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A Proposed Process for Reliably Updating the Common Rule

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Abstract

The recent Common Rule revision process took almost a decade and the resulting changes are fairly modest, particularly when compared to the ambitious ideas proposed in the advance notice of proposed rulemaking (ANPRM) and notice of proposed rulemaking (NPRM). Furthermore, the revision process did not even attempt to tackle any of the Common Rule subparts pertaining to vulnerable populations (i.e., pregnant women and fetuses, prisoners, children) where commentators think the rules unduly restrict important research. We believe that this was a missed opportunity to make desirable changes, and that given the usual process the next opportunity to revisit the Common Rule is unacceptably remote. In this article, we argue that the Common Rule should be regularly reassessed, with a mechanism for making substantive (and expeditious) changes. Drawing on lessons learned from the recent revision process, we make recommendations about ways to structure future attempts to maximize the ability to make timely and necessary changes.

Keywords

Common Rule; framework legislation; public consultation

Federal regulations governing research with human subjects have existed since 1974, but except for minor changes, the rules have been largely static for decades (Menikoff, Kaneshiro, and Pritchard 2017). Recognizing the need to revisit the Common Rule, the Obama administration began the process of making substantial changes to the regulations in 2011 with an advance notice of proposed rulemaking (ANPRM) (Federal Policy for the Protection of Human Subjects 2011). This document asked for public comment on a range of early ideas for ways to significantly change the Common Rule. After synthesizing the

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public comments regarding the ANPRM, a more concrete proposal was promulgated in a 2015 notice of proposed rulemaking (NPRM) (Federal Policy for the Protection of Human Subjects 2015).

Public comments revealed significant concerns about many of the proposed changes contained in the NPRM, and the final rule stripped away most of these controversial changes (Federal Policy for the Protection of Human Subjects, Final Rule 2017). Despite excluding many of the initially proposed ideas for change, the final rule does contain provisions that will improve protections for human subjects, and hopefully promote increased efficiency of institutional review board (IRB) review. For example, the Common Rule was changed to (1) clarify the information provided to subjects during informed consent; (2) create new types of exempt, low-risk, research; (3) require that multisite collaborative research protocols be reviewed by a single centralized IRB; and (4) end mandated continuing reviews of protocols in data analysis or follow-up stages.

In the end, the revision process took almost a decade and the resulting changes are fairly modest, particularly when compared to the ambitious ideas proposed in the ANPRM and NPRM. Furthermore, the revision process did not even attempt to tackle any of the Common Rule subparts pertaining to vulnerable populations (i.e., pregnant women, fetuses, prisoners, children) where commentators think the rules unduly restrict important research (Presidential Commission for the Study of Bioethical Issues 2013; Lyerly, Little, and Faden 2008). We believe that this was a missed opportunity to make desirable changes, and that given the usual process the next opportunity to revisit the Common Rule is unacceptably remote. In this article, we argue that the Common Rule should be regularly reassessed, with a mechanism for making substantive (and expeditious) changes. Drawing on lessons learned from the recent revision process, we make recommendations about ways to structure future attempts to maximize the ability to make timely and necessary changes.

AN ARGUMENT FOR REGULAR REVISION OF THE COMMON RULE

In our federal separation of powers, the legislative branch has the authority to make laws and the executive branch is tasked with implementing those laws. In practice, however, Congressional legislation typically lacks sufficient detail to serve as a workable regulatory regime; promulgation of precise and operative regulations is generally delegated to the executive branch. This is a powerful role, particularly when combined with the concurrent authority to execute the law. In order to ensure that the executive-branch rule-making process is sufficiently transparent and accountable to the public, various laws, policies, and practices have been established that require specific procedures (e.g., notice and comment) (Carey 2013). For better or for worse, the net result of this system is that federal regulations can be extremely difficult to make or alter (Kerwin, and Furlong 2010), particularly when a given set of regulations impacts a diverse range of agencies and stakeholders, as is the case with Common Rule. This at least partially explains why the Common Rule has remained largely unchanged for most of its existence. But there are at least three reasons why it might be important to push back against that regulatory inertia in the context of human subjects protections.

Changing Views About Research

First, as societal perceptions of the risks and benefits of research change, the underlying rationale for rules might shift accordingly. The early research ethics field and the U.S. regulations grew in response to a series of scandals (e.g., Nazi experiments, the Tuskegee study, etc.) and therefore understandably codified a predominantly protectionist stance (Institute of Medicine 2007). Over time, however, views about research have shifted (and continue to shift). While it is still important to protect potential subjects, strong protectionist views have been tempered by awareness that research can be beneficial, and that access to research should therefore be facilitated and promoted (Moreno 2001). Similarly, societal trust of investigators has ebbed and flowed; early strong protectionist views that saw researchers as requiring close oversight seem to have been softened by more willingness to trust researchers.

Two cases illustrate these shifts. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was charged with addressing the ethics of research with prisoners in 1976. It explicitly considered two ways in which respect for persons and justice could be applied to research with prisoners. On the one hand, those principles could require that prisoners, as autonomous agents, be free to volunteer for research and to access the potential benefits such participation might offer. On the other hand, respect for persons and justice could focus on prisoners' status as a vulnerable population that needs to be protected from potential exploitation (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1976). The commission chose to adopt this latter protectionist view, which subsequently led to the extremely restrictive Subpart C regulations (Department of Health and Human Services 1983). Thirty years later, however, an Institute of Medicine (IOM) committee reexamined this debate and chose to recommend rejecting strong protectionism, instead suggesting the adoption of a moderate protectionist stance that tried to find a more even balance between restrictive rules designed to avoid exploitation and permissive rules that promote access to beneficial research (Institute of Medicine 2007).

A similar shift was seen in the way that HIV activism transformed views on research toward recognition that protection needs to be balanced with access. In the late 1980s, researchers began conducting clinical trials to assess AZT as a treatment for AIDS. Given the lack of other therapeutic options to slow the disease's progression, AIDS activists publicly and persistently made the case that this research was potentially beneficial, that access was of paramount importance, and that barriers to participants should be removed. Describing this remarkably swift shift away from the protectionist view, Robert Levine wrote that "Investigational drugs, once regarded as dangerous, potential 'thalidomides,' are now described as 'promising new therapies' to which persons suffering with serious illnesses should have access" (Levine 1994, 95). This shift was so transformative that a new "parallel track" system was devised to provide patient access to certain drugs while clinical trials were still ongoing (Kolata 1989).

These cases demonstrate that changes in the understanding of and societal views on issues like trust of investigators and the characterization of research can shift dramatically over time. An ideal human subjects research regulatory regime would periodically be reassessed

to ensure that the rules in place accurately reflect an understanding of the evolving burdens and benefits of research on which they are supposed to be based.

Evolving Scientific Methods

A second reason for regularly revisiting the Common Rule relates to the rapid pace of scientific advances and the accompanying ethical issues that such progress can raise. As scientific technologies and methodologies evolve, the kinds of rules we need to govern research with humans will necessarily change as well. For example, the past decade has seen a radical transformation in the ability to sequence genomic data. Prior to 2005, sequencing genes was a laborious task, and the difficulty of producing genetic data limited the utility of genetic research (Mardis 2011). The invention of massively parallel sequencing platforms suddenly enabled researchers to quickly and cheaply sequence a person's genome (Feero, Guttmacher, and Collins 2010). This gave investigators a powerful new research methodology (Green, Guyer, and National Human Genome Research Institute 2011), but also raised significant ethical concerns (Tabor et al. 2011). Similarly, ethical questions have been raised by the past decade's proliferation of data and specimen research (Eiseman 2000), the increasing use of big data in research (Berkman et al. 2016), and the emergence of pragmatic trials (Sugarman and Califf 2014).

The emergence of new research methodologies and related practices was clearly a motivating factor in the attempt to modernize the Common Rule. For example, a number of the proposed (but not adopted) changes contained in the ANPRM and the NPRM were designed to address the possibility that "deidentified" samples are now potentially reidentifiable through advances in genomic research, and how changing notions of identifiability affect what types of research should be regulated as human subjects research (Emanuel and Menikoff 2011). Without taking a position on the relative merits of those proposed changes, we commend the effort to make the human subjects research oversight system keep pace with the evolving characteristics of scientific research. However, we also acknowledge that scientific methods will continue to shift over time, which should prompt more frequent reexaminations of the Common Rule.

Emerging Understanding of Regulatory Implementation

A third argument for regular updates to the Common Rule flows from the reality that necessarily technical or ambiguous regulatory language can be implemented in unexpected ways. Regulations can never fully specify how to deal with every situation, so some interpretation and extrapolation is often required, sometimes generating undesirable consequences. Furthermore, regulations are based on assumptions that can change, particularly as new evidence emerges. This points toward the need to understand how research practices are actually being influenced by regulations, and to regularly interrogate whether the rules are having the desired effect. In particular, it is important to ask whether some rules are being interpreted in an unduly restrictive way or implemented in an overly permissive way. Regular reevaluation of the regulations would allow for reaction to emerging evidence about how they are actually being interpreted and utilized.

There are at least three ways in which implementation issues can manifest. First, regulations contain some flexibility that can be used in unanticipated and potentially inappropriate ways. For example, the regulations outline a range of methods for review of research (i.e., full board, expedited, exempt), specifying the conditions under which protocols can be evaluated using each of those tracks. Yet IRBs have a tendency to unnecessarily utilize more rigorous review procedures than are otherwise required (Bell, Whiton, and Connelly 1998). There might be good reasons to maintain a flexible system where IRBs are free to select the level of review they deem to be most appropriate. On the other hand, if deviation from the intended design of the regulations results from inadequate education or unwarranted fear of violating the rules (Millum and Menikoff 2010), perhaps less flexibility would be beneficial.

Second, regulations can be unduly restrictive in ways that deleteriously overconstrain behavior. This has been observed in the rules limiting the categories under which research with vulnerable populations can be conducted. Given the original strong protectionist perspective, the regulations intentionally made it difficult to conduct certain kinds of research with pediatric (Presidential Commission for the Study of Bioethical Issues 2013) or pregnant subjects (Lyerly, Little, and Faden 2008). But given that there is evidence that these constraints are impeding important research, an exploration of whether or not to reorient the existing rule would be justified.

Third, regulations can contain language that does not anticipate new technologies or practices. For example, as electronic media have emerged, there has been much confusion about whether written consent forms could be displayed on computers and other devices. The updated Common Rule now has an expanded definition of “written” to explicitly include electronic media, but experimentation with novel ways to obtain informed consent was likely hampered by the previous uncertainty.

A PROPOSAL FOR FUTURE REVISIONS TO THE COMMON RULE

If one accepts that the Common Rule should be periodically reviewed, are there ways to create a system that facilitates regular reexamination, while maximizing the possibility of adopting changes in a way that improves the regulations without undermining important protections for research subjects? A continued reliance on the existing approach (which took nearly a decade and only produced incremental changes) will not ensure the proper balance. We believe that updates to the Common Rule would be facilitated by a framework and strategy that address two primary concerns: (1) the anticipatable roadblocks inherent to the rulemaking process, and (2) the competing goals of protecting subjects and facilitating research. In the next sections, we analyze these two problems and propose frameworks for improving the process of making changes to the Common Rule.

Creating Sufficient Political Momentum

Given that the Common Rule has only been updated sporadically since its adoption, and that it took nearly a decade to work through these recent changes, perhaps there is insufficient political will to ensure that changes are made as frequently and expeditiously as we have argued is necessary. One way to potentially solve this problem would be to employ the concept of framework legislation.

Framework legislation is a tactic used by legislatures when they can agree on the broad need to address a given problem, but when it will be difficult to settle on a particular course of action. Framework legislation attempts to bind a legislative body in a way that forces future collective action. Specifically, a piece of framework legislation will generally “establish internal procedures and rules that will shape legislative deliberation and voting with respect to a specific subset of laws or decisions in the future” (Garrett 2006). For example, the federal budget process includes a particular set of rules that require certain Congressional actions and that change voting procedures to more readily facilitate the important goal of passing a federal budget. Framework legislation is particularly useful as a strategy because it can address collective action problems, particularly by “entrenching certain macro-objectives so that future decisions are more likely to align with them” (Garrett 2005).

In the context of updating the Common Rule, since there is no clear constituency advocating for change, and since the changes would likely touch on politically controversial topics, there would almost certainly be a collective action problem. Nevertheless, it is likely that most people would agree with the “macro-objective” of regularly updating these important regulations as science advances and norms evolve. Framework legislation could put in place a structure whereby policymakers (in Congress, or more likely in the Executive Branch) would be required to revisit the Common Rule at a set interval, perhaps with instructions to pay particular attention to anticipatable issues. Without a timeline (and a deadline) for making change, it is likely that it will again be decades before the Common Rule is revised.

Adopting a framework legislation approach (i.e., “framework rulemaking”) can help to facilitate more frequent revisions, but this, of course, leaves a question about the appropriate frequency for these revisions and the length of the revision process. Changing rules has a cost because people and institutions have to update their existing policies and procedures accordingly, so it would not be prudent to set a schedule that resulted in relatively constant upheaval. Similarly, the revision process cannot take longer than the period of desired change. We preliminarily propose a 10-year revision cycle, including a 3-year revision process plus a subsequent year for implementation. If such a regular schedule were adopted, it might be the case that major revisions would not always be required, and that some cycles would lead to very few changes.

It is also important to explicitly consider the standard for making a change when setting up a prospective schedule for making changes. Even though we have argued that the Common Rule should be regularly reexamined, that does not necessarily imply that every reexamination should introduce radical changes. Since the Common Rule is an existing regulation, the bar for change should be higher than the one for enacting new regulations because practices and policies have been developed that rely on the existing rules. It is sensible to internalize a presumption in favor of not altering the regulations absent a compelling reason (e.g., the change is significantly, not marginally, better than the status quo, or the change is necessary given important changes in research methodology or societal norms).

As a final note, formal guidance could be useful as an additional strategy for expeditiously updating and clarifying aspects of the Common Rule. We believe, however, that guidance is

primarily useful for cases where existing regulatory language is unclear, where it allows for a range of options, or when the rules have not anticipated new practices (e.g., electronic informed consent). Formal guidance seems less relevant to more systemic issues like evolving scientific methods or shifting views about research. Nevertheless, formal guidance can be a useful tool for smaller changes and can serve as a way to make interim improvements. Interim guidance can also serve as a signal during each round of revisions for issues that need to be closely reexamined and revised if necessary.

Soliciting Appropriate Consultation and Input

Making major regulatory changes is designed to be difficult under the best of circumstances, and can be extraordinarily challenging when tackling complicated or controversial issues. In the absence of an explicit, distinct process for reexamining research regulations, we end up using the general process prescribed for rulemaking, which seems inadequate given the competing ethical issues raised by human subjects research—protection of participants and facilitation of needed research. This can be observed in the fact that the recent proposed changes to the Common Rule took on a number of controversial topics, almost none of which were ultimately adopted after significant pushback. Most of the criticism of the ANPRM and NPRM surrounded changes to rules about the secondary use of biospecimens in research. A study of universities that received funding from the National Institutes of Health (NIH) Clinical and Translation Science Awards found that the majority of institutions that commented on the ANPRM opposed the proposed biospecimen rules (Botkin et al. 2014). Some argued that, despite this sustained negative feedback from research institutions, the subsequent NPRM proposal on biospecimens still did not address concerns raised during the first comment period (Grizzle 2015). Stakeholders expressed similar worries during the NPRM comment period; one study estimated that 70% of comments on the NPRM referenced the biospecimen proposals and “more than half of the general public and 80% of the top 30-ranked universities opposed the proposed changes” (Sobel and Dreyfus 2017, 6).

The biospecimen proposal was also criticized as emblematic of the “unnecessary complexity” of the NPRM because it proposed more stringent regulation for secondary research with biospecimens than for research on existing data sets (Guerrini, McGuire, and Majumder 2016; Lynch, Bierer, and Cohen 2016). Some articles pointed out that this distinction could have unintended consequences and argued that treating biospecimens as unique required strong ethical reasoning that the NPRM did not provide (Williams and Wolf 2013; Robertson and Loe 2016). Although the NPRM cited surveys that indicated that the public wanted consent for biospecimen research, some argued that public opinion should not be the only guiding principle for policy (Robertson and Loe 2016).

As such, we argue for a process that starts narrowly. Before an ANPRM is promulgated, there should be a goal of identifying the most pressing issues that need to be addressed, as informed by the views of key stakeholders that have the strongest nexus with the Common Rule. Notably, the process for making the recent changes to the Common Rule started with just such an agenda-setting step. Shortly thereafter, this would be followed by broad consultation with the entire range of stakeholders to discuss the principles on which possible regulatory choices should be made. Specifically, in addition to the normal notice and

comment process, we propose a series of in-person meetings where stakeholders can assess and respond to a range of arguments. This kind of forum would give everyone (especially outspoken critics) an opportunity to have their views heard, but in the context of a cooperative environment where the goal is to articulate a shared set of principles for making difficult choices about changes to the Common Rule. Ideally, this broad consultation would include stakeholders within the relevant federal agencies, as well as direct representation from external stakeholders. Finally, there should be a very narrowly representative decision-making group that is responsible for making, and transparently justifying, concrete policy choices.

This process is responsive to the reality that when trying to regulate controversial topics, it is likely impossible to ever find complete consensus. Norm Daniels and James Sabin developed the “accountability for reasonableness” framework to address a similar concern in the context of health care system decision making. Although developed to address a distinct set of questions (namely, how to justify limitations on or refusals to provide certain types of care), this framework can also serve as a useful lens through which to think about how to balance important competing claims when making changes to the Common Rule. On their account, “Accountability for reasonableness is the idea that the rationales for important managed care plan decisions should not only be publicly available, but should also be those that “fair-minded” people can agree are relevant to pursuing appropriate patient care under necessary resource constraints” (Daniels and Sabin 1998, 51). Their framework acknowledges that a pluralistic society will find it difficult to agree on principles to settle difficult priority setting decisions, and therefore a focus on procedural fairness will help to facilitate decision making that is broadly viewed as legitimate (Daniels 2000).

Daniels and Sabin propose four conditions necessary to achieve accountability for reasonableness. First, there must be transparency about the reasoning being employed to justify policy decisions. Second, these arguments must flow out of principles and evidence that are broadly perceived to be relevant by the public. Third, there is a way to appeal disputed decisions. Finally, there is some enforcement mechanism for ensuring that these first three conditions are satisfied (Daniels and Sabin 1997).

We believe that these conditions are extremely relevant for effectively soliciting input about controversial topics where there are varied views about what is ethically acceptable. In order to effectively ensure that policy changes are based on widely supported principles and evidence, it is necessary to solicit input throughout the policymaking process. In practice, however, there are many questions about how to obtain appropriate input about a controversial policy change with wide-reaching implications. The first question concerns who should give input. Broad consultation can be beneficial because it gives more stakeholders an opportunity to present their views and to engage with the arguments and evidence being presented in support of a given policy proposal. This can increase procedural transparency, resulting in a higher likelihood of stakeholder buy-in. Following the accountability for reasonableness framework, we believe that significant opportunities for broad input of views are of paramount importance.

Broad consultation, however, is not a panacea; focused decision making is also vital for a number of reasons. First, a completely open process can privilege people with extreme views, so it is important to attempt to include specific groups to ensure a representative sample of perspectives. Second, a more focused decision-making process gives regulators more control over the direction of the policy's evolution and can avoid the paralysis of rulemaking by committee. For example, part of the reason it took so long for the revision process to move forward was the need for diffuse consultation within the many federal agencies that have signed onto the Common Rule. Even within the Department of Health and Human Services (DHHS), there are various stakeholders (e.g., NIH, Centers for Disease Control and Prevention [CDC], Food and Drug Administration [FDA]) that each have different views about how the rules should be structured. Getting them all to agree on a single approach is a daunting challenge, but could be facilitated by a representative decision-making group that can narrow the range of choices.

CONCLUSION

The preceding arguments are not an indictment of the hard work that many people put into efforts over the last decade to revise the Common Rule. Rulemaking is difficult, particularly in a controversial area like research ethics. Our hope, however, is that the next opportunity to revisit the Common Rule takes advantage of the lessons that the current update process affords. Specifically, we believe that there are important reasons to regularly revisit the Common Rule, and that there are procedural approaches (i.e., framework rulemaking and strategic consultation) that can be employed to facilitate that process. Commendably, the new changes to the Common Rule employ the former approach to a limited extent, for example, instructing the agencies that implement the Common Rule to collaborate on a process of redefining the definitions of “identifiable private information” and “identifiable biospecimen” at least every 4 years (Federal Policy for the Protection of Human Subjects, Final Rule 2017). Other countries (e.g., Japan) have successfully enacted a specified time frame for reviewing their human subjects research regulation. More of this kind of strategic procedural maneuvering would be productive, and should maximize the chances that our human subjects research regulations remain current and effective even in the face of the constant evolution of science and culture.

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