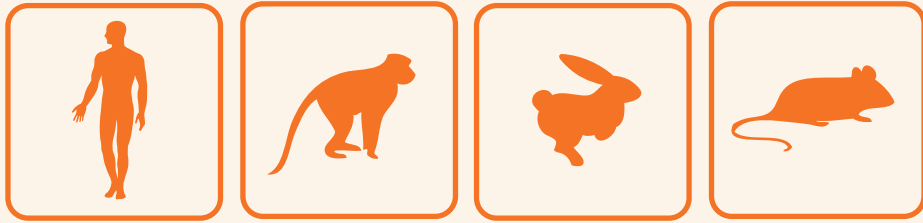


Gentest[®] Tissue Fractions

Reagents for Drug Metabolism





Gentest® Tissue Fractions

Reagents for Drug Metabolism

Tissue fractions from human and animal livers represent an important tool in preclinical metabolism studies for predicting the toxicity and pharmacokinetic properties of a drug compound. Liver microsomes from humans and animal species play an important role in evaluating drug compounds for metabolic stability, reactive metabolites, drug-drug interactions, reaction phenotyping, and metabolite identification.

For years, Gentest has been a trusted provider of a wide range of high-quality tissue fractions, including liver and intestinal microsomes, as well as ancillary products (e.g., cofactors, chemical substrates, metabolites, and inhibitors) necessary to perform metabolism-based assays.

Gentest® microsomes, cytosol, and S9 subcellular fractions provide a convenient, cost-effective source of native enzymes responsible for phase I and phase II metabolism of drugs. These enzymes include cytochrome P450 enzymes (CYP), UDP-glucuronosyl transferases (UGT), and flavin-containing monooxygenase (FMO).

Gentest has recently added a large donor pool of human liver microsomes (HLMs), the Gentest® UltraPool™ HLM 150, to the Gentest portfolio of human liver microsomes. This large donor pool better represents the average patient population and known CYP polymorphisms, enabling consistent experimental results in multi-year programs, and offering a time savings by reducing the time required qualifying new lots of HLMs.

The most rapid path to
more sound decision making.



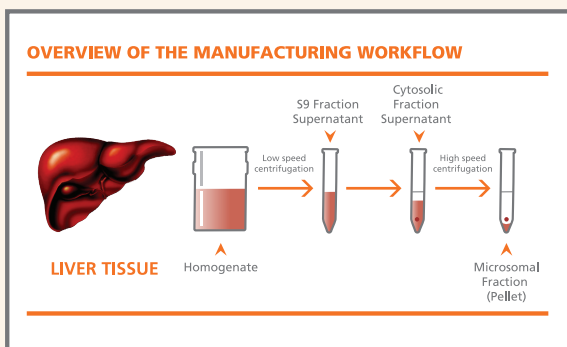
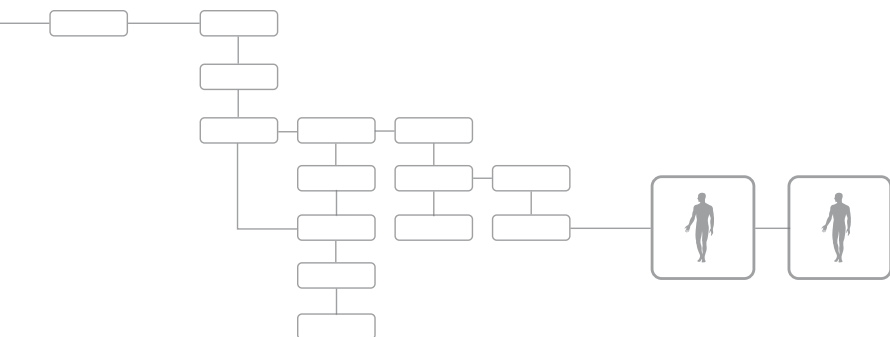
Gentest® Human Liver Microsomes

Gentest provides human subcellular fractions, as well as a variety of animal models. Each product contains an average representative pool of donors. Gentest UltraPool™ HLM 150 is fully characterized (K_m and V_{max}) according to GLP standards for major cytochrome P450 activities and select phase II enzymes using FDA-recommended substrates. Gentest UltraPool human liver microsomes are readily available as individual products, complete kits, or large lots for global supply.

Characterized for a range of enzymes

Gentest microsomes, cytosol, and S9 subcellular fractions provide a convenient, cost-effective source of native enzymes used in phase I and phase II metabolism of drugs. These enzymes include CYPs, UGTs, and FMOs.

Gentest HLMs (20-, 50-, and 150-donor pools) are manufactured in large lots and characterized for a range of important CYP, FMO, and UGT enzymes to ensure a high level of reproducibility.



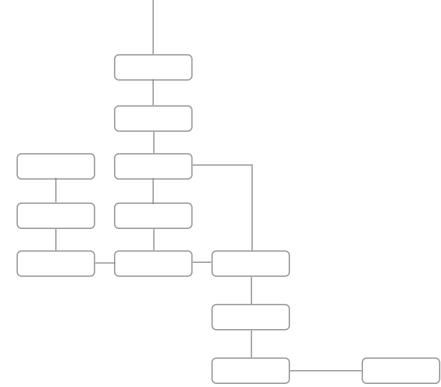
Gentest HLM, S9, and Cytosol—Isolation of subcellular fractions

Liver tissue contains enriched sources of native enzymes that metabolize xenobiotics. Homogenization and centrifugation of the liver product fractions enables a concentrated source of these enzymes.

Liver Microsomes (LMs): Endoplasmic reticulum membrane proteins containing phase I enzymes; CYPs and FMOs, and the membrane-bound phase II enzyme; UGTs—important enzyme systems for drug metabolism

Cytosol: Contains soluble phase II enzymes; GST, NAT, and SULT

S9: Contains both phase I and II enzymes; LMs and cytosol fractions

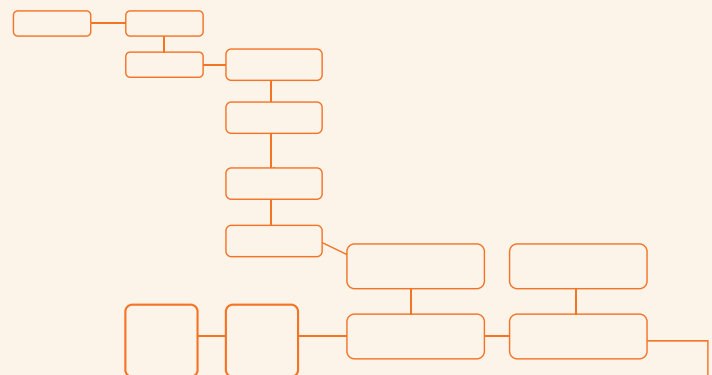


Gentest® Pooled HLMs Portfolio

| | 20 Donors | 50 Donors | 150 Donors |
|---------------------------|---|---|---|
| Catalog Number | 452161 (single vial) 452155 (80 vials in easy-count box) 452961 (S9) | 452156 (single vial) 452152 (80 vials in easy-count box) 452227 (1 vial each, HLM, S9, Cytosol) | 452117 (single vial) 452118 (80 vials in easy-count box) 452116 (S9) 452115 (Cytosol) |
| Donor Number | 20-30 | 50 | 150 |
| Quantity/Vial | 0.5 mL | 0.5 mL | 0.5 mL |
| Storage Buffer | 20 mg/mL 250 mM Sucrose | 20 mg/mL 250 mM Sucrose | 20 mg/mL 250 mM Sucrose |
| Gender Ratio | Seldom 50/50 | 50/50 (± 5%) | 50/50 |
| Donor Blend Method | Pre-selected donors mixed at ratios to give CYP activities for big 5 P450s (CYP1A2, 2C9, 2C19, 2D6, and 3A4) | Equal mix of donors on a per mg microsomal protein basis | Equal mix of donors on a per mg microsomal protein basis |
| CYP Activity | Targeted to meet a calculated mean of the average liver profile for the big 5 CYPs based on approx. 140 tested livers | Activities are similar to 452161 targeted values based on law of averages | Activities are similar to 452161 and 452156 values based on law of averages |
| Characterization | 10 CYP Assays: CYP1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, 3A4, 4A11 | 10 CYP Assays: CYP1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, 3A4, 4A11 | 10 CYP Assays: CYP1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, 3A4, 4A11 |
| | No Western Blot Assays | 2 Western Blot Assays: CYP3A4, 3A5 | 8 Western Blot Assays: CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 3A4, 3A5 |
| | 3 UGT Assays: (UGT1A1, 1A4, 1A9), and FMO | 5 UGT Assays: (UGT1A1, 1A4, 1A9, 2B7, 1A6), and FMO | 5 UGT Assays: (UGT1A1, 1A4, 1A9, 2B7, 1A6), and FMO 9 K_m/V_{max} Values: 3A4 Midazolam and Testosterone, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1 |

Gentest HLMs—Designed to speed the discovery process

- ▶ Tested for CYP, FMO, and UGT enzyme activity which enable lot selection best suited to meet your individual assay needs and quantities to meet multi-year global supply
- ▶ Supports strict tissue traceability with all human materials being sourced from US-based Organ Procurement Organizations
- ▶ Adheres to high safety standards including serological testing prior to acceptance, followed by PCR testing for HIV I/II, Hepatitis B, Hepatitis C, and HTLV - I/II



Gentest® UltraPool™ HLM 150— Consistent and rapid results

Gentest UltraPool HLM 150 is the first commercially available large donor pool. Gentest UltraPool HLM 150 enables consistency in experimental results in multi-site and long-term programs by delivering reproducible data across multiple CYP and UGT enzymes as compared to smaller pools of donors.

High degree of lot-to-lot consistency for CYP and UGT activity

Gentest UltraPool HLM 150 pool is statistically modeled so lot-to-lot variability represented as coefficient of variation (CV) is <10% (mean) for the more variable CYP enzyme (CYP2C19), and <5% (mean) for the key drug metabolizing CYP enzymes (CYP1A2, 2C9, 2D6, and 3A4). This lot-to-lot consistency is critical for researchers to achieve data consistency for metabolic stability, CYP inhibition, and reaction phenotyping assays year after year with multiple HLM lots.

Natural representation of the “average patient” and known CYP polymorphisms

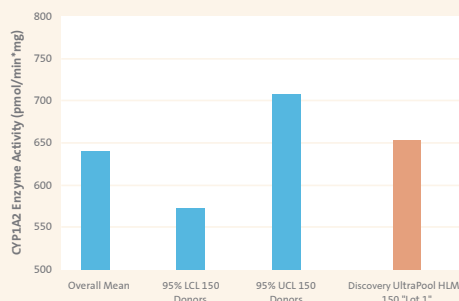
The large donor pool (150 donors, 300 alleles for diploid genes), consisting of an equal donor mix on a per milligram microsomal protein basis provides the best representation of an “average patient” drug metabolism activity. Gentest UltraPool HLM 150 provides consistency and confidence in the assay data across a wide selection of Gentest screening and development assays.

Large lots available for multi-year drug discovery programs

The Gentest UltraPool HLM 150 donor pool size is prepared from donors where considerable tissue is available and is manufactured in large lot sizes. This supports multi-year and multi-site programs by providing data consistency between ADME discovery screening and development groups. This donor pool size is specifically designed to serve the entire research organization—from drug discovery to drug development.



Gentest UltraPool HLM 150



CYP1A2 Activity Level Verification to Statistical Model

Illustration of the actual enzyme activity level for CYP1A2 in the Gentest UltraPool HLM 150 first lot and the calculated mean, upper and lower limits for a 150-donor pool based on Monte Carlo simulations. The bars are (from left to right): the overall mean, the 95% lower confidence limit (LCL), and the 95% upper confidence limit (UCL) calculated based on the CV from Monte Carlo simulations for a 150-donor pool, and the measured CYP1A2 activity in the first lot of Gentest UltraPool HLM 150.

Lot-to-lot Consistency

Monte Carlo Statistical Analysis

| | CYP1A2 | CYP2C9 | CYP2C19 | CYP2D6 | CYP3A4 |
|-------------------------------|--------|--------|---------|--------|--------|
| Mean (pmol/min*mg) | 640 | 2600 | 70 | 88 | 4800 |
| Standard Deviation | 520 | 1200 | 105 | 72 | 4100 |
| CV if Distribution was Normal | 82% | 47% | 150% | 82% | 85% |
| 50 Monte Carlo, mean (n=30) | 9% | 6% | 17% | 10% | 12% |
| 150 Monte Carlo, mean (n=30) | 5% | 3% | 9% | 4% | 5% |

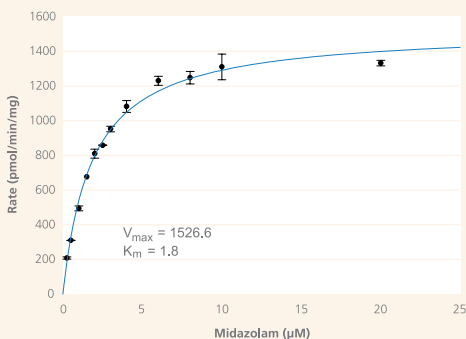
Mean, standard deviation and calculated CV for CYP activity is from HLM isolated from over 300 donors. CV decreases as the pool size increases and tends to level off after 150 donors. A reduction in CV as the donor number increases applies to all metabolic enzymes.

The data shown above resulted from a Monte Carlo analysis modeling the expected variability in HLM pools of differing sizes. Variability is measured by CV.

Kinetic Constants for CYP Isoform Activities for Gentest® UltraPool™ HLM 150

| Enzyme Measured | Substrate | Assay Protein Concentration (mg/mL) | Assay Time (min) | [S] Range (μM) | K _m (μM) | V _{max} [pmol/(mg x min)] |
|-----------------|------------------|-------------------------------------|------------------|----------------|---------------------|------------------------------------|
| CYP1A2 | Phenacetin | 0.2 | 10 | 2.5-150 | 24 | 1006 |
| CYP2A6 | Coumarin | 0.05 | 5 | 0.1-20 | 1.0 | 471 |
| CYP2B6 | Bupropion | 0.1 | 5 | 15-300 | 137 | 302 |
| CYP2C8 | Amodiaquine | 0.02 | 5 | 0.125-10 | 0.90 | 2023 |
| CYP2C9 | Diclofenac | 0.05 | 5 | 0.69-40 | 3.5 | 3973 |
| CYP2C19 | (S)-Mephenytoin | 0.3 | 10 | 5-200 | 24 | 53 |
| CYP2D6 | Dextromethorphan | 0.1 | 5 | 0.5-50 | 5.0 | 246 |
| CYP2E1 | Chlorzoxazone | 0.1 | 5 | 15-500 | 68 | 2311 |
| CYP3A4 | Midazolam | 0.02 | 5 | 0.25-20 | 1.8 | 1527 |
| CYP3A4 | Testosterone | 0.05 | 10 | 5.0-250 | 64 (n=1.2) | 5086 |

CYP3A4-Midazolam 1'-hydroxylation



Enzyme Kinetic Graph

- Method: Incubations for K_m and V_{max} determination contained 100 mM Phosphate (pH 7.4), 3.3 mM MgCl₂, NADPH generating system (1.3 mM NADP, 3.3 mM glucose 6-phosphate and 0.4 U/mL glucose 6-phosphate dehydrogenase) and CYP probe substrate (10 to 12 concentrations evenly spaced over the range). Metabolite formation was analyzed using validated LC-MS/MS methods with stable isotope labeled metabolites as internal standards.
- For testosterone, the K_m column represented as S50 (Hill coefficient = 1.2).

Gentest[®] HLMs

Additional options to enhance flexibility



Mixed Gender 50-Donor HLM Pool

The Gentest mixed gender 50-donor HLM pool is designed to improve predictions and scaling by minimizing metabolizing enzymes donor variability. The mixed gender pool is an equal mix of donors on a per mg microsomal protein basis as well as an equal male:female mix.

Features

- ▶ Western Blot testing for CYP3A5 and CYP3A4
- ▶ Activities for key CYP, FMO, and UGT isoforms are equal to an average patient

Mixed Gender 20-Donor HLM Pool

The Gentest mixed gender 20-donor HLM pool is formulated to represent an average profile of catalytic activities. The mixed gender pool targets the top five CYP enzyme activities to represent the average patient population.

Features

- ▶ Mixed gender with 20-30 male and female donors
- ▶ Activities for key CYP, FMO, and UGT isoforms

Human 50-Donor Tissue Fraction Kit

A convenient, cost-effective source of HLMs, cytosol, and S9 all isolated from the same 50 donors, this kit eliminates donor variability when performing a variety of studies including discovery screening and development services.

Features

- ▶ Suitable for metabolic stability testing, metabolite identification, reaction phenotyping, and inhibition testing

Each kit contains:

- ▶ 1 vial of 0.5 mL HLM
- ▶ 1 vial of 1.0 mL Cytosol
- ▶ 1 vial of 1.0 mL S9

Gentest[®] Specialty Tissue Fractions

Additional options to enhance flexibility

Gentest's portfolio of specialty pooled and single donor tissue fractions are designed to address differences in populations, catalytic activity, and genetic polymorphism. They are all highly characterized for catalytic activity measuring important metabolizing CYP, UGT, and other enzymes.

Specialty Human Pooled Tissue Fractions

Gentest's specialty pooled products are formulated to address metabolic differences between population groups. The portfolio of specialty tissue fractions include:

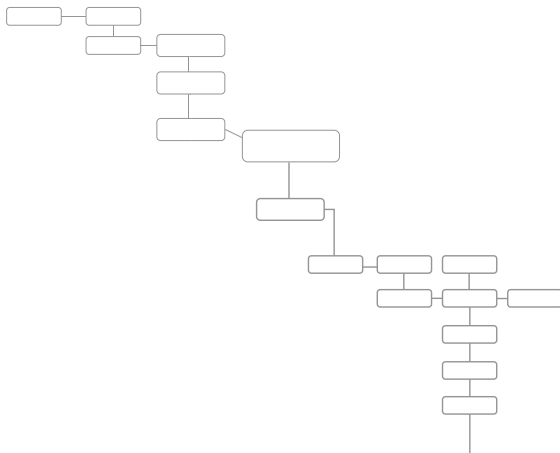
- ▶ Pooled Single Gender HLMs—formulated from five or more donors
- ▶ Mixed Pool CMV (cytomegalovirus) Negative HLMs—formulated from male and female donors testing negative serologically and with PCR-based testing

Non-hepatic Tissue Fractions

- ▶ Mixed Pooled Human Intestinal Microsomes—prepared from both the duodenum and jejunum sections of the small intestine for intestinal metabolism testing of CYP2C9, 3A4, 2J2/4F12, UGT1A, and carboxylesterase

High/Low P450 Single Donor HLMs

Gentest single donor HLM pools provide flexibility to select from a broad range of donors and CYP catalytic activity levels. Activity levels range from high to low representing the heterogeneity of expression of individual P450s found in the human population in order to study the metabolism of specific CYPs and to phenotype and correlate CYP activities.



Genotyped Allelic Variant HLMs

Human cytochromes P450 and UGTs exhibit a large number of allelic variants that may encode for defective enzymes, or no enzyme at all. Patients with diminished CYP and UGT activity may require lower than normal doses of specific drugs. HLMs isolated from donors with polymorphic genes can be valuable in understanding drug safety for all patients. Gentest has screened hundreds of donors to identify donors with allelic variants for important CYP and UGT isoforms.

Features

- ▶ 2C8(*3*3)
- ▶ 2C9(*2*2),(*2*3),(*3*3)
- ▶ 2C19(*2-*5)
- ▶ 2D6(*3-*8)
- ▶ 3A5(*1*1),(*1*3),(*3*3) Wild-type
- ▶ UGT1A1(*28*28),(*1*28),(*1*1) Wild-type

Gentest[®] Animal Tissue Fractions

Designed to speed metabolism studies

Gentest's animal subcellular fractions are prepared with the same quality, reproducibility, and characterization as our human liver products. Like human liver products, animal tissue fractions are well suited for metabolic stability testing, metabolite identification, and mechanistic studies.

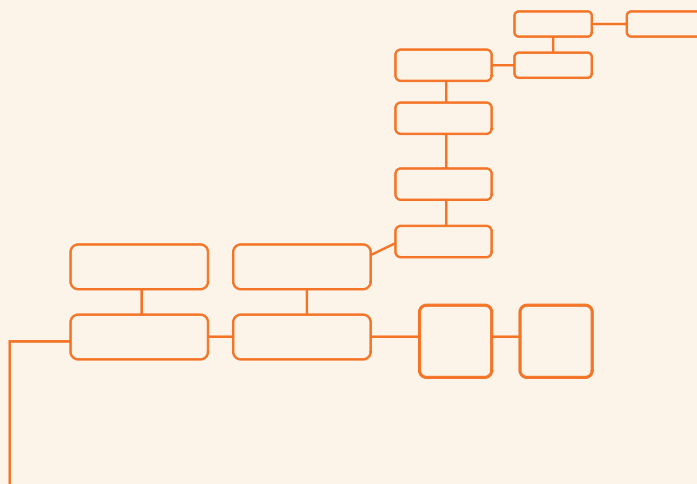
Animal Liver Tissue Fractions

Comparing *in vitro* profiles can aid in selecting a preclinical model for your *in vivo* studies. Gentest animal tissue fractions can be used to quickly generate metabolism data such as compound stability and metabolite formation. Animal liver microsomes are readily available, as well as S9 and cytosol for the select preclinical species listed:

- ▶ Mouse (B6C3F1, (CD-1)
- ▶ Rat (Sprague-Dawley, Wistar Han, Fischer 344)
- ▶ Guinea Pig (Dunkin Hartley)
- ▶ Rabbit (New Zealand White)
- ▶ Mini-Pig (Gottigen)
- ▶ Dog (Beagle)
- ▶ Monkey (Cynomolgus, Marmoset, Rhesus)

Features

- ▶ Large lots ensure product is readily available
- ▶ Pooled animal donors minimize lot-to-lot variability to better represent the average of the species
- ▶ Characterized for total P450, Cytochrome b₅, Oxidoreductase (OR), CYP3A, CYP2C, CYP2E1, CYP1A, and CYP4A



SERVICE AND SUPPORT

In Vitro ADME/Tox Services

Gentest is dedicated to the development of novel assay solutions for ADME/Tox research, including products and research services that are backed by a world-class service and support team. For over 25 years, Gentest has actively worked with ADME/Tox researchers to develop tools that help improve workflow, ease of use, and performance. This in-depth knowledge and experience is available to customers through application and technical support and expert contract research services.

Technical Applications Support

Gentest technical applications support specialists are available to provide e-mail and phone-based assistance and advice. Expert in a diverse array of topics, Gentest technical support specialists are well equipped to address customer needs in metabolism studies, drug transport, and other ADME /Tox applications.

Contract Research Services

Gentest Contract Research Study Directors have been helping customers test their drug compounds for over 15 years. This expertise gives Gentest Study Directors the ability to partner with clients to develop and deliver a broad range of *in vitro* ADME studies to meet their discovery and development project needs. Gentest ensures the highest level of quality standards and adheres to current regulatory requirements and applicable FDA-sponsored guidance documents.

To inquire about ADME/Tox Contract Research Services, e-mail us at salesorders@dls.com



Example Contract Research Services include:

- ▶ Permeability and Drug Transport
- ▶ Metabolic Stability
- ▶ Enzyme Inhibition
- ▶ Enzyme Induction
- ▶ Reaction Phenotyping
- ▶ Protein Binding

HLM Product List

Gentest® UltraPool™ HLM 150 Tissue Fractions – HLMs, S9, and Cytosol isolated from the same 150 donors

| Cat. No. | Description | Qty. | Protein Concentration |
|----------|--|-------------|-----------------------|
| 452117 | Mixed Gender Pooled 150-donor HLM | 0.5 mL | 20 mg/mL |
| 452118 | Mixed Gender Pooled 150-donor HLM (80 vials of 452117 packaged in an easy-count box) | 80 x 0.5 mL | 20 mg/mL |
| 452116 | Mixed Gender Pooled 150-donor S9 | 1.0 mL | 20 mg/mL |
| 452115 | Mixed Gender Pooled 150-donor Cytosol | 1.0 mL | 20 mg/mL |

Gentest™ Human Mixed Pooled HLMs, S9, and Cytosol

| Cat. No. | Description | Qty. | Protein Concentration |
|----------|--|----------|-----------------------|
| 452156 | Mixed Gender Pooled 50-donor HLM | 0.5 mL | 20 mg/mL |
| 452152 | Mixed Gender Pooled 50-donor HLM (80 vials of 452156 packaged in easy-count box) | 80 vials | — |
| 452227 | Human 50-donor Tissue Fraction Kit (Includes 1 vial each of HLM, S9, and Cytosol prepared from the same 50 donors) | 1 kit | — |
| 452161 | Mixed Gender Pooled 20-donor HLM | 0.5 mL | 20 mg/mL |
| 452155 | Mixed Gender Pooled 20-donor HLM (80 vials of 452161 packaged in easy-count box) | 80 vials | — |
| 452961 | Mixed Gender Pooled 20-donor S9 | 1.0 mL | 20 mg/mL |

Gentest Specialty Human Pooled Products

| Cat. No. | Description | Qty. | Protein Concentration |
|----------|---|--------|-----------------------|
| 452172 | Male Pooled HLM | 0.5 mL | 20 mg/mL |
| 452183 | Female Pooled HLM | 0.5 mL | 20 mg/mL |
| 452165 | Mixed Gender Pooled CMV Negative HLM | 0.5 mL | 20 mg/mL |
| 452210 | Mixed Gender Pooled Intestinal Microsomes | 0.2 mL | 10 mg/mL |

Custom HLM Pools are also available. For more information, e-mail gentestsupport@dls.com.

Gentest Individual HLMs Panel

| Cat. No. | Description | Qty. | Protein Concentration |
|----------|--------------------------------------|--------|-----------------------|
| 452138 | High/Low P450 Single Donor HLM Panel | 0.5 mL | 20 mg/mL |

Gentest Individual Allelic Variant Donor Panels

| Cat. No. | Description | Qty. | Protein Concentration |
|----------|----------------------------|--------|-----------------------|
| 452144 | CYP2C8(*3*3) | 0.5 mL | 20 mg/mL |
| 452142 | CYP2C9(*2*2),(*2*3),(*3*3) | 0.5 mL | 20 mg/mL |
| 452143 | CYP2C19(*2-*5) *PM | 0.5 mL | 20 mg/mL |
| 452141 | CYP2D6(*3-*8) *PM | 0.5 mL | 20 mg/mL |
| 452135 | CYP3A5(*1*1) | 0.5 mL | 20 mg/mL |
| 452136 | CYP3A5(*1*3) | 0.5 mL | 20 mg/mL |
| 452137 | CYP3A5(*3*3) Wild-type | 0.5 mL | 20 mg/mL |
| 452132 | UGT1A1(*28*28) | 0.5 mL | 20 mg/mL |
| 452133 | UGT1A1(*1*28) | 0.5 mL | 20 mg/mL |
| 452134 | UGT1A1(*1*1) | 0.5 mL | 20 mg/mL |

NOTE: Orders must include donor lot number as well as catalog number. Each lot number corresponds with a specific donor.

*PM: Poor Metabolizer

To view an up-to-date listing of donors with donor demographics, donor history, and characterization data, email GentestSupport@dls.com

Animal Liver Tissue Product List

Gentest® Animal Pooled Liver Microsomes, S9, and Cytosol

| Cat. No. | Description | Qty. | Protein Concentration |
|----------|---|--------|-----------------------|
| 452220 | Male Mouse Microsomes (B6C3F1) | 0.5 mL | 20 mg/mL |
| 452701 | Male Mouse Microsomes (CD-1) | 0.5 mL | 20 mg/mL |
| 452702 | Female Mouse Microsomes (CD-1) | 0.5 mL | 20 mg/mL |
| 452791 | Male Mouse S9 (CD-1) | 1.0 mL | 20 mg/mL |
| 452792 | Female Mouse S9 (CD-1) | 1.0 mL | 20 mg/mL |
| 452501 | Male Rat Microsomes (Sprague-Dawley) | 0.5 mL | 20 mg/mL |
| 452502 | Female Rat Microsomes (Sprague-Dawley) | 0.5 mL | 20 mg/mL |
| 452511 | Male Rat Microsomes (Wistar Han) | 0.5 mL | 20 mg/mL |
| 452521 | Male Rat Microsomes (Fischer 344) | 0.5 mL | 20 mg/mL |
| 452522 | Female Rat Microsomes (Fischer 344) | 0.5 mL | 20 mg/mL |
| 452591 | Male Rat S9 (Sprague-Dawley) | 1.0 mL | 20 mg/mL |
| 452593 | Male Rat S9 (Fischer 344) | 1.0 mL | 20 mg/mL |
| 452594 | Female Rat S9 (Fischer 344) | 1.0 mL | 20 mg/mL |
| 452581 | Male Rat Cytosol (Sprague-Dawley) | 1.0 mL | 20 mg/mL |
| 452311 | Male Guinea Pig Microsomes (Dunkin Hartley) | 0.5 mL | 20 mg/mL |
| 452313 | Female Guinea Pig Microsomes (Dunkin Hartley) | 0.5 mL | 20 mg/mL |
| 452201 | Male Rabbit Microsomes (New Zealand White) | 0.5 mL | 20 mg/mL |
| 452322 | Male Mini-Pig Microsomes (Gottigen) | 0.5 mL | 20 mg/mL |
| 452601 | Male Dog Microsomes (Beagle) | 0.5 mL | 20 mg/mL |
| 452602 | Female Dog Microsomes (Beagle) | 0.5 mL | 20 mg/mL |
| 452693 | Male Dog S9 (Beagle) | 1.0 mL | 20 mg/mL |
| 452413 | Male Monkey Microsomes (Cynomolgus) | 0.5 mL | 20 mg/mL |
| 452401 | Female Monkey Microsomes (Cynomolgus) | 0.5 mL | 20 mg/mL |
| 452424 | Male Monkey Microsomes (Rhesus) | 0.5 mL | 20 mg/mL |
| 452340 | Male Monkey Microsomes (Marmoset) | 0.5 mL | 20 mg/mL |
| 452341 | Female Monkey Microsomes (Marmoset) | 0.5 mL | 20 mg/mL |
| 452494 | Male Monkey S9 (Cynomolgus) | 1.0 mL | 20 mg/mL |
| 452491 | Female Monkey S9 (Cynomolgus) | 1.0 mL | 20 mg/mL |
| 452461 | Male Monkey Cytosol (Cynomolgus) | 1.0 mL | 20 mg/mL |
| 452462 | Female Monkey Cytosol (Cynomolgus) | 1.0 mL | 20 mg/mL |

Hazard Warning: Monkey tissue fractions are prepared from freshly frozen tissues. These materials are tested and found negative for Herpes B and SIV. We recommend that this material be considered a potential biohazard.

Warranty/Disclaimer: Unless otherwise specified, all products are for research use only. Not for use in humans. Not intended for use in diagnostic or therapeutic procedures. Discovery Life Sciences makes no claims regarding the performance of these products for clinical or diagnostic applications.

To place an order, contact Customer Service at: SalesOrders@dls.com

For technical assistance, contact Technical Support at: GentestSupport@dls.com

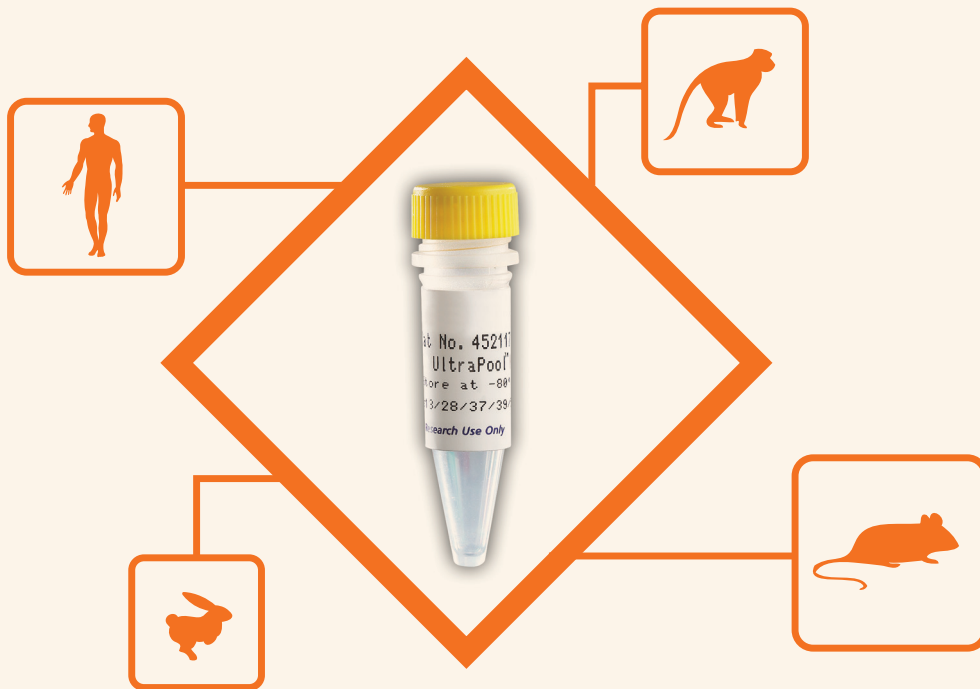
Chemical Product List

Chemicals to support CYP inhibition, reaction phenotyping, and metabolic stability assays

| Enzyme | Probe Substrate | Cat. No. | Metabolite | Cat. No. | Internal Standard | Cat. No. | Inhibitor | Cat. No. | Cofactor | Cat. No. |
|------------------|--------------------------------------|----------|--------------------------------|----------|--|----------|---|-------------------|-----------------------------------|------------------|
| CYP1A2 | Phenacetin | n/a | Acetamidophenol | n/a | Acetamidophenol- ^[13C2,15N] | 451001 | Furafylline | 451037 | NADPH Solution A Solution B | 451220 451200 |
| CYP2A6 | Coumarin | n/a | 7-Hydroxycoumarin | n/a | 7-Hydroxycoumarin-[D ₃] | 451002 | Tranylcypromine | n/a | | |
| CYP2B6 | Bupropion Hydrochloride | 451710 | Hydroxybupropion | 451711 | Hydroxybupropion-[D ₆] | 451003 | Ketoconazole | 451023 | | |
| CYP2C8 | Amodiaquine | n/a | Desethylamodiaquine | 451782 | Desethylamodiaquine-[D ₃] | 451004 | Montelukast | n/a | | |
| CYP2C8 | Paclitaxel | n/a | 6 α -Hydroxypaclitaxel | 451656 | 6-Hydroxypaclitaxel-[D ₃] | 451048 | Montelukast | n/a | | |
| CYP2C9 | Diclofenac | n/a | 4'-Hydroxydiclofenac | 451743 | 4'-Hydroxydiclofenac- ^[13C₆] | 451006 | Sulfaphenazole Tienilic Acid | 451019 451000 | | |
| CYP2C9 | Tolbutamide | n/a | Hydroxymethyl-tolbutamide | 451031 | Hydroxymethyl-tolbutamide-[D ₃] | n/a | Sulfaphenazole Tienilic Acid | 451019 451000 | | |
| CYP2C19 | (S)-Mephenytoin | 451032 | 4'-Hydroxymephenytoin | 451033 | 4'-Hydroxymephenytoin-[D ₃] | 451007 | (s)-(+)-(N)-(3)-Benzylrivanol | 451795 | | |
| CYP2D6 | Dextromethorphan | n/a | Dextrorphan | 451030 | Dextrorphan-[D ₃] | 451008 | Quinidine Paroxetine | n/a n/a | | |
| CYP2D6 | Bufuralol | 451034 | 1-Hydroxybufuralol | 451035 | 1-Hydroxybufuralol-[D ₃] | 451040 | Quinidine Paroxetine | n/a n/a | | |
| CYP2E1 | Chlorzoxazone | n/a | 6-Hydroxychlorzoxazone | 451036 | 6-Hydroxychlorzoxazone-[D _{2,15N]} | n/a | Chlormethiazole, disulfiram | n/a | | |
| CYP3A4 | Nifedipine | n/a | Oxidized Nifedipine | 451020 | Oxidized Nifedipine-[D ₁₂] | 451011 | Ketoconazole Azamulin | 451023 451785 | | |
| CYP3A4 | Midazolam | 451028 | 1'-Hydroxymidazolam | 451038 | 1'-Hydroxymidazolam- ^[13C₃] | 451010 | Ketoconazole Azamulin | 451023 451785 | | |
| CYP3A4 | Testosterone | n/a | 6 β -Hydroxytestosterone | 451012 | 6 β -Hydroxytestosterone-[D ₂] | 451009 | Ketoconazole Azamulin | 451023 451785 | | |
| UGT1A1, 1A6, 1A9 | *Acetaminophen | n/a | Acetaminophen-Glucuronide | n/a | Acetaminophen-[D ₃]-Glucuronide | 451046 | Alternative substrates: UGT1A1-Bilirubin UGT1A6-Naphthol UGT1A9-Propofol | n/a n/a n/a | | |
| UGT1A1 | Estradiol | n/a | Estradiol 3-Glucuronide | n/a | n/a | n/a | Bilirubin | n/a | | |
| UGT1A3 | 25-Trihydroxy-vitamin D ₃ | n/a | Estradiol 3-Glucuronide | n/a | n/a | n/a | 2-Hydroxyestradiol | n/a | | |
| UGT1A4 | Trifluorperazine | n/a | Trifluorperazine N-Glucuronide | n/a | n/a | n/a | Hecogenin | n/a | | |
| UGT1A6 | Serotonin | n/a | Serotonin Glucuronide | n/a | n/a | n/a | Naphthol | n/a | | |
| UGT1A9 | Propofol | n/a | Propofol Glucuronide | n/a | n/a | n/a | Propofol, 7-Hydroxy-4-Methylcoumarin | n/a | | |
| UGT2B7 | 3-Azidothymidine (AZT) | n/a | AZT Glucuronide | n/a | n/a | n/a | Eugenol, Morphine | n/a | | |
| UGT2B15 | S-Oxazepam | n/a | S-Oxazepam Glucuronide | n/a | n/a | n/a | n/a | n/a | | |

*Selectivity dependent on APAP concentration

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