

Against One-Size-Fits-All Research Ethics

by Michelle N. Meyer

Many feel the Common Rule treats an unwieldy range of activities identically under the monolithic label “human subjects research.” Past objections centering on the conflation of biomedical and behavioral research have gained new currency with the increase in biobanking and Internet-based research. A more nuanced approach to research is overdue. Regulation will no doubt remain a major component of any new approach. But in some research contexts, investigators and subjects should be permitted to reach voluntary, informed agreements about certain aspects of their relationship.

Consider the National Institutes of Health’s new “Guidelines for Human Stem Cell Research.”¹ The guidelines owe their existence to the NIH’s recognition that research diversity requires regulatory diversity. Under the Common Rule, the sources of existing, coded biological specimens are not considered research subjects when certain conditions are met. Thus, neither their consent to, nor even their knowledge of, research is required.² When the source’s only interest is in informational privacy, this rule is defensible. But when the source—or her relatives, or other genetic groups—objects to the *kind* of research being conducted, deidentification is irrelevant. While leaving the deidentification-is-enough rule otherwise intact, the NIH singled out human embryonic stem cell (hESC) research on deidentified embryos left over from in vitro fertilization, sensibly requiring

providers’ voluntary, informed consent, as defined by the guidelines’ criteria.

But if the guidelines as a whole show the promise of disaggregating research, one of the first decisions made in their name shows the peril of failing to do so. While newly derived lines must meet the guidelines’ rigorous informed consent criteria, the provenance of existing lines is reviewed by a specially formed working group of the Advisory Committee to the Director, “taking into account the principles articulated” in both the guidelines and the Common Rule.³ The working group found that lines derived by the Reproductive Genetics Institute fell short of these principles because donors were required to waive any legal claims arising from the research.⁴ The guidelines’ consent criteria, designed specifically for this context, say nothing about exculpatory language; however, the Common Rule—applicable here even to nonfederally funded entities like RGI as a source of ethical guidance—prohibits it. Although the NIH said it would approve the lines if donors consented without the waiver, deidentification makes contacting them again difficult.

Why is the exculpatory clause incompatible with the principles of ethical research? According to NIH Director Francis Collins, the “use of exculpatory language . . . was inconsistent with the basic ethical principle of voluntary consent.”⁵ But if voluntariness is a problem at all, it is so only with respect to the waiver term. The most plausible argument to be made from involuntariness is this: the waiver term was unfavorable,

but donating their embryos was so important, and the opportunity to do so without agreeing to a waiver so lacking, that donors’ acceptance of the waiver was coerced. If true, the solution is to sever the offending clause, not to invalidate the parties’ intent. Having agreed to donate despite the offending term, they needn’t be contacted to ask if they’re willing to donate without it. Instead, in exchange for approving the lines, the NIH should require RGI to waive *its* right to rely on the waiver in any lawsuit brought by donors. (Conversely, if the waiver somehow did infect the agreement to donate, it’s unclear how contacting donors again for their consent would constitute a cure. A party who didn’t authorize a contract made in its name can later ratify it, making her consent retroactive to the date of the contract. But here, consent today isn’t equivalent to initial consent: embryo destruction is a *fait accompli*, and donors may “choose” only between permitting the lines to be used for potentially beneficial research or insisting that they be wasted. Contact under these circumstances seems more like begging for forgiveness than asking for meaningful permission.)

Now consider a more provocative possibility: that in this particular case, the waiver itself is ethically acceptable. Like most contracts we sign every day, RGI’s was a take-it-or-leave-it offer—here, the opportunity to donate to hESC research in exchange for waiving any claims concerning that research. Although the opportunity to donate was no doubt important to many donors, it was not an offer they couldn’t refuse. Donors had alternatives for disposing of their embryos, for supporting hESC research (donating money), and possibly even for donating embryos to hESC research (donors could request that their embryos be returned and might have found a researcher who didn’t require the waiver).

The working group objected to the waiver on different grounds: that it “made it appear that the purpose of the document was to protect the practice more than [the] patient,” which “challenge[s] a key principle of

informed consent to protect the interests of the donors.”⁶ That is, even if voluntarily and knowingly agreed to, the waiver impermissibly altered the nature of the parties’ relationship. But, although the working group uses the term “patient,” donors of spare IVF embryos are subjects, not patients. And researchers, unlike physicians, are not fiduciaries obligated to avoid conflicts of interest that might interfere with their primary duty to pursue the beneficiary’s interests. Researchers’ primary aim is to pursue useful, generalizable knowledge. Their pursuit of that goal is subject to ethical side constraints: they’re obligated to avoid certain conflicts and promote certain interests of subjects. But they’re not obligated to indiscriminately rank subjects’ interests above their own or those of the research endeavor—nor could they, without crippling that endeavor. To point out that some interest of the subject is set back to promote some interest of the researcher, then, merely begs the question of the significance of those particular interests.

Indeed, the NIH itself does not view all waivers as contrary to ethical research: the guidelines require donors to be informed that they will not profit from any commercial development of the lines,⁷ and the NIH has approved lines where this was conveyed by requiring donors to waive all property rights.⁸ Though avoiding undue inducement is important, many subjects have a strong interest in ensuring that any fruits of the research to which they contribute are widely accessible.⁹ Overly broad waivers of rights not only to profits but also to control prevent donors from protecting this interest by conditioning their gift on acceptable intellectual property arrangements.

While it neglected donors’ property interests, the working group simply assumed that a waiver of tort claims would burden donors, and without any offsetting benefit to donors or science.¹⁰ Neither assumption is obviously true. Though the number of lawsuits brought by subjects is rising, subjects have limited prospects for relief from intangible harms unaccompanied by bodily injury—the most likely adverse outcome of

spare embryo donation, as the working group noted. Even if such psychosocial harms were legally cognizable, studies of medical malpractice show little overlap between those harmed by negligence and those awarded damages, and thus little liability-related deterrence of negligence. If true in the research context, tort liability may effectively amount to an arbitrary tax on research. That tax is likely to be passed on to patients through more expensive clinical applications, or to result in some research being foregone altogether—outcomes that would undermine what should be the shared interests of researchers and donors. Many argue that permitting patients and providers to contract out of medical malpractice liability would leave both parties better off. The same may be true here.

We should also consider whether researchers should bear the costs of any research-related misfortune that befalls subjects. If not, then rather than depriving donors of their due, the waiver may prevent a sort of unjust enrichment. When psychosocial risks are at issue, information asymmetries in professional-layperson relationships may be muted or even reversed. For instance, subjects are best able to avoid regret (a potential outcome the working group noted) by reflecting on their views about the moral status of the embryo, the likelihood that they will want more children through IVF, how they would feel about a genetic child being raised by others, etc. And while researchers are better able to avoid privacy breaches, only subjects know the magnitude of harm imposed if a breach occurs.

Finally, even if the waiver term constituted a net burden to donors, we can’t conclude that RGI’s overall protocol has a worse risk-benefit profile than standard donations without considering any unique benefits of that protocol. Unfortunately, the working group was reportedly instructed to ignore the considerable value of RGI’s forty-two rare, disease-specific lines.¹¹ Nonfederally funded researchers can still use them but are unlikely to foreclose the option of future federal funding by investing in ineligible lines. And since pharmaceutical

companies have little incentive to fund research on rare diseases, hESC research on such diseases may decrease. Finally, the protocol may offer RGI donors the unique benefits of contributing to research on those diseases from which they or their loved ones suffer.

It is ironic that the NIH applied as unimpeachable ethical wisdom the very Common Rule to which the guidelines are meant to be an exception. This isn’t about science versus ethics. It’s about rethinking what ethics requires in different contexts. We should take the growing consensus about the shortcomings of the Common Rule—in hESC research, biobanking, behavioral research, and elsewhere—as an opportunity to rethink its one-size-fits-all approach to human subjects research.

1. 74 Fed. Reg. 32170 (July 7, 2009).

2. See Department of Health and Human Services, Office for Human Research Protection, “Guidance on Research Involving Coded Private Information or Biological Specimens,” October 16, 2008, <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>.

3. Guidelines, at 32175.

4. Advisory Committee to the Director, Working Group for hESC Eligibility Review, “Findings and Summary Regarding Advanced Cell Technology Submission 2010-ACD-007,” June 3, 2010, http://acd.od.nih.gov/slides/061010/061010_files.pdf, at 67.

5. E.S. Collins, “Statement from the Director on the Addition of New Lines to the Human Embryonic Stem Cell Registry,” June 21, 2010.

6. Advisory Committee to the Director, Working Group for hESC Eligibility Review, “Findings and Summary,” at 37.

7. Guidelines, sec. II(A)(3)(e)(vi).

8. Advisory Committee to the Director, Working Group for hESC Eligibility Review, “Findings and Summary,” at 160 (Endeavour2 line).

9. See, for example, *Washington University v. Catalona*, 400 F.3d 667 (8th Cir. 2007); *Greenberg v. Miami Children’s Research Institute*, 264 F. Supp. 2d 1064 (S.D. Fla. 2003); R. Skloot, “Taking the Least of You,” *New York Times*, April 16, 2006; A.D. Marcus, “Putting Drug Development in Patients’ Hands,” *Wall Street Journal*, July 29, 2008.

10. See 45 C.F.R. 46.111(a)(1)–(2).

11. Editorial, “NIH Was Unwise to Reject Promising Stem-Cell Lines,” *Boston Globe*, June 27, 2010.

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