

# Corning® Gentest™ Human Tissue Fraction Products

## Frequently Asked Questions

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Corning Gentest microsomes, cytosol, and S9 subcellular fractions provide a convenient, cost-effective source of native enzymes used in the oxidation or glucuronidation of drugs. These enzymes include cytochrome P450 enzymes (CYP), glucuronosyltransferases (UGT), and flavin monooxygenases (FMO).

Corning Life Sciences human liver microsomes (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.

### **How should microsomes be stored, and how long are they stable under storage conditions?**

Microsomes, S9, and cytosol tissue fractions should be stored at -80°C. Studies conducted at Corning Life Sciences show that microsomes can be kept for at least 10 years with no loss in P450 activity when stored properly at -80°C.

### **How should microsomes be thawed and stored during applications? Can thawed microsomes be re-frozen without loss in activity?**

Microsomes can be thawed at room temperature or in a 37°C water bath. However, it is important that the microsomes be placed back on ice immediately after thawing to minimize any potential degradation of P450 or other drug metabolizing enzymes (e.g. FMOs which are known to be thermo-labile). A 0.5 mL vial of microsomes takes between 2 to 4 minutes to thaw at 37°C.

Thawed microsomes should be kept on ice during the entire time they are in use. Microsomes can be kept on ice for several hours without loss in enzyme activity.

Microsomes kept on ice can be re-frozen at -80°C without loss in enzyme activity. Microsomes incubated at 37°C or room temperature should not be re-frozen or used again.

### **What is the best method to mix microsomal suspensions, and what buffers should be used to dilute microsomes?**

It is a good practice to keep the microsomes on ice while mixing all other components of a reaction mix, and then add the microsomes last to initiate the reaction. Incubation mixes are typically pre-warmed to 37°C prior to start of the reaction; it is not advisable to pre-warm microsomal suspensions.

Microsomes should be mixed well immediately before addition to reaction mixes. Short bursts of vortexing (2 to 10 seconds) is recommended. Vortexing is also advised for mixing the reaction mix after addition of all components. Vortexing in short bursts will not harm the microsomes suspensions or reaction mixes.

Microsomes can be diluted with a variety of buffers or even H<sub>2</sub>O. Corning Gentest microsomes are provided in 0.25 M Sucrose, which can be used for dilution purposes. 0.1 M Phosphate buffer, pH 7.4, a 1:5 dilution of Cat. No. 451201, and Tris buffer, pH 7.5, a 1:5 dilution of Cat. No. 451202 are commonly used for diluting microsomes.

### **Are Corning® Gentest™ tissue fraction products tested for biohazardous agents? Does Corning Life Sciences take any special safety precautions?**

All human tissue fractions are derived from human tissue which is a potentially biohazardous material. Universal precautions should be used when handling, which means the material should be handled as if it were capable of transmitting disease. Materials used for Corning Gentest human tissue fraction products has been tested using FDA-approved methods and found negative for Human Immunodeficiency Virus (HIV-1/HIV-2), Human T Cell Leukemia Virus (HTLV-1/HTLV-2), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and Cytomegalovirus (CMV). However, no known test method can provide complete assurance that specimens of human origin will not transmit infectious disease. When handling or disposing, follow precautions described in CDC and FDA recommendations and OSHA blood borne pathogen recommendations.

### **Does Corning Life Sciences provide donor information about their human tissue fraction products? What information is provided?**

Yes, donor information is provided on the batch data sheet that is shipped with the product. The donor information includes donor gender, age, race, cause of death, social history, medical history, and medications taken while in the hospital.

### **How many donors are used to make pooled HLM, and how are the pools designed?**

The original HLM pool offered by Corning Life Sciences is Cat. No. 452161 which consists of 20 to 30 donors. The single donors used to make Cat. No. 452161 have all been pre-characterized for the major P450 activities. The amount of HLM used from each single donor is adjusted in order to achieve a pool with final “targeted” CYP activities consistent with the average activity in the Corning single donor data base (Corning has individual CYP activities data from over 300 single donor HLM). The average activities in the Corning 300-donor database are expected to be representative of the average activities in the general population.

Corning now offers a 50-donor pool (Cat. No. 452156) and Corning UltraPool™ HLM 150 (Cat. No. 452117), which contains 150 donors. Unlike catalog number 452161, these larger pools are mixed using equal amounts of protein from each HLM single donor. The larger number of donors achieves the best representation of the average individual and also minimizes lot-to-lot variability.

### **What other pooled HLM products are offered by Corning Life Sciences?**

Corning Life Sciences offers single gender pools (male and female) and CMV negative pools (negative serology for cytomegalovirus).

### **How does Corning Life Sciences ensure lot-to-lot consistency in their pooled HLM product? What steps are taken to ensure the quality of the single donors used to make the pooled tissue fraction products?**

Depending on the product, lot-to-lot consistency is maintained by careful formulation of the pools (Cat. No. 452161) or by using a large number of single donors in the pool composition (Corning UltraPool HLM 150 [Cat. No. 452117], and the 50-donor pool [Cat. No. 452156]). Donor tissues with evidence suggesting degradation (e.g. a high “P420” peak consistent with P450 degradation) are not used.

### **What are the advantages of the Corning UltraPool HLM 150?**

- ▶ The large number of donors used to make Corning UltraPool HLM 150 helps to ensure lot-to-lot consistency (please refer to Application Note 467).
- ▶ The Corning UltraPool HLM 150 is prepared as large lot sizes (same lot available for multiple years); suitable for long-term programs.
- ▶ Corning UltraPool HLM 150 (150 donors) is the best representation of an average patient in the population.

### **What types of single donor HLM products are offered by Corning Life Sciences?**

Corning Life Sciences provides allelic variants for CYP2D6, 2C8, 2C9, 2C19, 3A5, and UGT1A1. Individual donors carrying the different allelic variants are grouped together under a single catalog number. Consult the donor charts to identify the donors which best meet your needs and specify this donor with your order.

Corning Life Sciences also provides a single donor HLM panel (with high to low CYP activities). The single donor panel consists of 12 to 15 single donor HLM representing a broad range of CYP activities. The CYP activities from each donor vary independently from one another (low correlation between any two CYP activities). As with the allelic variants, these single donors are grouped under a single catalog number. Consult the donor charts to identify the donors which best meet your needs and specify this donor with your order.

### **What characterization data is provided with Corning® HLM products?**

The single donor and 20-donor pool (Cat. No. 452161) are characterized for 10 CYP activities, FMO, and 3 UGT activities (refer to web site/product data sheet for characterization details). Corning UltraPool™ HLM 150 and the 50-donor pool have additional characterization: 2 more UGT activities (UGT2B7 and UGT1A6) and immuno-quantitation of CYP3A4 and CYP3A5. Corning UltraPool HLM 150 also has full enzyme kinetics for the major drug metabolizing CYPs, more extensive immunoquantitation of CYPs, and the extrapolation factor (milligram microsomal protein per gm liver tissue) provided as supplemental data.

### **Does Corning Life Sciences offer HLM, S9, and cytosol prepared from the same single donors?**

Yes, both the 50-donor pool and Corning UltraPool HLM 150 have matching S9 and cytosol products. The 50-donor pool matched set product is available as a kit; the three fractions can be purchased together as Cat. No. 452227.

**Corning acquired the Gentest™ and UltraPool™ brands.**

For additional Corning product, technical, or distributor information, please e-mail us at [CLSTechServ@corning.com](mailto:CLSTechServ@corning.com), visit our website [www.corning.com/lifesciences](http://www.corning.com/lifesciences) or call 800.492.1110. Outside the United States, call 978.442.2200.

For information on the acquisition, visit [www.corning.com/discoverylabware](http://www.corning.com/discoverylabware).

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