Workshop Docket Comment Description

In conjunction with the January 24-25, 2022 virtual public workshop entitled *Endpoint Considerations to Facilitate Drug Development for Niemann-Pick Type C*, a public docket\(^1\) was open from January 21, 2022 until April 25, 2022 to collect further public input on the topic. As a supplement to the January workshop summary, this document provides a high-level summary of 15 submitted comments. Comments were submitted by parents and caregivers, health care providers, professional organizations, patient groups, and researchers. Comments received after the docket closed were also incorporated into this summary as applicable.

Docket submissions can be viewed in full here: Docket FDA-2021-N-1297

Summary of Comments

*The below summary of docket submissions includes a number of key themes expressed in the comments provided by the various stakeholders.*

Comments stressed that individuals with NPC have significant unmet treatment needs as there are no therapies currently approved in the United States for the treatment of NPC. For these patients, there is an urgent necessity for safe and effective therapies. It is important to consider input from patients, clinicians, and families when assessing the effectiveness of NPC investigational interventions to ensure meaningful improvements are captured.

The importance of regulatory flexibility for design, conduct, and analyses of NPC clinical trials was emphasized given the small patient population size and heterogeneity of disease presentation and progression. Comments acknowledged the complexity of this ultra-rare disease, and reiterated challenges discussed in the workshop including extremely heterogeneous disease presentation, the fact that NPC may cause degeneration in different areas and over different time-courses in each patient, and an acknowledgement that a one-year trial might be too short to demonstrate any meaningful change.

Comments described a strong patient preference for single-arm rather than placebo-controlled studies, use of existing natural history data, and acceptance of endpoint measures that are currently available and important to patients and their families. It was further noted that it is important to take into consideration invaluable information that has already been gathered through the natural history study at the National Institutes of Health (NIH) and the use of the NPC Clinical Severity Scale (NPCCSS).

\(^1\) A docket is a repository through which the public can submit electronic and written comments on specific topics to U.S. federal agencies such as FDA. More information can be found at [www.regulations.gov](http://www.regulations.gov).
Building upon the discussion at the workshop around swallowing studies, it was noted that the Modified Barium Swallow (MBS) study may not be available in the European Union. Thus, it was stressed that it is important to consider whether an assessment tool will be available at all study sites as to prevent unnecessarily constricting the trial population size, which could make it harder to enroll and see statistically significant differences between study arms of NPC clinical trials.

While not within the scope of this workshop, many stakeholders, including patients, therapists, and caregivers, stressed the importance of early and continued access to investigational products through the expanded access program. Stakeholders shared fears of what losing access to investigational products would mean for patients, especially for those who have been accessing these therapies for many years (such as arimoclomol and adrabetadex).

Letters that had been sent previously to the FDA on various investigational NPC therapies and detailing patient and caregiver perspectives on NPC and therapeutic development were also submitted to the docket. These letters echoed many of the experiences shared throughout the workshop on the successes patients and families have seen with investigational products and the urgent need to approve safe and effective treatments for patients with NPC. It was emphasized that clarity, collaboration, and action are needed immediately and that it is important for FDA to work with the NIH, industry, academia, health care providers, and the patient community to efficiently develop, approve, and ensure access to therapies.

Lastly, stakeholders submitted citations for published research articles on NPC that provided context on the topics under discussion during the workshop. Submitted references to publications included the following:

**Studies Related to NPC Natural History**


Defining natural history: Assessment of the ability of college students to aid in characterizing clinical progression of Niemann-Pick disease, type C. *PLoS ONE, 6*(10). https://doi.org/10.1371/journal.pone.0023666


**Studies Related to the NPCCSS**


A white paper providing a background and perspective on regulatory approach to several NPC investigational products.

https://www.regulations.gov/comment/FDA-2021-N-1297-0007

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