

# Building on Excellence to Tackle a Fundamental Scientific Challenge

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# What attracted me to the NTP?

- *Mission:*

- Evaluate agents of public health concern by developing and applying tools of modern toxicology and molecular biology.

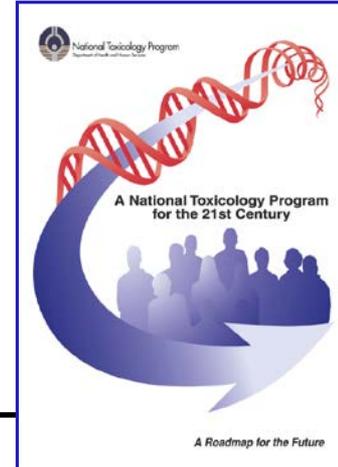
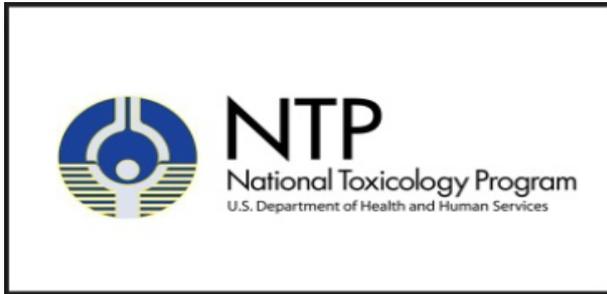
- *Goals:*

- Coordinate toxicological testing programs within the Department of Health and Human Services.
- Develop and validate improved testing methods that reduce, refine, or replace the use of animals.
- Develop approaches and generate data to strengthen scientific knowledge.
- Communicate information about potentially hazardous substances to the scientific, regulatory and public communities.





# What attracted me to the NTP?



## Mission

To evaluate agents of public health concern, by developing and applying tools of modern toxicology and molecular biology.

<http://ntp.niehs.nih.gov>; April 2015

## 21<sup>st</sup> Century Vision

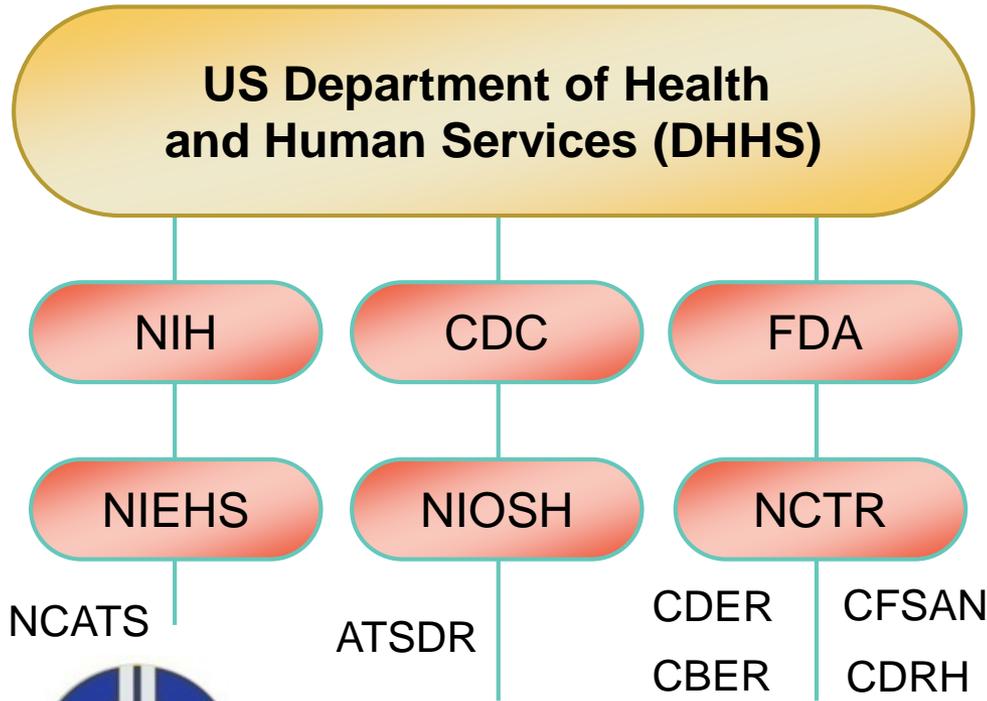
To support the evolution of toxicology from a predominately observational science at the level of disease-specific models to a predominately predictive science focused upon a broad inclusion of target-specific, mechanism-based, biological observations.

A National Toxicology Program for the 21<sup>st</sup> Century, November 2004



# What attracted me to the NTP?

## NTP – A program of partnerships



**National Toxicology Program**  
U.S. Department of Health and Human Services

<http://ntp.niehs.nih.gov>



Health and  
Environmental  
Sciences  
Institute



International Agency  
Research on Cancer



European Union Reference Laboratory  
for Alternatives to Animal Testing

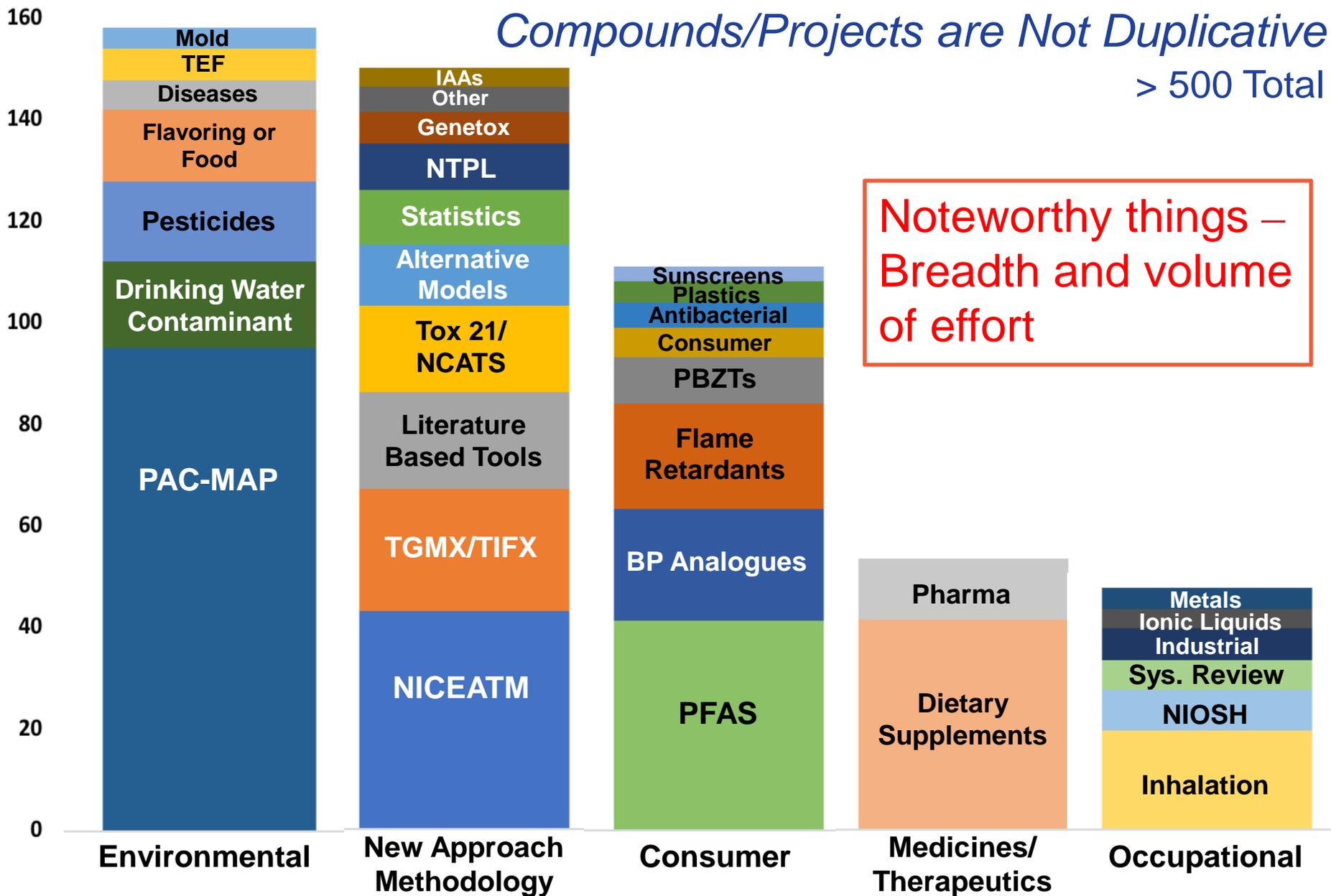


# **DNTP 2018 Portfolio Review Highlights**

6 days X 3 hours/day = 18 hours of  
presentation and discussion preceded  
by countless hours of preparation



# Ongoing Studies Grouped by Exposure





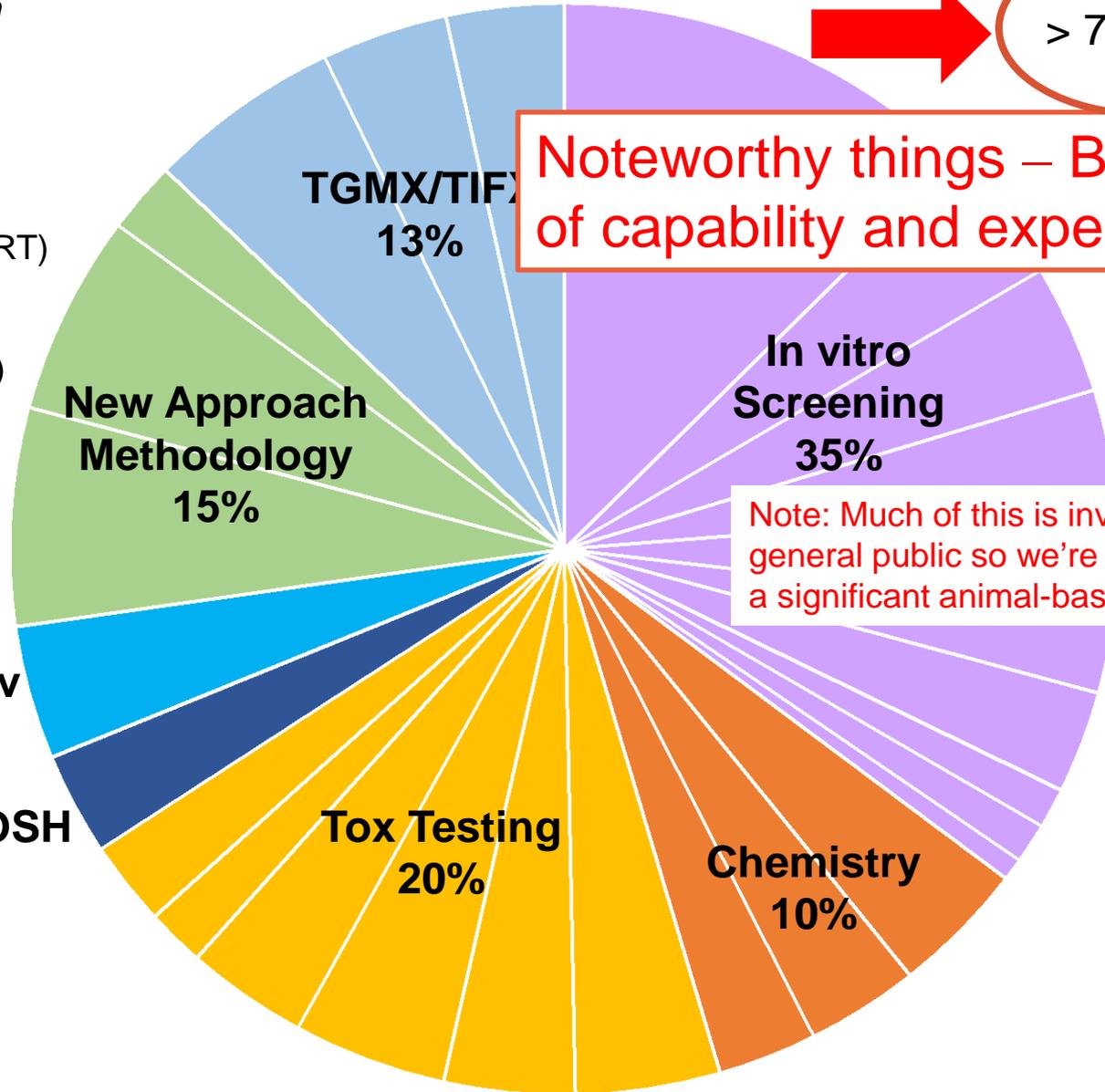
# Ongoing Studies Grouped by Study Type

Test Agents May Appear in Multiple Categories, Ex:

- **BP Analogues**
- Chemistry
- Biosample
- Toxicokinetics (TK)
- Dev/Repro Toxicity (DART)
- 5-day
- Immuno Toxicity
- Chronic Toxicity (NCTR)
- Scoping/Sys Rev
- In vitro
- Zebrafish

**Scoping/Sys Rev**  
4%

**NCTR/NIOSH**  
3%



> 700 Total

**Noteworthy things – Breadth of capability and expertise**

Note: Much of this is invisible to the general public so we're still seen as a significant animal-based program



# NTP Products, Research Areas, Resources

ABSTRACTS



## Developmental (Teratology) Abstracts

Evaluate the potential of chemicals to cause malformations and signs of toxicity during fetal development. [Go >](#)



## Drinking Water Abstracts

Studies of water distribution products provide their potential



## Botanical Dietary Supplements



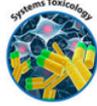
## Chemical Effects in Biological Systems

View individual data and summaries from NTP studies. Use guided searches to find organ sites with neoplasia, publications, and more. [Go >](#)



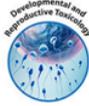
## DrugMatrix

Access a comprehensive database of toxicogenomic studies for hundreds of compounds including drugs and environmental chemicals. [Go >](#)



## Immunotoxicity Abstracts

The basic research program for the immunotoxicology studies conducted by NTP includes characterization of the potential for a substance to modulate immune function and



## Reproductive

Evaluate exposure to reproductive system



## Glyphosate Formulations

NTP is conducting a series of



## AIDS Therapeutics Toxicity Reports

Evaluate potential health effects of AIDS therapeutics in laboratory animals. [Go >](#)



## Genetically Modified Model Reports

Characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected agents in laboratory animals that have been genetically modified. [Go >](#)



## Polycyclic Aromatic Compounds

NTP is currently studying PACs to learn more about the toxicity of individual PACs and PAC mixtures. [Go >](#)



## Sulfolane

NTP is performing a set of studies to evaluate sulfolane toxicity and its potential health impacts of exposure. [Go >](#)



## Synthetic Turf/Recycled Tire Crumb Rubber

NTP is working to enhance the understanding of potential health impacts of chemicals released from synthetic turf. [Go >](#)



## West Virginia Chemical Spill

NTP has completed the West Virginia chemical spill research program. NTP's Final Update, collective findings, and supporting files are now



## Monographs

Assess evidence from the literature on substances in our environment that may cause adverse health effects. [Go >](#)



## Report on Carcinogens

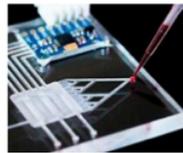
Identifies substances that may put people at increased risk for cancer. People can use the RoC to make informed decisions about their own health. Find [Scientific Review information](#) for substances evaluated since 1996. [Go >](#)

RESOURCES



## NTP Archives

Request access to an extensive collection of research specimens and supporting data from over 2000 NTP studies. [Go >](#)



## Alternative Toxicology

Gain access to research lists used to support methods development



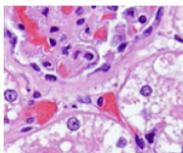
## Research Reports

Provide results of NTP research and literature-analysis activities that do not fall under the scope of existing report series. [Go >](#)



## Technical Reports

Describe long-term studies that characterize and evaluate the toxicologic potential of selected test articles in animals. [Go >](#)



## Nonneoplastic Lesion Atlas

Search the atlas for high-quality images and descriptions of rodent nonneoplastic lesions. [Go >](#)



## Tox21 Tool

Access useful tools for the Tox21 qHTS. [Go >](#)



## Toxicity Reports

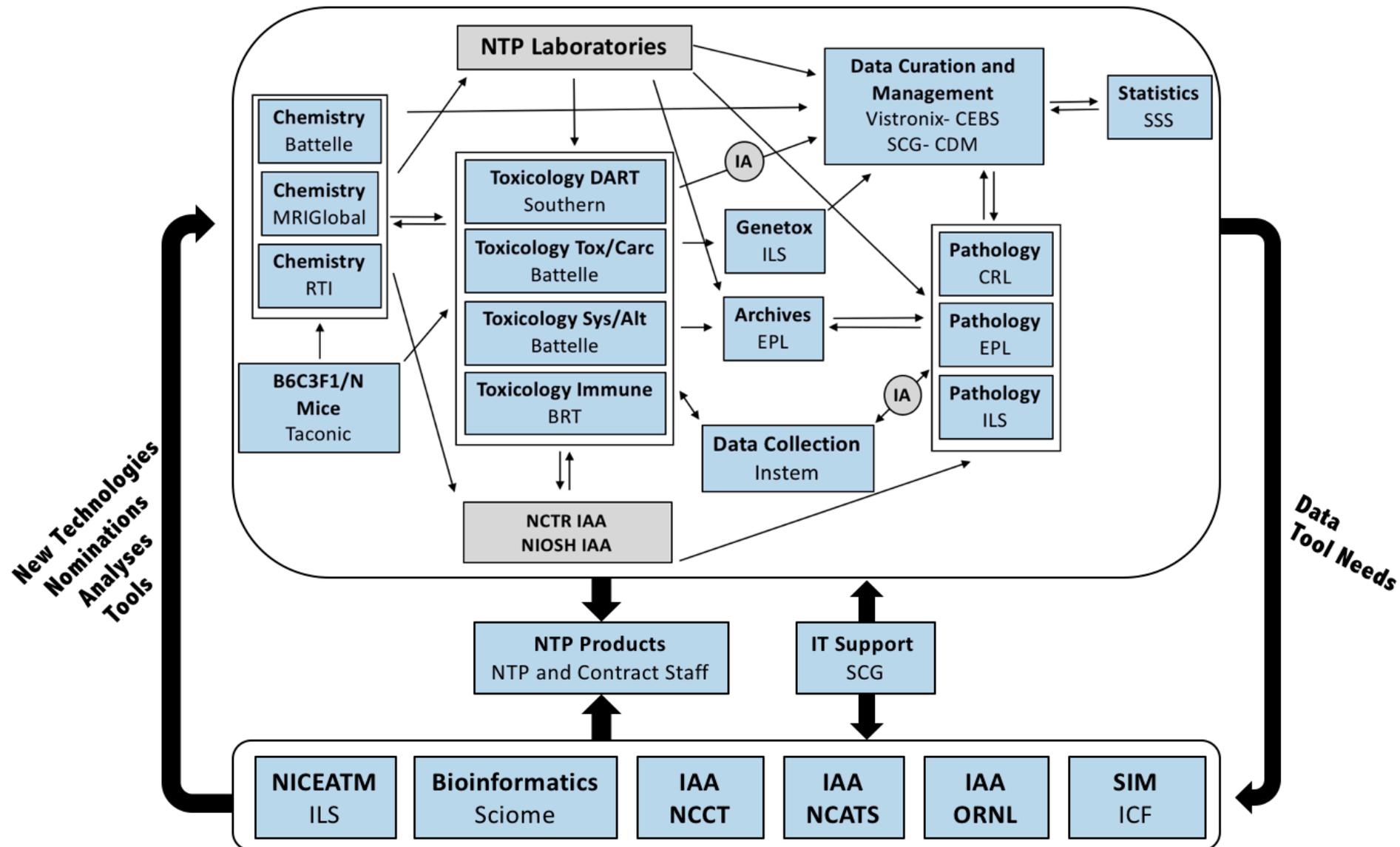
Describe short-term studies that characterize and evaluate the toxicologic potential of selected substances in laboratory animals. [Go >](#)

Noteworthy things – Breadth of products



# Noteworthy things – Breadth of complexity

# NTP Contract Support





- Multi-disciplinary expertise in toxicology
- Capabilities
  - General toxicology studies (with enablers like chemistry, TK/TD, etc.)
  - Repro/developmental
  - Immunotoxicity
  - Mechanistic/investigative toxicology
  - In vitro capabilities
  - Computational/in silico approaches
  - Literature/evidence-based assessments
  - Data management
- Taking on really hard problems!!!



- We can't animal study our way out of the growing need for insights into hazards from environmental exposures (chemical and non-chemical agents)
- Current non-animal approaches are better at producing data than enabling decisions
- The decision-making process of our stakeholders is still largely entrenched in the phenotypic outcomes of animal studies
- There is a gap in our ability to 'predict' human outcomes from higher throughput and more mechanistic *in silico* and *in vitro* assays
- Our resourcing is likely to remain relatively flat
- We've been too productive
- Our primary stakeholder (i.e., the public) is confused



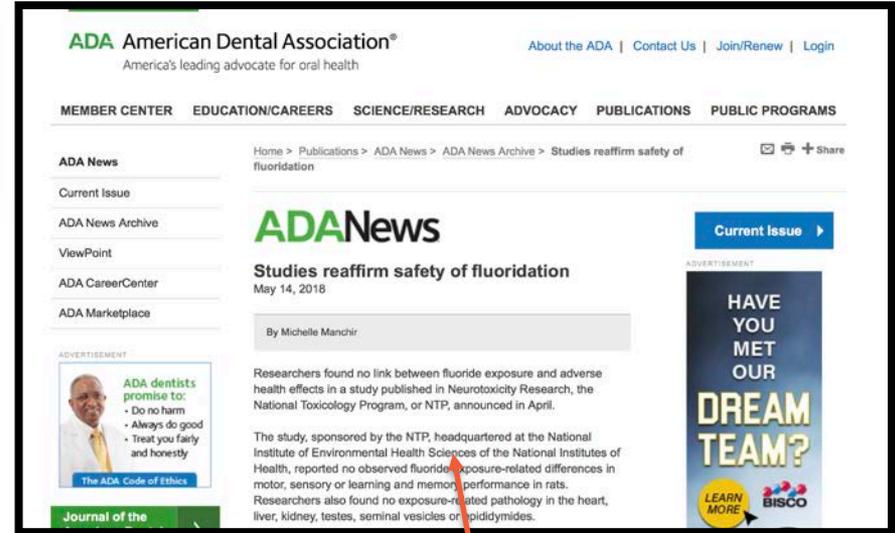
# Solutions – Understand What Stakeholders Care About



They want us to help them understand hazards in their environment

Dear Secretary Azar and Director Linda S. Birnbaum:

I am writing today to implore you to direct the National Toxicology Program and the Agency for Toxic Substances and Disease Registry to conduct additional research into the link between exposure to polychlorinated biphenyls (PCBs) and cancer. It is important for us to fully understand the public health implications between PCBs and cancer in order to develop a plan to protect those who have been exposed to these dangerous chemicals.



They care about how we do the work

They look to us to affirm their decisions





# Solutions – Align on a Vision

## Translational Toxicology at NTP

**Our impact**



**Our aims**

### **Inform** the present

- Engaging, informing and educating stakeholders
- Timely responses
- Contextualizing data

### **Innovate** the future

- Build mechanistic understanding
- Capability innovation
- Train next generation of translational toxicologists

**Our tools** Literature analysis Animal studies In vitro systems In silico/computational analytics

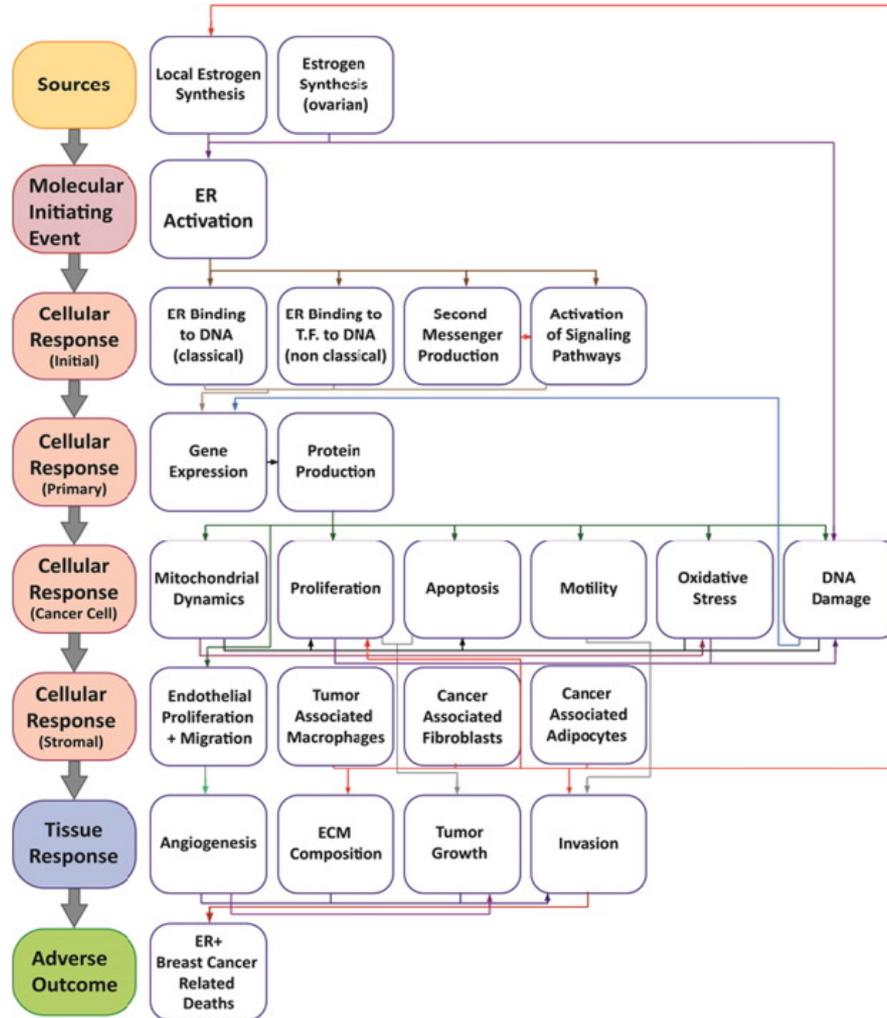
**Vision:** Advancing public health and the discipline of toxicology through the use of innovative tools and strategies that are translatable, predictive, and timely.





# Solutions – Focus on a Fundamental Problem

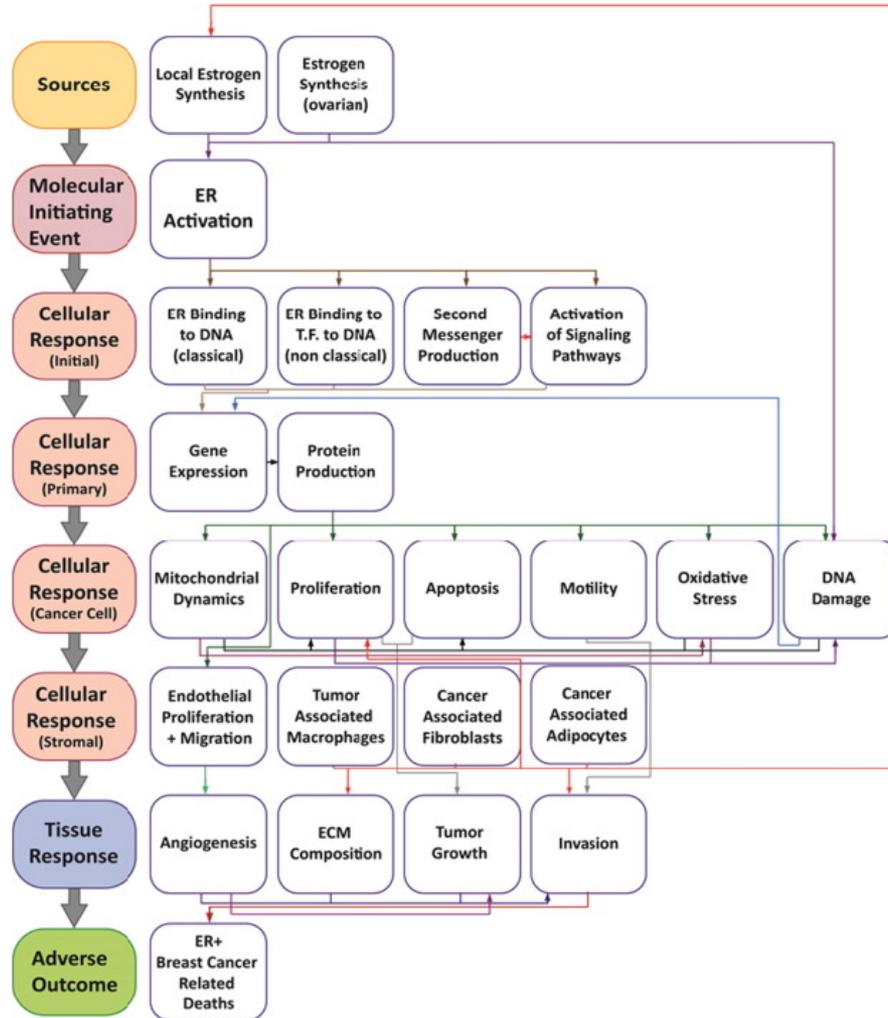
## Estrogen Receptor (ER) pathway to breast cancer





# Pathobiology – Predictive Toxicology Conundrum

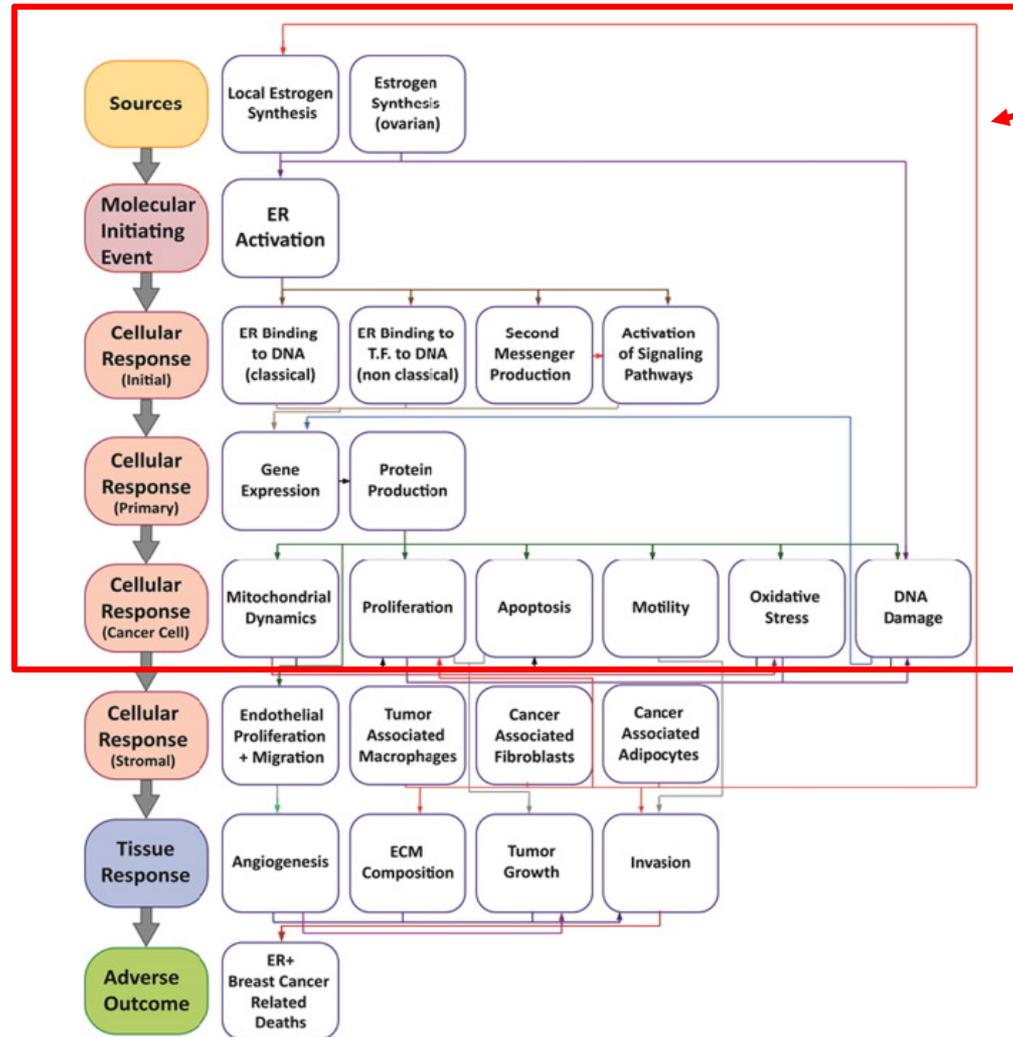
## ER pathway to breast cancer





# Pathobiology – Predictive Toxicology Conundrum

## ER pathway to breast cancer

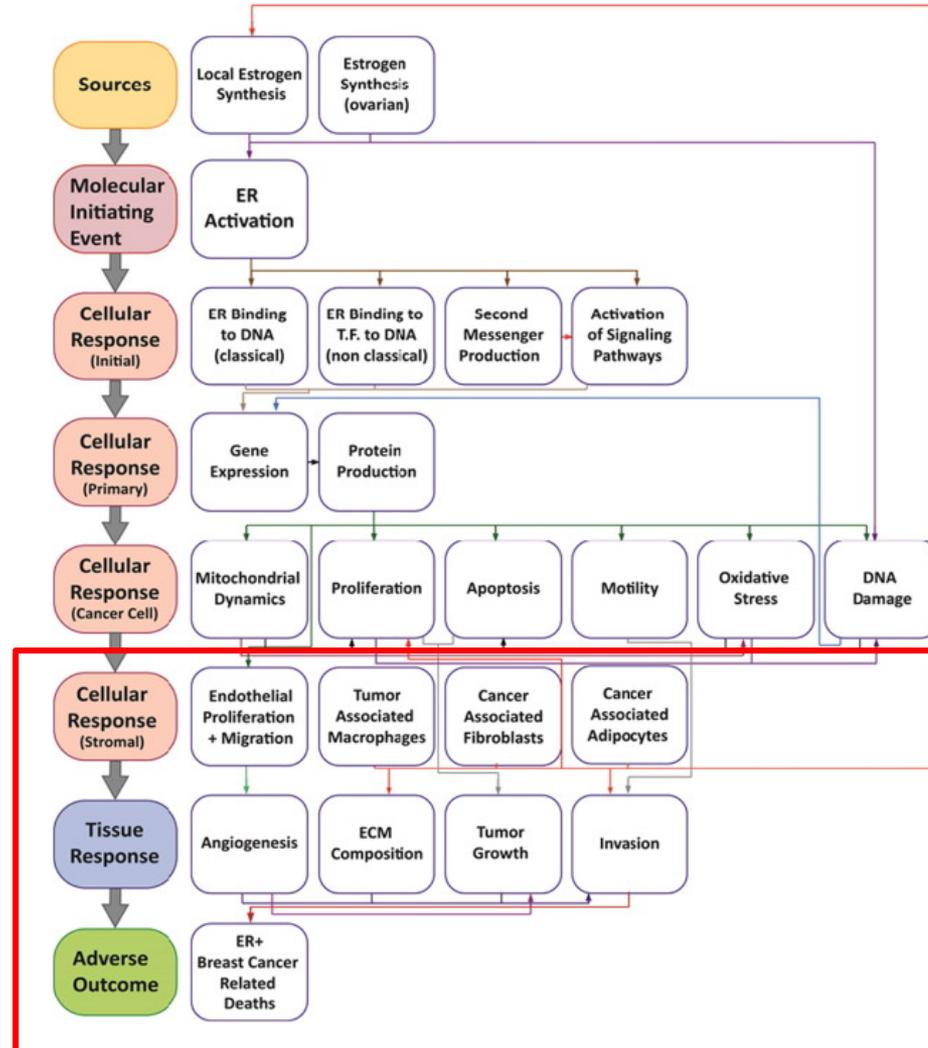


Normal adaptive biology



# Pathobiology – Predictive Toxicology Conundrum

## ER pathway to breast cancer



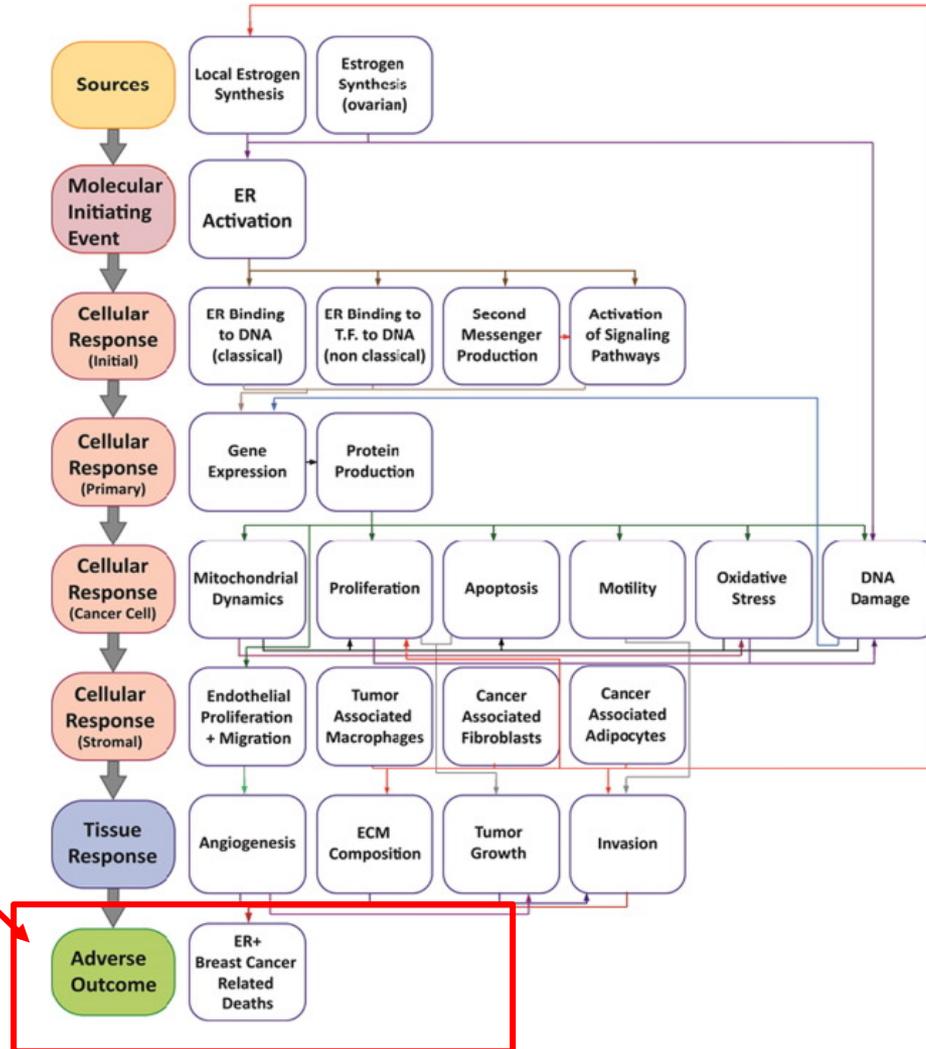
This is what we recognize to be bad.



# Pathobiology – Predictive Toxicology Conundrum

## ER pathway to breast cancer

This is what we traditionally model in observational ways.

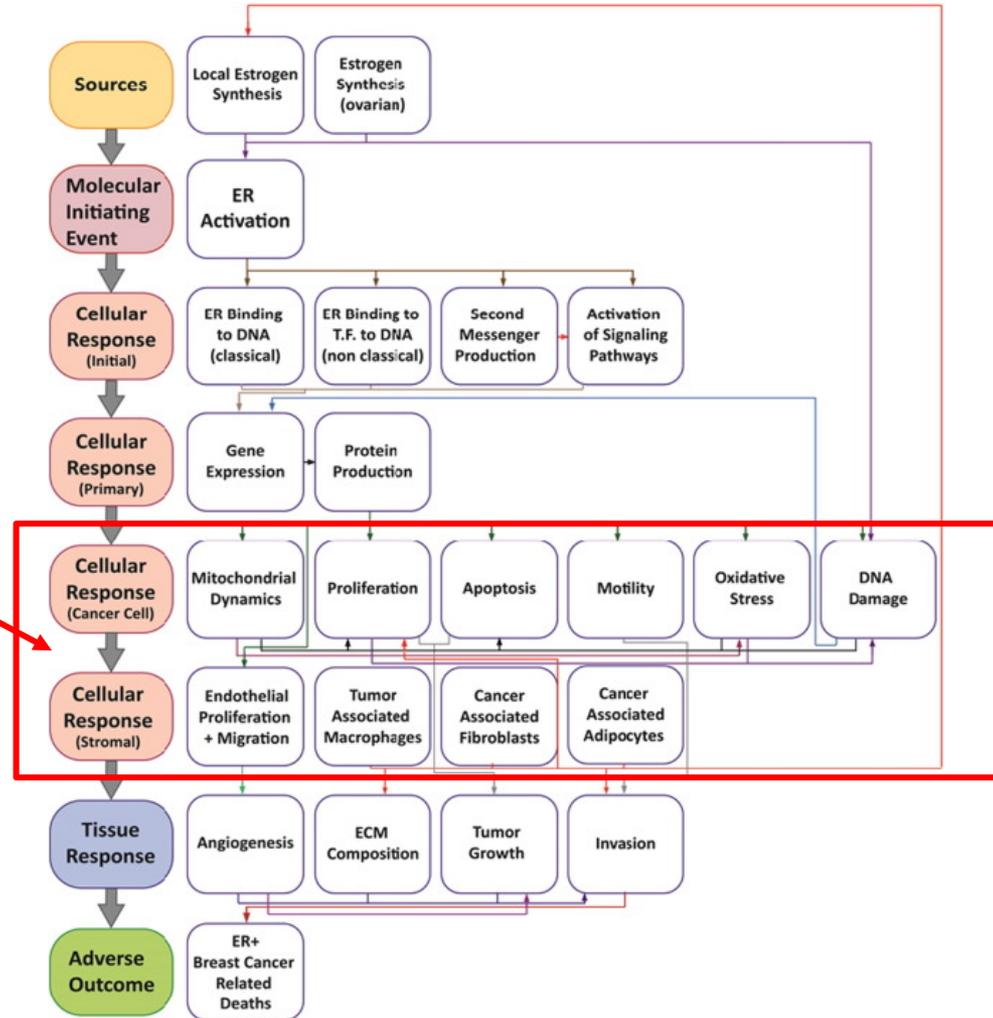




# Pathobiology – Predictive Toxicology Conundrum

## ER pathway to breast cancer

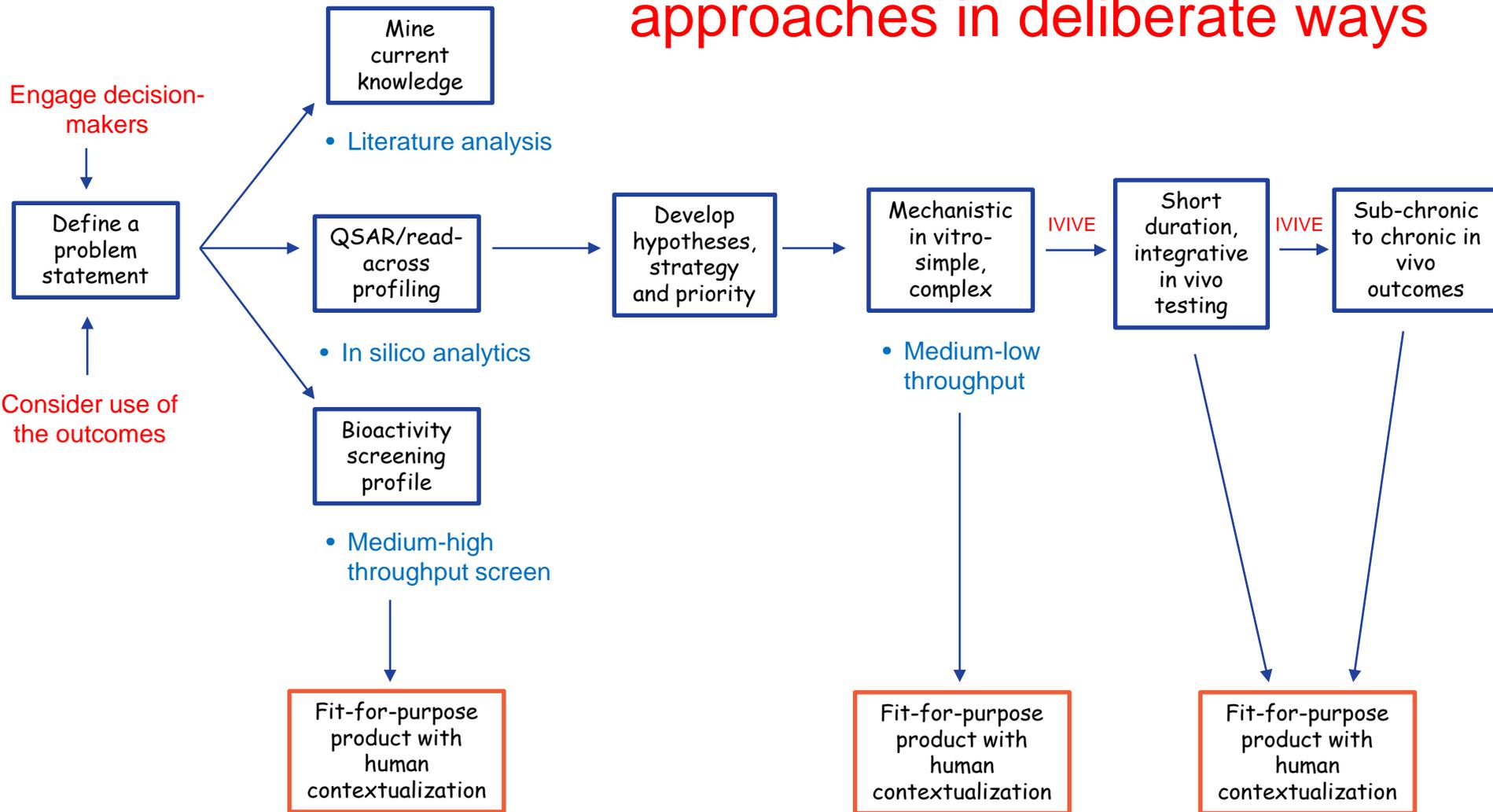
This is the inflection point we need to model since it represents the bridge between observation and prediction





# NTP Translational Toxicology Pipeline

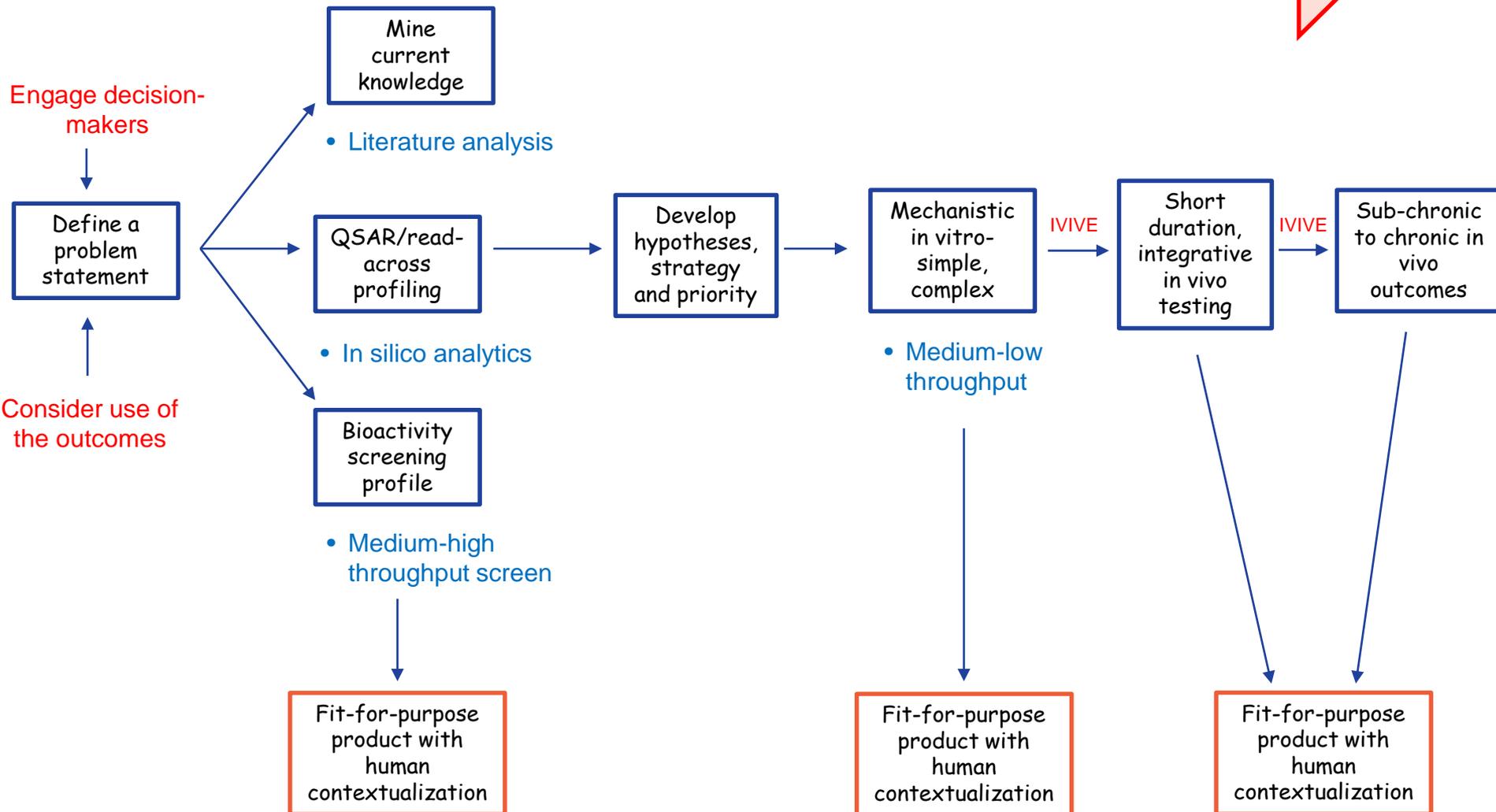
Apply our tools and approaches in deliberate ways





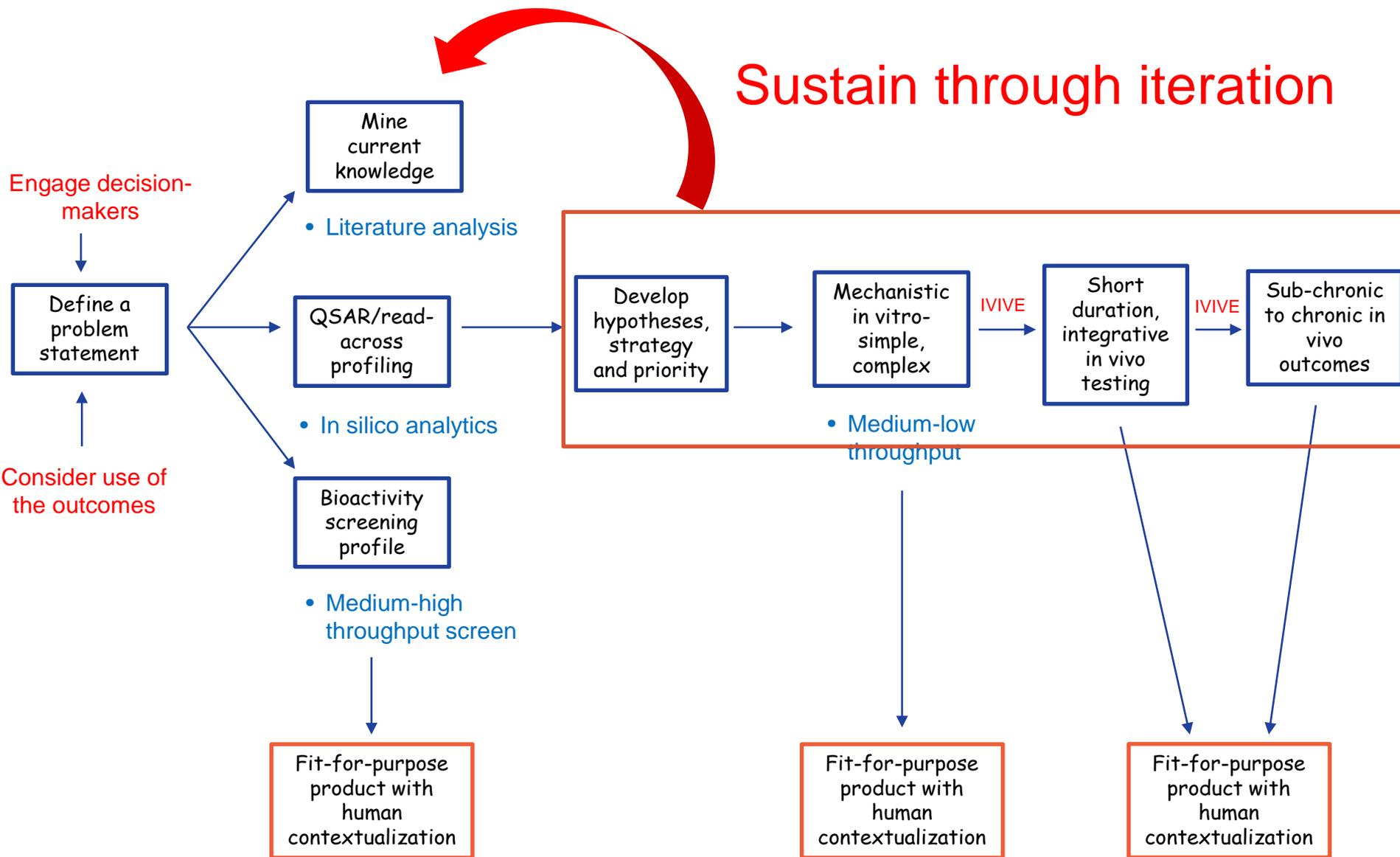
# NTP Translational Toxicology Pipeline

Enable by informed progression



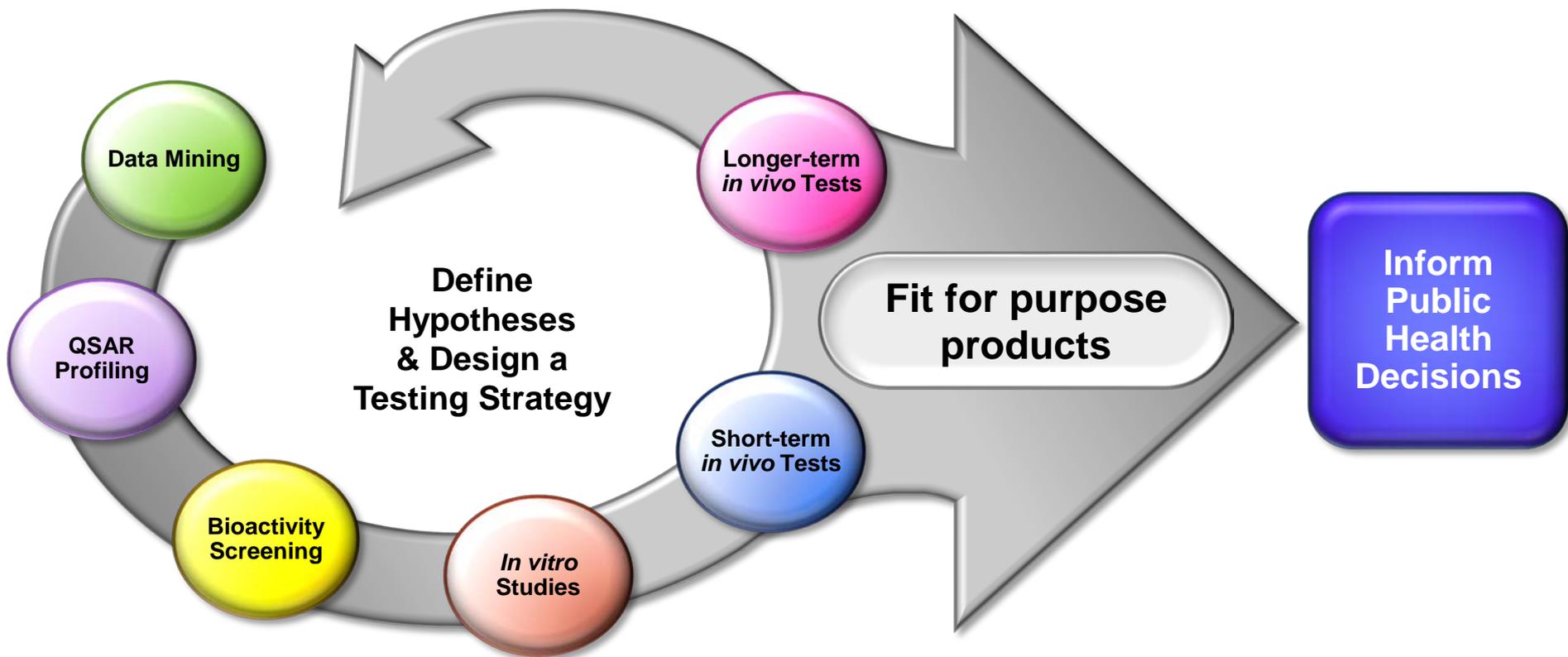


# NTP Translational Toxicology Pipeline



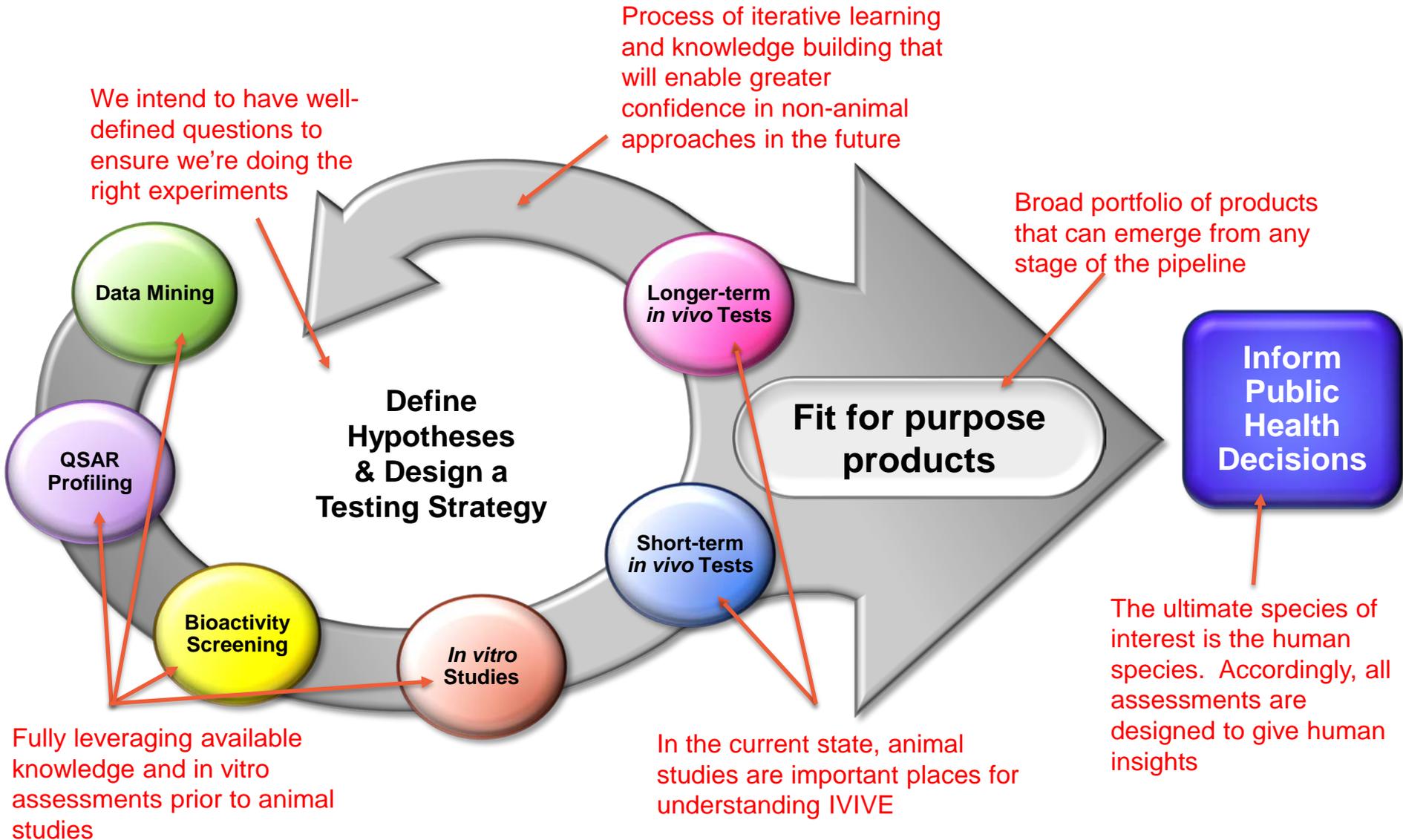


# DNTP Translational Toxicology Pipeline Plan





# DNTP Translational Toxicology Pipeline Plan





# Solutions – Define Ways of Working

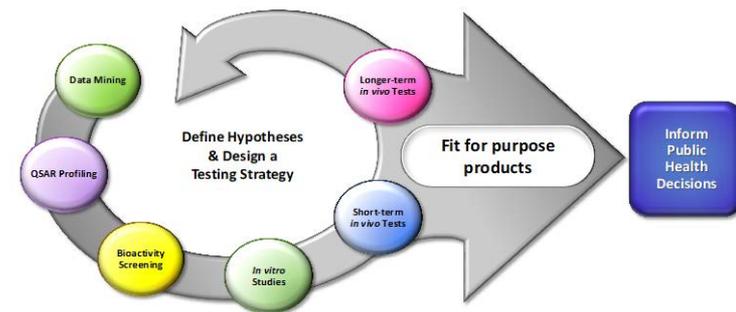
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- Innovate at pace and for cause
- Leverage partnerships
- Leverage technology
- A portfolio that reflects contemporary needs and concerns
- Dynamic portfolio management
- Disciplined prioritization
- Judicious animal use
- Communication as a first intent
- Public engagement and education



# NTP Portfolio Examples

- NTP Synthetic Turf/Recycled Tire Crumb Rubber Research
- Studies of Cell Phone Radiofrequency Radiation (RFR)
  - Report on March 26-28 2018 Peer Review of NTP Technical Reports
  - Follow-up Studies on RFR
- Activities on Bisphenols
  - CLARITY-BPA Research Program: Peer Review of Core Study and Next Steps
  - Evaluation of Bisphenol Analogues
- REACT Program for Per- and Polyfluoroalkyl Substances





**Questions?**