April 1, 2018

Dear Ms Kaeser:

I am responding to the Request for Information (RFI): ***Research Specific to Pregnant Women and Lactating Women***, NOT- HD-18-003 announced Feb 15, 2018.

I perform clinical pregnancy research using non-invasive imaging devices for fetal application under NIH-funding, and I supervise present and past FDA investigational device exemption (IDE) studies on approved biomagnetometer devices being used for fetal heart rhythm diagnosis, and similar experimental devices in developement. I participated in the writing group for the 2014 AHA Scientific Statement on Fetal Diagnosis and Treatment (Circulation, 2014), and also supported an application to the AMA for a Category III CPT code for fetal magnetocardiography. I have no conflicts of interest. Here are the areas that I personally feel require more evaluation in research in pregnancy:

Small companies develop pediatric, fetal, or pregnancy devices: Over 60% of the companies developing new technology for pregnancy or pediatrics are very small with limited experience in clinical research, applying for NIH grants, taking products through FDA, establishing subcontracts with universities, and commercializing their products.

I Agree with the American Academy of Pediatrics, they stated: *"In our view, the solution to the lack of pediatric devices lies in a comprehensive approach that includes providing assistance to innovators, streamlining regulatory processes, elevating pediatric device issues at the FDA and NIH, and improving incentives for devices for small markets -- while still preserving the ability to ensure the safety of new products once on the market. We look forward to working with Congress to pass legislation to ensure that when it comes to medical devices, children have access to the very best of what science and medicine have to offer."*

- **The principles listed above by the AAP should be implemented for pregnancy studies and for the fetus**. In addition to this lag in pediatric devices, devices supporting the health of the pregnant patient and her fetus, are also not coming through the pipeline at the same rate as for the adult. As an example, the fetal period is the only time in the human life-cycle when standard cardiac monitoring and electrocardiography are not a routine part of the care of the high risk patient.
- **NIH R grants, SBIR and STTR grants** currently support the technology development that is taking place. A reasonable portion of funding for these granting mechanisms should specifically target pediatric, fetal, and pregnancy research. In addition, I would like to see the NIH have more input from pediatric and pregnancy experts at the grant assignment level and within the review committees. Recently one of these committees, SBIB H82, was permanently closed by CSR. The time to market for pediatric-fetal-pregnancy (P-F-P) devices, about 17-20 years, is longer than for adult devices, and making adjustments in the length of current NIH or FDA funding mechanisms to account for this longer time to market is needed. Just one example of a difference between adult and P-F-P research and FDA IDE's, is the retrieval of medical records (source documents), particularly time consuming. It is necessary to track two subjects/two clinical outcomes, mother's and baby's. New surnames, hospital changes (mother and/or baby) and varying electronic medical records (EMR) formats make it very labor intensive to retrieve charts in order to track outcomes. In addition, many hospitals store parts

of the record, such as ECG's, on other software than the EMR software, and out-source their record requests to 3rd Parties.

- **FDA approval processes:** It is my understanding that external peer medical experts from industry and academics, are convened very late for FDA approval processes, often on the day that a device is proposed for approval before a panel of physicians, and scientists. This is completely different from the NIH where the experts are present from the beginning, to assess the design of the study and provide feedback. FDA could solicit and retain medical experts in each expertise area, and utilize them in the assessment of new pediatric-fetal-pregnancy (P-F-P) technologies.
- **Provide access to advisors within the FDA, NIH, and Universities** that facilitate device-based P-F-P research, especially clinical trials IDE development. To some extent this has been done for pediatrics with the Pediatric Device Consortium, but currently fetal device research is not covered under the pediatric umbrella, even though it is one of the most active areas of device research. A **Pregnancy Device Consortium** could be developed to support both maternal and fetal device development.
- **The current paperwork load for pregnancy clinical trials and for outcomes assessment is enormous** Universal templates and better study design support would help. Post-market surveillance, if made universal, could increase the need to retrieve P-F-P medical records. Many P-F-P studies recruit from around the country due to the rarity of disease. Thus, FDA post-market surveillance would be costly and difficult for companies, and academic investigators, unless a mechanism to support acquisition of source documents is developed.
- **Funding amount and time frames of SBIR/STTR grants:** Because some new devices have no predicate or CPT Code, or only a Category III CPT Billing code, there is little means for device developers to support the early clinical roll-out phase. SBIR and STTR grants can provide needed support for emerging technology**. But to be helpful, it is critical that the NIH remove the requirement of Third-Party investors for Phase IIB SBIR/STTR grant applications.** Eliminating this third-party investor requirement for Phase IIB SBIR/STTR grants would allow additional time and funding for P-F-P device developers to continue multicenter clinical trials and obtain a Category I CPT code.
- **CPT Code III and Payment.** Virtually all emerging devices have a Category III CPT code (T code or 4 digit code), and these are predominantly excluded from payment by insurance companies. As a result, Obstetrical and Children's Hospitals are reluctant to purchase emerging products, further slowing the pipeline to commercialization. Developing a plan with the AMA and stakeholders for evaluating P-F-P devices for possible early transition to Category I, with fewer centers owning the emerging devices, would be helpful.
- **Consenting Practices. Inclusion of minors, rural women, and minority women:** Removing the pregnant woman from the "vulnerable list" is a great step forward, and excluding onerous 2-person consent processes for non-invasive procedures in adult pregnant women may help stimulate research, and facilitate postnatal follow-up, which in turn should improve care and reduce mortality. Allowing women to consent for their infant (up to age 1 year) during the pregnancy, and having a single IRB of record, would also help for studies that involve neonatal follow-up of a condition. Many IRB's currently discourage recruitment of pregnant minors and non-English-speaking women (with a medical interpreter), even though in some cases, they stand to gain the most from results of certain studies. Also, incentives to encourage participation of rural and minority pregnant women, such as transportation re-imbursement or providing transportation should be encouraged.

Thank you for your consideration. And best wishes for supporting this difficult area of research.

Sincerely Yours,

Janette

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