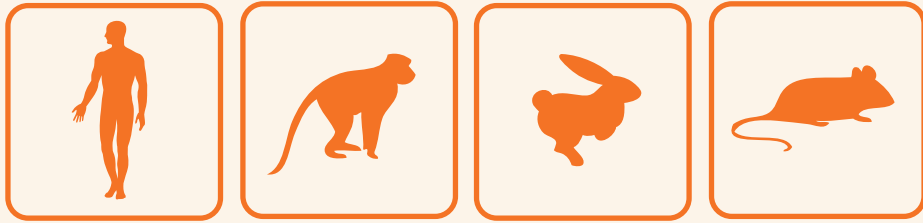


Corning® Tissue Fractions

Reagents for Drug Metabolism





Corning[®] 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, Corning 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.

Corning 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). As part of Corning Life Sciences' ongoing commitment to bringing innovative tools to life scientists and emerging areas of ADME/Tox research, Corning added a large donor pool of human liver microsomes (HLMs), the Corning UltraPool[™] HLM 150, to the Corning 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.



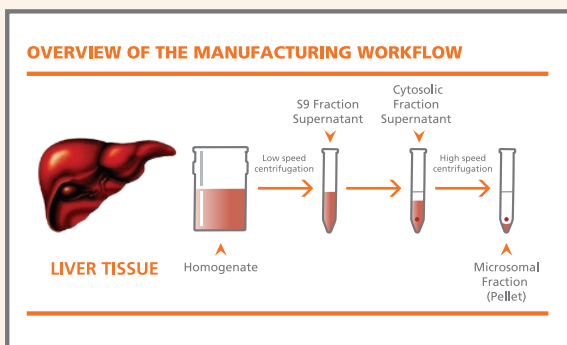
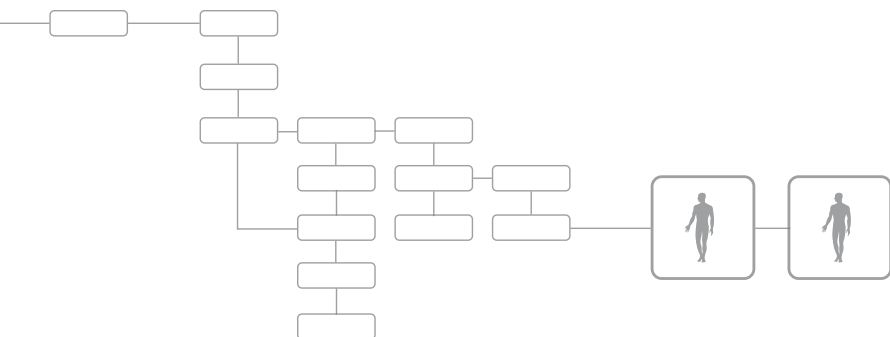
Corning® Gentest™ Human Liver Microsomes

Corning provides human subcellular fractions, as well as a variety of animal models. Each product contains an average representative pool of donors. Corning 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. Corning Gentest and Corning UltraPool human liver microsomes are readily available as individual products, complete kits, or large lots for global supply.

Characterized for a range of enzymes

Corning 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.

Corning 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.



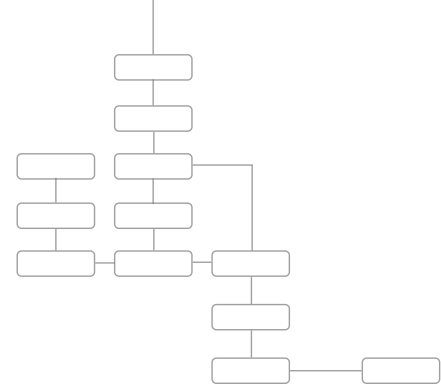
Corning Gentest HLM, S9, and Cytosol—Isolation of subcellular fractions

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

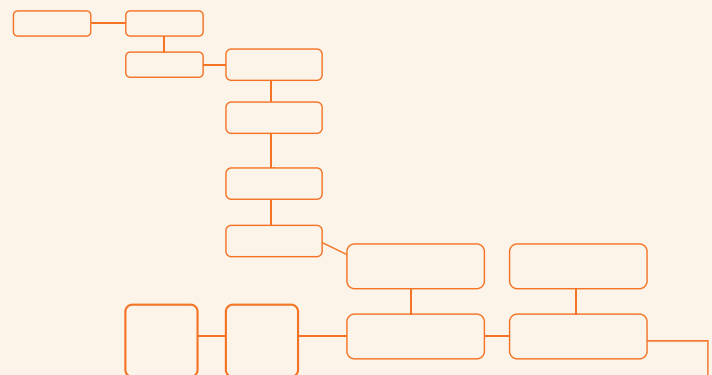


Corning® Gentest™ Pooled HLMs Portfolio

	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

Corning 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



Corning® UltraPool™ HLM 150— Consistent and rapid results



Corning UltraPool HLM 150 is the first commercially available large donor pool. Corning 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

Corning 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.

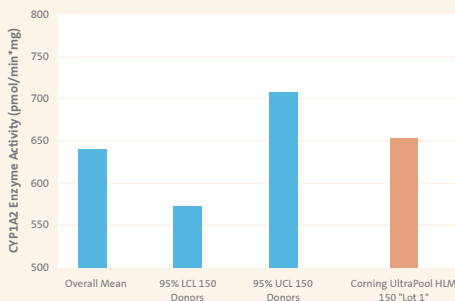
Natural representation of the “average patient” and known CYP polymorphisms

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. Corning UltraPool HLM 150 provides consistency and confidence in the assay data across a wide selection of discovery screening and development assays.

Large lots available for multi-year drug discovery programs

The Corning 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.

Corning UltraPool HLM 150



CYP1A2 Activity Level Verification to Statistical Model

Illustration of the actual enzyme activity level for CYP1A2 in the Corning 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 Corning 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%

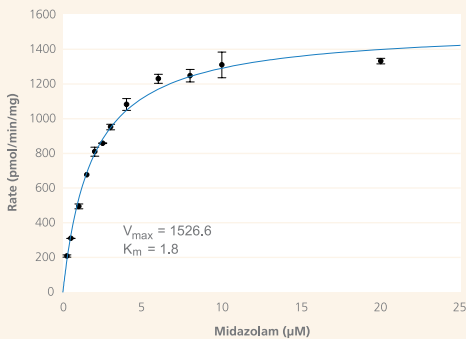
Mean, standard deviation and calculated CV for CYP activity is from HLM isolated from over 300 donors. CV decreases as the pool size increases and tends to level off after 150 donors. A reduction in CV as the donor number increases applies to all metabolic enzymes.

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 Corning® 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).

Corning® Gentest™ HLMs

Additional options to enhance flexibility



Mixed Gender 50-Donor HLM Pool

The Corning 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 Corning 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

Corning® Specialty Tissue Fractions

Additional options to enhance flexibility

Corning Life Sciences' 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

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

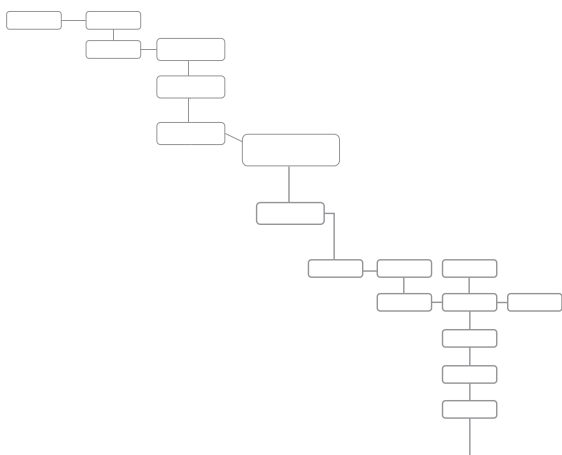
- ▶ Pooled Single Gender HLMs—formulated from five or more donors
- ▶ Mixed Pool CMV (cytomegalovirus) Negative HLMs—formulated from male and female donors testing negative serologically and with PCR-based testing

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

Corning 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. Corning Life Sciences 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

Corning[®] Animal Tissue Fractions

Designed to speed metabolism studies

Corning Life Sciences' 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.

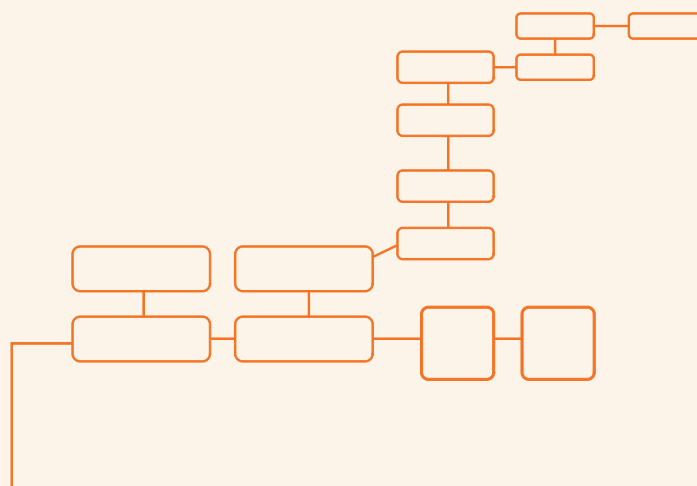
Animal Liver Tissue Fractions

Comparing *in vitro* profiles can aid in selecting a preclinical model for your *in vivo* studies. Corning 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

Corning Life Sciences 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, Corning 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

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

Special Order HLM Products

Corning HLM pools can be customized to meet specific customer requirements. Please e-mail ADMETOX@corning.com for more information.

Contract Research Services

Corning Life Sciences Contract Research Study Directors have been helping customers test their drug compounds for over 15 years. This expertise gives Corning Life Sciences 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. Corning 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 CLSTechServ@corning.com or call 888.334.5229 x2246 or 781.935.5115 x2246.



Example Contract Research Services include:

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

HLM Product List

Corning® 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

Corning 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

Corning 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 ADMETOX@corning.com.

Corning Gentest Individual HLMs Panel

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

Corning 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, visit www.corning.com/lifesciences.

Animal Liver Tissue Product List

Corning® 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. Corning Life Sciences makes no claims regarding the performance of these products for clinical or diagnostic applications.

To place an order in the U.S., contact Customer Service at:
tel: **800.492.1110**, fax: 978.442.2476, email: CLSCustServ@corning.com

For technical assistance, contact Technical Support at:
tel: **800.492.1110**, fax: 978.442.2476, email: CLSTechServ@corning.com

Outside the U.S., contact your local distributor or visit www.corning.com/lifesciences to locate your nearest Corning office. For additional Corning product, technical, or distributor information, call **978.442.2200**.

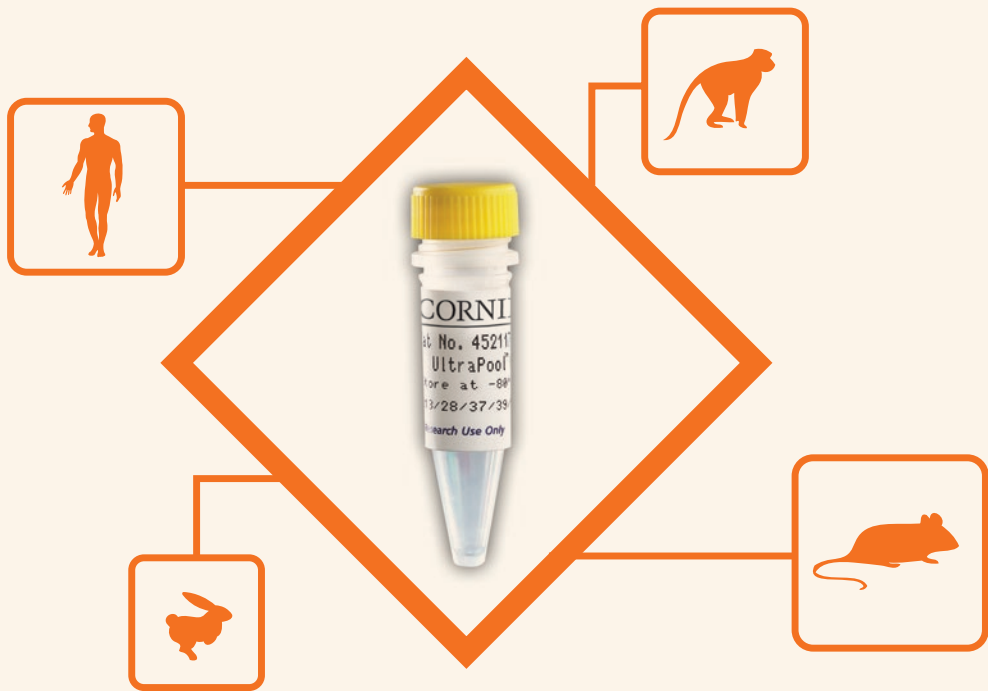
Chemical Product List

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-[¹³ C ₂ , ¹⁵ N]	451001	Furafylline	451037	NADPH Solution A Solution B	451220 451200
CYP2A6	Coumarin	n/a	7-Hydroxycoumarin	n/a	7-Hydroxycoumarin-[D ₃]	451002	Tranlycypromine	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-[¹³ C ₆]	451006	Sulfaphenazole Tienilic Acid	451019 451000		
CYP2C9	Tolbutamide	n/a	Hydroxymethyl-tolbutamide	451031	Hydroxymethyl-tolbutamide-[D ₉]		Sulfaphenazole Tienilic Acid	451019 451000		
CYP2C19	(S)-Mephenytoin	451032	4'-Hydroxymephenytoin	451033	4'-Hydroxymephenytoin-[D ₃]	451007	(s)-(+)-(N)-(3)-Benzylirivanol	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 ₉]	451040	Quinidine Paroxetine	n/a n/a		
CYP2E1	Chlorzoxazone	n/a	6-Hydroxychlorzoxazone	451036	6-Hydroxychlorzoxazone-[D ₂ , ¹⁵ N]	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-[¹³ C ₃]	451010	Ketoconazole Azamulin	451023 451785		
CYP3A4	Testosterone	n/a	6 β -Hydroxytestosterone	451012	6b-Hydroxytestosterone-[D ₇]	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 D3	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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