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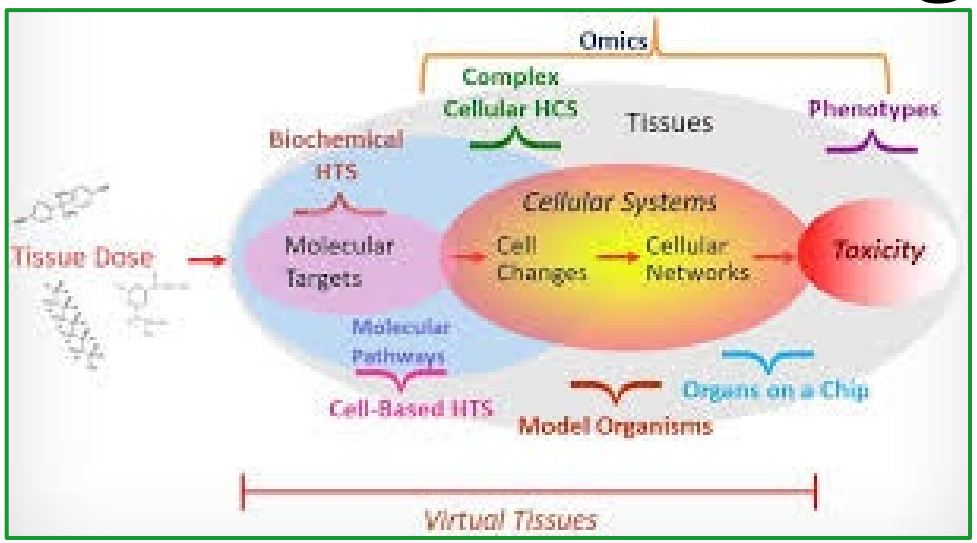
Application of Cost Effectiveness and Value of Information Analyses in Evaluating the Utility of Toxicity-Testing Methodologies



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U.S. EPA Board of Scientific Councilors

November 5, 2021

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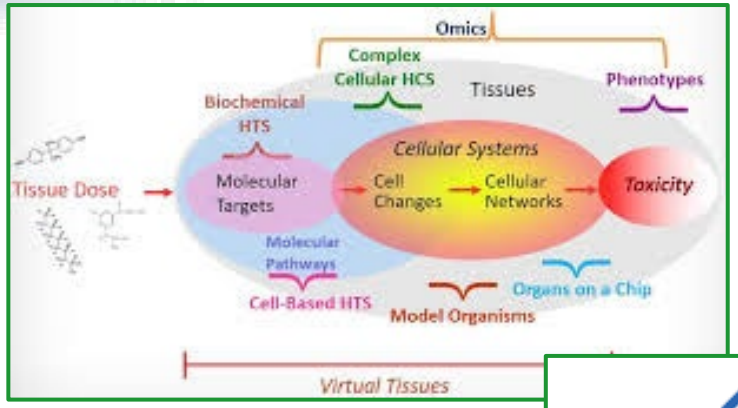
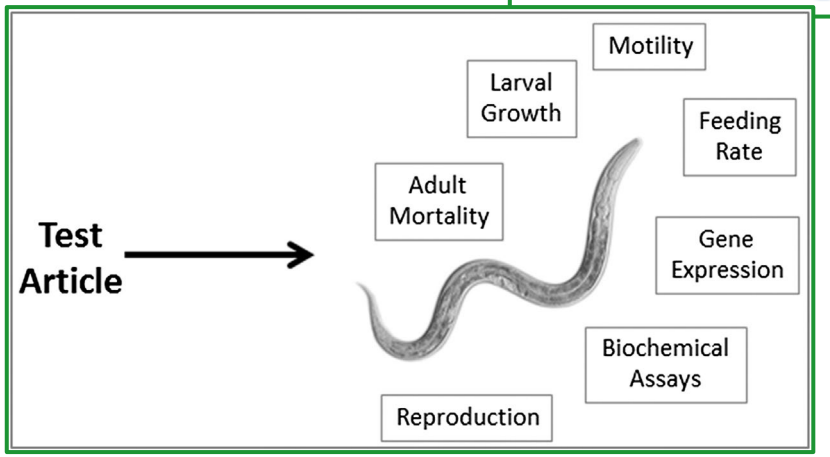
Purpose of the project

- Toxicology continues to develop new testing methodologies
- A framework is needed to evaluate the new tests –
  - Are they better then existing approaches?
  - In what ways?
  - Are they useful for testing large numbers of chemicals?
- Key elements to evaluate are– differences in cost, duration, and uncertainty
  - Very different aspects of a test
  - How to do tradeoffs?





The impacts of cost, duration, and uncertainty

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- The vast majority of the 100,000+ chemicals in commerce have not been tested
  - Testing for a new pesticide: 8-16 million dollars
  - Cost has been identified as the major factor limiting testing
- Complete testing can take from 3 to > 8 years.
  - Exposures and risks are ongoing while we wait for test results
  - Can not address immediate needs (e.g., spills)
- Uncertainty in toxicity data increases probability of under or overestimating the need for controls leading to higher social costs

50-Million-dollar annual budget	
Cost per chemical	Annual number of chemicals tested
10 million dollars	**5**
50 thousand dollars	**1000**

Evaluating toxicity tests using existing tools from decision analysis

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- The project investigated the use of two tools
  - Cost Effectiveness Analysis (CEA)
  - Value of Information (VOI)
- CEA and VOI
  - Each has different strengths and limitations
  - Both have the ability to assess the impacts of cost, duration, and uncertainty
- CEA work was recently published in Risk Analysis. VOI work has been submitted to Risk Analysis.

Differences

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Cost Effectiveness Analysis:

"What is the most cost effective test for correctly determining if a chemical's risk is above or below a target risk level?" Measured using the cost effectiveness ratio

$$Cost\ Effectiveness\ Ratio = \frac{Cost\ in\ dollars}{Desired\ outcome}$$

Value of Information:

"Is it worth spending additional money to reduce the uncertainty in an estimate of toxicity that is driving a regulatory action?"

$$Net\ Benefit = Costs\ saved\ by\ reducing\ uncertainty\ - cost\ of\ testing$$

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Cost Effective Analysis

Cost Effectiveness Ratio

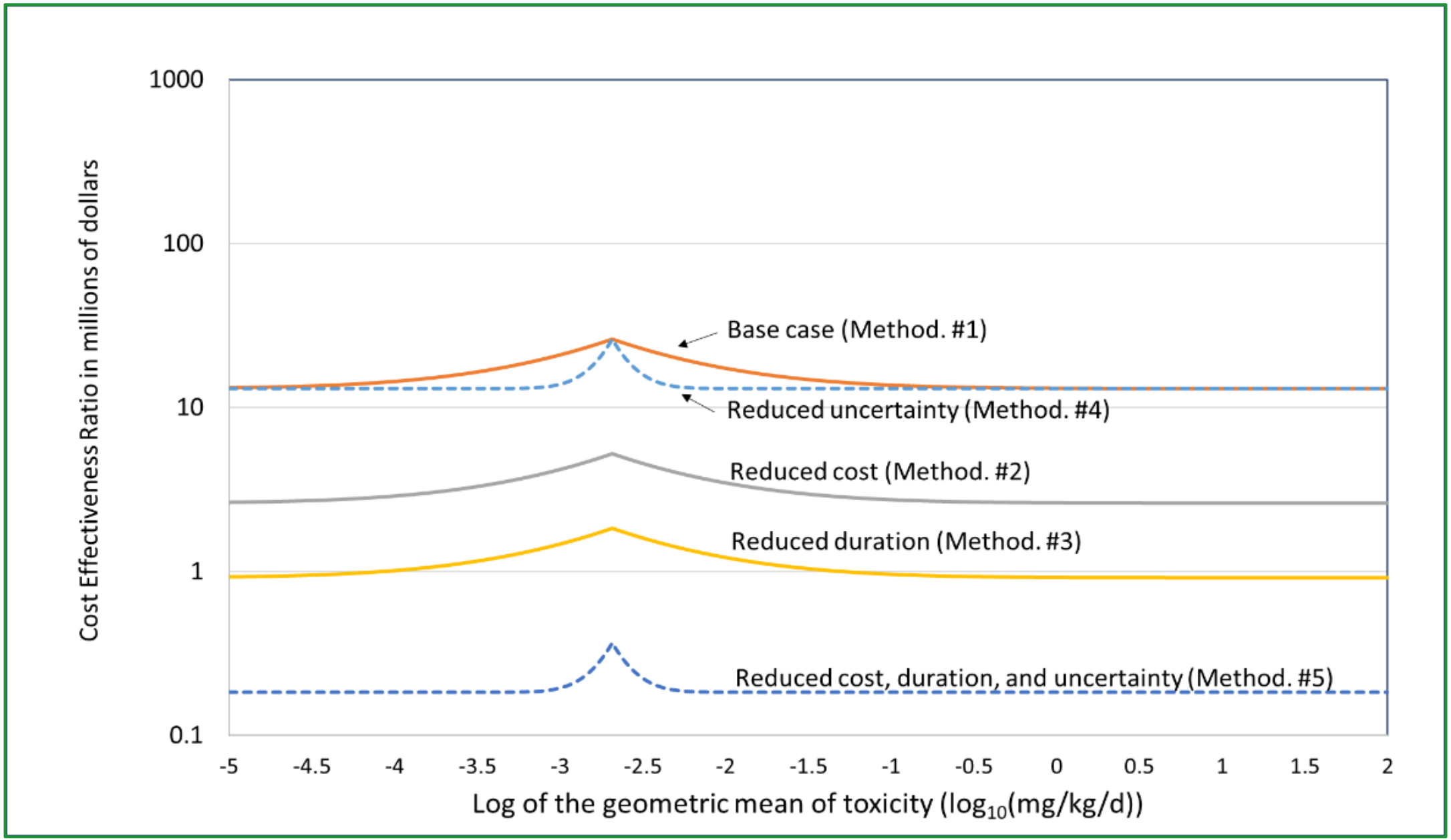
- The net present value of cost of a correct l^{th} decision for one chemical for one year using the j^{th} toxicity methodology
- Decision Making Value (DMV) is the ability to make the same decision as one based on perfect toxicity information
- Costs and DMV are discounted to reflect when they occur
- Time horizon (y_{TH})- period of time when costs and benefits accrue

$$CER^{j|l} = \frac{\sum_{y=1}^{y_{T,j}} \frac{C_y^j}{(1+r)^{y-1}}}{\sum_{y=y_{T,j}}^{y_{TH}} \frac{DMV_y^{j|l}}{(1+r)^{y-1}}}$$

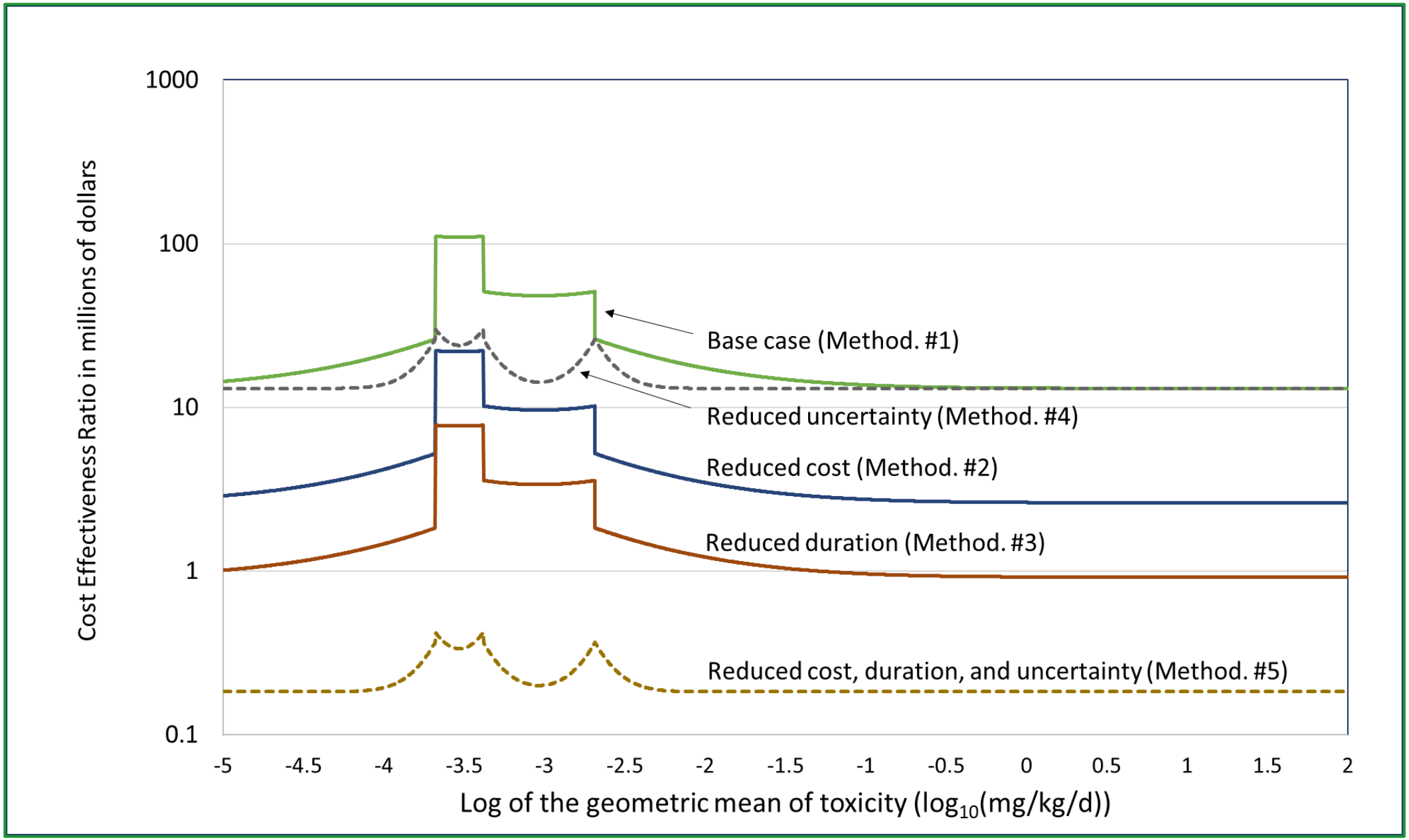
Setting up the CEA illustration

- A program is envisioned that tests large numbers of the chemicals every year
- The results of the testing are used to generate risk estimates for two decision making processes (binning exercises)
  - Are exposures above a level of concern? (Yes/No)
  - Which level of regulatory action is needed (None, level 1, level 2, or level 3)
- Five toxicity-testing methodologies (hypothetical)
  - Base case: high cost, high uncertainty, and long duration
  - Four alternatives: reduce cost, reduce uncertainty, reduce duration, reduce all three

CER values for the 5000 chemicals for the simple decision



CER values for the 5000 chemicals for the complex decision



Findings on the relative importance of reducing cost, duration, and uncertainty

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- In the example illustrations, reductions in cost and duration have as large, or larger, impacts on CER than reductions in uncertainty
- The impact of differences in uncertainty on decision making varies with the decision-making process and the chemical's toxicity
- There is no single standard for the "acceptable" level of uncertainty in a toxicity finding

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Value of Information

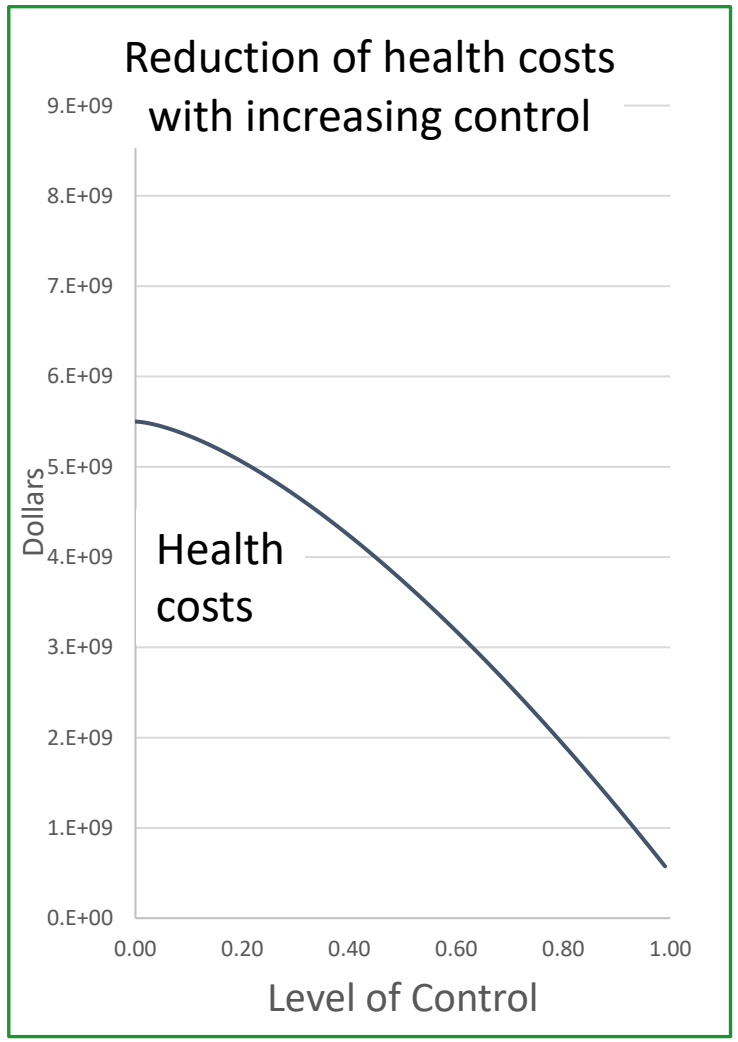
Value of Information

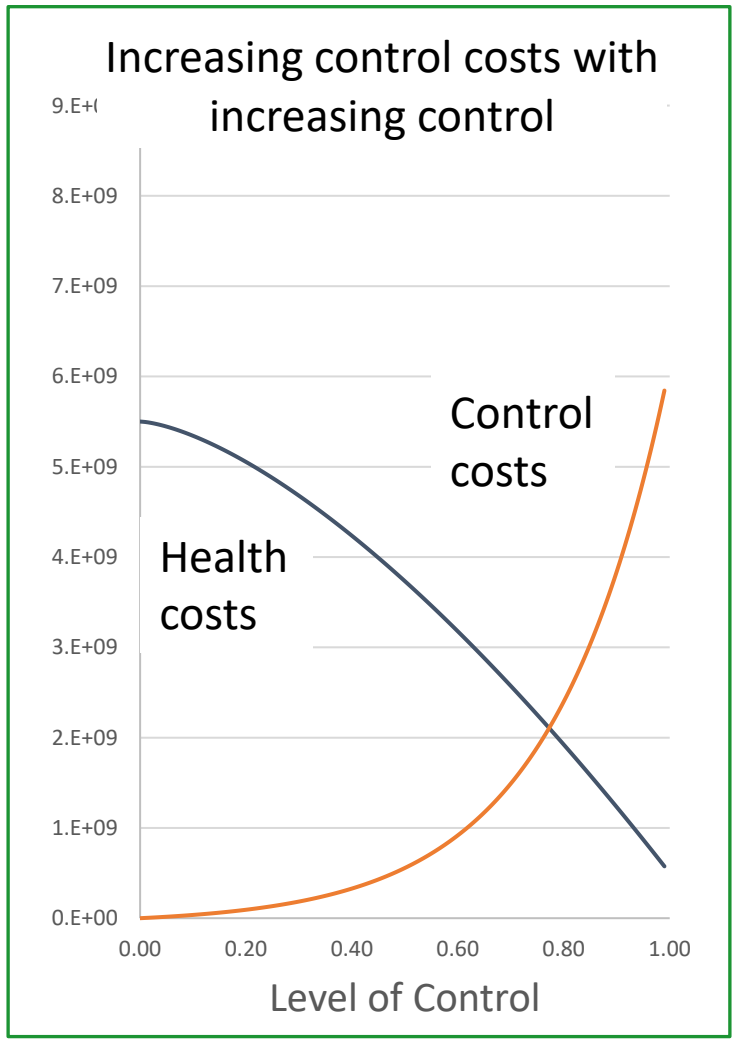
- Does the improvement in a decision that results from more certain data worth the time and cost of obtaining such data
- The metric to address this is the Total Social Cost (TSC) ($)

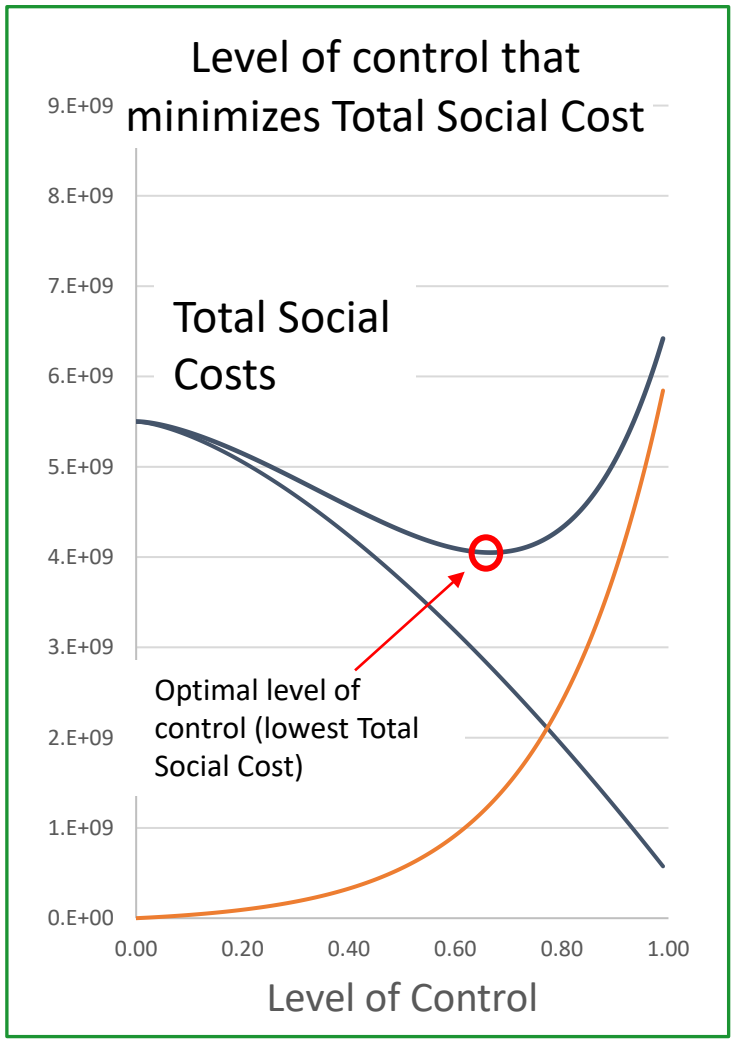
$$Total\ Social\ Cost = Total\ Control\ Cost + Total\ Health\ Cost$$

$$= \sum_{y=y_{\mathrm{imp},j,k}}^{y_{TH}} \frac{C_k}{(1+r)^{y-1}} + \left[\sum_{y=1}^{y_{TH}} \frac{N_y B_y RV}{(1+r)^{y-1}} - \sum_{y_{\mathrm{imp},j,k}}^{y_{TH}} \frac{N_y B_y (R - R_k) V}{(1+r)^{y-1}} \right]$$

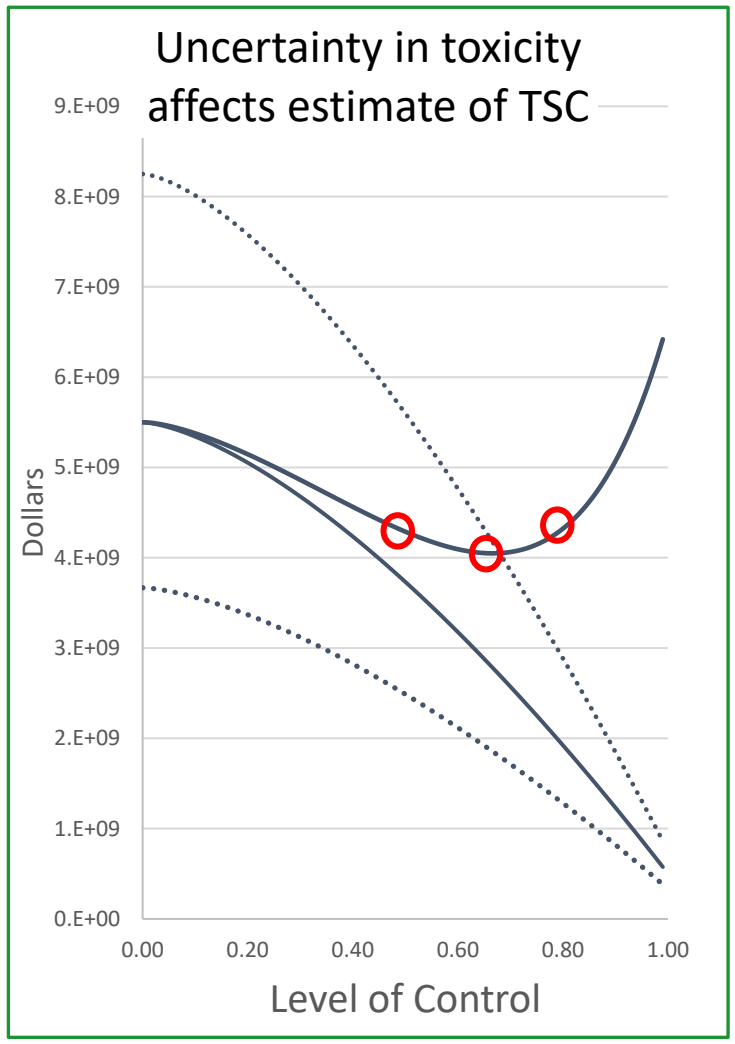
Determining the cost of uncertainty for benefit cost analysis

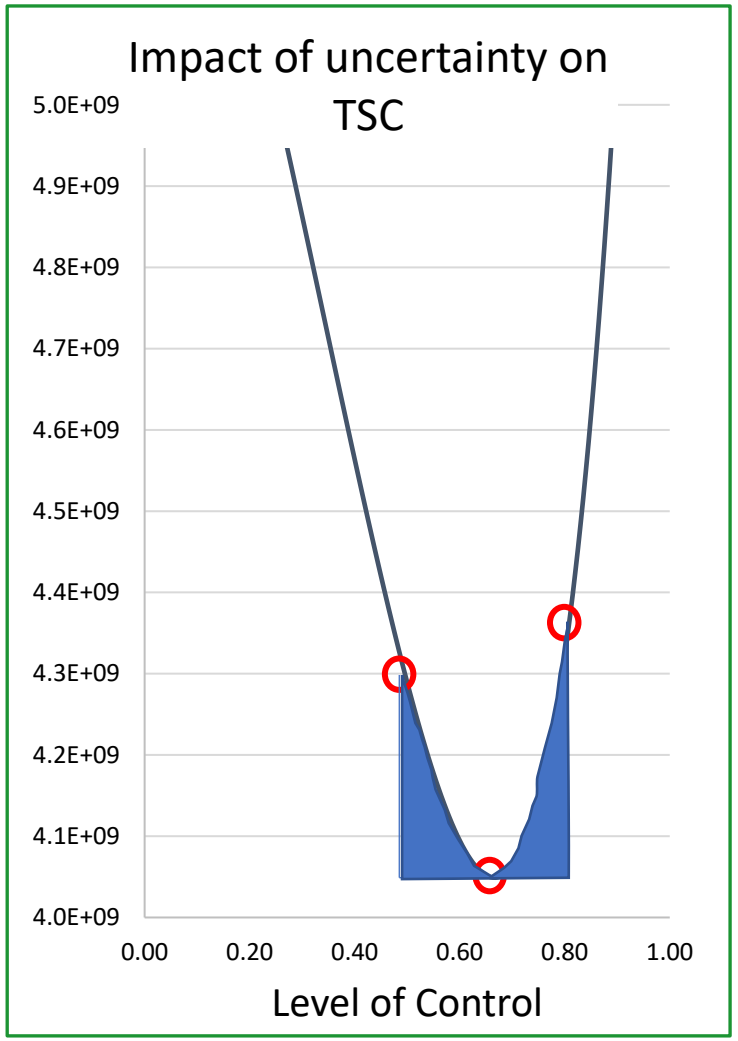


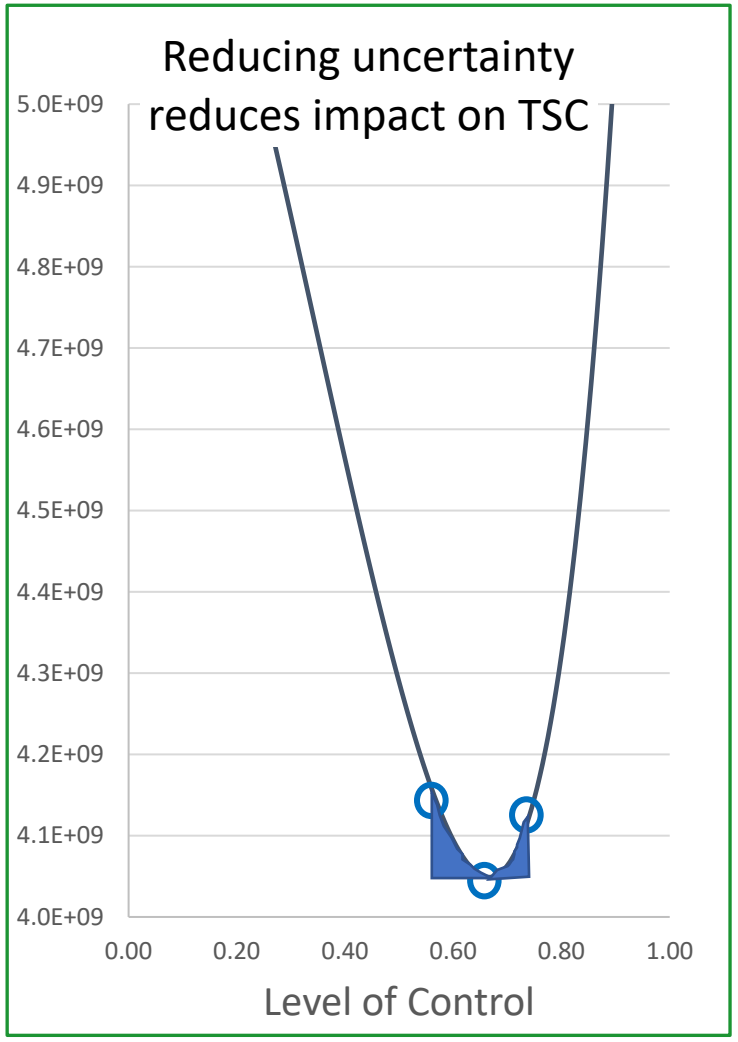




Determining the cost of uncertainty







VOI case studies

- Evaluated two toxicity tests
  - Test A – lower cost, shorter duration, higher uncertainty
  - Test B – high cost, long duration, lower uncertainty
- Evaluated chemicals with significant health costs
  - One with chronic effect leading to early mortality
  - One with acute effect leading to multiple days of illness
- Look at a range of chemicals and decisions
  - Chemicals with of high and relatively low uncertainty
  - Chemicals regulated based on benefit-cost analysis and target risk levels

Impacts of reduced uncertainty and duration

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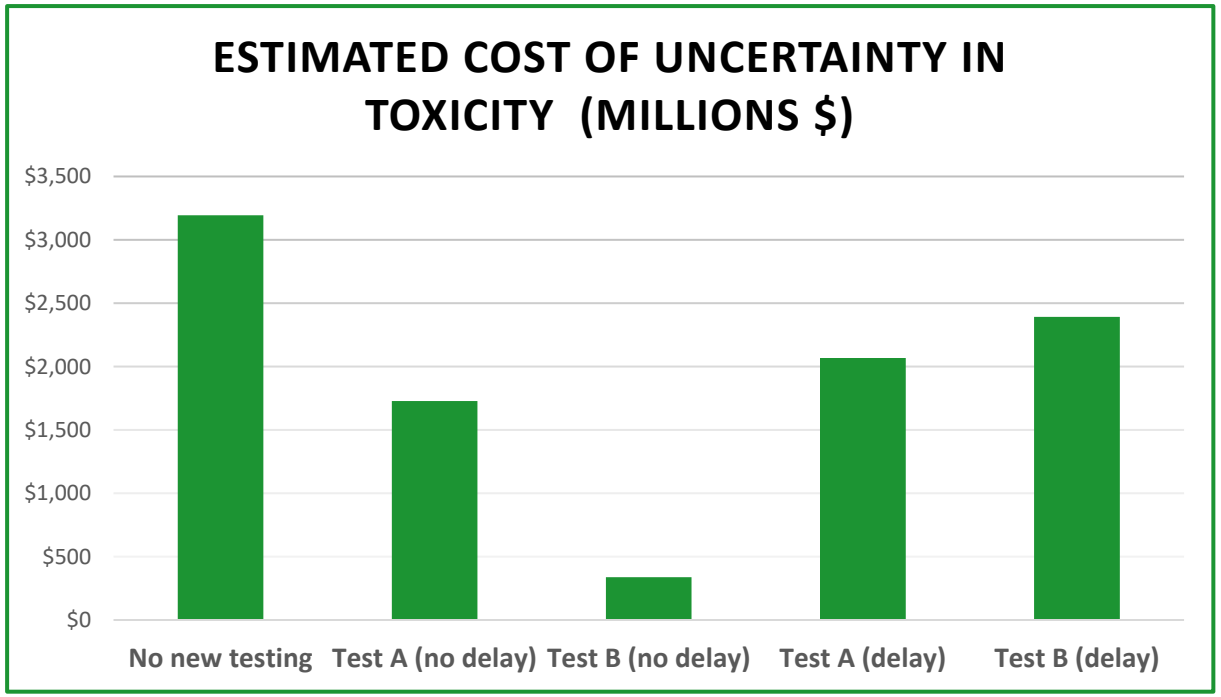
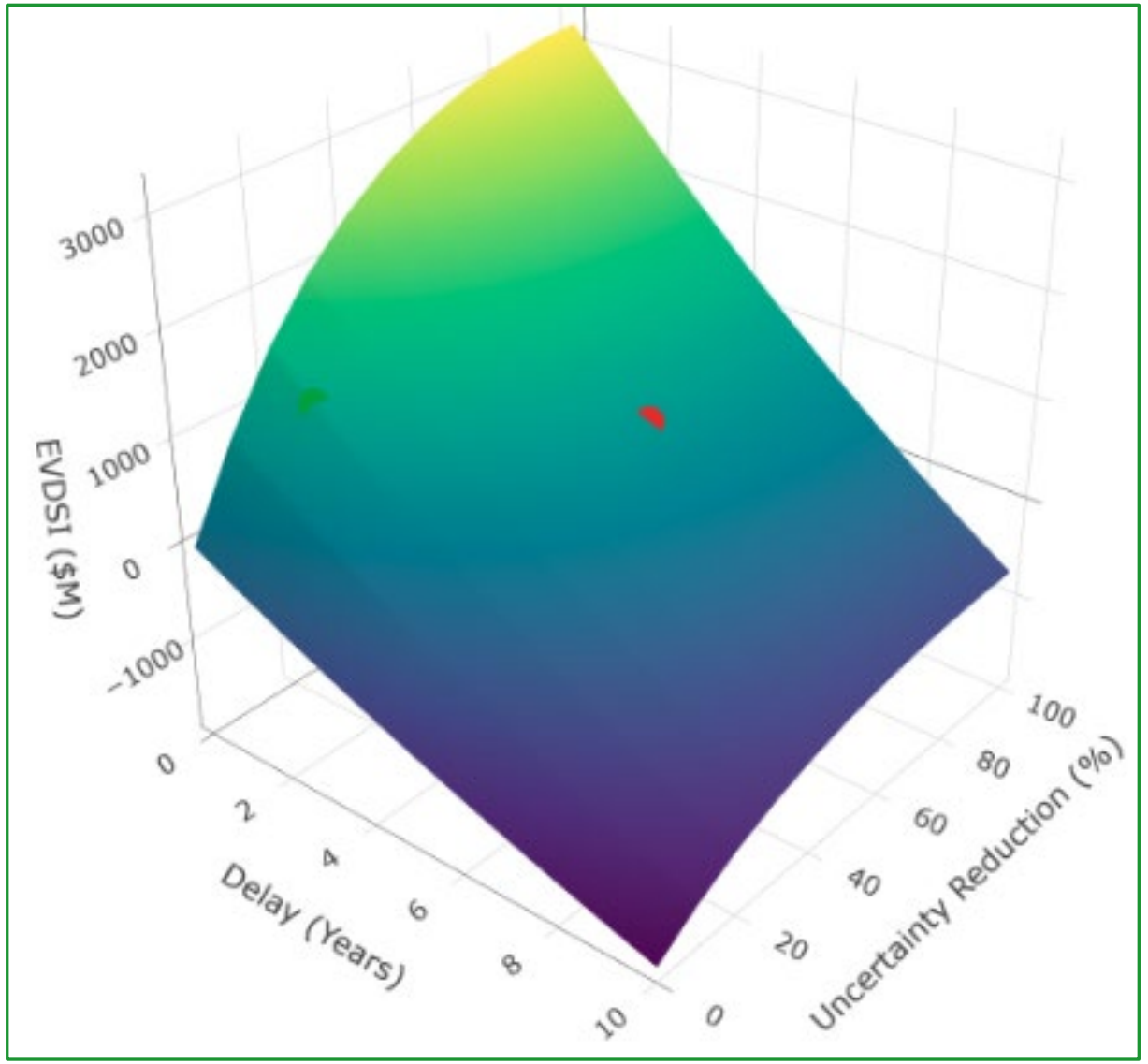
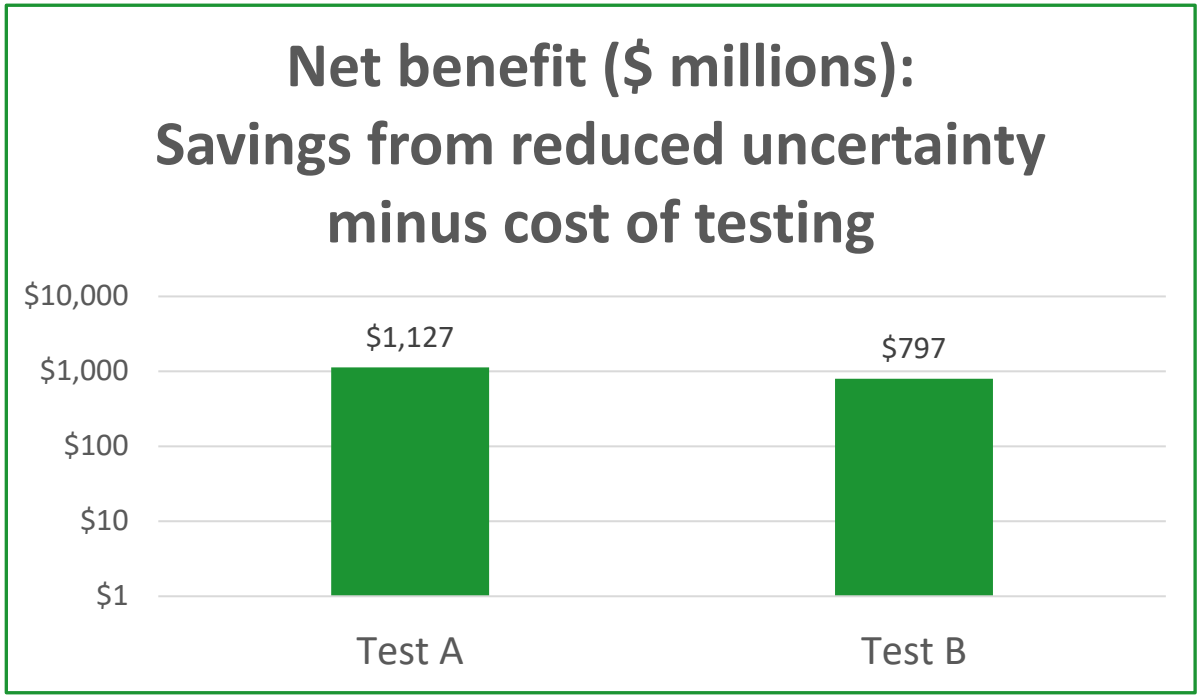
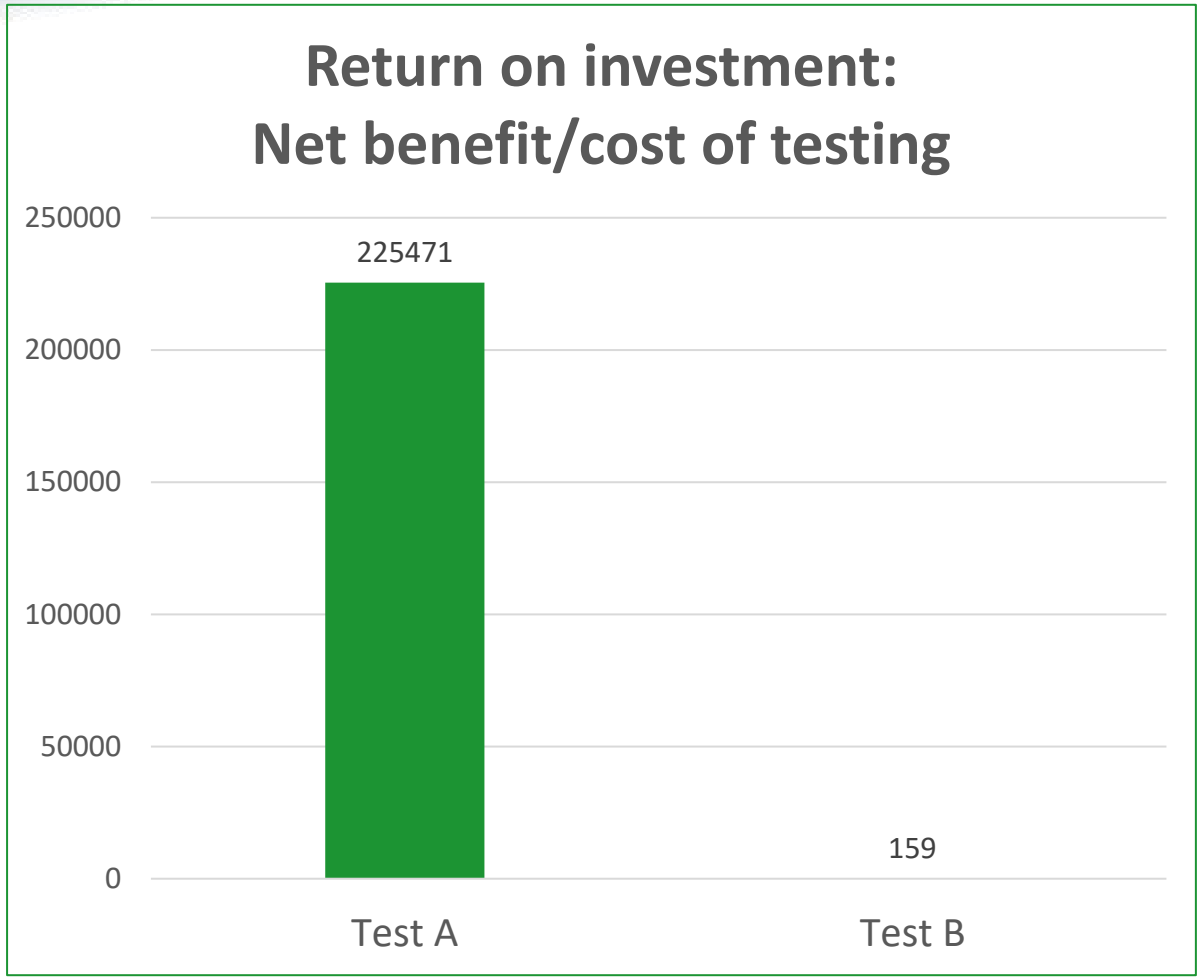




Impact of Cost of testing





Findings for project

- Two tools for determining preferred toxicity tests were developed
  - Both addressed duration, cost, and uncertainty
  - Approaches are complementary: addressing different uses of the toxicity findings
- Both approaches found similar patterns of impact for cost, duration, and uncertainty
  - Reduction in all three elements are desirable
  - Reduction in cost and duration can have effects equal to greater than reductions in uncertainty
  - Impact of uncertainty varies with the decision, the toxicity of the chemical, and level of exposure

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Thank you.

Questions?