# Hepatotoxicity Contract Services

## Hepatotoxicity Contract Services from HemoGenix®

Toxicity to the liver, hepatotoxicity, is usually at the top of the organ and tissue toxicity list during drug development. The liver is considered the most important detoxification organ in the body. The cytochrome P450 system is designed to cope with the removal of toxicants by either induction or inhibition of specific P450 enzymes. In addition, hepatocytes are in a very active state of metabolism and therefore demonstrate high levels of intracellular ATP (iATP). Since the iATP concentration is proportional to cellular and mitochondrial integrity, changes in iATP levels are an indication not only of viability but cellular functionality. The most sensitive hepatotoxicity marker is the standardized and validated measurement of iATP using a luciferin/luciferase-based, bioluminescence readout, a procedure HemoGenix® calls Bioluminomics™. This procedure is used in the "gold standard" HALO® Platform for stem cell hemotoxicity testing and has now been incorporated into HepatoGLO™-Tox HT, an *in vitro,* high throughput hepatotoxicity testing platform. This information sheet provides information on the HepatoGLO™-Tox HT assay and associated multiplexing assays that can be provided to produce a wealth of information to help improve safety and efficacy of potential drug candidates at any time during drug development and determine hepatotoxicity of xenobiotic agents.

## HepatoGLO™-Tox HT Contract Service Applications

- High throughput *in vitro* toxicity, safety and efficacy testing for primary and iPS-derived hepatocytes and hepatocyte cell lines.
- ADME/Tox screening.
- Hepatocyte cellular drug-drug interaction (DDI) studies.
- Oxygen-tension response studies.
- Cell type comparison testing using the ComparaTOX™ 1 Platform

### Hepatocyte Types

- Fresh or cryopreserved primary cells
- Male
- Female
- Individual or pooled lots
- iPS-derived hepatocytes
- Hepatocyte cell lines, e.g. HepG2

### Species

- Human
- Non-human primate
- Dog
- Rat
- Mouse

HemoGenix® *Changing the Paradigm*

**Assays** You Can Trust
**Innovative Expertise** You Can Count On

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## Benefits of Using HepatoGLO™-Tox HT

- Incorporates an ATP-based luciferin/luciferase bioluminescence signal.
- Bioluminomics™ measures intracellular ATP (iATP) (the cell's energy source) to determine viability, cellular functionality, proliferation/cytotoxicity and cell number, all of which are proportional to the iATP concentration.
- Designed for all stages of drug development, from screening to pre-clinical animal studies.
- For fresh, cryopreserved and iPS-derived hepatocytes.
- From individual or pooled cells.
- Suspension or adherent cell cultures.
- 96- or 384-well plate high throughput formats.
- Most sensitive non-radioactive signal detection readout available.
- Single-addition reagent with a 10 minute bioluminescence developing time.
- Non-subjective, instrument-based and quantitative assay system.
- All assays are calibrated and standardized with an external ATP standard and controls, providing additional validation, when required.
- Assay standardization allows for comparison of results over time.

## Multiplexing with HepatoGLO™-Tox HT

- Cellular functionality/viability assays (LIVEGlo™, MTT etc).
- Low oxygen tension studies.
- Growth factor/cytokine assay production and release assays.
- Apoptosis assays: caspases.
- Oxidative DNA damage.
- LDH assays.
- Hepatocyte specific assays.
- CYP450 assays: CYP1A2, 2C9, 3A4, 2C19, 2D6.

## Parameters Uses to Define a Study

- Number of test compounds.
- Number of reference, positive and/or negative compounds.
- Primary assay(s) to be used and add-on assays to be performed.
- Type and number of cell populations to be tested.
- Type and number of species to be tested.
- Compound dose range.
- Number of compound doses (usually 6-12).
- Type of test compound addition.
- Culture conditions.
- Curve fit analysis, number of EC/IC values (if relevant) and statistics (if applicable).
- GLP/non-GLP/QA audit.

## Contract Services Workflow

- The CSO of HemoGenix® will advise and consult with our clients regarding the best assays to perform to achieve the goals of the study.
- Prepare quote and revise if required to suit budget.
- Prior to the start of the study, a detailed Study Plan will be prepared by the Study Director for the Study Monitor's approval.
- Sponsor shipment of test compounds.
- Procurement of test items (target cells) for study.
- Initiate study on arrival of tissues.
- Completion of study will depend on the target cells being used.
- Phase I report provided between 4-7 business days after study completion.
- Audit of study data and Phase I report.
- Phase II Final Report and study termination.