

Safety Pharmacology Solutions

In Vitro Safety Profiling for Early De-Risking

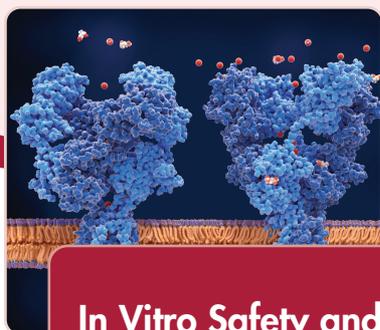
Tiered Off-Target Screening For Every Development Stage

Off-target activity is a leading cause of late-stage drug failure. *In vitro* safety pharmacology profiling evaluates compounds against GPCRs, ion channels, transporters, enzymes, and nuclear receptors clinically linked to adverse drug reactions—enabling discovery teams to design around liabilities before costly *in vivo* studies.

Reaction Biology’s InVEST platform provides tiered panels from hit confirmation (InVEST18) through extensive profiling (InVEST77). Functional assays distinguish agonist from antagonist activity. **Kinases profiled at 1mM ATP** reduce false positives. **10 business day turnaround** from Malvern, PA.

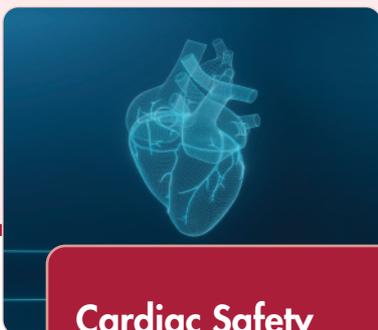
Our Solutions for Safety Pharmacology

Determine compound interactions across target classes associated with adverse drug reactions in humans.



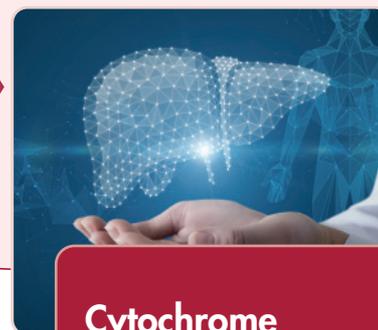
In Vitro Safety and Toxicity Screening

- Tiered panels: InVEST18, 44, 59, 77
- Radioligand binding, fluorescence polarization, enzymatic, and functional assays
- GPCRs, ion channels, transporters, kinases, nuclear receptors, and other enzymatic targets
- All kinases at 1mM ATP
- 10 business day turnaround



Cardiac Safety Assessment

- hERG binding (fluorescence polarization)
- Manual patch clamp: hERG, Nav1.5, Cav1.2, KCNQ1
- Automated patch clamp: GABAA, expanded throughput
- Tissue-based action potential recording (Purkinje fibers)



Cytochrome P450 Assays

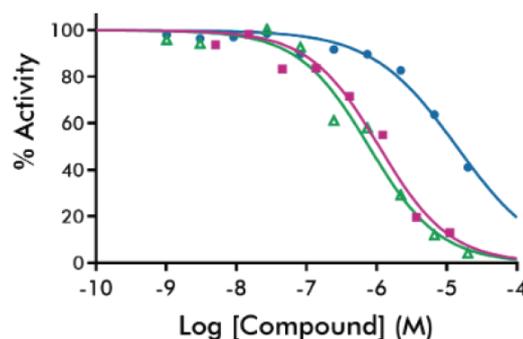
- 14 CYP isoforms including 1A2, 2C9, 2C19, 2D6, 3A4
- Reversible inhibition screening
- Time-dependent inhibition (TDI) assessment
- CYP induction screening
- High-throughput P450-Glo™ format

Why Choose InVEST?

- **Speed:** 10 business day turnaround for all panel sizes
- **Efficiency:** Monthly screening runs with predictable scheduling
- **Flexibility:** Single-concentration or full dose-response for any target
- **Translational Relevance:** Kinases at 1 mM ATP reduce false positives
- **Quality Assurance:** Reference compound IC50 values included for each assay

Test your compound against our preselected targets or build your own panel suited to your unique project needs

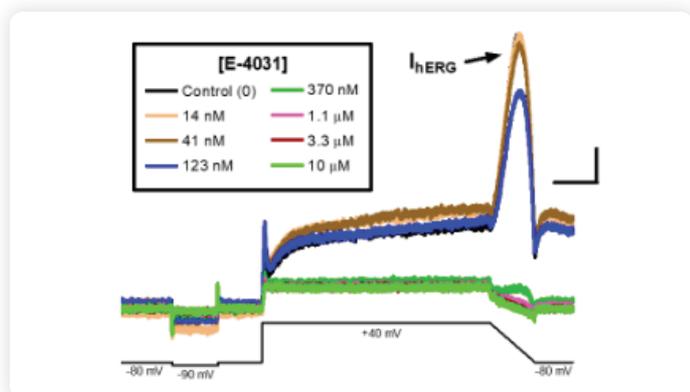
Sample Data: Enzymatic Activity Assay with a PDE



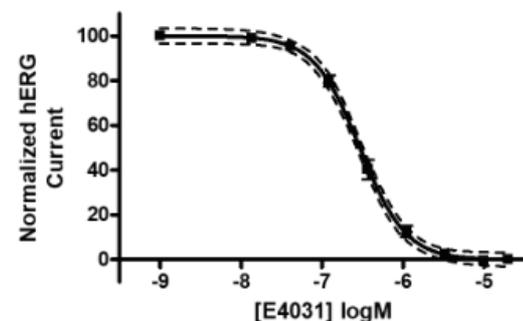
Three reference compounds IBMX, methoxyquinazoline, and Rolipram were tested against the activity of cAMP-specific cyclic phosphodiesterase 4A (PDE4A). Concentration-response curves are shown with semi-log concentrations in singlicates with the following parameters:

- IBMX (blue): $IC_{50} = 1.4 \times 10^{-5}$, hillslope = -0.72
- Methoxyquinazoline (green): $IC_{50} = 7.82 \times 10^{-7}$, hillslope = -0.86
- Rolipram (purple): $IC_{50} = 1.1 \times 10^{-6}$, hillslope = -0.86

Sample data from InVEST Cardiac 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 Targets

InVEST Panels

Target Family	Target Name	Assay Format	InVEST18	InVEST44	InVEST59	InVEST77	PDE	CYP
Bromodomain	BRD4	AlphaScreening Binding			x	x		
COX	COX-1	Enzymatic Activity		x	x	x		
	COX-2	Enzymatic Activity		x	x	x		
Cytochrome P450	CYP1A2	Enzymatic Activity						x
	CYP2A6	Enzymatic Activity						x
	CYP2B6	Enzymatic Activity						x
	CYP2C8	Enzymatic Activity						x
	CYP2C9	Enzymatic Activity						x
	CYP2C19	Enzymatic Activity						x
	CYP2D6	Enzymatic Activity						x
	CYP2E1	Enzymatic Activity						x
	CYP2J2	Enzymatic Activity						x
	CYP3A4	Enzymatic Activity						x
	CYP3A5	Enzymatic Activity						x
	CYP4A11	Enzymatic Activity						x
	CYP4F3B	Enzymatic Activity						x
CYP19A	Enzymatic Activity						x	
GPCR	Adenosine A2A	Radioligand Filter Binding		x	x	x		
	Adrenergic α1A	Radioligand Filter Binding	x	x		x		
	Adrenergic α2A	Radioligand Filter Binding		x	x	x		
	Adrenergic β1A	Radioligand Filter Binding		x	x	x		
	Adrenergic β2A	Radioligand Filter Binding	x	x		x		
	Cannabinoid CB1	Radioligand Filter Binding	x	x		x		
	Cannabinoid CB2	Radioligand Filter Binding		x	x	x		
	Cholecystokinin CCK1	Radioligand Filter Binding		x	x	x		
	Cholecystokinin CCK2	Radioligand Filter Binding			x	x		
	Dopamine D1	Radioligand Filter Binding	x	x		x		
	Dopamine D2L	Radioligand Filter Binding		x	x	x		
	Dopamine D2S	Radioligand Filter Binding						
	Dopamine D3	Radioligand Filter Binding			x	x		
	Endothelin ETA	FLIPR/Ca Assay			x	x		
	GPBA	Cell Reporter			x	x		
	Histamine H1	Radioligand Filter Binding	x	x		x		
	Histamine H2	Radioligand Binding		x	x	x		
	Mas-related GPCR	FLIPR/Ca Assay			x	x		
	Muscarinic M1	Radioligand Filter Binding			x	x		
	Muscarinic M2	Radioligand Filter Binding			x	x		
	Muscarinic M3	Radioligand Filter Binding	x	x		x		
	NK3 receptor	Radioligand Filter Binding			x	x		
	Opioid (δ)	Radioligand Filter Binding			x	x		
	Opioid (κ)	Radioligand Filter Binding			x	x		
	Opioid (μ)	Radioligand Filter Binding	x	x		x		
	Serotonin 5-HT1A	Radioligand Filter Binding			x	x		
	Serotonin 5-HT1B	Radioligand Filter Binding			x	x		
	Serotonin 5-HT2A	Radioligand Filter Binding			x	x		
	Serotonin 5-HT2B	Radioligand Filter Binding	x	x		x		
	Serotonin 5-HT6	Radioligand Filter Binding			x	x		
Vasopressin V1A	Cell Reporter			x	x			
Ion Channel	Cav1.2	Patch Clamp	x	x		x		
	GABAA (α1/β2/γ2)	Patch Clamp (automated)				x		
	GABAA (Central BDZ)	Radioligand Filter Binding	x	x		x		
	hERG (Kv11.1)	Fluorescence Polarization	x	x		x		
	KV7.1	Patch Clamp			x	x		
	nAChR (α1)	FLIPR/Ca assay			x	x		
	nAChR (α4/β2)	FLIPR/Ca assay		x				
	Nav1.5	Patch Clamp	x	x		x		
	NMDA	Radioligand Filter Binding		x	x	x		
	Serotonin 5-HT3	Radioligand Filter Binding		x	x	x		
Kinase	ATM	HotSpot		x	x			
	Aurora A	HotSpot		x	x			
	Aurora B	HotSpot		x	x			
	c-KIT	HotSpot		x	x			
	EGFR	HotSpot		x	x			
	FGFR1	HotSpot		x	x			
	FMS (VEGFR1)	HotSpot		x	x			
	GSK3B	HotSpot		x	x			
	IR	HotSpot		x	x			
	KDR (VEGFR2)	HotSpot		x	x			
	LCK TK	ADP-Glo	x	x		x		
	MKK7	HotSpot			x	x		
	PDK1	HotSpot			x	x		
	PI3Kg (p110g)	ADP-Glo			x	x		
	PTK2	HotSpot			x	x		
	ROCK1	HotSpot			x	x		
	ROCK2	HotSpot			x	x		
	SRC	HotSpot			x	x		
	STK35	HotSpot			x	x		
	TRKA	HotSpot			x	x		

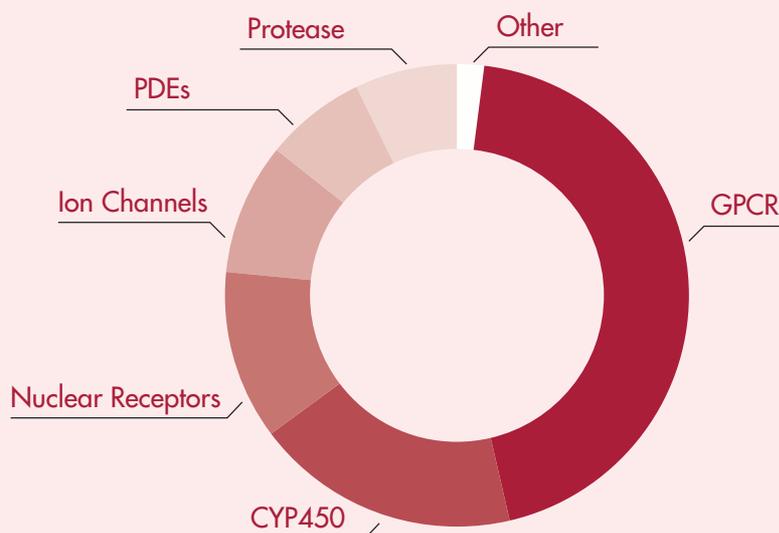
InVEST Panels

Target Family	Target Name	Assay Format	InVEST18	InVEST44	InVEST59	InVEST77	PDE	CYP
MAO	MAO-A	Enzymatic Activity		x	x	x		
	MAO-B	Enzymatic Activity		x	x	x		
Nuclear Receptor	Androgen	Cell Reporter		x	x	x		
	Estrogen- α (ER α)	HotSpot			x	x		x
	Glucocorticoid	Fluorescence Polarization		x	x	x		x
	Progesterone PR	Fluorescence Polarization			x	x		x
Other Enzyme	Retinoic Acid RAR α	Cell Reporter			x	x		x
	Acetylcholinesterase	Enzymatic Activity	x	x		x		x
Phosphodiesterase	PDE1A	Enzymatic Activity					x	x
	PDE1B	Enzymatic Activity					x	x
	PDE1C	Enzymatic Activity					x	x
	PDE2A	Enzymatic Activity					x	x
	PDE3A	Enzymatic Activity	x	x		x	x	x
	PDE3B	Enzymatic Activity					x	x
	PDE4A	Enzymatic Activity					x	x
	PDE4B	Enzymatic Activity					x	x
	PDE4C	Enzymatic Activity					x	
	PDE4D	Enzymatic Activity					x	
	PDE4D2	Enzymatic Activity	x	x		x	x	
	PDE5A	Enzymatic Activity					x	
	PDE7A	Enzymatic Activity					x	
	PDE7B	Enzymatic Activity					x	
	PDE8A	Enzymatic Activity					x	
	PDE8B	Enzymatic Activity					x	
PDE9A	Enzymatic Activity					x		
PDE10A	Enzymatic Activity					x		
Protease	Cathepsin D	Enzymatic Activity			x	x		
	Paracaspase	Enzymatic Activity			x	x		
Transporter	Dopamine (DAT)	Radioligand Filter Binding	x	x		x		
	GAT1	Radioligand Filter Binding			x	x		
	Norepinephrine (NET)	Radioligand Filter Binding	x	x		x		
	Serotonin (SERT)	Radioligand Filter Binding		x	x	x		

Validated Targets by Family

InVEST target selection is derived from industry consensus publications establishing the molecular targets most frequently associated with clinical adverse drug reactions. The Bowes *et al.* (2012) 44-target panel remains the industry standard for early safety screening. Brennan *et al.* (2024) expanded this foundation with additional kinases, transporters, and emerging targets based on post-market safety data.

Our validated targets span **10 families across 100+ individual targets.**



Scan to learn more

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