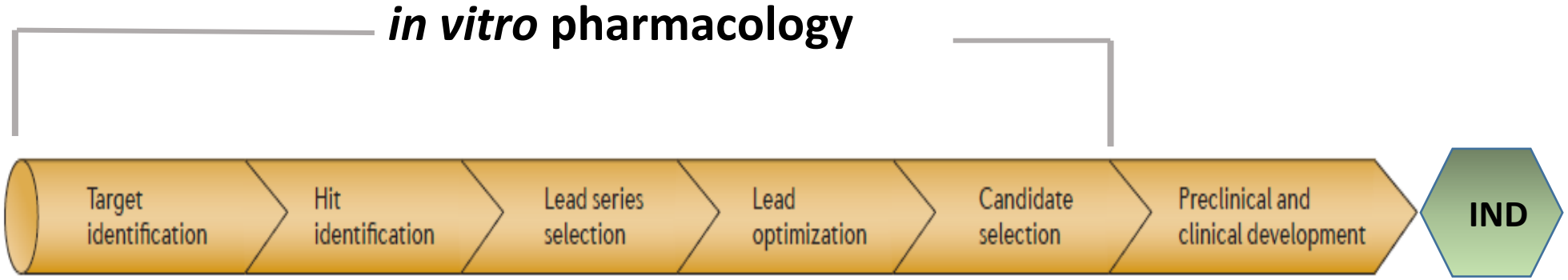
In Vitro Pharmacology Working Group

The *In Vitro* Pharmacology working group

- The In Vitro Pharmacology Working Group (IVP) is the product of a Public-Private Partnership (PPP) between FDA and Pistoia Alliance
- **History:** Researchers at FDA performing work on *in vitro* pharmacology data noted variable assay formats →Making regulatory review and research difficult
- In early 2021, FDA and the Pistoia Alliance began discussing the scope of the IVP
- PPP finalized in June 2022
- Initial focus is on secondary and safety pharmacology

What is *in vitro* Pharmacology?



Screening of large libraries of chemicals for molecules with the necessary properties from a pool of potentially useful compounds ("hits") and narrowed down to identify more promising compounds ("leads")

the most promising molecules undergo further screening

in vitro pharmacology assays are performed at this stage to extensively optimize the biological activity and properties of the leads.

Identification of the best drug candidate that may proceed to pre-clinical trials

Adapted from Reducing safety-related drug attrition: the use of *in vitro* pharmacological profiling. Bowes J. *et al.,* 2012

As per ICH Topic S7A Safety Pharmacology Studies for Human Pharmaceuticals

- **Primary Pharmacology** is defined as “studies on the mode of action and/or effects of a substance in relation to its desired therapeutic target”

- **Secondary Pharmacology** is defined as “studies on the mode of action and/or effects of a substance not related to its desired therapeutic target”
- **Safety Pharmacology** is defined as as “studies that investigate the potential undesirable pharmacodynamic effects of a substance on physiological functions in relation to exposure in the therapeutic range and above.”

Challenges

- Lack of harmonization in terminology and file structure
- Target synonyms and multiple naming conventions
- Code name in assay results needed to be confirmed in other submission documents
- Table structure can differ significantly, making automated extraction difficult

Value Proposition

- Creation of a working platform for collaboration between Biopharm, CROs, technology platform and regulators to develop data standards for *in vitro* bioassays.

- Numerous R&D organisations are initiating a transformation internally to improve drug research agility through new modalities → Rather than working in silos, this approach will achieve more thorough and valuable results faster and cost effectively.

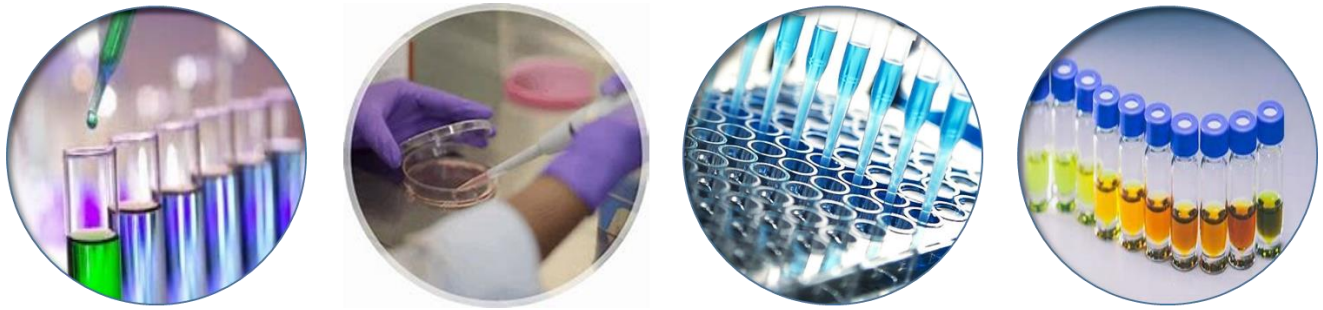
- This approach would also enable seamless collaboration and focus on data centricity

- A common and standardized data structure will be developed, utilizing new or existing ontologies for the description of common assays.

- Creation of a data standard will provide more consistency with regulatory submissions, enabling faster reviews and interpretations of IND submissions by regulatory agencies → This enables more effective analysis leading to deeper insights that result in better decision making.

- Output will be computer and human readable, exportable and the creation of a standardized and common data template would enable cross site collaboration and data transparency → FAIR

		CHALLENGES	BENEFITS OF IMPLEMENTING DATA STANDARD	
Regulators	**Consistency and Clarity**	Inability to evaluate data across studies, difficulty interpreting in vitro pharmacology data leading to slow review	Streamlined data ingestion into GSRS or other system, organized data easier to interpret, **faster review** process	
	Life cycle activities	Mapping assay over time is time consuming	**Faster review**	
	Knowledge management activities		Facilitate identification of of risk factors --> these information would be published and readily available and help to identify more easily candidate molecule that could potentially pose safety problems	
			More efficient *in vitro* pharmacology testing	
Biopharma		Review of dossier may take time delaying drug development progress	Improve speed and efficiency in data processing and review by regulatory agencies, potentially **shortening the time** to deliver therapy to patients in need.	**FASTER & CHEAPER**
CROs		Diverse clients with diverse reporting needs, some clients with limited or no resources for standardizing data, inability to search & analyze across multiple platforms	Provide standardized template to all clients regardless of resources	



IN VITRO PHARMACOLOGY WORKING GROUP

We propose a 3-pronged solution:

- **An agreed standard set of information to be reported for each assay**
- **A public assay database for *in vitro* pharmacology assays**
- **A mechanism for transmission of *in vitro* pharmacology data during IND submission**

How to enable FAIRification of IVP?

1

Standardized Template

Agreed set of information which will comprise of the critical sections required for review by regulatory bodies

2

Ontology

Ontology (A set of concepts and categories in a subject area or domain that shows their properties and relations between them) :

- A controlled vocabulary
- A well-curated ontology → BioAssay Ontology ?

3

Assay protocol registration

- Steps required to run an experiment
- Assay purpose, design time conditions (target and concentration, substrate…), biological model and run-time conditions

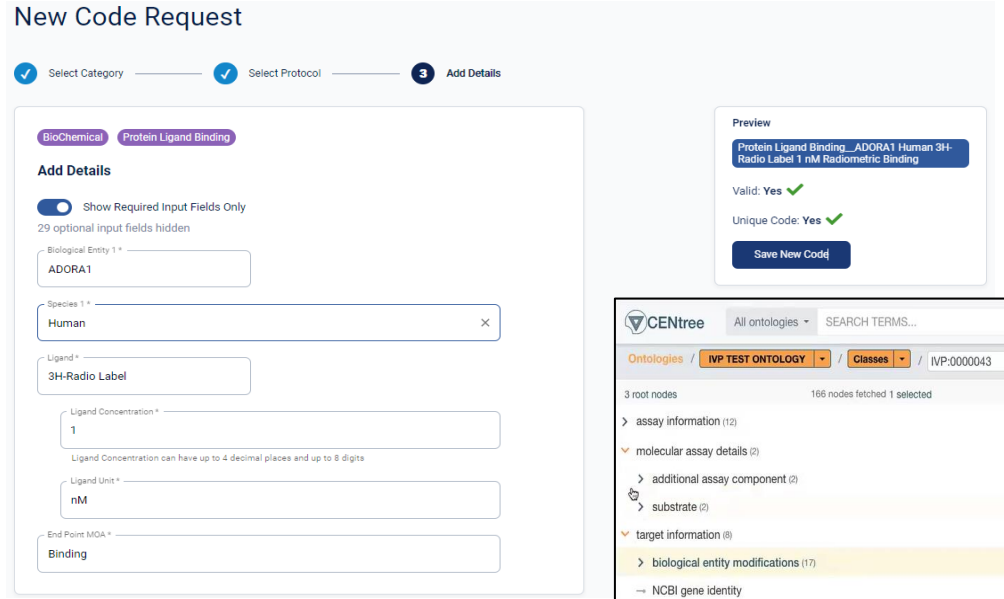
4

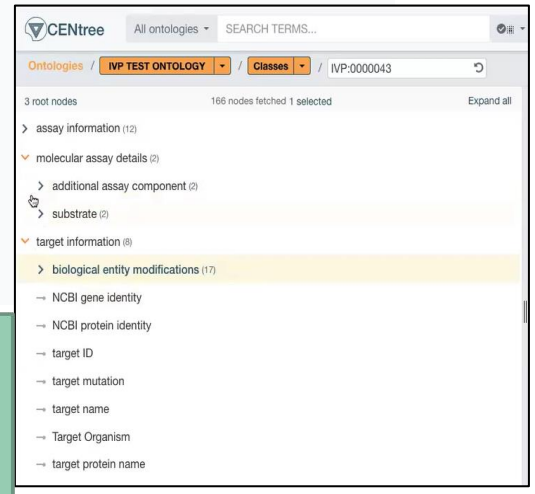
Repository of assays

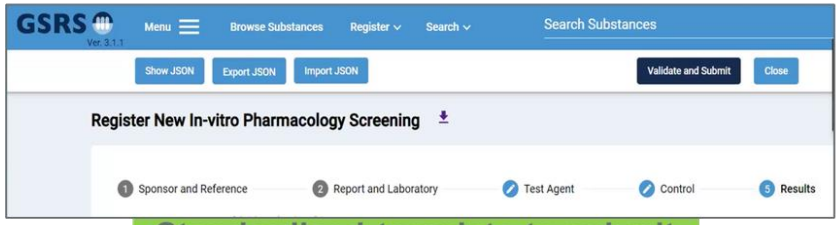
Benefits:

- Provides a global protocol registration platform
- Enables improved assay data searchability
- ID label of each assay to refer in the standardised template.

Project Deliverables







Repository of Assays

A single, open sourced centralised protocol repository

- Integrated Ontology
- Unique Identifier
- Open sourced/accessible

Standardised template to submit *In Vitro* secondary and safety pharmacology to regulatory bodies

- Agreed set of information which will comprise of the critical sections required for review by regulatory bodies
  - Screening assays
  - Quantitative data
- A controlled vocabulary & a well-curated ontology

Global Substance Registration System – GSRS

Assist agencies in registering and documenting information about substances found in medicines.

- A common identifier for all of the substances used in medicinal products
- Utilizing a consistent definition of substances globally, including active substances under clinical investigation
- consistent with the ISO 11238 standard.

What are the key risks and issues?

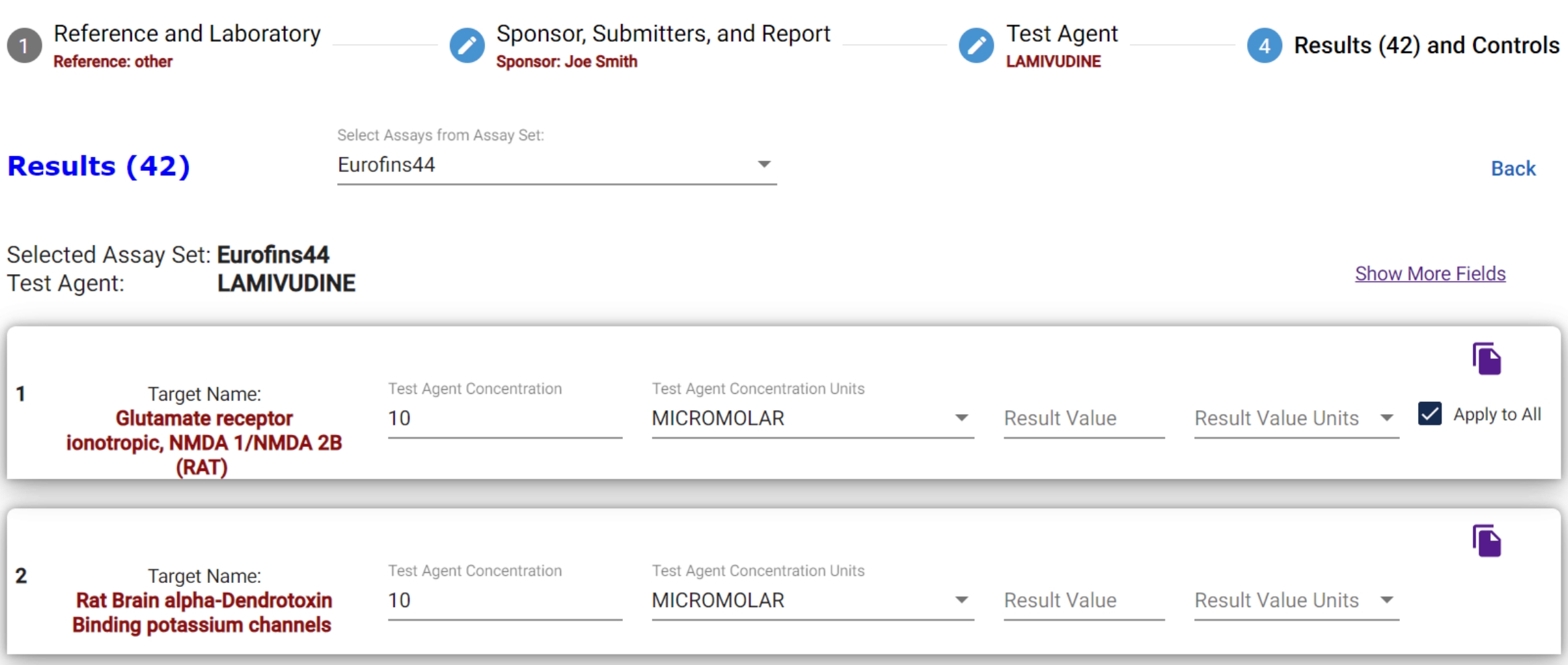
- Key risks and issues
  - Lack of support from Pharma, CRO and regulatory bodies
  - Reluctance to share data across Pharma and/or CRO
  - Lack of funding → End of the IVP working group

Consequences of ending the IVP WG

- IND dossier continues to be submitted in a pdf format → Lack in FAIRification and standardization resulting in a time-consuming process for the regulatory bodies to absorb this data into their information systems.

- A standardized template may become mandatory for submission of IND in the future → Biopharma and CROs would then have to conform to this template which may be completely different to their current process.

Linked to the GSRS



Current Members of the IVP Working Group

Public Private Partnership with the FDA

More information here: https://www.pistoiaalliance.org/community/in-vitro-pharmacology/

Get in touch: ProjectInquiries@PistoiaAlliance.org