

# Zebrafish Platform

An evaluation model for biosafety and effectiveness of drugs, extracts and ingredients

Neuron Bio has developed a range of technologies based in the use of zebrafish to boost the development process of products of our clients. Thus, the zebrafish provides scientific evidence on the best products under development as a previous stage to their validation in mammals. Costs and development times are much more reduced in comparison with the rodent model



## Toxicology

### Fish Embryotoxicity (FET) Test

Analysis of the biosafety by measuring toxicological effects in embryo zebrafish model based on [OCDE TG 236](#). Endpoints: (a) Lethal: coagulated embryos, lack of somite formation, non-detachment of the tail, heart rate alteration; (b) Sub-lethal: non-spontaneous movements, depigmentation, formation of edemas, blood coagulation; (c) Teratogenic: malformation of organs, scoliosis, general growth retardation; (d) Tox Parameters: half lethal concentration (LC50); no observed effect concentration (NOEC) and lowest observed effect concentration (LOEC).

### Ototoxicity

Ototoxicity studies on neuromasts of the lateral line of larvae zebrafish (detected by fluorescence microscopy) caused by any kind of compound.

### Ocular Toxicity

Use of zebrafish embryo/larvae/adult to predict adverse visual effects in early drug safety assessment (by histology&histopathology and immunohistochemistry).

### Limit Test

Using the procedures described in the [OECD TG 203](#), a limit test may be performed at 100 mg/l in order to demonstrate that the LC50 is greater than this concentration. If any mortality occurs, a full study should be conducted. If sublethal effects are observed, these should be recorded.

### Single Dose Toxicity

Analysis of the biosafety by measuring toxicological effects of a single dose of a compound in adult zebrafish based on [OECD TG 203](#). Endpoints: (a) Mortality; (b) Sub-lethal effects: loss of equilibrium, erratic swimming behaviour, abnormal respiratory function, alteration of pigmentation.

### Fish Acute Toxicity Test

Analysis of the biosafety by measuring toxicological effects in adult zebrafish based on [OECD TG 203](#). Endpoints: (a) Mortality; (b) Kaplan-Meier analysis; (c) Sub-lethal effects: loss of equilibrium, erratic swimming behaviour, abnormal respiratory function, alteration of pigmentation; (d) Tox Parameters: half lethal concentration (LC50); no observed effect concentration (NOEC) and lowest observed effect concentration (LOEC) values.

## Efficacy

### Neuroprotection in Zebrafish Embryo/Larva

Analysis of protective effect against neuronal damage caused by neurotoxin.

### Central Nervous System Development

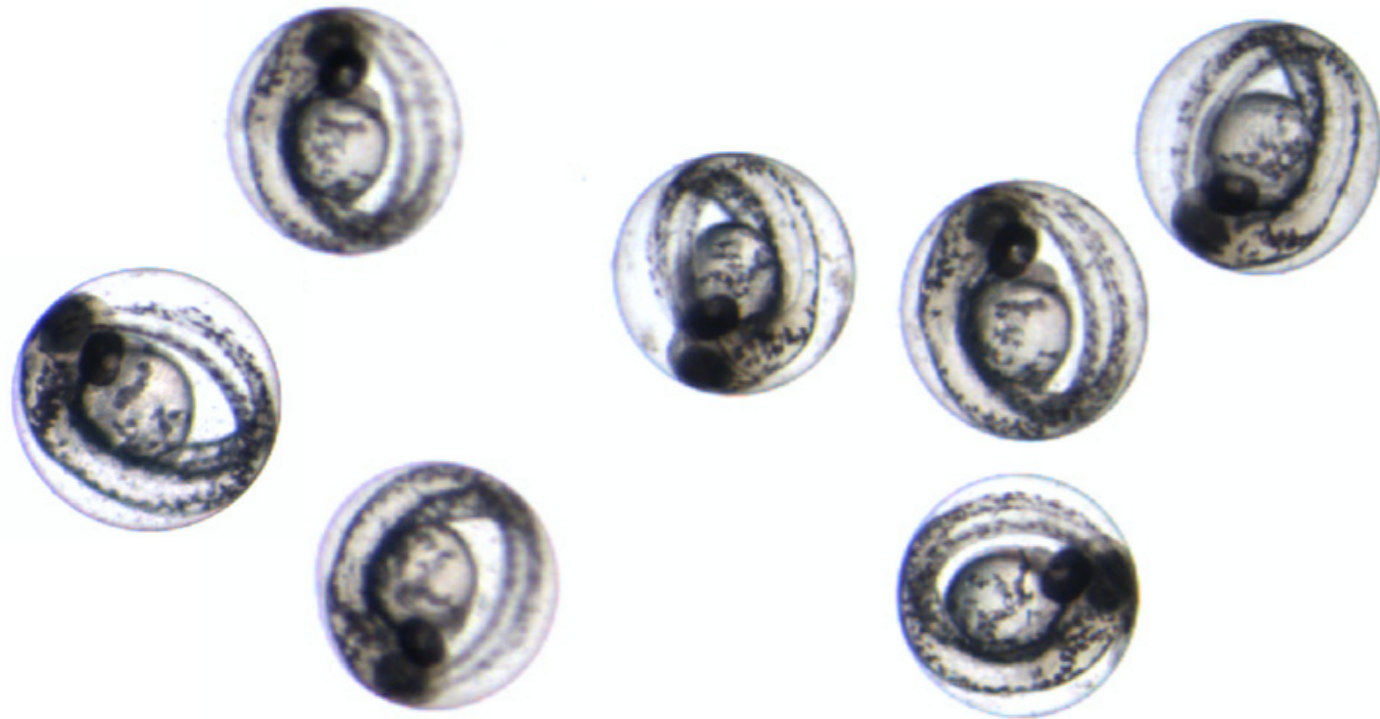
Effect of compounds in CNS development. Endpoints: (a) Axonal growth, (b) Motoneurons detection and (c) Specific neuronal biomarkers.

### Neuroprotection in Adult Zebrafish

Study of  $\alpha$ -,  $\beta$ - and  $\gamma$ -secretase activities in zebrafish brain measured by fluorescent specific substrates.

### Epilepsy Model

Study of compounds in an epilepsy model measuring behaviour seizure-stage score in adult zebrafish after kainate injection. Endpoint: (a) Mortality; (b) Kaplan-Meier analysis; (c) Latency: time of seizure onset; (d) Racine's scale: seizure



## An alternative to mice with the goal of reducing the use of mammals in research

One of the most important advantages of this animal model is that it is excluded from the animal testing regulation because it is not considered as a vertebrate organism until 6 days after birth, thus allowing experimentation with them, avoiding long bureaucratic periods related to animal testing

score; (e) Status epilepticus (SE): % of animals with SE; (f) Seizures: % of animals with seizures.

### Locomotor Activity and Anxiety

**Open Field.** Endpoints: (a) Latency; (b) Swimming velocity; (c) Resting time; (d) Swimming distance; (e) Thigmotaxis.

### Cognitive Status and Spatial Memory

**T-Maze.** Endpoints: (a) Latency; (b) Swimming activity; (c) Total time in enriched chamber.

### Screening of Antipsychotics in Adult Zebrafish

Investigation of potential antipsychotic effects. The blockade of the hyperactivity induce by a NMDA receptor antagonist is predictive of

antipsychotic-like efficacy.

### Protection Against Ototoxicity Phenomena

Protective effect of a compound against ototoxicity caused by aminoglycoside antibiotics on neuromasts of the lateral line of larvae zebrafish (detected by fluorescence microscopy).

## Tools

### Histology/Histopathology

Cytoarchitecture (H&E).

### Immunohistochemistry/Immunofluorescence

Neuronal markers (Acetylated  $\alpha$ -tubulin, TH,

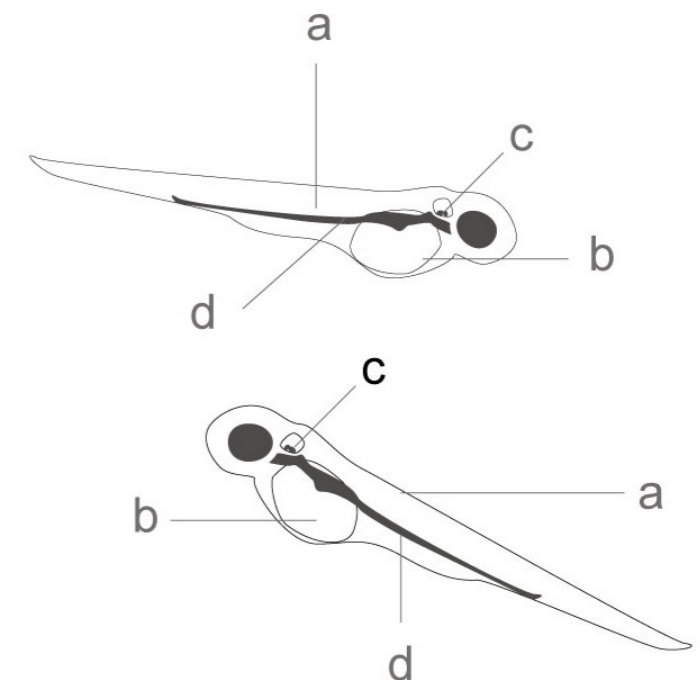
Isl 1/2), astrogliosis (GFAP)...on whole mount (embryo/larva) and histological samples (adult).

### Western Blot

Brain neuronal markers.

### Behaviour

- Cognitive status: Spatial memory (T-maze).
- Global motor activity: Global activity (Open-Field).



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