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## Product Information

### CYTOCHROME P450 CYP2D6 ISOZYME Human, Recombinant Microsomes with Cytochrome P450 Reductase

Product Number **C 5232**  
Storage Temperature  $-70\text{ }^{\circ}\text{C}$

#### Product Description

The microsomal product is prepared from insect cells (*Sf 9*) infected with recombinant baculovirus containing cDNA inserts for the human cytochrome P450 isozyme and rabbit cytochrome P450 reductase. Metabolism by endogenous insect cytochromes P450 has not been detected.

Cytochrome P450 enzymes are a superfamily of heme containing monooxygenases, which are found primarily in the mammalian liver and catalyze the oxidative metabolism of xenobiotics. This metabolism is the initial step in the biotransformation and elimination of a wide variety of drugs and environmental pollutants from the body. These reactions are achieved through a mixed monooxygenase system with the general EC number of 1.14.14.1.<sup>1</sup>

The CYP2D6 isozyme is responsible for the 4-hydroxylation of debrisoquine and for the metabolism of many antidepressant and neuroleptic drugs. It is the major enzyme involved in the formation of both R- and S-norfluoxetine, though on long-term exposure, the enantiomers of fluoxetine and norfluoxetine inhibit CYP2D6. CYP2D6 may be involved in the formation of the hepatotoxic N-acetyl-p-benzyquinone imine from acetaminophen.

The cytochrome P450 enzymes range in molecular weight between 45 to 60 kDa.

The product is supplied as 0.5 nmole of cytochrome P450 isozyme in a solution of 100 mM potassium phosphate, pH 7.4, with 1.0 mM EDTA, 1.0 mM DTT, and 20% (v/v) glycerol. Cytochrome c reductase activity, turnover activity, and protein content of the microsomes are reported on a lot-to-lot basis.

Cytochrome P450 Content:  $\geq 80$  pmole cytochrome P450 (spectral analysis) per milligram protein.

#### Precautions and Disclaimer

In general,  $\leq 1\%$  of the total reaction volume may be organic solvent. Any solvent at a concentration between 1 and 5% will have a serious effect on P450 activity. If it is necessary to use concentrations  $> 1\%$ , acetonitrile should be used since it has less of an effect on substrate metabolism. DMSO should never be used, since a concentration as low as 0.2% may inhibit certain types of cytochrome P450 activity.

This product is for laboratory research use only. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

#### Preparation Instructions

1. Quickly thaw at  $37\text{ }^{\circ}\text{C}$  using a water bath. Keep on ice until ready to use.
2. If not using entire contents, aliquot to minimize freeze-thaw cycles.
3. Store aliquots at  $-70\text{ }^{\circ}\text{C}$ .

#### Storage/Stability

The product is shipped on dry ice and should be stored at  $-70\text{ }^{\circ}\text{C}$ . The product as supplied is stable for at least 18 months. For prolonged storage, freeze in working aliquots at  $-70\text{ }^{\circ}\text{C}$ . Avoid repeated freezing and thawing.

#### References

1. Enzyme Nomenclature, IUBMB, Academic Press (1992).
2. Anzenbacher, P., and Anzenbacherova, E., Cytochromes P450 and metabolism of xenobiotics. *Cell Mol. Life Sci.*, **58**, 737-747 (2001).
3. Ishii, M., et al., Interaction of plasma proteins with cytochromes P450 mediated metabolic reactions: inhibition by human serum albumin and alpha-globulins of the debrisoquine 4-hydroxylation (CYP2D) in liver microsomes of human, hamster and rat. *Toxicol. Lett.*, **119**, 219-225 (2001).
4. Otani, K., and Aoshima, T., Pharmacogenetics of classical and new antipsychotic drugs. *Ther. Drug Monit.*, **22**, 118-121 (2000).

5. Ring, B.J., et al., Identification of the human cytochromes P450 responsible for in vitro formation of R- and S-norfluoxetine. *J. Pharmacol. Exp. Ther.*, **297**, 1044-1050 (2001).
6. Dong, H., et al., Involvement of human cytochrome P450 2D6 in the bioactivation of acetaminophen. *Drug Metab. Dispos.*, **28**, 1397-1400 (2000).
7. Kronbach, T., et al., High-performance liquid chromatographic assays for bufuralol 1'-hydroxylase, debrisoquine 4-hydroxylase, and dextromethorphan O-demethylase in microsomes and purified cytochrome P-450 isozymes of human liver. *Analytical Biochemistry*, **162**, 24-32 (1987).

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