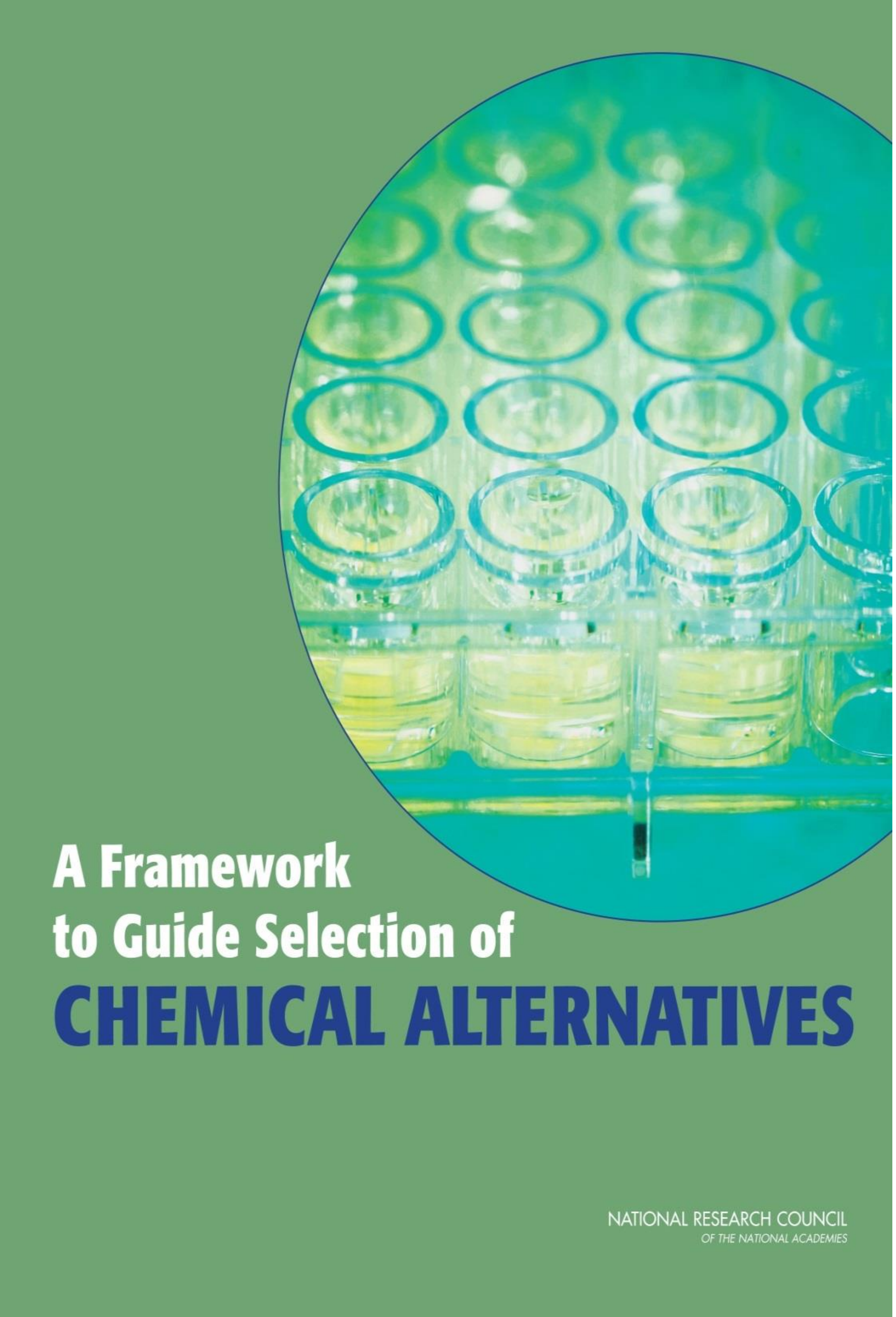
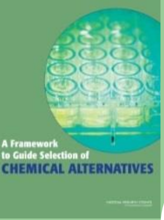


Helen Holder

Hewlett Packard



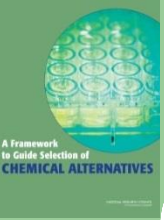
Committee on Design and Evaluation of Safer New Chemicals – A Framework to Inform Government and Industry Decisions

Sponsor

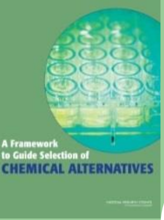
- EPA, Office of Research and Development (with support from Office of Chemical Safety and Pollution Prevention (OCSPP))

National Research Council’s Division on Earth and Life Studies

- Board on Chemical Sciences and Technology
- Board on Environmental Studies and Toxicology



STATEMENT OF TASK



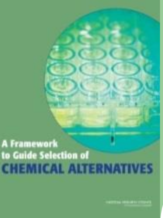
Statement of Task

Decision framework for evaluating potentially safer substitute chemicals to:

- support consideration of potential impacts early in chemical design
- consider both human health and ecological risks
- integrate multiple and diverse data streams
- consider tradeoffs between risks and factors such as product functionality, product efficacy, process safety and resource use
- identify the scientific information and tools required

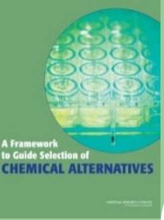
Demonstrate the framework's:

- application by users with contrasting decision contexts and priorities
- use of high throughput/content data streams



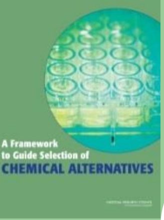
Considered

- Existing frameworks and tools
- Previous reports
  (e.g. Toxicity Testing in the 21st Century, Science and Decisions)
- Invited presentations to the committee:
  - Existing frameworks
  - California Department of Toxic Substances Control (DTSC) activities
  - Industry, retailer, and NGO viewpoints
  - Life cycle analysis
  - Multi-criteria decision analysis (MCDA)



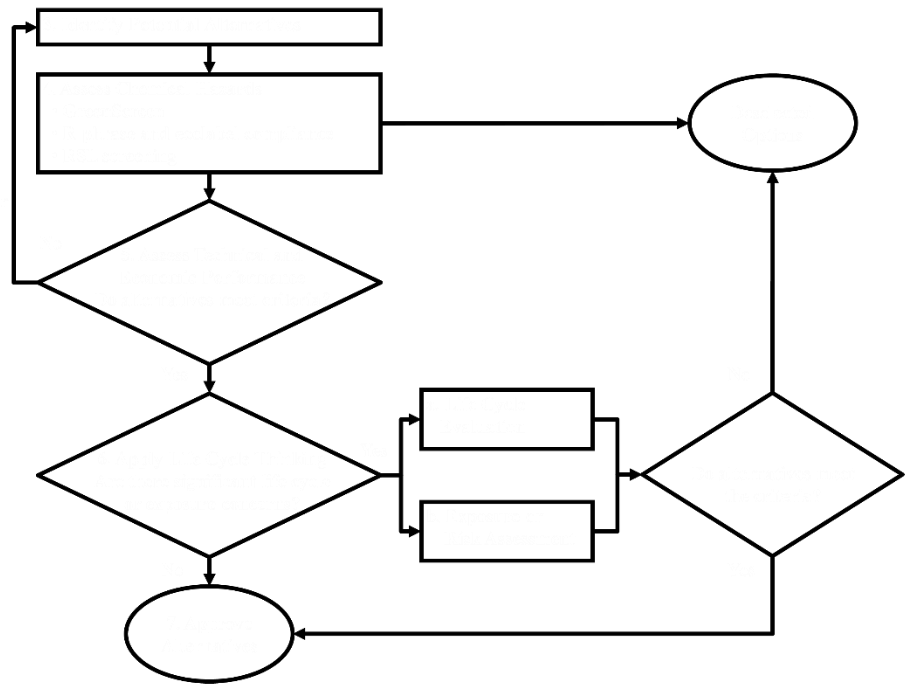
Key Issues

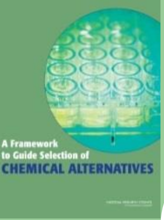
- How to consider exposure and hazard
- Consideration of contextual information
- How data gaps and uncertainty are handled
- How to integrate information of different types
- Use of new data streams (e.g., high throughput screens)
- Research opportunities



Framework

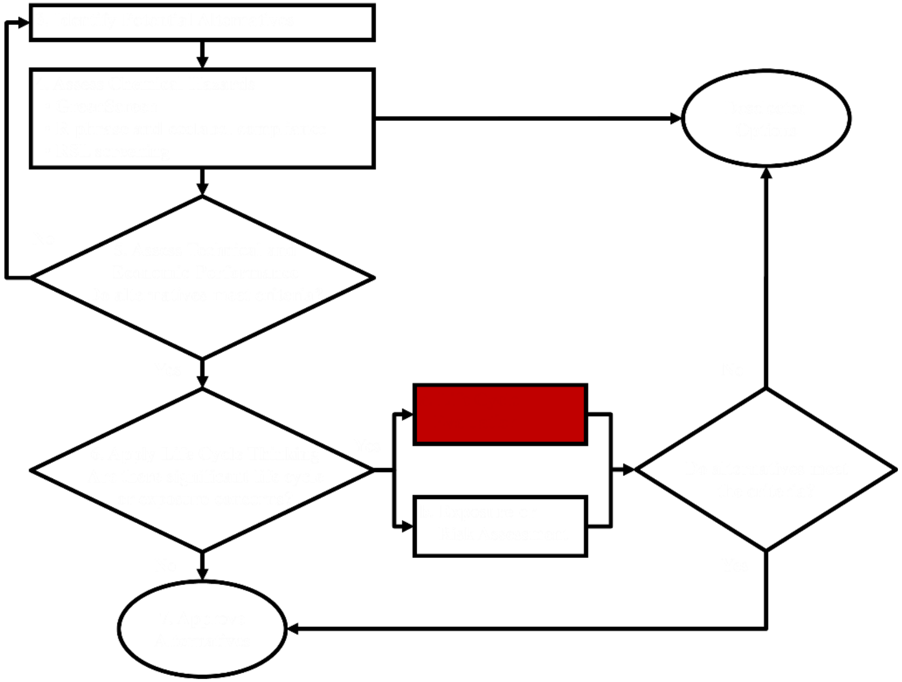
- Structured approach to compare human health and environmental hazards associated with different chemicals or chemical-dependent processes.
- Description of a specific arrangement of assessments and decisions used to conduct an AA
- Usually represented as a flowchart or sequential steps
- Order and decision points may be fixed
- *Examples: IC2, Lowell, CA SCP, BizNGO, DfE Steps*





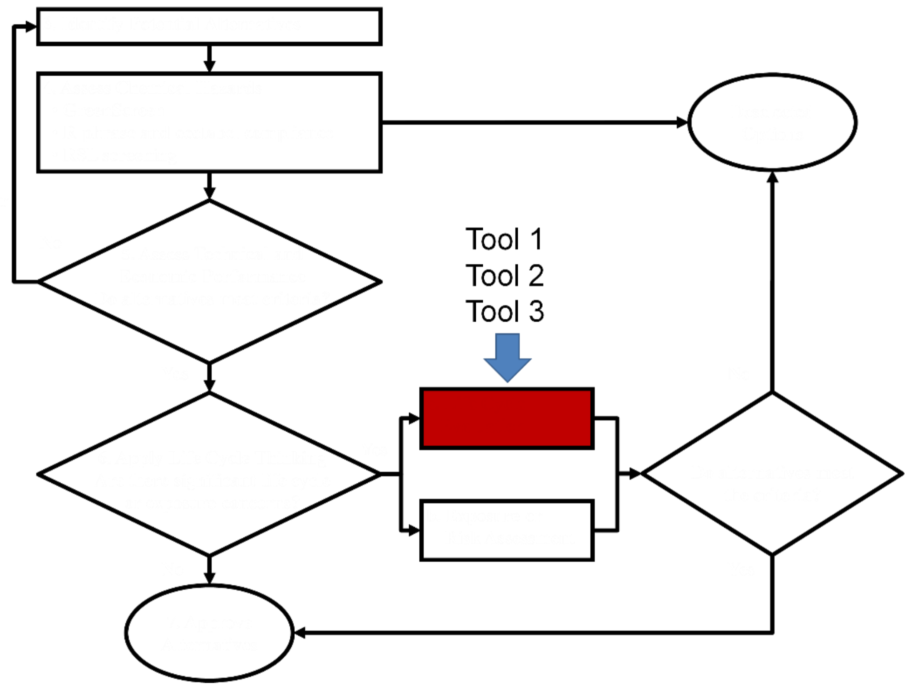
Step

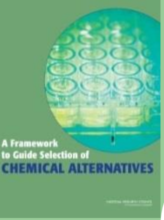
- A documented approach for assessing a substance, material, or process for the purpose of comparative analysis
- Often an established method that can be used for stand-alone analysis
- Represented by a single step/box within framework
- *Examples: life cycle analysis (LCA), risk or exposure assessment, and hazard assessment*



Tool

- An approach for assessing a chemical, material and/or process for the purpose of attribute analysis
  - Can be computer programs, paper-based tools, information sources, etc.
  - *Examples: GreenScreen, SimaPro*





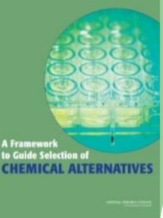
FRAMEWORK

↓

STEP

↓

TOOL



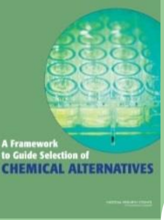
Alternatives Assessment

is

- is a process for identifying, comparing and selecting safer alternatives to chemicals of concern
- informed consideration of the advantages and disadvantages of alternatives to a chemical of concern

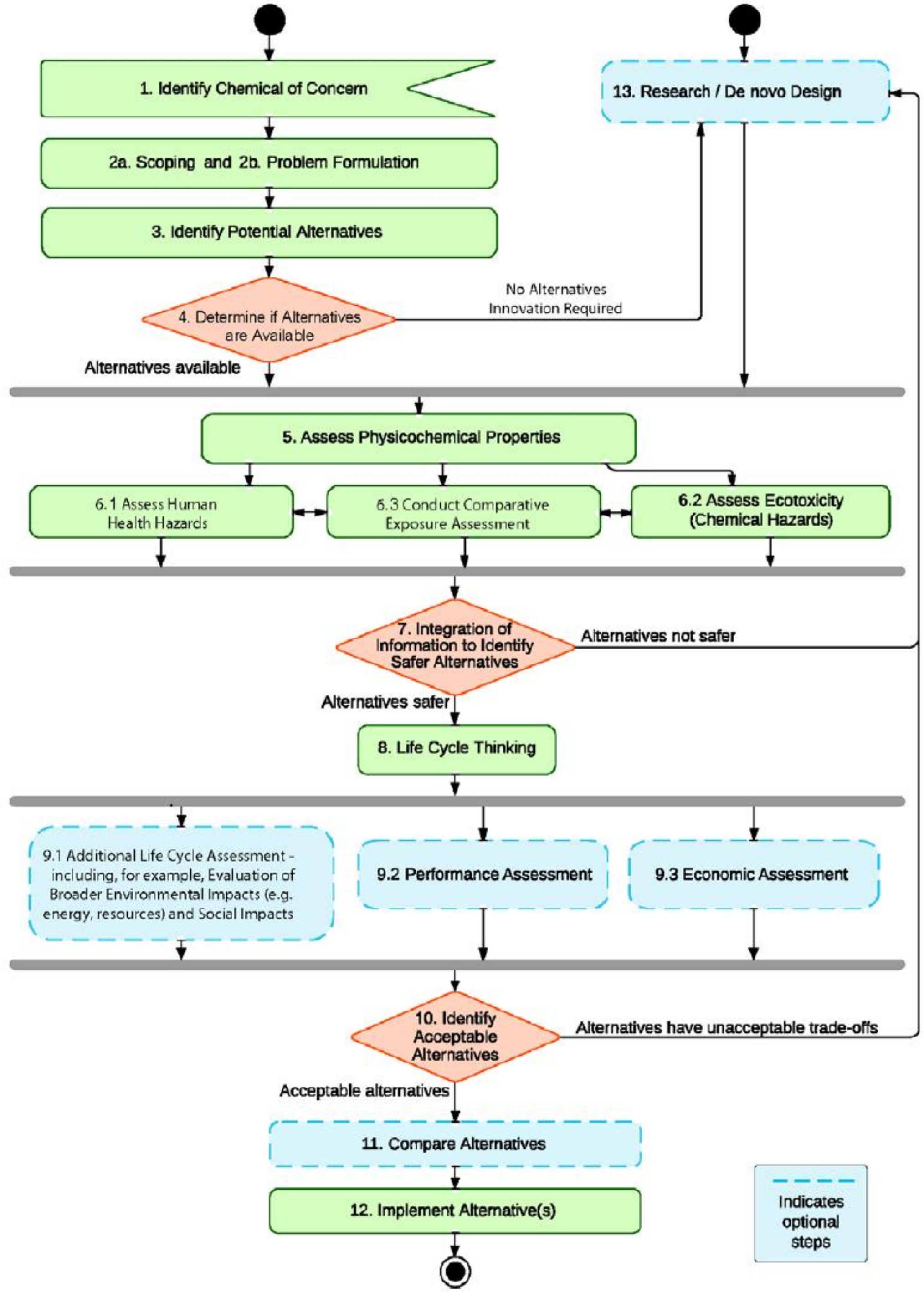
is not

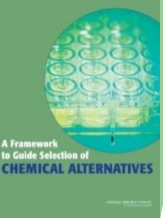
- *risk assessment* where risk associated with a given level of exposure is calculated
- *safety assessment*, where the primary goal is to ensure that exposure is below a prescribed standard
- a *sustainability assessment* that considers all aspects of a chemicals' life cycle, including energy and material use.



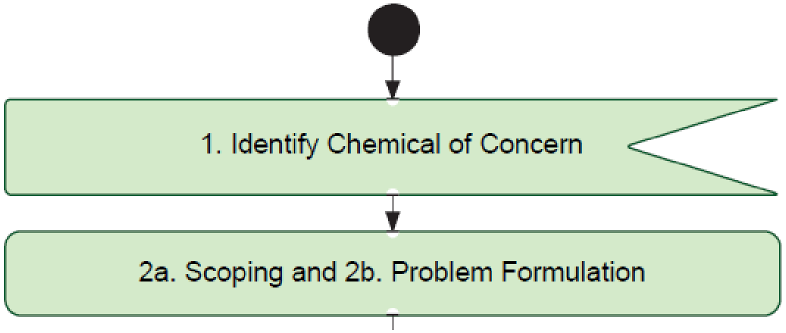
Framework

- Two phases
  1. Health, ecotoxicity, and comparative exposure
  2. Followed by a consideration of broader impacts
- Required minimum steps and optional steps
- Decision and data integration points
- Acknowledged need for research and innovation





Scoping and Problem Formulation



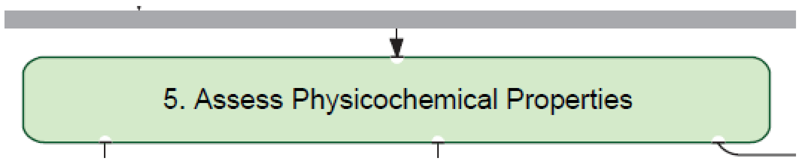
2a: Scoping:

- Documentation of *goals, principles, and decision rules* guiding the assessment.
- Make preferences of the decision-maker explicit in the form of decision rules or algorithms to be applied in the face of tradeoffs and uncertainty
- Decision rules established a priori.
- Documenting assumptions, data, and methods in the assessment.

2b Problem Formulation

- Characterization of *function and performance requirements*
- Characterize chemical of concern
- Initial screening if necessary

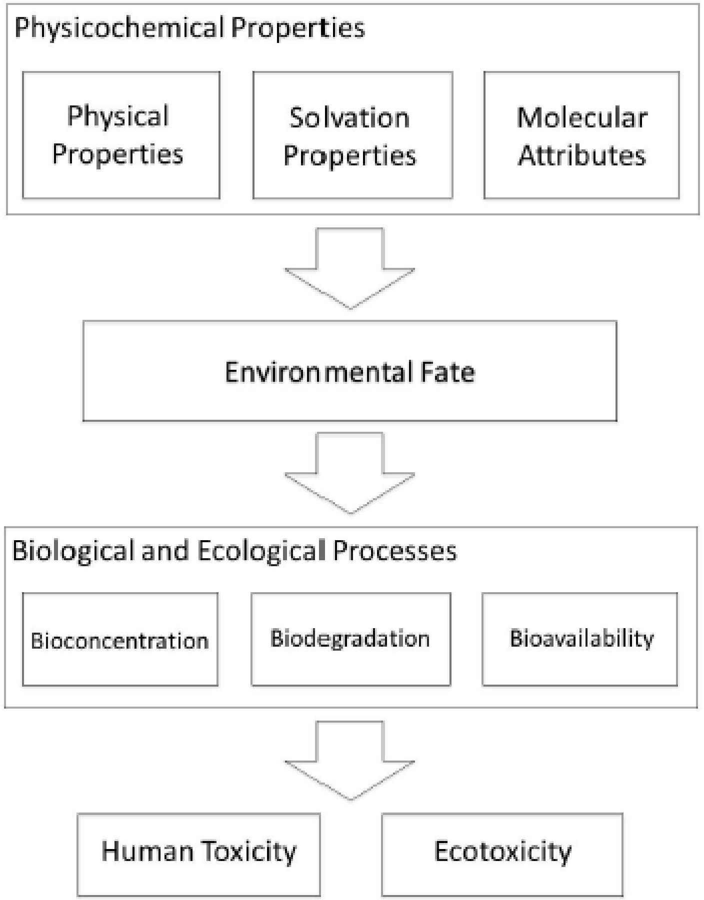
Expanded physicochemical properties



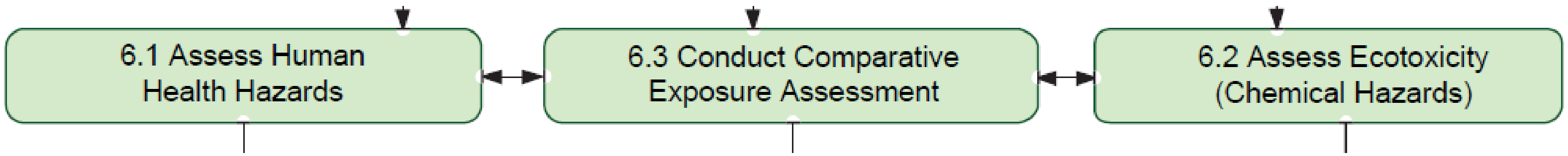
- Beyond physical hazards (like explosivity and corrosivity)
- Use for determining environmental compartments of chemical partitioning
- Estimating potential for bioconcentration and bioavailability
- Estimating likely routes of mammalian exposure and bioavailability
- Estimating likelihood for high aquatic toxicity

Why expand consideration?

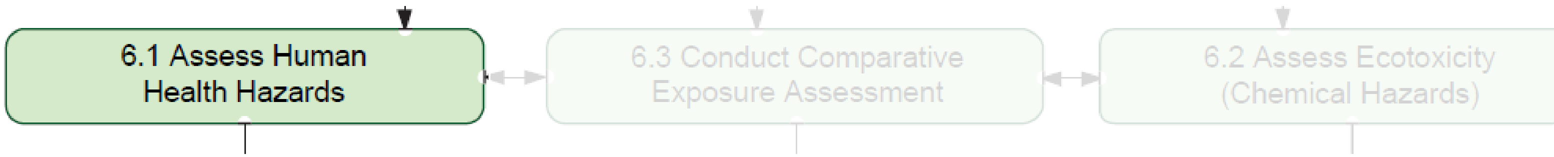
- Physicochemical properties related to human toxicity and ecotoxicity
- Easy to obtain
    - Growing body of literature
    - In silico prediction
    - Can be obtained experimentally



Step 6


6.1 Assess Human Health Hazards
6.3 Conduct Comparative Exposure Assessment
6.2 Assess Ecotoxicity (Chemical Hazards)

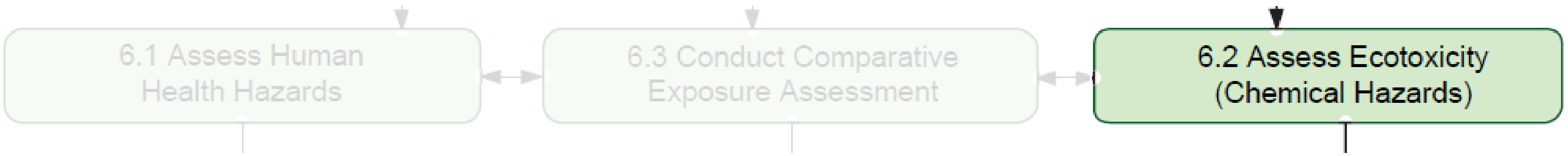
Step 6



Human health

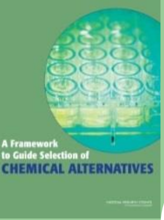
- Endorses GHS-tied criteria with a few refinements
- Can use thresholds to categorize hazard (H, M, L) and describe certainty
- Use in vitro and in silico data as primary data (e.g., mutagenicity) and to fill data gaps
- Document which endpoints were not considered
- Apply appropriate expert judgment

Step 6



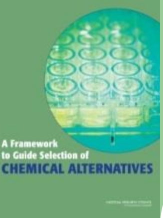
Ecotoxicity

- Review physicochemical data to determine environmental compartments of concern
- Compile ecotoxicity data, especially for identified compartments
- Address missing data (read across, QSAR, etc.)
- Can use thresholds to categorize hazard (H, M, L) in different environmental media (soil, water, sediment, air) and describe certainty

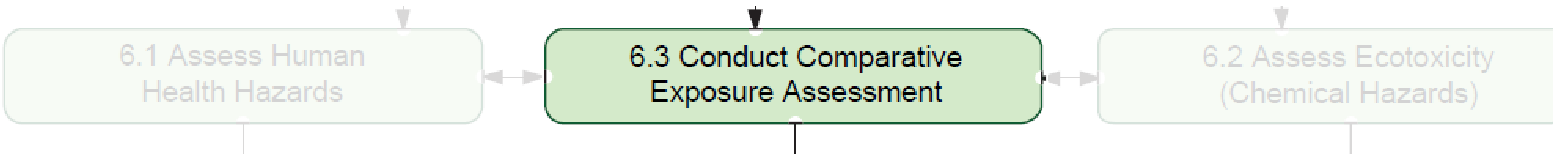


Incorporation of In Vitro Data and In Silico Models

- Move beyond sole reliance on traditional toxicology data
- Foster greater use of high throughput in vitro data and in silico modeling data
  - Primary evidence for a given endpoint
    - Currently limited (e.g., mutagenicity assays)
  - Fill gaps in data for a particular endpoint
  - Screen for possible unintended consequences
- Principles or tools to support benchmarking and integration of high throughput data are needed



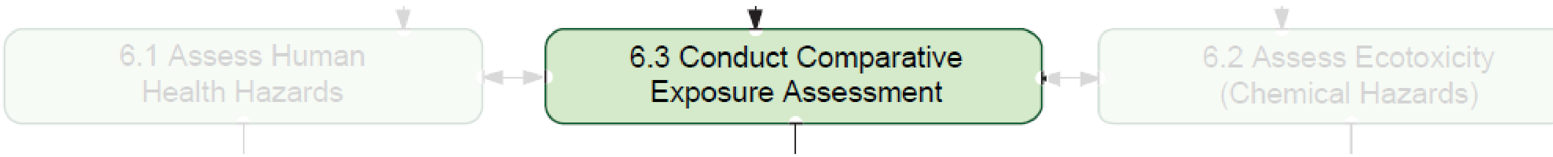
Step 6



Comparative Exposure

- Asks: Is the exposure potential of the alternatives expected to be substantially equivalent to the original chemical?
- Equivalent exposure is a commonly used assumption by EPA DfE and others
- Makes the question explicit
- Not intended to limit the hazards considered → lens

Step 6

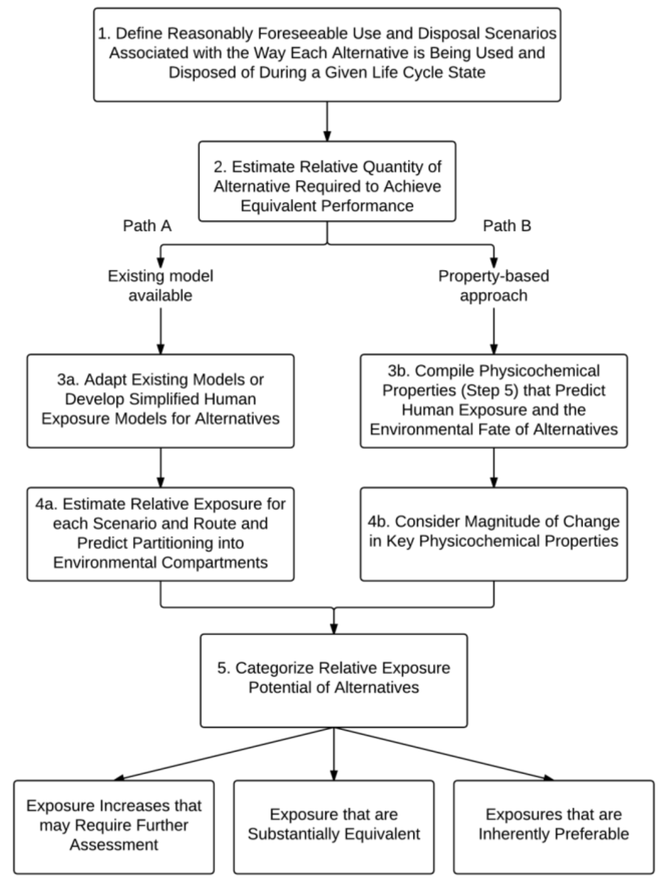


Comparative Exposure

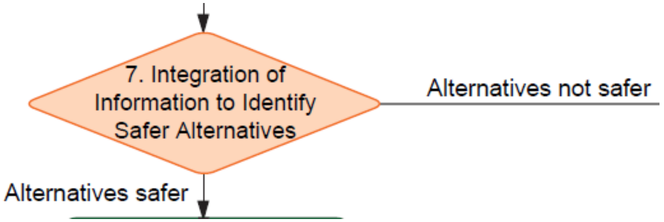
- If substantially equivalent exposure is expected, then the assessment can be mainly hazard based
- Some alternatives preferable due to lower inherent exposure potential and exposure-related properties (consider in decisionmaking)
- If an alternative has substantially higher potential for exposure, more detailed assessment may be appropriate if further analysis suggests the effort is warranted

Substantially Equivalent Exposures

- Outputs of simple exposure models (especially those considering estimates based on observed use patterns)
- Comparing key physicochemical properties of alternatives
- Exposure estimates should be derived in the absence of assumptions about controls



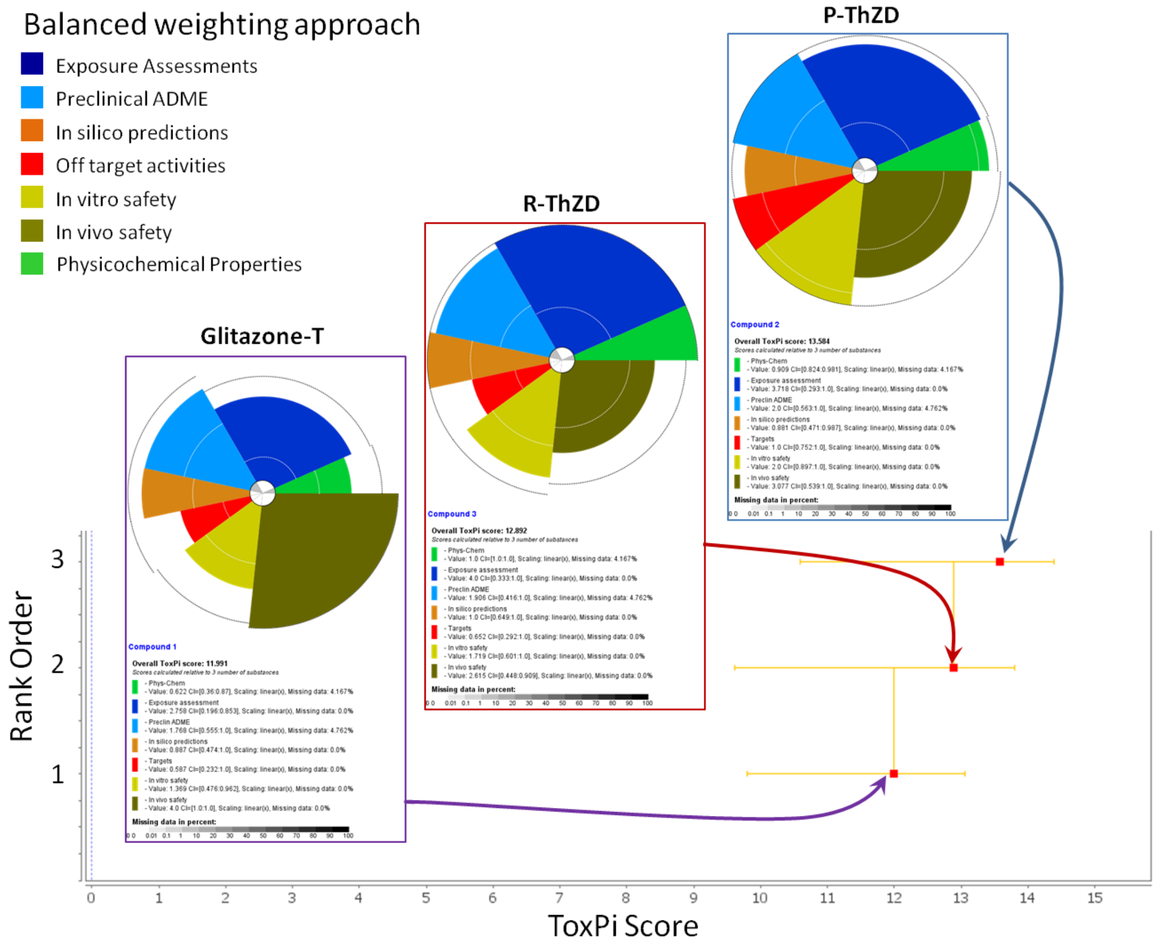
Step 7

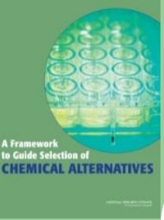


Identify Safer Alternatives

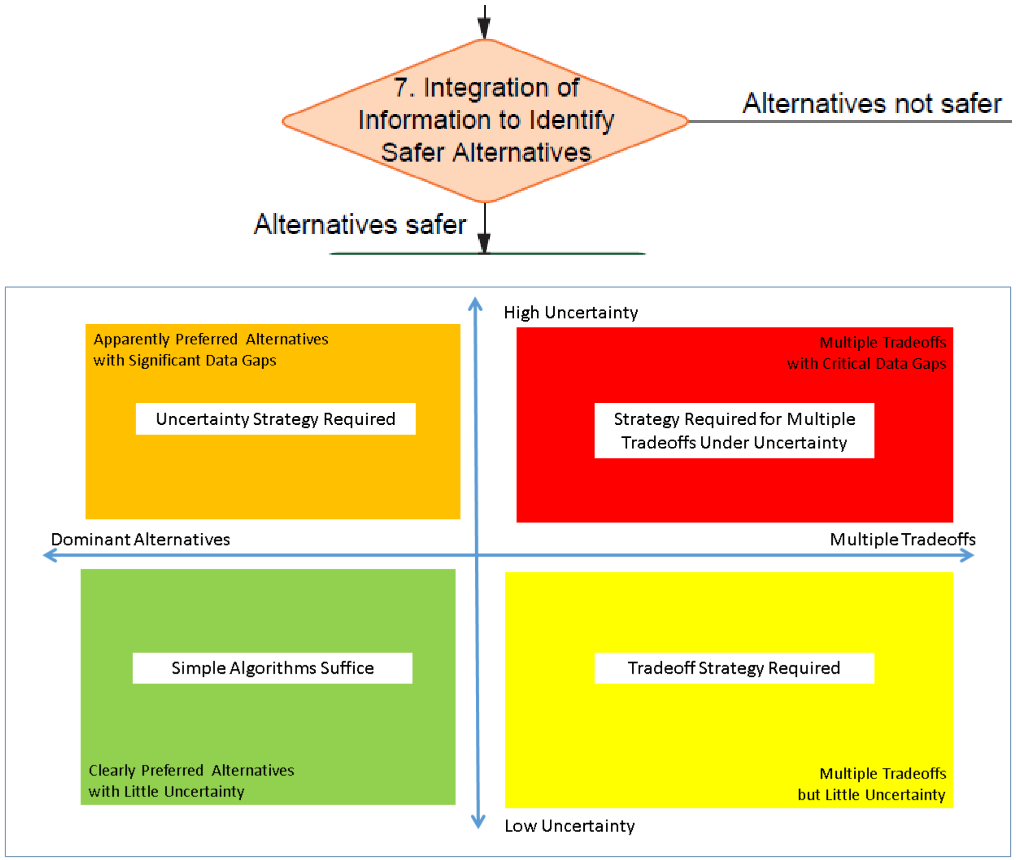
- Acceptable trade-offs are values-driven
- Report:
  - Provides strategies for integrating data
  - Recommends setting goals, requirements, and definition of “safer” in advance
  - Recommends requiring improvement in original area of concern
- Definition of “safer” is up to the entity performing the assessment

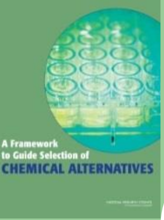
Example: ToxPi Visualization of Data





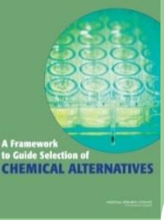
Data Integration And Identification Of Viable Alternatives – Decision Rules





Uncertainty Strategies/Decision Rules

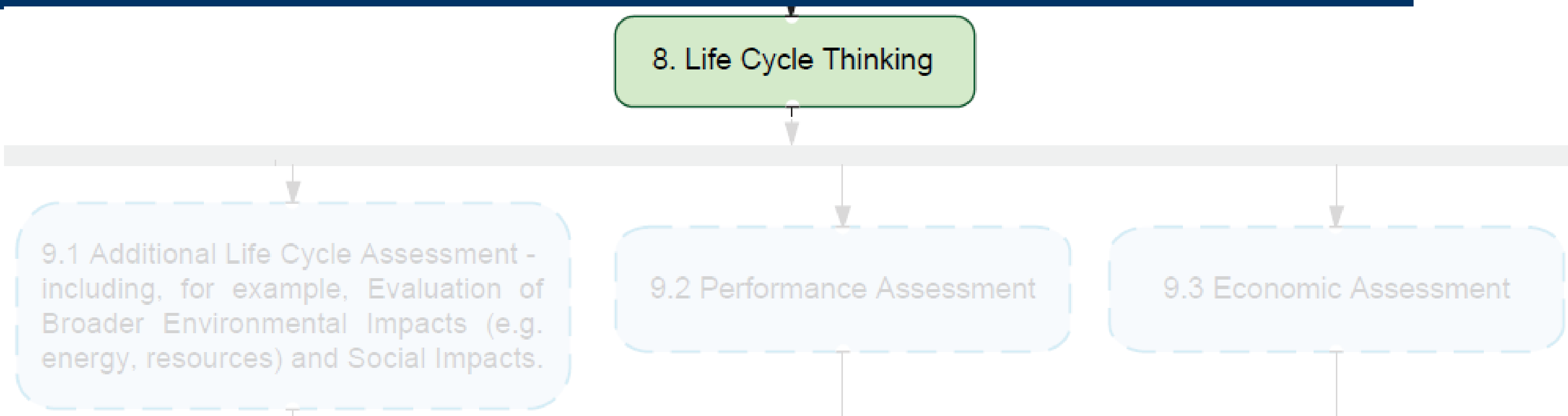
- Known best estimates basis
- Uncertainty downgrade basis
- Quantitative uncertainty analysis
- Remaining neutral about uncertainty and missing data



Tradeoffs Strategies/Decision Rules

- Improvement on key end point
- Strict ordering of end points
- Equal weighting of end points
- Weighted scoring of end points
- Rule-based ranking
- Eliminate the "high" rating
- Exposure weighting
- Relative risk assessment with disease burden estimation
- Expert-manager judgment
- List-based preference ordering

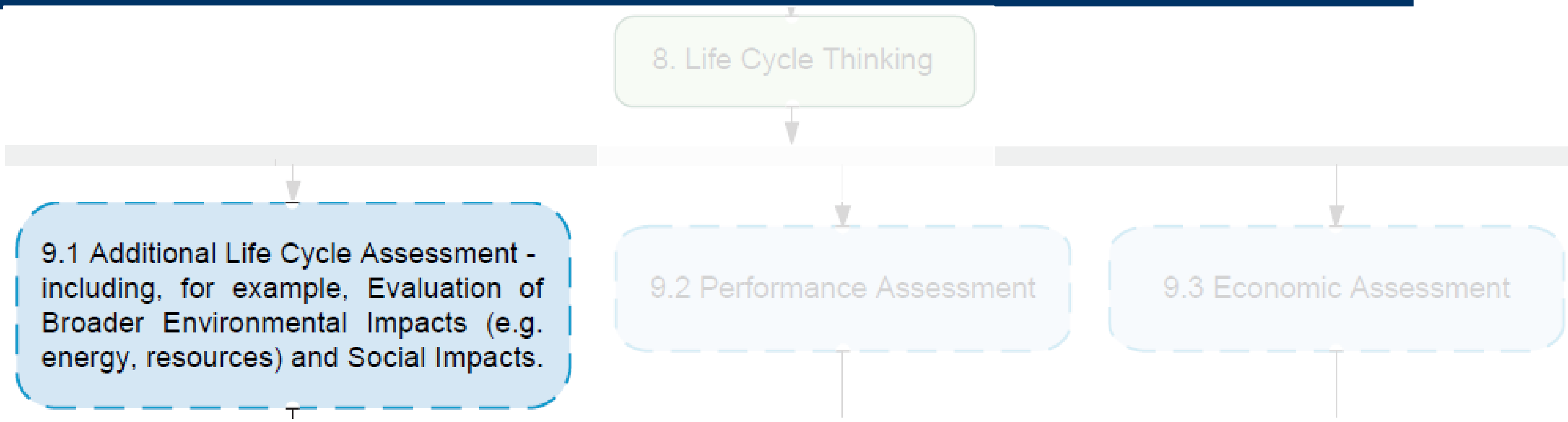
Life Cycle Thinking and Optional Steps



Life cycle thinking

- Consideration of life cycle **differences** between the chemical of concern and alternatives and their implications for broad environmental impacts (e.g. material, water, or energy use)
- Looks beyond time and place of use and disposal

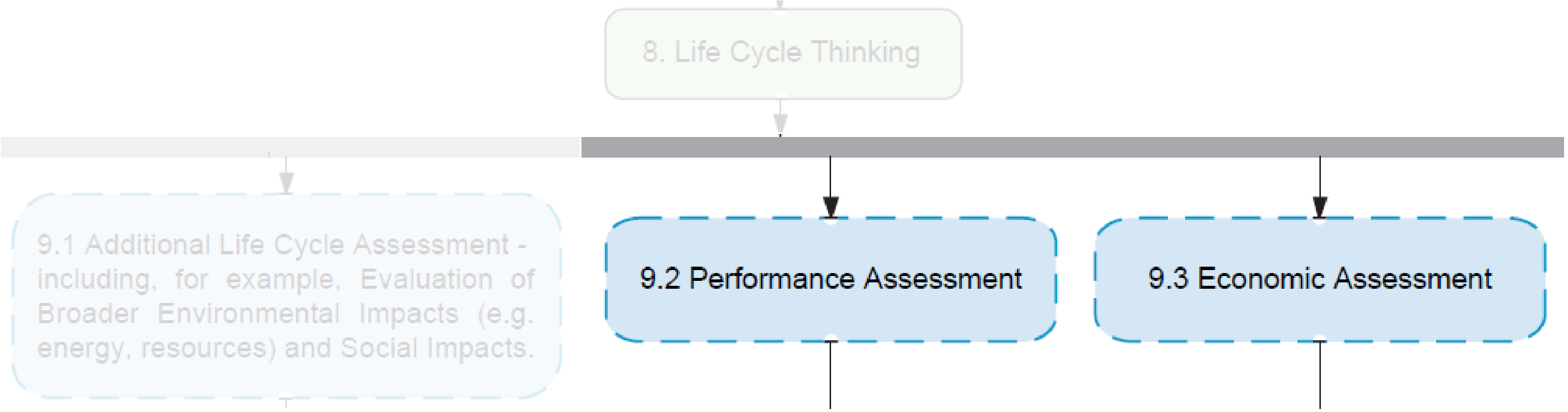
Life Cycle Thinking and Optional Steps



LCA and Social Impacts

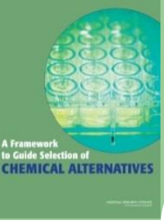
- Based on findings from Step 8 (Life cycle thinking) more analysis might be needed to evaluate differences between the chemical of concern and alternatives and their implications for broad environmental or social impact

Life Cycle Thinking and Optional Steps

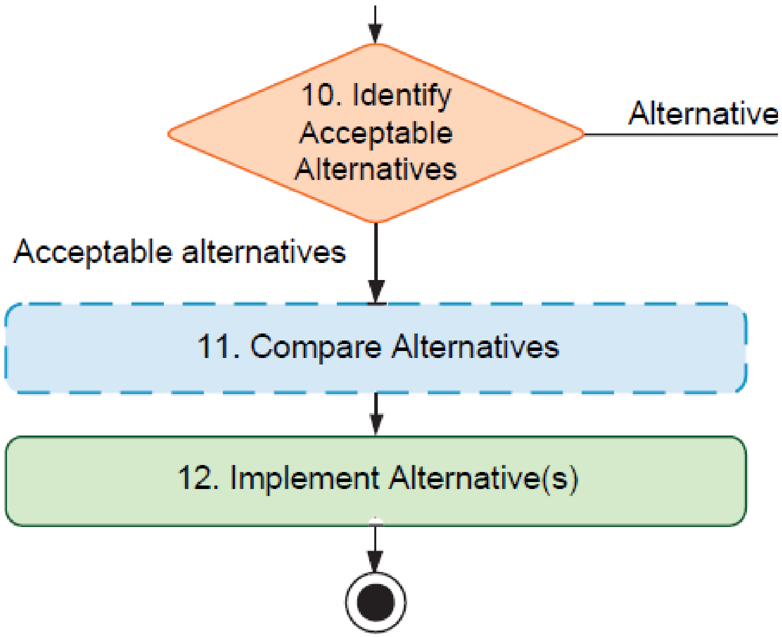


Performance and Economic Assessment

- Completed according to Step 2
- May not be possible or needed in some cases
- Addressed in less detail in the report



Steps 10-12



Identify Acceptable Alternatives

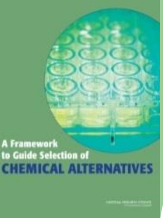
- Use criteria from Step 2
- Acceptable trade-offs are values-driven

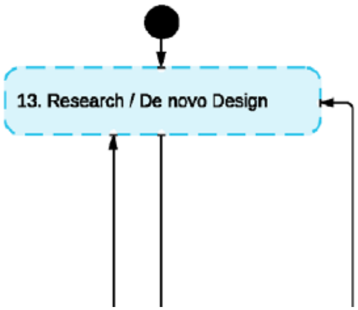
Compare Alternatives

- Methods for selecting single option

Implementation

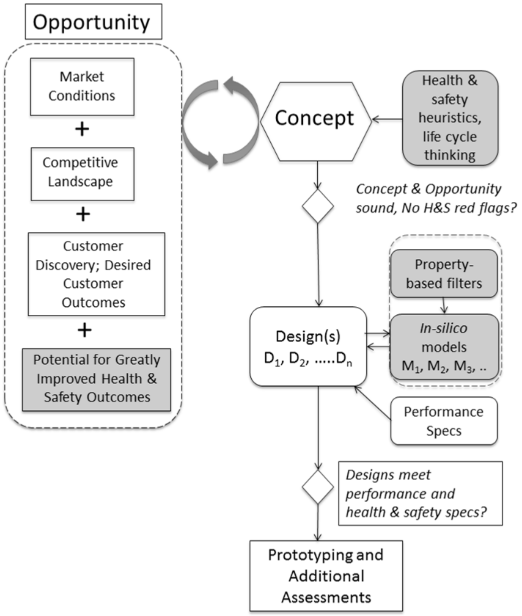
- Expanded section
- Includes monitoring for unintended consequences

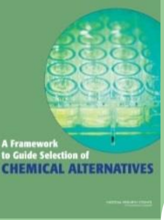




Design of New Chemicals

- Opportunity to address lack of viable alternatives
- Consider environmental and health impacts in parallel with performance criteria.
  - Apply rules of thumb, or general principles; computational methods; and expert systems to predict both physicochemical properties and biological impacts during chemical design phase
  - Chemical candidates could be screened through a battery of in vitro tests, to provide baseline hazard and performance information





For More Information

http://dels.nas.edu/Report/Framework-Guide-Selection/18872?bname=bcst

Free PDF available at:

http://www.nap.edu/catalog.php?record_id=18872

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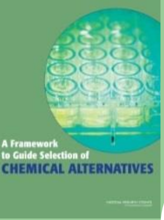

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