ADME/Tox products and services

At Life Technologies, we strive to offer industry-leading ADME/Tox products that provide physiologically relevant results, so you can make the right decisions related to your compounds. We are a team of hepatic scientists helping fellow scientists—supporting IND and NDA submissions with our products and services, and participating in the advancement of research in enzyme induction, CYP inhibition, hepatic transport, and other metabolism-related fields. Our goal is to provide the right tools and technical support for your needs.

ADME/Tox products for drug metabolism and safety
Physiologically relevant in vitro systems, such as primary hepatocytes and liver subcellular fractions, can be used to address a wide array of research questions related to in vivo applications, including those related to xenobiotic metabolism, drug–drug interactions, and cytotoxicity (Table 1). We offer products for:

- CYP450 inhibition and enzyme induction
- Metabolic profiling and stability
- Transporter applications

Complete selection of in vitro hepatic cell products
Our comprehensive offering includes hepatocytes and subcellular fractions isolated from human, rat, mouse, dog, rabbit, nonhuman primate, trout, and other species upon request. Our products are prequalified for particular research applications, and most are supplied as pooled or single donors, often in large lot sizes to facilitate multiple and multi-site experiments. These products include:

- Cryopreserved primary hepatocytes and Kupffer cells
- Freshly isolated primary hepatocytes (North America only)
- HepaRG® cells
- Cell culture media

Gibco® quality—every step of the way
As hepatic scientists, we deeply understand the importance of a high-quality, reliable supply chain and stringent characterization methods. We offer:

- A robust, extensive tissue procurement network
- Carefully honed isolation techniques
- Rigorous quality control standards
- Ongoing research and development
- Hepatic product specialists to provide technical support
<table>
<thead>
<tr>
<th>Application</th>
<th>Purpose</th>
<th>FDA guidance*</th>
<th>Plateable hepatocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug development research (ADME, DMPK, toxicology)</td>
<td></td>
<td></td>
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<tr>
<td>Enzyme induction and inhibition</td>
<td>Determine if a compound has the potential to induce or inhibit hepatic enzymes</td>
<td>Yes</td>
<td>+++</td>
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<tr>
<td>Hepatotoxicity</td>
<td>Determine if a compound and its metabolites have the potential to be hepatotoxic</td>
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<td>+++</td>
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<td>Metabolic profiling</td>
<td>Determine which enzymes metabolize a compound</td>
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<td>+++</td>
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<td>Metabolic stability</td>
<td>Measure the disappearance of a compound in the presence of metabolizing enzymes</td>
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<td>++</td>
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<tr>
<td>Reaction phenotyping (metabolic identification)</td>
<td>Identify the metabolites formed from a compound when exposed to metabolizing enzymes</td>
<td>Yes</td>
<td>++</td>
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<td>Transporter uptake</td>
<td>Determine if a compound has the potential to inhibit or induce liver transporter uptake</td>
<td>No</td>
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</tr>
<tr>
<td>Transporter efflux</td>
<td>Determine if a compound has the potential to inhibit or induce liver basolateral transporter efflux</td>
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<td>Other research applications (R&amp;D, toxicology, environmental safety)</td>
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<tr>
<td>Environmental bioaccumulation</td>
<td>Evaluate bioaccumulation of drugs or chemicals in humans and fish</td>
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<td>Liver disease research</td>
<td>Improve understanding of how the liver is involved in disease</td>
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<td>+++</td>
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<tr>
<td>siRNA, basic research</td>
<td>Identify the effects of gene suppression on disease</td>
<td>No</td>
<td>+++</td>
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+++ Product highly recommended for this application.
++ Product recommended for this application.
+ Our lowest recommendation, but product may still be useful for some assays.
<table>
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<tr>
<th>Suspension hepatocytes</th>
<th>Liver microsomes</th>
<th>Liver S9 fractions</th>
<th>Other</th>
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<td>Gibco® Human Cryopreserved Plateable Hepatocytes, Induction Qualified</td>
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<td>+++</td>
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<td></td>
<td>Gibco® Human Pooled Microsomes</td>
<td>HMMCP1</td>
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<td></td>
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<td>Gibco® Human Cryopreserved Plateable Hepatocytes, Metabolism Qualified</td>
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<td></td>
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<td>Also available:&lt;br&gt;• Fresh and cryopreserved human and animal hepatocytes</td>
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<tr>
<td>+++</td>
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<td></td>
<td>Recombinant CYP450 enzymes</td>
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<td>Gibco® Human Microsomes, Single Donor</td>
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<td></td>
<td>Also available:&lt;br&gt;• BACULOSOMES® Plus reagents and Vivid® kits</td>
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<tr>
<td>+++</td>
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<td></td>
<td></td>
<td>Gibco® Human Cryopreserved Suspension Hepatocytes, Transporter Qualified</td>
<td>HMCPS1</td>
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<td></td>
<td></td>
<td>Also available:&lt;br&gt;• Human plateable hepatocytes, transporter qualified&lt;br&gt;• Animal hepatocytes</td>
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<td></td>
<td></td>
<td>ABC vesicles</td>
<td>HMCPS1</td>
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<td>Gibco® Human Cryopreserved Plateable Hepatocytes, Transporter Qualified</td>
<td>HMCPS1</td>
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<td></td>
<td>Also available:&lt;br&gt;• GeneMembrane™ ABC inside-out vesicles&lt;br&gt;• Animal plateable hepatocytes</td>
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<tr>
<td>++</td>
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<td>Gibco® Fish (rainbow trout) S9 Fractions</td>
<td>TRS9PL</td>
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<td></td>
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<td></td>
<td></td>
<td>Also available:&lt;br&gt;• Animal and human, fresh and cryopreserved hepatocytes</td>
<td></td>
</tr>
<tr>
<td>+++</td>
<td></td>
<td></td>
<td></td>
<td>Gibco® HEP10® Pooled Human Cryopreserved Hepatocytes</td>
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<td></td>
<td>Also available:&lt;br&gt;• Animal and human, fresh and cryopreserved hepatocytes&lt;br&gt;• Animal and human microsomes</td>
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<td>Gibco® Human Cryopreserved Plateable Hepatocytes, Transporter Qualified</td>
<td>HMCPS1</td>
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<td></td>
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</table>
Primary hepatocytes isolated from the liver are effective tools for the \textit{in vitro} evaluation of metabolism, drug–drug interactions, hepatotoxicity, and transporter assessment. Our technicians are extensively trained in proper techniques to help ensure optimal cell health. As a result, Gibco® hepatocytes have high viabilities, \textit{in vivo}–like enzyme expression levels, and if released as plateable cells, excellent confluencies that contribute to polarization and functioning cell–cell contacts (Figure 1). Our primary hepatocytes offer:

- Viabilities routinely >80%
- Large and multiple lots—ideal for long-term studies across sites
- Characterization for phase I and phase II drug-metabolizing activities

### Characterization and quality control

- 10-point cell morphology check backed by photomicrographs—cell membrane integrity, organelle size, presence of lipid droplets, nucleus size and shape, cytosolic clarity, cell shape, level of cell debris, cell excretion products, cell–cell contacts (plateable cells only), and reestablishment of bile canalicular networks (plateable cells only)
- Metabolic activity testing—ECOD, 7-HCG, 7-HCS; human hepatocytes include testing for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A, and FMO
- Application qualification tests—attachment efficiency, monolayer confluency (Figure 2), fold induction with prototypical inducers, transporter uptake and efflux, \textit{in situ} intrinsic clearance
- Additional characterization data—genotyping, optimal seeding densities (Figures 3 and 4), viability stabilities, donor demographic

### Figure 1. Confluent, healthy, sandwich-cultured human hepatocytes shown after five days of culture.

The high level of confluency (>90%) and observable canaliculi are signs that this lot is suitable for metabolism, induction, and transporter uptake experiments.

### Characterization and quality control

- Low confluency (<70%)
- Limited cell–cell contact
- Grainy cytoplasm
- Visible cell stretching
- Severe cell flattening
- Absence of bile canaliculi

- High confluency (>90%)
- Good cell–cell contact
- Clear cytoplasm
- 3D configuration
- Cuboidal cell structure
- Bile canaliculi formation

### Figure 2. Monolayer integrity of human hepatocytes.

Representative images that demonstrate lack of monolayer integrity and ideal monolayer integrity from cryopreserved human hepatocytes isolated of separate donor tissues and cultured for multiple days. Note: An unhealthy monolayer can demonstrate confluence but lack integrity due to cell stretching and flattening.
These plateable and suspension hepatocytes are assessed for transporter function using uptake transporter assays. These cells:

- Contain functional membrane receptors and transporters
- Facilitate effective transporter uptake and basolateral efflux (plated) experiments
- Have stringent release specifications: >80% viability and >80% confluency (plated cells)

**Measurement of transporter uptake using suspension hepatocytes**

Transporter-qualified cryopreserved suspension hepatocytes are suitable for hepatic uptake studies, which typically measure the rate of appearance of substrate in cells after a relatively short incubation period, in most cases from 15 seconds to 3 minutes. Each of our transporter-qualified lots (suspension and plateable) has been functionally tested for the activities of NTCP, OATP1B3, and OATP transporter pathways using the substrates taurocholate, digoxin, and estradiol 17β glucuronide (E2-17G), as well as phase I and phase II metabolic activities. Visualization of the bile canalicular networks is attained by fluorescence microscopy using the compound 5-(6)-carboxy-2',7'-dichlorofluorescein diacetate (CDFDA). CDFDA is a substrate of the MRP2 transporter protein and accumulates in the bile canaliculi as the cells polarize and form bile canaliculi over 3–4 days in culture (Figure 5). Transporter uptake data have been compared before and after cryopreservation with similar results, suggesting that transporter gene expression in suspension hepatocytes is not affected by cryopreservation (Figure 6).
These plateable hepatocytes are tested with clinically relevant inducers and are suitable for use in experiments monitoring in vitro enzyme induction:

- Prequalified for CYP1A2, CYP2B6 and CYP3A induction
- ≥80% viability and ≥80% confluency (plated cells)
- Minimum specific activities:
  - ≥10-fold induction of CYP1A2
  - ≥5-fold induction of CYP2B6
  - ≥3-fold induction of CYP3A

Qualification of lots for use in experiments monitoring in vitro enzyme induction

Our induction-qualified hepatocytes have passed our quality tests for specific activity and mRNA levels in response to prototypical inducers. We culture our cryopreserved hepatocytes in 24-well collagen-coated plates and dose in triplicate with vehicle (0.1% DMSO), omeprazole, phenobarbital, and rifampicin for 72 hours.

Once monolayers are washed, they are incubated with substrates phenacetin, bupropion, and testosterone to determine CYP1A2, CYP2B6, and CYP3A activities, respectively (Figure 7). Fold induction of specific activity is expressed as the ratio of induced activity to vehicle activity. mRNA content is also determined by TaqMan® qRT-PCR analysis after 48 hours of treatment.
Gibco® Human Cryopreserved Hepatocytes, Plated, Metabolism Qualified

These plateable hepatocytes are suitable for use in applications involving metabolism of compounds:
- Useful for the assessment of intrinsic clearance ($CL_{int}$) of low-turnover compounds
- Prequalified according to $CL_{int}$ of midazolam, tolbutamide, and dextromethorphan
- ≥80% viability and ≥75% attachment efficiency

Metabolic assay conditions for plated metabolism-qualified human hepatocytes

Our plated metabolism-qualified hepatocytes have been tested for the enzymatic functions of CYP3A4, CYP2C9, and CYP2D6, using the prototypical CYP450 substrates midazolam, tolbutamide, and dextromethorphan, respectively (Figure 8). Using 48-well collagen-coated plates, hepatocytes are allowed to attach prior to incubation in serum-free Williams Medium E, with reactions stopped with ice-cold acetonitrile. Well contents are stored at −70°C prior to analysis. The disappearance of the parent compound is monitored by LC-MS/MS and intrinsic clearance values determined by linear regression.

Figure 8. Cryopreserved human hepatocytes prequalified for plated metabolism (intrinsic clearance). $CL_{int}$ [µL/1 x 10^6 cells/min] results were midazolam, 14.6; tolbutamide, 134; dextromethorphan, 7.20.

Gibco® Human Cryopreserved HEP10™ Pooled and Single Donor Hepatocytes, Metabolism Qualified

Our HEP10™ pooled and single donor human cryopreserved suspension hepatocytes are ideal for metabolism studies such as metabolic profiling and metabolic stability. As an industry leader in liver tissue sourcing and hepatocyte isolations, we offer one of the largest selections of single-donor and pooled lots (Figure 9). Our pooled lots are produced from normal donors with average CYP450 values, simplifying your experiments that may require the use of multiple donors. HEP10™ hepatocytes are:
- Characterized for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A, ECOD, 7-HCG, and 7-HCS activities
- Pooled as high-quality lots with batch sizes of >500 vials
- Available as specialty lots, including low CYP2D6 metabolizers

Figure 9. Human hepatocytes qualified for suspension metabolism applications.
Gibco® Animal Cryopreserved Plateable and Suspension Hepatocytes

Our animal cryopreserved hepatocytes are prepared using the same careful isolation and cryopreservation techniques as our human lots. We routinely isolate hepatocytes from mouse, rat, dog, and nonhuman primate, with other major toxicology research species available upon request. Viabilities for these cells are routinely >80%. Characterization methods include ECOD, 7-HCG, and 7-HCS for phase I and phase II enzyme activities. We also closely monitor cell morphology, attachment efficiency, monolayer confluency (plateable cells), and viability stability over time.

Gibco® Cryopreserved Kupffer Cells

**Kupffer cells provide improved physiological modeling**

Growing evidence shows that under both normal and pathological conditions, many hepatocyte functions are regulated by substances released from neighboring nonparenchymal cells (NPCs). These cells, particularly Kupffer cells, play an important role in the modulation of xenobiotic metabolism in the liver. Kupffer cells secrete potent mediators of the inflammatory response that controls liver inflammation. These cytokine mediators control hepatocyte metabolic rates through direct interactions with phase I and phase II enzymes.

Co-cultured Kupffer cell and hepatocytes can self-assemble within 72 hours of treatment with pro-inflammatory cytokines or lipopolysaccharides (LPS), and can function by effectively modulating P450 expression, thus giving a more physiologically relevant result (Figures 10 and 11). Studies indicate that co-cultures of hepatocytes with NPCs better represent both normal liver physiology and disease states. Cryopreserved purified human and rat Kupffer cells are a convenient way to produce hepatocyte and Kupffer cell co-cultures for the study of various hepatic functions. With Gibco® Cryopreserved Kupffer Cells, you get:

- High viability and purity, routinely >90%
- Response to activation with LPS
- Minimum 1 million viable cells per vial
- Hepatocyte co-culture protocols

**Figure 10. Co-cultures modeling normal and inflamed liver states.** These models enable researchers to study the interactions between hepatocytes and Kupffer cells during liver inflammation.

**Figure 11. IL-6 production in co-cultures of Kupffer cells and hepatocytes after LPS and IL-2 stimulation for 24, 48, and 72 hours.** Note that IL-6 is significantly up-regulated in co-cultures at all time points. This suggests cellular self-assembly between Kupffer cells and hepatocytes that synergistically allows those cells to function together during resolution of inflammation.
HepaRG® cells

The HepaRG® cell line is an immortalized hepatic cell line that retains many characteristics of primary human hepatocytes. HepaRG® cells are terminally differentiated and provided in a convenient cryopreserved format. For scientists who need reproducible metabolism data, HepaRG® cells are an in vitro tool that provides results in a metabolically complete and scalable system. These cells enable you to:

- Obtain biologically relevant results from a metabolically complete system
- Assess the drug–drug interaction potential of your compound
- Experience reproducible results from a single population of cells

Biologically relevant

HepaRG® cells exhibit many characteristics of primary human hepatocytes, including morphology, expression of key metabolic enzymes, expression of nuclear receptors, and drug transporters. Unlike HepG2 and Fa2N-4 cells, HepaRG® cells have high P450 activity and complete expression of all nuclear receptors.

Predict metabolism-based drug–drug interactions

HepaRG® cells respond to prototypical P450 inducers and inhibitors to the same extent as primary hepatocytes, allowing HepaRG® cells to be used to evaluate potential drug–drug interactions.

Consistent performance

HepaRG® cells are essentially a single donor. This enables users to obtain physiologically relevant results for metabolism-based drug–drug interactions without the concern of donor variability and limited lot sizes that come with relying on donor tissue. Note: The cells provided by Life Technologies are terminally differentiated.

Cell culture reagents

Thawing media

Hepatocyte Thaw Medium (HTM) and Cryopreserved Hepatocyte Recovery Medium (CHRM®) are proprietary formulations designed to enhance the recovery of viable hepatocytes while removing cryoprotectant after cell cryopreservation. When used appropriately, they have proven to result in healthier hepatocytes with consistently higher viability (Figure 12). Both are easy to use: simply add one vial of thawed hepatocytes to the conical tube, centrifuge briefly, remove the medium, and gently resuspend the cell pellet.

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**Figure 12.** Typical results of HTM or CHRM® vs. DMEM in the ability to enhance hepatocyte viability post-cryopreservation.
Williams Medium E
We recommend a phenol red–free Williams Medium E for hepatocyte research involving LC-MS/MS analysis.

Hepatocyte Plating Supplement Pack
The Hepatocyte Plating Supplement Pack contains prequalified fetal bovine serum, dexamethasone, and a cocktail solution of penicillin-streptomycin, bovine insulin, GlutaMAX™ medium, and HEPES to supplement up to 500 mL of Williams Medium E without phenol red, or a suitable alternative basal medium, for the purpose of plating fresh or cryopreserved hepatocytes.

Hepatocyte Maintenance Supplement Pack
The Hepatocyte Maintenance Supplement Pack contains dexamethasone and a cocktail solution of penicillin-streptomycin, ITS+ (insulin, transferrin, selenium complex, BSA, and linoleic acid), GlutaMAX™ medium, and HEPES to supplement up to 500 mL of Williams Medium E without phenol red, or a suitable alternative basal medium, for the purpose of incubating hepatocytes in suspension or plated cultures.

Collagen I, Rat Tail
Collagen is the most widely used extracellular matrix (ECM) protein for cell culture, facilitating cell attachment and differentiation. In addition to our 5 mg/mL Collagen I solution, we also offer Collagen I precoated 6-, 24-, and 96-well plates for your hepatocyte experiments.

Geltrex™ LDEV-Free Reduced Growth Factor Basement Membrane Matrix
Geltrex™ matrix is a soluble form of reduced growth factor (RGF) basement membrane extract (BME) purified from continuous sheets of specialized extracellular matrix that form an interface between Engelbreth-Holm-Swarm (EHS) tumor cells. The major components of Geltrex™ matrix include laminin, collagen IV, entactin, and heparin sulfate proteoglycan, which provide the foundation for three-dimensional (3D) culture studies.
Gibco® Fresh Hepatocytes (North America only)

Primary human hepatocytes, under appropriate culture conditions, model metabolism, induction, and inhibition similar to the *in vivo* liver. Fresh human hepatocytes are used to test potential therapeutic compounds for their metabolic stability, metabolic profile, probability of hepatotoxicity, and ability to inhibit or induce metabolic enzymes and hepatic transporters. To achieve optimal *in vitro* results, primary hepatocytes must be carefully isolated to preserve their drug-metabolizing enzymes, transporters, and cellular activities. Our technicians are highly trained in the proper techniques to help ensure optimal cell health. As a result, our fresh hepatocytes have high viabilities, excellent confluencies (Figure 13), and *in vivo*-like enzyme expression levels. Our fresh hepatocytes:

- Offer a reliable supply from one of the industry’s largest sourcing networks
- Have stringent release specifications: ≥80% viability and ≥80% confluency (plated cells)
- Are ready for use—plated to your specifications or provided in suspension

**Gibco® Human Fresh Hepatocytes**

We source liver tissue from a network of hospitals that perform surgical resections on living donors, as well as from deceased donors whose organs were rejected for transplant. Typically, we have access to one or more tissues per week. With such a large sourcing network, we can supply healthy human hepatocytes on a consistent basis, as well as keep you informed of tissues that meet your study’s specific requirements.

- Weekly availability (typically)
- Rapid Alert™ emails keep you informed

**Gibco® Animal Fresh Hepatocytes**

We carry hepatocytes from the major toxicology research species and accept many custom requests. Isolations are conducted weekly to facilitate your research. To view our animal isolation calendar, visit our website at lifetechnologies.com/hepatocytes.

- Multiple isolations every week
- Published calendar to facilitate planning your experiments

Species of animal fresh hepatocytes routinely available include:

- Rat (Sprague-Dawley)
- Mouse (CD-1)
- Dog (beagle)
- Nonhuman primate (cynomolgus)

Our formats are flexible—you can order hepatocytes in suspension or let us do the plating for you. We plate our cells to maximum confluency and offer an optional Geltrex™ matrix overlay to create a more *in vivo*-like environment. Available in:

- Multi-well plates (6-, 12-, 24-, 48-, and 96-well)
- Suspension culture

For information on our Rapid Alert™ notifications, see the back cover.
Gibco® Liver Microsomes and S9 Fractions

Subcellular fractions derived from the endoplasmic reticulum of liver contain a variety of metabolic enzymes for assessing the in vitro metabolism of drug candidates (Table 2) and are suitable for a variety of experiments:

- Metabolite characterization
- Cytochrome P450 inhibition studies and phenotyping
- Metabolic stability

We provide liver microsomes from a variety of human and other toxicology research species. Each product contains an average representative pool of donors. Human microsome pools are fully characterized ($K_m$ and $V_{max}$) according to GLP standards for major cytochrome P450 activities and selected phase II enzymes using FDA-recommended substrates (Table 3). We have:

- Large pooled lots for reproducible, long-term studies
- Specialty human pools based on age, BMI, high CYP3A4, or high CYP2D6
- Other subcellular fractions available, including S9 and cytosol fractions

S9 fractions are available from the following species:

- Human [single donor, specialty pools, population pools]
- Rat [Sprague-Dawley]
- Mouse [CD-1]
- Dog [beagle]
- Nonhuman primate [cynomolgus]
- Fish [rainbow trout]
Table 2. Metabolic enzymes found in liver subcellular fractions.

<table>
<thead>
<tr>
<th>Metabolic enzymes</th>
<th>Liver microsomes</th>
<th>Liver S9 fractions</th>
<th>Liver cytosol</th>
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<tr>
<td>Aldehyde oxidase</td>
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<td>Cytochromes P450 (CYP)</td>
<td>X</td>
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<tr>
<td>Flavin monooxygenases (FMO)</td>
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<tr>
<td>Glutathione transferase (GST)</td>
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<tr>
<td>Monamine oxidase (MAO)</td>
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<tr>
<td>Sulfurotransferases (SULT)</td>
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<tr>
<td>Uridine glucuronide transferase (UGT)</td>
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Table 3. Kinetic parameters for the current lot of Gibco® Human Liver Microsomes, 50 Donor Pool.

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<th>$V_{max}$ (nmol/min/mg)</th>
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<td>Hydroxyltolbutamide</td>
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<td>1'-Hydroxymidazolam</td>
<td>1.6</td>
<td>1.1</td>
</tr>
</tbody>
</table>
Cytochrome P450 BACULOSOMES™ Plus Reagents and Vivid® CYP450 Screening Kits

CYP450 BACULOSOMES™ Plus Reagents are microsomes prepared from insect cells infected with a recombinant baculovirus containing a human CYP450 isozyme, as well as human cytochrome P450 reductase. Vivid® CYP450 Screening Kits are high-throughput, fluorescence-based assays for detection of enzyme–drug interactions and CYP450 inhibition. CYP450 BACULOSOMES™ Plus Reagents and Vivid® CYP450 Screening Kits offer:

- A single human P450 isozyme for detailed drug metabolism studies
- An easy three-step procedure, “mix and read” format; reactions performed at room temperature or 37°C
- High signal-to-background ratio, broad dynamic range
- Compatibility with multiple assay formats from 96-well to 1,536-well

**Unique Vivid® reagents for bright fluorescent signals and low background**

Vivid® fluorogenic substrates are blocked dyes that yield minimal fluorescence signal until cleaved or hydroxylated. Oxidation at either of two potential sites releases the highly fluorescent product. They have superior fluorescence, solubility, and kinetic properties compared to conventional fluorogenic probes. This results in higher sensitivity, greater signal-to-noise ratios, and better assay reproducibility. The choice of substrate yields a product that emits blue, green, red, or cyan fluorescence.

**Flexible assay formats for optimized results**

The sensitivity of the Vivid® CYP450 assays allows detection of weak inhibitors and miniaturization to as little as 2 µL per reaction. Assays may be set up in kinetic mode or in endpoint mode to facilitate multi-plate screening. Assays may be performed at room temperature or 37°C.

**Single overexpress human CYP450 isozyme**

CYP450 BACULOSOMES™ Plus Reagents offer a distinct advantage over human liver microsomes in that only one CYP450 isozyme is expressed, thereby preventing metabolism by other CYP450 isozymes or other classes of drug-metabolizing enzymes.

For full listings of CYP450 enzymes and Vivid® kits, visit lifetechnologies.com/admetox
ABC Transporter Vesicles

ATP-binding cassette (ABC) transporter vesicles are easy-to-use, efficient reagents for early assessment of a drug candidate’s substrate and drug interaction potential. Prepared from Sf9 cells, which have been engineered to overexpress specific ABC transporters, these “inside-out” vesicles provide high levels of transporter activity with low background, giving you a clear signal if your compound is a substrate or inhibitor of a specific efflux transporter.

ABC Transporter Vesicles are prepared from ABC transporter membranes for use in vesicular transport assays. While ABC transporters typically mediate the efflux of substrates from cells, transporters expressed on these inside-out vesicles import substrates into the vesicles. It is therefore possible to quantitatively evaluate transport activity for your compound by determining the amount incorporated into the vesicles.

These vesicles, manufactured by GenoMembrane, are prepared by advanced methodologies using plasma membrane purified from an insect cell system (Sf9 cells transfected with baculovirus) that overexpresses ABC transporters.

For a full listing of ABC vesicles, visit lifetechnologies.com/admetox
ADME/Tox support

Protocols for ADME/Tox products
- Cell counting of primary hepatocytes using trypan blue exclusion analysis
- Metabolic stability using suspension and plated hepatocytes
- Induction potential in plated hepatocytes
- Co-culture of hepatocytes and Kupffer cells

Need assistance selecting a product?
Our product specialists are available to help you with product and lot selection, usage protocols, and orders.

Americas and Asia Pacific—orders and technical support
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Toll-Free Tel: +1 866 952 3559
Email: hepaticproducts@lifetech.com

Europe—orders and technical support
Tel: +44 (0) 141 814 5900
Email: hepaticproducts@lifetech.com

Japan—orders and technical support
Tel: +81 3 6832 6980
Email: JPCS@lifetech.com

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Find out more at lifetechologies.com/admetox

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