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January 2, 2015

Jerry Menikoff, MD, JD  
Director, Office for Human Research Protections  
Department of Health and Human Services  
1101 Wootton Parkway, Suite 200  
Rockville, MD 20852

Regarding docket number HHS-OPHS-2015-0008 on [www.regulations.gov](http://www.regulations.gov): Comments on NPRM amendments to the Common Rule.

Dear Dr. Menikoff:

We, the undersigned, organized by Genetic Alliance, offer the following comments. Genetic Alliance is a nonprofit health advocacy organization with a 29-year track record of engaging individuals, families, and communities to transform health. Genetic Alliance is a network of more than 1,200 advocacy organizations as well as thousands of universities, private companies, government agencies, and public policy organizations.

#### *Overall impressions*

We think that this NPRM does not meet the standard of a proposed Rule, since it raises more questions than the ANPRM that preceded it four years ago. This NPRM is not responsive to most of the issues that many organizations raised in 2011. In general, the NPRM lacks the clarity and precise definitions and concepts required by an NPRM. Instead, the document states that the agency will develop critical elements in the future, rather than offering them here as part of the NPRM. The resulting Final Rule will cause confusion and unintended consequences that will not protect research participants, nor further the benefits of research.

We agree that “science has continued to advance, as has the dialogue regarding the changing nature of research and the preferred balance of protections for research participants among the principles of respect for persons, beneficence, and justice.” In fact, we recommend that the terms ‘subject’ and ‘patient’ be replaced with the term ‘participant’ for all references to individuals in research. In fact, the Common Rule should refer to human participants, *not* human subjects. Employing the term “human subjects” denigrates participants’ involvement as essential partners in these critical aspects of biomedical research. Likewise, labeling participants ‘patients,’ continues to assign us a passive role and undercuts the very dignity and respect the NPRM aims to instill throughout updated research regulations. Employing the term ‘participant’

recognizes agency and autonomy. President Barack Obama and the National Institutes of Health Director, Francis Collins, have gone on record declaring that individuals engaged in research are partners and participants, not subjects or patients, and we recommend these terms as well.

**Informed consent should be simple and offer more meaningful, culturally appropriate engagement**

We agree with the NPRM's recommendation to shorten and simplify consent forms; we particularly applaud the emphasis placed on meaningful choices and decisions informed by pertinent information "a reasonable person would want to know". We believe that is contextual.

The Common Rule should recognize consent as a process, and not a translational form. A form, particularly one is not responsive to context cannot not be meaningful. In the process of shortening and simplifying consent forms, we recommend the Common Rule support and enable culturally and clinically appropriate consent processes — these should be contextually appropriate. The Common Rule should also rely on the Fair Information Practice Principles, and employ other relational methods of engaging individuals in research.

We recommend including the proposed notifications of potential commercial profit, of return of clinically relevant results, and of possibilities for re-contact, as standard procedure in consent forms unless researchers can justify their omission through documented approval from an appointed oversight professional or participating IRB. We also recommend that results are returned in accordance with the preferences of the participant and in the context of their family, community, and situation.

The provision regarding allowable waivers of signatures with cultural groups in which signatures are not normally employed is a reasonable provision in that it acknowledges the specific needs of various cultures. However, it assumes that researchers can sufficiently evaluate cultural norms and make culturally appropriate judgments regarding minimal risk. To preserve justice, beneficence, and proper respect for participants' autonomy, we advise that a waiver of signature should only be permitted after documented consultation with a recognized cultural expert and/or the community under consideration.

**Broad informed consent for primary and secondary research conducted on biospecimens and for the storage of biospecimens and identifiable private information is not sufficient for responsible participant engagement**

We agree that biospecimens should be afforded the same protections as other information from human research participants with consent required for inclusion in research.

However, we have reservations about the use of broad consent for biospecimens-related research as described in the NPRM. Broad consent is a valid option, but should

not be the only option. The NPRM fails to provide clear definitions of broad consent and how and when it should be used. As described, it appears to be a binary choice, which denies participants autonomy and respect.

Broad consent would exclude participants who might hesitate to include their specimens in secondary research for which they had insufficient knowledge. This could be, for example, out of fear the research may conflict with certain religious beliefs or other convictions. It might also prevent participants from choosing to share their biospecimens more broadly than solely in one institution or study.

It has been documented through numerous studies that participants prefer to be offered relevant information, granular choices, the opportunity to withdraw, and research results. Broad, one-size-fits-all, consent, cannot achieve these goals.<sup>1,2</sup>

We are aware that there is resistance to even broad consent for biospecimens, let alone dynamic and granular consent. Researchers and institutions are concerned that the added costs and complications will be prohibitive. We suggest that 1) the value of engaging participants trumps cost and convenience, 2) consent does not equal engagement, 3) true engagement might include notification, ongoing communications, and various kinds of consent processes. Various technologies can now support novel methods of engagement and decrease associated costs and time. For example, the Reg4ALL, based on the Platform for Engaging Everyone Responsibly (PEER), enables community based, contextual, granular, dynamic consent for much lower costs than traditional written paper consent<sup>3</sup>.

### **NPRM exclusions and exemptions in general support improved research and participant engagement, subject to certain concerns**

The systematic changes described in the NPRM could have the inadvertent effect of encouraging researchers to design studies eligible for exemption or exclusion, and discourage researchers from planning more rigorous and involved human research due to the perceived “penalty” of needing to undergo IRB review.

#### *Common Rule exclusions*

We find most of the exclusions listed sensible, though we hesitate to allow the determination of exclusion to rest primarily on researchers’ judgment. Studies excluded from oversight under the Common Rule should still be reviewed with some regularity by someone other than the principal investigator. IRBs generally have a great deal of

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<sup>1</sup> Melham K, Moraia LB, Mitchell C, Morrison M, Teare H, Kaye J. The evolution of withdrawal: negotiating research relationships in biobanking. *Life Sci Soc Policy*. 2014;10:16. doi: 10.1186/s40504-014-0016-5. Epub 2014 Oct 5. PubMed PMID: 26573981; PubMed Central PMCID: PMC4512976.

<sup>2</sup> Kaye J, Whitley EA, Lund D, Morrison M, Teare H, Melham K. Dynamic consent: a patient interface for twenty-first century research networks. *Eur J Hum Genet*. 2015 Feb;23(2):141-6. doi: 10.1038/ejhg.2014.71. Epub 2014 May 7. PubMed PMID: 24801761; PubMed Central PMCID: PMC4130658.

<sup>3</sup> Terry SF, Shelton R, Biggers G, Baker D, Edwards K. The haystack is made of needles. *Genet Test Mol Biomarkers*. 2013 Mar;17(3):175-7. doi: 10.1089/gtmb.2012.1542. PubMed PMID: 23428177.

experience and skill in dealing with the possibility of exemption and should be consulted, albeit in a streamlined process.

Invoking HIPAA to convey privacy and security protections is illogical since HIPAA regulations specifically do not apply to de-identified biospecimens.

*Additional categories of exempt research*

It seems peculiar to leave enormous gaps in processes for determining exemption and relegate these uncertainties to a Rule. As written, determination of exemption would depend on web-based tools that are not yet developed. These tools should be developed before becoming part of the Rule.

Moreover, these tools will depend on accurate input for success. Oversight should be built in, not necessarily as much to check exemption status but to verify the accuracy of the information provided in order to secure exemption. While it could be acceptable for researchers to provide the information determining their work's status either to the proposed tool or to an oversight expert, it would be possible for researchers to contrive their answers to secure exempt status in either case. An outside auditor therefore seems advisable. Notification given to participants of exempt status is also advisable.

The exemption for the secondary use of identifiable private information is confusing and lacks specificity. The term 'identifiable private information' is not well defined, and may be at odds with similar definitions in federal laws, rules, and acts. This creates a troublesome lack of harmonization.

***Guidelines around obtaining a waiver of consent require further clarity***

A waiver of consent for biospecimens research may make sense in certain contexts. We are concerned about instances of researchers wishing to take advantage of this waiver. However, the NPRM states that these instances are intended to be "extremely rare", without precisely defining *how* rare or who will have authority to grant such a waiver, including exercising the oversight to ensure that waivers are, overall, indeed "rare" in practice. From the point of view of the institution this might signal that this waiver should almost never be used. For the participant, 'rare' lacks specificity and might elicit distrust.

The current requirements stipulate that waivers will only be considered for work that is scientifically compelling and that cannot secure consented biospecimens. Again, this creates an incentive for researchers to argue for the difficulty of obtaining consent. There should be clear guidelines about the characteristics of situations in which a waiver is appropriate.

***Using a single IRB for multi-site collaborations should be optional***

A single IRB for multi-site collaborations should be context dependent, since experts have argued both that it might either relieve or impose greater burden on researchers. There are a number of models of efficient use of IRBs in multi-center studies. It is not

clear from the NPRM whether the agency means an IRB of record with associated reliance agreements, or a true 'single' IRB. We recommend refining systems that accelerate study review and conserve resources. Just as engagement should be contextual, the needs of various communities with regard to oversight should be carefully considered with the ultimate goal of improving research processes for the sake of research participants.

**Eliminate continuing review when appropriate**

We agree with the proposition to eliminate continuing review and posit that regularly maintained and updated documentation establishing research progress (and subject to random audits) is sufficient.

**All clinical trials should be subject to the Common Rule**

We heartily approve of this amendment, as it creates more consistency across regulations that would uniformly promote responsible participant engagement.

**Summary:** The Common Rule is of paramount importance in protecting research participants while also promoting research—in this historic shift to modernize the Common Rule, the NPRM should take advantage of the opportunity to support responsible participant partnership, choice, and engagement. No Rule should be finalized without sufficient engagement, and responsiveness to the recommendations, of the community that participates in research: patients, participants, families, communities, providers, investigators, and health systems. Various agencies within Health and Human Services are using modern methods of robust engagement that the Office of Human Research Protections should avail itself of before any rule is finalized. It is our opinion that this NPRM has a long way to go before it is finalized.

Sincerely,

A handwritten signature in black ink, appearing to read "Sharon F. Terry". The signature is fluid and cursive, with a long, sweeping tail on the final letter.

Sharon F. Terry, MA  
President & CEO

Organizations:

AliveAndKickn  
Haworth, NJ

Alstrom Syndrome International  
Mount Desert, ME

American Association for Respiratory Care  
(AARC)  
Irving, TX

American Behcet's Disease Association  
(ABDA)  
Rochester, MI

American Multiple Endocrine Neoplasia  
Support  
Maryville, TN

Angioma Alliance  
Norfolk VA

Association of Gastrointestinal Motility  
Disorders, Inc. (AGMD)  
Bedford, MA

Beautiful You MRKH Foundation, Inc.  
Bethesda, MD

CADASIL Together We Have Hope Non-  
Profit Org  
Round Rock, TX

Center for Medical Technology Policy  
Baltimore, MD

Children's PKU Network  
Encinitas, CA

Christopher and Dana Reeve Foundation  
Short Hills, NJ

Colorado Developmental Disabilities  
Council  
Denver, CO

Council for Bile Acid Deficiency Diseases  
Rockville, MD

Cure HHT  
Monkton, MD

Cutaneous Lymphoma Foundation  
Birmingham, MI

Detroit Medical Reserve Corps  
Detroit, MI

Dyskeratosis Congenita Outreach, Inc.  
New York, NY

Everyminute.org  
Old Hickory, TN

Family Voices NJ  
Newark, NJ

Fight Colorectal Cancer  
Washington, DC

FOD (Fatty Oxidation Disorders) Family  
Support Group  
Okemos, MI

Geneforum.org; Genomics For Everyone  
Portland, OR

Hannah's Hope Fund  
Rexford, NY

HCMA  
Denville, NJ

Hemophilia Federation of America  
Washington, DC

Hepatitis Foundation International  
Silver Spring, MD

ICAN, International Cancer Advocacy  
Network  
Phoenix, AZ

Immune Deficiency Foundation  
Towson, MD

InnoThink Center for Research in  
Biomedical Innovation  
Indianapolis, IN

International Foundation for Autoimmune  
Arthritis  
St. Louis, MO

Joubert Syndrome & Related Disorders  
Foundation  
Cincinnati, OH

Law Office of Robert S Chase  
Fall River, MA

Lupus and Allied Diseases Association  
Verona, NY

M-CM Network  
Chatham, NY

MLD Foundation  
West Linn, OR

National Multiple Sclerosis Society  
Washington, DC

NBIA Disorders Association  
El Cajon, CA

Organic Acidemia Association  
Golden Valley, MN

PPD  
Wilmington, NC

PXE International  
Washington, DC

QE Philanthropic Advisors  
Potomac, MD

RASopathies Network USA  
Altadena, CA

Statewide Parent Advocacy Network  
Newark, NJ

Sudden Arrhythmia Death Syndromes  
(SADS Foundation)  
Salt Lake City, UT

The Moebius Syndrome Foundation  
Pilot Grove, MO

The National Adrenal Diseases  
Foundation  
Great Neck, NY

The TMJ Association  
Milwaukee, WI

The Ultra Rare Disease, Disorders &  
Disabilities Foundation  
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