ENDOCRINE SOCIETY
Hormone Science to Health

July 28, 2020

Lowell Schiller, JD
Principal Associate Commissioner for Policy
U.S. Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Re: Docket No. FDA-2020-N-0837 "Rare Disease Clinical Trial Networks; Request for Information and Comments"

Dear Dr. Schiller,

The Endocrine Society appreciates the opportunity to comment on approaches to setting up and sustaining a global clinical trial network to support the Rare Diseases Cures Accelerator. Founded in 1916, the Endocrine Society is the world's largest professional organization of endocrinologists, representing the interests of over 18,000 physicians and scientists engaged in the treatment and research of endocrine disorders. Several endocrine conditions, including acromegaly, adrenocortical carcinoma, growth hormone deficiency, Cushing's syndrome, and familial chylomicronemia syndrome (FCS), qualify as rare diseases, and patients still lack effective treatments for many of these and other conditions. We enthusiastically support the Rare Diseases Cures Accelerator and welcome the opportunity to participate in a global clinical trial network for rare diseases. Our comments are aimed at ensuring the immediate and long-term success of such an initiative.

What should be the immediate (<3 years) and long-term objectives of a global clinical trials network?

The immediate goals for the project should include setting up the infrastructure and databases required for the analyses of trials. This will involve establishing systems and personnel to conduct ethical reviews consistent with the various legal requirements and patient protections in each country. Because the universe of rare diseases is extremely large, we suggest that FDA first define a limited initial scope and parameters for the network. In the near-term, it may be more practical to prioritize specific themes or disease categories identified through a separate solicitation. Prioritization could be guided by areas of greatest need, or diseases where resources and expertise from existing networks can be leveraged to advance new treatments more quickly. For example, the National Cancer Institute Cancer Gene Atlas Program (TCGA) rare cancer projects – particularly TCGA-ACC (adrenocortical carcinoma) was facilitated by a robust international consortium with databases and repositories already operational. Such leverage is essential to secure buy-in from industry partners, funding agencies and patient groups who are often already engaged/partnering with international rare disease experts and cooperative groups.

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Long-term objectives should include scaling-up the network by adding more disease states and conditions. FDA should also develop and deploy educational resources for patients and providers with the aim of bringing rural and underserved populations into the network.

How could a global clinical trials network for rare disease be organizationally structured?

The governance and decision-making structure should ideally involve organizations (both international and domestic) that are recognized as neutral/independent partners. International scientific societies for example would be well positioned to assist as an impartial convener of relevant experts and other stakeholders within specific disease areas. In addition to independent expertise, early involvement of industry partners, patient-focused civil society organizations and patient-run advocacy groups will be critical both at start-up and throughout development. Examples of such groups include:

- The National Adrenal Disease Foundation – https://www.nadf.us
- CARES Foundation – www.caresfoundation.org
- ACC C.U.R.E – www.acccure.org
- Pheo Para Alliance – www.pheopara.org

Making the network itself a resource for patients, e.g., through educational or support resources, will ensure buy-in from the patient community and increase participation.

Importantly, FDA must very clearly define for patients and investigators how data will be used and where primary responsibility lies for the data. The network must also have a transparent structure with clear rules to provide proper attribution for investigators who contribute to the network for the different diseases and outcomes.

What are potential opportunities to leverage and/or complement other existing networks?

There exist international networks for several rare endocrine diseases that could be leveraged for expertise, including the European Lipodystrophy Registry[1], the i-DSD (disorders of sexual development) and i-CAH (congenital adrenal hyperplasia) registries[2] , A5[3] (American Australian Asian Adrenal Alliance) and ENSAT[4] (European Network for the Study of Adrenal Tumors). There may also be opportunities to learn from existing large international networks outside of the rare disease space, such as the Type-1 Diabetes TrialNet[5]. Collectively, these networks can help identify barriers, develop realistic estimates for startup costs, and propose achievable goals. We recommend that FDA convene a virtual

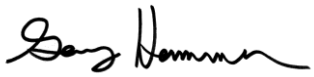
[1] https://ojrd.biomedcentral.com/articles/10.1186/s13023-020-1295-y
[2] https://home.i-dsd.org/
[3] https://a5adrenalalliance.com
[4] https://www.ensat.org
[5] https://www.trialnet.org/

conference of these and other successful endocrine-related networks to identify best practices that will facilitate FDA's efforts.

Concluding Comments

Thank you for considering the Endocrine Society's comments; our members stand ready to provide additional input and guidance to facilitate the long-term success of the FDA rare disease clinical trial network. We would welcome the opportunity to further discuss how rare endocrine diseases could be incorporated into the network. If we can be of any additional assistance, please contact Joseph Laakso, PhD, Director of Science Policy at jlaakso@endocrine.org.

Sincerely,



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