Asthma and Allergy Foundation of America

January 6, 2016

Jerry Menikoff, M.D., J.D.
Office for Human Research Protections (OHRP)
Department of Health and Human Services
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Re: HHS-OPHS-2015-0008 Federal Policy for the Protection of Human Subjects
Submitted electronically via http://www.regulations.gov

Dear Dr. Menikoff:

On behalf of the Asthma and Allergy Foundation of America (AAFA, www.aafa.org), I am pleased to submit comments in response to the above referenced request for comments. AAFA, a not-for-profit organization founded in 1953, is the leading patient organization for people with asthma and allergies, and the oldest asthma and allergy patient group in the world. AAFA is dedicated to improving the quality of life for people with asthma and allergic diseases through education, advocacy and research. AAFA first provides general comments about the proposed rule and then includes more specific comments about certain sections/components.

General Comments

AAFA applauds the Department of Health and Human Services' (HHS; the Department) efforts to modernize and strengthen the Federal Policy for the Protection of Human Subjects, promulgated as a Common Rule. For patients with chronic conditions such as asthma and allergies, clinical research is a crucial component of the effort to develop more effective, affordable treatments, and ideally a cure. Improving and enhancing the Common Rule offers HHS an opportunity to demonstrate that it appreciates the value of clinical research and will take steps to ensure that patients' role in this important process is protected and elevated.

AAFA supports and encourages patient engagement in basic, clinical, preventive, and health services research. Patients are critical members of the research team, and they must be given the opportunity to be full and active participants. Unfortunately, a divide between clinical researchers and patients can form due to barriers such as a lack of transparency about potential risks or the research process itself. When patients are not able to make informed decisions about their participation in clinical trials or other forms of clinical research, the entire process suffers.

AAFA is disappointed that the Notice of Proposed Rulemaking (NPRM) lacks specificity, clarity and precise definitions and concepts. We are concerned that the NPRM states that the Department will develop several critical components in the future. Therefore, the Final Rule will likely cause confusion and unintended consequences, will not protect research participants, and will not 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." We recommend that the terms 'subject' and 'patient' be replaced with the term 'participant' for all references to individuals in research. We suggest that 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.

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

Improvements to the informed consent procedure are a vital aspect of the proposed updates to the Common Rule. By eliminating the use of unduly long and complex documents, researchers can be sure that informed consent forms will highlight the key information necessary for patients to make knowledgeable decisions about their involvement in the trial. The one-time posting requirement for clinical trial consent forms will allow the public to view the documents and to ensure that the most important information is presented in a clear and concise manner. A more succinct, understandable informed consent process will go a long way towards dismantling some of the barriers between patients and researchers.

Beyond informed consent, AAFA was pleased to see the proposed rule includes other components that aim to remove excessive burdens in clinical research. Changes to the risk oversight system will make the level of review more proportional to the seriousness of the research's potential harms/dangers, thereby eliminating cumbersome requirements that decrease efficiency, waste resources, and convolute the research objectives. As a result, some studies would become exempt from IRB approval, saving time and resources that would normally be directed to the administrative process of obtaining IRB approval. This measure is a step towards a more efficient clinical research process.

AAFA is supportive of the proposed revision to the IRB operations, functions, and membership requirements that would add "economically or educationally disadvantaged persons" as an example of vulnerable populations. It is undeniably important for researchers to have an awareness of patients' health literacy levels and the health implications of their socioeconomic statuses, and the effect that these factors could have on a patient's

understanding of the research.

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 such choices and decisions are contextual.

The Common Rule should recognize consent as a process, and not a translational form. A form, particularly one that is not responsive to context, cannot 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 consider the Fair Information Practice Principles, and employ other methods of engaging individuals in research. Issues related to health literacy should also be addressed within the NPRM.

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, culture, community, and circumstances.

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 appropriately and sufficiently evaluate cultural norms and make culturally appropriate judgments regarding minimal risk. To preserve justice, beneficence, and proper respect for participants' autonomy, we believe that a waiver of signature should only be permitted after documented consultation with a recognized cultural expert and/or the community under consideration. The NPRM should provide additional details in this area.

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 about which they had insufficient or incomplete 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 exclusively in one institution or study.

We are aware that there may be resistance to even broad consent for biospecimens, let alone dynamic and granular consent. Researchers and institutions are concerned that the added costs and processes and complexities 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. We believe that various information systems and communications technologies can now support innovative methods of ongoing engagement and therefore will decrease associated costs and time.

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 unintended consequence 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 or burden" 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 experience and skill in dealing with the possibility of exemption and should be consulted, albeit in a streamlined process.

It is not clear why the NPRM invokes HIPAA to convey privacy and security protections since HIPAA regulations specifically do not apply to de-identified biospecimens. That said, some might suggest or argue that no biospecimens are truly ever completely de-identified. We urge the Department to further address these issues.

Additional categories of exempt research
AAFA is concerned that the NPRM does not address processes for determining exemption and instead relegates these uncertainties to the Final Rule. As written, determination of exemption would depend on web-based tools that are not yet developed. We urge the department to develop such tools and make them available for public review and comment in advance of issuing any Final Rule.

Moreover, these tools will depend on accurate input for success. Oversight should be built in, not necessarily to check exemption status but to verify the accuracy of the information provided in order to secure exemption. Any new processes should be pilot tested for accuracy, reliability and usability. An outside auditor /reviewer 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. We urge the Department to review and harmonize disparate terms, terminology, definitions and usage.

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. Examples should be developed and widely disseminated.

Using a single IRB for multi-site collaborations should be optional
AAFA believes that a single IRB for multi-site collaborations should be context dependent. Lesson learned and processes can be adapted from a number of models of efficient use of IRBs in multi-center studies. It is not clear from the NPRM whether the Department means an IRB of record with associated reliance agreements, or a true 'single' IRB. We urge the

Department to clarify what is meant by “a single IRB for multi-site collaborations”.

All clinical trials should be subject to the Common Rule

We strongly support this amendment, as it creates more consistency across regulations that would uniformly promote responsible participant engagement.

Summary

There is no known cure for asthma or allergic diseases. Because the best hope for identifying more effective treatments and therapies for these conditions lies with clinical research, AAFA recognizes the importance of improving and advancing the research process. The patient safeguards that exist in order to protect both the patients involved and the integrity of the research must be strengthened and modernized. The Common Rule was first promulgated in 1991, and since then the research field has experienced many shifts and transformations, notably due to technological advancements. With improved and updated patient safeguards in place, researchers can attain results that will help improve the lives of people living with chronic conditions such as allergies and asthma.

AAFA thanks HHS for providing the opportunity to offer comments. Please do not hesitate to contact me at Csennett@aafa.org or Meryl Bloomrosen, AAFA’s Senior Vice President for Policy, Advocacy and Research at mbloomrosen@aafa.org for further information.

Regards,

Cary Sennett

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President and CEO