**Background Information**

- Human carboxylesterases (CE) are Phase I drug metabolising enzymes of the serine hydrolase superfamily. They hydrolyse a variety of ester containing drugs and prodrugs.

- Carboxylesterase inhibitors may play a role in improved efficacy of compounds inactivated by this class of enzymes and/or reduce the toxicity of agents that are activated by these enzymes.

- Cyprotex’s carboxylesterase inhibition assay identifies if your compound is an inhibitor of the carboxylesterase (CE) isoforms, hCE1, using hCE1-b and hCE1-c recombinant enzymes.

---

**Protocol**

- **Test System**
  hCE1-b and/or hCE1-c expressed enzymes

- **Substrates**
  Trandolapril (hCE1)

- **Metabolites**
  Trandolaprilat (hCE1)

- **Test Article Concentrations**
  0, 0.4, 1, 4, 10, 40 and 100 µM (different concentrations available)

- **Positive Control Inhibitors**
  Benzil (hCE1)

- **Test Article Requirements**
  100 µL of a 40 mM DMSO solution (or equivalent amount in solid)

- **Analysis Method**
  LC-MS/MS

- **Data Delivery**
  IC$_{50}$
  Standard error of IC$_{50}$
  % Control at each concentration

---

*Hatfield M.J. and Potter P.M. (2011) Expert Opin Ther Pat 21(8): 1159-1171*
‘modulation of CE activity’ may present an opportunity to alter drug metabolism and pharmacokinetics, with the ultimate goal of improving therapy.\textsuperscript{11}

Figure 1

Inhibition of trandolapril (hCE1 substrate) metabolism in recombinant hCE1-b by benzil.

References

\textsuperscript{1} Hatfield M.J. and Potter P.M. (2011) Expert Opin Ther Pat 21(8);1159-1171