



September 29, 2021

Re: NOT-OD-21-131: Request for Information: Developing Consent Language for Future Use of Data and Biospecimens

Dear Sir or Madam,

Thank you for the opportunity to submit comments on behalf of the National Organization for Rare Disorders (NORD) regarding the National Institutes of Health (NIH) Request for Information (RFI): *Developing Consent Language for Future Use of Data and Biospecimens*. Founded in 1983, NORD represents the estimated 1 in 10 Americans living with a rare disease and 328 rare disease patient organizations.

NORD applauds the NIH for issuing this RFI and demonstrating its ongoing commitment to ensuring that the U.S. continues to lead the world in biomedical research and reduce the costly burden of illness and disability in the U.S. and worldwide. As noted in the RFI, ensuring that all such research is based upon robust informed consent practices is critical. NORD supports the goal of the RFI to foster sharing of data and biospecimens which cannot occur in the absence of properly consented research. If future uses of data and biospecimens aren't feasible because of consent failures, the pace of research will slow. The various points to consider and sample informed consent language that NIH has set forth in the RFI will, when finalized, provide a valuable resource for stakeholders.

NORD submits the following comments to urge NIH to clarify in the informed consent resource that is ultimately created research areas for which such a resource would be inapplicable or inappropriate for use. In particular, prior to finalizing this resource, NORD urges that NIH carefully assess the ways in which it could be interpreted and applied in the context of subsequent research uses of biospecimens obtained in the course of newborn screening to ensure that it does not have the unintended effect of hampering this critical area of research.

Use of Biospecimens in Newborn Screening

Newborn screening (NBS) is an area in which subsequent research uses of dried blood spots (DBS) is critical. NBS is a largely state-run process by which, within 24-48 hours after an infant is born, a small sample of blood is taken in the form of a DBS, and used to test for indicators for certain heritable conditions.¹ It is one of the most successful public health programs, screening almost 4 million babies and saving the lives of 12,500 infants each year.² Once the testing for the

¹ Baby's First Test. Newborn Screening 101. Accessed 9/29/21. <https://www.babysfirsttest.org/newborn-screening/screening-101>

² CDC. (2012). CDC Grand Rounds: Newborn Screening and Improved Outcomes. Morbidity and Mortality Weekly Report. Accessed 9/29/21. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6121a2.htm>

state-required panel of heritable conditions is complete, residual DBS may be stored by the state-accredited lab that conducted the initial testing. Critically, these DBS are stripped of all identifying information.³ Usually, state law governs how long the DBS samples are kept and what type of research can be done with them.⁴ There are also steep penalties for misuse of DBS, including losses of funding and other punitive actions. Each state and institution have their own policies to address misuse as well the Department of Health and Human Services Office of Human Research Protections.⁵

Depending on the state's laws, there are opportunities to use the residual DBS to conduct additional research on a deidentified biospecimen. The lab ensures the biospecimen contains no information that can link it back to the donor, either by a state lab or an external party.⁶ For example, DBS are used to conduct quality assurance and quality control testing to ensure laboratory equipment is functioning properly.⁷ They are also used to develop new or improve existing newborn screening tests for future infants.⁸ Finally, DBS can be used in biomedical research to advance research into a disease or identify public health needs.⁹ To conduct research on DBS, an investigator who has gained approval from an Institutional Review Board (IRB) can request deidentified residual DBS for use in the IRB-approved research.¹⁰

While consent is not usually required when a sample is taken, we believe that the current system to protect identifiable information is working as intended, as there are no reported abuses of DBS research in the program's history.¹¹ Additionally, gaining consent for NBS has proven to be exceedingly difficult and presents many logistical challenges for the state programs and the hospitals and birthing centers. Several states, like Michigan and Texas, have requirements that require informed consent for future research to be collected from the parents of a newborn at or near the time of birth. This has been problematic because of the additional time and cost of gaining consent in the short time frame of a stay at a hospital or birthing center.¹² In theory, the practice of receiving consent at the hospital or giving the parents a form to return sounds simple, but in reality, it is a complex and resource-intensive endeavor. In instances where consent forms

³ Baby's First Test. Dried Blood Spot Storage and Usage. Accessed 9/27/21.

<https://www.babysfirsttest.org/newborn-screening/dried-blood-spot-storage-and-usage>

⁴ APHL. APHL Position Statement Newborn Screening Residual Dried Blood Spot Specimens. Accessed 9/29/21.

https://www.aphl.org/policy/Position_Documents/DBS%20Final.pdf

⁵ Office for Human Research Protections. Compliance Oversight Procedures for Evaluating Institutions (2009). HHS. Accessed 9/29/21. <https://www.hhs.gov/ohrp/compliance-and-reporting/evaluating-institutions/index.html>

⁶ Baby's First Test. Dried Blood Spot Storage and Usage. Accessed 9/27/21.

<https://www.babysfirsttest.org/newborn-screening/dried-blood-spot-storage-and-usage>

⁷ Ibid.

⁸ Ibid.

⁹ Ibid.

¹⁰ Ibid.

¹¹ Ibid.

¹² Feuchtbaum, L, Cunningham, G, Sciortino, S. (2007). Questioning the Need for Informed Consent: A Case Study of California's Experience with a Pilot Newborn Screening Research Project. *Journal of Empirical Research on Human Research Ethics: An International Journal*, 2(3), 3-14. Accessed 9/29/21.

<https://journals.sagepub.com/doi/10.1525/jer.2007.2.3.3>

are required, there are huge discrepancies in the percentage of individuals who return the form, which can skew later research.¹³ In Michigan, the real-world impact of the consent requirement has led to a more than 40% reduction in the number of biospecimens that are able to be used for future research.¹⁴ Reduced access to samples negatively impacts NBS research because such research can require tens, if not hundreds, of thousands of DBS samples.¹⁵

Recently, the federal government reiterated its longstanding view that research on nonidentified biospecimens, including residual DBS, is “secondary research” and therefore not subject to the same protections as research involving human subjects. The 2019 revision to the Common Rule, the regulation that sets the standard for the ethical procedure of government funded research studies and requires elements such as informed consent, was revised to make clear that it only applies to human research and not deidentified biospecimens.¹⁶

NORD believes that NBS is not, and should not, subject to the same informed consent processes and requirements as biospecimens for a research study. It is critical that this informed consent resource, once issued in final form, clearly delineates the types of research that could benefit from it, and those for which it is inapplicable. Otherwise, the goal of supporting viable biomedical research could be thwarted in the confusion that would ensue. NORD urges NIH to provide this clarification in the final informed consent resource.

Thank you for the opportunity to submit comments on this RFI. If you have any questions, please contact Rick White at rwhite@rarediseases.org.

Sincerely,

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¹³ Rothwell, E., Johnson, E., Riches, N. et al. Secondary research uses of residual newborn screening dried bloodspots: a scoping review. *Genet Med* 21, 1469–1475 (2019). <https://doi.org/10.1038/s41436-018-0387-8>

¹⁴ Rothwell, E., Goldenberg, A., Johnson, E., Riches, N., Tarini, B., & Botkin, J. R. (2017). An Assessment of a Shortened Consent Form for the Storage and Research Use of Residual Newborn Screening Blood Spots. *Journal of empirical research on human research ethics: JERHRE*, 12(5), 335–342. Accessed 9/29/21. <https://doi.org/10.1177/1556264617736199>

¹⁵ Rothwell, E., Johnson, E., Riches, N. et al. Secondary research uses of residual newborn screening dried bloodspots: a scoping review. *Genet Med* 21, 1469–1475 (2019). <https://doi.org/10.1038/s41436-018-0387-8>

¹⁶ Federal Policy for the Protection of Human Subjects. 45 C.F.R. § 46.