A LEGAL APPROACH TO THE USE OF HUMAN BIOLOGICAL MATERIALS FOR RESEARCH PURPOSES

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Abstract

Human Biological Materials (HBM) come from individuals in a variety of circumstances. The use of HBM for research purposes raises a host of difficult ethical questions. The law is important in this arena because, in most cases, legal principles significantly influence the making of ethical choices. Following a general overview of research regulation in the United States generally, and a few comments on the relevance of international statements for this country, this article explores several specific legal issues, and their ethical implications, related to the obtaining and handling of HBM for research purposes, namely: informed consent, privacy, and commercial or ownership (property) interests in HBM. The article concludes that, although the realistic liability risks are low, the law's important role in characterizing the rights and responsibilities involved will be very influential in shaping the ways that the chasm between science and ethics is resolved within the context of the use of human tissue for research purposes.

Key Words

Legal, Human tissue, Research, Ethics

1. INTRODUCTION

Increasingly, biomedical and behavioral researchers are conducting genetic research involving the use of human biological material (HBM). The conduct of research using human beings (referred to interchangeably in this article as "human subjects," "human participants," or "patients") generally, and entailing the use of HBM particularly, raises a broad collection of complex social issues that have received substantial attention during the past decade in the public and professional literature. In identifying and analyzing the ethical challenges posed within the context of research with HBMs, attention to a legal approach should be one consequential component of the inquiry.

The next section of this article comments on the importance of a legal approach to this subject. This discussion is followed by an identification of the various sources of HBM and then a general overview of American human subjects research regulation. Subsequently ensuing are some comments on the [limited] relevance of international statements for practice in the United States. Finally, this article explicates several specific legal issues and their ethical implications related to the obtaining and handling of HBM for research purposes.

2. WHY A LEGAL APPROACH?

The Symposium from which this article is derived focused on the chasm between science and ethics regarding the use of HBMs in the biomedical and behavioral research context.[1] One might well ask whether the explication of a legal approach to this ethics-focused discussion adds any value.

Examining a legal approach does add value to this discussion because one primary function of the law is to establish certain boundaries or parameters that, in most cases, significantly influence which ethical and policy choices are made and carried out. More particularly, the law may provide useful—albeit not necessarily complete—guidance regarding the basic issues of

[1] Symposium, Creighton University Center for Health Policy & Ethics, *The Use of Human Tissue and Public Trust: The Chasm Between Science and Ethics* (Sept. 19, 2011).

duty (What are we obligated to do?), power (If we want to act, do we have the authority to engage in that chosen action?), and limits (If we want to exercise authority to act, what constraints are there on our power to act?). Within the broad boundaries set by the law's delineation of duty, power, and limits, there is substantial opportunity and necessity for the implementation of ethical and policy discretion.

In the specific context of biomedical and behavioral research involving the use of human participants, the purpose of the law is neither to delay nor to expedite the research project, but rather to protect actual or potential human participants.[2] The fundamental ethical principles underlying the present elaborate legal apparatus overseeing the conduct of human subjects research in the United States (described below) are beneficence (a concern about participants' well-being), autonomy (a concern about participants' right to freely and knowledgeably choose whether or not to voluntarily participate in the research), and justice (a fair, equitable distribution of benefits and burdens).[3]

3. SOURCES OF HUMAN BIOLOGICAL MATERIAL (HBM)

Before proceeding to a discussion of the pertinent legal issues, it is useful to briefly lay out the most likely independent or overlapping scenarios that may result in the collection and retention of HBM. Excess HBM may be left over and retained from a clinical procedure that was performed for diagnostic or treatment purposes.[4] Alternatively, HBM may be obtained just for use in an ongoing clinical research protocol.[5] Further, HBM

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[2] Richard S. Saver, *Medical Research Regulation After More Than Twenty-Five Years: Old Problems, New Challenges, and Regulatory Imbalance*, 19 ANNALS HEALTH L. 223, 223 (2010).

[3] BARUCH A. BRODY, THE ETHICS OF BIOMEDICAL RESEARCH: AN INTERNATIONAL PERSPECTIVE 35 (1998).

[4] Laura B. Rowe, *You Don't Own Me: Recommendations to Protect Human Contributors of Biological Material After* Washington University v. Catalona, 84 CHI.-KENT L. REV. 227, 227-28 (2009).

[5] Lori Andrews, *Who Owns Your Body: A Patient's Perspective on* Washington University v. Catalona, 34 J.L. MED. & ETHICS 398, 398 (2006).

might be obtained at one point in time in anticipation of its potential use in future, currently undefined research protocols.[6] Increasingly, HBM obtained for use either in a current or future research protocol or for a variety of other potential purposes (such as DNA retained for law enforcement purposes or sperm, ova, and embryos retained for reproductive purposes) is being stored in biobanks or tissue repositories.[7] These biobanks may provide HBM to researchers for use in their investigations either gratuitously or for a fee.

4. BRIEF OVERVIEW OF RESEARCH REGULATION IN THE UNITED STATES

A. GENERAL PROVISIONS

The Federal Department of Health and Human Services (DHHS) regulations governing the conduct of research using human participants in the United States[8] are based mainly on the recommendations of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (the Belmont Commission). The Belmont Commision was established by the 1974 National Research Act.[9] Additionally, a number of other federal agencies have adopted the DHHS regulations as a Common Rule to protect human participants in any research protocol for which that agency provides financial support.[10] Most American academic and

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[6] *Id*. at 399.

[7] Leslie E. Wolf, *Advancing Research on Stored Biological Materials: Reconciling Law, Ethics, and Practice*, 11 MINN. J. L. SCI. & TECH. 99, 100 (2010).

[8] 45 C.F.R. §§ 46.101–46.505 (2009).

[9] *The Belmont Report*, U.S. DEP'T OF HEALTH & HUMAN SERVS (April 18, 1979), http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html.

[10] These agencies and departments are: Department of Agriculture, Department of Energy, National Aeronautics and Space Administration, Department of Commerce, Consumer Product Safety Commission, Agency for International Development, Department of Housing and Urban Development, Department of Justice, Department of Defense, Department of Education, Department of Veterans Affairs, Environmental Protection Agency, National

health care institutions conducting human subjects research agree to adhere to the Common Rule for all of their research protocols regardless of the funding source for a specific study, as a condition of the institution receiving a Federalwide Assurance (FWA) from the DHHS Office of Human Research Protections (OHRP).[11]

The regulations define "research" to which the Common Rule applies as the systematic collection and analysis of data from which generalizable conclusions may be drawn that may assist in improving the future care of presently unknown beneficiaries.[12] So delimited, research is distinguishable from diagnostic and therapeutic interventions (which are intended to directly benefit the person being intervened upon, rather than using that person primarily as a source of data with the possibility of some incidental or secondary direct benefit) or consultation (collecting data to benefit one specific client in terms of a specific need, rather than to benefit the larger public).

Prior to enrollment of any human participants, covered research projects must be reviewed and approved by an Institutional Review Board (IRB) recognized by OHRP.[13] Once approved initially, the research activity is then subject to continuing IRB oversight and at least annual formal review thereafter.[14]

To approve (or renew the approval for) a research protocol involving human participants, an IRB must find that each of the following requirements is met: (1) Physical and psychological

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Science Foundation, and Department of Transportation. *See Federal Policy for the Protection of Human Subjects ("Common Rule")*, U.S. DEP'T OF HEALTH & HUMAN SERVS., http://www.hhs.gov/ohrp/humansubjects/commonrule/index.html (last visited Oct. 15, 2012); *Federalwide Assurance (FWA) for the Protections of Human Subjects*, U.S. DEP'T OF HEALTH & HUMAN SERVS., http://www.hhs.gov/ohrp/assurances/assurances/filasurt.html (last updated June, 17, 2011).

[11] *See Office for Human Research Protections (OHRP)*, U.S. DEP'T OF HEALTH & HUMAN SERVS., www.hhs.gov/ohrp (last visited Oct. 15, 2012).

[12] 45 C.F.R. § 46.102(d) (2012).

[13] 45 C.F.R. § 46.109(a) (2012).

[14] 45 C.F.R. § 46.109(e) (2012).

risks to subjects are minimized; (2) physical and psychological risks to subjects are reasonable in relation to anticipated benefits to those subjects and to the importance of the general knowledge that might reasonably be expected to result; (3) selection of subjects is fair and equitable; and (4) informed consent will be obtained, based on communication to potential participants, or their decision making substitutes, of at least the following informational items (basically consisting of a codification and expansion of the common law informed consent doctrine that was developed on a case-by-case basis in the diagnostic and therapeutic context):[15] (a) reasons for the research, the protocol's anticipated duration, and the specifics of any interventions that are part of the protocol; (b) reasonably foreseeable risks and benefits of volunteering to participate and any reasonable alternatives to volunteering for the specific protocol; (c) confidentiality provisions relating to the research project records; (d) any remuneration and/or treatment available for research related injuries; (e) the potential volunteer's right to decline participation or to withdraw from participation at any time, without penalty or prejudice.[16] Additionally, informed consent must be documented appropriately.[17]

On July 26, 2011, DHHS published an Advance Notice of Proposed Rulemaking (ANPRM).[18] Public comments were

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[15] *See* RUTH R. FADEN & TOM L. BEAUCHAMP, A HISTORY AND THEORY OF INFORMED CONSENT (1986). *See* John M. Conley, Adam K. Doerr, & Daniel B. Vorhaus, *Enabling Responsible Public Genomics*, 20 HEALTH MATRIX 325, 376 (2010) ("[R]esearchers, just like other physicians, must not expose their subjects to potential harm without their consent."); Omri Ben-Shahar & Carl E. Schneider, *The Failure of Mandated Disclosure*, 159 U. PA. L. REV. 647, 655 (2011) ("Few disclosure mandates have been as richly favored as the doctrine of informed consent. Courts, legislatures, and administrative agencies have mandated it in many forms and for a for decades. The medical *and research* establishments have made it their conventional wisdom with barely a whisper of dissent.") (emphasis added).

[16] 45 C.F.R. § 46.116(a) (2012). *See also* FADEN & BEAUCHAMP, *supra* note 15, at 212.

[17] 45 C.F.R. § 46.117(a) (2012).

[18] Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 143 (July 22, 2011) (to be codified at 45 C.F.R. pts.

sought on the following proposals: (1) providing uniform guidance on federal regulations; (2) extending federal regulatory protections to all research conducted at United States institutions receiving funding from the Common Rule agencies, regardless of whether the particular research protocol in question was funded by a federal agency; (3) implementing a systematic approach to collecting and analyzing data on unanticipated problems and adverse events across all trials; (4) establishing mandatory data security and information protection standards for all studies involving identifiable or potentially identifiable data; (5) updating the forms and processes used for informed consent, potentially using a standardized template; (6) using a single institutional review board for review of all domestic sites of multisite studies; and (7) revising the risk-based framework to more accurately calibrate the level of review to the level of risk.[19]

Research involving the testing of investigational drugs or medical devices is also regulated by the Federal Food and Drug Administration (FDA). The Common Rule and the FDA regulations[20] overlap a great deal (including requirements pertaining to IRB review), but are not totally identical.

Human subjects research may be regulated concurrently by both the Federal Government and individual states. A few states have enacted statutes or promulgated regulations providing safeguards for human research participants, some of them compelling prior review and continuing oversight beyond the federal Common Rule.[21] By contrast, some states have codified existing federal regulatory ambiguities concerning biobanking and genetic research.[22] The specific content of the different state

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46, 160, 164 & 21 C.F.R. pts. 50, 56), *available at* http://www.ofr.gov/OFRUpload?OFRData/2011-18792_PI.pdf.

[19] *Id.*

[20] *Compare* 21 C.F.R. § 50 (2012), *and* 21 C.F.R. § 56 (2012), *with* 21 C.F.R. § 312 (2012), *and* 21 C.F.R. § 812 (2012).

[21] *See, e.g.*, MD. CODE ANN., HEALTH-GEN. §§ 13-201–13-206 (LexisNexis 2012).

[22] Katherine Drabiak-Syed, *State Codification of Federal Regulatory Ambiguities in Biobanking and Genetic Research*, 30 J. LEGAL MED. 299, 299 (2009).

laws vary. Also, a particular HBM source might bring a private civil lawsuit against researchers and protocol sponsors for violating the common law tort standard of care (that is, for committing medical malpractice) in conducting research involving and harming that plaintiff.[23]

On December 15, 2011, the Presidential Commission for the Study of Bioethical Issues issued a report that assessed the present system for protecting human subjects enrolled in research studies, both in the United States and abroad.[24] The central finding of the Commission was that the United States' system for protecting human subjects provides "substantial protections" for the health, rights, and welfare of research subjects.[25]

B. INTERNATIONAL STATEMENTS

This article concentrates exclusively on the legal situation in the United States. Nevertheless, we may be able to learn helpful lessons by observing the regulatory regimes regarding the use of HBM in research elsewhere in the world.[26] It also is important to acknowledge the growing international consensus[27] and the various international pronouncements touching on the benefits of biomedical research, the value of privacy, the subject's right of self-determination, and the imperative to avoid or minimize harm. Common themes in these statements are individual dignity, informed consent as a core requirement in both research and clinical contexts, concern about the psychosocial damage that might occur for some people that could be associated with research done with their stored HBM, and

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[23] *See generally* Roger L. Jansson, *Researcher Liability for Negligence in Human Subject Research: Informed Consent and Researcher Malpractice Actions*, 78 WASH. L. REV. 229 (2003).

[24] PRESIDENTIAL COMM'N FOR THE STUDY OF BIOETHICAL ISSUES, MORAL SCIENCE: PROTECTING PARTICIPANTS IN HUMAN SUBJECTS RESEARCH (2011).

[25] *Id.* at 5.

[26] *See generally* Jessica Wright, Corrette Ploem, Marcin Sliwka & Sjef Gevers, *Regulating Tissue Research: Do We Need Additional Rules to Protect Research Participants?*, 17 EUR. J. HEALTH L. 455 (2010).

[27] M.G. Hansson, *Ethics and Biobanks*, 100 BRIT. J. CANCER 8, 8 (2009).

unease or even stronger negative feelings (especially in Europe) toward the idea of commercialism involving the sale of HBM or resulting products.[28]

These international statements often represent valuable assertions of ethical aspirations. However, these statements do not have the force of binding and enforceable law on, or within, the United States, unless and until any particular provision has either been ratified by Congress and signed by the President or has been included in a valid Presidential Executive Order.

5. RESEARCH REGULATION AND HBM

A. SHOULD RESEARCH INVOLVING HBM BE REGULATED?

By contrast, FDA regulations concerning the collection and use of HBM in current or future research protocols entailing the testing of investigational drugs or medical devices continue to fully apply to all HBM research protocols, without exception.[29] The inconsistency in regulatory requirements exists because the FDA's definition of "human subject" differs from the definition employed in the Common Rule, with the FDA including in its definition the use of unidentified (as well as identified) HBM.[30] However, on April 25, 2006, the FDA published a guidance document indicating that it would not object to research done without IRB review or oversight on leftover HBM collected for routine clinical care that would otherwise have been discarded, as long as the HBM is not identified with a particular individual.[31]

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[28] *Id.* at 9-11.

[29] *OHRP - Guidance on Research Involving Coded Private Information or Biological Specimens*, U.S. DEP'T OF HEALTH & HUMAN SERVS., http://www.hhs.gov/ohrp/policy/cdebiol.html (last visited Oct. 15, 2012) ("This guidance document does not apply to research regulated by FDA that involves coded private information or specimens.").

[30] Barbara J. Evans & Eric M. Meslin, *Encouraging Translational Research Through Harmonization of FDA and Common Rule Informed Consent Requirements for Research With Banked Specimens*, 27 J. LEGAL MED. 119, 126 (2006).

[31] U.S. DEP'T OF HEALTH & HUMAN SERVS., OMB CONTROL NO. 0910-0582, GUIDANCE ON INFORMED CONSENT FOR IN VITRO DIAGNOSTIC DEVICE STUDIES

Applicability of the Common Rule and the FDA regulations will always depend upon the specific facts regarding a specific research protocol. Consequently, each institution that conducts or sponsors research should have policies in place that designate the individual or entity that is authorized to determine whether research involving coded private information or HBM constitutes "human subjects research." It should also be noted that the July 25, 2011 ANPRM referenced above:

> asks for comment on a proposal to clarify procedures and enhance protections related to research with biospecimens. In almost all cases, persons would have the right to allow or disallow the use of their biospecimens for research, regardless of whether the specimens were originally collected for research purposes or as part of clinical care. Recognizing the huge benefits to be gained from such research, the ANPRM includes a suggestion that a standard, brief, and general form be used to obtain consent for the future open-ended use of biospecimens in research. Further, such a form need not be signed each and every time a specimen is collected. Rather, researchers or hospitals might ask participants to sign one form in which they agree to such future use of all specimens (existing or to be collected in the future).[32]

USING LEFTOVER HUMAN SPECIMENS THAT ARE NOT INDIVIDUALLY IDENTIFIABLE (2006), *available at* http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm078384.htm.

[32] Ezekiel J. Emanuel & Jerry Menikoff, *Reforming the Regulations Governing Research With Human Subjects*, 365 NEW ENG. J. MED. 1145, 1149 (2011).

B. INFORMED CONSENT

1. Why Informed Consent?

Whether or not particular federal regulations apply to research protocols involving the use of stored HBM, the ethical principle of respect for autonomy—which is closely connected to an individual's interest in bodily integrity and exercise of liberty and privacy rights—requires consideration of the legal doctrine of informed consent in this setting, regarding both the original obtaining of the HBM from the source and its storage and use in research studies. One reason informed consent is implicated is that the conduct of research using HBM entails certain risks of harm to the individual sources of the HBM used.[33] Direct harms to the HBM source include the potential compromise of one's privacy and the misuse of personally identifiable genetic information by insurers, employers, or others to discriminate improperly against the source of the HBM, despite provisions in the 2008 Genetic Information Nondiscrimination Act (GINA)[34] that expressly forbid such discrimination.[35]

Apart from specific harms that could directly jeopardize a source of HBM because of the use of that HBM in research investigations, there are dignitary (as opposed to physical or financial) reasons that an individual source might care about—and therefore might want to retain a high degree of control over—the research uses of his or her own HBM.[36] These reasons might apply not just to the individual source of the HBM, but additionally to an ethnic or cultural group of which the source is a member. For example, concerns might surface about the

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[33] *See* Katherine Drabiak-Syed, *Lessons from* Havasupai Tribe v. Arizona State University Board of Regents*: Recognizing Group, Cultural, and Dignitary Harms as Legitimate Risks Warranting Integration Into Research Practice*, 6 J. HEALTH & BIOMED. L. 175, 217-24 (2010).

[34] Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, § 1, 122 Stat. 881 (2008) (codified as amended in scattered sections of 42 U.S.C.).

[35] Genetic Information Nondiscrimination Act §§ 201-205 (prohibiting the use of genetic information by employers, employment agencies, labor unions and training programs, for discriminatory purposes).

[36] Drabiak-Syed, *supra* note 34, at 220.

potential emotional or cultural meaning of some kinds of genetic information for the community to which one belongs (for example, studies of the genetics of sickle cell anemia among African-Americans or Tay-Sachs disease among Ashkenazi Jews). Some types of research protocols might offend some persons (if they eventually learn about their existence), even if individual HBM sources' privacy is not breached.

> Recent studies have tried to link genetics to race or ethnic groups, thus creating the possibility that some groups will become known as a greater insurance risk, less healthy, or more expensive to treat. Research studying the genetic causes of mental illness, alcoholism, or criminal propensities are other examples of such studies. In 2006, a researcher made the controversial claim that he had discovered a "warrior" gene in the Maori Tribe, which allegedly makes them more aggressive, more violent, and more likely to be criminals. The Maori and others protested this claim as stigmatizing and scientifically questionable.[37]

Other individuals might be morally upset by the notion of investigators, drug companies, or other players in the biotechnology industry making large financial profits in the future from research involving HBM. In sum, "in current practice, the only moment when a person is really able to make a choice about participating in clinical research is when they sign the Informed Consent form. At this moment, the balance of power between overall research goals and individual interests should find equilibrium."[38] Put differently:

> [a]lthough participant consent to donate tissue and information to biobanks is likely to fall short of the robust requirements of a fully informed act

[37] Julie A. Burger, *What Is Owed Participants in Biotechnology Research*?, 84 CHI.-KENT L. REV. 55, 72 (2009).

[38] Deborah Mascalzoni, Andrew Hicks, Peter Pramstaller & Matthias Wjst, *Informed Consent in the Genomics Era*, 5 PLOS MED. 1302, 1302 (2008).

> of self-determination,...it should not be dismissed as lacking moral value...The process of giving consent was valued by participants as a valued act, which encompassed a declaration of their role in society as a person who contributed and cared for others. Seen in this light ...participants saw the giving of consent as a valued act of self-determination.[39]

2. Parameters of Informed Consent

The specific parameters of legally required informed consent for the use of HBM in research are shaped by two factors.[40] First, what were the circumstances (the when and how) under which the HBM was obtained from a particular source? Second, to what degree is the source's privacy protected by the manner in which particular HBM can or cannot be identified as coming from a specific source? Let us consider several scenarios.

If a person is having some tissue removed (with that person's informed consent) as part of a diagnostic intervention or treatment and is requested to permit a portion of that tissue to also be available for use in a related ongoing genetic study, legally sufficient permission for the extra research use would require that the investigator clarify for the participant whether the genetic research study is an essential component of the therapeutic treatment plan or, alternatively, is a completely separate project.[41] Only in the former situation (with the investigation as an integral part of the treatment protocol) may the investigator properly condition access to the treatment protocol on the participant's acquiescence with his or her tissue being included for analysis in the research study. By contrast, if the genetic study is a separate project, the person who is the source of the tissue may refuse to have it used for research

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[39] Judy Allen & Beverley McNamara, *Reconsidering the Value of Consent in Biobank Research*, 25 BIOETHICS 155, 165 (2011).

[40] *See generally* Canterbury v. Spence, 464 F.2d 772, 787 (D.C. Cir. 1972) (regarding legal standards for informed consent).

[41] Wendy Prime, Mark E. Sobel & C. Simon Herrington, *Utilization of Human Tissue in Breast Cancer Research*, 2 BREAST CANCER RES. 237, 239 (2000).

without giving up the opportunity to participate in the treatment protocol.

Whether or not it is yoked to current patient treatment, the details of a present research project can be described to a prospective HBM source with enough precision to support a meaningful informed consent process. By contrast, it is, at the least, hard for a research subject to give legally and ethically valid prospective consent to the use of his or her HBM in a potential future research protocol whose details cannot now be explained. This is true regardless of whether the HBM is excess tissue obtained from a patient during the course of treatment or it is requested from a volunteer purely so that it can be placed and stored in a biobank for use in a possible future research protocol. In either event, the potential future research protocol has not yet even been imagined, and therefore cannot be described adequately.

In an analogous vein, some investigators may wish to conduct retrospective studies using HBM that was obtained and archived long ago, originally for non-research purposes. The only way to obtain true informed consent in this kind of situation would be for the current investigators to somehow go back and locate the individuals who were the sources of the HBM (and who by this time may be dead, mentally incapacitated, without an ascertainable address, or otherwise unavailable to consent to research participation), explain the current research protocol to those individuals, and secure their informed consent for research participation based on the information provided to them

3. Alternative Consent Processes

As a practical matter, IRBs ordinarily (but not universally) permit investigators to ask patients who are undergoing treatment to provide a generic or "blanket" consent for the present banking of tissue, premised clearly on the condition that use of the tissue in any particular future research protocols would require another, supplementary permission of the patient, founded on specific information about that particular study at that later point in time.[42] Many researchers have

[42] *See generally* Debra Harry, *Indigenous Peoples and Gene Disputes*, 84 CHI.-KENT L. REV. 147 (2009).

argued for acceptance of one blanket consent by itself (without the need to secure a subsequent, specific supplementary consent from the HBM source), obtained at the time that the HBM is initially taken from its source.[43] Their argument is that the need to go back to every individual to obtain explicit consent for each subsequent investigation undertaken with the initial HBM would significantly hamper or even prevent the conduct of potentially valuable research.[44] For researchers, the idea of blanket consent carries a great deal of practical appeal in terms of saving time, reducing administrative burden, and avoiding confrontations with IRBs, risk managers, bioethicists, and patients and their families about the details of planned HBM use. In the concurring view of one leading legal commentator, "[a]s long as the potential research subjects are clearly apprised of the range of possible future uses of their sample, they should be permitted to give one-time blanket consent to such uses."[45]

Another approach would go even further, by not requiring even blanket consent.[46] Under this view, implied consent to future research use takes place whenever HBM is taken as part of a diagnostic or therapeutic procedure to which the patient gave express consent, since the patient has effectively abandoned the excess HBM that would be thrown out anyway.

One hybrid or compromise approach would be to encourage people to execute advance directives agreeing to have their HBM used in subsequent, presently unforeseen research protocols

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[43] NAT'L BIOETHICS ADVISORY COMM'N, RESEARCH INVOLVING HUMAN BIOLOGICAL MATERIALS: ETHICAL ISSUES AND POLICY GUIDANCE, Vol. 1, at 64-66 (1999).

[44] *See generally* Michael J. Malinowski, *Taking Genomics to the Biobank: Access to Human Biological Samples and Medical Information*, 66 LA. L. REV. 43 (2005).

[45] Mark A. Rothstein, *Expanding the Ethical Analysis of Biobanks*, 33 J.L. MED. & ETHICS 89, 92-93 (2005).

[46] *See* Jacki Cassell & A. Young, *Why We Should Not Seek Individual Informed Consent for Participation in Health Services Research*, 28 J. MED. ETHICS 313 (2002); Peter Furness, *Consent to Using Human Tissue*, 327 BMJ 759, 759 (2003).

that meet certain broad conditions.[47] In this model, a potential HBM source could order or reject (by tailoring an advance directive) from a menu of possible types of future research involving HBM (for example, research on Alzheimer's disease versus research on contraception).

4. Informed Consent Disclosures

Whatever consent process is followed, the informational component of "informed consent" requires that the researcher disclose to the potential source of HBM material facts—facts that might make a difference in the decision of a reasonable, normal person—about the risks involved in allowing the use of the source's HBM for research purposes.[48] As explained by one set of authors:

> While it remains untenable to fully anticipate the specifics of future use, it is critical to inform prospective participants about the potential for future use, track consent information to ensure appropriate use, and adopt standards that address when and how results should be communicated back to the participant. Developing and providing standardized informed consent templates with modular provisions for specific human specimens and data allows investigators to adapt the template and establishes common approaches to issues such as future use. [49]

Specifically, the potential HBM source must be adequately warned about the potential for a compromise of the source's

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[47] *See generally* Henry T. Greely, *Breaking the Stalemate: A Prospective Regulatory Framework for Unforeseen Research Uses of Human Tissue Samples and Health Information*, 34 WAKE FOREST L. REV. 737, 754 (1999).

[48] *See generally* Christopher White, Arnold J. Rosoff & Theodore R. LeBlang, *Informed Consent to Medical and Surgical Treatment, in* LEGAL MEDICINE 337, 337-45 (Shafeek S. Sanbar ed., 7th ed. 2007).

[49] Geoffrey S. Ginsburg, Thomas W. Burke & Phillip Febbo, *Centralized Biorepositories for Genetic and Genomic Research*, 299 J. AM. MED. ASS'N 1359, 1360 (2008).

privacy and discriminatory misuse of the individual's personal genetic information by insurers, employers, educators, or others.[50] Additional informational disclosures necessary to assure the validity of a source's consent would include the following: the reason(s) for collecting the HBM (namely, to conduct research as opposed to therapy); the intervention or collection procedure to be used; the expected duration of the research; any financial costs to the source associated with research participation; any financial incentives of the HBM collectors and researchers, financial conflicts of interest, and the HBM source's lack of any ownership interest in the HBM or projects derived from it; how the research results will be used (for example, possible commercial applications); confidentiality provisions; provisions, if any, for compensating parties who are injured during research participation; and alternatives to participating in research, including the participant's right to refuse as well as the right to withdraw from an ongoing research protocol at any time without any penalty.[51]

Regarding informed consent, the American Medical Association (AMA) provides in its Code of Medical Ethics, among other things:

> Physicians contemplating the commercial use of human tissue should abide by the following guidelines: (1) Informed consent must be obtained from patients for the use of organs or tissues in clinical research[;] (2) Potential commercial applications must be disclosed to the patient before a profit is realized on products developed from biological materials[; and] (3) human tissue and its products may not be used for commercial purposes without the informed consent of the

[50] AM. MED. ASS'N, CODE OF MED. ETHICS, Op. E-2.079 (2002), *available at* http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion2079.page? (last visited Sept. 14, 2012).

[51] 45 C.F.R. § 46.116(a)(8).

> patient who provided the original cellular material.[52]

In a number of other contexts, courts and legal commentators have shown deference to AMA Code provisions in enunciating legal rulings or recommendations.[53]

5. Refusing Research Participation

There are several reasons that someone might decline to participate in a genetic study through the provision of his or her HBM. These reasons might include: concerns about personal risks such as discrimination in employment, insurance, or educational opportunities;[54] "concerns about the potential meaning of some types of genetic information for the community to which one belongs"[55] —in other words, cultural objections or the fear of social stigmatization; ethical or political objections to the nature of future studies;[56] a belief that one's identity or character is communicated by one's HBM;[57] political or philosophical objections to others possibly profiting from the use of the source's HBM;[58] religious objections;[59] and a general distrust of medicine and/or research.[60]

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[52] AM. MED. ASS'N, CODE OF MED. ETHICS, Op. E-2.08 (1994), *available at* http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion208.page (last visited Sept. 16, 2012).

[53] Marc A. Rodwin, *Reforming Pharmaceutical Industry-Physician Financial Relationships: Lessons from the United States, France, and Japan*, 39 J.L. MED. & ETHICS 662, 664-67 (2011).

[54] Mark A. Rothstein & Carlton A. Hornung, *Public Attitudes*, *in* GENETICS AND LIFE INSURANCE: MEDICAL UNDERWRITING AND SOCIAL POLICY 17, 17-22 (Mark A. Rothstein ed., 2004).

[55] ROBERT F. WEIR & ROBERT S. OLICK, THE STORED TISSUE ISSUE: BIOMEDICAL RESEARCH, ETHICS, AND LAW IN THE ERA OF GENOMIC MEDICINE 145 (2004).

[56] Natalie Ram, *Assigning Rights and Protecting Interests: Constructing Ethical and Efficient Legal Rights in Human Tissue Research*, 23 HARV. J.L. & TECH. 119, 121 (2009).

[57] Kathleen Liddell & Alison Hall, *Beyond Bristol and Alder Hey: The Future Regulation of Human Tissue*, 13 MED. L. REV. 170, 176 (2005).

[58] WEIR & OLICK, *supra* note 55, at 145.

C. PRIVACY

When we consider the privacy interests of the individual who is the source of HBM we must take into account that there are four basic ways in which HBM may be maintained. First, HBM may be "identified" in the sense that the HBM and resulting data remain linked to the particular person from whom the HBM was obtained.[61] "Identifiable" HBM and resulting data can be unlinked from the source, but the linkage can be restored through access to a key or code.[62] "De-identified" HBM and resulting data can be unlinked from the source, with the key or code to re-link available only to an intermediary and not to the investigator.[63] Finally, "unidentified" HBM is collected anonymously from the source and, hence, cannot ever be connected to that person.[64]

This categorization engenders at least a couple of questions. First, should the specific informed consent process that we legally and ethically require for participation in a research protocol vary depending upon the extent of the privacy protection afforded the HBM involved? Moreover, does the unlinking of HBM and the source's individual medical record decrease the scientific research value of the HBM?

The federal standards for Privacy of Individually Identifiable Health Information (the Privacy Rule)[65] promulgated under the authority of the Health Insurance Portability and Accountability

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[59] Ellen Wright Clayton et al., *Informed Consent for Genetic Research on Stored Tissue Samples*, 274 J. AM. MED. ASS'N, 1786, 1788 (1995).

[60] Giselle Corbie-Smith, Stephen B. Thomas & Diane Marie M. St. George, *Distrust, Race, and Research*, 162 ARCHIVES INTERNAL MED. 2458, 2460 (2002).

[61] Michael D. Volk, Jr., Christine Meis McAuliffe & May Mowzoon, *Genebank Management: A Review of Salient Ethical, Legal, and Social Issues*, 45 JURIMETRICS J. 205, 211 (2005).

[62] *Id.*

[63] *Id.*

[64] *Id.*

[65] 45 C.F.R. §§ 160, 164(A), (E) (2012).

Act (HIPAA)[66] are important in this context. The Privacy Rule requires specific (not blanket) written consent from a patient before anyone else may use or disclose protected health information (PHI) about that person for non-routine purposes such as research.[67] PHI is defined as any "individually identifiable health information" transmitted or maintained by a "covered entity" such as a health care provider, health insurance plan, or data processing firm.[68] Under the Privacy Rule biobanks are not "covered entities" unless they also engage in diagnosing and treating patients.[69] HIPAA applicability is triggered by a health care provider sending HBM to a biobank for storage, but not by the recipient's act in maintaining the repository.[70]

Additionally, the Privacy Rule is relevant only to a covered entity that attaches medical information containing explicit patient identifiers to the HBM that it is sending to a biobank. De-identified data (including anonymously collected data) is not classified as PHI and therefore does not trigger HIPAA. According to the DHHS:

> In general, OHRP considers private information or specimens to be individually identifiable as defined at 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.
>
> Conversely, OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. For example, OHRP does

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[66] Health Insurance Portability and Accountability Act of 1996, Pub. L. No. 104-191, §§ 261-264, 110 Stat. 1936 (1996).

[67] 45 C.F.R. §§ 164.502, 164.508 (2012).

[68] 45 C.F.R. § 160.103 (2012).

[69] *Id.*

[70] Michael D. Allen, *Commercial Tissue Repositories: HIPAA Raises Sponsors' Fears*, 26 IRB: ETHICS & HUM. RES., Sept.-Oct. 2004, at 9, 10.

> not consider research involving **only** coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:
>
> 1. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
>
> 2. the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
>
>   a. the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
>
>   b. there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
>
>   c. there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.[71]

Even if the privacy of the potential source of HBM is maximally protected, the informed consent process should at the least include disclosures about the following: the reasons for

[71] U.S. DEP'T HEALTH & HUMAN SERVS., *OHRP - Guidance on Research Involving Coded Private Information or Biological Specimens* (2008), *available at* http://www.hhs.gov/ohrp/policy/cdebiol.html (last visited Sept. 16, 2012).

collecting the HBM; the collection procedure; the financial incentives of those involved in the HBM collection and research; and how the participants intend to use the data derived from research with the HBM. The particular details of informed consent vary according to individual state laws.[72] For example, Nebraska law requires a consent document executed by the HBM source that declares:

> After a full discussion of the risks, benefits, and alternatives [relating to predictive genetic testing], I agree to be tested . . . For a short time after testing, the lab will keep any remaining sample in case the test must be repeated. After that, the lab may destroy the sample, or it may remove all identifying information and use the sample for research. Two additional options are storage of the sample for your future use (for a fee), or participation in research as an identified subject.[73]

The potential Nebraska HBM source must then select one of the following options: "I want my sample to be stored for my future use. I will be charged for this" or "I am willing to be contacted if research options are available, and I will decide whether to participate."[74]

6. COMMERCIAL OR OWNERSHIP (PROPERTY) INTERESTS IN HBMS

A. GENERAL ABSENCE OF PROPERTY RIGHTS

Investigators and biobank owners ordinarily have a proprietary (that is, a commercial, ownership, or property) interest in products that may be developed as a result of the

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[72] Leili Fatehi & Ralph F. Hall, *Enforcing the Rights of Human Sources to Informed Consent and Disclosures of Incidental Findings From Biobanks and Researchers: State Mechanisms in Light of Broad Regulatory Failure*, 13 MINN. J. L. SCI. & TECH. 575, 611-13 (2012).

[73] 181 NEB. ADMIN. CODE, ch. 5, Attachment C (2011).

[74] *Id.*

research being conducted with the use of HBM.[75] By contrast, the person who is the source of the HBM with potential commercial value has an autonomy (or liberty) right to decide whether an HBM may be taken and stored in the first place, but he or she has no legally enforceable ownership or property interest in the HBM itself or in the profits from any commercially valuable products developed out of the research conducted with the HBM.[76] The right to control the use of the HBM and the release of information about the source of the HBM does not translate into an ownership interest in the commercial value of research products derived from the HBM, according to courts in California[77] and Florida.[78]

Thus, the owner of the HBM is the entity (ordinarily a research institution) to which the source originally made the "gift" or "donation." Once the "donation" has been made, the source cannot subsequently decide to transfer the HBM to somewhere else.[79] All of the HBM source's rights are concentrated in the initial informed consent process and the applicable privacy protections. As summarized by one author:

> [W]e can draw the following conclusions about the current state of the law...Property law does apply to human tissue: only while it is in our bodies, it is our property. What property rights we retain in tissue samples (other than blood, sperm or eggs) after they have been removed from the body depends upon the circumstances. By intentionally and voluntarily providing samples for research, we transfer ownership in the form of a gift, and if we have not very explicitly placed conditions on acceptance of the sample, it is an unconditional gift. Consequently, when the donor takes

[75] Ram, *supra* note 55, at 134.

[76] *Id*.

[77] Moore v. Regents of Univ. of Cal., 793 P.2d 479, 488-89 (Cal. 1990).

[78] Greenberg v. Miami Children's Hosp. Res. Inst., 264 F. Supp.2d 1064, 1074 (S.D. Fla. 2003).

[79] Washington Univ. v. Catalona, 490 F.3d 667, 673 (8th Cir. 2007).

> possession of the gift (the sample), it becomes his or her property.[80]

The September 7, 2011 Federal Register contains a Draft Guidance on Exculpatory Language in Informed Consent that was released jointly by the OHRP and the FDA on August 19, 2011. According to this Draft Guidance:

> [A] subject's waiver of any [property] rights he or she may have with respect to a biospecimen obtained by investigators for research purposes would *not* be exculpatory because it does not have the effect of freeing the investigator, sponsor, institution, or others involved in the research from malpractice, negligence, blame, fault, or guilt. Accordingly, including such waiver language in an informed consent document would be permissible under 45 CFR 46.116 and 21 CFR 50.20.[81]

B. SHOULD PROPERTY RIGHTS BE RECOGNIZED?

Many are offended by the legal system's failure to recognize an ownership interest on the part of the source of HBM that is used in research that turns out ultimately to be financially profitable.[82] As argued by one commentator:

> Denying individuals property rights in the cells of their body is ... a remarkably paternalistic approach to protecting individuals from coercion, particularly in light of the fact that we seem to grant property rights in those cells to research labs. The law, in essence, would be saying: "You have no property rights in the cells of your body

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[80] Patricia Roche, *The Property/Privacy Conundrum Over Human Tissue*, 22 HEC F. 197, 206 (2010).

[81] OFFICE FOR HUMAN RES. PROTS., GUIDANCE ON EXCULPATORY LANGUAGE IN INFORMED CONSENT (2011) (draft), *available at* http://www.regulations.gov/#!documentDetail;D=HHS-OPHS-2011-0014-0002.

[82] REBECCA SKLOOT, THE IMMORTAL LIFE OF HENRIETTA LACKS (2010).

> when they are outside your body because we must protect you from economic exploitation, but we are perfectly comfortable letting biotechnology companies and research labs profit from the transfer of such cells."[83]

One obvious response to the situation described would be to permit the sharing of financial profits with the source of the HBM leading to those profits. The AMA Code of Medical Ethics includes a guideline stating that "profits from the commercial use of human tissue and its products may be shared with patients, in accordance with lawful contractual agreements."84 In a stronger vein would be the enactment of legislation recognizing a personal property interest in the HBM source and a corresponding right to share in (or to own exclusively) any financial gain derived from research using the HBM.[85] Genetic Bills of Rights recognizing that HBM has a "fair market value" and therefore assigning property rights to the sources of that HBM were introduced in 2011 in the states of Massachusetts and Vermont.[86]

A proposed property right owned by the source of the involved HBM inspires several significant concerns. First, permitting commercial trade in HBM would likely encounter resistance in the face of strong international sentiment against the buying and selling for money of human body parts.87 Second, if one may legally barter with an investigator regarding

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[83] Robin Feldman, *Whose Body Is It Anyway? Human Cells and the Strange Effects of Property and Intellectual Property Law*, 63 STAN. L. REV. 1377, 1385 (2011).

[84] AM. MED. ASS'N, *supra* note 52.

[85] Donna M. Gitter, *Ownership of Human Tissue: A Proposal for Federal Recognition of Human Research Participants' Property Rights in Their Biological Material*, 61 WASH. & LEE L. REV. 257, 315-17 (2004); Rowe, *supra* note 4.

[86] Eriq Gardner, *Gene Swipe: Few DNA Labs Know Whether Chromosomes are Yours or if you Stole Them*, 97 A.B.A. J. 50, 52 (2011).

[87] Eike-Henner W. Kluge, *The Remains of the Body: Human Tissue, Competence and Consent in an Age of Profit*, 26 CAN. OPERATING ROOM NURSING J. 6, 7-8 (2008).

the disposition of his or her HBM in the research context, does that mean that the person is allowed to sell, use, trade, destroy, or give away the whole body or any of its parts for any purpose at all? Once a property interest is recognized, it would become much more difficult for the state to justify restricting the individual's freedom to contract about something that he or she personally owns.[88]

In addition, if one is deemed to own his or her body, would that person's heirs inherit the right to the body when the individual dies, just as they inherit the deceased's money and other tangible assets today? If so, could the heirs demand—presumably, rather disruptively in most cases—the return of the person's HBM from a researcher or a biobank? This would be a large departure from the status quo, under which every state (adopting a version of the Uniform Anatomical Gift Act) permits families to donate a deceased relative's organs for transplantation purposes and every jurisdiction recognizes a family's interest in the proper, respectful treatment and disposition of the deceased's body, but none recognize a property or ownership right to profit from the commercial value of a deceased's body.[89]

There are a few reasonable alternatives to codifying a straight property rights approach regarding HBM. One possibility might be enactment of federal regulation (which would pre-empt any inconsistent state laws[90]) permitting and regulating the buying and selling of HBM for research purposes, thus treating HBM as a commodity or commercial property but explicitly restricting that legal status to research situations. If challenged, Congress would need to justify its differential treatment of the HBM's source in the research context, as opposed to the legal treatment of HBM sources in other spheres

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[88] R. Alta Charo, *Body of Research—Ownership and Use of Human Tissue*, 355 NEW ENG. J. MED. 1517, 1519 (2006).

[89] *See generally* Richard J. Bonnie, Stephanie Wright & Kelly K. Dineen, *Legal Authority to Preserve Organs in Cases of Uncontrolled Cardiac Death: Preserving Family Choice*, 36 J.L. MED. & ETHICS 741 (2008).

[90] Regarding federal preemption of inconsistent state laws, see Mary J. Davis, *On Preemption, Congressional Intent, and Conflict of Laws*, 66 U. PITT. L. REV. 181 (2004).

of activity in which the source's property interests would remain unrecognized.[91]

> A somewhat different approach would [R]ecognize[] a limited right to control how the information contained within one's cells is used. This approach adopts the contours of American intellectual property. In particular, a rights regime adapted from copyright appears to capture many of the needs and interests to be protected in research involving human tissue. Unlike tangible property, copyright cannot be lost through unconscious abandonment during its statutory period. Moreover, copyright attaches even to unpublished (i.e., undisclosed) works. Personal genetic information protected by a copyright-like informational privacy right would thus be unavailable for unauthorized use no matter how or from where it was obtained.[92]

Another approach meriting consideration might be the creation of community trusts (based on a consortium of medical institutions, researchers, and potential sources of HBM) that would exercise ownership rights regarding HBM, with corresponding trust or fiduciary duties to administer biobanks in a fashion that maximizes benefit to the general public.[93] This concept of assigning ownership rights to a public or communal trust may not be warmly received in a society with a strong history of respect for private property ownership.[94]

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[91] Such a challenge might be based on Equal Protection grounds. *See* U.S. CONST. amend. XIV, §1.

[92] Ram, *supra* note 56, at 141-42.

[93] David E. Winickoff & Richard N. Winickoff, *The Charitable Trust as a Model for Genomic Biobanks*, 349 NEW ENG. J. MED. 1180, 1182-83 (2003).

[94] Bartha M. Knoppers, *Biobanking: International Norms*, 33 J. L. MED. & ETHICS 7, 10-12 (2005).

7. CONCLUSION

The use of HBM in biomedical and behavioral research protocols is a culturally, personally, and emotionally sensitive area that engenders a broad panoply of legal, as well as ethical, questions and concerns. Further progress in the diagnosis and treatment of complex medical conditions will increasingly rely on the continued conduct of genetic research involving the use of HBM. To sustain and expand this kind of research in the future, however, public trust and credibility must be continually fostered by the research community. The "third party" to research—the public—cannot be safely ignored.[95]

"The likelihood that a patient will make claims against researchers who are using tissues that would normally be discarded is probably low. However, as studies on genetic material become more prevalent, the frequency of lawsuits may increase."[96] Regardless of the magnitude of legal liability risks in this arena, the law has a fundamental role to play; how society, through its legal instruments, categorizes the sometimes complementary and sometimes conflicting rights (autonomy/liberty, privacy, property, or contract) of the respective actors in the field of genetic clinical research utilizing HBM will no doubt make a large difference in shaping tomorrow's research enterprises and the medical practice it enables.

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[95] Gail Javitt, *Why Not Take All of Me? Reflections on* the *Immortal Life of Henrietta Lacks and the Status of Participants in Research Using Human Specimens*, 11 MINN. J. L. SCI. & TECH. 713, 747-48 (2010).

[96] Monica J. Allen, Michelle L. E. Powers, K. Scott Gronowski & Ann M. Gronowski, *Human Tissue Ownership and Use in Research: What Laboratories and Researchers Should Know*, 56 CLINICAL CHEMISTRY 1675, 1682 (2010).