders . . . is that their disorders may compromise their capacity to understand the information presented and their ability to make a reasoned decision about participation."\(^\text{98}\) The Guidebook mentions that the DHHS regulations require IRBs to have "one or more individuals who are knowledgeable about and experienced in working with those subjects" and require that "additional safeguards are in place."\(^\text{99}\) Again, "additional safeguards" are not defined. The Guidebook then notes, "[u]nlike research involving children, prisoners and fetuses, . . . no additional DHHS regulations specifically govern research involving persons who are cognitively impaired."\(^\text{100}\)

2. Additional Protections for Pregnant Women Involved as Subjects in Research

The DHHS regulations, at Subpart B, provide additional protections in connection with research involving pregnant women, fetuses, and human in vitro fertilization.\(^\text{101}\) The special protections given to pregnant women will be looked at in this section.

According to the Guidebook, this subgroup warrants "special attention from IRBs because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus."\(^\text{102}\) The Guidebook adds, "[s]pecial attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society."\(^\text{103}\)

The first protection mandates that the Secretary of DHHS establish "Ethical Advisory Boards" to serve as advisors on any ethical issues that may be raised by individual research proposals or by any general policies or guidelines.\(^\text{104}\)

\(^{\text{97}}\)45 C.F.R. § 46.109(e) (1994).

\(^{\text{98}}\)PENSLAR, supra note 47, at 6-26.

\(^{\text{99}}\)Id. at 6-27.

\(^{\text{100}}\)Id. "Cognitively impaired" is defined as having a psychiatric disorder, an organic impairment, or a developmental disorder that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Id. at 6-26.

\(^{\text{101}}\)45 C.F.R. §§ 46.201-46.211 (1994).

\(^{\text{102}}\)PENSLAR, supra note 47, at 6-11.

\(^{\text{103}}\)Id.

\(^{\text{104}}\)45 C.F.R. § 46.204(a) and (b) (1994).
The Boards must be "competent to deal with medical, legal, social, ethical, and related issues."\textsuperscript{105} The second protection requires IRBs to monitor the informed consent process by actual participation of the IRB or through the use of "subject advocates."\textsuperscript{106} This entails a third party overseeing the informed consent process, in at least a sampling of the subjects, to ensure that "approved procedures for induction of individuals into the activity are being followed."\textsuperscript{107} This section also allows for visits to research sites, by IRBs or subject advocates, to continually monitor and evaluate activities "to determine if any unanticipated risks have arisen."\textsuperscript{108} The regulations forbid pregnant women from being involved as subjects in research unless the research activity meets the health needs of the mother and places the fetus at minimal risk.\textsuperscript{109}

3. Additional Protections for Prisoners Involved as Subjects in Research

The DHHS regulations, at Subpart C, provide additional protections in connection with research involving prisoners.\textsuperscript{110} These special safeguards exist with the recognition that "prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research."\textsuperscript{111} The first protection requires that a majority of the IRB, exclusive of prisoner Board members, have no affiliation with the particular prison seeking review and approval of research at its facility.\textsuperscript{112} This section also requires that at least one member of the IRB is a prisoner or "a prisoner representative with appropriate background and experience to serve in that capacity."\textsuperscript{113} The second protection involves additional duties placed on the IRB when reviewing research.\textsuperscript{114} For example, the IRB may not approve research which would create advantages to the prisoner (in terms of medical care, quality of food, etc.), thereby impairing his or her ability to weigh the risks of the research against such desirable advantages in his or her limited environment.\textsuperscript{115} The IRB has the duty to ensure that "information is presented in language which is..."
understandable to the subject population." The IRB is also to determine if follow-up examination or care of research participants, following their formal participation, is needed and, if so, that adequate provisions have been made.

4. Additional Protections for Children Involved as Subjects in Research

The DHHS regulations, at Subpart D, provide additional protections in connection with research involving children. According to the Guidebook, this subgroup warrants extra protection because of children's "special vulnerability." The Guidebook adds, "To safeguard their interests and to protect them from harm, special ethical and regulatory considerations are in place for reviewing research involving children."

Protections for children vary depending on the amount of risks and benefits involved. Informed consent is only mentioned in this section to define children as persons who have not reached the legal age to consent to research participation.

One form of protection for children involves the IRB's requirement to solicit the "assent" of the child to participate in research if the child is capable of providing it. "Assent" is defined as an "affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent." In determining if a child is capable of assenting, the IRB is to consider the age, maturity, and psychological state of the child. Parental permission is also required. "Permission" is defined as "the agreement of parent(s) or guardian to the participation of their child or ward in research."

This section also provides special protection to children considered wards of the state or any other agency or institution. The protection applies to

119 PENSULAR, supra note 47, at 6-18.
120 Id.
122 45 C.F.R. § 46.402(a) (1994).
123 45 C.F.R. §§ 46.404, 46.405(c), 46.406(d), 46.407(b)(2)(iii), 46.408(a) and (e) (1994).
124 45 C.F.R. § 46.402(b) (1994).
125 45 C.F.R. § 46.408(a) (1994).
126 45 C.F.R. §§ 46.404, 46.405(c), 46.406(d), 46.407(b)(2)(iii), 46.408(b) and (d) (1994).
127 45 C.F.R. § 46.402(c) (1994).
research involving greater than minimal risk\textsuperscript{129} to the subject with no direct benefit to the subject, or, to research involving the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children.\textsuperscript{130} If such research is carried out with children who are wards, the IRB must do the following:

[T]he IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.\textsuperscript{131}

In sum, the DHHS regulations recognize the mentally disabled as a "vulnerable" group of research participants, yet fail to provide this group with additional protections as it does so clearly and elaborately for pregnant women, prisoners, and children. This is problematic as the mentally disabled also have unique circumstances, which warrant special protections which are not given.

IV. THE NATURE OF SCHIZOPHRENIA

In order to think about providing more protection to persons participating in schizophrenia research, the reader must first have an understanding of what schizophrenia is. This is a necessary step as a significant number of people are uninformed or misinformed about this disease.\textsuperscript{132} This writer will attempt to familiarize the reader with the disease of schizophrenia, using the testimony of Gregory Aller,\textsuperscript{133} when possible, to illustrate key concepts.

\textsuperscript{129}"Minimal risk" is defined by the regulations as "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." 45 C.F.R. § 46.102(i) (1994).

\textsuperscript{130}45 C.F.R. § 46.409(a) (1994).

\textsuperscript{131}45 C.F.R. § 46.409(b) (1994).

\textsuperscript{132}Dr. E. Fuller Torrey, a clinical and research psychiatrist, contends that: Despite its being a common disease, schizophrenia is remote to most people. A remarkable number of people do not even know what schizophrenia is. A recent survey of college freshman found that 64 percent of them believed 'multiple personalities' to be a common symptom of schizophrenia. Schizophrenia has nothing to do with multiple or split personalities . . . .


\textsuperscript{133}Problems in Securing Informed Consent of Subjects, supra note 2, at 4-9 (statement of Gregory Aller).
First, some general information and statistics on schizophrenia are given. Second, the criteria necessary to diagnose schizophrenia are reviewed and, lastly, the course of the disease is examined.

A. General Information and Statistics on Schizophrenia

Schizophrenia has been described as "arguably the worst disease affecting mankind" because of its complexity of symptoms, its potentially deteriorating course, and because there is no cure for this disease. Schizophrenia is actually a common disease in our society today. In the United States, it is estimated that 1.2 million persons have schizophrenia, which means "approximately one out every hundred persons in the United States will be diagnosed with schizophrenia during his or her lifetime." Of this 1.2 million, it is estimated that 482,000 live with family members in the community; 250,000 live in foster homes or board-and-care homes; 165,000 reside in nursing homes; 100,000 live alone; 85,000 are in hospitals; 87,000 are in public shelters or live on the streets; and 31,000 are in jails or prisons.

Today, many persons with schizophrenia, and those with other mental disabilities, live in the community as opposed to hospitals due to the reform movement of deinstitutionalization. This movement, started in the 1960's, grew from society's recognition that large mental institutions had become inhumane, warehouse-like facilities for those with chronic mental illnesses such as schizophrenia. Thus, mental hospitals began to discharge patients to more humane facilities or, more often, to their families and the community. This "emptying" of mental hospitals has significantly reduced hospital populations: from 524,878 in 1970 to 267,638 in 1986. Deinstitutionalization has not been without its problems. For example, many residents of such institutions had no families or homes to go to; facilities in the community (e.g., the board-and-care homes) have been deemed substandard; and a significant portion of those discharged have become homeless and vul-


135 OFFICE OF TECHNOLOGY ASSESSMENT, 102D CONG., THE BIOLOGY OF MENTAL DISORDERS, DOC. NO. OTA-BA-538, 6-7 (Sept. 1992) [hereinafter OFFICE OF TECHNOLOGY ASSESSMENT].

136 TORREY, supra note 132, at 3.

137 Id. at 8.


139 Id.

140 Id.

141 Id. These figures indicate reduction of hospital patients overall, not only those with schizophrenia. That is, the figures include other diagnoses, too.
nerable to victimization. Of those with families, it has been observed, "there are enormous tensions in caring for a mentally ill member," with some families experiencing "burn-out."

The socioeconomic data on persons with schizophrenia reveal that "[i]ndividuals who have never been married or who are divorced or separated suffer schizophrenia two to three times as often as their married or widowed counterparts." Also, compared to the general population, persons with schizophrenia are less likely to have earned a college degree or to be employed and, if employed, they are likely to earn less than their counterparts without schizophrenia. Schizophrenia is five times more prevalent in lower socioeconomic groups as compared to higher socioeconomic groups.

B. The Diagnostic Criteria for Schizophrenia

Schizophrenia is a disease characterized by a mixture of certain signs and symptoms, involving "a range of cognitive and emotional dysfunctions," which must persist for a specified amount of time before this disease can be diagnosed. To be diagnosed with schizophrenia, six criteria (A through F) must be met.

Criterion A requires the presence of certain characteristic symptoms, referred to as active-phase symptoms, which include: (1) delusions, (2) 

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142Carson & Butcher, supra note 138, at 694-95.


144LeRoy Spaniol & Hal Jung, Effective Coping: A Conceptual Model, in Families of the Mentally Ill, supra note 143, at 93. Mr. Aller was fortunate to have his family advocate for him during his ordeal at UCLA. However, not all families would/could have been so responsive. Therefore, the protection of such subjects cannot be expected to come from families.

145Office of Technology Assessment, supra note 135, at 51.

146Id.

147Id.

148The information in this discussion has been obtained from the American Psychiatric Ass'n, Diagnostic and Statistical Manual of Mental Disorders (4th ed. 1994) [hereinafter APA], a manual used by many mental health professionals to diagnose mental disorders. The manual is very informative and descriptive. It was originally published by the American Psychiatric Association in 1952 and was recently updated in 1994.

149Id. at 274.

150Id. at 285-86.

151Id. at 273.

152APA, supra note 148, at 285; e.g., "I started to have paranoid delusions about Government agents chasing me." Problems in Securing Informed Consent of Subjects, supra note 2, at 6 (statement of Gregory Aller).
hallucinations,\(^{153}\) (3) disorganized speech,\(^{154}\) (4) grossly disorganized behavior\(^{155}\) or catatonic behavior,\(^{156}\) and (5) negative symptoms\(^{157}\) which include affective flattening,\(^{158}\) alogia,\(^{159}\) or avolition.\(^{160}\) If at least two of these symptoms persist for a significant portion of time during a one-month period (or less if successfully treated), then a diagnosis of schizophrenia is given if other criteria are also met.\(^{161}\)

Criterion B requires that the person's "work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset" of the disease.\(^{162}\) Criterion C requires that continuous signs of the disease persist for at least six months, with at least one month of symptoms which satisfy Criterion A,\(^{163}\) as stated above. Criterion D involves ruling out the diagnosis of schizophrenia if the diagnosis of schizoaffective disorder or mood disorder would be more appropriate.\(^{164}\) Criterion E also rules out schizophrenia if the disturbance is due to the direct effects of drug abuse, medication, or a general medical condition.\(^{165}\) Finally, Criterion F, reads: "If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated)."\(^{166}\)

\(^{153}\) APA, supra note 148, at 285; e.g., "I woke up screaming actually believing that I was sprouting another leg." Problems in Securing Informed Consent of Subjects, supra note 2, at 6 (statement of Gregory Aller).

\(^{154}\) APA, supra note 148, at 285; e.g., the person may slip easily from one topic to another, unable to stay on topic, or the person's "answers to questions may be obliquely related or completely unrelated." Id. at 276.

\(^{155}\) Id. at 285; e.g., appearing markedly disheveled, dressing in an unusual manner. Id. at 276.

\(^{156}\) APA, supra note 148, at 285; e.g., "marked decrease in reactivity to the environment." Id. at 276.

\(^{157}\) Id. at 285.

\(^{158}\) Id.

\(^{159}\) APA, supra note 148, at 285; e.g., the person answers questions with brief and empty replies. Id. at 276-77.

\(^{160}\) Id. at 285; defined as "an inability to initiate and persist in goal-directed activities." Id. at 277.

\(^{161}\) APA, supra note 148, at 285.

\(^{162}\) Id.

\(^{163}\) Id.

\(^{164}\) Id. at 285-86.

\(^{165}\) APA, supra note 148, at 286.

\(^{166}\) Id.
Clinicians are warned to take cultural differences into account when diagnosing schizophrenia since "[i]deas that may appear to be delusional in one culture (e.g., sorcery and witchcraft) may be commonly held in another."\textsuperscript{167} They are also warned to take socioeconomic and cultural differences into account as there has been some evidence of over-diagnosing this disease within some ethnic groups.\textsuperscript{168}

C. The Course of Schizophrenia

"The median age at onset for the first psychotic episode of Schizophrenia is in the early to mid-20s for men and in the late 20s for women."\textsuperscript{169} The onset of the disease may be sudden or insidious.\textsuperscript{170} The majority of individuals slowly develop certain signs and symptoms such as "social withdrawal, loss of interest in work or school, deterioration in hygiene or grooming, unusual behavior, [and] outbursts of anger."\textsuperscript{171} Eventually, however, the active-phase symptoms of the disease appear.\textsuperscript{172}

The course of this disease varies from person to person, but "is often unpredictable and can change rapidly."\textsuperscript{173} Some individuals display periodic exacerbations and remissions of the disease while others remain chronically ill.\textsuperscript{174} Complete remission, however, is uncommon in this disorder\textsuperscript{175} and a “substantial number of patients continue to manifest symptoms of schizophrenia throughout their lives.”\textsuperscript{176} The negative symptoms of the disease are particularly persistent over the course of the illness.\textsuperscript{177} Persons with schizophrenia are also at a higher risk for suicide. Suicide is the number one cause of premature death among individuals with schizophrenia (ten to fifteen percent of persons with schizophrenia commit suicide).\textsuperscript{178}

\textsuperscript{167}Id. at 281.
\textsuperscript{168}Id.
\textsuperscript{169}APA, \textit{supra} note 148, at 282.
\textsuperscript{170}Id.
\textsuperscript{171}Id.
\textsuperscript{172}Id.
\textsuperscript{174}APA, \textit{supra} note 148, at 282.
\textsuperscript{175}Id.
\textsuperscript{176}OFFICE OF TECHNOLOGY ASSESSMENT, \textit{supra} note 135, at 51.
\textsuperscript{177}APA, \textit{supra} note 148, at 282-83.
\textsuperscript{178}OFFICE OF TECHNOLOGY ASSESSMENT, \textit{supra} note 135, at 52.
There is no cure for schizophrenia, but medication can be used to control the psychotic symptoms, such as hallucinations and delusions. However, such antipsychotic medications have a number of troublesome side effects, and are not effective for the negative symptoms of the disease. Some commentators suggest that the pharmacologic approach, i.e., treatment by drugs, to treating schizophrenia is grossly over-rated, and that medication plus psychosocial treatment, a rarity, is more beneficial in treating this disease.

V. THE UNIQUE PROBLEM OF SCHIZOPHRENIA AND INFORMED CONSENT

Given the fact that schizophrenia is a cognitive disorder which can "impair[] the ability to integrate information, to reason, to concentrate, or to focus attention or purpose," do individuals with this disorder have trouble understanding information conveyed during the informed consent process? Research by Paul R. Benson indicates that the answer to this question is "yes," though understanding can be improved if innovative methods of information delivery are used, as opposed to the traditional method in which the unassisted psychiatric researcher conveys the information to the subject. Also, research by Thomas Grisso and Paul S. Appelbaum indicates there is "a greater risk of very poor understanding of treatment disclosures among schizophrenic patients."

Benson, with four colleagues, directly observed eighty-eight consent sessions, looking at investigator information disclosure and subject understanding in four psychiatric research settings. They noted that their research differed greatly from previous research on informed consent because previous researchers had not focused on the direct observation of the interaction between subject and researcher, citing this as a deficiency in past informed consent research.

The Benson study observed and taped the consent process in eighty-eight consent sessions involving twenty-four subjects diagnosed with major depression, forty-four subjects diagnosed with chronic schizophrenia (all living in the community), and twenty subjects diagnosed with borderline

179CARSON & BUTCHER, supra note 138, at 613.
180Id. at 613-14.
181Id. at 464-66.
182OFFICE OF TECHNOLOGY ASSESSMENT, supra note 135, at 47.
185Benson et al., supra note 183, at 455.
186Id. at 456-57.
personality disorder. Following each disclosure session between investigator and subject, "subjects were questioned regarding their understanding of the psychiatric research project using a semi-structured interview," and they were also questioned as to "the consent process itself and the requirements of their prospective roles as a psychiatric study participant." Standardized interactional rating forms were completed by the observers.

The Benson study used four different disclosure techniques to ascertain whether information delivery and subject understanding could be improved. The following disclosure techniques were used: 1) unassisted disclosure in which the subject's consent was obtained in the psychiatric researcher's traditional manner; 2) unassisted disclosure with videotape in which the subject received disclosure from the researcher and viewed an informational videotape prepared by the researcher; 3) assisted disclosure with "improved" videotape in which the subject viewed a second instructional tape and "received whatever additional information the investigator deemed appropriate to disclose"; and 4) disclosure provided to the subject by a "neutral educator" and the researcher.

The Benson results show that the three innovative disclosure methods significantly improved the quality of information communicated to subjects, with the neutral educator method showing the largest improvement. The results further indicated that subject understanding showed "substantive improvement" especially with the use of the neutral educator. However, for the subjects with schizophrenia, Benson found that the degree of improvement was substantially lower compared to those with major depression and those with borderline personality disorder. Benson concluded:

Findings indicate that the use of experimental techniques generally increases the quality of information delivered to prospective subjects, with disclosures by subject educators generating the most complete information. Subject understanding was also found to be significantly associated with the quality of information provided. Diagnosis and

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187 Id. at 459.
188 Id.
189 Benson et al., supra note 183, at 459.
190 Id. at 457-58.
191 Id. at 458.
192 Id. at 463-64 (showing that third party neutral educators, as opposed to researchers, give more detailed information to subjects, explain more clearly that participation in the research is voluntary, and allow more time for subjects to read consent forms. The educators are to assist in understanding, in a neutral fashion, as they are not advocates for either side).
193 Benson et al., supra note 183, at 469.
194 Id. at 473.
level of psychopathology, however, were found to be the most important predictors of subject understanding, with schizophrenics and the highly impaired most likely to demonstrate poor comprehension. These results suggest that the degree of improvement in understanding obtainable for severely disordered subjects is substantially lower than it is for others.  

In another study, Grisso and Appelbaum compared the abilities of two groups of hospitalized mentally ill patients (schizophrenia and major depression) with two groups of hospitalized non-mentally ill patients (heart disease and non-ill primary care patients) to understand informed consent disclosures about treatment with medication. Understanding of information was determined by the patient's ability to paraphrase the information given to him or her regarding treatment, and by the patient indicating, by choosing from various statements, whether each statement is the "same" or "different" from the information disclosed to him or her. The Grisso and Appelbaum results show that "the group of hospitalized schizophrenic patients manifested significantly poorer understanding of information related to decisions about consent to treatment with medication" in comparison to the others. They noted that, among those with schizophrenia, the risk of poorer understanding was more likely. The risk of poorer understanding also existed for those with major depression, but to a lesser extent.  

These studies indicate that persons with schizophrenia have special needs that deserve extra attention from the DHHS regulations akin to the additional protections already provided to pregnant women, prisoners, and children. The informed consent process has come under attack as an "empty ritual," where "researchers concentrate more on obtaining signatures than on talking and listening to the patients." This process further deteriorates when persons with cognitive problems are involved. Stricter overall regulations may be

195Id. at 455.
196Grisso & Appelbaum, supra note 184, at 377.
197Id. at 379-81.
198Id. at 385.
199Id. at 386.
200See supra parts III.C.2-4.
201Katz, supra note 9, at 13-14.
202David L. Wheeler, Informed Consent Questioned in Research Using Humans, CHRON. HIGHER EDUC., Dec. 4, 1991, at A14. In this short article, Arthur Caplan, then director of the Center for Biomedical Ethics at the University of Minnesota, now at the Center for Bioethics at the University of Pennsylvania (and the third witness at the congressional hearing on May 23, 1994) is quoted as saying, "[i]f I have one more medical student come up to me with a piece of paper in hand and say, 'I have informed consent,' I'm going to amputate an arm."
needed in this area, and are certainly needed where vulnerable subjects, such as those with severe psychiatric disabilities, are concerned.

VI. SUGGESTED IDEAS FOR PROVIDING ADDITIONAL PROTECTIONS TO PERSONS WITH SEVERE PSYCHIATRIC DISABILITIES, SUCH AS SCHIZOPHRENIA, INVOLVED AS SUBJECTS IN RESEARCH

Several commentators have proposed suggestions indicating that the mentally disabled, involved as subjects in research, could be better protected. This writer will present an overview of these ideas.

Some ideas from the congressional hearing include: 1) to create a federal oversight board to perform special reviews of some research involving vulnerable groups and to make periodic visits to IRBs; 2) to require IRB members to be more active in protecting subjects by having contact with research participants beyond sitting in committee rooms reviewing research and consent forms; 3) to create special regulations for research involving the mentally ill so that IRBs will have guidance in this area; and 4) to have at least one subject representative on an IRB that reviews research involving subjects with severe psychiatric disabilities.

Other suggestions, from various sources, include: 1) modifying the informed consent process to improve upon information disclosure and understanding through the use of innovative techniques, particularly the use of independent subject educators; 2) increasing the monitoring/observation of the informed consent process by IRB members which is an existing, but infrequently used, part of the regulations; 3) requiring a mandatory waiting period between the investigator's request of the subject to participate in research and the signing of the consent form; and 4) using subject advocates to assist participants in understanding their rights.

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203 Problems in Securing Informed Consent of Subjects, supra note 2, at 20 (statement of Arthur Caplan, Ph.D).

204 Id.

205 Id. at 32 (statement of Arthur Caplan, Ph.D); id. at 53 (statement of Donald Rockwell, M.D.).

206 Problems in Securing Informed Consent of Subjects, supra note 2, at 46, 52 (statement of Donald Rockwell, M.D.).

207 Benson et al., supra note 183, at 455, 471, 473.

208 Jesse A. Goldner, An Overview of Legal Controls on Human Experimentation and the Regulatory Implications of Taking Professor Kate Seriously, 38 ST. LOUIS U. L.J. 63, 132 (Fall 1993). The regulations allow an IRB "to observe or have a third party observe the consent process." 45 C.F.R. § 46.109(e) (1994).

209 Goldner, supra note 208, at 133.

210 Subject advocates differ from subject educators in that educators explain the research to subjects in a neutral manner (i.e., not on the side of the researchers or the subjects) whereas advocates would act on the behalf of the subjects' interests.
Other sources take a different view. They suggest that tighter regulations are unnecessary, and will only lead to the restriction of much needed research on persons with schizophrenia. 212

VII. A PROPOSED SOLUTION TO PROVIDE TRUE PROTECTION FOR PERSONS WITH SEVERE MENTAL DISABILITIES, SUCH AS SCHIZOPHRENIA, INVOLVED AS SUBJECTS IN RESEARCH

This writer will now propose how the DHHS regulations could better protect the forgotten group of persons with severe psychiatric disabilities, such as those with schizophrenia, serving as research subjects. Clear and distinct protections do not exist for this group of research participants, but are provided for other vulnerable groups. The usefulness of each protection will be justified by relying on the information regarding this particular population, although the ultimate justification is the expectation that the federal regulations provide additional protections to all groups considered vulnerable. The proposed additions to the regulations will appear in italics followed by, in regular typeface, the rationale for each one.

The proposed additions are as follows and are placed in a separate subpart of the regulations devoted to this subgroup of participants:

Subpart E - Additional Protections Pertaining to Research Involving the Mentally Disabled, Such as Persons With Schizophrenia, as Subjects.

§ 46.410 Applicability.
(a) The regulations in this subpart are applicable to all research conducted or supported by the Department of Health and Human Services involving the mentally disabled, such as persons with schizophrenia, as subjects, and are applicable to all research regardless of where the subjects may reside (in institutional settings or in the community).
(b) The requirements of this subpart are in addition to Subpart A of 45 C.F.R. Part 46.

§ 46.411 Purpose.
Inasmuch as persons with cognitive disabilities, such as those with schizophrenia, may need extra assistance in considering whether or not to participate in research, which could affect their ability to make a truly voluntary decision, the purpose of this subpart is to provide additional safeguards for the protection of persons with schizophrenia involved as subjects in research.

§ 46.412 Ethical Advisory Boards.
(a) The creation of Ethical Advisory Board(s), established by the Secretary of DHHS. Members of the Board, collectively, shall be competent to deal with medical, legal, social,

212 Torrey, supra note 132, at 332-34.
ethical, and related issues relevant to research involving the particular population within.

(b) To provide advice, at the request of the Secretary, to IRBs or researchers, on ethical issues in research involving persons with severe psychiatric disabilities such as schizophrenia.

These boards would be similar to the ones mandated to protect pregnant women.\textsuperscript{213} The justification for this additional safeguard is based on the fact that schizophrenia is a complex disease involving potentially complex ethical questions. For example, the ethics of the UCLA research, which withdrew medication from subjects, is contested.\textsuperscript{214}

\textsection{46.413 Composition of Institutional Review Boards when research to be reviewed involves persons with schizophrenia as subjects.}

(a) At least one member of the Board shall be a person with schizophrenia to serve as a subject representative, to represent the interests of subjects.

(b) If the IRB is larger than the minimally required five members (per \textsection{46.107(a)}, then the number of subject representatives should increase in proportion to the enlargement of the Board. For example, if the Board contains ten members, two of the ten shall be subject representatives.

This requirement is similar to the one for board composition of research involving prisoners,\textsuperscript{215} and is similar to a requirement that UCLA has been ordered to follow.\textsuperscript{216} This writer decided to deviate from the protections for prisoners by adding the proportionality requirement in (b) to achieve balance\textsuperscript{217} and to have true subject representation as opposed to a token-like version.

\textsection{46.414 Additional duties of the Institutional Review Boards in connection with activities involving persons with schizophrenia.}

(a) To provide, at a minimum, a subject educator to every potential research participant to assist during each phase of informed consent (e.g., if a study consists of

\textsuperscript{213} 45 C.F.R. \textsection{46.204} (1994).
\textsuperscript{214} See supra note 7.
\textsuperscript{215} 45 C.F.R. \textsection{46.304(b)} (1994).
\textsuperscript{216} Problems in Securing Informed Consent of Subjects, supra note 2, at 52 (statement of Donald Rockwell, M.D.). UCLA is now under stricter scrutiny due to its schizophrenia study, and has been ordered by the Office for Protection from Research Risks to include a subject representative on its IRB when review entails psychiatric research. This is a good plan that should be implemented overall, not just when a research facility is being reprimanded for unethical behavior.
\textsuperscript{217} Unequal power relations between professional and lay members of review committees have been recognized. Paul M. McNeill, The Ethics and Politics of Human Experimentation 91-94, 188-92, 210-14 (1993). Since the subject representative is likely, though not necessarily, to be a lay member, increasing the number of representatives is important to achieve balance.
multiple phases with informed consent obtained at each phase, then the subject educator is to be present at each stage). The subject educator must be properly trained in such areas as the elements of informed consent, be knowledgeable of the research study involved, and be familiar with the potential needs of this subgroup. One subject educator may serve as educator for more than one subject, but not for more subjects than could be reasonably served, allowing for adequate time to educate each subject. The general requirements of informed consent (at § 46.116 (a)) must still be met.

This additional safeguard is justified by the fact that persons with schizophrenia, in general, can experience difficulty in comprehension.218

(b) If the research involves more than minimal risk,219 a subject advocate must be assigned to the activity site to determine if any unanticipated risks have arisen. The subject advocate shall make periodic visits to the site, and may serve as an advocate for a reasonable number of subjects at a reasonable number of sites (a roving subject advocate is allowable). The advocate must have the background and experience to act in the best interest of the subjects and may have no affiliation with the research or investigators.

This requirement, based on an increase of risk in the research, is necessary due to the fluid nature of schizophrenia and with the increased risk for suicide among this population.220 Considering these facts, increased monitoring is warranted. Also, some, if not most, of the burden of monitoring should fall on the research facility rather than solely on the subject’s family.221

VIII. CONCLUSION

Modern history shows the world’s attempt to protect research participants from harm, from the Nuremberg Code established after the criminal convictions of numerous physician-experimenters,222 to our own country’s establishment of regulatory protections.223 However, people are still being harmed, as attested to by Gregory Aller, a research participant in a schizophrenia study at UCLA.224

While the regulations are designed to protect all research subjects, the regulations also recognize that vulnerable subjects, with special circumstances, deserve extra protection. For instance, pregnant women are given special

218 See supra part V.
219 See supra note 129 (for definition of “minimal risk”).
220 See supra notes 173-78 and accompanying text.
221 See supra notes 143-44 and accompanying text.
222 Annas, supra note 35, at 120-22.
224 Problems in Securing Informed Consent of Subjects, supra note 2, at 4-9 (statement of Gregory Aller).
protections because of the third party (the fetus) involved, and prisoners are given special protections because of the potentially coercive environment in which they live. However, not all groups deemed "vulnerable" have been afforded special protection, resulting in an unjust system. Persons with severe mental disabilities, such as schizophrenia, have special circumstances deserving of extra protection, yet no clear and distinct regulations govern research involving this population.

Persons with schizophrenia, in general, may need extra time and assistance in understanding information, and live with a condition that is somewhat unpredictable. These are special circumstances warranting extra protection in the areas of informed consent and monitoring for such research subjects. The revelation of the Gregory Aller incident, followed by the concerns expressed at the congressional hearing on May 23, 1994, show that it is time to update the regulations to provide true protection for persons with severe mental disabilities, such as schizophrenia, serving as research subjects.

ANNE J. RYAN

\[225\] 45 C.F.R. § 46 (Subpart B, Subpart C) (1994).

\[226\] See generally Problems in Securing Informed Consent of Subjects, supra note 2.