**\*Otoscopy**

1. Otoscopy result:
   1. Pre-auricular region

Normal

Abnormal, explain:

Periauricular pit(s)

Preauricular pit(s)

Sinus tract(s)

Skin tag(s)

Other, specify:

Cannot assess, explain:

Exam not done

* 1. Pinna

Normal

Abnormal, explain:

Location

Microtia

Shape

Size

Other, specify:

Cannot assess, explain:

Exam not done

* 1. External auditory canal

Normal

Abnormal, explain:

Atresia

Cerumen impaction

Edema

Erythema

Erythema annulare centrifugum (EAC)

Granulation tissue

Stenosis

Other, specify:

Cannot assess, explain:

Exam not done

* 1. Tympanic membrane

Normal (translucent and mobile)

Abnormal, explain:

Erythematous

Granulation tissue

Immobile

Indwelling tympanostomy tube

Opaque

Otorrhea

Perforation

Retraction

Other, specify:

Cannot assess, explain:

Exam not done

**\*Tympanometry:**  Did not assess, explain:

Tympanogram results:

|  |  |  |
| --- | --- | --- |
|  | **Right Ear** | **Left Ear** |
| **Probe Tone** | 226 Hz  1000 Hz | 226 Hz  1000 Hz |
| **Ear Canal Volume (cc)** | Data to be filled in by site | Data to be filled in by site |
| **Compensated Amplitude** | Data to be filled in by site | Data to be filled in by site |
| **Peak (daPa)** | Data to be filled in by site | Data to be filled in by site |
| **\*\*Gradient (re: +200)** | Data to be filled in by site | Data to be filled in by site |
| **\*\*Est. Middle Ear Resonance** | Data to be filled in by site | Data to be filled in by site |

**\*\*Acoustic Reflexes:**  Done  Not Done

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Tone Activator** | | | | |
| **500 Hz** | | **1000 Hz** | | **2000 Hz** |
| **dB HL** | **Reflex Decay** | **dB HL** | **Reflex Decay** | **dB HL** |
| **Probe Right, Stimulus Left** | Data to be filled in by site | Positive  Negative | Data to be filled in by site | Positive  Negative | Data to be filled in by site |
| **Probe Right, Stimulus Right** | Data to be filled in by site |  | Data to be filled in by site |  | Data to be filled in by site |
| **Probe Left, Stimulus Right** | Data to be filled in by site | Positive  Negative | Data to be filled in by site | Positive  Negative | Data to be filled in by site |
| **Probe Left, Stimulus Left** | Data to be filled in by site |  | Data to be filled in by site |  | Data to be filled in by site |

**\*Pure Tone Audiometric Thresholds:**  Did not assess, explain:

Alternative stimuli:

Test location:

Transducer used:  Headphones/insert  Bone vibrator  Non-ear specific/speakers

1. Air conduction thresholds (dB HL)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **\*\*125 Hz** | **250 Hz** | **500 Hz** | **\*\*750 Hz** | **1000 Hz** | **\*\*1500 Hz** | **2000 Hz** | **3000 Hz** | **4000 Hz** | **6000 Hz** | **8000 Hz** |
| **Right Ear**  **(dB HL)** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Masking Status** | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked |
| **Left Ear**  **(dB HL)** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Masking Status** | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **9000 Hz** | **10000 Hz** | **11200 Hz** | **12500 Hz** | **14000 Hz** | **16000 Hz** | **18000 Hz** | **20000 Hz** |
| **Right Ear**  **(dB HL)** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Masking Status** | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked |
| **Left Ear**  **(dB HL)** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Masking Status** | Masked | Masked | Masked | Masked | Masked | Masked | Masked | Masked |

1. Bone conduction thresholds (dB HL)

|  | **250 Hz** | **500 Hz** | **\*\*750 Hz** | **1000 Hz** | **\*\*1500 Hz** | **2000 Hz** | **3000 Hz** | **4000 Hz** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Right Ear**  **(dB HL)** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Left Ear**  **(dB HL)** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Non-specific**  **(dB HL)** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

**\*Speech Audiometry:**  Did not assess, explain:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Right Ear** | **Left Ear** | **Binaural** |
| **Test 1** | | | |
| **Test Material** | Data to be filled in by site | | |
| **# of Test Items** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Transducer** | Headphones/insert  Bone vibrator  Non-ear specific/ speakers | Headphones/insert  Bone vibrator  Non-ear specific/ speakers | Headphones/insert  Bone vibrator  Non-ear specific/ speakers |
| **Speech Threshold (dB HL):**  **SRT/SAT** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Word Recognition** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Score** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Level (dB HL) Indicate** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Masking Status** | Masked | Masked |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Right Ear** | **Left Ear** | **Binaural** |
| **Test 2** | | | |
| **Test Material** | Data to be filled in by site | | |
| **# of Test Items** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Transducer** | Headphones/insert  Bone vibrator  Non-ear specific/ speakers | Headphones/insert  Bone vibrator  Non-ear specific/ speakers | Headphones/insert  Bone vibrator  Non-ear specific/ speakers |
| **Speech Threshold (dB HL):**  **SRT/SAT** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Word Recognition** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Score** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Level (dB HL) Indicate** | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| **Masking Status** | Masked | Masked |  |

**\*\*OAEs: Distortion Product Otoacoustic Emissions (DPOAE):**  Done  Not Done

1. **DPOAEs**
   1. Present (frequencies):
   2. Absent (frequencies):
   3. Artifact (frequencies):
2. **TEOAEs**
   1. Present (frequencies):
   2. Absent (frequencies):
   3. Artifact (frequencies):

**\*\*ABR/Auditory Evoked Potential:**  Done  Not Done

Air conduction  Bone conduction

Stimulus: Click

Test location:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | **Right Ear** | | **Left Ear** |
| **Stimulus Level** | | Data to be filled in by site | | Data to be filled in by site |
| **Threshold** | | Data to be filled in by site | | Data to be filled in by site |
| **Latency** | | Data to be filled in by site | | Data to be filled in by site |
| **\*\*\*ASSR** | | Data to be filled in by site | | Data to be filled in by site |
| **If abnormal:** | | | | |
| **Wave Peak Latencies** | **I** | Data to be filled in by site | | Data to be filled in by site |
| **III** | Data to be filled in by site | | Data to be filled in by site |
| **IV** | Data to be filled in by site | | Data to be filled in by site |
| **Waveform Morphology** | | Data to be filled in by site | Data to be filled in by site | |

Air conduction  Bone conduction

Stimulus: Tone

Test location:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | **Right Ear** | | **Left Ear** |
| **Stimulus Level** | | Data to be filled in by site | | Data to be filled in by site |
| **Threshold** | | Data to be filled in by site | | Data to be filled in by site |
| **Latency** | | Data to be filled in by site | | Data to be filled in by site |
| **\*\*\*ASSR** | | Data to be filled in by site | | Data to be filled in by site |
| **If abnormal:** | | | | |
| **Wave Peak Latencies** | **I** | Data to be filled in by site | | Data to be filled in by site |
| **III** | Data to be filled in by site | | Data to be filled in by site |
| **IV** | Data to be filled in by site | | Data to be filled in by site |
| **Waveform Morphology** | | Data to be filled in by site | Data to be filled in by site | |

**\*\*\*Electrocochleography**

1. ECochG: Done  Not Done

Result: Normal Abnormal, explain:

1. Promontory nerve stimulation: Done  Not Done

Result: Normal Abnormal, explain:

Recorder Signature: Date:

## General Instructions

Hearing loss is a common clinical manifestation of mitochondrial diseases. This case report form (CRF) contains data elements that collect information related to the characterization of the hearing loss and that assess its severity in the affected individual. Data may be collected at multiple time points to show progression over time. Questions on this CRF are also applicable to trials/studies.

Important note: Some of the data elements are classified as Core (i.e., strongly recommended for all mitochondrial disease clinical studies to collect), others as Supplemental – Highly Recommended (i.e., essential information for specified conditions, study types, or designs) or Exploratory, as indicated by asterisks below.

\*Element is classified as Core

\*\*Element is classified as Supplemental – Highly Recommended

\*\*\*Element is classified as Exploratory

Please see the Data Dictionary for element classifications.

## Specific Instructions

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

* Otoscopy – Examination informs regarding status of the external canal, tympanic membrane, middle ear.
* Tympanometry – Testing informs regarding objective site of lesion measurement: functional integrity of the sound-conduction system (ear canal patency, tympanic membrane mobility, middle ear status).
* Hearing thresholds – Record threshold.
  + Mild: 20-34 dB
  + Moderate: 35-49 dB
  + Moderately Severe: 50-64 dB
  + Severe: 65-79 dB
  + Profound: 80-94 dB
  + Complete: 95+ dB
* Air conduction thresholds – Extended high frequencies are Supplemental – Highly Recommended for the adult population and Exploratory for the pediatric population.
* Bone conduction thresholds – Ear specific bone conduction values are presumed to be masked. Non-specific values are presumed to be unmasked.
* Speech audiometry – Test 1 and 2 are included on the CRF, data for additional tests may be collected as needed.
* OAEs – Testing is used as an objective site of lesion measurement: functional integrity of the cochlear outer hair cell subsystem. Present OAEs are defined as 6 dB SNR.
* ABR/Auditory Evoked Potential – Testing is used as an objective site of lesion measurement: to assess neural response integrity. Not used for determining thresholds in adults unless unable to do behavioral tests. Bone conduction is not needed in adults.

## References

Sue CM, Lipsett LJ, Crimmins DS, Tsang CS, Boyages SC, Presgrave CM, Gibson WP, Byrne E, Morris JG. Cochlear origin of hearing loss in MELAS syndrome. Ann Neurol. 1998 Mar;43(3):350-9.

World report on hearing. Geneva: World Health Organization; 2021. License: CC BY-NC-SA 3.0 IGO.