REACTION BIOLOGY

Safety Pharmacology Solutions

In Vitro Safety Profiling for Early De-Risking

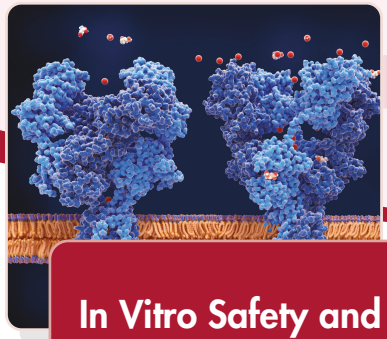
Tiered Off-Target Screening For Every Development Stage

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.

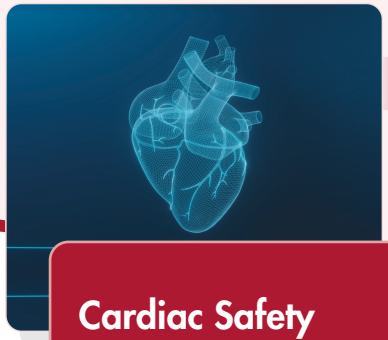
Our Solutions for Safety Pharmacology

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



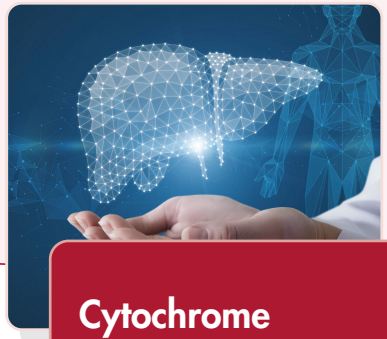
In Vitro Safety and Toxicity Screening

- 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 (MultiClamp 700B): hERG, Nav1.5, Cav1.2, Kv7.1
- Tissue-based action potential recording (Purkinje fibers)
- Langendorff isolated heart (ex vivo whole-heart preparation)



Cytochrome P450 Assays

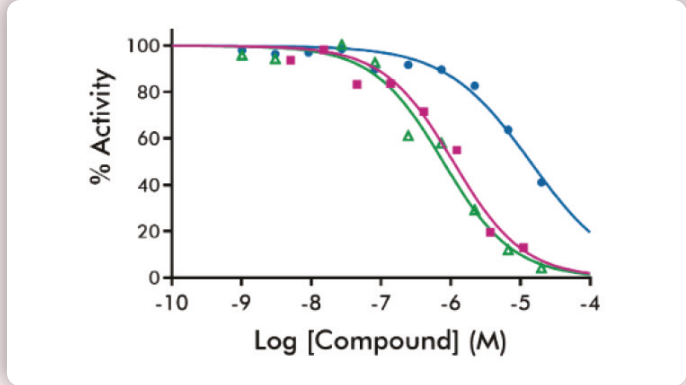
- 14 CYP isoforms including 1A2, 2C9, 2C19, 2D6, 3A4
- Reversible inhibition screening
- Time-dependent inhibition (TDI) assessment
- CYP induction screening
- High-throughput P450-Glo™ format

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 1mM ATP reduce false positives
- **Quality Assurance:** Reference compound IC50 values included for each assay

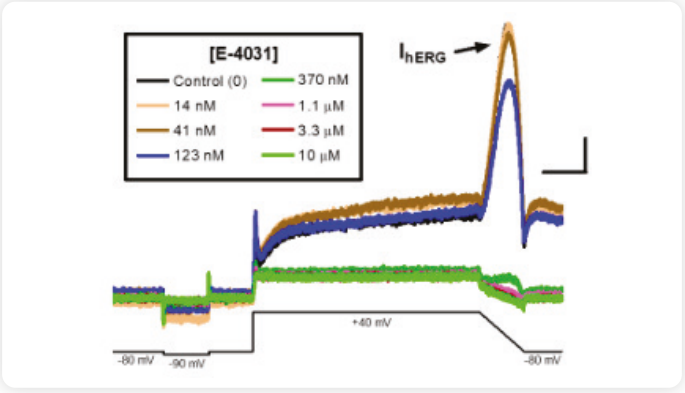
Test your compound against our preselected targets or build your own panel suited to your unique project needs

Sample Data: Enzymatic Activity Assay with a PDE

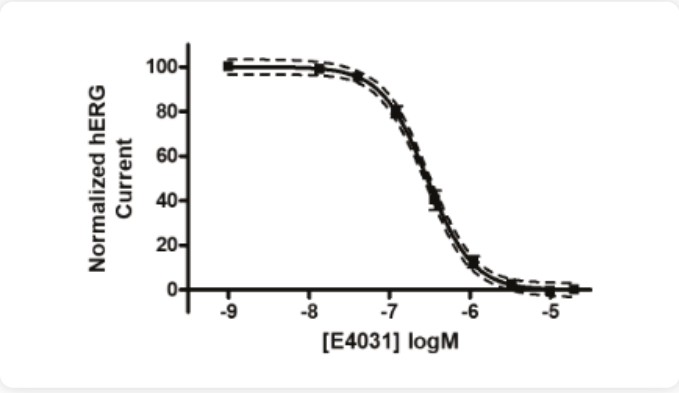


Three reference compounds IBMX, methoxyquinazoline, and Rolipram were tested against the activity of cAMP-specific cyclic phosphodiesterase 4A (PDE4A). Concentration-response curves are shown with semi-log concentrations in singlicates with the following parameters:
- IBMX (blue): IC_{50}= 1.4e-05, hillslope= -0.72
- Methoxyquinazoline (green): IC_{50}= 7.82e-07, hillslope= -0.86
- Rolipram (purple): IC_{50}= 1.1e-06, 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 β1	Radioligand Filter Binding		x	x	x		
	Adrenergic β2	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	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	x		
	Muscarinic M2	Radioligand Filter Binding		x	x	x		
	Muscarinic M3	Radioligand Filter Binding	x	x		x		
	NK3 receptor	Radioligand Filter Binding			x	x		
	Opioid (δ)	Radioligand Filter Binding		x	x	x		
	Opioid (κ)	Radioligand Filter Binding		x	x	x		
	Opioid (μ)	Radioligand Filter Binding	x	x		x		
	Serotonin 5-HT1A	Radioligand Filter Binding		x	x	x		
	Serotonin 5-HT1B	Radioligand Filter Binding		x	x	x		
	Serotonin 5-HT2A	Radioligand Filter Binding		x	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	x		
Ion Channel	Cav1.2	Patch Clamp	x	x		x		
	GABA(A) α1β2γ2L	FLIPR/Membrane Potential				x		
	GABA(A) (Central BDZ)	Radioligand Filter Binding	x	x				
	hERG (Kv11.1)	Fluorescence Polarization	x	x		x		
	Kv7.1	Patch Clamp			x	x		
	nAChR α1	FLIPR/Ca assay			x	x		
	nAChR α4β2	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	HTRF		x	x	x		
	Aurora A	HotSpot		x	x	x		
	Aurora B	HotSpot		x	x	x		
	c-KIT	HotSpot		x	x	x		
	EGFR	HotSpot		x	x	x		
	FGFR1	HotSpot		x	x	x		
	FMS (VEGFR1)	HotSpot		x	x	x		
	GSK3B	HotSpot		x	x	x		
	IR	HotSpot		x	x	x		
	KDR (VEGFR2)	HotSpot		x	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		

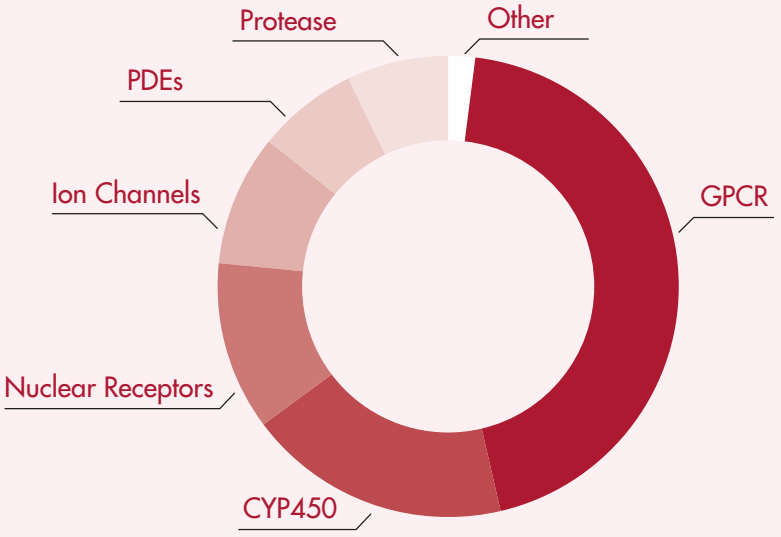
InVEST Panels

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 (AR)	Cell Reporter		x	x	x		
	Estrogen-α (ERα)	Fluorescence Polarization			x	x		x
	Glucocorticoid (GR)	Fluorescence Polarization		x	x	x		x
	Progesterone (PR)	Fluorescence Polarization			x	x		x
	Retinoic acid-α (RARα)	Cell Reporter			x	x		x
Other Enzyme	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.**



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v1.2 Mar. 2026