

# ADME and Safety

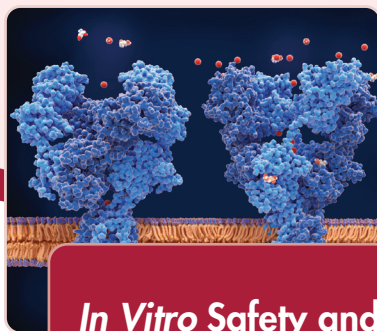
Unlocking the Potential of *In Vitro* Solutions for Safer Pharmaceuticals

## Obtain early read on potential drug safety issues

Predicting potential safety liabilities early in drug discovery is paramount for effective lead compound selection. *In vitro* safety screening enables you to test your compound's selectivity based on its structure and activity to efficiently select a lead candidate with minimal off-target effects and optimal potency.

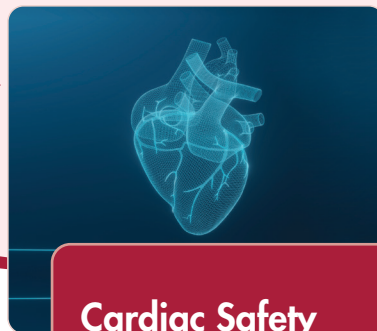
## Our Solutions for ADME and Safety

Our solutions for *in vitro* safety profiling allows you to determine the interaction between your compounds and a broad range of targets that may cause adverse drug reactions in humans.



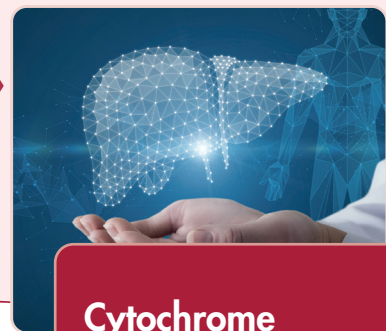
### *In Vitro* Safety and Toxicity Screening

- Enzymatic, biochemical binding, radioligand binding, and functional assays
- A range of available targets including GPCRs, nuclear receptors, cytochrome P450s, ion channels, and more



### Cardiac Safety Assessment

- *In vitro* hERG binding assays
- Ion channel screening with patch clamp
- Tissue-based action potential recording using isolated Purkinje fibers
- Organ-based ECG recording using Langendorff preparations



### Cytochrome P450 Assays

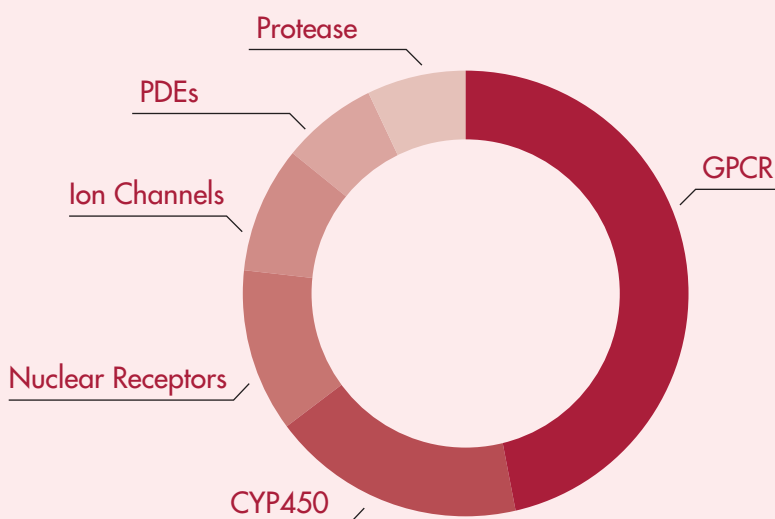
- Small to large scale CYP profiling
- High throughput CYP screening
- Tailored solutions

# Validated Targets by Family

Our validated targets include receptors, transporters, enzymes, and ion channels.

Early safety profiling includes more than 50 targets across 6 target families for broad coverage of potential adverse drug effects.

All of our selected targets are clinically relevant. Their inhibition was shown to cause potentially serious health problems.



## Discover our InVEST™ Panels

### *In Vitro* Evaluation of Safety and Toxicity (InVEST) Made Simple

Our InVEST panels are specifically designed to help you investigate your compound's effects on a large selection of targets. Adding your compound to our monthly screening runs is an efficient and economical way to address your *in vitro* safety screening needs.

- More than 50 targets
  - Radioligand binding, enzymatic activity, and fluorescent polarization assay formats
  - Cell-based patch clamp for ion channel screening including hERG, NaV1.5, and CaV1.2
  - Manual and automated patch formats
  - Compound profiling against the 12 most important CYP isoforms to provide early guidance on a compound's toxicity
  - Simple "mix-and-read" fluorescent assay for high-throughput analysis
- #### InVEST Biochemical

  - A growing panel of more than 15 targets
  - Fully customizable target selection

#### InVEST Functional

#### InVEST Cardiac

#### InVEST Kinase

  - A kinase safety panel including more than 25 kinase targets

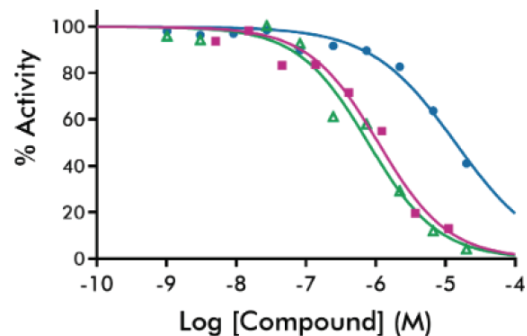
#### InVEST CYP

# Why Choose from our InVEST Panels?

- **Efficiency:** selected targets from our InVEST panels are enrolled in monthly screening runs
- **Robustness:** InVEST Panel screens are set up as single concentration testing in duplicates
- **Quality Assurance:**  $IC_{50}$  values of reference controls are included for each assay
- **Expertise:** direct access to our safety pharmacologists for expert consultation

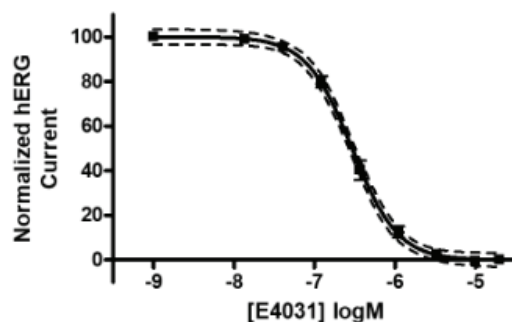
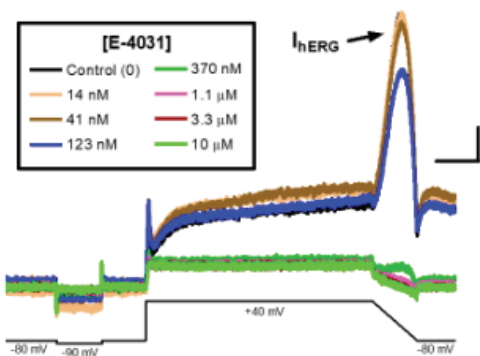
Test your compound against our pre-set panels or build your own panel suited to your unique project needs

## Sample Data



IBMX (blue,  $IC_{50}$ = 14 $\mu$ M, Slope=-0.72) methoxyquinazoline (green, 782 nM, -0.86) and Rolipram (red, 1.1  $\mu$ M, -0.86) tested against activity of cAMP-specific cyclic phosphodiesterase 4A (PDE4A)

## Recording of hERG current by manual patch



Example recording of hERG current ( $I_{hERG}$ ) from CHO hERG-Duo cells (B'Sys) using manual patch.

Concentration-dependent effect of E-4031 on hERG current recorded using manual patch (n=23, 6 independent preparations):  $IC_{50}$ =294 nM, Hill Slope=-1.53).

# Discover our Panels

InVEST Biochemical Panel			
Target Family	Target Name	Assay Format	Species
Biogenic amine transporter	Serotonin transporter	Radioligand filter binding	Human
Cholinesterase	Acetylcholinesterase	Enzymatic activity	Human
Cyclooxygenase	COX-1	Enzymatic activity	Ovine
	COX-2	Enzymatic activity	Human
Cytochrome P450	CYP1A2	Enzymatic activity	Human
	CYP2A6	Enzymatic activity	Human
	CYP2B6	Enzymatic activity	Human
	CYP2C19	Enzymatic activity	Human
	CYP2C8	Enzymatic activity	Human
	CYP2C9	Enzymatic activity	Human
	CYP2D6	Enzymatic activity	Human
	CYP2E1	Enzymatic activity	Human
	CYP2J2	Enzymatic activity	Human
	CYP3A4	Enzymatic activity	Human
CYP3A5	Enzymatic activity	Human	
GPCR	Adenosine A1 Receptor	Radioligand filter binding	Human
	Adrenergic α1A Receptor	Radioligand filter binding	Human
	Adrenergic α2A Receptor	Radioligand filter binding	Human
	Adrenergic β1	Radioligand filter binding	Human
	Adrenergic β2	Radioligand filter binding	Human
	CCK1 Receptor	Radioligand filter binding	Human
	Dopamine D1 Receptor	Radioligand filter binding	Human
	Dopamine D2S Receptor	Radioligand filter binding	Human
	Dopamine D3 Receptor	Radioligand filter binding	Human
	Histamine H1 Receptor	Radioligand filter binding	Human
	Muscarinic M1 Receptor	Radioligand filter binding	Human
	Muscarinic M2 Receptor	Radioligand filter binding	Human
	Muscarinic M3 Receptor	Radioligand filter binding	Human
	Muscarinic M4 Receptor	Radioligand filter binding	Human
	Muscarinic M5 Receptor	Radioligand filter binding	Human
	Opioid δ Receptor	Radioligand filter binding	Human
	Opioid κ Receptor	Radioligand filter binding	Human
Opioid μ Receptor	Radioligand filter binding	Human	
Serotonin 5-HT1A Receptor	Radioligand filter binding	Human	
Serotonin 5-HT1B Receptor	Radioligand filter binding	Human	
Ion Channel	GABAA Receptor hERG	Radioligand filter binding Fluorescence Polarization	Rat Human

InVEST Functional Safety Panel*		
Name	Assay Format	Technology
5-HT2A Human Serotonin	Agonist/Antagonist	FLIPR/Ca assay
5-HT2B Human Serotonin	Agonist/Antagonist	FLIPR/Ca assay
α1A Human Adrenoceptor	Agonist/Antagonist	FLIPR/Ca assay
CB1 Human Cannabinoid	Agonist/Antagonist	FLIPR/Ca assay
DAT Human Dopamine Transporter	Inhibitor	FLIPR/NT assay
D1 Human Dopamine	Agonist/Antagonist	Envision/cAMP assay
H1 Human Histamine	Agonist/Antagonist	FLIPR/Ca assay
M3 Human Muscarinic	Agonist/Antagonist	FLIPR/Ca assay
μ Human Opioid	Agonist/Antagonist	FLIPR/Ca assay
δ Human Opioid	Agonist/Antagonist	FLIPR/Ca assay
κ Human Opioid	Agonist/Antagonist	FLIPR/Ca assay

\*for targets currently not listed please get in touch



## Reaction Biology Corp.

- 1 Great Valley Parkway, Suite 2 Malvern, 19355, PA, USA
- sales@reactionbiology.com
- +1.610.722.0247

v1.1 March 2024

**REACTION**  
**BIOLOGY**