GLP PRECLINICAL SERVICES FOR AUDITORY SAFETY

Clinical data confirms that many therapeutic compounds, including those targeting indications unrelated to hearing and otic disorders, should be tested for auditory safety. Ototoxicity and associated auditory pathology may affect millions of patients taking medications, potentially contributing to diminished quality of life. Additionally, several promising drugs and devices are currently in development for improving the lives of more than 360 million people suffering from hearing loss, the majority of which are suffering from conditions for which regulatory agencies recognize no efficacious therapy.

To meet these challenges, the auditory specialists at CILcare and Boston-based, GLP-compliant CRO CBSET, Inc. have created a strategic alliance to offer drug and device developers cutting-edge preclinical services for the evaluation of auditory functions in a regulated GLP environment.

Well-known ototoxic drug classes include:

- Antibiotics (aminoglycosides)
- Chemotherapeutic agents (cisplatin, carboplatin)
- NSAIDS (salicylate)
- Cardiovascular drugs (diuretics)
- Antimalarial drugs

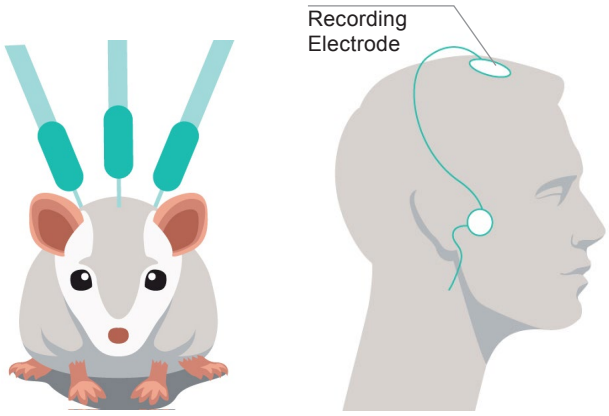
Prevalence of hearing loss:

- 15% of global population
- 1 in 3 adults > 65 years

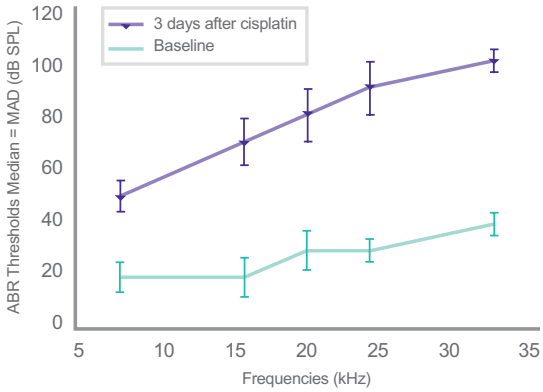
How to Evaluate Auditory Safety?

FDA guidance documents specify auditory safety evaluation utilizing two methodologies*:

- ***In vivo* assessment: measure of Auditory Brainstem Responses (ABR):**

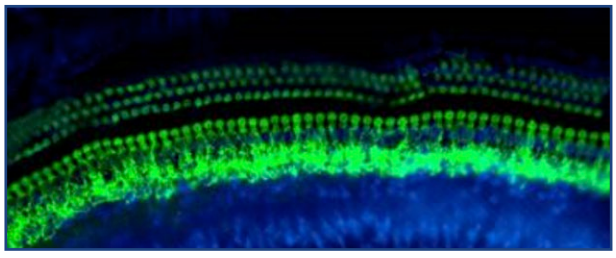


Auditory Brainstem Responses (ABR) are electric potentials recorded from scalp electrodes. This non-invasive method allows determination of auditory response thresholds. It is translational between rodents and humans, and is commonly used for screening newborns.



Auditory Brainstem Response thresholds in a cisplatin-induced ototoxicity model

- ***Ex vivo* assessment: cytocochleogram:**



The cytocochleogram allows histopathological assessment of ototoxic damage on inner hair cell and outer hair cell of the cochlea, with anatomical localization corresponding to predicable patterns of functional deficits.

**Source: Nonclinical Safety Evaluation of Reformulated Drug Products and Products Intended for Administration by an Alternate Route. Guidance for industry and Review Staff - Oct 2015 - FDA.*

Fortify Your IND Application

CBSET and CILcare combine scientific excellence in otology with experienced, GLP-compliant, preclinical experience to reduce risk in your regulatory filings. From general toxicology studies to surgical services, our team has the capability to customize a full preclinical program in line with your IND approach and project milestones. The collaboration between CBSET and CILcare creates a highly experienced team offering complex transtympanic and intracochlear drug delivery methods, which limit systemic exposure and provide robust, reproducible data in support of your ototoxicity or auditory function program.

Surgical Services
Interventional & minimally-invasive
Otic procedures (intracochlear)

General Toxicology
Single & repeat dose toxicology studies
Local tolerance (otic route)

Pharmacokinetics
Perilymph & cochlea sampling
Tissues & organs samplings
Bioanalysis

Animal Species
Rodents
Non-rodents

Safety Pharmacology
Central nervous system
Cardiovascular system
Respiratory system

Routes of Delivery
Transtympanic
Intracochlear
Systemic

Data & Endpoints
Electrophysiology (ABR)
Hematology & clinical chemistry
Gross pathology & necropsy
Histology analysis: cytocochleogram, immunostaining, electron microscopy

ABOUT CBSET

CBSET is a translational research institute providing high quality collaborative GLP studies from proof-of-concept through regulatory filling, to IND-enabling GLP studies:

- Full preclinical programs, plus specific study design supporting a range of applications in therapeutic and device development
- OLAW-assured, AAALAC-accredited animal research facilities
- GLP-compliant analyses
- Multispecies housing

CBSET is established in Lexington, MA (USA).

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ABOUT CILcare

CILcare is the world's leading CRO specializing in the development of novel therapies for ear disorders.

The company offers a range of services to assess the efficacy, safety and exposure of drug candidates and medical devices on preclinical models for:

- Hearing loss
- Tinnitus
- Otitis
- Ototoxicity

CILcare is based in Montpellier (south of France), Paris, and Boston, MA (USA).

www.cilcare.com