A Brief Introduction to Informed Consent in Research with Human Subjects

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1. Introduction

All modern codes of ethics concerning research with human subjects affirm the moral importance of a principle of informed consent. It is a principle born of outrage at the atrocities committed by German physicians and scientists under the Hitler regime. As is well known, thousands of concentration camp prisoners were used as human guinea pigs against their will in experiments that were typically excruciatingly painful and generally led to death or permanent disfigurement. As a part of its written decision, the war crimes tribunal that convicted several of the notorious "Nazi Doctors" produced what has since become known as the Nuremberg Code (1), widely regarded as the first international code of human experimentation ethics. The code begins simply, with one statement set apart from all the rest:

> "The voluntary consent of the human subject is absolutely essential."

The document goes on to detail the informational and other elements inherent in the notion of voluntary consent, and to establish nine additional principles of ethical research. Clearly, however, the principle of informed consent predominates. Later international codes of research ethics, such as the Declaration of Helsinki (2), outline key considerations of informed consent. Most recently, the International Ethical Guidelines adopted by the Council for International Organizations of Medical Sciences (CIOMS) (3) reassert the primacy of informed consent.

If the impenetrable barrier of the historical record makes it virtually impossible to dismantle a principle of informed consent, it does not in any obvious way support such a principle in less extreme research. That is, we can all condemn the practice of forcing prisoners into ice baths to see how long it takes them to freeze to death without necessarily agreeing that informed consent is required in virtually risk-free research, such as surveys or interviews. The memory of the Third Reich has to be supplemented by sound reasoning to flesh out the extent and nature of the principle of informed consent.

2. Justifying a principle of informed consent

In general, two types of reasons might be offered to justify the status of informed consent as a fundamental principle of ethical research involving human subjects: consequentialist ones and nonconsequentialist ones.

Consequentialist reasons are grounded in the conviction that the action with the best overall expected consequences is, generally, the action we ought to take. The primary consequentialist reason for adopting a principle of informed consent, then, is that doing so has the best expected consequences compared with alternatives. This view can be supported by a number of contentions, including the following:

a) Obtaining subjects' informed consent to participation tends to increase their adherence to the protocol, and hence the quality of the research.

b) Since investigators are not always able to identify the risks their research may pose to subjects, a process of informed consent provides the benefit of an additional layer of risk review tailored to the interests of the individual subject.

c) Affirming a principle of informed consent is likely to foster public trust of the research community; without such trust the research enterprise could not flourish.

Important though they are, consequentialist reasons for adhering to a principle of informed consent in research may not be the most compelling ones. Perhaps the most obvious weakness of a consequentialist approach is that strong consequentialist arguments *against* adopting a principle of informed consent can also be adduced. Securing the informed consent of subjects can be cumbersome and expensive, and potentially creates a self-selection bias in the subject pool. Moreover, the consequentialist reasons offered in support of a principle of informed consent can all potentially be invalidated: in some cases, the process of informed consent may *not* substantially increase participants' adherence to protocol and may *not* effectively individualize the risk/benefit assessment. Worst of all, some researchers may believe that public trust of the research community may be protected by successfully *concealing* non-consensual research practices – this may be particularly tempting to researchers for whom deception of subjects is an important tool.

In contrast, *nonconsequentialist* reasons for adopting a principle of informed consent are grounded in intrinsic qualities of persons or actions. For example, if one believes that persons have an inherent capacity – even a need – for self-determination, this provides the grounds for an obligation to avoid interfering with their actions and decisions (e.g., by withholding relevant information). In some respects, the nonconsequentialist approach provides a more robust foundation for the principle than does a consequentialist one, since it requires researchers to secure the informed consent of subjects irrespective of the overall expected consequences of doing so.

The *Belmont Report* (4) invokes the most common nonconsequentialist rationale for a principle of informed consent, one that has its origins in Kantian deontological theory. This rationale holds that investigators have an obligation to respect persons, particularly, their distinctive capacity for autonomous decision making. To use a person merely as an instrument to some other end, without regard for that individual's preferences and values, is a moral perversion. While the Nazi experiments present perhaps the most extreme example of this kind of offense in the research context, *all* cases of *merely using* persons have the same offensive character, according to this view. However, the obligation to respect persons doesn't prohibit *ever* using others in the pursuit of one's goals; rather, it requires that any such use be *cooperative* in nature, and hence that individuals be included in research only if they freely and knowingly choose to participate.

An alternative nonconsequentialist rationale[1] starts from the premise that certain kinds of endeavors, in view of their optional and noble nature, impose on parties higher standards of behavior than those of ordinary life. For example, in marriage it is not enough simply to avoid harming one's spouse; loving promotion of the spouse's welfare is required. Similarly, human subjects research must do more than ensure that an experiment offers a reasonable risk/benefit profile to subjects; rather, it should aspire to a genuine partnership between investigator and subject as embodied in the principle of informed consent.

3. Two notions of informed consent

Faden and Beauchamp, whose influential analysis of informed consent forms the basis of much of this essay, identify two distinct meanings of the term. The first sense – which we call the *moral* sense of the term – defines informed consent as an "autonomous authorization" (5, at 276) of one's participation in research. The second sense – which we refer to as the *socio-legal* sense of the term – defines informed consent as a "legally or institutionally *effective* (sometimes misleadingly called *valid*) authorization" (5, at 281).[2] Informed consent in the moral sense is the sort of authorization that transforms what would otherwise be "merely using" a person as a research subject into a morally acceptable, cooperative activity – a *morally effective* authorization, if you will. It is the kind of authorization made by a person with *decision making capacity* who has a substantial *understanding* of the relevant *information* and who is *free* from controlling influences in making the decision. Each of these elements of informed consent is developed briefly in the section 4, below.

Informed consent in the *socio-legal* sense of the term refers to the practices and conventions that make it socially or legally acceptable to use a person as a research subject, and includes the rules, regulations, and cultural and professional practices governing informed consent to research. Presumably these practices and conventions exist in order to produce the morally effective authorization that lies at the heart of the *moral* sense of informed consent, but, of course, the *socio-legal* and *moral* senses of informed consent may not always correspond in practice. For example, despite a well-constructed informed consent document and consent-related discussions that make it clear no medical benefit is anticipated for subjects in a clinical trial, a patient may nevertheless agree to participate expecting to receive some medical benefit. In such a case, informed consent in the *socio-legal* but not in the *moral* sense is obtained. To the extent that these two senses of informed consent do not or may not always correspond in practice, it is useful to keep the distinction in mind. For the most part, this essay is concerned with the *moral* conception of informed consent, although the last section considers exceptions to the regulatory obligations of informed consent.

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[1] The authors are indebted to David H. Smith for both the form of the argument and the example.

[2] Faden and Beauchamp identify these different conceptions of informed consent as *sense*$_1$ and *sense*$_2$, respectively. We adopt what seems to us a more natural, descriptive terminology simply for reasons of style and readability.

Finally, it is important to note that if the "use" of the research subject is to be morally legitimate throughout the course of her or his involvement, the subject's autonomous authorization must persist for that period. Thus, as many people involved in human experimentation ethics have stressed, informed consent should be thought of not as an event, such as the signing of an informed consent form, but rather as a process that extends both before and after documentation of the subject's willingness to participate. All of the elements of informed consent that are described below – conditions of adequate information, understanding, voluntariness, and decisional capacity – should characterize the subject's authorization at every point of his or her participation in research.

4. Four elements of informed consent

Information. One cornerstone of informed consent is the idea that potential subjects ought to be provided with all the available information that is relevant to a decision concerning participation. The concept of "relevance," however, is notoriously thorny. Three different standards for disclosing information have evolved in legal and bioethical contexts (6, at 147-150):

1) a *professional practice* standard, which requires disclosure only of the information that professionals typically provide;

2) a *reasonable person* standard, which requires disclosure of the information that a thoughtful layperson would consider relevant to such a decision; and

3) a *subjective* standard, which requires disclosure of the information considered to be material to the decision by the specific person who must make it.

Note that none of these standards articulates a notion of *full* or *complete* information, an unattainable and perhaps even undesirable goal.

If one goal of informed consent is to ensure that subjects have sufficient information to be able to determine which decision about research participation is most compatible with their individual interests and values, then a *subjective* standard of disclosure would seem to be the most appropriate. However, it is impossible for an investigator to know in advance what information each potential subject of a given experiment will take to be relevant. In practice, the best way to facilitate informed consent may be to design consent forms and other informational materials to satisfy a *reasonable person* standard, supplemented by conversations intended to elicit and answer any questions that are not otherwise addressed. As a minimum, federal regulations identify eight different types of information that ought to be provided to potential subjects, such as the nature and purposes of the experiment, the procedures involved, likely burdens and benefits, among others.[3]

[3] For examples of required information, see: 7, at §116; 8, at Chapter III; and 3, at Guideline 2.

Understanding. It is not enough simply to *have* the information that is relevant to a decision about participation, subjects must *understand* that information. As is the case with informational disclosure, informed consent does not entail anything like *perfect* or *complete* understanding. Instead, it requires a level of comprehension or appreciation of information that is *adequate* for meaningful deliberation about the decision, or what Beauchamp and Childress call "substantial" understanding (6, at 143). This element of informed consent speaks to the idea that autonomous decisions reflect what one *intends* to do, and this is possible only if the individual adequately apprehends the relevant information. Empirical studies on informed consent suggest that even when provided with information about the nature of research and the studies in which they are asked to participate, subjects "systematically misinterpret the risk/benefit ratio of participating in research because they fail to understand the underlying scientific methodology" (9, at 21). In such cases, what the subjects *actually* authorize differs substantially from what they *intend* to authorize, and thus informed consent is frustrated.

The informed consent process, then, should be directed not only at providing relevant information to potential subjects but also at promoting their understanding. Obvious implications of this conclusion include the need to ensure that consent forms are written in lay language, at a level of difficulty suited to the reading and comprehension skills of the expected subject population. Less obvious is the need to focus attention on aspects of the informed consent process other than the consent forms, which may be useful for ensuring and documenting that subjects have access to relevant information, but which may not be ideal for promoting understanding. Investigators may want to consider using alternative media and methods for presenting relevant information as a part of the informed consent process, as well as testing subjects' comprehension (10).

Voluntariness. The genuinely autonomous authorization that defines informed consent is one that is freely given, representing the determination of one's own will and not that of any other person. This is not to say that a decision is non-voluntary unless it is made without any constraint whatsoever, but merely that the decision is not controlled by anyone other than the subject. Even this requirement, however, seems too strong: virtually every decision is controlled *to some extent* by others. So, if the concept of voluntariness is ever to have any application in the real world, it will have to consist in *substantially* non-controlled decisions and action (5, at 259), rather than *complete* freedom from external control. [4]

As Faden and Beauchamp point out, "control is exerted through influences . . ., but not all influences are controlling" (5, at 256). Of the three types of influences they identify, Faden and Beauchamp suggest that:

1) *coercion* is *always fully controlling*; and thus is incompatible with informed consent;

[4] It should be noted that Faden and Beauchamp (5) avoid the term "voluntary" entirely, preferring instead to use the less 'loaded' term, "noncontrol."

2) *persuasion* is *never controlling*, and so is always compatible with informed consent; and

3) *manipulation* – of an individual's options, of the information with which the person is provided, and/or of the psychological and emotional components of decision making – *constitutes the continuum between fully controlling and noncontrolling* and so will sometimes be compatible with informed consent, sometimes not (5, at 355].

Coercion is always controlling, on Faden and Beauchamp's analysis, because its hallmark is the irresistible imposition of another's will by means of a threat of serious but avoidable harm. It should be noted that this concept of coercion excludes the possibility of "coercive offers," unless they are simply veiled threats. Rather, even the most irresistibly attractive offer, such as a large monetary payment for participation, is an occasion of manipulation (albeit, potentially a controlling one) since it does not diminish the available options. At the opposite extreme is persuasion, which is defined as influence by means of rational argument. Persuasion may appear controlling insofar as it may be used to elicit a desired decision from another person, but it can do so only if that person chooses to accept the reasons offered as compelling. The only element of force is that exerted by reason itself. In practice, however, it is not always easy to distinguish strictly persuasive discourse from that involving psychological or informational manipulation.

Finally, manipulation is the most complex set of influences, essentially comprising all influences that are neither strictly persuasive nor coercive. In the research context, the informed consent process may unavoidably exhibit at least two forms of manipulation: a) manipulation of choice, since the opportunity to participate in research is itself an alteration of the options available to the potential research subject, and b) manipulation of information, since no presentation of information can be entirely neutral; it always involves some selection of what information is to be provided, how it is to be framed it, etc. The key is to minimize manipulation, particularly that which interferes with subjects' ability to identify and pursue their own values and goals. If the interference is substantial and invidious, it presents an *undue* influence and the decision cannot be considered substantially voluntary. On the other hand, if the manipulation is benign and resistible -- that is, not so great that the consent represents more the will of the investigator than that of the subject -- then the decision to participate is sufficiently voluntary to be compatible with informed consent.

Decision Making Capacity. [5] In addition to having adequate information, understanding, and freedom from controlling influences, informed consent requires that potential subjects have the capacity to make a decision about participation. That is, they must have the ability to determine whether participation or non-participation is most consistent with their authentic preferences, goals and values. As a precondition of decision making capacity, persons giving consent must *have* reasonably stable preferences, goals and values with which they genuinely identify, suggesting that a certain level of maturity is necessary. Decision making capacity further

[5] Although the term "decision making capacity" is often used interchangeably with "competence," the latter is a technical legal term.

requires that prospective subjects must be able to assess the possible consequences of participation/non-participation with respect to their individual interests, and must be able to come to a reliable decision as a result of these deliberations. Finally, despite having the requisite skills, some individuals may not be able to exercise their decision making capacity while in environments that significantly limit opportunities for individual choice (such as prisons or other detention facilities) or which encourage dependency on others for decision making (e.g., some health care settings and relationships). Since these conditions may erode decision making capacity, care must be taken when informed consent to research is sought in such settings.

If a potential subject does not have the capacity to make an authentic decision about research participation and is not likely to acquire or regain it, proxy consent may be an acceptable substitute. Ideally, the proxy should be a legally authorized representative (LAR) who knows and will faithfully adhere to the potential subject's previously expressed autonomous preferences, values and goals in deliberating about participation. Or, if the potential subject has never developed the capacity for autonomous choice, it seems appropriate that a surrogate decision maker ought only authorize research participation when doing so appears to be in the individual's best interests.

5. Is informed consent always necessary?

Informed consent (in the socio-legal sense) to research participation is not always required, but in federally regulated research (e.g., that covered by 7, 11 and 12), the circumstances under which it need not be obtained are limited. Investigations that do not require informed consent may be thought of in four classes:

1) investigations that do not constitute *research* involving *human subjects*,

2) human subjects research that is exempt from compliance with federal regulations,

3) non-exempt human subjects research in which it is not *possible* to obtain participants' written informed consent, and

4) non-exempt human subjects research in which it is not *desirable* to obtain participants' written informed consent.

5.1 Investigations that do not constitute research involving human subjects.

Many types of interactions are aimed at gathering information that may be widely disseminated, but nonetheless do not constitute research. According to federal regulations: "*Research* means a systematic investigation . . . designed to develop or contribute to generalizable knowledge" [7, at §102(d)]. Thus, journalistic inquiries, legal and criminal investigations, quality assurance testing, studies conducted purely for personal edification, etc., do not qualify as research under current

regulations.[6] In addition, research that does not involve *living*, *human* subjects generally does not require informed consent. For example, research involving persons who are dead usually is not considered human subjects research for purposes of regulation and informed consent. On the other hand, research involving tissues or other specimens prospectively collected from living individuals and/or the recording of personally identifiable information about living persons in connection with research on biological materials is regarded as research with human subjects and typically requires informed consent to the collection and use of these samples.[7]

5.2 Human subjects research that is exempt from compliance with federal regulations.

The Common Rule identifies six types of "exempt" research activities that are not covered by its regulations, including those pertaining to written informed consent [7, at §101(b)(1)-(6)]. Fully half of these categories concern forms of research that pose very little risk to subjects because they involve only "normal educational practices" or relatively unobtrusive research methods (educational tests, surveys, observation, etc.) that ensure that individual subjects cannot be linked to any sensitive information. When such research does record personally identifiable information, it may still be exempt if federal statutes offer protection against the disclosure of the information or if the subjects are public officeholders or candidates. Other categories of exempt research include studies of the taste or quality of food made with safe ingredients, projects concerning public benefit or service programs, and the use of existing materials (specimens, documents, data, etc.) that are either publicly available or in which only "anonymized" information is recorded. In each exempt category, it is clear that the risks of research are similar to those of everyday life. Moreover, for many such exempt projects individual refusals would be very difficult to accommodate and the effort to obtain informed consent would be prohibitively burdensome. It should be noted, however, that exemption from federal regulations does not mean that the research is exempt from any regulation or oversight nor from a moral obligation to inform subjects about their inclusion in research.

5.3 Non-exempt human subjects research in which it is not possible to obtain individuals' written informed consent to participate.

For reasons of age, cognitive impairment, or the like, some individuals are incapable of providing informed consent/refusal in response to an invitation to participate in research. LARs may provide proxy informed consent on behalf of those who lack decision making capacity,

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[6] Some of these activities arguably require the informed consent in the moral sense (though not the socio-legal sense) under most circumstances. For example, journalists performing interviews are surely morally obliged (under most circumstances) to secure the informed consent of the interviewee by providing information ("I'm a reporter for the *New York Times*") that the interviewee can understand (generally a given) and the interviewee should participate voluntarily (not under threat of bad publicity, for example). It is also generally bad journalistic practice to interview persons who lack the capacity to agree or disagree to be interviewed.

[7] See 7, §102(d) and (f) for definitions of research and human subjects, respectively. For more on the special circumstances involving the collection and use of human biological materials, see 13.

although regulations and human protections policy significantly restrict the types of research in which such subjects may participate and outlines additional consent requirements.[8]

Research in emergency medicine presents special difficulties for informed consent, since prospective subjects may not have decision making capacity, and experimental procedures may have to be undertaken before a proxy decision maker can be located. IRBs may grant a waiver of the informed consent requirement for research in emergency medicine, but under very restricted conditions including, among other requirements: community representation in the research review process, community notification of the experiment and its findings, debriefing and deferred consent of the subject and/or a LAR, and oversight by a data and safety monitoring board.[9]

Finally, some researchers contend that not all societies share the same ideal of individual autonomy in which the principle of informed consent is grounded This is a substantial empirical claim that requires significant justification; nonetheless, it raises the possibility that in such communities individual informed consent to research is meaningless, at best, offensive and disrespectful, at worst. This is an area in which human experimentation ethics is rapidly evolving. Assuming that the contention is well grounded in some particular instances, it may be appropriate to step back from the practice of informed consent and instead focus on making a sincere effort to uphold the underlying principle of respect for persons. Precisely how the principle would be honored in such circumstances would depend intimately upon the details of the case.[10]

5.4 Non-exempt human subjects research in which it is not desirable to obtain individuals' written informed consent to participate.

There are at least two circumstances in which it may not be desirable to obtain informed consent from subjects in non-exempt research: 1) a signed informed consent document may pose a risk to subjects, and 2) obtaining informed consent may diminish the scientific merit of the research. It should be noted that in the first case, only the *documentation* of the subject's informed consent is undesirable; in the second case the problem is with the informed consent process itself.

In some kinds of research, the very existence of a signed informed consent form, as a written record of a subject's participation in a project, may present a risk to that individual. For example, a subject's signature on a consent form for research investigating illegal drug use, deviant sexual

[8] For research involving children, see: 7, at subpart D; 8, at Chapter VI (C); and other OHRP guidance. For the most recent guidance on research involving people with cognitive impairments, see 14.

[9] For more on the emergency research waiver, see the amendment noted in 11 as well as OHRP guidance materials.

[10] Among other documents, CIOMS International Guidelines for the Review of Epidemiological Studies briefly discusses community agreement for research in communities in which collective decision making is the norm (15, at guidelines 5-8; also see 3, at guidelines 8 and 9]. Community agreement is one possible response to the concern raised above.

practices, or a serious heritable condition, may reveal highly sensitive information about that subject, constituting a significant confidentiality or other risk. It may be advisable for investigators to obtain a Certificate of Confidentiality, which protects against some forms of compulsory disclosure of information about subjects. In other cases, the best way to manage the risk of disclosure may be to waive the written informed consent requirement. An IRB may grant such a waiver under certain conditions (see below), but it should be stressed that such waivers do not necessarily relieve the investigator of the obligation to *obtain* the subject's informed consent, only of the need to collect signed consent forms from all participants.

In contrast, the desire to waive written informed consent requirements may not be motivated by the subjects' needs, but rather by concern for experimental design. Being aware that one is the subject of an experiment or knowing the purpose of the experiment may sometimes alter the subject's behavior to such an extent that it is no longer revealing. Consider, for example, a controversial study of the accuracy of self-reports of cocaine use (16). Subjects agreed to participate in an experiment concerning asymptomatic carriage of sexually transmitted diseases (STDs). To this end, they provided urine samples and completed a questionnaire that included questions about recent cocaine use. What subjects were not told, however, was that a second study was being conducted in conjunction with the STD study, and that their urine samples would be tested for cocaine metabolites and matched with their responses to drug-history items on the STD questionnaire. Had subjects' informed consent been obtained, the study about the accuracy of self-reported cocaine use would have been invalid.

Local IRBs have the authority to grant waivers of the written informed consent requirement for reasons of experimental design, but only under limited conditions: the research may not involve more than minimal risk to subjects and any deviation from the ordinary informed consent process may not infringe on subjects' rights or welfare. In essence, these requirements insure that participation in research in the absence of informed consent poses only the degree or type of risk ordinarily encountered in daily life, that is, to the sorts of risks to which we implicitly consent simply by engaging in ordinary activities. If so, then it is only the *purposes* of the research, and not the risks, for which consent is presumed. Moreover, when the presumption of consent may be remediable by debriefing and/or obtaining their deferred consent (with the opportunity to withdraw their data), debriefing and/or deferred consent are required [7, at §116(c) and (d)].

6. Conclusion

Despite these exceptions to the requirement to secure socio-legal informed consent, informed consent in both the socio-legal and moral senses is an indispensable component of ethically conducted research. More than anything, perhaps, the principle and the practice of informed consent outlined in this brief survey reflect an attitude of the researcher toward the subject that is inextricably linked to the scientific enterprise itself. Consistency demands that the same respectful and benevolent attitudes that motivate the search for generalizable knowledge about humankind also guide researchers' dealings with the individuals who serve as subjects.

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