NTP
National Toxicology Program

Assessing NTP's Effectiveness: A Case Study on Hexavalent Chromium

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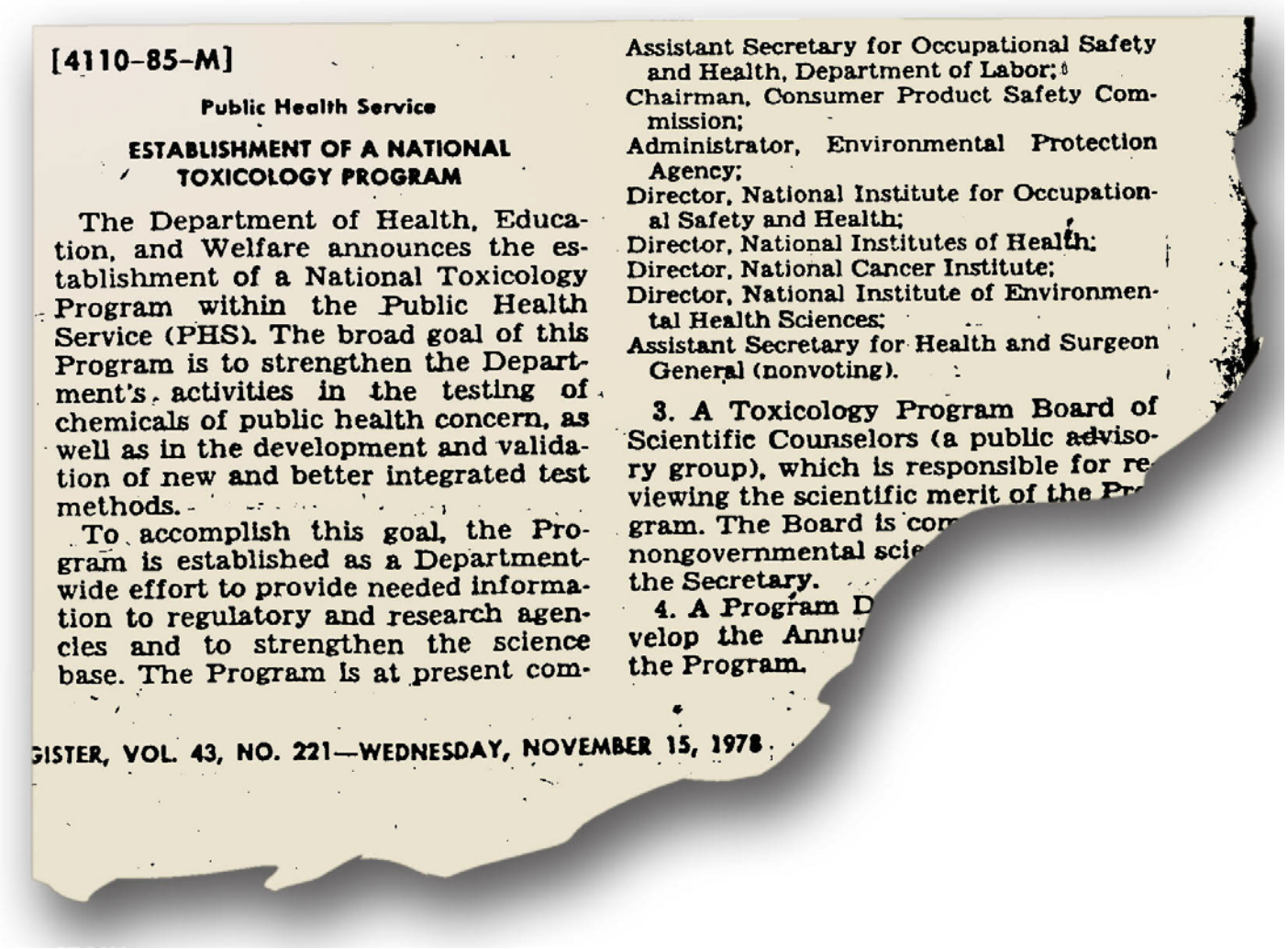
Office of Liaison, Policy and Review
National Institute of Environmental Health Sciences

NTP Board of Scientific Counselors Meeting
December 10, 2014

Establishment of NTP



[4110-85-M]

Public Health Service

ESTABLISHMENT OF A NATIONAL TOXICOLOGY PROGRAM

The Department of Health, Education, and Welfare announces the establishment of a National Toxicology Program within the Public Health Service (PHS). The broad goal of this Program is to strengthen the Department's activities in the testing of chemicals of public health concern, as well as in the development and validation of new and better integrated test methods.

To accomplish this goal, the Program is established as a Department-wide effort to provide needed information to regulatory and research agencies and to strengthen the science base. The Program is at present com-

Assistant Secretary for Occupational Safety and Health, Department of Labor;
Chairman, Consumer Product Safety Commission;
Administrator, Environmental Protection Agency;
Director, National Institute for Occupational Safety and Health;
Director, National Institutes of Health;
Director, National Cancer Institute;
Director, National Institute of Environmental Health Sciences;
Assistant Secretary for Health and Surgeon General (nonvoting).

3. A Toxicology Program Board of Scientific Counselors (a public advisory group), which is responsible for reviewing the scientific merit of the Pr
gram. The Board is com
nongovernmental scie
the Secretary.

4. A Program D
velop the Annu
the Program.

GISTER, VOL. 43, NO. 221—WEDNESDAY, NOVEMBER 15, 1978

“NTP exists to develop the information and the tools that both agencies of government and industry need so that we can all live together safely in the same world.”

David P. Rall, 1981

Since Its Establishment, NTP Has

- Studied >2500 substances for variety of cancer and noncancer health effects
- Developed new methods, tools, and approaches
- Prepared and published
  - 580 NTP Technical Reports (~200 from NCI cancer bioassay program)
  - 79 NTP Toxicity Reports
  - 16 Genetically Modified Models Reports
  - 13 editions of Report on Carcinogens
  - 23 NTP Monographs (Center for Evaluation of Risks to Human Reproduction and Office of Health Assessment and Translation)
  - 1000s of journal publications

NTP Is Recognized as Authoritative by

- OSHA Hazard Communication Standard: Report on Carcinogens
- EPA Toxic Substances Control Act for ocean dumping permits and export notification requirements: Report on Carcinogens
- California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65)
  - Report on Carcinogens and NTP Technical Reports for identification of chemicals causing cancer
  - CERHR Monographs for identification of chemicals causing reproductive toxicity
- NTP Website: http://ntp.niehs.nih.gov/go/regact

What We Hoped to Gain

- Develop a useful approach
  - Identify methods that will yield comprehensive and credible assessments of NTP's effectiveness.
  - Demonstrate the feasibility of assessing NTP's impacts in multiple sectors:
    - Academia, industry, non-government groups, and federal, state, and international agencies
  - Identify strategies to improve existing methods for assessing research impacts.
- Successfully test the approach with a pilot project
- Hexavalent chromium case study
  - Demonstrate the effectiveness of NTP's science at advancing toxicology and being translated to public health decision-making.

Acknowledgements

Contributors

- Yun Xie, PhD
- Stephanie Holmgren, MSLS, MBA
- Danica Andrews
- Mary Wolfe, PhD

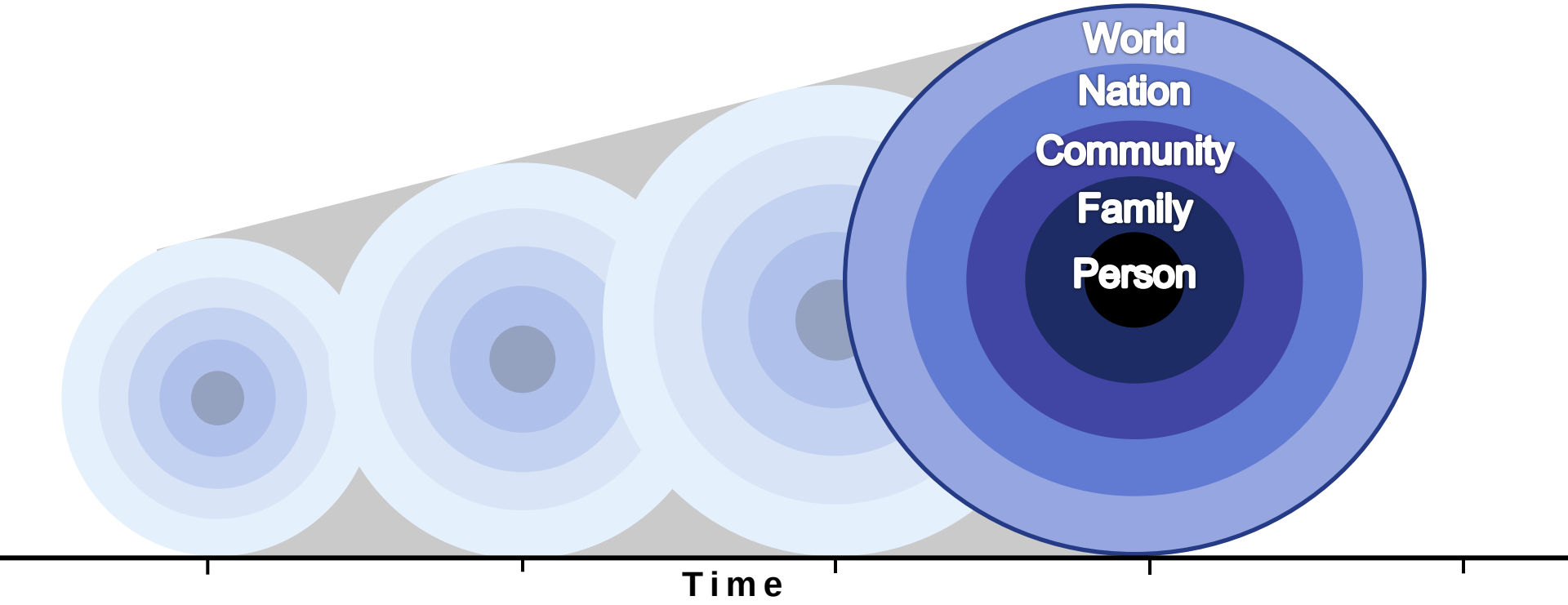
Expert Advisers

- Christina Drew, PhD
- Michelle Hooth, PhD
- Matt Stout, PhD
- James Stojan
- Sylvia Richardson

Outline

- Background information for assessing research impact.
- Our logic model to assess NTP's research effectiveness.
- The results from our hexavalent chromium case study.

Impact of NTP Research Is Dynamic



- NTP studies can impact different groups of people.
- Impact changes over time.
- How do we measure impact?

Image adapted from NIH Scientific Management Review Board Working Group on the Value of Biomedical Research, June 4, 2013

Challenges to Measuring Impact

- Attribution
  - Must show connection between our work and impact.
  - Must work without a counter factual (i.e., what would happen without NTP research).
- Lag Time
  - Time from research to publication can be years.
  - Time from publication to citation is on average 3+ years.
  - Time from research to policy impact can be 10+ years.
  - Time from policy change to health impact can be many years.
- External Factors
  - We have no direct control over regulations, public health, etc.
  - External factors influence how our research leads to impact.

Strategies from the Literature

Identified strategies that will yield impact assessments that are:

- Comprehensive
- Credible
- Responsive
- Rigorous

NTP Mission and Goals

- NTP mission:
  - Evaluate agents of public health concern by developing and applying the tools of modern toxicology and molecular biology.
- NTP goals:
  - Coordinate toxicology testing programs within the federal government.
  - Strengthen the science base in toxicology.
  - Develop and validate improved testing methods.
  - Provide information about potentially toxic chemicals to health, regulatory, and research agencies, scientific and medical communities, and the public.

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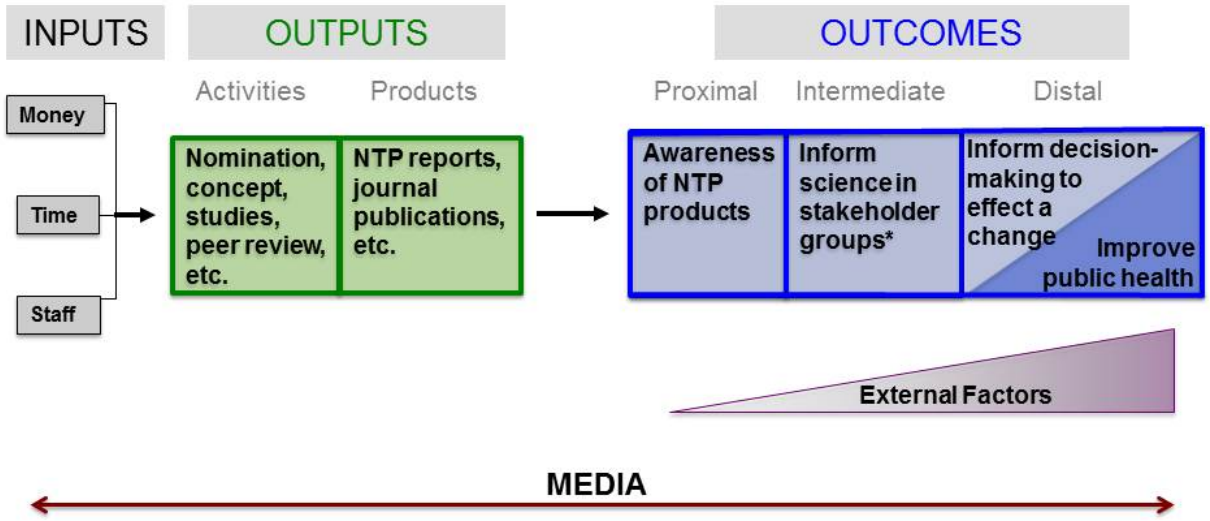
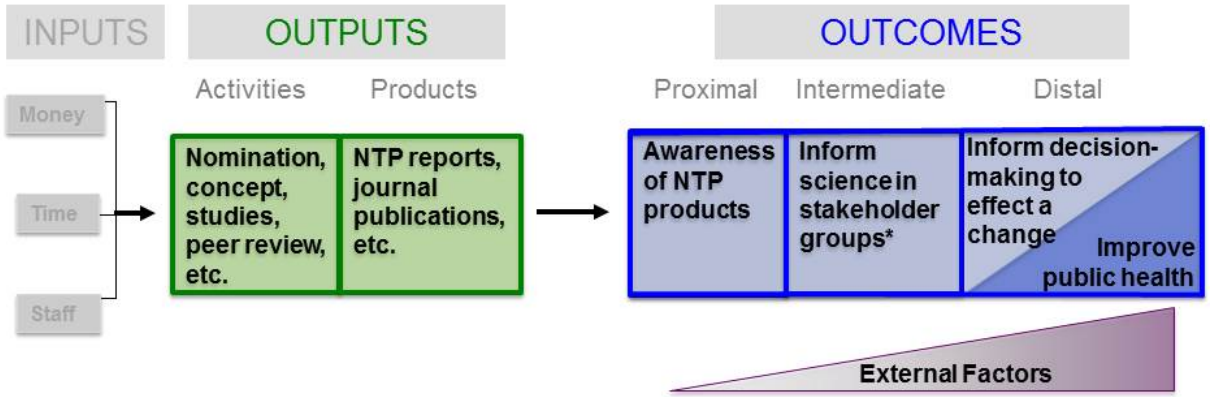
Logic Model for NTP Studies



*Stakeholder groups include academia, industry, federal regulatory and non-regulatory agencies, state agencies, non-government groups, and international agencies.

Logic Model for NTP Studies



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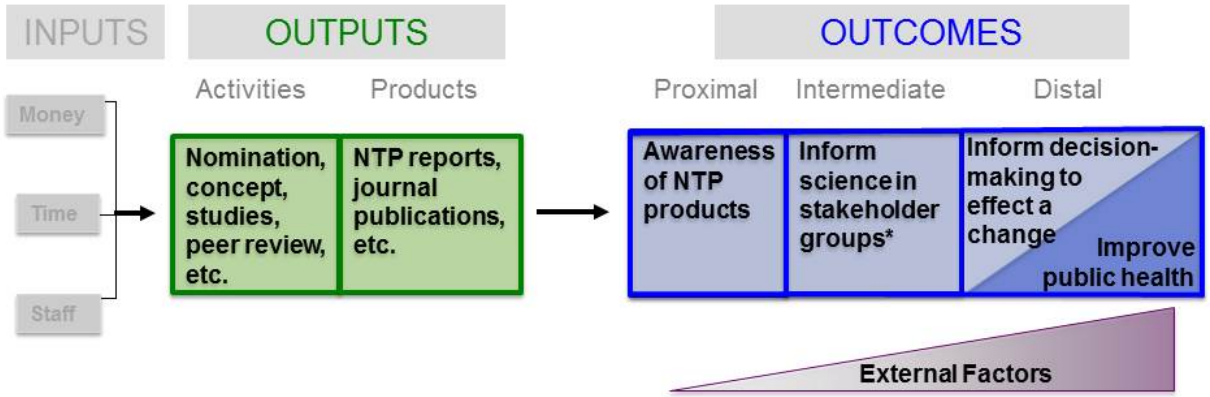
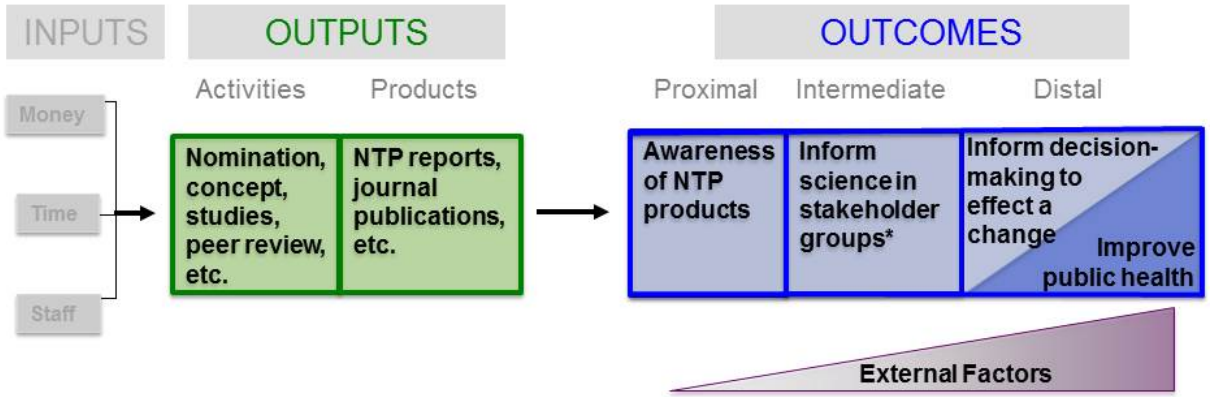


OUTPUTS
Activities & Products
Number and dates of milestones of what NTP did and produced

*Stakeholder groups include academia, industry, federal regulatory and non-regulatory agencies, state agencies, non-government groups, and international agencies.

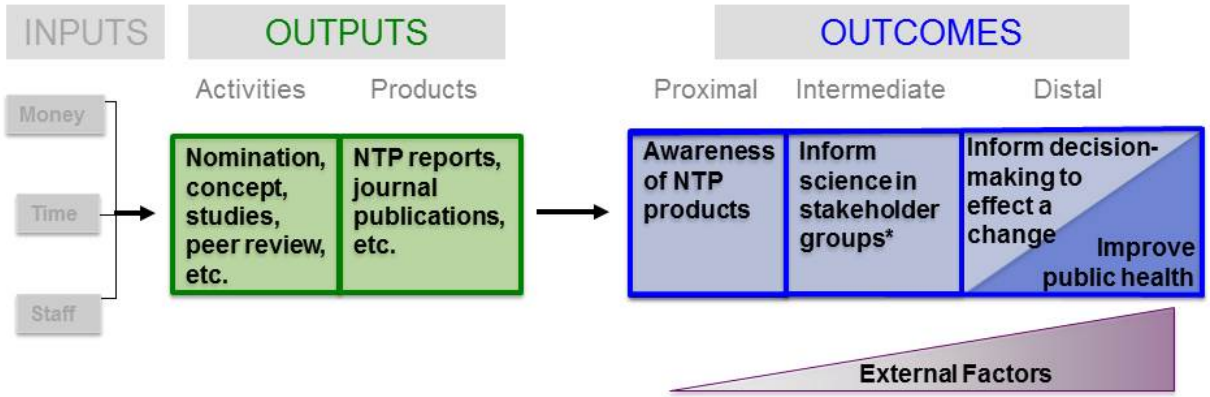
Logic Model for NTP Studies



OUTPUTS	OUTCOMES (Impacts)	
Activities & Products	Proximal	
Number and dates of milestones of what NTP did and produced	Number of downloads and requests for NTP products	

*Stakeholder groups include academia, industry, federal regulatory and non-regulatory agencies, state agencies, non-government groups, and international agencies.

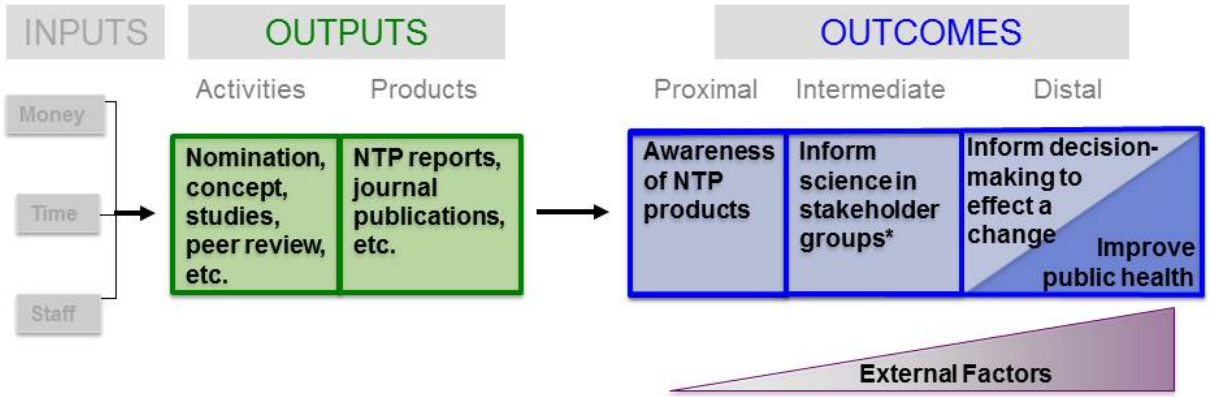
Logic Model for NTP Studies



OUTPUTS	OUTCOMES (Impacts)		
Activities & Products	Proximal	Intermediate	
Number and dates of milestones of what NTP did and produced	Number of downloads and requests for NTP products	Number and nature of citations in science publications, grants, and reports from stakeholder groups*	

*Stakeholder groups include academia, industry, federal regulatory and non-regulatory agencies, state agencies, non-government groups, and international agencies.

Logic Model for NTP Studies



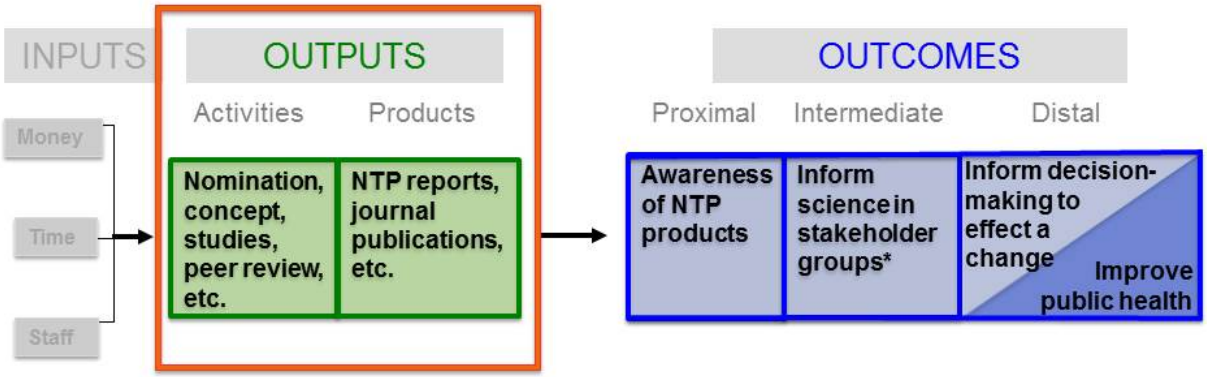
OUTPUTS	OUTCOMES (Impacts)		
Activities & Products	Proximal	Intermediate	Distal
Number and dates of milestones of what NTP did and produced	Number of downloads and requests for NTP products	Number and nature of citations in science publications, grants, and reports from stakeholder groups*	Citations in documents that led to a change or action in legislation, lawsuit, policy, etc.

*Stakeholder groups include academia, industry, federal regulatory and non-regulatory agencies, state agencies, non-government groups, and international agencies.

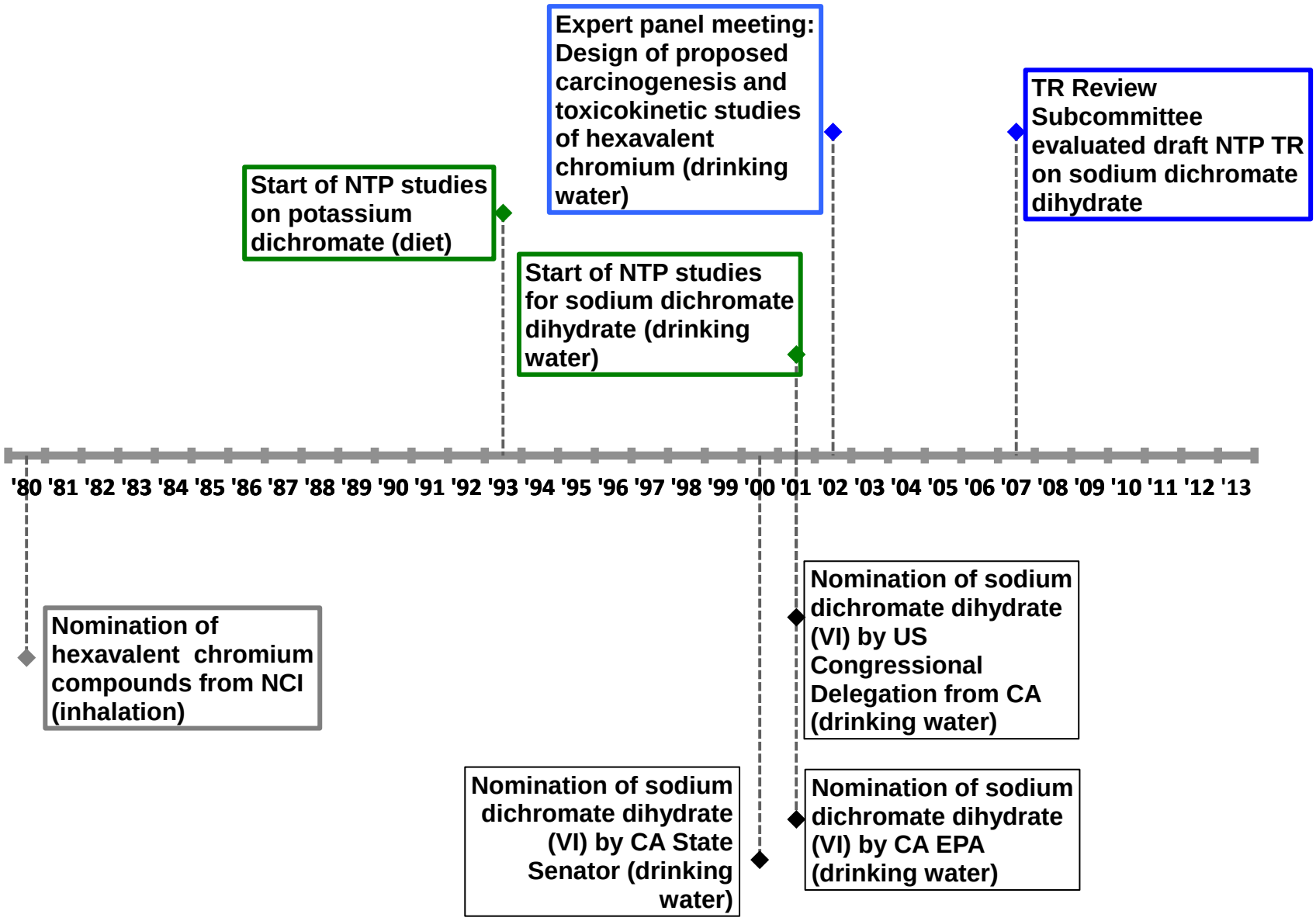
Choosing Chromium (VI)

- This impact evaluation focuses on chromium (VI).
- NTP's work on chromium (VI) was completed several years ago with presumably sufficient time to identify its use by stakeholders and evaluate impacts.

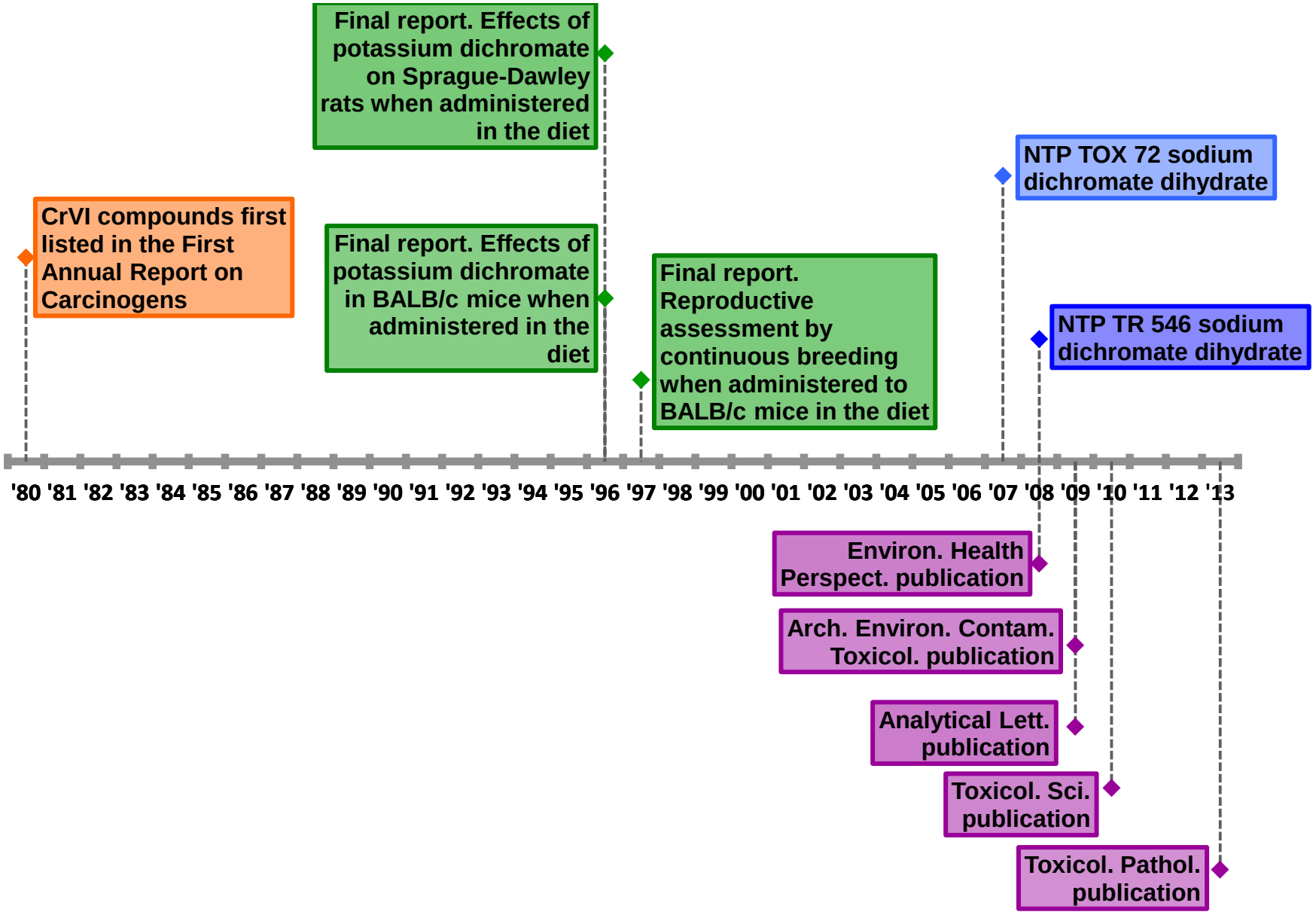
NTP Outputs: Activities and Products



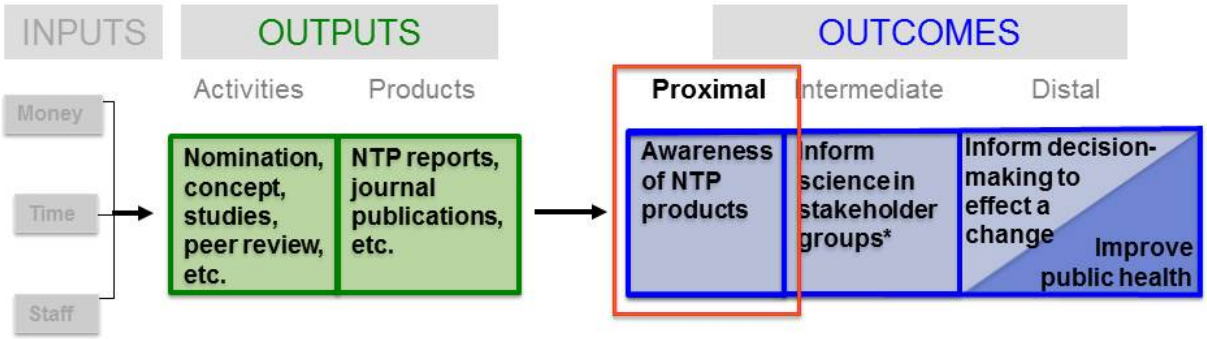
Outputs: A Timeline of Main Activities



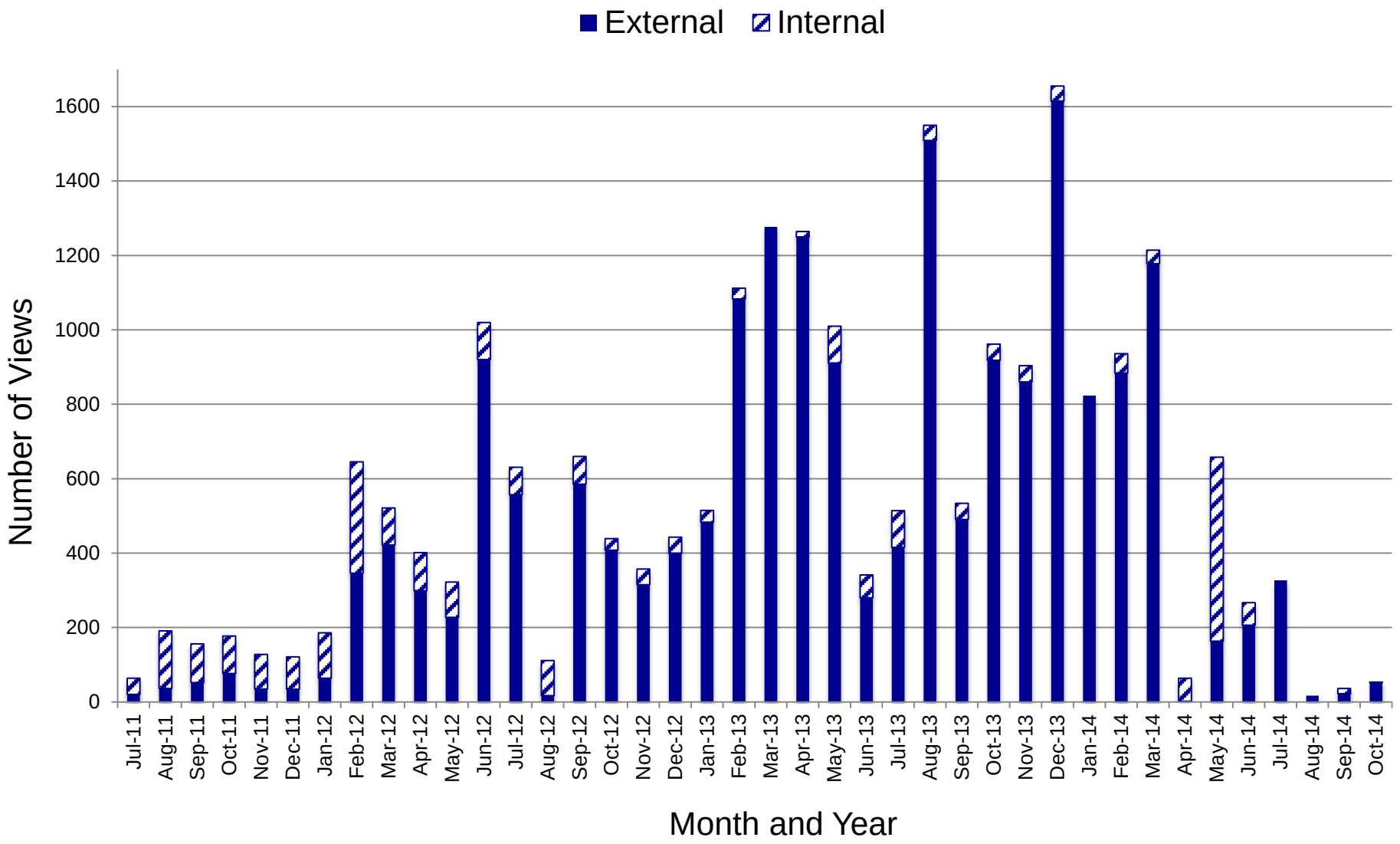
Outputs: NTP Products



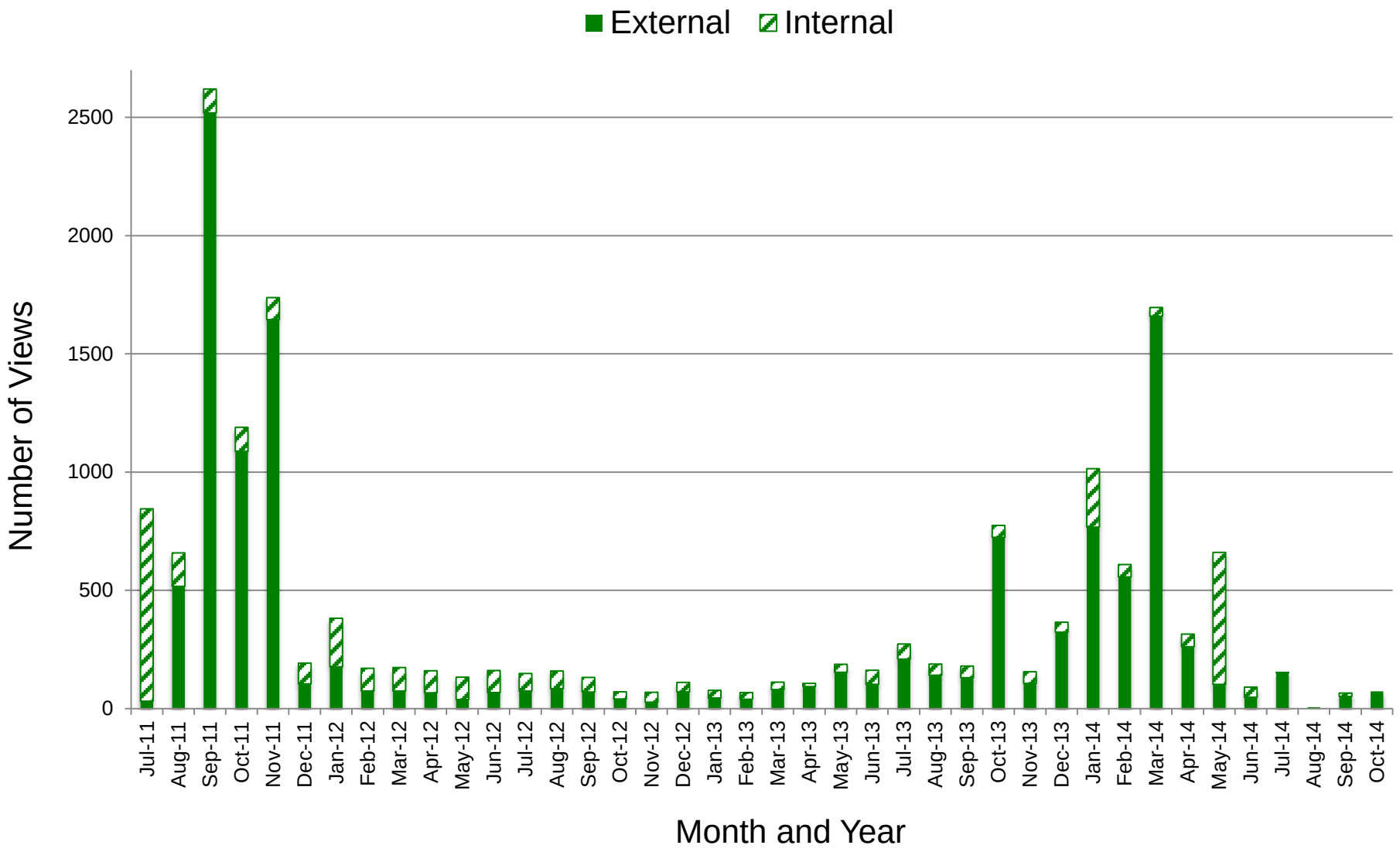
Outcomes


INPUTS
OUTPUTS
OUTCOMES
Activities
Products
Proximal
Intermediate
Distal
Money
Time
Staff
Nomination, concept, studies, peer review, etc.
NTP reports, journal publications, etc.
Awareness of NTP products
Inform science in stakeholder groups*
Inform decision-making to effect a change
Improve public health

Webpage Views for TR 546: July 2011 – October 2014



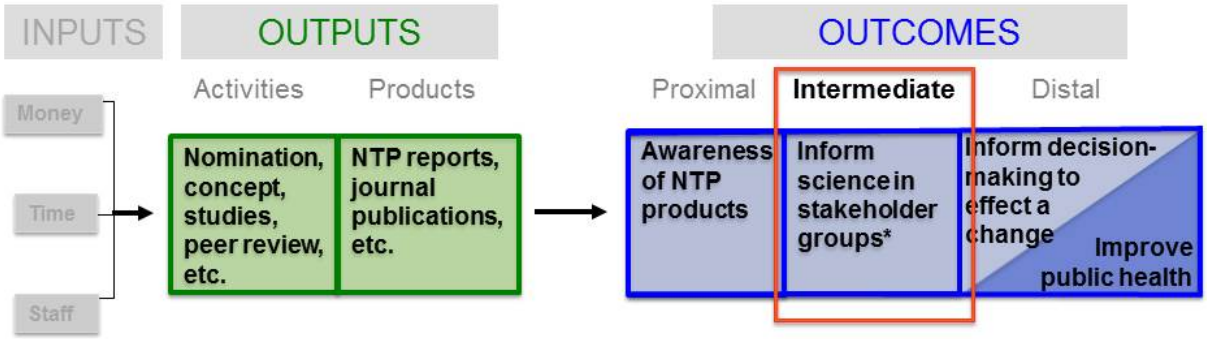
Webpage Views for TOX 72: July 2011 – October 2014



Requests to NTP's Document Management Team

- 15 Total requests for chromium (VI):
  - 2 Related to RoC
  - 13 Related to TR 546 or TOX 72
- Requests came from multiple groups:
  - Industry
  - U.S. EPA
  - U.S. House staff
  - NJ state agency
  - Academia

Intermediate Outcomes



NTP goal:

Strengthen the science base in toxicology.

Intermediate Outcomes

Bibliometrics

Citations in Scientific Literature

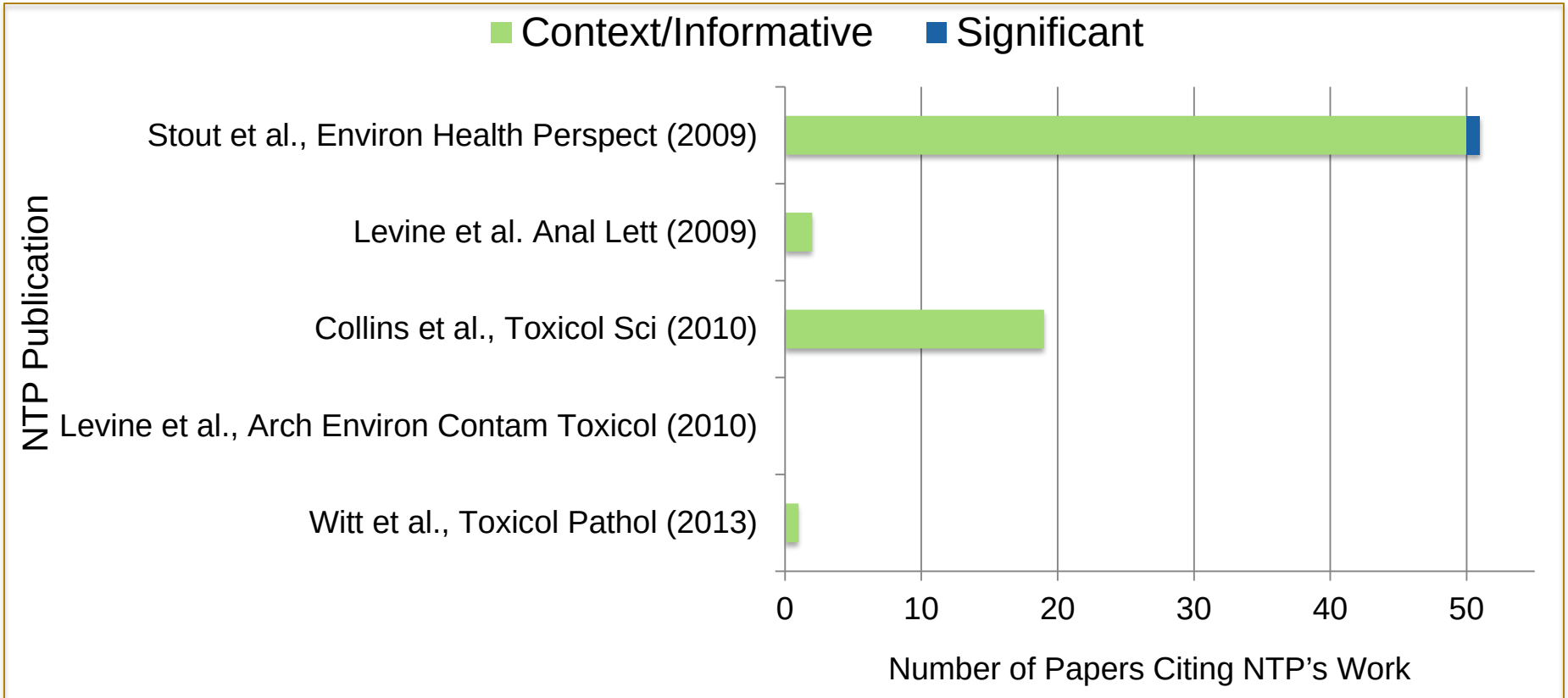
(Journal Articles, Book Chapters, and Reviews)

Citations of NTP Journal Publications

Searched by Web of Science and Scopus

Context/Informative: Cited NTP product to provide context for their study or to inform experimental design and/or data interpretation.

Significant: Used NTP data and/or method in their study.



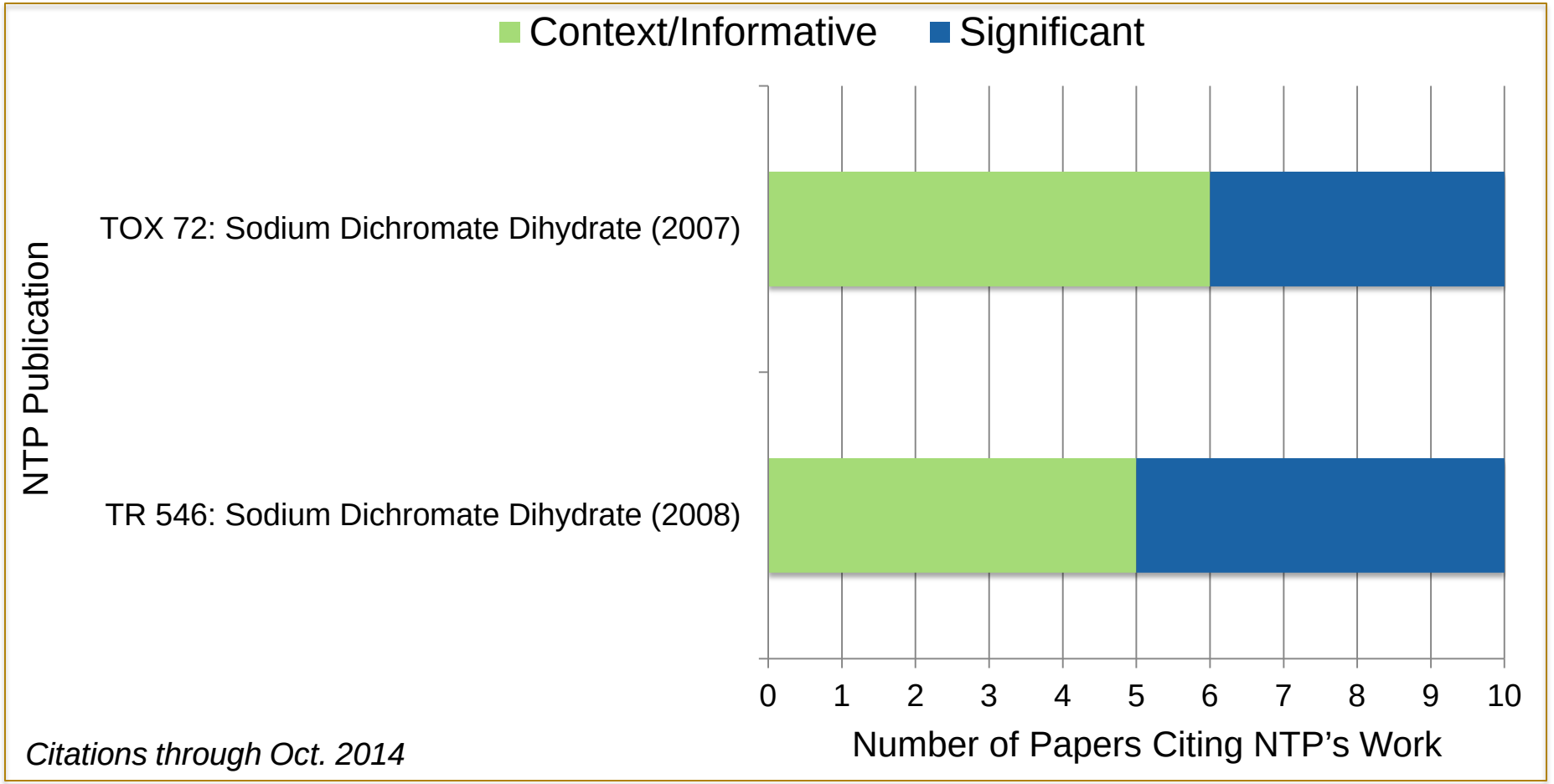
Citations through Oct. 2014

Citations of NTP Technical Report and Toxicity Report

Searched by PubMed

Context/Informative: Cited NTP product to provide context for their study or to inform experimental design and/or data interpretation.

Significant: Used NTP data and/or method in their study.



Citations through Oct. 2014

Intermediate Outcomes

Bibliometrics

Citations in Grants

NIH-Funded Grants that Cite NTP's Work

- References from grants are not searchable on NIH database.
- Searches were performed for grants that related to chromium.
  - Available references were checked for NTP products.
  - 4 grants were found that reference TR 546 or RoC:
    - **NIEHS:** Zhitkovich, Anatoly. *Genotoxicity of Chromium Compounds* (TR 546 Sodium Dichromate Dihydrate).
    - **NIEHS:** Puga, Alvaro. *Molecular Mechanisms of Complex Mixture Toxicity* (TR 546 Sodium Dichromate Dihydrate).
    - **NIEHS:** Chen, Aimin. *Human developmental toxicity of metal mixture exposure from e-waste recycling* (RoC).
    - **NIEHS:** Chang, Howard Y. *LncRNA regulation of environmental response* (RoC).

Bibliometrics

Citations in State, Federal, and Non-Government Reports

Search Strategies

Searched for NTP product references in

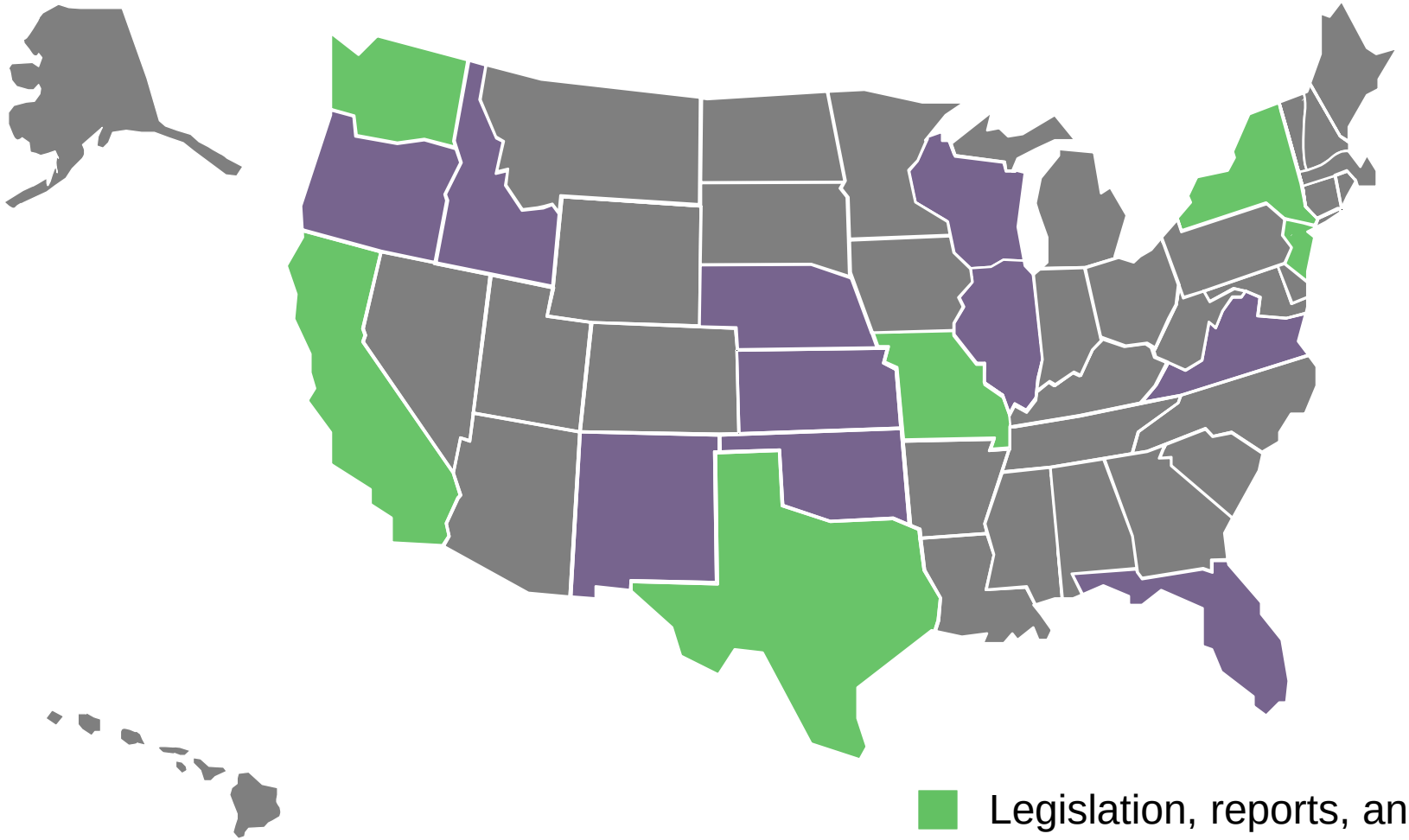
- Regulations
- Policy documents
- Science reports from other agencies
- Legal documents

Searches were done for

- All 50 states
- U.S. federal agencies
- U.S. non-government groups
- International community

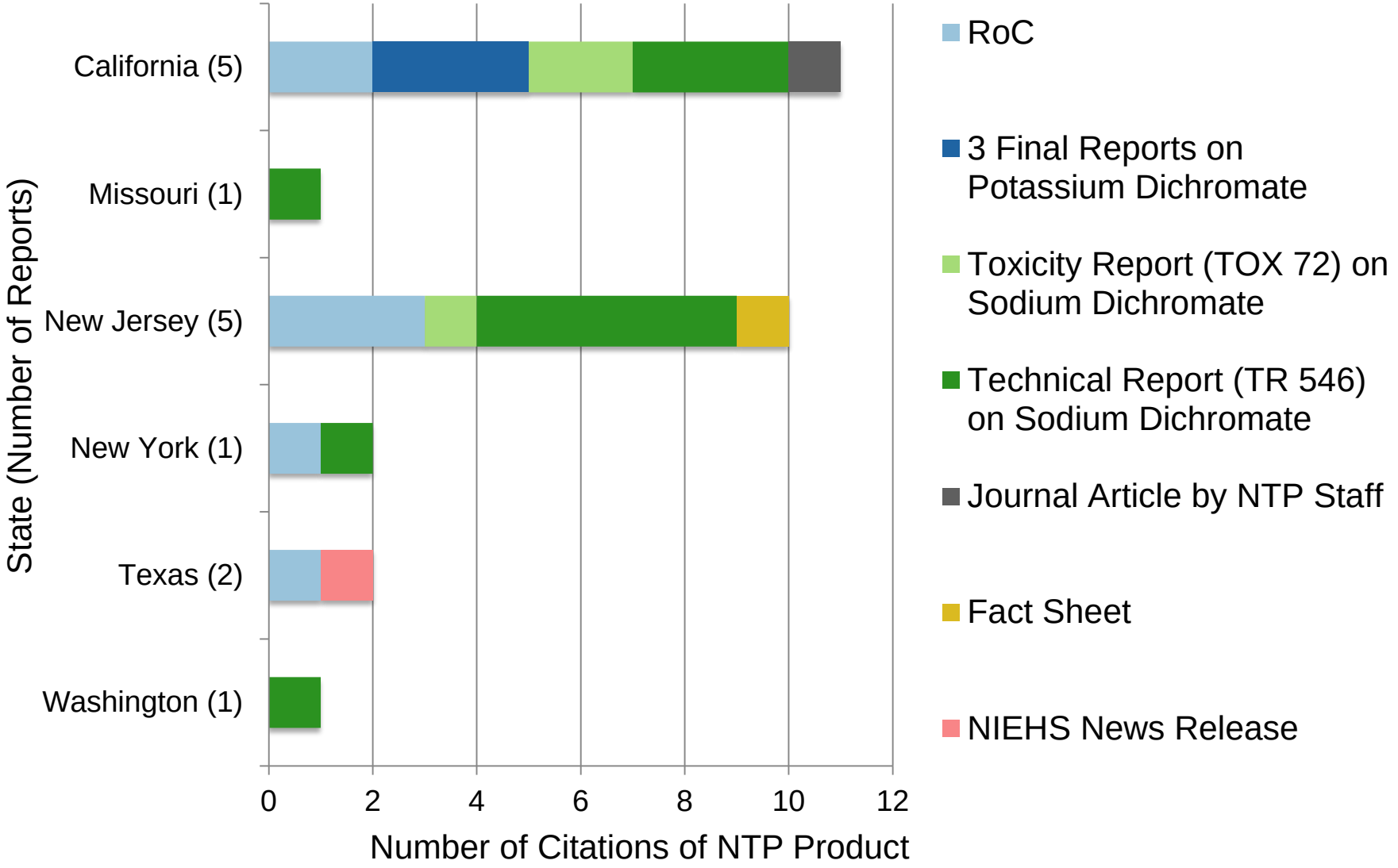
Intermediate Outcomes

Impact of NTP's Work in Individual States



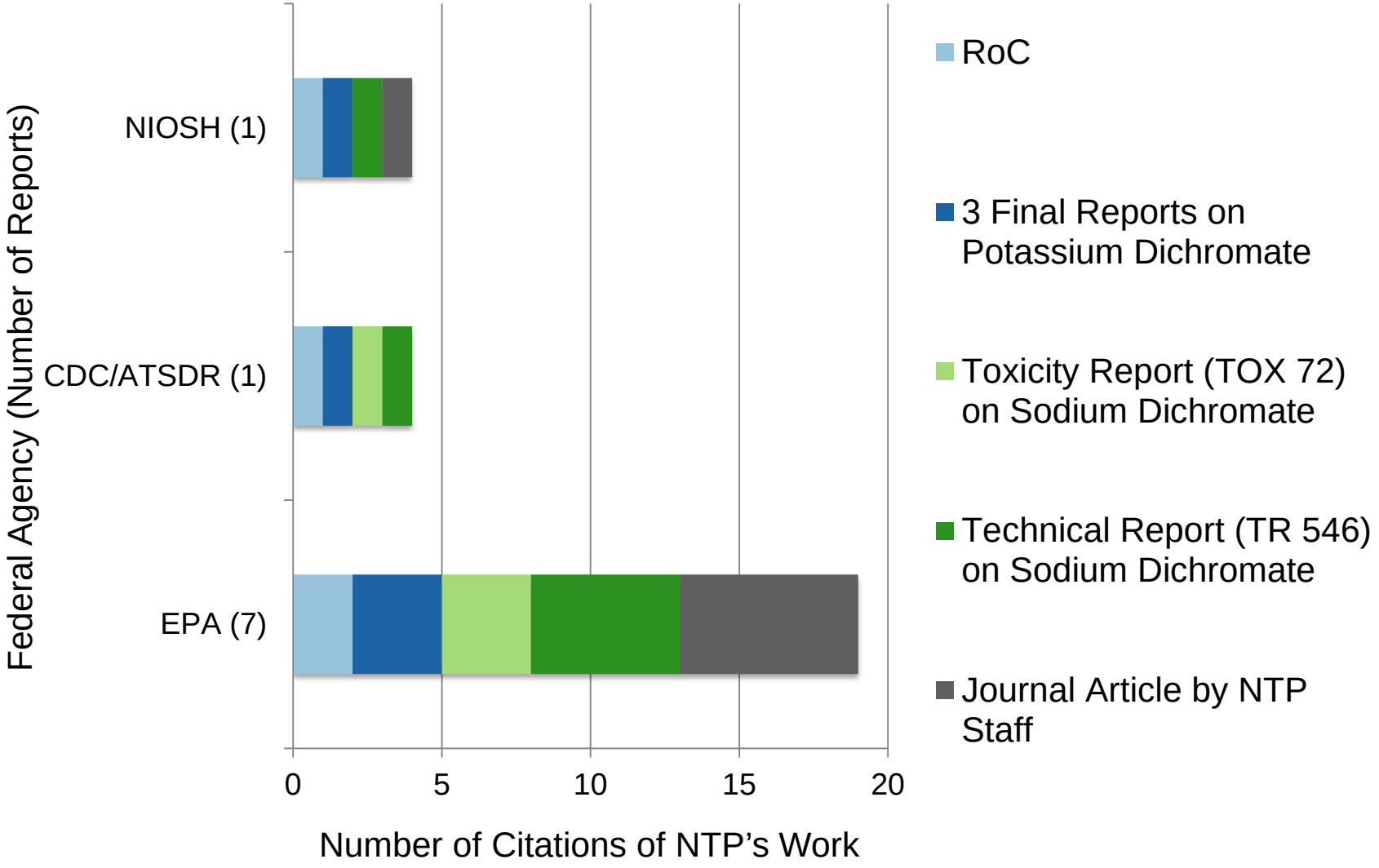
Intermediate Outcomes

Bibliometric Data: States



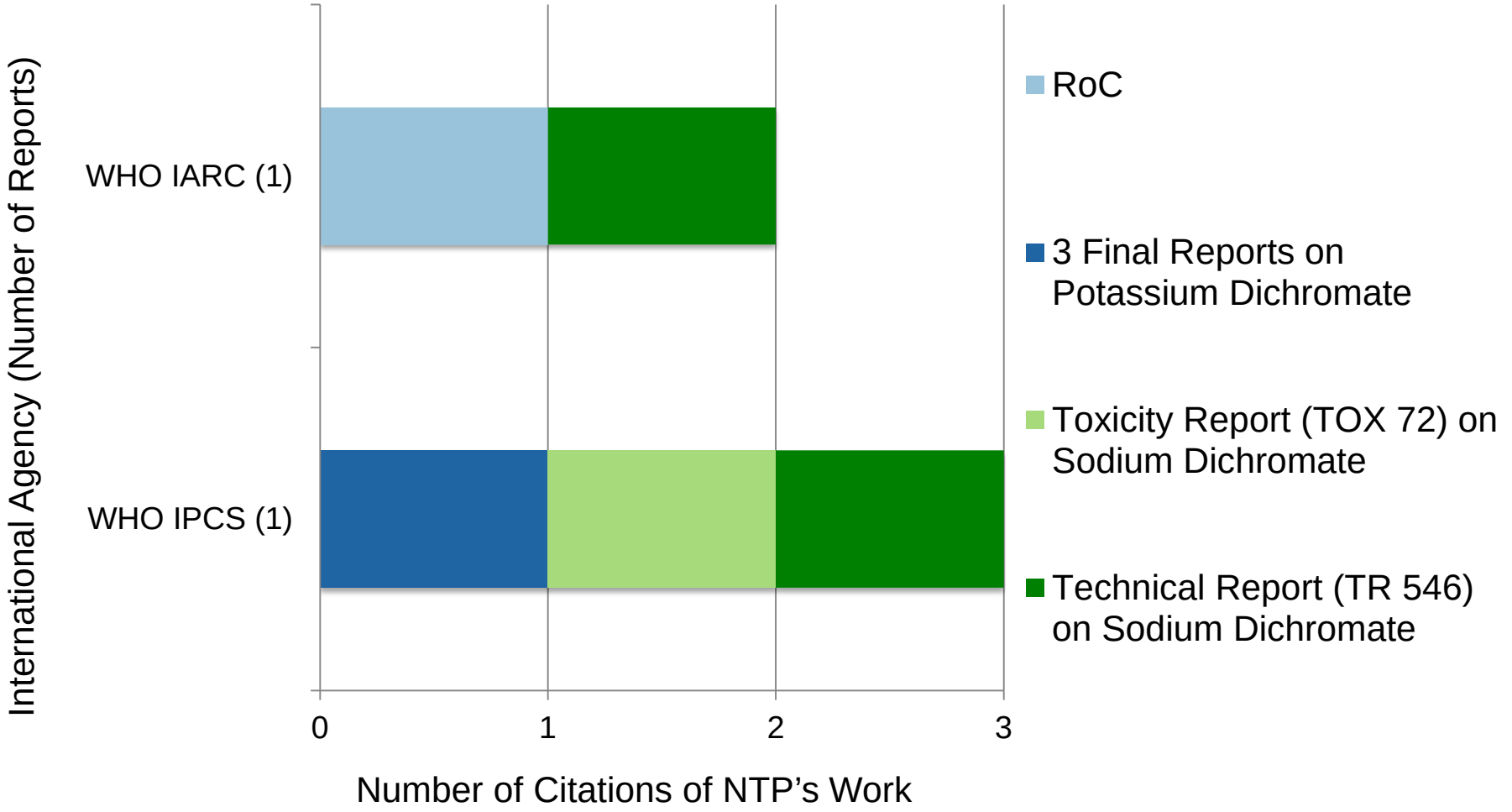
Intermediate Outcomes

Bibliometric Data: Federal Agencies

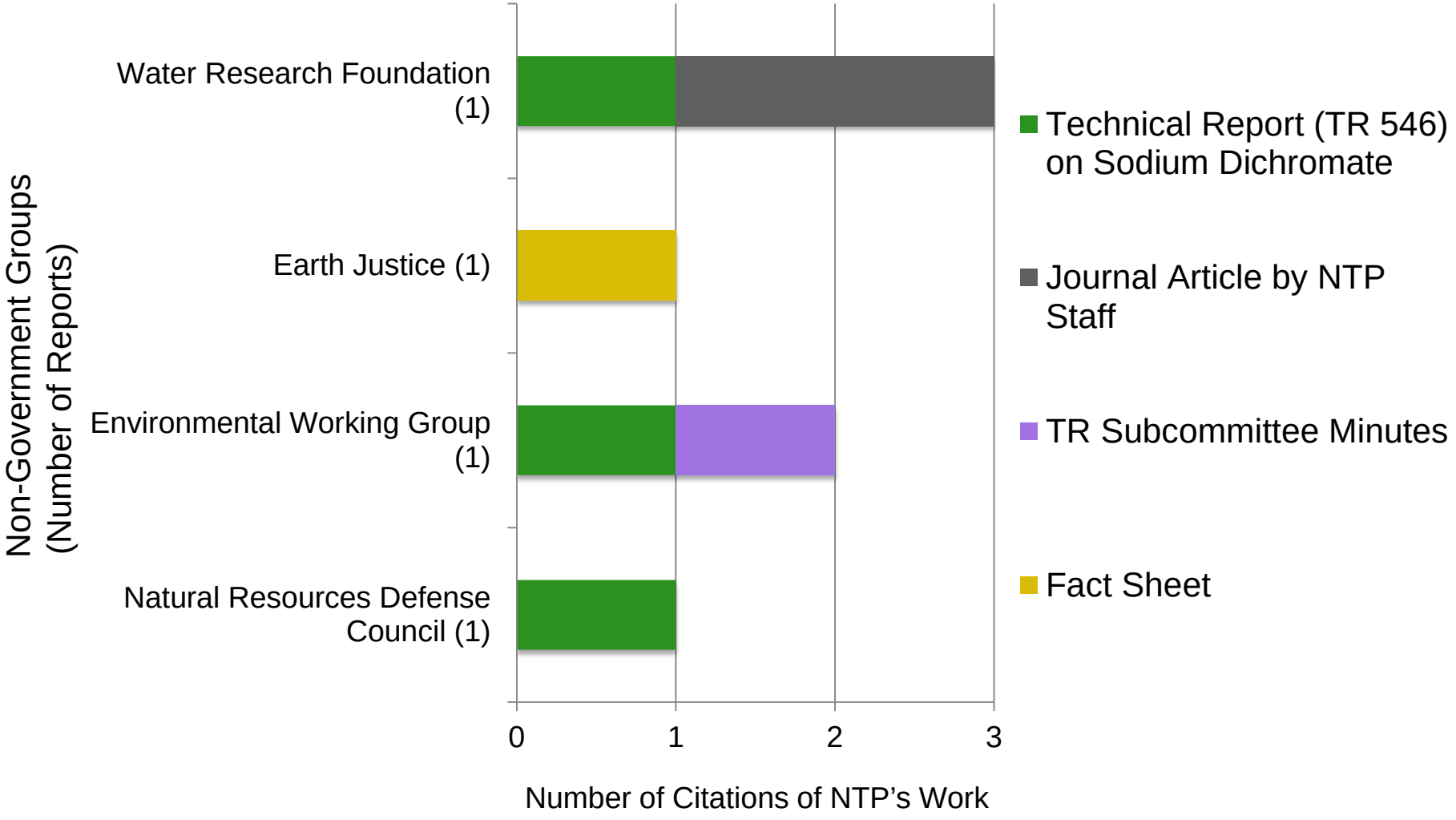


Intermediate Outcomes

Bibliometric Data: International Agencies

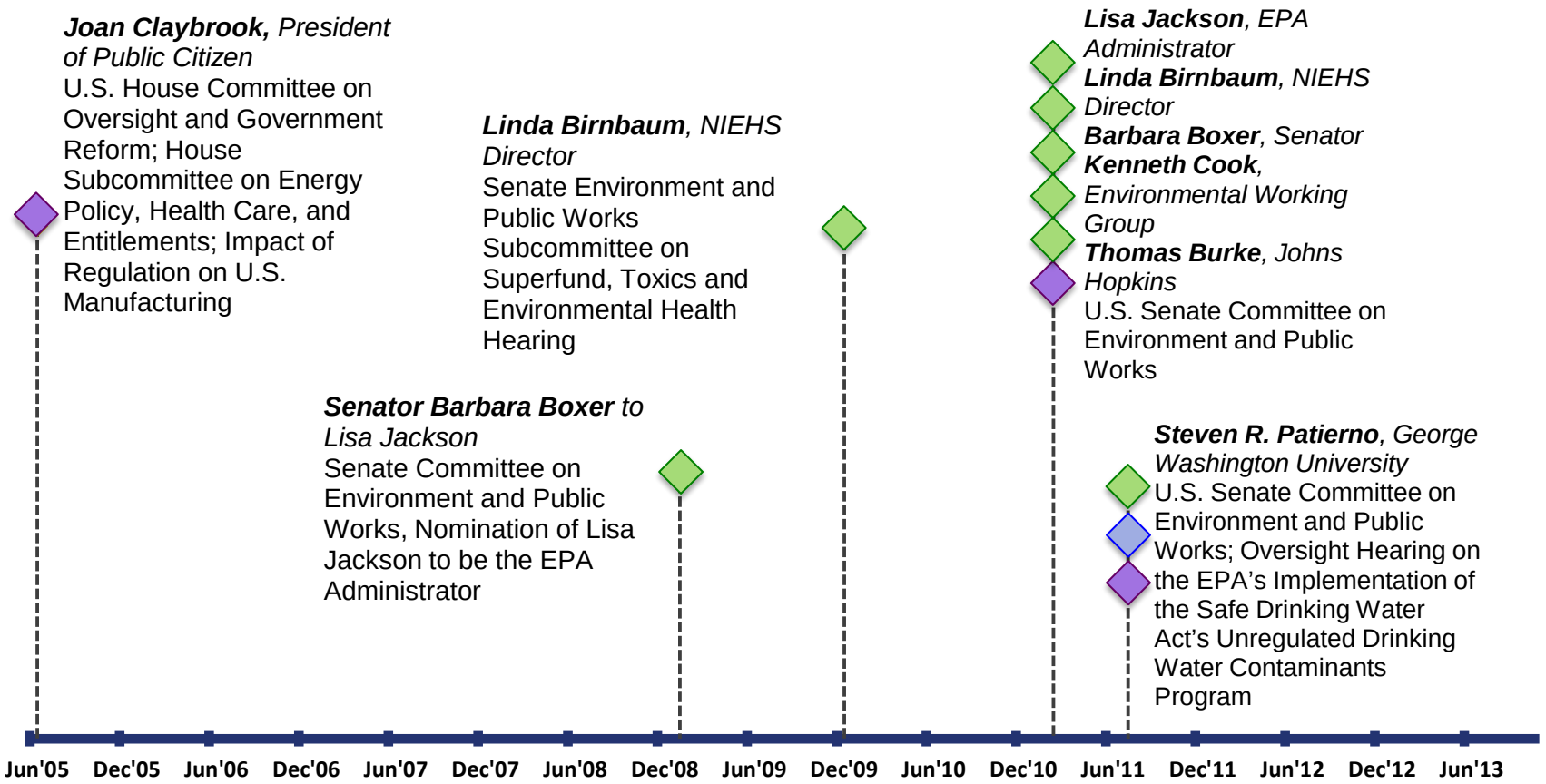


Bibliometric Data: Non-Government Groups



Intermediate Outcomes

Congressional Hearings



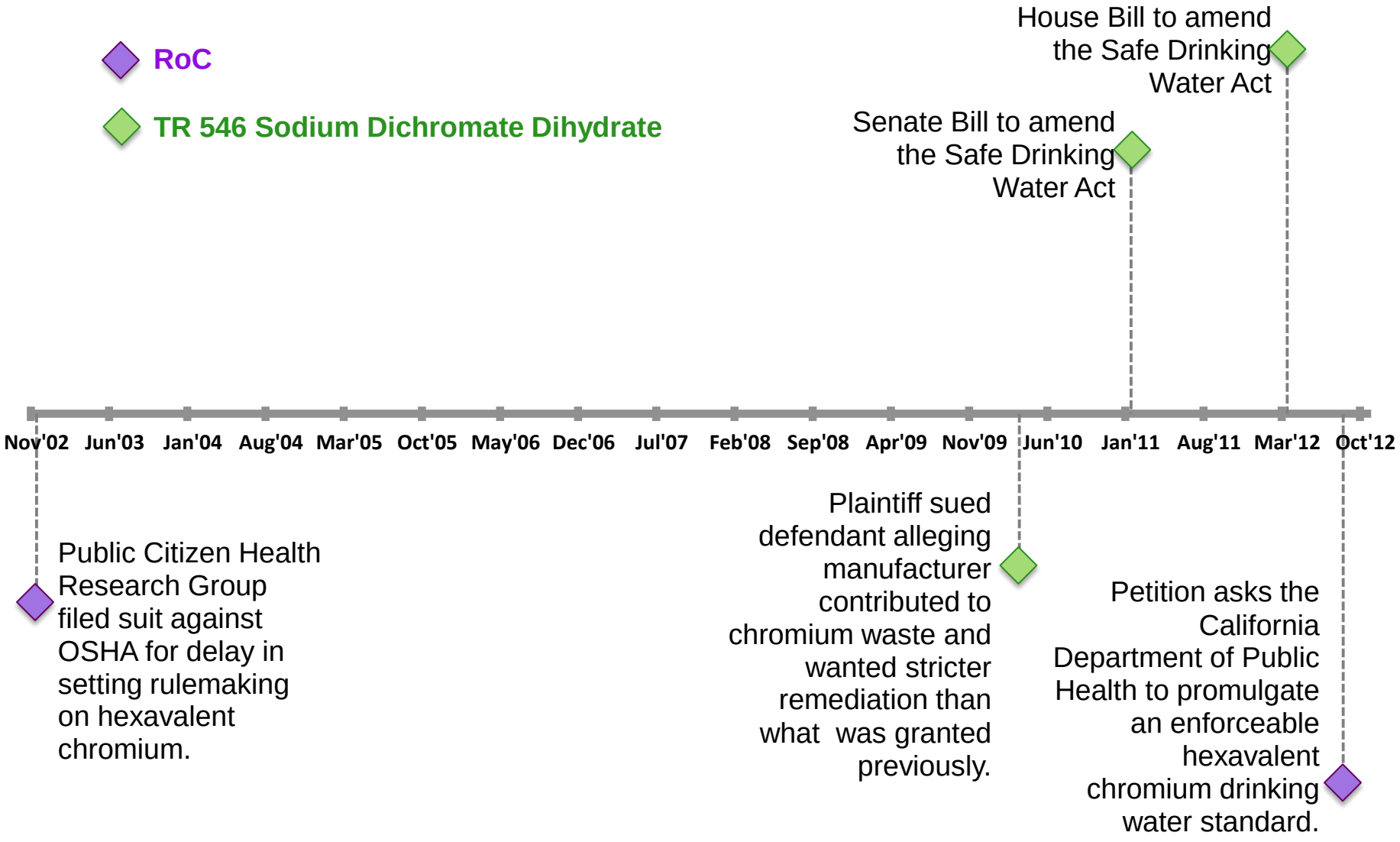
RoC

Journal publication

TR 546 Sodium Dichromate Dihydrate

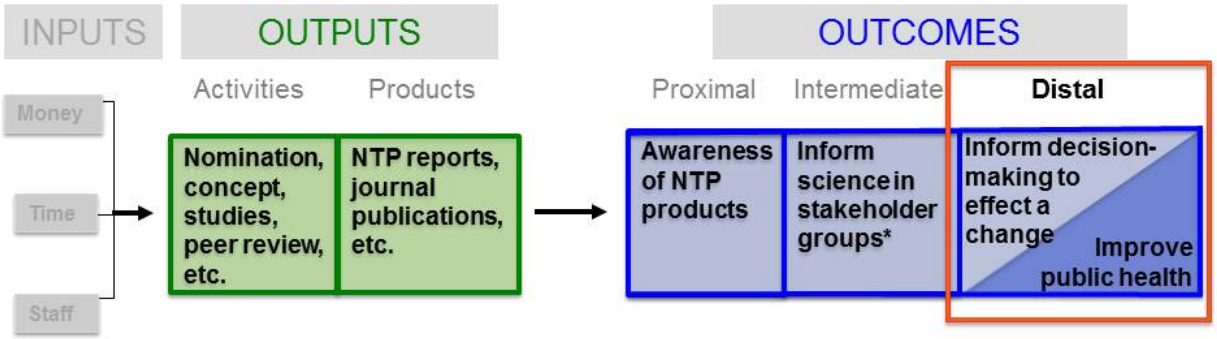
Intermediate Outcomes

Federal Legislative and Judicial Impact



Distal Outcomes

Inform Decision Making to Effect a Change



NTP goals:

Provide information about potentially toxic chemicals to health, regulatory, and research agencies, scientific and medical communities, and the public.

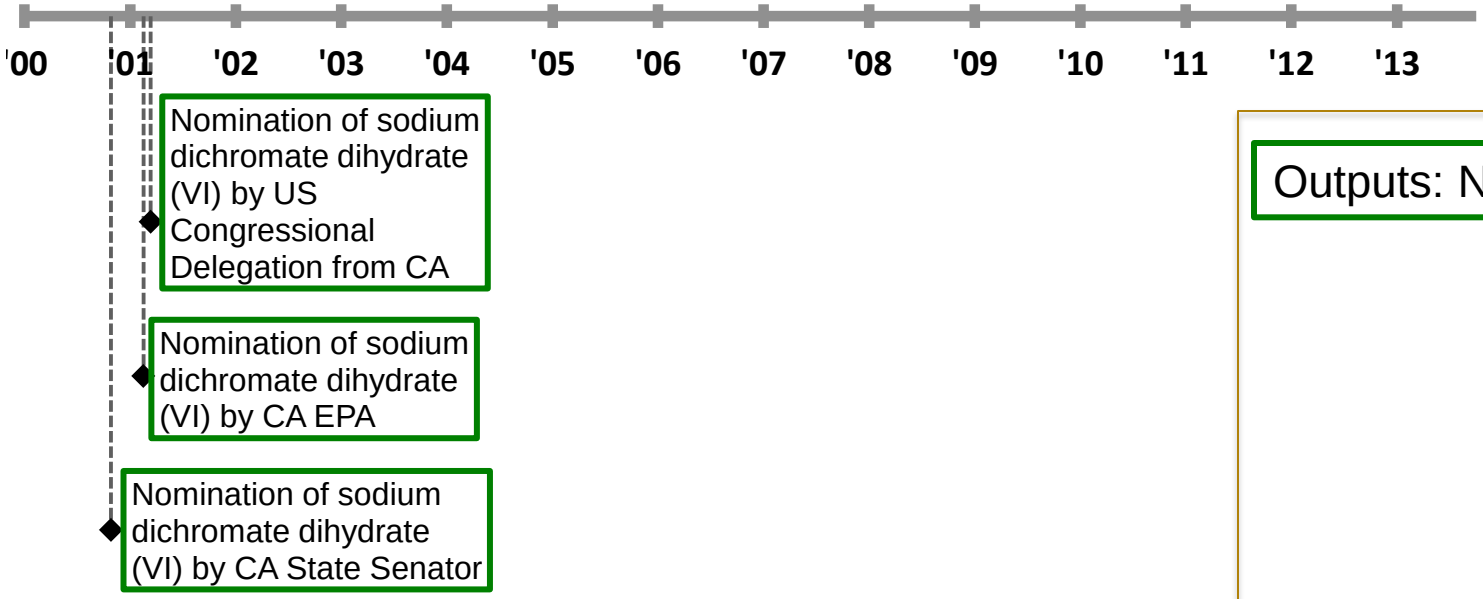
Distal Outcomes: NTP Impact in California

- **In May 2014, the regulation for a maximum contaminant level (MCL) of chromium-6 was approved by the Office of Administrative Law.**

- **The 0.010-milligram per liter MCL became effective on July 1, 2014.**

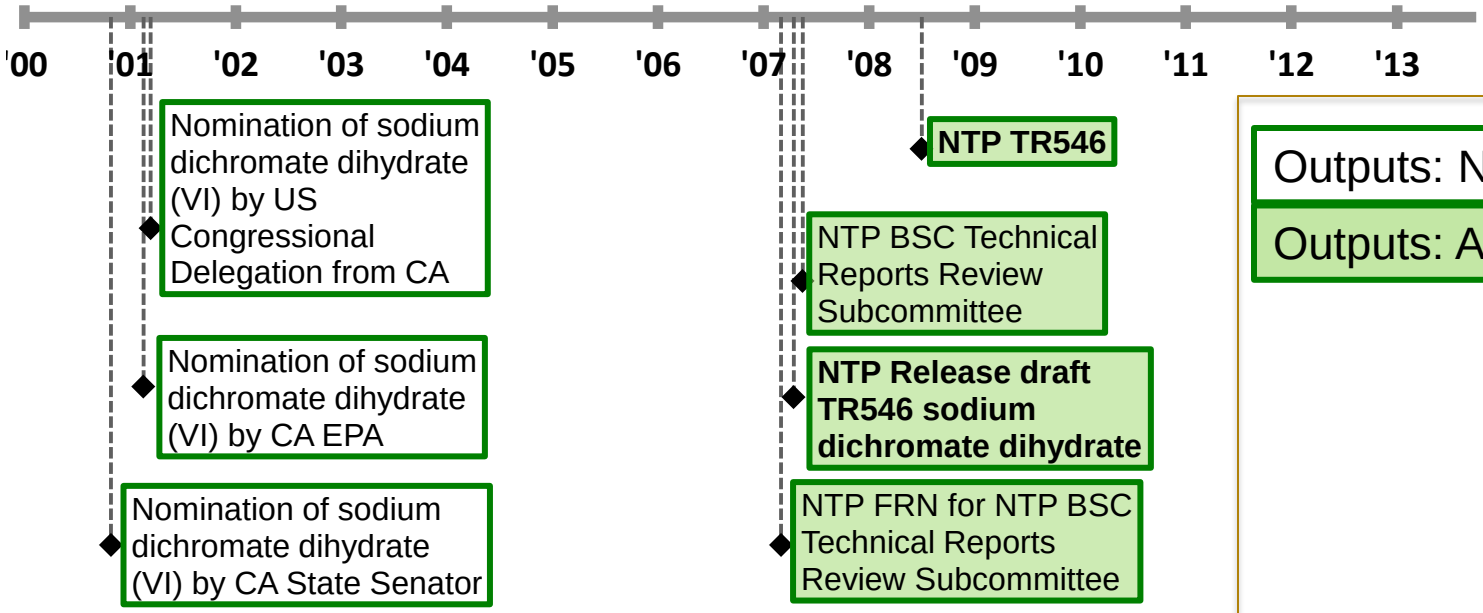
NTP's research was key to California's drinking water standard for chromium (VI).

Path to Distal Outcomes in CA: TR 546



Outputs: Nomination Activity

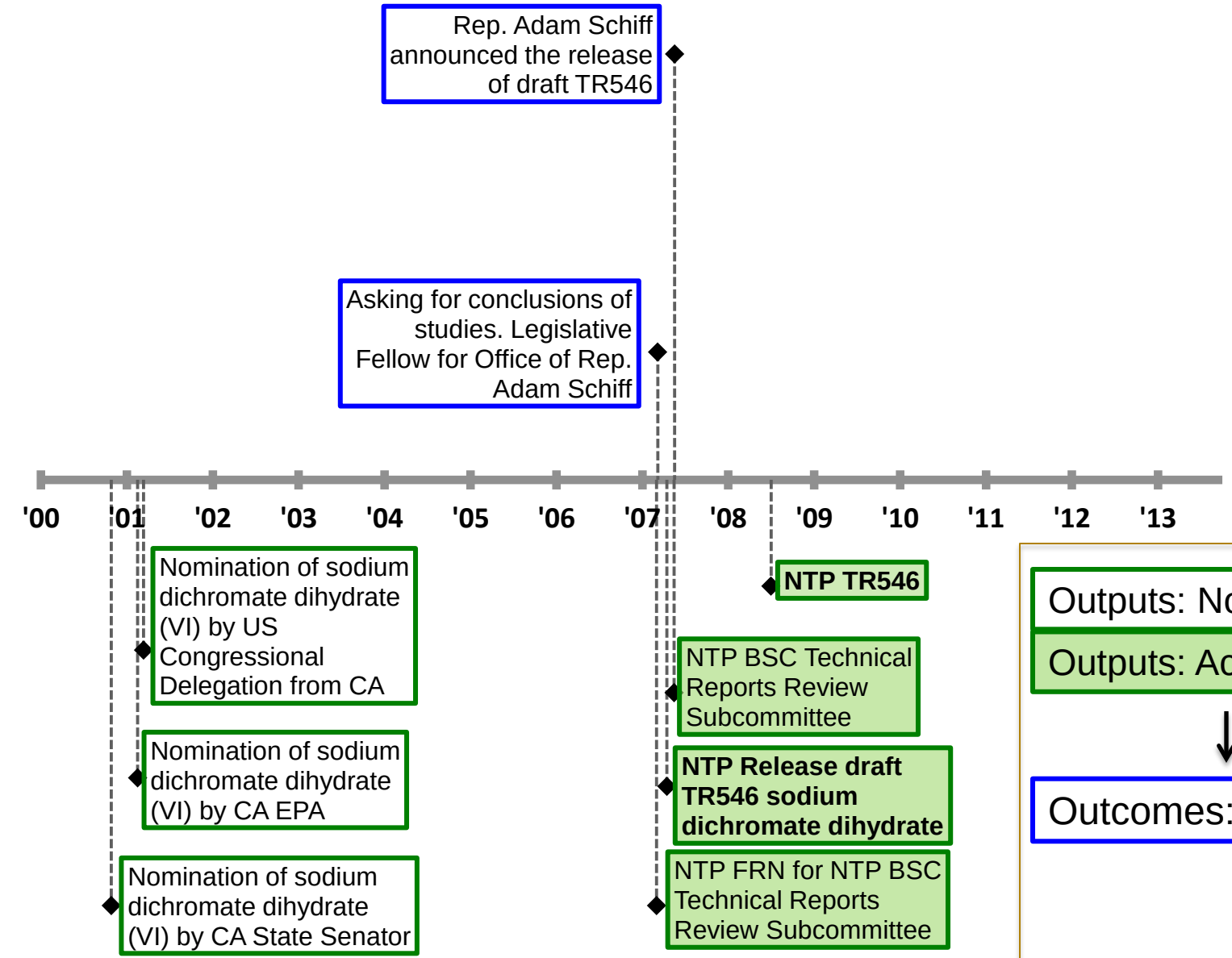
Path to Distal Outcomes in CA: TR 546



Outputs: Nomination Activity

Outputs: Activities/Products

Path to Distal Outcomes in CA: TR 546



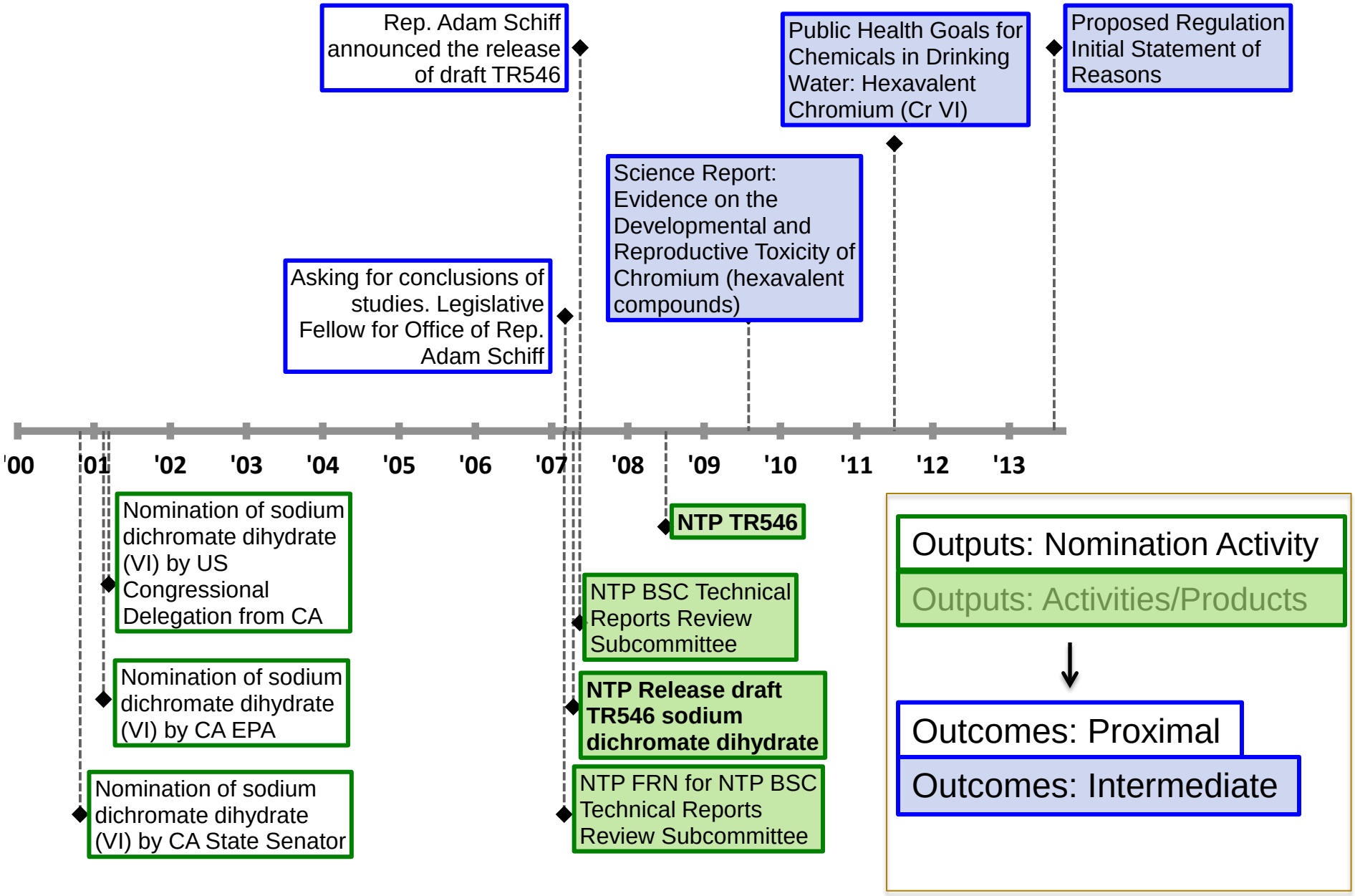
Outputs: Nomination Activity

Outputs: Activities/Products

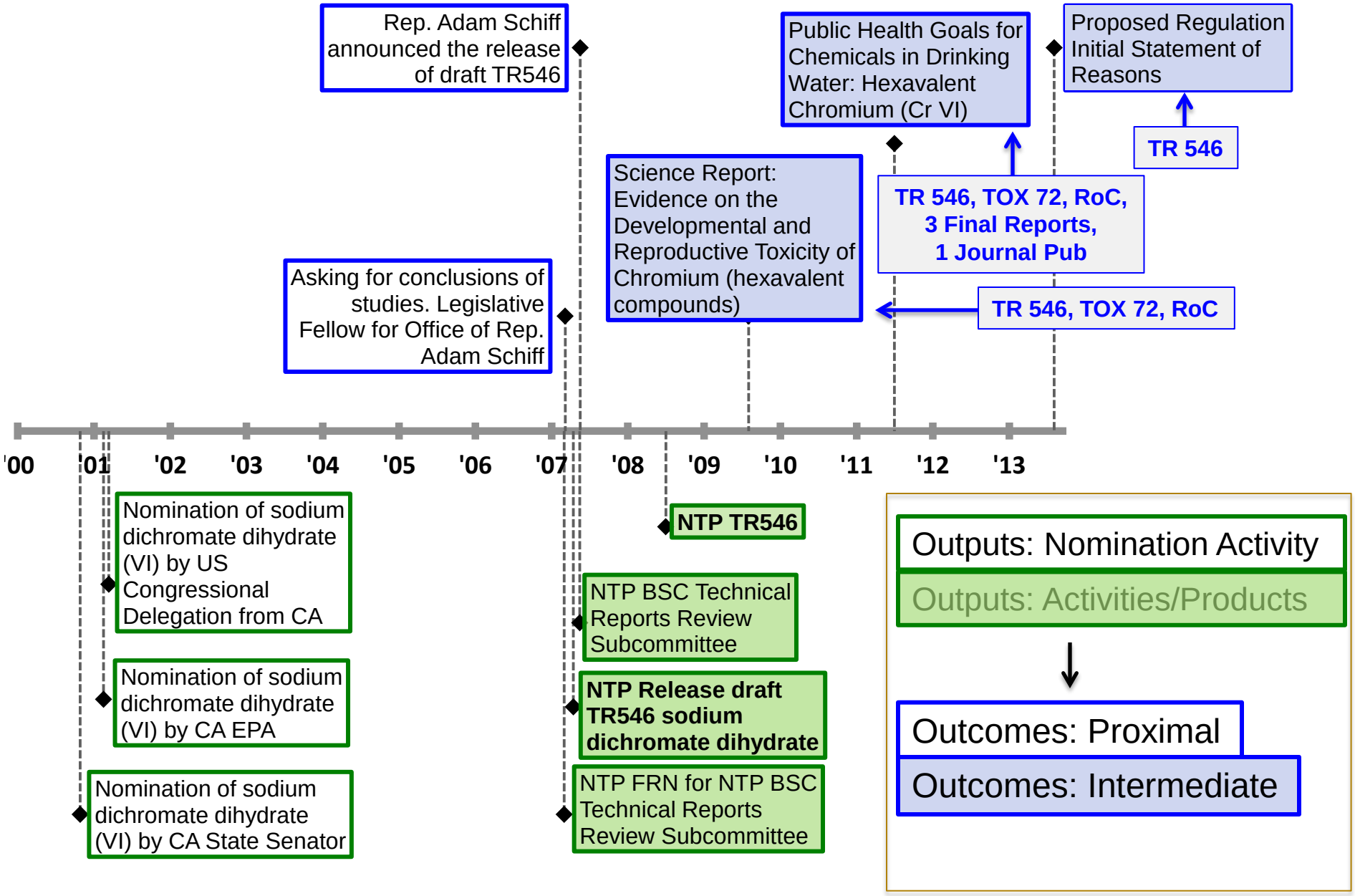
↓

Outcomes: Proximal

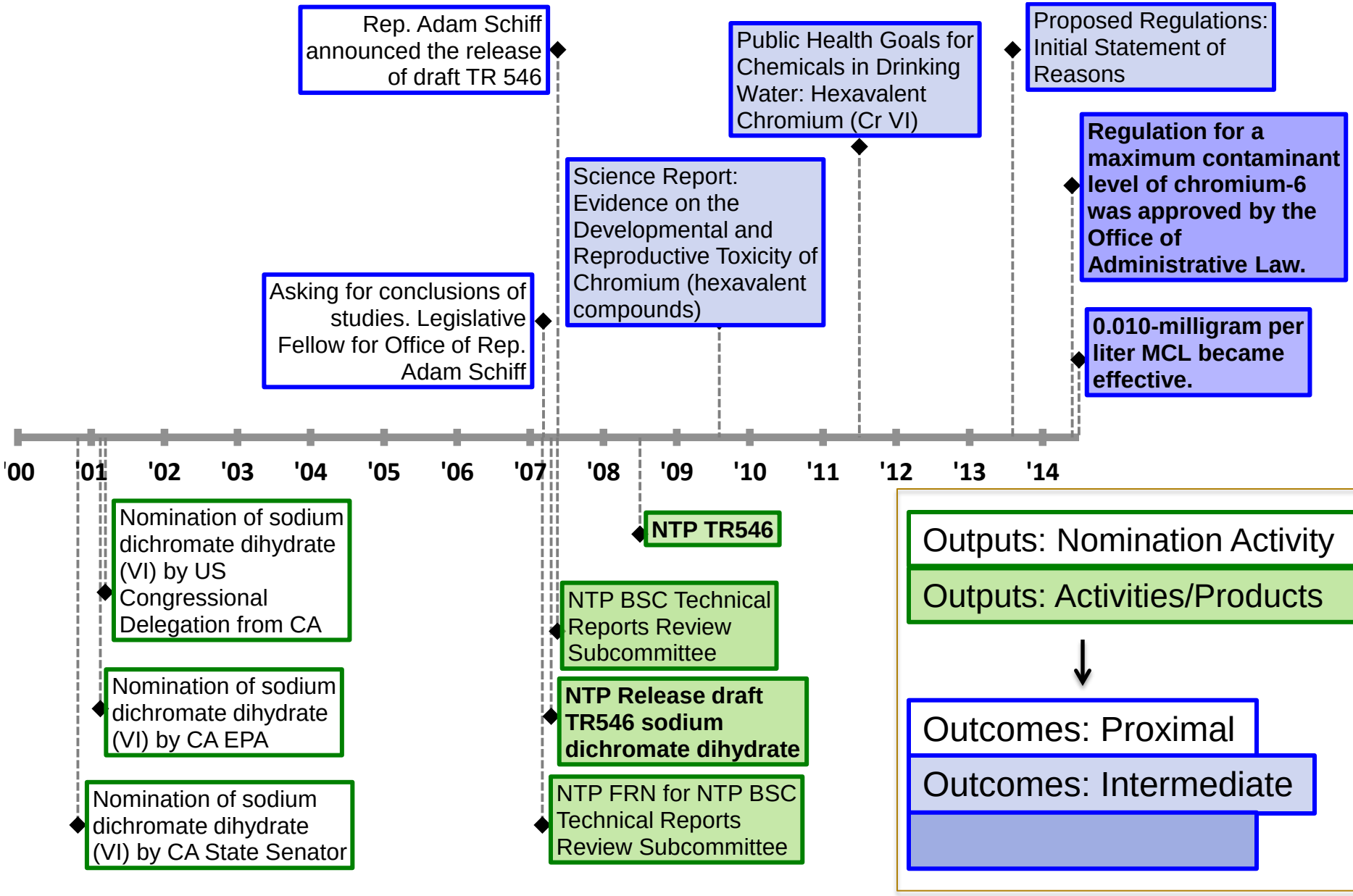
Path to Distal Outcomes in CA: TR 546



Path to Distal Outcomes in CA: TR 546



Path to Distal Outcomes in CA: TR 546



Examples of Challenges

For distal outcomes, there is increased lag time and reliance on external factors.

"…a protracted timeframe introduces many variables that are difficult to track and are often beyond the control of NIH."

NIH. 2013. Scientific Management Review Board Report on the Approaches to Assess the Value of Biomedical Research.

NTP Impact in Washington

DATE	SUBJECT	NTP Reference
6/1/10	Draft Revisions Model Toxics Control Act Method A Groundwater Cleanup Levels	TR546

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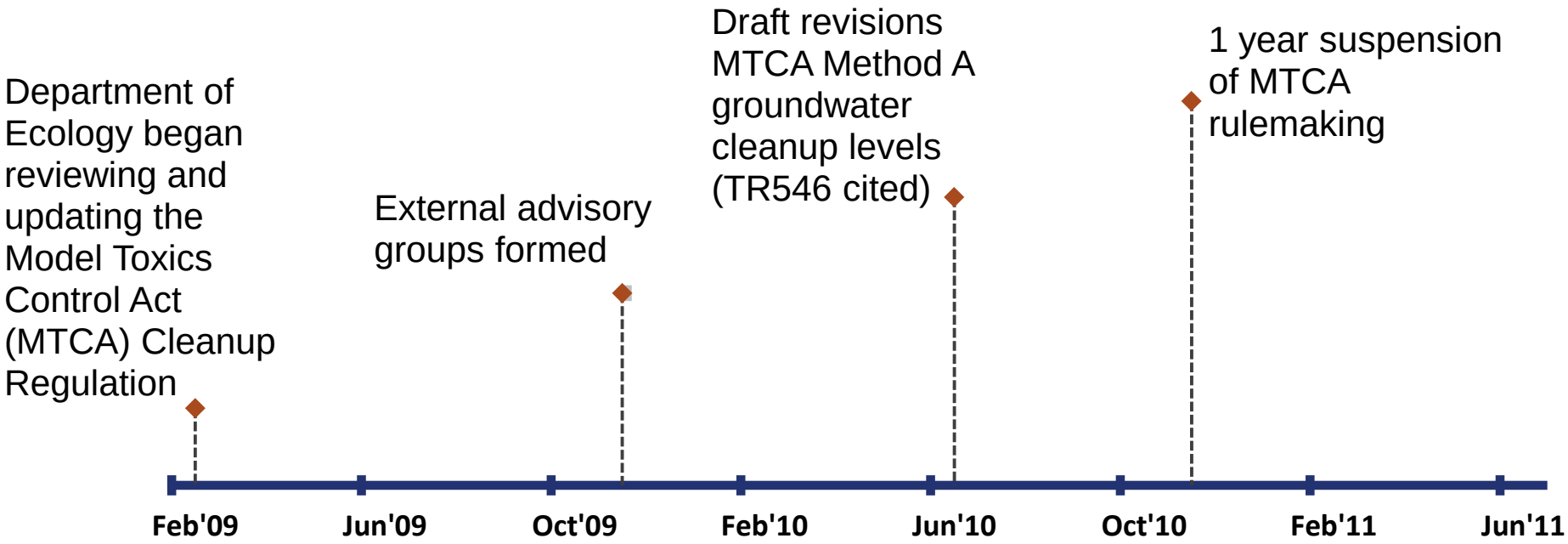
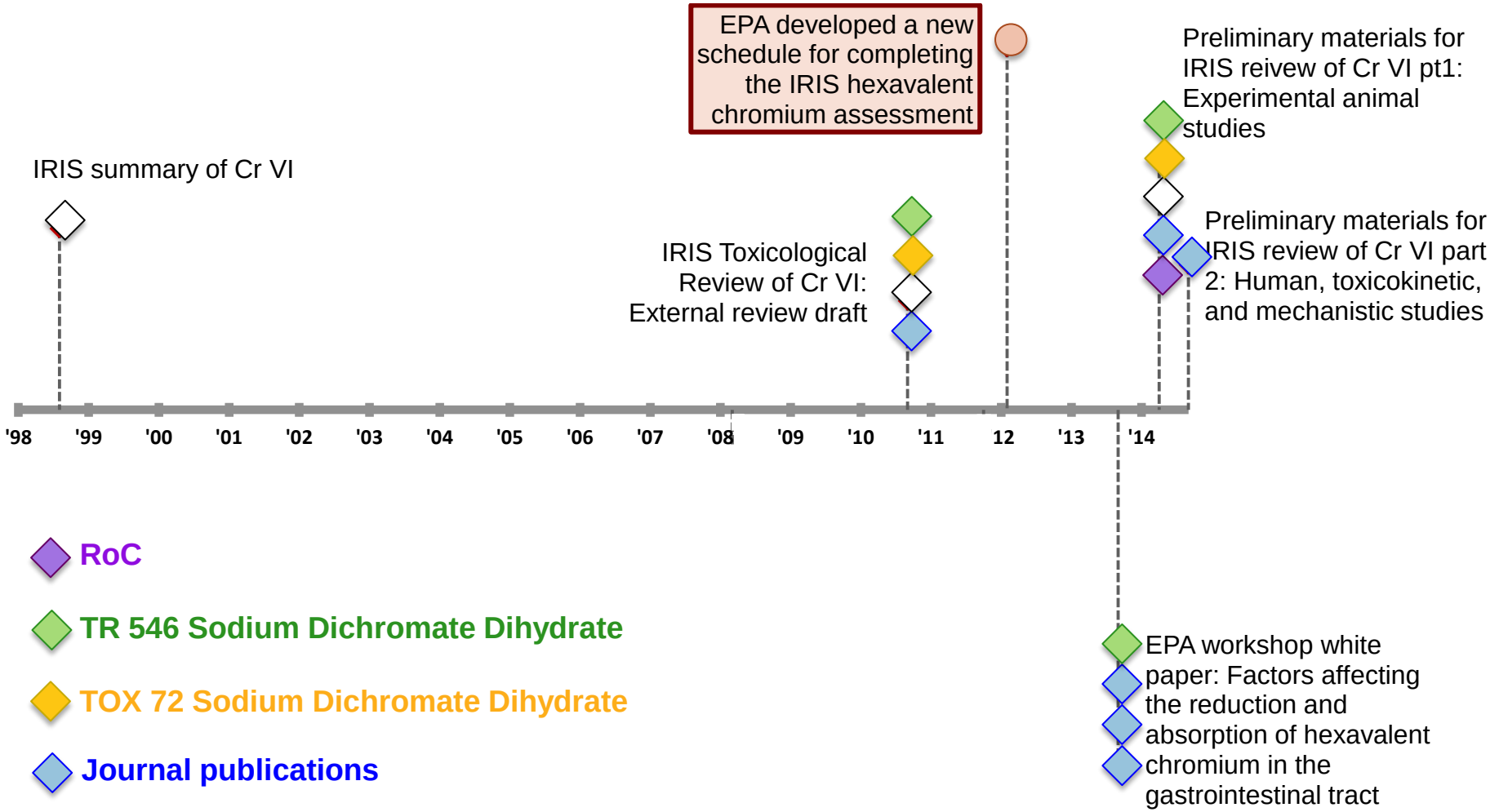


EPA IRIS


EPA developed a new schedule for completing the IRIS hexavalent chromium assessment
Preliminary materials for IRIS reivew of Cr VI pt1: Experimental animal studies
IRIS summary of Cr VI
IRIS Toxicological Review of Cr VI: External review draft
Preliminary materials for IRIS review of Cr VI part 2: Human, toxicokinetic, and mechanistic studies
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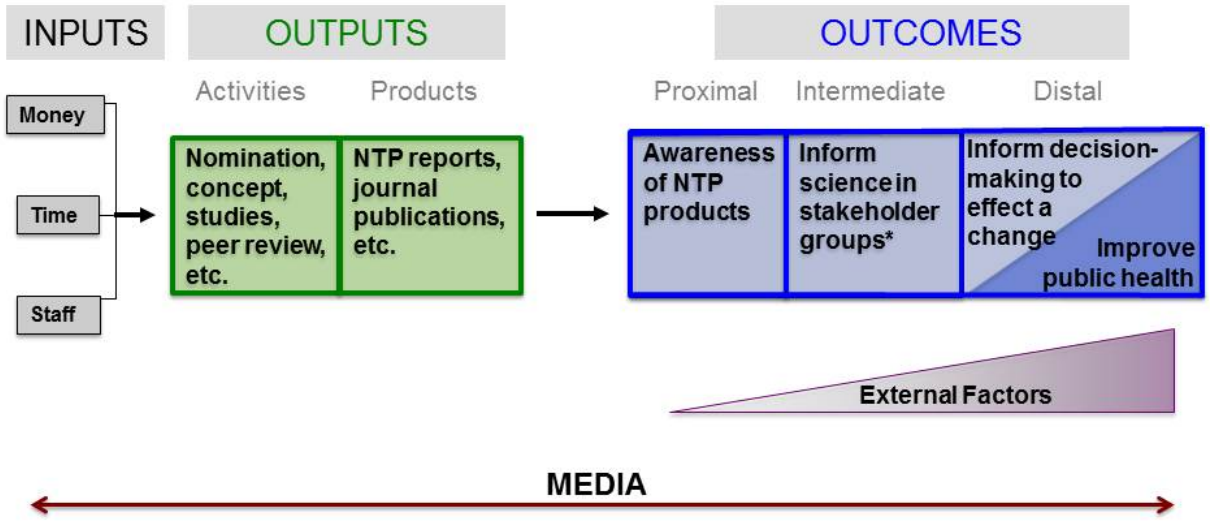
RoC
TR 546 Sodium Dichromate Dihydrate
TOX 72 Sodium Dichromate Dihydrate
Journal publications
Final reports (set of 3) on the reproductive toxicity of potassium dichromate
EPA workshop white paper: Factors affecting the reduction and absorption of hexavalent chromium in the gastrointestinal tract

Logic Model for NTP Studies on Chromium (VI)



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Media

- Analyzed over 400 media articles related to the NTP and chromium.
- Media coverage paralleled NTP outputs and outcomes.

Media

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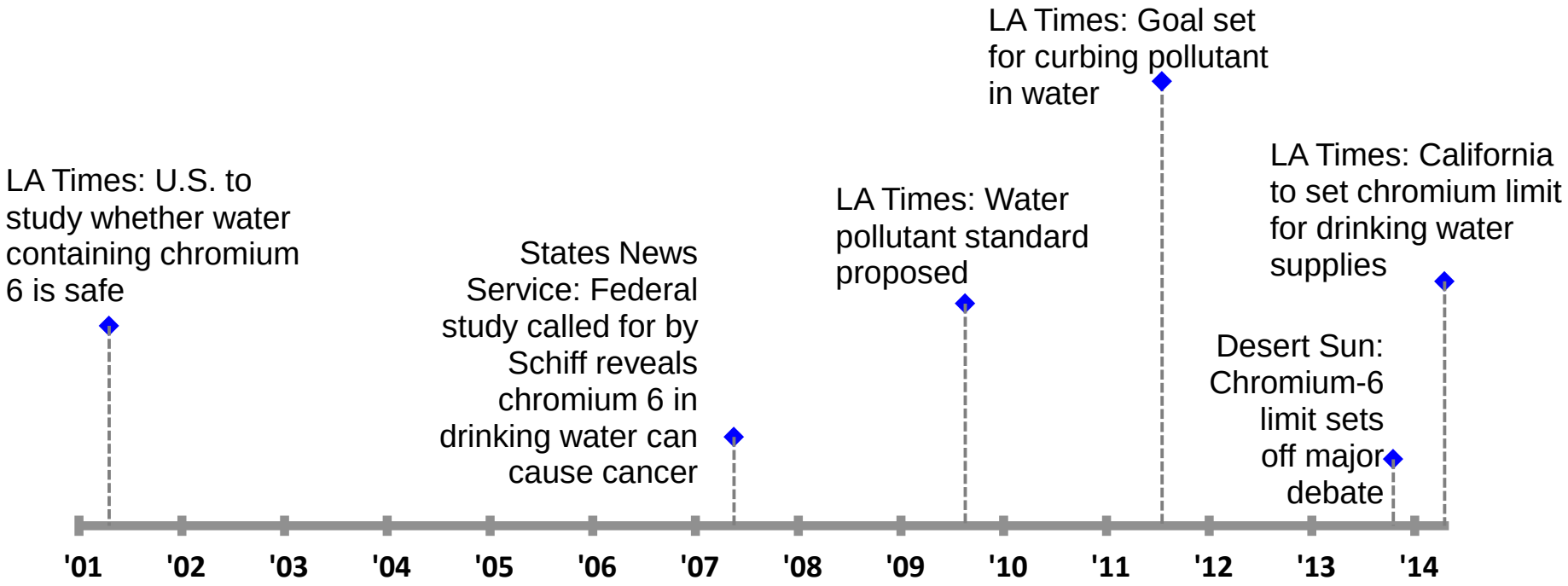
- Media coverage paralleled NTP outputs and outcomes.
- For example:



Conclusions

- This case study demonstrated NTP's science on chromium VI had impact in many areas including public health.
- We identified a broad and objective approach for assessing NTP's effectiveness.
- Discovered data and methodological gaps that need to be addressed for more thorough and efficient assessments in the future.

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- Distal Outcomes
  - Working with Sciome, Inc. subcontractors on web-mining tools (e.g., search automation and text mining).

Actions for Improving Future Evaluations

Overall Improvements

- Use methods learned from retrospective work to track current NTP projects (e.g., systematic review).
  - Timely tracking of activities, products, and impacts.
  - Ensure NTP work is effectively communicated to the public and stakeholders.

Next Steps

- Develop an approach to conduct a retrospective evaluation that more broadly examines NTP effectiveness:
  - Random selection of NTP reports in a certain time range that accounts for:
    - Lag time.
    - Availability of data.
  - Identify differences in achieving distal impacts.
    - Determine why there are differences in achieving distal impacts if differences are found.
    - Potentially identify additional distal outcomes not currently measured.

Questions