Value of Information Case Study

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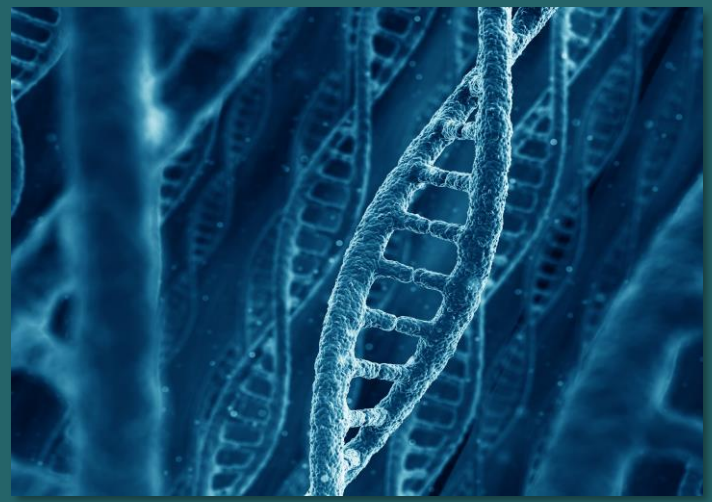

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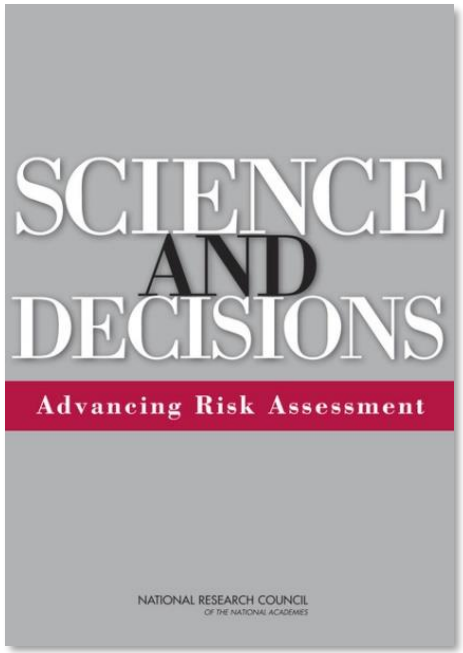
How Can ORD Assess the Value of a New Assessment Paradigm, Like ETAP?



NRC, 2009

- The National Research Council stated that the **timeliness** is a "*major and rarely acknowledged influence in the nature and quality*" in risk assessment
- Additional studies or improvements in the assessment may reduce **uncertainty**, but they require additional resources and the **delay** "*can have significant impact on communities who are awaiting risk assessment results*."
- **Value-of-information** (VOI) analysis was recommended as providing a **more objective** decision framework
- VOI is a method for quantifying the **expected gain in economic terms** of reducing uncertainty through the collection of additional data
- To date, application of VOI in toxicology and chemical risk assessment have not explicitly considered the impact of **timeliness of data collection**

Value of Information Framework Used in the Case Study

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ORIGINAL ARTICLE

A value of information framework for assessing the trade-offs associated with uncertainty, duration, and cost of chemical toxicity testing

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Abstract

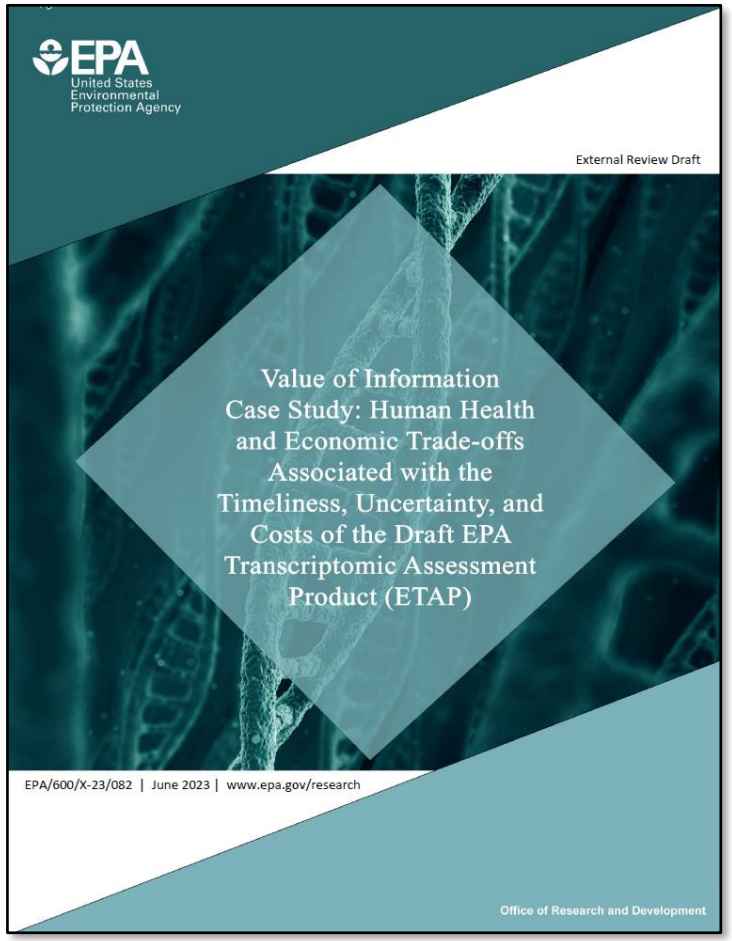
A number of investigators have explored the use of value of information (VOI) analysis to evaluate alternative information collection procedures in diverse decision-making contexts. This paper presents an analytic framework for determining the value of toxicity information used in risk-based decision making. The framework is specifically designed to explore the trade-offs between cost, timeliness, and uncertainty reduction associated with different toxicity-testing methodologies. The use of the proposed framework is demonstrated by two illustrative applications which, although based on simplified assumptions, show the insights that can be obtained through the use of VOI analysis. Specifically, these results suggest that timeliness of information collection has a significant impact on estimates of the VOI of chemical toxicity tests, even in the presence of smaller reductions in uncertainty. The framework introduces the concept of the expected value of delayed sample information, as an extension to the usual expected value of sample information, to accommodate the reductions in value resulting from delayed decision making. Our analysis also suggests that lower cost and higher throughput testing also may be beneficial in terms of public health benefits by increasing the number of substances that can be evaluated within a given budget. When the relative value is expressed in terms of return-on-investment per testing strategy, the differences can be substantial.

KEYWORDS
cost of delay, return on investment, risk decision making, social cost, toxicity testing, value of information

1 | INTRODUCTION

Evidence-based risk assessment has become a cornerstone of public and population health risk decision making, integrating evidence on toxicity and exposure from multiple evidence streams. When the available evidence is insufficient to allow a decision to be made with confidence, consideration can be given to gathering additional evidence to strengthen the evidence base. The present paper focuses on the use of value of information (VOI) analysis to evaluate the utility of gathering additional evidence on the toxicity of chemicals. Specifically, we present a VOI analytic framework that builds on previous methodological work in this field, explicitly incorporating the value of additional test data resulting from reductions in the uncertainty in estimates of a chemical's toxicity, the cost of delay in decision making that results

Hagiwara et al., Risk Analysis, 2022



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- The VOI framework provides a basis for objectively evaluating trade-offs between **timeliness**, **uncertainty**, and **cost** in toxicity testing and chemical risk assessment
- The case study applies this framework to assess and compare the value of information provided by two alternate testing and assessment processes

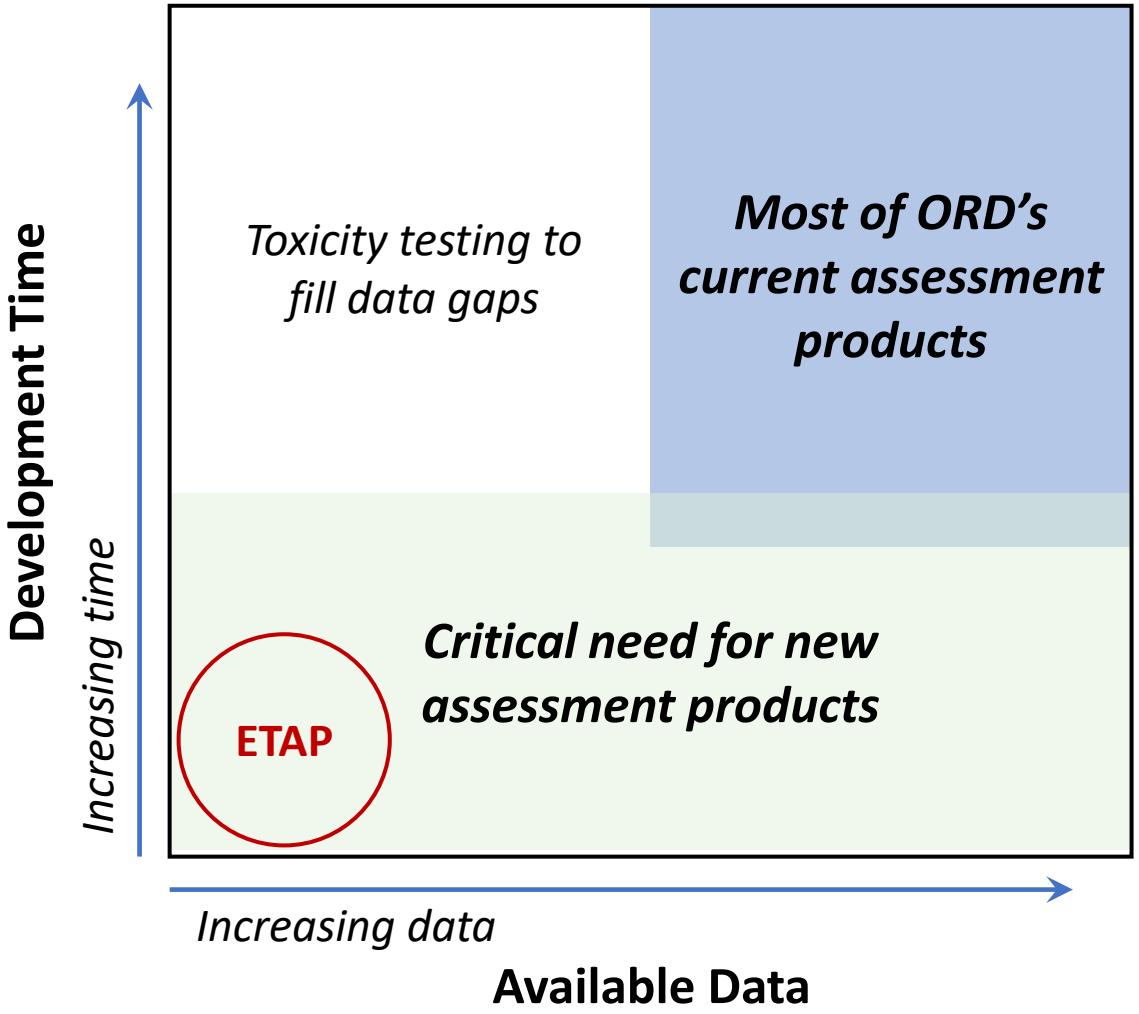
Focus of the Case Study

- Case studies provide an important tool for understanding the strengths and weaknesses of proposed new methodological approaches prior to their application in regulatory practice (*Kavlock et al., 2018*)

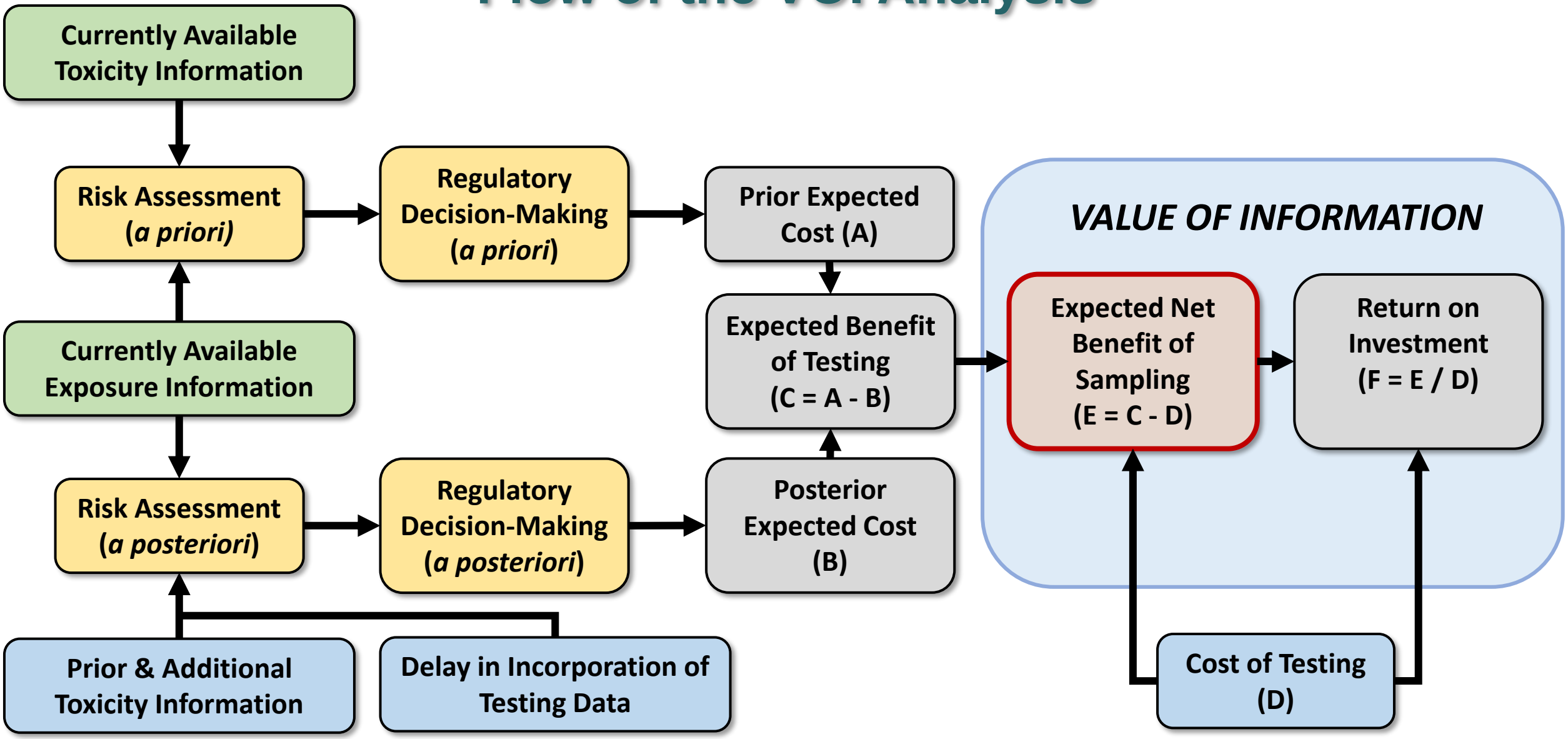
- The present case study uses an expanded VOI framework to compare two chemical toxicity testing and risk assessment options:

    1. The five-day, repeated dose *in vivo* transcriptomic study and the EPA Transcriptomic Assessment Product (**ETAP**) process

    2. The two-year rodent chronic toxicity test with traditional human health assessment (**THHA**) process.

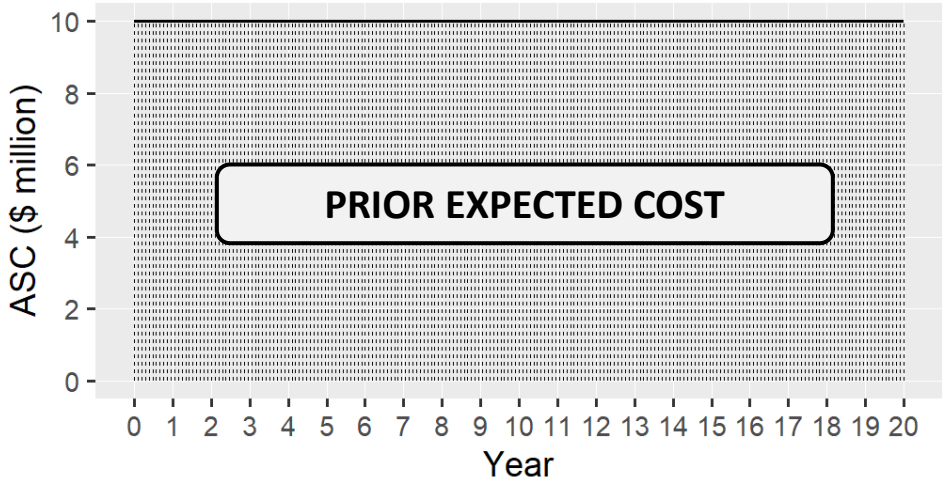


Flow of the VOI Analysis



Benefits of Testing – Incorporating both Annual Risk Reduction and Timeliness

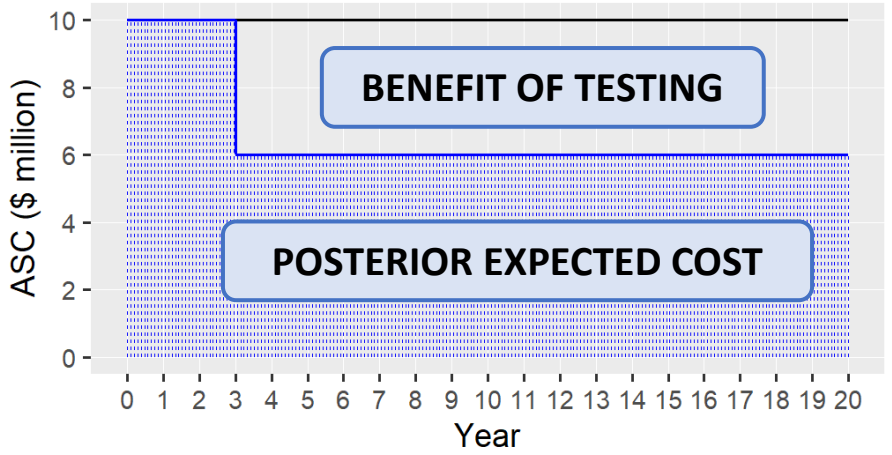
With currently available information

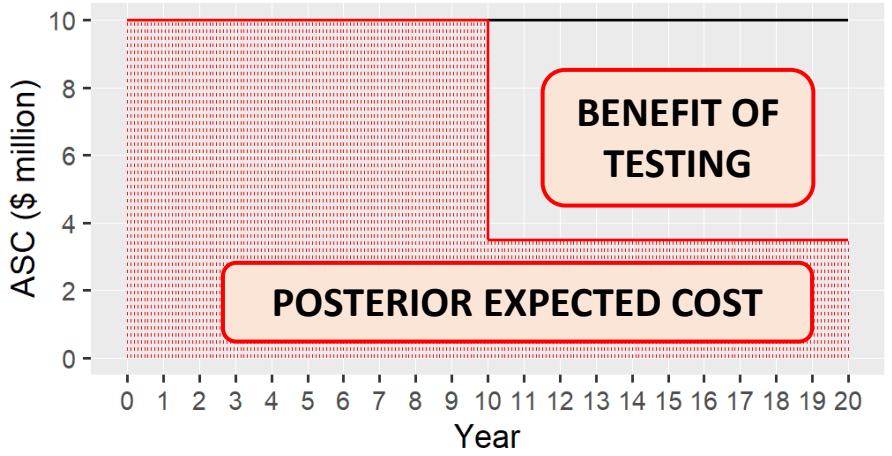


Less certain;
More timely

More certain;
Less timely

With additional information





Case Study Parameters Informed by Empirical Data

Toxicity Information

- Prior uncertainty in chemical toxicity is gauged using toxicity information on 608 chemicals spanning diverse health outcomes (*Chiu et al., 2018*)
- Reduction in uncertainty guided by results reported by previous investigators for **ETAP** (*Gwinn et al., 2020; EPA 2023; WHO, 2017; Chiu et al., 2018*) and for **THHA** (*Sand et al., 2011; WHO, 2017; Chiu et al., 2018*)

Valuing Adverse Health Outcomes

- Valuation of adverse health outcomes based on economic valuation assigned to acute, chronic, and fatal outcomes in the health economic literature (*Shahat and Greco, 2021; EPA, 2022*)
- Social discount rate based on recommendations from US EPA Science Advisory Board (*EPA SAB, 2004*)

Exposure Information

- Exposure data on 1,578 chemicals abstracted from SHEDS-HT (*Isaacs, 2014*)
- Emission rates for seven key air pollutants between 1990 and 2021 used in determining trends in exposure reduction over time (*EPA, 2022*)

Cost of Exposure Mitigation

- Exposure mitigation cost guided by US EPA analysis of cost of reducing levels of criteria air pollutants in ambient air (*EPA, 2011*)
- Cost of 33 chemical exposure reduction programs under the EU REACH program also considered (*ECHA, 2021*)

Decision-Making Contexts

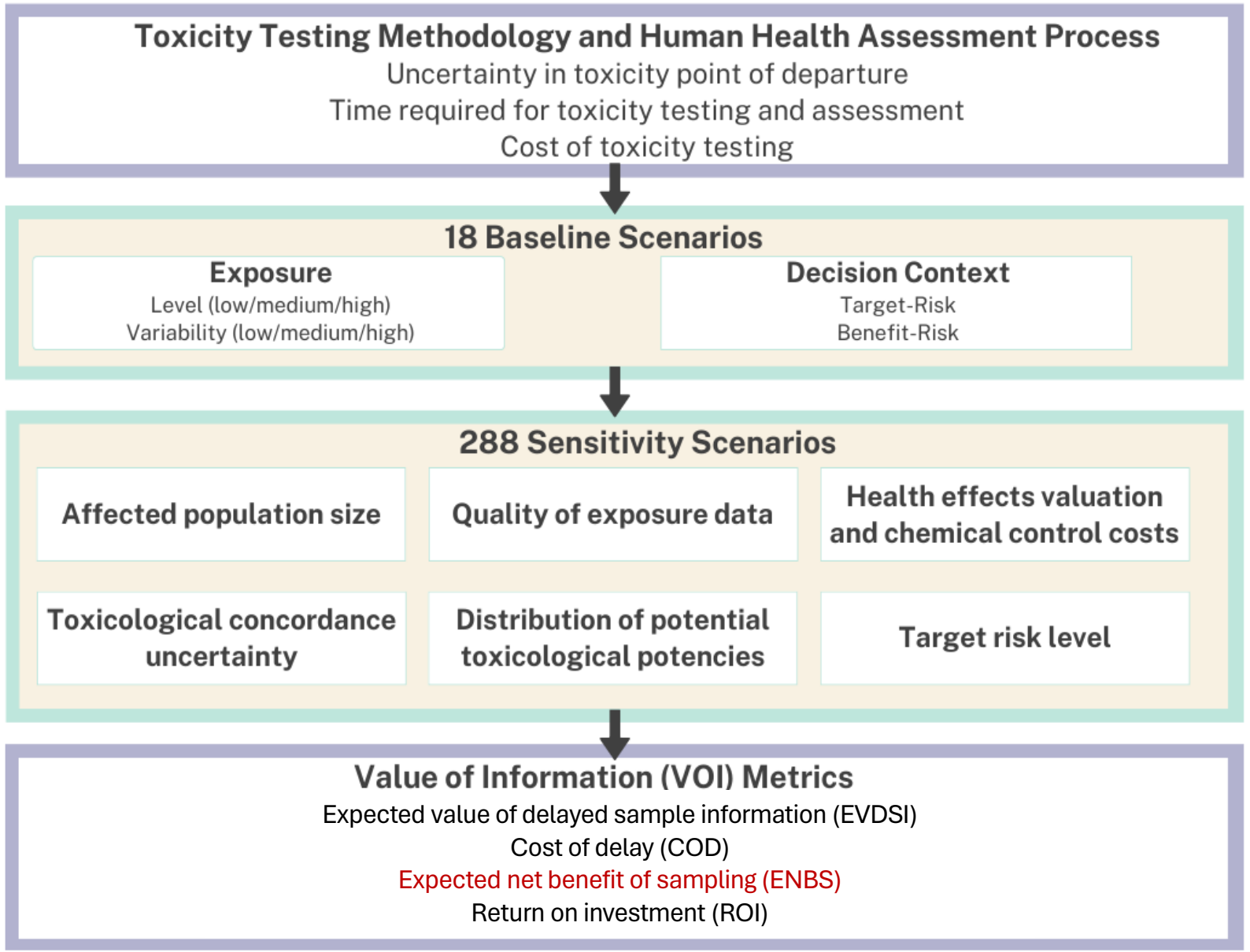
Benefit-Risk Decision-Maker (BRDM)

- The BRDM seeks to **balance population health risks and the societal costs of risk reduction**

Target-Risk Decision-Maker (TRDM)

- The TRDM seeks to **reduce potential risks whenever the risk is anticipated to exceed a specified target risk level**

Summary of Case Study Scenarios



Case Study Results

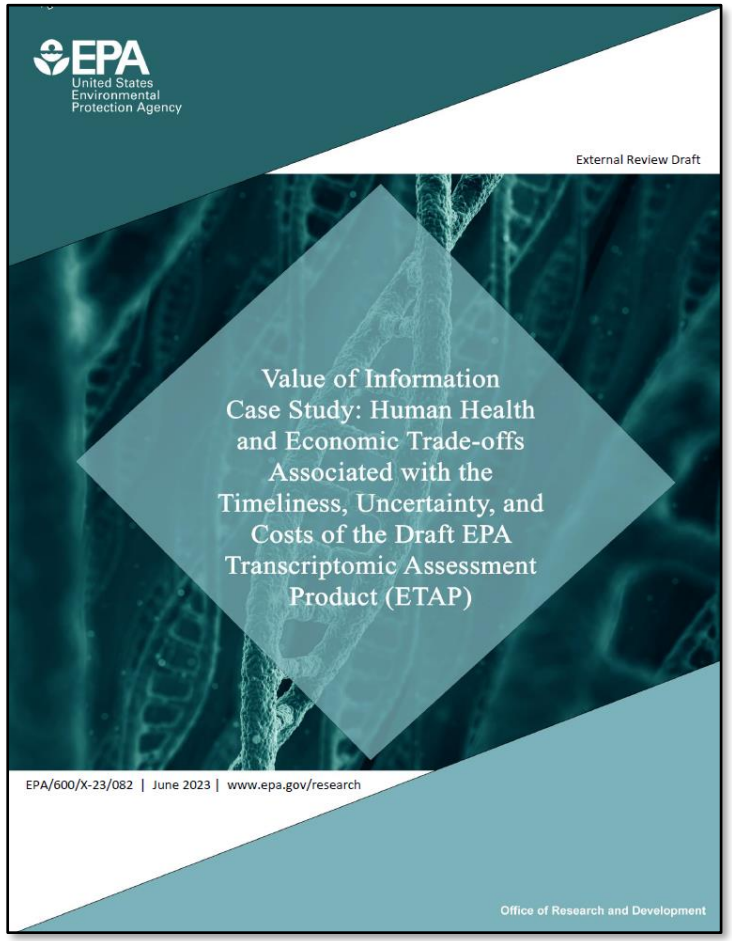
For the **BRDM**, of the 153 scenarios considered

- **153 (100%)** scenarios **preferred ETAP** over THHA using ENBS
  - **29 (19%)** of the scenarios had **negative** ENBS values for ETAP
  - **73 (48%)** of the scenarios had **negative** ENBS values for THHA
- The median ENBS value for ETAP was greater than that of THHA by **$47 B**
  - For the entire U.S. population over 20 years using 5% discount rate

For the **TRDM**, of the 153 scenarios considered

- **127 (83%)** scenarios **preferred ETAP** over THHA using ENBS
- The median ENBS value for ETAP was greater than that of THHA by **$81 B**
  - For the entire U.S. population over 20 years using 5% discount rate

Summary and Conclusions



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- A new VOI framework that incorporates the **cost**, **timeliness** and **reduction in uncertainty** associated with different toxicity testing strategies has been developed, meeting an important methodological need identified in *Science and Decisions (NRC, 2009)*
- The case study results emphasized the importance of **timely decision making**, as indicated by the **greater public health benefits from the use of ETAP** compared to THHA in different decision-making contexts, for evaluating data-poor chemicals with no existing toxicity or human health data
- The **benefits of ETAP will increase proportionately** as more and more chemicals are evaluated with the new EPA Transcriptomic Assessment Product.

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