Informational NBS Webinar on Notice of Proposed Rulemaking: The Common Rule

November 9, 2015

Jelili Ojodu: Good morning, everyone, and welcome to this informational webinar on the NPRM, on the Common Rule, and specifically implications to newborn screening programs. As a number of you know, we've had a number of discussions related to the changes to the Common Rule or the Notice of Proposed Rule Making to the Common Rule and specific discussions around Section 12, the Newborn Screening Saves Lives Act; not only us but a number of federal partners, including NIH earlier on this year, CDC. We brought together a number of folks from different states to talk about this.

Ideally, this webinar would have been better to have been done in person, but unfortunately, due to time and funding specifically, we're not able to do that. This is our second best effort to be able to hear from you, the newborn screening community, discussions related to those implications around the proposed rulemaking for the common rule as it relates to newborn screening programs.

There are a number of people to thank, and I won't be able to get to all of them, but specifically, our main speaker this morning, Dr. Huckaby-Lewis, who needs no introduction. Dr. Huckaby-Lewis is going to go over a number of slides that we have sent to you all earlier on. Those slides have been updated slightly. We'll want to leave a good amount of time for discussion. As I noted earlier, we left all of the phone lines open so that you can ask questions. We didn't want to mute them at this point in time, but if we start to hear a lot of interference, we are going to mute all lines and then you'll have to mute yourself manually by pressing star-7, so please mute your phones.

Dr. Huckaby-Lewis is a pediatrician and an attorney with training in bioethics and health services research. She is with the Berman Institute of Bioethics at Johns Hopkins University. With that, I'm going to quickly pass this on to Dr. Huckaby-Lewis to start the presentation.

If you have any questions, there are two ways to actually provide questions. We're going to open the lines or we're going to prompt you all to ask questions verbally on the phone. At that point, you can just ask your questions in an

orderly manner and I'll be able to monitor that. The other way to ask questions on this webinar would be typing your question into the textbox at the bottom left side of your webinar screen. There's a chat box in there. You'll be able to type in your questions and we'll be able to read them off at the specific time. Again, many thanks to Dr. Huckaby-Lewis and all the folks that have helped in asking the right questions for this particular webinar. With that, Michelle.

M Huckaby-Lewis: Thank you, Jelili. It's a pleasure to be here. Good morning. Thank you all for your interest in this topic. Before I dive into details, I want to acknowledge that my work on this topic has been funded by the CDC. I'd like to thank Carla Cuthbert of the CDC for helping me think through these issues; Denise Chrysler for helping me wrestle with some of the real questions that I had; and Dr. Jerry Menikoff at OHRP for his willingness to answer some questions.

I want to make clear that these opinions are my own. They're not those of the CDC. This presentation is not constituting legal advice for newborn screening programs or anyone else. If you have legal questions, you need to seek the advice of counsel within your own institution.

As I go through this presentation and this information, I ask you to keep in mind the goals here. I have multiple goals. First is to provide information. What I have tried to do is go through the NPRM and the related materials to pull out the provisions that might be relevant to newborn screening, newborn screening laboratories and newborn screening research. Again, these are my own opinion, and so if there are aspects of this which you disagree then that's fine, but just remember the spirit of this conversation.

I also hope to facilitate discussion amongst you all about these issues. I think it's important that the newborn screening community have a voice that it's heard in this conversation. As you probably know that we are in the comment period for responses to these proposed regulations and I think it's very important for the newborn screening community to have a voice in that conversation. The OHRP presentations, the town meeting and the webinars, they have specifically sought public feedback about these proposed regulations. This is an opportunity to have a voice in that conversation to potentially shape what the final rules may look like in the long run.

Just to give you an idea of what to expect, there are many, many slides here with lots and lots of words. I'm not going to go through all these word by word, but part of what I wanted to do, the first part of this presentation is going to through the actual rules themselves, highlighting the rules, summarizing so that you have the actual language because for legal purposes, the actual language matters. In some instances, I have paraphrased the rules slightly, but you'll be able to see as we go through. The second part of the presentation will be thinking about how these proposed rules would potentially apply to newborn screening so digging in a little bit more into the details of how these rules might apply.

Before I get started, one other announcement that I'd like to make. Some of you may have heard me speak before about the legal toolkit that Denise Chrysler, Aaron Goldenberg and I developed looking at issues related to the retention and use of residual dried blood samples and related information. This legal toolkit brings together state statutes and regulations regarding these issues. I just wanted to give you information on how to access that legal toolkit. That legal toolkit has been live now for about a week, a week and a half.

Diving in, the current version of the Common Rule, and that's the federal regulations that govern human subjects research in the United States, the current version was adopted in 1991. The goal was to create a uniform body of regulations across all human subject research across federal departments. However, since 1991, the landscape within which human subjects research is conducted in the United States has changed significantly. The oversight mechanism, the Common Rule, has remain largely unchanged. In 2011, the Advance Notice of Proposed Rulemaking was published to request comment on how the current regulations might be revised to become more effective.

My goal today is not to give you a primer on the NPRM and all of the potential changes. This list on this slide are the most significant changes as detailed by the NPRM document itself, and this is all I'm going to say in general about the NPRM.

Significant changes include: improving the informed consent process; requiring informed consent for the use of stored biospecimens; excluding from the Common Rule certain categories of activities; adding additional categories of exempt research. I'll go into the differences between exemption and exclusions in a few moments. Changing requirements for waiver of consent. I'm not going to speak much today about waiver of consent for causing intent in the NPRM for newborn screening purposes, particularly with respect to residual dried blood samples. Obtaining waivers will be very difficult under the new rules.

The NPRM calls for the mandatory use of a single IRB for cooperative research. It eliminates continuing review requirements for some studies. Extend the scope of the policy to cover all clinical trials, regardless of their funding source. That's the new requirement.

Jelili Ojodu: Michelle, one second, please. We're getting an echo of Michelle's voice. That means that someone is listening to the presentation on both their computer and their phone. Can you please mute your computer if you're listening to both? Please mute your phones too as well. Thank you very much.

M Huckaby-Lewis: Let me know if you need me to stop again. As I mentioned, my goal today is not to provide detailed information about the NPRM. Rather, to consider potential implications on newborn screening and newborn screening research if the rules are adopted as written. As a reminder, these rules are not yet law. Amendment 12 of Newborn Screening Saves Lives Reauthorization Act is the current law.

Amendment 12 applies only until the new rules are promulgated under the NPRM. If the new rules for some reason were not to be promulgated, Amendment 12 would remain in effect.

The main areas that I am going to discuss today are changes in definitions, particularly with respect to human-subjects research, exclusion, exemptions, what these terms mean for the secondary use of identifiable private information and dried blood spots, privacy safeguards, changes in requirements regarding informed consent and the requirements for broad consent. What I'm going to do is walk you through what these provisions mean. You'll see in the textboxes in blue, those are the actual provisions themselves or a paraphrased version and then there's some explanatory language. Again, these are my interpretations.

The threshold question is to what does this policy apply? This policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency, but there are exclusions and exemptions. The difference between exclusions and exemptions is that for exclusions, the rules do not apply to excluded activities. There are no procedural or other kind of requirements that apply to those activities. For activities that are considered to be exemptions, only certain parts of the Common Rule apply to exempt activity. As we'll see in the second part of my presentation, some activities that use residual dried blood samples or related information fall into this category.

First, let's talk about exclusions. There are two types of exclusions. There are exclusions for categories that are deemed not to be researched, and there are exclusions for activities that are considered to be researched but they are such low risk that they are excluded from the Common Rule requirement. One of the exclusions that is deemed not to be researched is data collection analysis, including the use of biospecimens for an institution's own internal operational monitoring and program improvement purposes. These are activities that are designed for administrative purposes related to using the information to improve quality or services.

Examples for newborn screening. Again, we're going to go back over this in the second part of my presentation. Examples would be cases diagnosed through newborn screening program, case dismissed, case is lost to followup, etc.

Another exclusion would be for quality assurance for improvement activities involving the implementation of an accepted practice to improve the delivery or quality of care or services. The purpose has to be limited to altering the utilization of the accepted practice. This exclusion does not cover evaluation of the accepted practice. It's thought that this type of activity is not considered research and can be excluded because independent privacy, confidentiality and security safeguards are in play that would minimize the risk of harm.

The last bullet is a quote from the NPRM's documentation. "These efforts, some of which could be judged to be researched should be carried out because of the recognized public good that they achieve. This exclusion is intended to avoid impeding these efforts where the Common Rule requirement might have a chilling effect."

This exclusion is proposed to deal with QI activities that are aimed at implementing practices that are already accepted. Again, this exclusion does not include evaluation of different accepted practices themselves. It's designed only to improve the implementation of a practice that is already accepted.

Another exclusion is for public health surveillance activities. We'll go into this in more detail in the second part of my presentation as well. Public health surveillance activities, including the collection and testing of biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority and limited to those necessary to allow the public health authority to identify, monitor, assess, or investigate potential public health signals. An example here would be the use of dried blood samples to determine the prevalence of HIV in newborn. That type of activity may fall under this exclusion.

There are other types of exclusions as I mentioned that are considered to be researched but they're considered to be low risk, again, because they're already subject to other independent kinds of controls. These exclusions do not apply when the research includes a collection or analysis of biospecimens.

One of these exclusions involve the collection or study of information that has been or will be acquired solely for non-research activities or for research studies other than the proposed research study when the information is publicly available or it's recorded by the investigator in such a manner that the human subjects cannot be identified. This is exclusion does not include secondary research use of biospecimens. This involves research that doesn't involve direct interaction with human subjects, and the idea is that it poses no additional personal or informational risk and that the Common Rule requirements would not provide any additional protection.

There is also an exclusion for activities that are covered under the HIPAA privacy rule. There's also another category of low-risk exclusions that are considered to be low risk that don't meaningful diminish subject autonomy. This is for the secondary research use of an unidentified biospecimen that it is designed only to generate information about an individual who's already known. This exclusion includes but is not limited to development and validation of certain tests and assays such as research to develop diagnostic test for a condition using specimens from individuals known to have the condition and those known not to have the condition, different QA, QC activities and proficiency testing.

This kind of activities are excluded from the Common Rule provisions not because they are not researched but because the information that would be obtained in the course of the research is information that is already known.

The NPRM also contains provisions related to the transition period allowing the use of prior collections of biospecimens if they were collected either for research or non-research purposes for the compliance state and that the research used occurs only after removal of identifiable information.

There are a few definitions of which I would like to make you aware. The first one that's the most important for our purposes today in considering the implications for newborn screening are the changes related to the definition of human subjects. Human subject means a living individual about whom an investigator conducting research … If you skip down to item number three … obtains, uses, studies or analyzes biospecimens. It's important to know here that there's nothing mentioned about identifiability. Activities involve obtaining, using, studying or analyzing biospecimens. That is included in the definition of human subjects. It's important to note that compliance with this provision will be delayed until three years after the publication of a final rule.

The rationale for these provisions, there was concern about risk from inappropriate disclosure of information generated from biospecimens. It was thought that one way to protect subjects is to bring under oversight research for which the risks are greater of subjects being identified and information being disclosed improperly. It's also recognized that it may be difficult to identify individuals from their non-identified biospecimens at present that in the future. It may be easier to re-identify the individuals with the use of certain technologies and databases and that it is likely that it will be increasingly difficult to make biospecimens fully non-identifies. It may not be possible in the future to guarantee that an individual could not be re-identified.

That is one proposed definition of human subjects, to include biospecimen activities as human subjects. The NPRM proposes two alternative proposals. For the next few slides, forget the definition that we discussed.

This is alternative proposal A, is to expand the definition of human subject to include whole genome sequencing. We're not talking about biospecimens here. We're talking about whole genome sequencing. This alternative proposal would expand the definition to include only whole genome sequencing data or any part of the data generated from whole genome sequencing, regardless of the identifiability of the biospecimen. These regulations would apply to research that would generate whole genome sequencing data, the use of any part of that data and the research involving secondary use of any part of that data. Whole genome sequencing data would meet the definition of human subjects.

A new exemption would be created to allow this research to be exempt if consent for secondary future research were obtained. Again, this would not

matter if identifiers were removed for whole genome sequencing data. Consent would be needed. Other types of secondary research, use of non-identified information or non-identified biospecimens will continue to fall outside the scope of [audio glitch 00:20:51]. Really, what this alternative proposal A does, it would prevent the secondary research use of de-identified dried blood samples without consent as long as whole genome sequencing was not involved.

Alternative proposal B expands the definition of human subjects to include research use of information that was produced using technology applied to biospecimens that generates information that can be considered bio-unique. The idea here is if there are, in the future, other types of information technology aside from whole genome sequencing, it could be used to obtain information that is unique to an individual. This definition would cover the use of other types of technology. Under this definition, consent would be required for genomic sequencing of even a small portion of a person's genome, not just the whole genome, and for use of other technologies that might generate information unique to a person.

For this proposal, three criteria would have to be met. Technology would have to be applied to a biospecimen that's capable of producing information unique to an individual. Enough information has to be produced that this information is likely to be unique to an individual. It would have to be a publicly available database that when combined with that information produced from the use of that technology would create the possibility that some of the individuals whose bio-assessments were analyzed could be identified. The concern with this alternative is that it would require that HHS would continually have to evaluate the new technology to be able to determine whether those technologies were capable of generating bio-unique information.

This slide just gives you information about private information definitions and identifiable private information. This slide gives you the definition of research. Again, it's about generalizable knowledge. That's something to keep in mind as we get further along in these discussions.

Now, let's talk about exemptions. What does exempt mean? NPRM proposes to require that exempt research compliant with certain provisions of the proposed rule such as the privacy safeguards but not all provisions of the rule. Again, just as a reminder, there's the definition between exempt and excluded activities.

The NPRM proposes to have the federal government create a decision tool, a web-based decision tool that will help investigators determine what category their proposed activity falls into, whether it is considered excluded, exempt or subject to full Common Rule requirements. There are a few things that I'd like to point out about this decision tool.

It is proposed that the tool could be used by an individual who's knowledgeable about exemption categories or by the investigator, and that if this decision tool

is used and accurate information is obtained, it is entered into the tool, further assessment of the exemption determination is not required. The investigator can enter the information. The decision tool is a safe harbor if accurate information is entered and there is not audit requirement.

Now let's discuss exempt research, first thinking about data. One of the exempt categories is for data not involving biospecimens, and this is the secondary research use of identifiable private information that was acquired for non-research purposes if prior notice was given to the individuals that the information may be used for research and their information is used only for purposes of the specific research study for which the investigator requested access to the information.

The idea here is really to facilitate secondary research use of identifiable private information that had been collected for non-research purposes once prior notice has been given and privacy safeguards are in place. The idea is that if these privacy safeguards are in place that the Common Rule requirement would not add significantly greater protections for this category of activity. Recognizing that technological development and big data have significantly increased the potential benefits of this kind of research that it's considered to be low risk, and it allows IRBs instead to focus on higher risk research. Consent is not required. Prior notice has to be given but there is no [audio glitch 00:26:07] is not permitted and the exemption applies only if the following criteria are met.

Jelili Ojodu: Dr. Lewis, can you pause for one second?

M Huckaby-Lewis: Yeah.

Jelili Ojodu: Please mute your lines, both your phone line and your computer. We're getting an echo back. We're still getting the echo, so please mute your phone. Dr. Lewis, please go ahead. No, we're still getting it. No. There is someone on the line that has their phone line open. Please mute your phone or computer. Please try again. Lovely. Thank you.

M Huckaby-Lewis: This exemption only applies if prior notice has been given, privacy safeguards are met and the information is used only for those specific purposes.

Now let's discuss broad consent. One of the proposed changes is to allow broad consent for maintenance and storage of residual samples and information and then secondary use of these samples or information. Really, these are two exemptions that work in tandem. For this exemption, it involves bio-assessments or identifiable private information have to recorded. Privacy standards have to be put in place. Limited IRB is required, but informed consent is required. We'll discuss that more in detail.

The consent for storage will be for research studies other than for the proposed research study or for non-research study, so written consent for the storage is

required. The secretary of HHS will develop a template to facilitate obtaining informed consent. In order for this exemption to apply, the secretary's template must be used. The IRB will make the determinations. Really the IRB review has determined that the informed consent process was appropriate.

For broad consent for the research, this is research involving the use of biospecimens or identifiable information that has been stored for secondary use. If consent for that storage was obtained, it should be important to note that if the investigator anticipates that individual research results will be provided to research subjects, the research will not be exempt under this provision. These exemptions propose to require that a consent be obtained but to allow for that consent to be broad. It would not require study-specific consent. Research activities falling under this exemption will be subject to certain requirements, including using the decision tool about the exemption through that tool.

The goal of this is to enable the conduct of research while recognizing the autonomy interest of people to decide whether or not to participate. The idea is that there's growing evidence that people want some control of the circumstances in which their information or their biospecimens are used. That desire for control is distinct from concerns about inappropriate disclosure. In coming up with these rules, there was concern that if the appropriate weight was not given to concerns about these autonomy interests, public support for the research enterprise would be diminished.

It was also thought that continuing to allow secondary research use of biospecimens collected without consent for research is not consistent with the majority of the public's wishes. The exemption for storage only allows for the storage or maintenance for secondary research. It does not exempt creation of any data or the actual new collection of biospecimens. Again, as I mentioned, the purpose of the limited IRB review is to ensure the process of obtaining consent has occurred in an appropriate way or will occur.

For the exemption for research, activity is not exempt if the researcher anticipates that individual research results will be returned. If the activity is not exempt, there must be full IRB and full informed consent must be obtained. This exemption is for the actual secondary research for biospecimens and identifiable private information that is then stored for unspecified research. One of these exemptions is for storage. One of them is for research, but they work together.

Requirements for the exemption are that the privacy safeguards are met, broad consent has been obtained, and using the secretary's template. It's important to note that within the NPRM, there is language that says that it is presumed that research involving newborn blood spots which frequently take place using this provision. The processes … provisions honor the principles with respect for

persons and provide protection for information through privacy safeguards and limited IRB review.

I've already mentioned information about return of result, but I think it's important to point out that these provisions, in my opinion, discourage the return of result for research conducted using information or residual dried blood samples because that would require full IRB review and obtaining individual consent rather than the broad consent. This slide just realizes that this rule could have a negative impact on efforts to increase willingness to allow biospecimens to be used if people are going to be less inclined to consent, to give broad consent if they know that they're not going to get any information back.

This slide deals with the protection of the biospecimens and individual private information. This talks about the privacy safeguards and there are two ways that institutions, investigators can comply with the privacy safeguards requirement. One way is that the secretary will develop basically a checklist that will list the criteria for filling the requirement and the other one is for an investigator to agree to follow the HIPAA rules. This is again needed to apply the safeguards identified by the secretary or to apply a HIPAA privacy standard.

This slide explains that these privacy safeguards are also applicable to the research use of identifiable private information when notice is given. The other exemption, not the broad consent but the other exemption for data. This slide provides information that there are limitations on the use, release and disclosure after research has been conducted. This slide provides information about criteria for IRB approval of research, and it really is just looking at the procedures for obtaining consent.

There are a few changes to the general requirement for informed consent. I'm going to go through this quickly. One of them is that the prospective subject must be provided with information that a reasonable person would want to know in order to make an informed decision. This provision is borrowing from the jurisprudence related to medical malpractice informed consent whereby the standard in many states is what a reasonable person would want to know. Another point to point out to you is regarding the order in which information can be presented to potential participants and that the consent forms have to include only the requirements of informed consent and other information should be included in appendices.

There are a few new requirements for informed consent that need to be included if applicable. Research that involves the collection of identifiable private information, the consent needs to include a statement either that identifiers might be removed and the data could be used for future research without additional consent or that the subject's data will not be used for future research studies.

Also, additional elements of informed consent that must be included if applicable: a statement that the subject's bio-assessment may be used for commercial profit and whether the subjects will or will not share in that profit; a statement whether research results will be returned to the participants and an option to consent or refuse to consent to being re-contacted in the future.

For the broad consent exemption for the storage and secondary research use that biospecimens are identifiable private information, there are specific requirements that need to be included in that consent as well. Part of those requirements include a description of the types of biospecimens or information; the period of time during which the collection will occur.

That period of time cannot exceed 10 years or for research involving children, 10 years after parental permission is obtained or until the child reaches the legal age for consent. That 10 years if not how long the samples or information can be used. That's how long the information or samples can be collected from the time of intent. Another issue that must be included in the consent form, the broad consent form is a description of the period of time during which an investigator continue to conduct research. Statement that the participant can withdraw if they won't be informed of the details of specific research. You can see the other … I'm hearing a phone ringing.

Speaker 1: [inaudible 00:37:41]

Jelili Ojodu: I am too. Dr. Lewis, can you pause for a second as we're going to get some water? We're going to mute all lines now. Bear with us one second.

Speaker 2: The conference has been muted.

Jelili Ojodu: Star-7? [crosstalk 00:37:58] All right, Michelle, please press star-7 on your phone. You should be fine. Yeah, you're good, all right.

M Huckaby-Lewis: I'm behind schedule so in the interest of promoting discussion, you will have access to all of these slides. I will just tell you what's on the slides and then keep going. This provides information about the templates for consent and the documentation for consenting or declining to consent needs to be maintained. This rule gives permission for an IRB to approve a proposal for investigators to obtain information without consent for the purpose of recruiting, to determine eligibility of human subjects for research.

We've talked about changes in definitions, exclusions, exemptions and what some of these issues may mean for newborn screening. I'd like to dive in a little bit more and think about what some of these issues may mean in particular for newborn screening.

We see that the change in definition of human subjects to include biospecimens. It brings all secondary research with biospecimens that's

supported by a federal agency under the provisions of the Common Rule. That's actually slightly broader than Amendment 12. As we're going through this discussion, I'd like you to consider newborn screening-related activities and then research unrelated to newborn screening because there may be some differences.

Here on this slide, what I've created for you is a framework for consideration of the extent to which Common Rule would apply to a particular activity. The first question is, is it activity deemed to be human subjects research? It has to be a human subject and it has to be research. If no, the Common Rule requirements do not apply. If yes, the activity is deemed to be human-subjects research, is it research that is excluded from the Common Rule? Some type of activities are considered to be a subsequent risk that they are excluded. If no, the activity is deemed to be research that is not excluded, is it exempt research?

First, speaking about if this activity is deemed to be human-subjects research. There's some activities that are deemed not to be research: internal operational monitoring; either QA, QC activities; troubleshooting technical issues. I've given you a few examples of newborn screening activities that would fall within this exclusion in my opinion.

Another area of activities that are excluded because they are deemed not to be research are public health surveillance activities. Public health surveillance refers to the collection, analysis and use of data to target public health prevention. To me, that's a big part of what newborn screening is. As I was thinking about this exclusion, I thought a little bit more about the definition of public health surveillance.

CDC published a paper in 2012 that took another look at whether the working definition of public health surveillance was appropriate, evaluated the definition and determined that it still was an appropriate definition. This is a systematic, ongoing collection, management, analysis and interpretation of data followed by dissemination to public health programs to stimulate public health action. That same document considered the distinction between surveillance and research. Surveillance is used to gather data and knowledge that can be used to identify and control a health problem or improve a public health program or service. Whereas, the purpose of research is to generate generalizable knowledge.

Some examples of newborn screening activities that fall within this exclusion. This is going back to some of the work that was done earlier after Amendment 12 came out, thinking about research and not research activities. In my opinion, newborn screening is a public health program that is a hybrid of laboratory and clinical components. I know there's more involved in newborn screening than just lab and clinical components, but for my purposes right now, I think that's an important distinction.

I think the purpose of the laboratory component is to identify infants with increased risk of disease and that secondary prevention. The laboratory component involves identification of at-risk infants so that they can be transferred to the clinical care component for further diagnostic treatment and follow-up. In my opinion, certain activities related to new test development should fall within the public health surveillance exclusion. I would argue that these activities are part of the public health function of newborn screening programs and therefore should fall within this exclusion.

For example, activities designed to establish reference ranges for new conditions within a specific population. This is information that's not generalizable to another newborn screening program. Each lab would have to determine its own appropriate reference ranges in its own specific population.

I think initial development of a lab test in the public health lab or in a research lab that is in collaboration with a public health program, so state lab feasibility process involving the implementation of a newborn screening test for conditions for which screening has been mandated by the state. The primary intent of this activity is to take steps necessary to implement screening for new conditions as mandated by the state. Dried blood samples in this situation could be used for known effective. That's information that's already known exclusion, and I'll talk about that in a moment. Lab created specimens that mimic effective samples or anonymized dried blood samples. Again, the primary intent is not to create generalizable knowledge.

For purposes of the Common Rule, a state mandate to include a new test in newborn screening panels may be irrelevant, but the state mandate may mean that practice is now part of clinical care. That presents a challenge for state because the newborn screening program can't conduct research activities to evaluate the appropriateness of inclusion in the state panel without consent. If a state mandates that the condition be included on the panel even without supporting evidence, there's not a way to obtain the evidence without consent if the activity is not considered excluded, but seeking consent to evaluate appropriateness of the inclusion on the panel would be in conflict with the state mandate.

Analytical validation of a stable newborn screening method or test system is another example. This would include validation of LDT or home group and verification of an unmodified FDA-cleared or FDA-approved test system. These activities I would argue are necessary prerequisites to the performance of the public health function of newborn screening and should fall within the public health surveillance exclusion.

Other examples: determination of the clinical validity of an analytically validated newborn screening method or test system. As a reminder, clinical validity represents the accuracy with which the newborn screening test that was developed by that particular lab identifies the patient's clinical status. It

monitors statistical measures of the performance of the tests. That includes sensitivity, specificity, true involved positives and negatives and the positive and negative predictive value. These are all part of public health surveillance.

Clinical utility establishes the risk and benefits resulting from the use of a newborn screening test in that particular population. This requires long-term follow-up and monitoring of the impact of the testing. Again, that's public health surveillance in my opinion. If an activity is deemed to be human-subjects research, is it research that is excluded from the Common Rule?

Before we were talking about activities that were not considered to be research. There are some types of exclusions as I mentioned. QA, QI implementation activity, this involves implementation of an accepted practice to improve the delivery of services. The purpose must be limited to all utilization of the accepted practice. It cannot cover evaluation of the practice itself. These activities could be just to be researched but they should be carried out because of the recognized public good that they achieve. This exclusion was proposed to deal with QI activities that are aimed at implementing practices that has already been established.

Implementing a validated method or test system for newborn screening conditions that was previously validated in another laboratory. If a public health exclusion is not applicable to most newborn screening-related activities, this exclusion likely would not apply to the first state to employ a newborn screening test, but it would likely apply to the subsequent adoption of a new test in other states.

This exclusion relates to information that is already know. Inclusive development and validation of tests and assays. I have a question about this, and I'd like to hear the thoughts of this community about this. This relates to specimens for individuals known to have the condition and knows not to have the condition. My question is whether this can include presumed negative in the general population.

This exclusion includes QA, QC, sharing material, but, again, relating to my earlier question, can this exclusion apply to the controls too? They're using known positives … I'm sorry. Not as controlled as cases under this exclusion. Could using presumed negatives from the general population as control apply as well? For example, to determine reference ranges for a test that has not been adopted previously in that state. Here are some examples. Development of new testing from initial concept to stable test. There are certain times when information will be obtained that is already known about a participant.

If the research is not excluded, is it exempt? We've already talked about these exemption categories. First, the one for data, that data only, required notice is given. Then, the exemption for broad consent and these are the requirements so that you have them. In these requirements, there are requirements from the

general consent requirements. The requirements are slightly different than what is required in informed consent in general.

Here is information about that content. I've gone over this. This is just so that you have it clearly what those requirements are and what the additional requirements are. There are additional requirements that explain the types of research that might be conducted in the future, the types of institutions who may have access to the information and other kinds of requirements that you have here.

I have a list of questions that if we have time, I'd like to go over and I'd like to open the floor for discussion, but before I do that, Dr. Jerry Menikoff from OHRP I believe is on the phone, and I'd like to first thank him for his hard work on these issues and thank him for his time today to be available to the Newborn Screening Committee and give him the first opportunity to open the floor. Dr. Menikoff?

Jelili Ojodu: Thank you Dr. Lewis. Dr. Menikoff is here on the phone. Please press star-7 to unmute yourself.

Jerry Menikoff: Can you hear me?

Jelili Ojodu: Absolutely.

Jerry Menikoff: Thanks, Michelle, a great discussion. I'm here with some of my colleagues: Julia Gorey and Julie Kaneshiro. The only point I'd make now is just to add in the federal funding, in particular the Common Rule funding issue here because none of this is going to apply to activities that are not basically funded by Common Rule agencies. We're talking about NPRM. That could probably significantly narrow the scope of these rules since our understanding is obviously, a lot of this activity is done at the state level and is done by states doing their own thing, not doing it because the federal government is telling them to do one thing or another or funding one or another of the activities. Why don't I leave it at that for now?

M Huckaby-Lewis: Can I ask you a clarifying question about that? If the state wants to use residual newborn screening dried blood samples for a research project that is funded by the state, a de-identified residual dried blood sample for a project that is funded by the state, then the Common Rule provisions would not apply. Is that correct?

Jerry Menikoff: Yes, you're right. We're not talking about the Section 12 of the current law because that's a little different. Yes, in terms of the NPRM, if the activity is not funded by federal agency or department that's covered by the Common Rule, this would have no applicability to that.

M Huckaby-Lewis: Thank you.

Jerry Menikoff: Sure.

Jelili Ojodu: Dr. Lewis, there was a question that we got online, and I know that this is a topic for discussion. Quickly, for anyone who wants to ask a question, you can ask verbally by pressing star-7 on your phone to unmute yourself or you can type in your question in the chat box at the bottom left end side, corner of your screen. I'll wait for the first question to come in. Michelle, there was a question about in your opinion, is there any clarification on the use of data for long-term follow-up to determine whether screening improves outcomes? I could see this being both as program operations and research.

M Huckaby-Lewis: I will defer to others about distinguishing between program operations and research, but I think that under the proposed rules, using … If the information is de-identified then these rules don't apply. Using identifiable private information, there are two different ways that that information could be exempt from full applicability of the Common Rule. One is if prior notice is given to the participant. That is one possibility. Information will be given that the information could be used for a specific process.

I'm sorry. Prior notice will be given that the information could be used for future research, then a researcher could only use information for a specific project. It limits broad data sharing in that way. That kind of information also could be subject to the exemption for which broad consent would be obtained. Does that answer the question?

Jelili Ojodu: I hope so. The question came from someone from a state. If you want additional clarification, please just let us know either verbally by unmuting yourself or let us know online. Go ahead.

M Huckaby-Lewis: I had a list of questions that I would love to throw out to participants. Again, the purpose of these questions is multifaceted. The big question is, what do these proposed changes mean for the newborn screening program? I tried to go through and pull out what I see is my interpretation of how some of these provisions might apply. In thinking about it, and hopefully I … At least in my experience, it takes several times going through this information to be able to wrap your head around it. What do you see as the biggest challenges that newborn screening programs will face if these proposed rules are adopted? As part of that conversation, how might they address these challenges?

Jelili Ojodu: Dr. Comeau was trying to unmute herself. Were you able to do that, Anne? Star-7 on your phone. How about this? Let's unmute all lines? It's going to be a little loud, but let's do it.

Speaker 2: The conference has been unmuted.

Jelili Ojodu: Anne, are you there? Maybe not.

Anne Comeau: Can you hear me now?

Jelili Ojodu: Yes, ma'am. Please go ahead.

Anne Comeau: Finally. Okay, thanks. I have one practical question then I wanted to address Michelle's question. I was wondering whether OHRP would be willing to send to each state laboratory director a list of these questions, asking the state laboratory director to get opinions from their newborn screening people. I ask that because we often hear that newborn screening people feel that they cannot lobby or make their opinions known. Such a direct information request from OHRP might actually help you to get more information. I just wanted to put that out there.

As to Michelle's first question, I certainly am of the opinion that the whole issue of the biospecimen identifiability is a major, major problem. I would welcome using instruments that we have now such as having investigators prevented from relinking any information that they generate or have access to with anything that would identify the person. I understand that one might say that that doesn't address autonomy, but I think that the autonomy gets us into a circular argument. If one doesn't know that it's your information then how can you claim that it's your information?

I'm going to finish by saying that while I think that a lot of the legal issues are covered, I really worry about the administration of this and the public perception of what's going on that if public health has all of these exclusions and exemptions that the public perception of big brother and big government looking at data won't be changed. I think we're much better off using some of the less complex rules that we have now and enforcing those rules. I'm hoping that the answer is what I heard at town hall which is that you would still be willing to reconsider the identifiability issue, the biospecimen and identifiability.

M Huckaby-Lewis: Others on this issue?

Anne Comeau: I was asking Dr. Menikoff and his team.

Jerry Menikoff: Do you want us to respond? You can hear me?

Jelili Ojodu: Yes, we can. Please go ahead, Dr. Menikoff.

Jerry Menikoff: In terms of the point about information from all the newborn screening or public health departments, in terms of the procedures, this proposal is out there for public comment. I don't think it's for us to specifically target particular entities in terms of providing information. Whoever wants to provide information, we certainly encourage them to do so. If people on your end or APHL or whoever wants to do things to collect that information, of course, that will be great.

In terms of what the NPRM will ultimately include on the provision relating to use of de-identified biospecimens, yeah, it is out for public comment and it's providing people comment. Of course, hopefully, our expectation is the comments will be reviewed. It will be reviewed and we'll see what comes of that. Again, we certainly encourage people to comment about whether they think this is a good idea and what alternatives are, etc. We certainly are supportive of that. I'll leave it at that.

Anne Comeau: Thank you.

Jelili Ojodu: Any other verbal comments or questions for discussion with the questions that are on the screen there? Dr. Lewis, we did get two questions and one prior question and I could read that off from the chat box when you …

M Huckaby-Lewis: Okay.

Jelili Ojodu: The question is, who decides whether a project is research? Is it a federal agency that's funding a project? Do they determine whether it's research?

M Huckaby-Lewis: I think the question of what is research and what is not research is a challenging question that there are not always clear answers, so I'm not going to be able to give a clear answer. What I have tried to do, and again these are my interpretations of some of these activities of where they potentially fall within exclusions and potentially exemptions, but I think … For example, if an entity has a grant to conduct research then that is research. I don't have a great answer for that. I think part of the issue is trying to parse through these different activities and how they could potentially apply to the new rules. [crosstalk 01:03:11]

Jelili Ojodu: Can you please mute your phones if you're not speaking or asking a question? Thank you. Go ahead, Dr. Lewis. I apologize.

M Huckaby-Lewis: No, I was finished.

Jelili Ojodu: This is a multipart question that also came in. If broad consent provisions were implemented by a state for research uses of newborn screening, would consent necessarily need to be obtained at a birthing facility? For example, would prenatal consent be acceptable? [crosstalk 01:03:50] Oh my, goodness.

M Huckaby-Lewis: Would prenatal consent be allowed? It's basically the [crosstalk 01:04:01]

Jelili Ojodu: Michelle, let's go ahead and mute everyone again. Sorry.

Speaker 2: The conference has been muted.

Jelili Ojodu: Please go ahead. Press star-7 to unmute yourself. It should be okay.

M Huckaby-Lewis: Can you hear me?

Jelili Ojodu: We could hear you now.

M Huckaby-Lewis: Okay, great. That particular topic is not addressed in NPRM. I know that there has been much discussion of increasing education during the prenatal period, but I think that's an open question whether consent obtained from a parent during the prenatal period would be considered to be valid after the baby is born. I can answer that.

Jelili Ojodu: This is also part of that multipart question. Would linkage between the blood spot form and a separate consent form be acceptable?

M Huckaby-Lewis: I will defer to Dr. Menikoff on that question. It's my understanding that that would not be acceptable.

Jelili Ojodu: Dr. Menikoff, any thoughts on that?

Jerry Menikoff: Can you hear me?

Jelili Ojodu: Yes, sir.

Jerry Menikoff: I guess we'd say it may be okay. It just isn't specifically resolved, but we're not saying it's just probably … The NPRM doesn't address that, but it shouldn't necessarily be problematic.

M Huckaby-Lewis: We may come back to this slide, but I'd like to go to the next slide.

Jelili Ojodu: Go ahead.

M Huckaby-Lewis: I think that there are a couple of issues that I'd like to make sure that we have time to discuss in today's conversation. One issue. As I mentioned before, part of today's purpose is to provide the newborn screening community with the opportunity to have a discussion about these issues. Also, to try to inform the debate and inform responses, comments that gets sent back to OHRP about the NPRM. I think it's important to consider both the issues that are challenging but also the aspects of the NPRM that the newborn screening things are good things for the newborn screening community. If there are elements of the proposal that you think are a good thing, it's important that that support be voiced as well. That's one question that I'd like us to discuss.

The other issue is whether there are activities or types of activities that will be difficult to conduct if these proposed changes are adopted. Dr. Comeau earlier made a comment that identifiability related to biospecimens … I'm paraphrasing. I apologize … is a major problem. I'd like to elicit from this community why that's a major problem. What types of activities will be difficult

to conduct? Are there any kinds of activities that these new rules would make impossible to that going forward?

The third bullet point here, it's been estimated in Texas and Michigan, parents have only approximately 65% of newborn consent to the secondary research use of their baby's dried blood samples. What does that mean? Why is 65% a problem? Is that a problem? What does that mean for newborn screening research and for newborn screening test development?

In some of the time that we have left, I think it would be very helpful if we could spend some time thinking about these three issues. First, what is right about this proposal? What are the aspects of it that are positive in a meaningful way for the newborn screening community?

Jelili Ojodu: Thank you, Dr. Lewis. We have approximately 103 people on the phone, and as far the state, this question is directed towards you all at the state level. To respond, please press star-7 to unmute yourself.

Susan: Hi, Jelili. This is Susan. Can you hear me?

Jelili Ojodu: I can hear you crystal. Please go ahead.

Susan: Okay, great. In response to what was helpful, I guess I'll say, I think it's helpful to have some of the exclusions spelled out. I know that definitely we worked a lot on is it research or is it not research? As a community, we've discussed that and I think ultimately, this goes back to the previous questions too. I think when we had those conversations previously, it was to guide our own institutional review boards. I think ultimately, having the exclusions will help, and then it becomes an interpretation of which category does it fall in? Dr. Lewis outlines some of those, but ultimately then, it would be our institutional review boards that would have to answer, is it research or not? I think the exclusions help.

In regards to what's going to be difficult, if you don't already have some form of consent mechanism in place that's already going to have to be adapted, so what's going to be difficult? We have to adapt out current procedures. Even though we have a consent mechanism in Texas now, we will have to adapt our form and we'll have to establish some sort of procedures. It is a concern for us. Probably the most difficult thing is that we, the newborn screening programs, don't collect a single specimen. We rely on healthcare providers to collect specimens. In Texas, that's probably 2,000 different providers who we have to rely upon to follow a procedure that our institutional review board has approved.

The only thing I can think of to even put some sort of regulation on that procedure is to put it in our administrative code through rules, but we really have no authority over that. That's probably my biggest concern. In the absence

of broad consent, then there is no research or anything that falls into the category as deemed by our institutional review board as research.

M Huckaby-Lewis: Thank you.

Speaker 3: Hi. This is [inaudible 01:11:45]. One of the things that I think is right and it may not be so much for the newborn screening programs is a single IRB for multi-institutional studies because I know that's been quite a challenge in activities that have tried to use multiple states and multiple areas for newborn screening research. Having a single IRB would be very helpful for that particular purpose.

Jelili Ojodu: Dr. Lewis, we did also get a couple of questions online in reference to the topic for discussion here. One in particular is … Let's see here. As to point 2, I'm curious about what responsibility an agency has if DBS were to be obtained for use in public health surveillance or used under the state law, but then the DBS is requested for us by another agency or a different state to conduct federally funded research.

M Huckaby-Lewis: First, I want to remind the listeners that that explanation of public health surveillance activities, that's my interpretation, so that is not necessarily … I can't speak for OHRP clearly for how OHRP would interpret the public health surveillance exclusion and the extent to which different newborn screening-related activities would fall within that exclusion. Just to be very clear, that's my interpretation.

In answer to that question, if a state is using a residual dried blood sample under a public health surveillance exclusion, so no consent has been obtained, and then the sample is requested for use for federally funded research, that can't happen unless consent has been obtained, either specific informed consent or exemption through the broad consent for storage and secondary research use.

Jelili Ojodu: I also got more comments here so let me just quickly shoot them off to you. One is a quick comment about extending the scope of the policies to cover all clinical trials as good. We should all be on the same playing field. Another comment or question here is, could we get clarification on first adopter states developing a new test for a condition not previously screened for newborn screening panel? It seems first adopter states might fall in the public health surveillance and previously known information exclusion. Is this correct?

M Huckaby-Lewis: That is an argument that I made as my interpretation. Again, that's not … I can't speak for OHRP, so that would be their determination for whether the first adopting state activities would fall under the public health surveillance activity. I would argue that a strong case can be made for why those activities should fall within that exclusion, but, again, that's my interpretation.

Jelili Ojodu: Please, go ahead.

Anne Comeau: This is Anne. I was the one that put in that extending the scope to cover all is good. I think that Dr. Menikoff and his group needs to understand that some states will follow the federal rules, whether they have to or not. The even playing field as to who might be a first adopting state or just having the public perception be the same across all states as to what is research and what isn't. I welcome that part of the rules to say that everyone should be following the same rules.

As to the first adopting states, I think that is a big, big challenge. Michelle, I think that when you said that you thought it was going to be a public health surveillance, that's cutting the fine line of doing it versus evaluating clinical utility. Many of the first adopting states are actually evaluating the clinical utility of a new condition in order to know whether or not they want to mandate that new condition.

M Huckaby-Lewis: Right. I would argue that that is part of the public health function of the newborn screening program.

Anne Comeau: The evaluation? I would argue that too, but that's not how I read the rules. That's a challenge in that interpretation, right?

M Huckaby-Lewis: What I'm saying is that my interpretation is that activities related to newborn screening programs performing their function as convention and control related to public health that those activities should fall within the public health surveillance exclusion.

Anne Comeau: I think a big challenge for us will be knowing where to draw that line. I would agree with what you just said, but I think that there are going to be multiple interpretations of where that line is drawn. That's the problem.

M Huckaby-Lewis: Also remember, there can be differences between newborn screening-related activities that help newborn screening programs fulfill their public health function and dried blood samples or information that are used or nonrelated activities that are not related to newborn screening.

Anne Comeau: Right, like the HIV seroprevalence study, which the first one out the door with that, it probably would have been research. It would be considered … After that, if people are going to use it for public health activities, it might be considered surveillance. I think that we don't want to prevent the development of surveillance, and that's part of the big problem here.

M Huckaby-Lewis: Go ahead. I was just going to ask if others have thoughts on this issue.

Jelili Ojodu: The line is open for anyone who has any other discussions to what we're discussing. Please press star-7 to unmute yourself. I have a number … Go ahead.

M Huckaby-Lewis: I'd also like discussion … We only have a few minutes left, but if people on the phone have something to say about that last bullet about the 65%. If 65% is not enough then I'd like to hear your reasons why.

Jelili Ojodu: Silence could mean that 65% is enough or maybe they'll just email you later.

M Huckaby-Lewis: If we don't respond … If we have evidence that 65% is really what we get when we say consent6, then if the newborn screening community does not think that 65% is sufficient to do what newborn screening programs need to do then the newborn screening community needs to articulate why that's a problem.

Speaker 3: Hello.

Jelili Ojodu: Yes, we can hear you. Go ahead.

Speaker 3: One of the things that there are concerns about are healthcare disparities in terms of who's consenting and who's not. Although I don't think we have any evidence right now, I think that that's been a big concern about you'll be looking at healthcare disparities. The other thing too is you're not looking at … With that in mind, you may not be looking at true population, statistics or evaluation because you only have a portion of that population. The portion that consents may be a biased proportion.

M Huckaby-Lewis: Thank you.

Michelle: Hi. This is Michelle. Can you hear me?

Jelili Ojodu: Yes, ma'am. Please, go ahead.

Michelle: I agree 100% with that. I'm from New York. We have a very mixed population in New York. When you're doing the work to establish ranges, we know there are examples in our previous work where certain populations have different levels of marker than others just by biology. That's a big concern when we're trying to establish ranges for a test and we know we have a large proportion of people in New York State that don't speak English as a first language. We were trying to tell them how I would get consent in multiple languages, if it has to be part of a collection form. Those sorts of things will present themselves as a bias.

Two, newborn screening being one of the only programs that's universally available to everyone, I think it will have a broad impact on how we're able to deliver the service.

Jelili Ojodu: Thank you, Michelle.

M Huckaby-Lewis: Thank you. Are there any examples that people can think of, of research that would not be able to be conducted if the rules were adopted as written?

Anne Comeau: This is Anne. Again, when we first began … Can you hear me?

M Huckaby-Lewis: Yes.

Jelili Ojodu: Yes, ma'am. Please.

Anne Comeau: When we first began tandem mass spec screening way back when, we had some estimate of how frequently we would see MCT but we didn't know. We really had no idea how frequently we would see that. We used anonymized specimens and tested for the common mutation. That allowed us to project a frequency of homozygotes and match that with what we were finding by tandem mass spec. I wouldn't be able to do that now because supposedly, there's no such thing as anonymized.

When you're starting off on something brand new that no one else has done before, you want to have checks and balances. That was just purely research. We didn't get back to anybody with these results. It was anonymized specimen. That's another example of the kind of thing we wouldn't be able to do.

M Huckaby-Lewis: Thank you.

Jelili Ojodu: Dr. Lewis, I want to make sure that we are able to accommodate all of the questions that are coming in. I know that we said this is going to be 90 minutes long. We have the ability to extend for another 10 to 15 minutes depending upon folks and what kind of questions they have. I just want to make that option available. If you're available, we can proceed and get in as many questions as possible.

M Huckaby-Lewis: Absolutely.

Jelili Ojodu: Good. Let's see here. A quick question or comment that came in. While this applies to federal funding, it is almost all or nothing. Let me see. While this applies to federal funding, it almost has to be all or nothing. More consenting is the broad consent for storage. As I understand, we need to get consent to store sample. This is problematic on several fronts. First, we will introduce bias. Furthermore, families and providers requesting subsequent samples from us to confirm disease in a deceased sibling, etc. If they don't consent, samples will be destroyed. It was the comment that we got online. I don't know if there's any additional comments to that. Another question is …

M Huckaby-Lewis: Can I interrupt for a second and just respond to that?

Jelili Ojodu: Please.

M Huckaby-Lewis: States still have reason to retain samples beyond just retaining them for research purposes. The exemption in the NPRM is related to retaining and storage for future research purposes. It's not related to storing samples for non-

research purposes. In many states, there are state laws that specifically authorize states to keep samples for a certain period of time. States need to keep samples for their own QA activities that are independent of any potential future research use.

Jelili Ojodu: Thank you. Another question that came in. For NBS assay development, is it correct to presume that the use of prepared dried blood spots for non-newborns, for example, children and adults already diagnosed with a syndrome or condition, does not fall under the requirement of the Newborn Screening Saves Lives Act, but rather the research and determination for IRB to review as they follow general requirements of biospecimen under the new NPRM.

M Huckaby-Lewis: I didn't follow all of that. I'm sorry.

Jelili Ojodu: I'll try and read it again as written. For a newborn screening assay development, is it correct to presume that the use of prepared dried blood spots for non-newborns, for example, children and adults diagnosed with a condition, does not fall …

M Huckaby-Lewis: Wait. Hold on one second. This is for dried blood samples not obtained as part of newborn screening?

Jelili Ojodu: I would assume so, yes.

M Huckaby-Lewis: It is my interpretation that, again, I'm not giving any legal advice, but it would be my interpretation that the Newborn Screening Saves Lives Act amendment 12 does not apply to those samples.

Jelili Ojodu: Let's see here. Concern from a small state where the birthrate is less than 20,000, states will struggle with applying for a research grant if they are … That was too fast. Sorry. If they cannot provide enough participants.

M Huckaby-Lewis: That's in response to why is the 65% a problem?

Jelili Ojodu: Another question that came in … coming in rapidly now. Given the complexity to this rule, exemptions and exclusions, it is unreasonable to assume that all newborn screening programs will be able to follow these new procedures and activities subject to the Common Rule and will fall to a minority of programs.

M Huckaby-Lewis: I think that's a comment more than a question.

Jelili Ojodu: It is a comment as noted. Another comment or question, depending on the interpretation. For states with small birth volume, this might impact a new test development, assuming 65% participation and low population incidence for a new condition. I fear we will shift new test development to larger programs. This might ultimately favor regional lab development and make newborn screening for small states difficult.

M Huckaby-Lewis: I agree. I think that's a comment.

Jelili Ojodu: The line is open for anyone who has questions or comments. You can ask verbally by unmuting yourselves, star-7.

M Huckaby-Lewis: I think some of those comments further supports consideration of public health surveillance exclusions for some of these activities because that offers a way to conduct some of these activities in a way that they could not be performed in an unbiased way otherwise. Any other comments or questions?

Jelili Ojodu: Can you scroll up, please? There was a question about HIPAA there that I've missed. Scroll up. I'm not sure if this is a question or a comment. HIPAA definition of de-identification is not adopted for data.

M Huckaby-Lewis: I think that's a comment.

Jelili Ojodu: Okay, scroll up. Did we get everyone? Okay, here. What if routine monitoring of screening efficacy becomes generalizable at some point and then there needs to be communicated in the scientific literature for public health benefit? Exempt activity can become or appear to become research that should be disseminated.

M Huckaby-Lewis: At some point, it becomes generalizable information. I think that is a question. Again, the line between what is research and what is not research is a difficult line to draw because even the QA, QI activities that occur in hospitals, you can say these we're doing out of our own experience but we've had great experience here so we'd like to share this with the broader hospital community or in this case, the broader newborn screening community. It's not clear to me exactly how those lines should be drawn.

Jelili Ojodu: There's another one. Let's see. Can you clarify the 10-year timeframe for broad consent? Go ahead. It's a multipart question.

M Huckaby-Lewis: It's my understanding that the 10-year timeframe, it's not as applicable in a newborn screening context, but the 10-year timeframe is 10 years from the time the consent is obtained to when the sample or information will be collected. The 10-year timeframe is not related to the time period during which the activity, whether it'd be considered research or exclusions or whatever, however you define the activity, but for the sake of clarity, for answering this question. It's not that you have 10 years to conduct the research. It's not that you have 10 years to use the sample. It's that for other kinds of bioassessment collection or detailed collection, you have 10 years from the time that you consent to actually get the sample or get the information.

For our purposes, what needs to be included in the consent form is that you need to give participants information about the time period during which their sample or information may be used. The NPRM very clearly says that that time period may be a certain number of years or maybe indefinitely. The NPRM very

specifically considers the secondary research use of a biospecimen or identified information for an indefinite period of time.

Jelili Ojodu: Just additional thoughts for that particular question. I have heard that this is for both the timeframe to collect subsequent specimens and data and alternatively that it was the amount of time that specimens could be retained based on broad consent. Can OHRP specify which is correct?

M Huckaby-Lewis: You want to hear the answer from OHRP, not from me.

Jelili Ojodu: That was from the person who typed up the question initially. I'm not sure if Dr. Menikoff is there to respond to that.

Jerry Menikoff: We're here, but could you repeat the question?

Jelili Ojodu: Absolutely. It starts off by saying can you clarify the 10-year timeframe for broad consent? I have heard that this is for both the timeframe to collect subsequent specimens and data and alternatively that it is the amount of time that specimens could be retained based on broad consent.

Jerry Menikoff: It's certainly the former in terms of the period during which, which specimens you could then use for the research purpose. I'm not sure in terms of … Julie Kaneshiro.

M Huckaby-Lewis: Just verifying what Jerry was saying, but go ahead if you want to clarify the question.

Jerry Menikoff: It's not a limitation. Once you've collected this stuff, if it shows up within that 10-year period, you could of course use it forever, as long as the consent said that you could use it forever. No problem saying it can be used indefinitely. It's just a question of … The notion was somebody's biospecimen may show up because blood is drawn 35 years from now or something and there was a concern that a person couldn't really wrap their mind around something that goes that far into the future. The original consent was only contemplating the researcher having access to the biospecimens collected during the next 10 years.

M Huckaby-Lewis: Just to clarify. I think that there's … I've heard this concern mentioned before. It's my interpretation that the 10-year applies to the time period from when the consent is obtained to when the specimen or information is collected. The time period during which the specimen or information can be used could be indefinite.

Jerry Menikoff: That's correct. As long as the consent form said that. That's correct.

Jelili Ojodu: Thank you, Dr. Menikoff and Dr. Lewis. Another question came in. Is the exclusion for public health surveillance's suggestion/recommendation all part of the Common Rule/NPRM?

M Huckaby-Lewis: That is my interpretation that there is an exclusion for public health surveillance. That is part of the NPRM, but what categories would apply under that exclusion, the kinds of activities that I mentioned, that is my interpretation. For our examples in the NPRM of types of activities that would fit within the public health surveillance exclusion but they're not all geared towards newborn screening activities. For purposes of the presentation today, I tried to consider newborn screening-related activities that would potentially fall within the public health surveillance exclusion.

Jelili Ojodu: Thank you, Dr. Lewis. There are no other questions online at this point.

M Huckaby-Lewis: Thank you, Dr. Menikoff for being available to participate in the call.

Jerry Menikoff: Our pleasure. Just one final point on the comment we just made. There are issues relating to when a minor reaches the age of consent. That might qualify. It does qualify to my point about indefinitely, but that's similar to the current rules. It's something that was under the Common Rule. There are issues about you can continue to do research after the minor becomes an adult. You then have to re-consent them. I just want to clarify that.

M Huckaby-Lewis: Thank you.

Jelili Ojodu: Thank you. Michelle, you have some slides over … I'm not sure if you're done with your slide presentation there. Did you want to proceed?

M Huckaby-Lewis: Just other questions, topics for discussion about different concerns. Part of me, putting these questions out there are again that the comment period is open for public comment and response to the NPRM. Also, within the NPRM document, there are questions where public comment is specifically solicited on particular issues. The last few slides are questions from the NPRM where they are specifically seeking public comment about these issues. That's the last few slides.

Jelili Ojodu: We did get a couple of more comments/questions here so I'm just going to shout them out. Given the exclusion for public health surveillance, the newborn screening laboratory is able to use 100% of the specimens for method development, for QA, QC purposes, "65% for sufficient research." Is that the question? Just a comment, okay.

Let's see here. What did the NPRM get right? The NPRM works towards making research using newborn screening dried blood spots, a transparent process for the public. It is important that the public perception of newborn screening

remain focused on the life-saving public health effort, not on the perceived research which shrinks consent responsibility. I think that was a comment.

Speaker 4: Jelili, I have a question.

Jelili Ojodu: Please, shout it out.

Speaker 4: Given that we don't have a crystal ball as to what we're going to be doing for research or test development, and let's say that our state decides that we're not going to use broad consent because we just don't think that anyone can give broad consent in a knowledgeable way or that we can't exercise it. Ten years from now or five years from now, we come up with a research project that involved identifiable subjects and accessing their stores specimen but we didn't get permission for research storage. We would typically approach the subject and get their permission, but are we going to be in conflict with not having previously gotten this broad consent for storage, for research storage?

Jelili Ojodu: Good question. Dr. Lewis or anyone on the phone, comments?

M Huckaby-Lewis: If you are retaining them for … The exemption is for retention and maintenance for secondary research purposes. If you have another reason to be keeping them for long periods of time, then you may not be in conflict. I think there's some ambiguity there.

Speaker 4: Yeah.

Jelili Ojodu: One final question here. I'll do my best to read it from where I am. The NPRM exclusion for public health surveillance appears to address surveillance that is determined to be research. However, it leaves the process open to first determine that the surveillance activities may first be determined to be non-research that would not be subject to the new Common Rule anyway. Is that correct?

M Huckaby-Lewis: No. Part of going through these exclusions is not necessarily having to answer the question, is it research or not research? It's more, in my interpretation, more a question of assessing whether the activity falls within the criteria in that exclusion. The exclusions list criteria that have to be met in order for the exclusion to apply. Again, what I have presented here is my interpretation of the public health surveillance exclusion. That is not necessarily saying that these activities are not research. It's saying that these activities are excluded if they are determined to be public health surveillance.

Again, I'd like to make the point. I said this before. This is my interpretation, but if this is an interpretation that your program supports or you as an individual support, then you need to write OHRP. You need to respond and make comments because that is the way that your feedback and your views about these issues will be heard. I as an individual can develop comments and submit

them, but if you have concerns about how these issues will affect your newborn screening programs, your laboratory, your research, then the way to have your voice be heard is to develop written comments, responses to the NPRM. Otherwise, if you are sidelined then they don't hear either positive feedback or potential criticism, potential suggestions for interpretation.

Jelili Ojodu: Thank you, Dr. Lewis. We've been on the phone for the past 1 hour and 47 minutes. I'd like to thank Dr. Lewis for answering all of the questions and giving this presentation today.

Just to note a couple things. We will have these slides archived on our website. We will send the link out this afternoon. This webinar would also be archived on our website. That will be done shortly. I think we have to transcribe it to make sure that we got all of the points. If you have any additional questions or comments, please feel free to shoot them my way and we can add it to the frequently asked questions as part of this webinar page that we've already developed on the NewSTEPs website.

I have a number of people to thank. Obviously, Dr. Michelle Huckaby-Lewis; folks from CDC that funded this activity under the auspices of APHL; newborn screening legal and legislative issues, the workgroup that's been working on these kinds of activities; and also, a number of folks from state newborn screening programs that submitted questions to us.

APHL is going to be submitting public comments directly on this notice NPRM before December 7th, the deadline there, and we're hoping to make those publicly available to any state that may be planning to send their comments from their individual states. If you would like to see what we're planning to share out, then we'll send it to a good number of states or pretty much every state. Please let me know directly and we'll make sure that we send that to you. It's highly encouraged that I restate newborn screening program to at least send their comments in reference to the NPRM.

I can't think of anything else that I'm missing here. Did I cover everything? I'm looking at within … I'm looking at the good reader, these two and anyone else. Dr. Lewis, do you have any … Please.

M Huckaby-Lewis: Can I make one more comment?

Jelili Ojodu: Absolutely.

M Huckaby-Lewis: There's a concern that some of the individuals from state newborn screening programs are prohibited from submitting comments.

Jelili Ojodu: That's a good point.

M Huckaby-Lewis: If people have suggestions for having the voices of those individuals be heard in another way, it would be great if they could share them with the community. As I said, I will also be developing comments. If people would like to work with me on that, I would be happy to do that because as an individual, I can freely submit.

Jelili Ojodu: We can too. That's a very good point, Dr. Lewis. If you are precluded in submitting comments for whatever reason but you do have pertinent comments to submit to this process, please send them our way, directly to me or Dr. Lewis and we'll make sure that that gets included as part of a collective that's being submitted. Any final thoughts, Dr. Lewis?

M Huckaby-Lewis: No. Thank you all for your participation, your interest and your patience. I know this was a long couple of hours. Again, a lot of it, I just wanted to make the information available to you.

Jelili Ojodu: Thank you everyone. That concludes the webinar. Have a good Monday afternoon.

M Huckaby-Lewis: Thank you.