Mitochondrial Disease Version 2.0 NINDS CDE Project
Audiology Outcomes Subgroup Summary

The NINDS Mitochondrial Disease v2.0 Common Data Element (CDE) Audiology Outcomes Subgroup (SG) convened a panel of experts to draft recommendations on guidance/CDEs to be used for research studies. The SG centered its recommendations on approaches and tools known in the audiology and vestibular clinical practice, accounting for considerations for the various phenotypes of patients affecting both children and adults with mitochondrial disorders. In addition, the SG selected tools that would be useful in a natural history study and would help to characterize a population as well as tools that may be better at demonstrating change over time to be used in clinical trials.

Mitochondrial disease encompasses a broad group of conditions characterized by a biochemical defect in energy metabolism. Disorders can be caused by pathogenic variants in the mitochondrial genome or in the nuclear genome and can be hereditary. Age of onset varies from birth to old age. Hearing loss is particularly characteristic of most mitochondrial disorders given the reliance of the hair cells in the organ of Corti upon mitochondrial for both energy generation and proper functions and localization of the ribbon synapse.

The SG acknowledges that hearing loss accompanying mitochondrial disorders is multifactorial, varies across individuals, and that functional declines are not always fully captured nor characterized in standard diagnostic tests in the auditory and vestibular clinical practice. Thus, depending on the research questions to be addressed, different methods of assessment, focused on revealing specific aspects of dysfunction, may be indicated. Additionally, the complexity of hearing evaluation means that no single assessment can meet all research needs. Therefore, a multi-faceted set of measures is essential, encompassing both physiological and functional aspects of hearing. Approaches and tools ultimately selected also will be shaped by constraints imposed by the participant including age and abilities, where the assessments will be conducted and the equipment and personnel resources available.

Audiologic outcomes in individuals with mitochondrial disease are determined by a series of hearing assessments conducted throughout their lives. These evaluations should focus on both initial identification and ongoing monitoring.

Key elements to consider include the following:
Historical items:
Pediatric

- Results of newborn or school-based hearing screening, if available
- Early recognition of changes in hearing ability, as reported by parents or guardians. This may include changes in response to sounds, difficulties with using devices at a normal volume, or challenges in noisy environments.
- The child's developmental milestones related to balance, such as the age when they learned to ride a bicycle or their ability to engage in balance-intensive activities like skating or gymnastics.

Adult

- Adult-onset changes in hearing, such as increased difficulty hearing using devices like cell phones or headphones, challenges in understanding speech in noisy environments, and feeling excluded from conversations.
- The individual's perception of balance issues, including onset and progression. For adults, this may involve challenges with activities that require balance, like yoga, recreational sports, or navigating uneven surfaces.

Both pediatric and adult historical aspects are essential for a comprehensive understanding of the individual's auditory and balance functions. This life course perspective on hearing loss emphasizes the importance of monitoring and assessing changes over time, from childhood through adulthood. Evaluation of auditory and balance functions in individuals with mitochondrial disease should ideally be conducted by an audiologist whenever feasible. Audiologists possess the specialized expertise necessary to accurately assess and interpret the complex nature of hearing and balance. This professional approach ensures that assessments are thorough, tailored to the individual’s age and specific needs.

Summary of Recommendations

Subdomain	Instrument/CRF Name	Classification	Population
Audiology	Hearing Loss in Mitochondrial Disease	Core; Supplemental – Highly Recommended; Exploratory	Adult; Pediatric
	Sensory Organization Test (SOT)	Exploratory	Adult; Pediatric
	Vestibular Function in Mitochondrial Disease	Supplemental – Highly Recommended; Exploratory	Adult; Pediatric
Motor Function	6 Minute Walk Test	Supplemental	Adult; Pediatric