

The Systems Toxicology Challenge

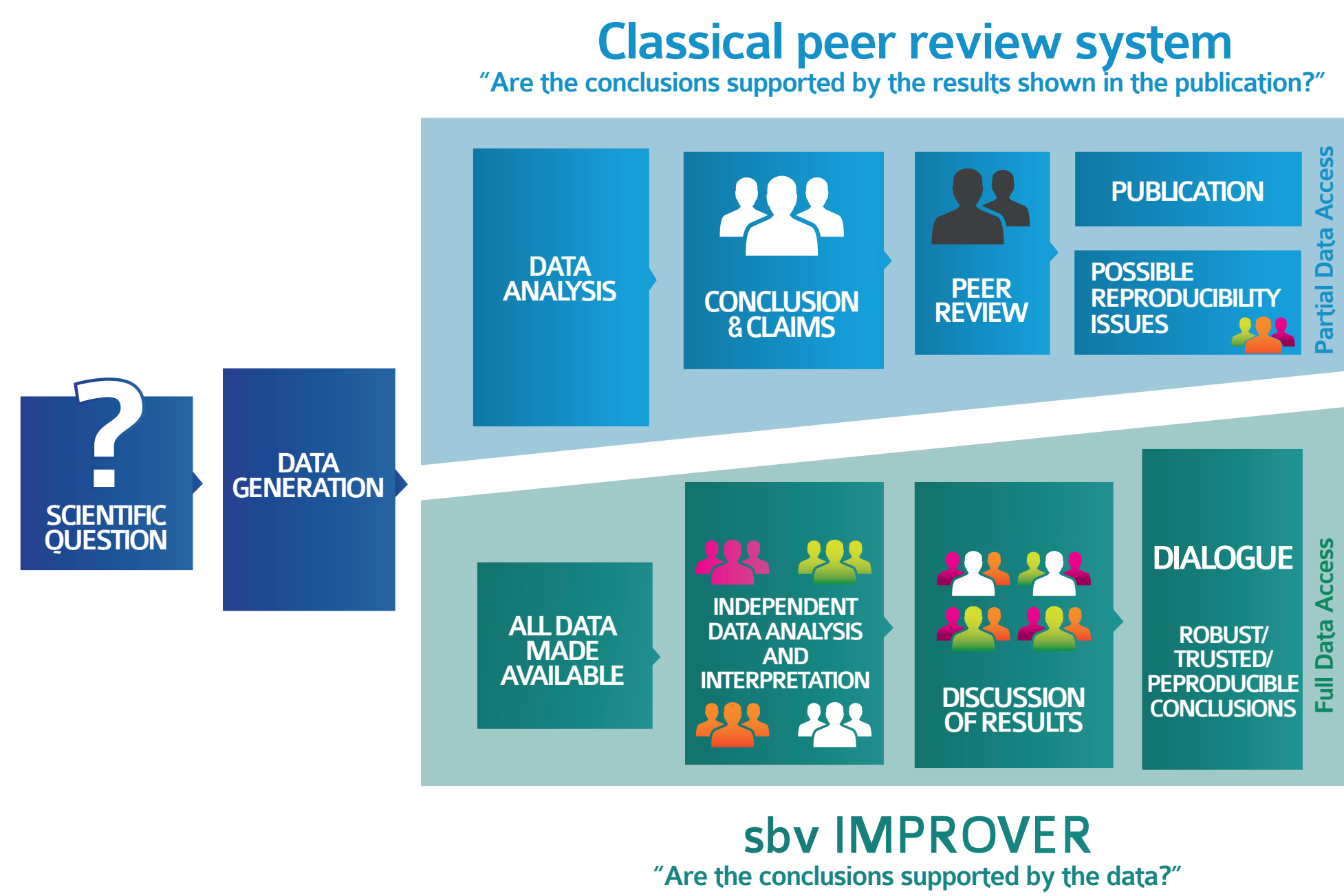
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Abstract

Risk assessment in the context of 21st century toxicology relies on the elucidation and understanding of mechanisms of toxicity. For that purpose, datasets generated by high-throughput technologies (e.g., high-throughput/content screening) combined with various omics data types are now generated in vitro to test diverse set of chemicals (e.g. ToxCast). The development of relevant computational approaches for the analysis and integration of these big data remains challenging. The current scope of sbv IMPROVER (Industrial Methodology for Process Verification in Research; www.sbvimprover.com) is the verification of methods and concepts in systems biology research via challenges opened to the scientific community. Previous challenges brought new insights on methods and their associated results that address questions about diagnostic signatures, the translatability of biological responses/processes across species, and the relevance of biological causal network models. A new sbv IMPROVER challenge will be introduced aiming at evaluating methodologies for the identification of specific biomarkers of exposure when organisms are exposed to individual chemical molecules or mixtures. Participants will be provided with high quality data sets to develop predictive models/classifiers. For this challenge, the integration of a priori biological knowledge in the development of computational approaches may be required to enable biological interpretability/understanding of the predictions. The results and post-challenge analyses will be shared with the scientific community, and will open new avenues in the field of systems toxicology.

sbv IMPROVER

sbv IMPROVER stands for Systems Biology Verification combined with Industrial Methodology for Process Verification in Research. This approach aims to provide a measure of quality control of industrial research and development by verifying the methods used. The sbv IMPROVER project is a collaborative effort led and funded by PMI Research and Development.



sbv IMPROVER Challenges

2014/2015 Network Verification Challenge (NVC)

The NVC Challenge aims at verifying the biological network models to ensure their relevance to lung biology and COPD.

Symposium 2014, Montreux (Switzerland)
Symposium 2015, Barcelona (Spain)

2013 Species Translation Challenge (STC)

Changes in phosphorylation status and gene set activation induced by cellular response to 52 different perturbations in human cells can be predicted to a certain extent given responses generated in rat cells.

Symposium 2012, Boston (USA)

2015-2016 Systems Toxicology Challenge (SysTox)

Objective: to verify that robust and sparse human specific- and species-independent gene signatures of exposure response can be extracted in whole blood gene expression data from human, or human and rodent to predict exposed and non-exposed group labels.

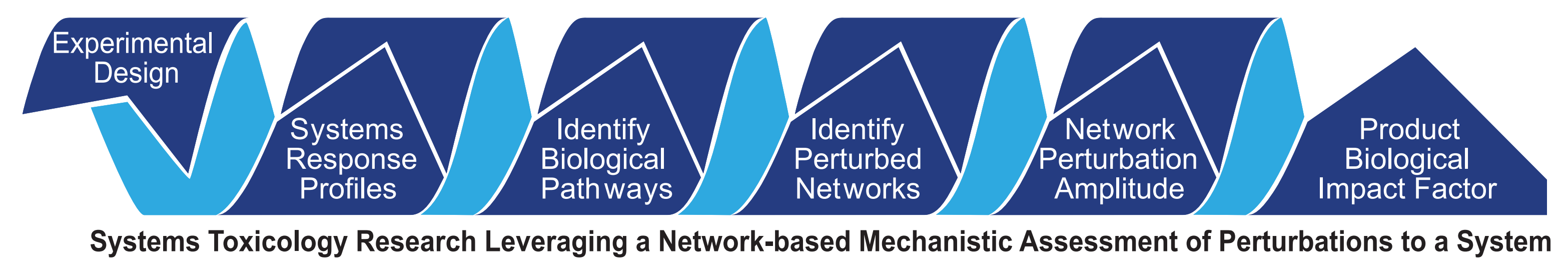
a. Blood samples are collected from human and mouse subjects belonging to exposed or non-exposed groups.
b. Gene expression profiles (GEX) are measured using microarray-based technology.
c. Participants are provided with GEX and asked to develop a classification approach that identifies a gene signature capable to associate subjects to the correct exposure group:

- Sub-challenge1: Human blood signature as exposure response marker for smoking
- Sub-challenge 2: Species translatable blood signature as exposure response marker

Everyone can participate
Knowledge in computational science is an asset

Fall 2015 - Spring 2016

www.sbvimprover.com
sbvimprover.rd@pmi.com

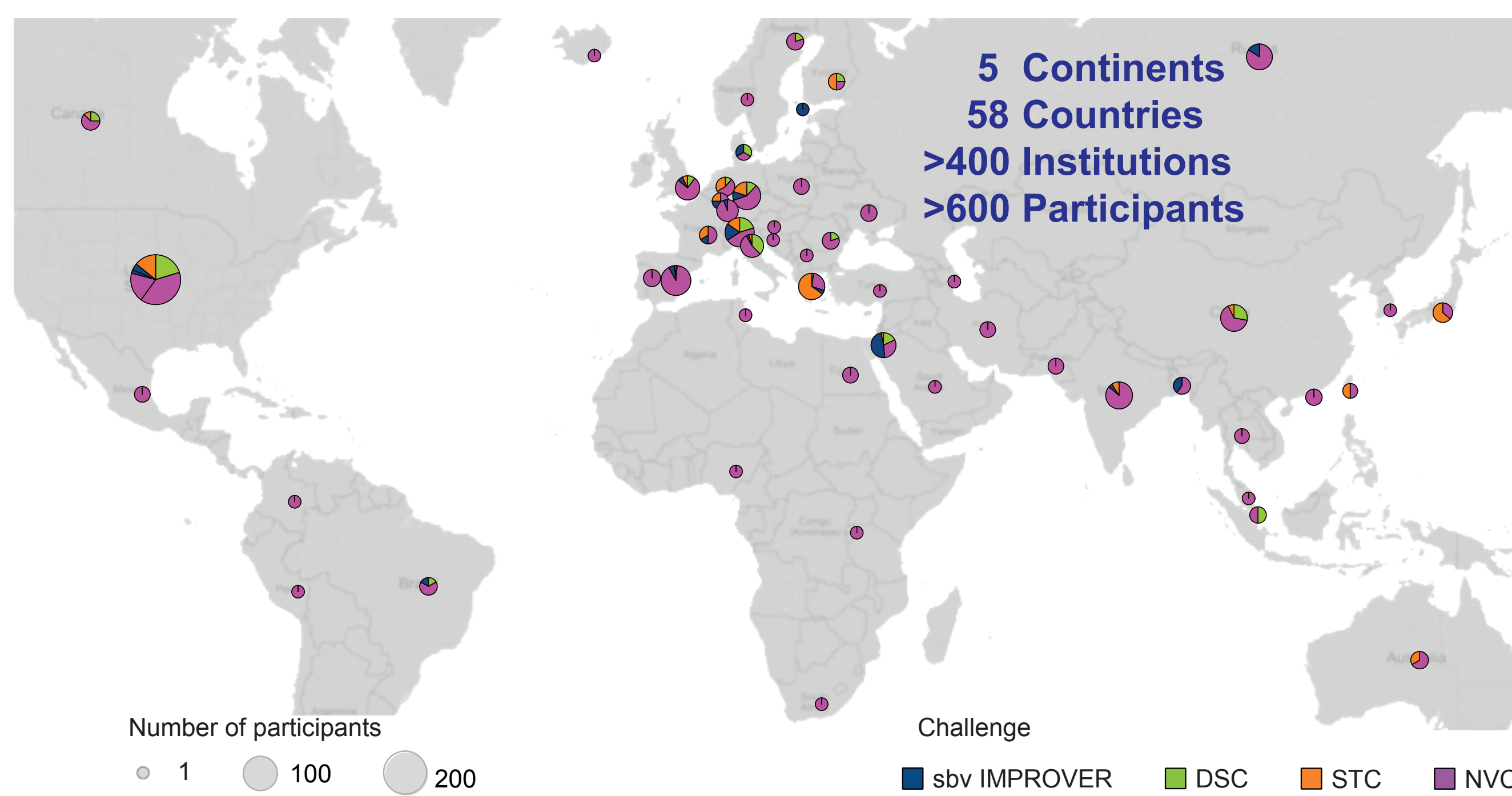


Systems Toxicology Verification

Systems toxicology or 21st century toxicology, aims to create a detailed understanding of the mechanisms by which biological systems respond to toxicants, so that this understanding can be leveraged to assess the potential risk associated with chemicals, drugs, and consumer products. This project will start by conducting a peer review of a Systems Toxicology-based inhalation study performed in rodents across diverse expertise fields. The intention of this review is to go beyond classical peer-review and pilots the SciPi process (scipinion.com) as a model for a more in depth review of a complex study by an independent panel of experts.

Worldwide Participation in sbv IMPROVER

March 2012 - June 2015 / per Country



References

SysTox

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DSC

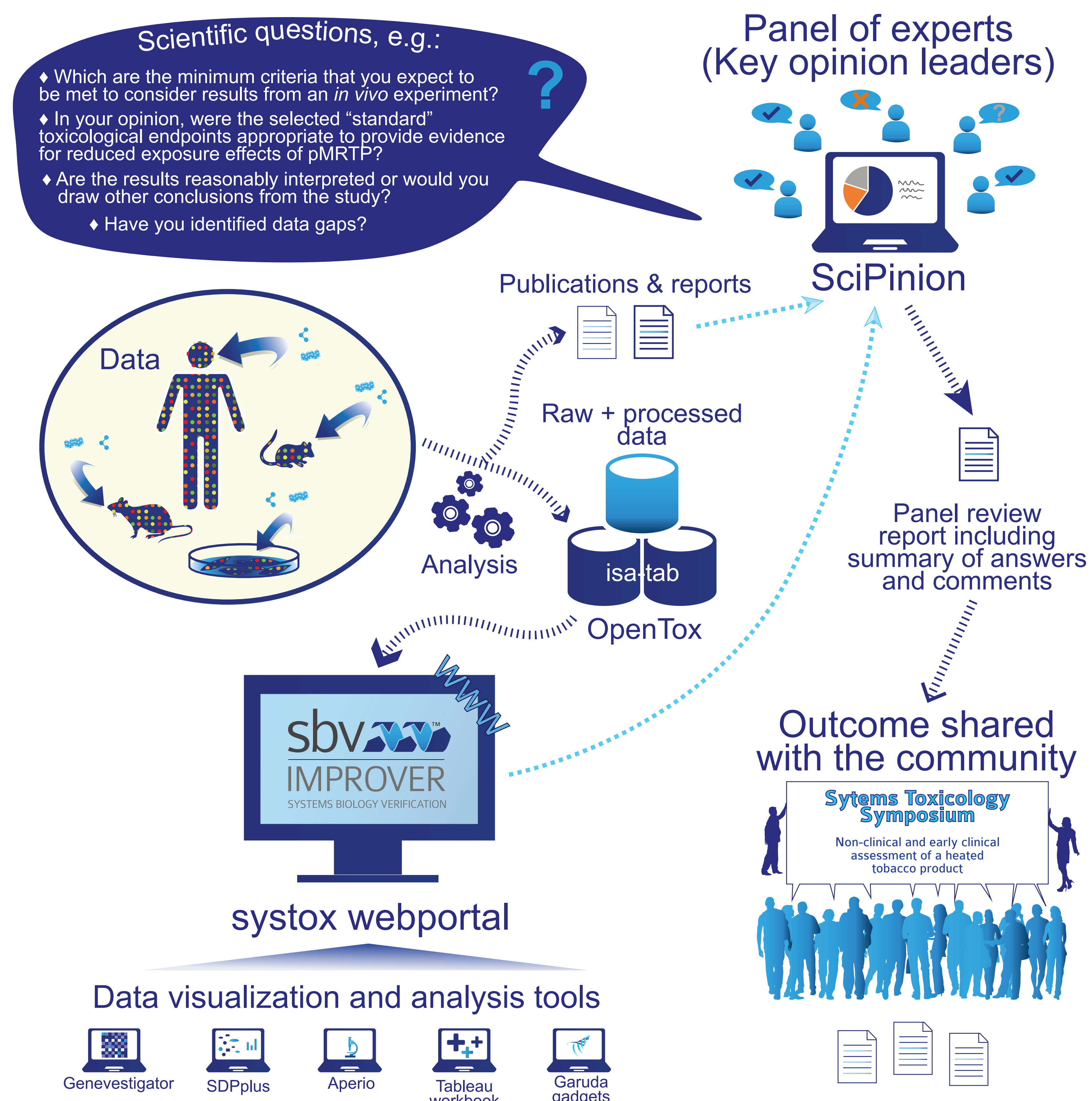
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NVC

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The sbv IMPROVER project, the websites and the Symposia are part of a collaborative project designed to enable scientists to learn about and contribute to the development of a new crowd sourcing method for verification of scientific data and results. The project is led and funded by Philip Morris International. The current challenges, website and biological network models were developed and are maintained as part of a collaboration with Selventa, Douglas Connect, SBX-Garuda, Nebion, OrangeBus and ADS. For more information on the focus of Philip Morris International's research, please visit www.pmscience.com.

