From: MDHHS-IRB
Sent: Tuesday, December 22, 2015 1:47 PM
To: Stanbury, Martha (DHHS)
Cc: Scott, Robert L. (DHHS);Dykema, Linda D. (DHHS);Mona Hanna-Attisha
Subject: RE: For your review (Hurley amendment)
Attachments: Study Proposal IRB BLL MHA revised 10 1 15.docx

Hello Martha,

Thank you again for the prompt and thorough response to the IRB comments. Your most recent e-mail was very helpful to my understanding of the proposed revision. What I think has caused confusion to this point, is that the originally approved study protocol (submitted to the MDHHS IRB on 10/1/2015) included only a limited analysis of pediatric blood lead data. In fact, a power analysis had been performed with the initial proposal indicating only a relatively small population sample would be required for the researchers to address the proposed aims. Because no revised protocol is yet available to me, it was my understanding with this revision that the scope of the research proposed had only changed with respect to the time frame to be studied.

It appears, however, given the description provided with your last e-mail, that the researchers now intend to perform a much more detailed characterization of the pediatric population in Flint. The request for a prospective waiver of informed consent that has been submitted reads much more appropriately for a descriptive study. I think what would be most helpful here, and what would likely allow our board to view a waiver request positively, is a revised research protocol that captures the new design of the research to be conducted at Hurley Medical Center.

I've attached the protocol that is currently approved in case that is a helpful reference. Please note that our IRB acknowledges the minimal risk nature of this proposal, we agree that there is the potential for benefit to this research, and we think the data security measures proposed should protect the data requested. At this point, we simply want to verify that the privacy rights of subjects under HIPAA are appropriately respected. If it is not necessary to disclose protected health information for this research without authorization from subjects, then we don't want to violate that right. If it is necessary to disclose protected health information without authorization for this research to occur, then we can approve the waiver and this revision to the research. I look forward to reviewing an updated research protocol. Do not hesitate to contact me with any questions or concerns.

Thank you,
-Ian

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From: Stanbury, Martha (DHHS)
Sent: Monday, December 21, 2015 2:56 PM
To: MDHHS-IRB <MDHHS-IRB@michigan.gov>
Cc: Scott, Robert L. (DHHS) <ScottR9@michigan.gov>; Dykema, Linda D. (DHHS) <DykemaL@michigan.gov>; Mona Hanna-Attisha <MHanna1@hurleymc.com>
Subject: RE: For your review (Hurley amendment)

Hello Ian: Thank you for your comments. In the attached document I have prepared some remarks that hopefully address your concerns. I look forward to hearing from you on this. Regards, Martha

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From: MDHHS-IRB
Sent: Monday, December 21, 2015 10:54 AM
To: Stanbury, Martha (DHHS) <stanburym@michigan.gov>
Cc: Scott, Robert L. (DHHS) <ScottR9@michigan.gov>
Subject: RE: For your review (Hurley amendment)

Hello Martha,

Thanks to you and to Dr. Hanna-Attisha for the very prompt response to my initial inquiry. I appreciate the comments provided. It does not appear (at this point) the threshold for impracticability of obtaining authorization and therefore the threshold for approval of a prospective waiver of authorization has been met. I'm hopeful the following questions will be helpful in thinking through alternative approaches to this research or the details of the waiver request:

1. Is it not possible for MDHHS to receive data from Hurley that allows MDHHS to perform the removal of duplicate test results? If MDHHS (the non-research entity and the entity holding the more inclusive data set) received information from Hurley that allowed for duplicate data to be screened out of prospective data transfers, MDHHS would appear to only need to send address, age, test date and result (that is, less protected health information than proposed) to the researchers. This would minimize the risk of providing additional identifying information (Child ID Number) about non-Hurley patients to the researchers. Understanding that the retrospective data transfer included a large number of records that perhaps prohibited MDHHS from performing this function prior to data transfer, it appears any subsequent data exchanges will be relatively small in comparison. Minimization of risks is important to IRB approval generally. If MDHHS involvement at this level is not possible, please document that.
2. There are two weaknesses with the current justification for the waiver related to the impracticability of conducting the research without the waiver.
    a. The case is made that obtaining authorization would be difficult, but it is not clear this meets the threshold of impracticability. The researcher does not indicate how many potential subjects will be included in the prospective research. If there are hundreds of subjects being tested each day, it would seem more likely that coordination across Hurley practitioners and/or others would be difficult to the point of impossible. If there are relatively few tests performed per day, then coordination typical of routine clinical research should not be an issue. Also, the opportunity to obtain authorization does not appear limited to the time of the testing. It appears there is additional opportunity to obtain

authorization during follow-up contact with subjects (presumably contact information for subjects won't be as likely to change in the matter of days following a test as it might over the course of years as was discussed in the approved waiver request for the retrospective data).

b. It is not clear what sample size is needed for the researcher to conduct the proposed analysis. The argument that a sample that excludes the 25% of children not tested at Hurley would bias study results would be better supported with a routine power analysis documenting that greater than 75% response rate is needed. The current justification includes a claim that population-level data is required. Given the relative rarity of elevated blood lead levels among the general population, it appears reasonable that a somewhat large sample will be needed to provide accurate characterizations of differing rates by geography and over a certain time scale, but to state that the analysis couldn't be conducted without population level data is certainly not supported in the documentation provided. A discussion that demonstrates the need for a minimum response rate and additional proof that such a response would not be achieved if authorization from each subject was required would be helpful in documenting why the research cannot be conducted without an approved waiver.

Thank you for considering these points. I look forward to a response addressing these concerns. Regards,
-Ian

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From: Stanbury, Martha (DHHS)
Sent: Friday, December 18, 2015 1:23 PM
To: MDHHS-IRB <MDHHS-IRB@michigan.gov>
Cc: Scott, Robert L. (DHHS) <ScottR9@michigan.gov>
Subject: RE: For your review (Hurley amendment)

Hello Ian: Attached is the HIPAA waiver form amended that has been signed by Dr. Hanna-Attisha, which hopefully addresses your concerns. Please let Bob and me know. Many thanks, Martha

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From: MDHHS-IRB
Sent: Tuesday, December 15, 2015 4:36 PM
To: Scott, Robert L. (DHHS) <ScottR9@michigan.gov>
Cc: Stanbury, Martha (DHHS) <stanburym@michigan.gov>
Subject: RE: For your review (Hurley amendment)

Hello Bob and Martha,

I want to send a note right away as I'm actually not sure this proposed revision is as straight forward as I thought it might be earlier (when I spoke with Martha). This IRB application was approved while thinking of this research as retrospective and involving data that had already been collected. Our IRB approved of the research with a waiver of the requirement for informed consent and a waiver of authorization for the Department to disclose protected health

information to Hurley. The justification that permitted approval of those waivers (attached) included the following language:

"This study could not be practically conducted without Waiver of Authorization. The number of subjects would be greatly reduced if authorization was not waived for several reasons:

1) At best, possibly 75% of Flint children (and even less non-Flint children) have their labs processed at Hurley.
2) Of the patients whose labs were processed at Hurley, the contact information on file is often outdated or wrong.
3) Finally, a considerable percentage of subjects may not return calls/contacts even if the information on file was correct for them.

It is critical for this issue that we have the most data to get an accurate assessment of the impact of the water change on children's lead levels. This will help to determine risk and prioritize response. A biased sample may make any issues seem worse or better than the actual situation.

(A greatly reduced sample size would also lead to power issues with the analysis as the sample size with authorization would likely not be adequate for the analysis considering the percentage of children with elevated blood levels.)"

This language doesn't clearly support a waiver that pertains to prospective data collection. Although the issue of a biased sample may still be compelling, problems with contact information being outdated or wrong are not applicable if the potential to interact with subjects at the time of lead testing is present (that is, if the test hasn't occurred yet).

This isn't to say that a waiver of informed consent or a waiver of authorization to disclose protected health information isn't possible, but a new justification that accounts for the fact that the desired data is now to be collected prospectively is necessary. Our IRB requests that the attached document be updated to reflect this change in the research. It appears that for potentially 75% of subjects, the researcher/her institution will have an opportunity at the time blood is sampled to obtain informed consent and authorization from Hurley patients (or parents) for the use of the test result and other patient information (address specifically) in research. If a consent process is appropriate, one should be proposed. Alternatively, a justification for why that can't occur, and/or why MDHHS must still provide identifiable data to the researcher without authorization from subjects is needed for the research to proceed.

I'm available and very willing to discuss any questions related to this. I certainly understand the interest in making data available to study this important issue. I'm also sensitive that children involved in this research have rights under the Common Rule regulations/HIPAA that prohibit the use of their identifiable information in research without consent of a parent, or without an approved waiver of the requirement for informed consent. Aside from having the researcher respond with an informed consent proposal or a revised version of the attached document, let me know if you have questions or concerns at this point.

Thank you,
-Ian

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From: Scott, Robert L. (DHHS)
Sent: Tuesday, December 15, 2015 10:59 AM
To: MDHHS-IRB <MDHHS-IRB@michigan.gov>
Cc: Stanbury, Martha (DHHS) <stanburym@michigan.gov>
Subject: For your review (Hurley amendment)

Ian,

Please see attached.

Thanks,
Bob

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