

# CYP Induction & RIS Services

## Supporting confident decision-making in drug development

Cytochrome P450 (CYP) enzymes metabolize many drugs. Some compounds induce CYP expression, accelerating their own metabolism or that of co-administered drugs, which can lower exposure, reduce efficacy, or cause toxicity or therapeutic failure.

## Why CYP induction studies matter

Regulatory agencies (FDA, EMA) recommend early assessment of CYP induction potential to guide clinical study design and manage drug–drug interaction (DDI) risks.



## Our Capabilities:

- Solubility pre-screening
- Cytotoxicity evaluation
- Primary human hepatocyte assays for CYP1A2, CYP2B6, CYP3A4
- Optional screening for CYP2Cs (CYP2C8, CYP2C9 and CYP2C19) when induction of CYP3A4 is positive
- mRNA and enzyme activity analysis for transcriptional and functional induction
- Relative Induction Score (RIS) approach to predict clinical relevance from in vitro data
- Qualified positive controls spanning non-inducers to strong inducers
- Expedited study options: 4 weeks TAT with draft report for three donors and three major isoforms (1A2, 2B6, 3A4)
- Custom study designs from early discovery through to NDA submission

## Discovery to Development – From Insight to Impact

Pharmaron's experienced scientists deliver high-quality, reproducible data packages to support decision-making, DDI risk mitigation, and regulatory filings. Our validated platforms and deep DMPK expertise help accelerate your development timelines.

## Relative Induction Score (RIS)

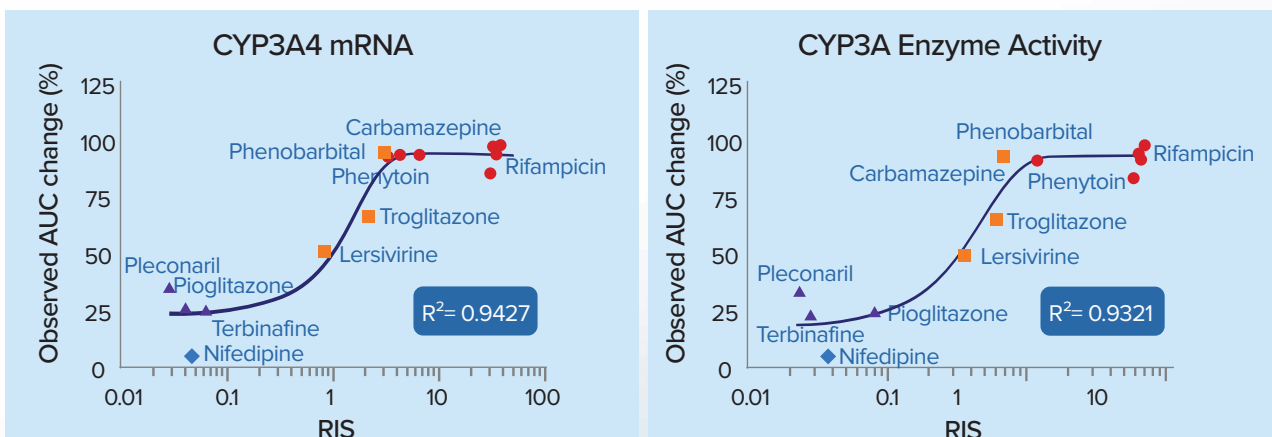
### Pharmaron's RIS Methodology

- Uses cryopreserved plated human hepatocytes treated with 7-point concentration curves for each model compound
- Is validated with a wide range of known clinical inducers: rifampicin, phenytoin, carbamazepine, phenobarbital, troglitazone, lersivirine, pleconaril, pioglitazone, terbinafine, and nifedipine
- Covers the full clinical induction spectrum — from non-inducers to strong inducers
- Generates robust, regulatory-accepted predictions to inform clinical study design

### Why Pharmaron?

Our RIS platform is internally validated and embedded within our broader range of DMPK service offerings. We deliver reliable data and expert interpretation to help clients manage DDI risk and meet global regulatory requirements.

### RIS Calibration Curves for mRNA and Enzyme Activity



The data demonstrates a strong correlation, with  $R^2 > 0.9$ , between the observed midazolam AUC change in humans (as reported in the literature [1, 2]) and the calculated RIS values from both CYP3A enzyme activity and CYP3A4 mRNA.

1. J. George Zhang et al., Drug Metabolism and Disposition, 2014, 42, 1379-1397
2. Odette A. Fahmi et al., Drug Metabolism and Disposition, 2008, 36 (9), 1971-1974



Laboratory Services



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Biologics & CGT

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