

Avengers Assemble! A Day in the Life of the BSC Technical Working Groups

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BOTANICAL
SAFETY CONSORTIUM

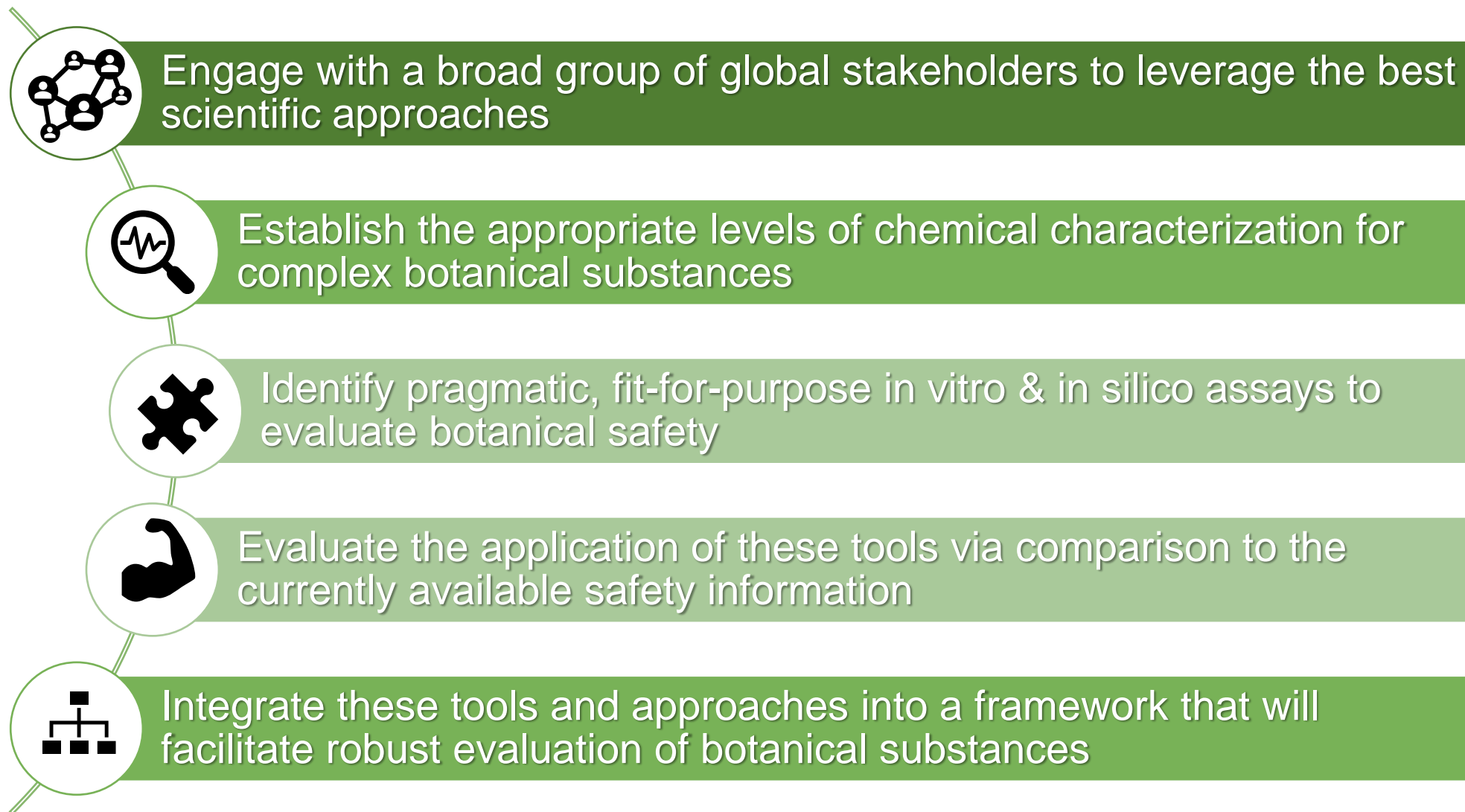
Technical Working Groups

- Technical Working Groups are the **core** technical entities responsible for designing and executing the BSC's scientific mission.
- **Focused on specific scientific questions** related to evaluation of botanical ingredient safety, as defined by each TWG's mission and objectives.
- Being apart of a TWG involves
 - participating in teleconferences;
 - providing technical and strategic input and perspectives during the TWG's ongoing scientific discussions;
 - experimental research;
 - data analysis;
 - writing;
 - communicating on behalf of the TWG.
- Sub-teams within a TWG may be formed as needed on key topics related to the overall TWG mission & objectives.

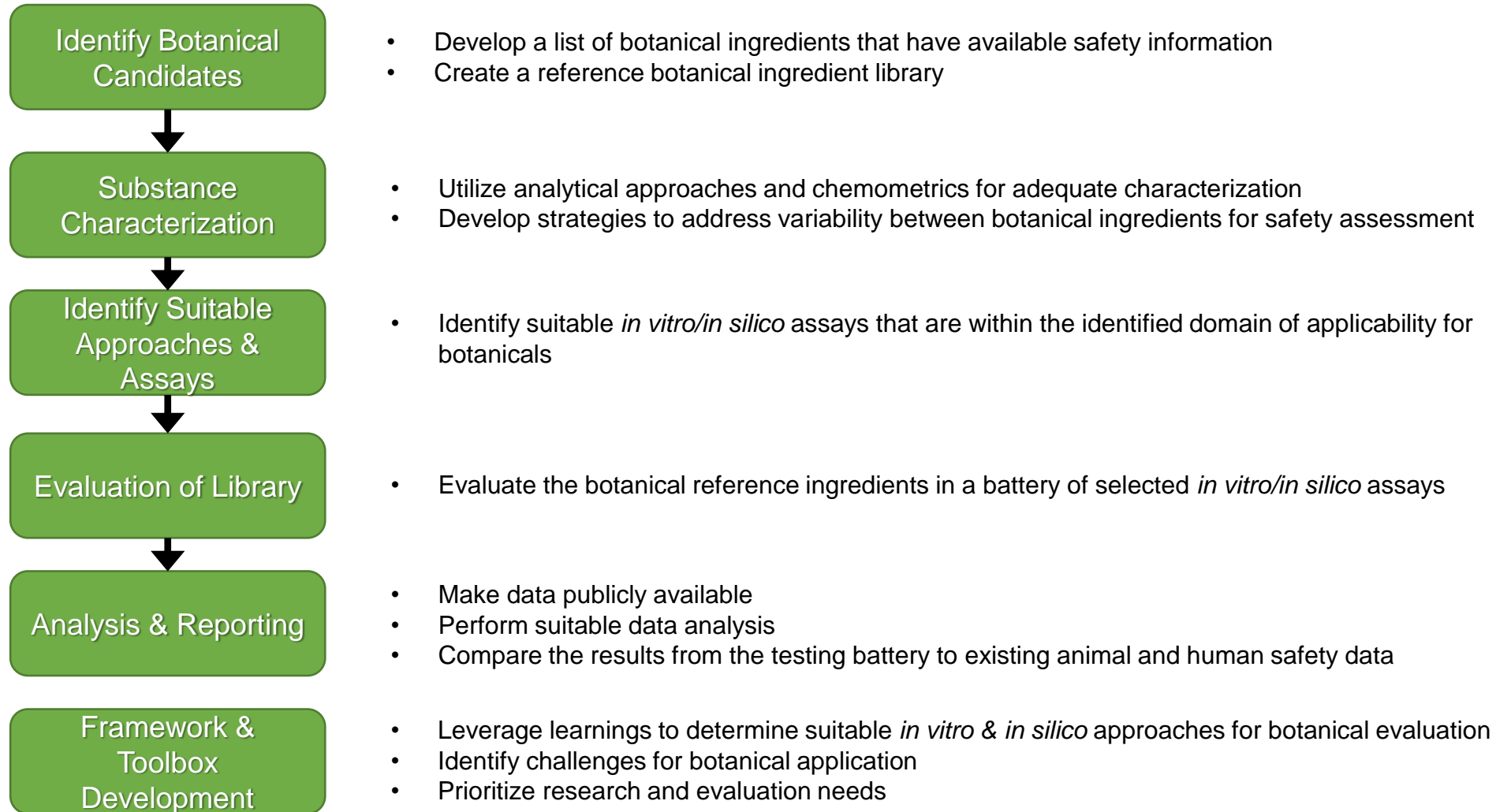
Technical Working Groups: *Composition & Process*

- TWG members may be nominated by BSC Steering Committee, Stakeholder Council members, TWG members, themselves, or staff.
- Eligibility for TWG participation will be evaluated by the BSC Steering Committee and TWG co-chairs **based on scientific and technical expertise** via submission of an application and CV.
- As is feasible, all TWGs will **strive for balance across sectors** (public / private), areas of expertise, and geography.
- Members of the TWG will review membership on a yearly basis

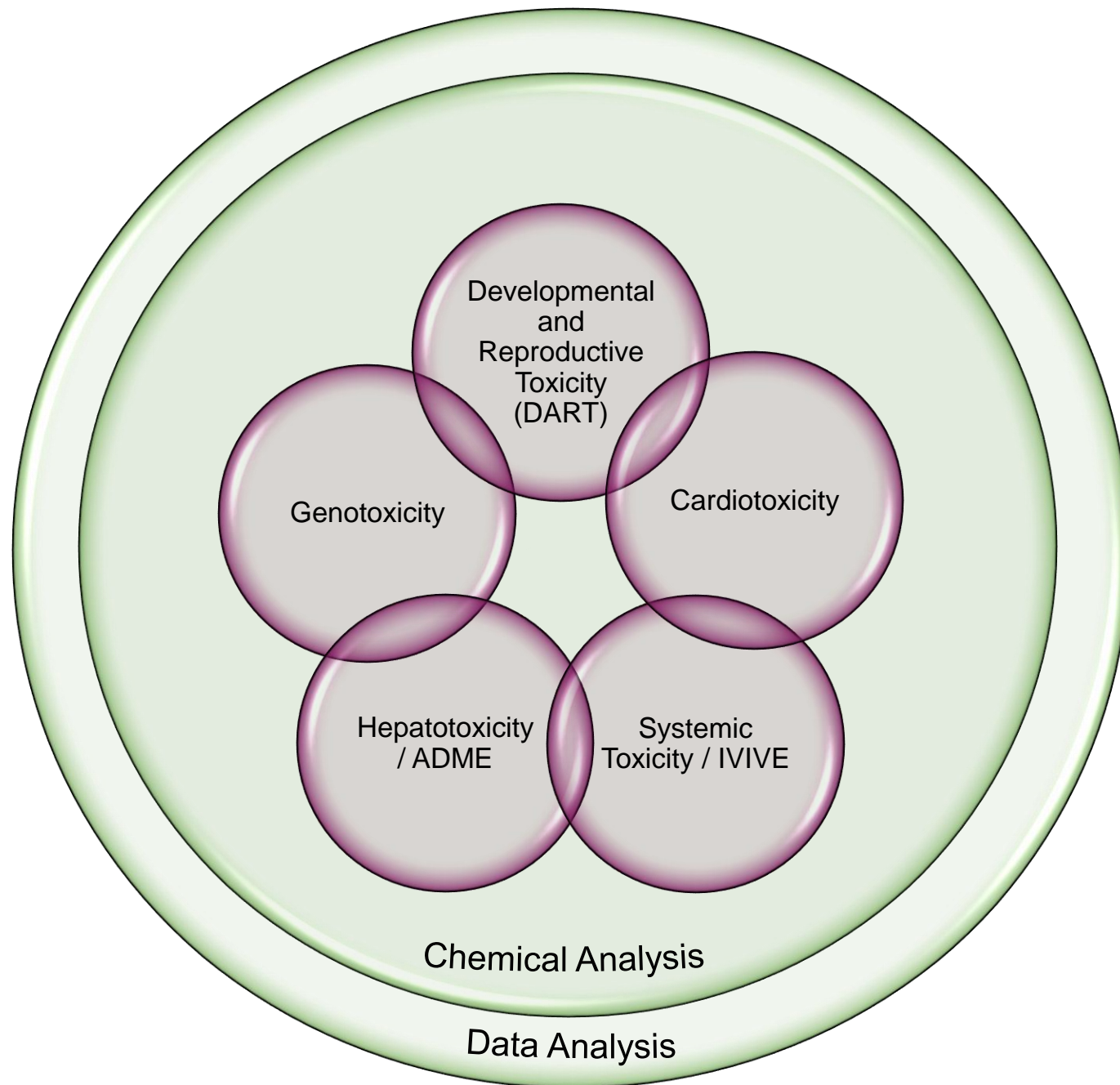
Botanical Safety Consortium Objectives



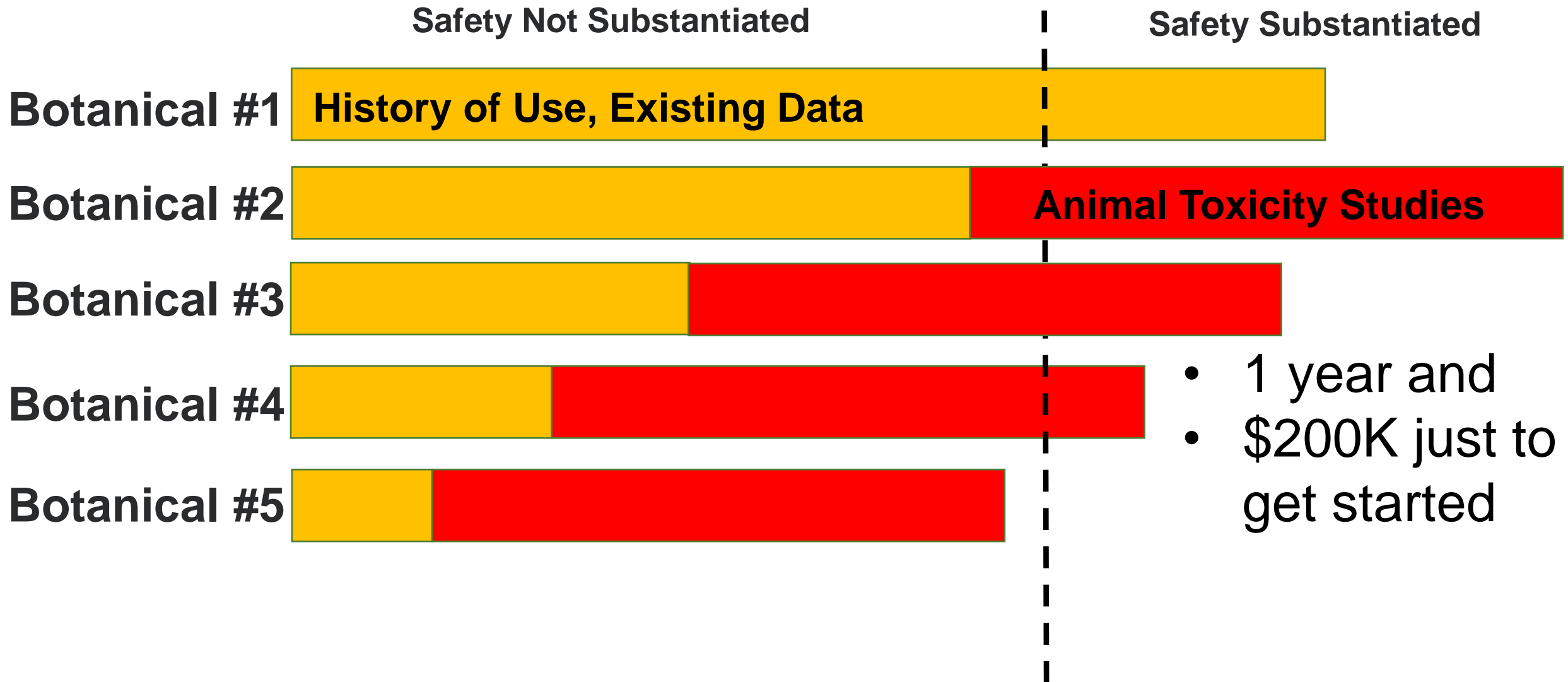
Botanical Safety Consortium Strategy



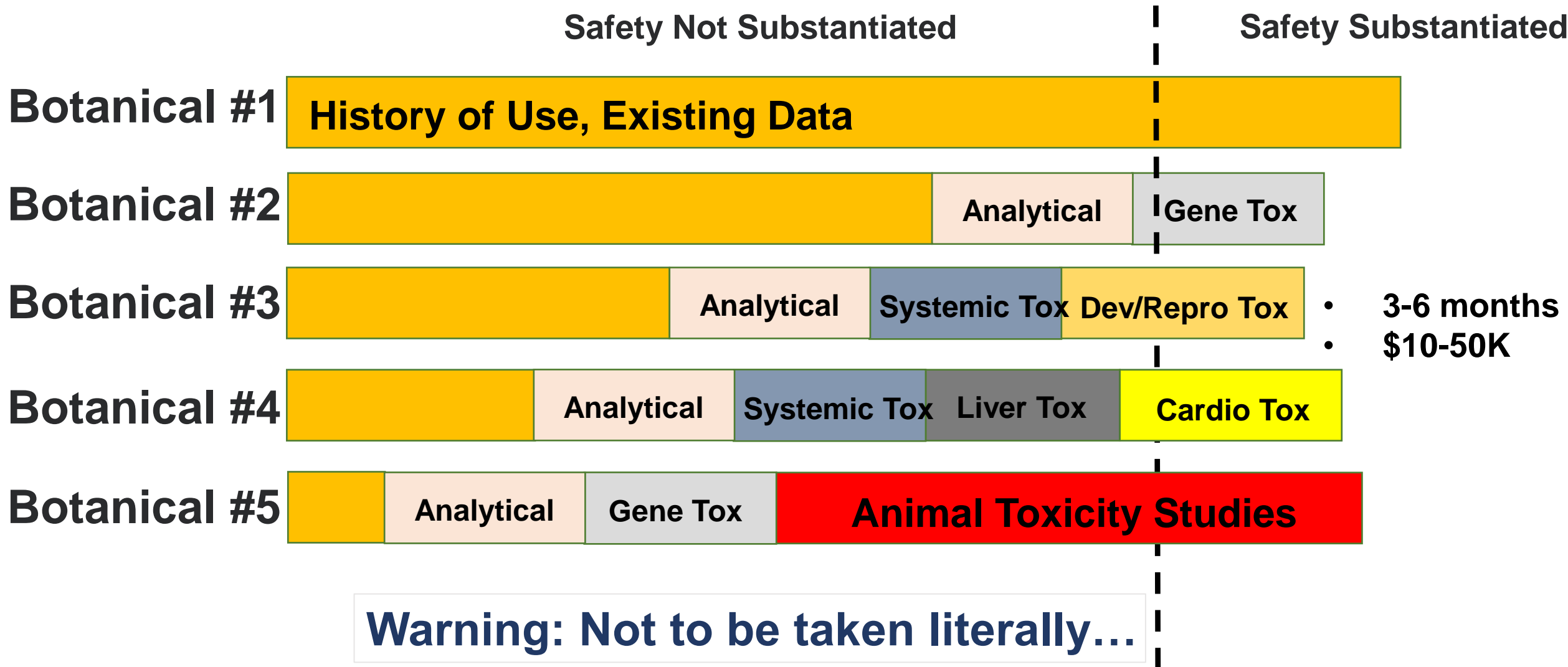
Technical Working Groups



Traditional Botanical Safety Paradigm



Modern Botanical Safety Paradigm



Technical Working Groups

– Current status

- Formation of teams of experts for each of the focus areas
 - Balance of industry, government, and academic scientists
 - Global representation, where possible
- Refining goals and objectives
- Reviewing the state of the science on botanicals research in each of the key areas





Chemical Analysis Mission: To develop a strategy and methodologies to characterize botanical ingredients for the purpose of enabling safety assessments.

Objectives:

- **Prioritize selected candidates for comprehensive chemical characterization** based on the needs of other Technical Working Groups;
- **Identify a strategy to compile existing literature on analytical methods used and chemical composition** of selected botanical ingredients;
- **Select resource-efficient analytical approaches, methods, and partners that can comprehensively characterize botanical ingredients with respect to safety**, including, but not limited to, identifying and quantifying constituents of botanicals to the degree required for material selection and safety assessment.



Chemical Analysis

Current Members

- Rajiv Agarwal (FDA)
- Tim Baker (co-chair, P&G)
- Nadja Cech (UNC Greensboro)
- Kan He (Herbalife Nutrition)
- Ikhlas Khan (University of Mississippi)
- Adam Kuszak (NIH/OD)
- Eike Reich (HPTLC-Association)
- Catherine Rimmer (NIST)
- Elan Sudberg (Alkemist Labs)
- Micheal (Bhodi) Tims (Maryland University of Integrative Health)
- Richard van Breemen (Oregon State University)
- Suramya Waidyanatha (co-chair, NIEHS)
- Hong You (Eurofins)
- Yanjun Zhang (Herbalife Nutrition)



Genotoxicity Working Group Mission: To develop a screening strategy that can reliably identify potential genotoxic botanical ingredients, with future application to evaluate associated human health risks

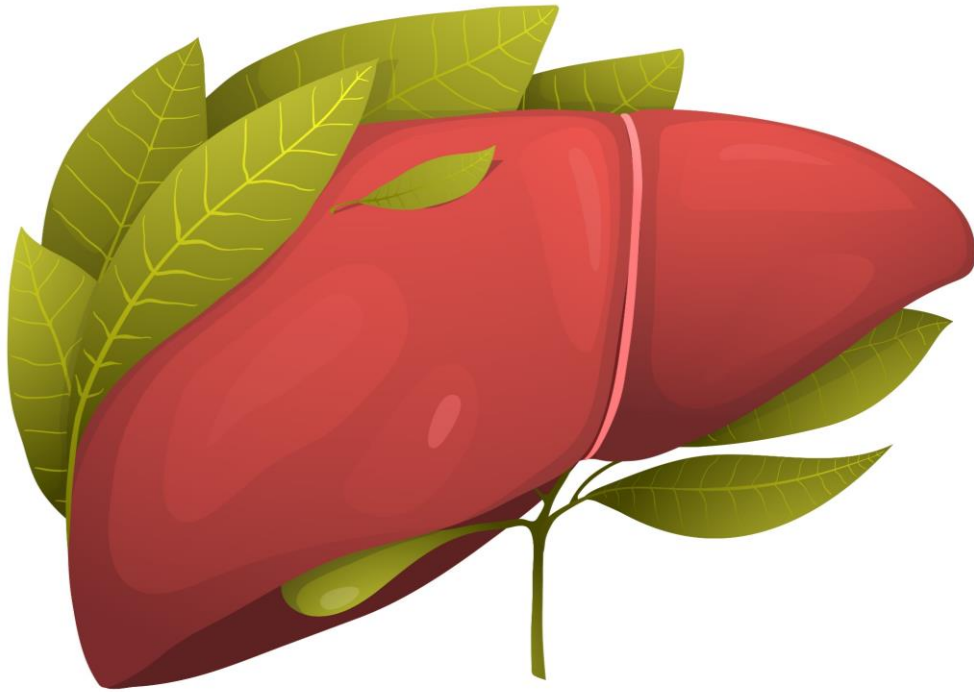
Objectives:

- **Select resource-efficient *in silico* and *in vitro* tools that can identify genotoxic agents** in complex mixtures represented by botanical ingredients;
- **Recommend criteria for identifying significant genotoxic hazards;**
- **Select candidate botanical ingredients** based on suspected toxicity or safety with respect to genotoxicity endpoints;
- **Use a series of botanical case studies** to evaluate the usefulness and reliability of a growing genotoxicity toolbox in the context of *in vivo* outcomes and exposure (where such data are available).



Genotoxicity Working Group Members

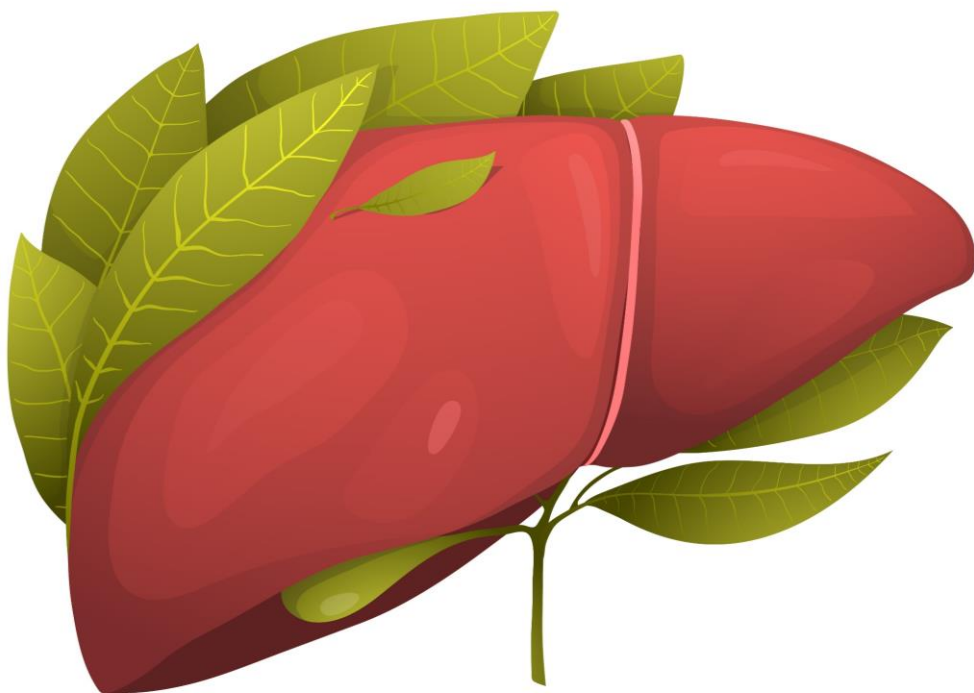
- Gerhard Eisenbrand (Consultant)
- Jim MacGregor (Consultant)
- Nan Mei (FDA/NCTR)
- Stefan Pfuhler (co-chair, Procter & Gamble)
- Ivonne Rietjens (Wageningen University)
- Stephanie Smith-Roe (NIH/NIEHS)
- Helga Stopper (University of Wurzburg)
- Kristine Witt (co-chair, NIH/NIEHS)
- Dan Xi (NIH/NCI)



Hepatotoxicity Working Group Mission: To develop a screening strategy that can reliably identify hepatotoxic botanical ingredients, inform mechanisms of toxicity, and characterize the ‘botanicokinetic’ properties of botanical ingredients.

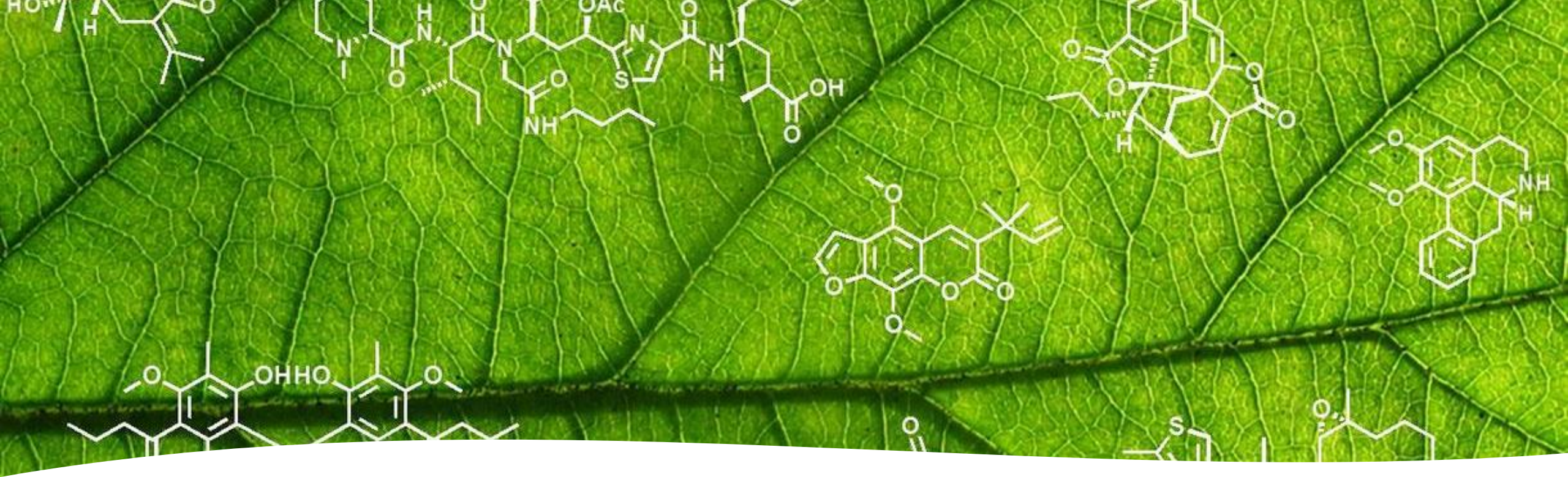
Objectives:

- **Select resource-efficient *in silico* and *in vitro* tools** that can accommodate complex mixtures represented by botanical ingredients. These tools will estimate human liver potential or ADME properties;
- **Select candidate botanical ingredients with respect to hepatotoxicity** based on suspected toxicity or safety, and ADME endpoints;
- **Evaluate the potential and limitations of these tools** to predict and understand botanical ingredient -induced hepatotoxicity;
- **Explore the potential of drug-botanical interactions** using candidate methods.



Hepatotoxicity Working Group Members

- Dennis Cladis (Purdue University)
- Stephen Ferguson (co-chair, NIH/NIEHS)
- Shabana Khan (University of Mississippi)
- Igor Koturbash (U of Arkansas for Medical Sciences)
- Katelyn Lavrich (NIH/NIEHS)
- Albert Li (In Vitro ADMET Laboratories)
- Yitong Liu (FDA)
- Scott Masten (NIH/NIEHS)
- Merrie Mosedale (UNC)
- Amy Roe (co-chair, Procter & Gamble)
- Mathieu Vinken (Vrije Universiteit Brussel)
- Heather Walker (Bayer)
- Paul Walker (Cyprotex)
- Charles Wu (FDA/CDER)



ADME Group

- Will work with all technical working groups to obtain knowledge on toxicokinetic properties of botanical constituents
 - Metabolites need to be examined for potential toxicity



Developmental and Reproductive Toxicity Working Group Mission: To develop screening strategies that can reliably identify potential developmentally or reproductively toxic botanical ingredients.

Objectives:

- **Select *in silico* and *in vitro* tools** that can accommodate complex mixtures represented by botanical ingredients;
- **Select candidate botanical ingredients** based on suspected toxicity or safety with respect to DART endpoints;
- **Establish a series of DART botanical case studies**, such that we can evaluate the usefulness of a growing toolbox.



Developmental and Reproductive Toxicity Working Group Members

- Mark Cronin (Liverpool John Moores University)
- Corrado Galli (University of Milan)
- Amy Inselman (FDA/NCTR)
- Catherine Mahony (co-chair, Procter & Gamble)
- Raymond Pieters (Utrecht University)
- John Rogers (US EPA)
- Vicki Sutherland (co-chair, NIH/NIEHS)



Systemic Toxicity Mission: To develop tools that can reliably identify botanical ingredients with the potential to induce adverse effects within multicompartmental biological systems

Objectives:

- **Develop systematic literature review strategies and tools** to efficiently gather existing history of use and traditional use data for botanical ingredients.
- **Select and leverage multi-compartmental *in vitro* models** to generate systemic safety data for botanicals
- **Improve *in vitro* to *in vivo* extrapolation (IVIVE)** using toxicokinetic modeling to support safety assessments and margin of safety calculations



Systemic Toxicity Working Group Members

Current Members:

- Steven Dentali (Dentali Botanical Sciences)
- Joe Dever (co-chair, Amway)
- Esther Haugabrooks (PCRM)
- Michael Lawless (Simulations Plus)
- Annie Lumen (FDA)
- Jim McKim (IONTOX)
- Bhashkar Mukerji (Givaudan)
- Jürgen Schnabel (Givaudan)
- Nisha Sipes (co-chair, NIH/NIEHS)
- Sibyl Swift (NPA)



Data Analysis Mission: To develop and apply data analytic methods that use *in vitro/in silico* data for safety/hazard assessment of botanical ingredients

Objectives:

- Work with other Technical Working Groups to design experiments;
- Support the data analysis needs of other Technical Working Groups;
- Development, evaluation and/or application of data analysis methods for the determination of botanical ingredient sufficient similarity;
- For a subset of botanical ingredients, characterize the degree of similarity between the toxicological profiles derived from *in vitro/in silico* data compared to those obtained from traditional animal tests

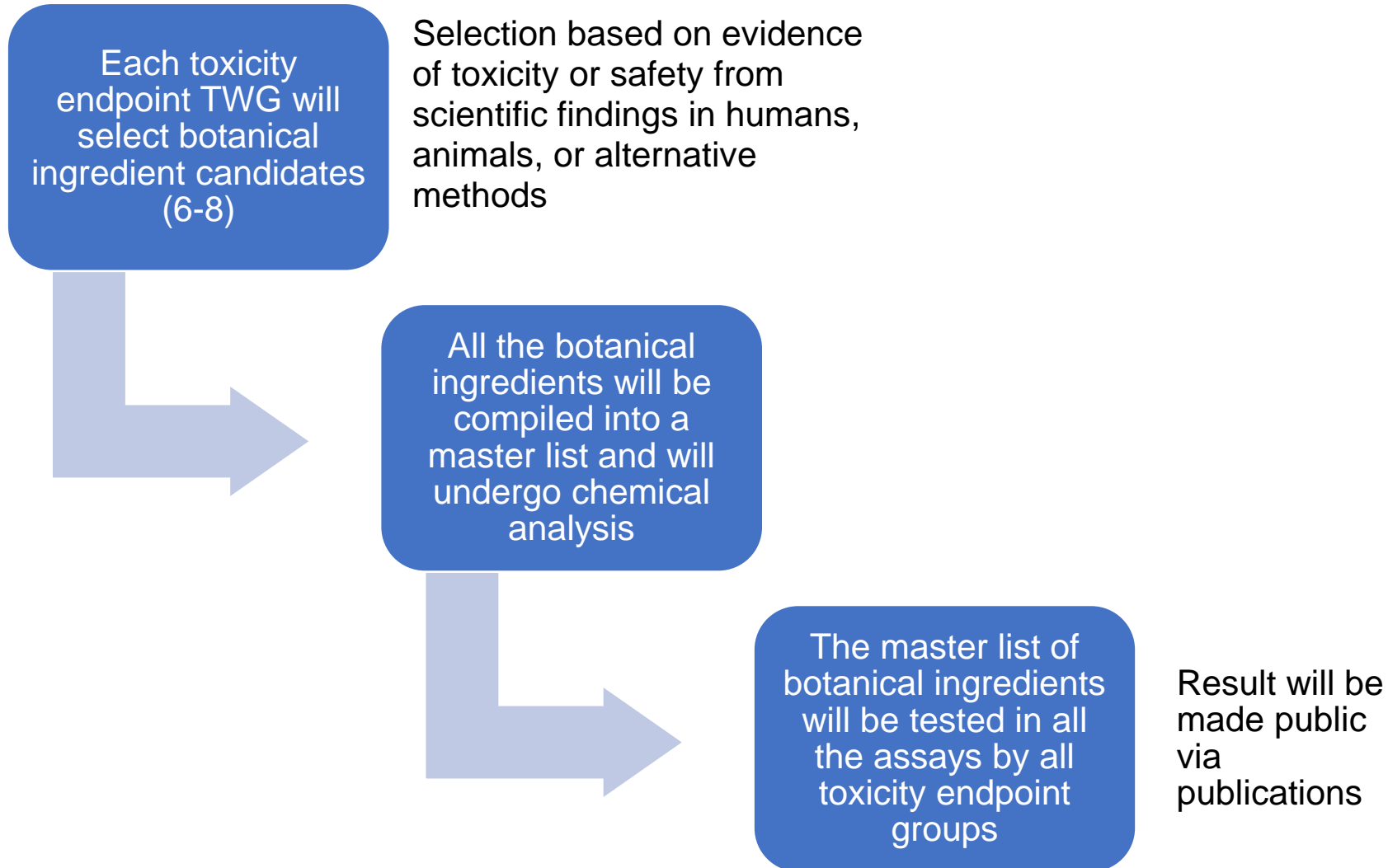


Data Analysis Working Group Members

Current Members:

- Scott Auerbach (co-chair, NIH/NIEHS)
- Minjun Chen (co-chair, FDA)
- Laura Egnash (Consultant)
- Dagney McCready (Eurofin)
- Andrew Nguyen (PISC)
- Julia Rager (University of North Carolina)
- David Reif (co-chair, North Carolina State University)

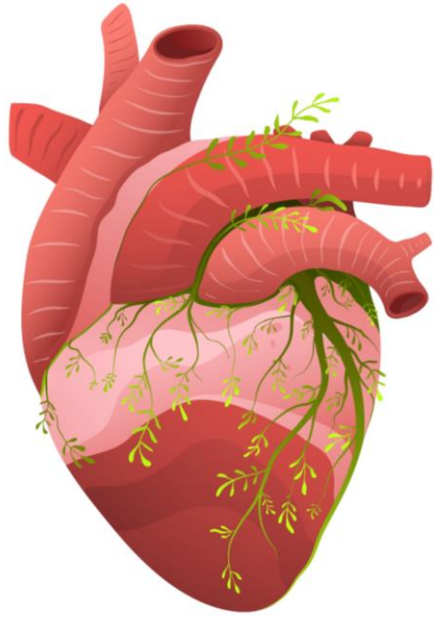
Botanical Candidate Criteria



A photograph of two Erlenmeyer flasks on a reflective surface. The flask on the left contains a small green plant with serrated leaves. The flask on the right contains a red liquid and a thermometer with a red bulb. The background is a blurred laboratory setting with shelves and equipment.

Methodology Criteria and Considerations

- Focus on *in silico* and *in vitro* methodologies
- Establish as suitable for botanicals (**mixtures**)
- **Leveraging history of use** data for individual botanicals
- ***In vitro* to *in vivo* extrapolation**
- **Practicality** (cost, time and technical requirements)



Other Potential Groups

- Cardiotoxicity
- Immunotoxicity
- Nephrotoxicity
- Neurotoxicity
- Others?



Summary

- The BSC has established 6 technical working groups to execute the TWG's mission and objectives.
- We thank all current and future TWG members for their dedication, time, expertise, and determination.

Captain America: "We need a plan of attack!"

Iron Man: "I have a plan. Attack!"