Innovative CRO+Explorer
ICE Bioscience

ICESTP Safety Panel™

Harnessing Functional Assays for Deeper Insights into Drug Safety

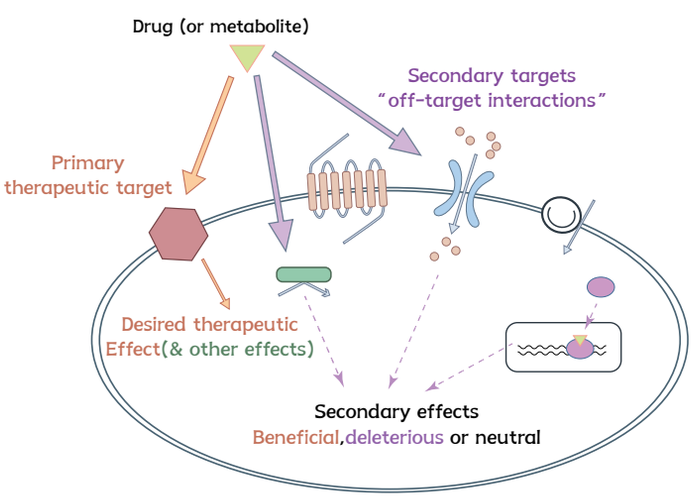
The ICESTP Safety Panels™ 44 and 77 are fully functional secondary pharmacology panels designed to deliver quantitative, mechanism-relevant insights. ICESTP 77, in particular, is the first functional Safety 77 panel available in the market. These panels are built on the latest scientific consensus surrounding secondary pharmacology, as outlined in recent publications such as Nature Reviews Drug Discovery (2024)[1]. These references emphasize the value of early in vitro profiling to identify off-target liabilities and reduce the risk of late-stage failure due to adverse pharmacology.

Why Functional Assays Give You Better Answers:

- Binding ≠ true activity — often overestimates hits
- Functional assays reduce false positives and unnecessary follow-up
- Better at detecting allosteric or agonist effects, especially for ion channels
- Relying on binding alone risks missing key liabilities or rejecting good compounds

Target Class	ICESTP Safety Panel™ 44	ICESTP Safety Panel™ 77
GPCRs	24	30 (6*)
Ion channels	8	8
Enzymes	6	10 (4*)
Kinases	1	20 (19*)
Transporters	3	4 (1*)
Nuclear receptors	2	5 (3*)
No. of Targets	44	77
No. of Assays	74	116
Assay Mode	Single-point or dose–response	Single-point or dose–response

* Numbers in parentheses indicate new targets added in ICESTP Safety Panel™ 77 compared to Panel 44.



ICESTP Safety Panel™ 44

The ICESTP Safety Panel™ 44 reflects the historical core set of off-targets derived from the original Bowes-44[2] panel, aligned with ICH guidelines and regulatory expectations.

ICESTP Safety Panel™ 77

The ICESTP Safety Panel™ 77 expands this scope based on modern data-driven target selection, incorporating additional receptors, enzymes, kinases, and transporters relevant to human safety pharmacology. This panel is fully aligned with the recently published "Safety 77" industry standard.

1. Brennan, R. J. et al. The state of the art in secondary pharmacology and its impact on the safety of new medicines. Nat. Rev. Drug Discov. 23, 525–545 (2024).
2. Bowes, J. et al. Reducing safety-related drug attrition: the use of in vitro pharmacological profiling. Nat. Rev. Drug Discov. 11, 909–922 (2012).

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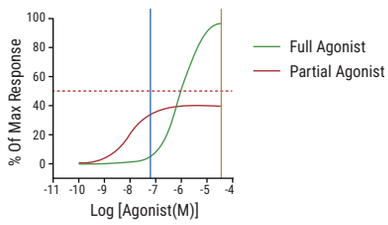
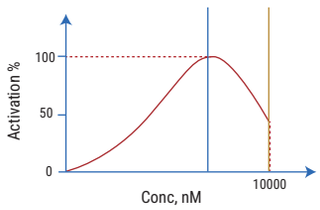
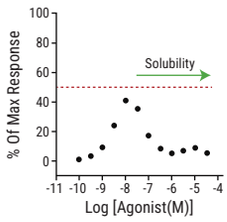
Compared to single-point binding assays, functional screening provides greater predictive value, helping uncover true off-target effects, including agonist or allosteric activity that binding assays might miss.

All ICESTP Safety Panels™ are available in both **single-concentration** and **full dose–response** formats.

Why Dose Response Panel Matters







Distinguish Full vs Partial Agonism

Only dose–response curves can reveal whether a compound is a full or partial agonist. Single-point data may miss functional nuances critical for risk prediction.

Identify Non-Linear Effects

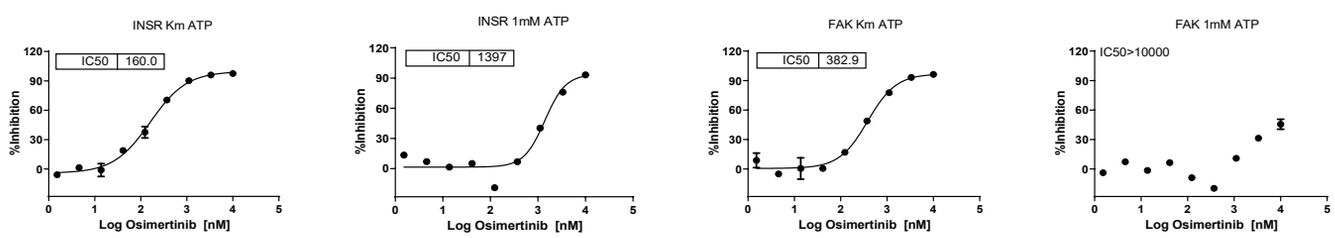
Some targets show bell-shaped dose–response curves. Without full profiling, these effects may be misinterpreted or overlooked entirely.

Avoid Solubility-Driven Misreads

Apparent activity loss at higher doses could result from solubility issues, not biology. Dose–response testing helps differentiate real effects from artifacts.

Functional Kinase Profiling Under Physiological ATP Conditions

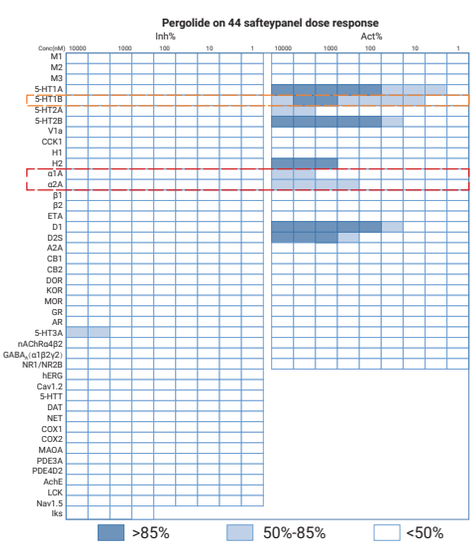
All kinase targets in the ICESTP Safety Panels™ are profiled using **1 mM ATP**, reflecting near-physiological intracellular levels. This helps filter out compounds that appear active only under low-ATP assay conditions but lack meaningful activity at physiological ATP levels — reducing false positives and improving data relevance.



Osimertinib shows potent inhibition of INSR (IC_{50} = 160.0 nM) and FAK (IC_{50} = 322.9 nM) at Km ATP concentrations. However, under 1 mM ATP conditions, its activity is markedly reduced, with an IC_{50} of 1397 nM for INSR and >10,000 nM for FAK, indicating strong ATP-competition sensitivity.

What Makes ICESTP Dose Response Panels Different

- **Top Dose in Duplicate**
  Highest concentration tested in duplicate for data consistency and to confirm borderline signals.
- **Dual Visual Outputs**
  Radar plots and IC_{50}/EC_{50} curves provided for both quick overview and in-depth analysis.
- **Flexible Panel Options**
  ICESTP 44 and 77 support different needs from early screening to pre-IND safety assessment.
- **1 mM ATP for Kinase Assays**
  Kinase profiling at physiological ATP levels (1 mM) to reduce false positives and enhance relevance.
- **Visual Reports with Expert Insights**
  Reports include interactive visuals and expert interpretation—suitable for internal review or regulatory submission.



5-HT1B (orange box) shows a bell-shaped curve—only detectable through full concentration profiling. α1A and α2A (red box) display partial agonist activity, with submaximal effects even at the highest dose.