



Overview of the QSAR Application Toolbox

Environment Health and Safety Division,
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Recognizing the Need for the QSAR Application Toolbox

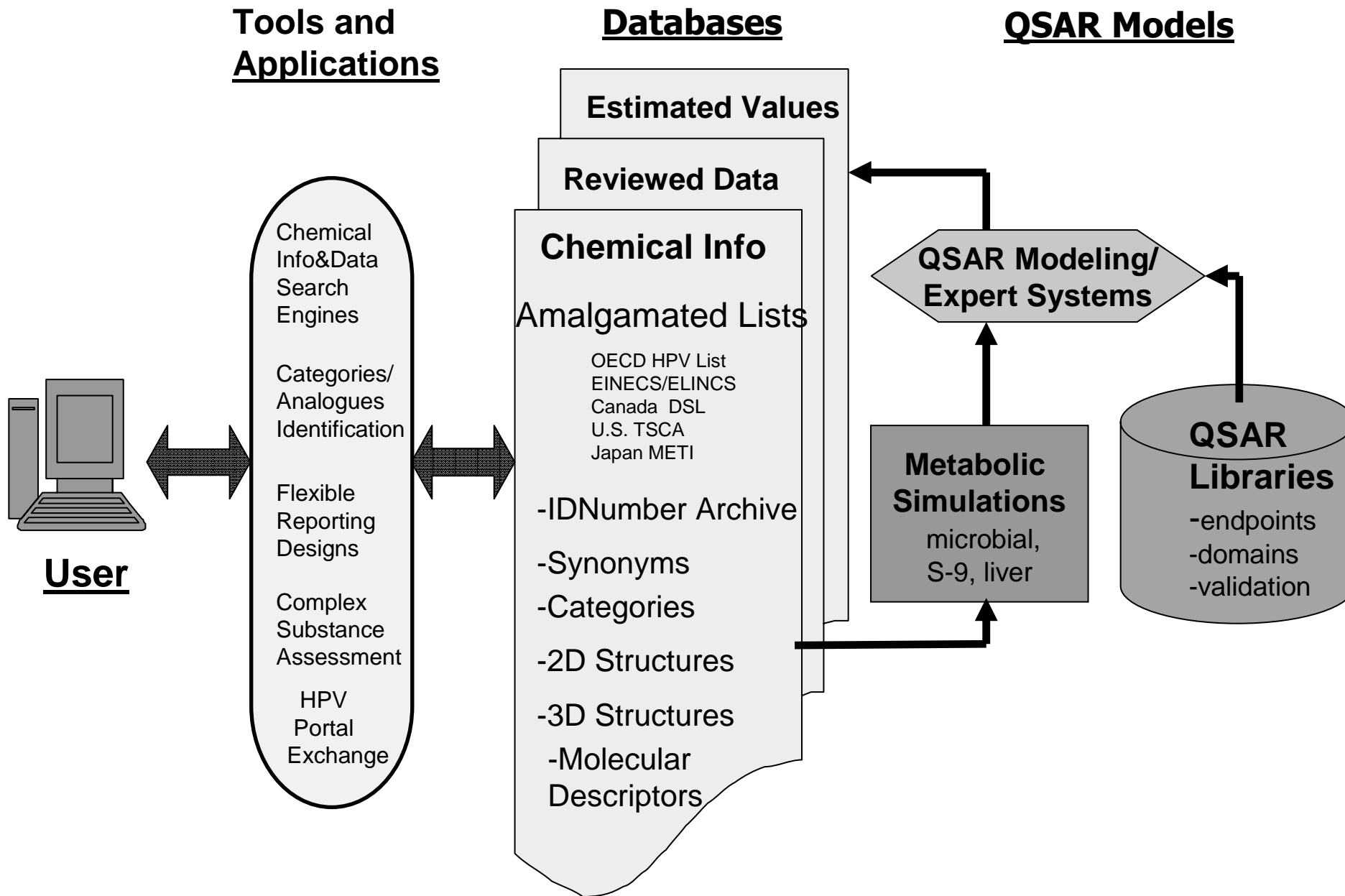
- Required data for risk assessments are available for a small percentage of chemicals
- QSAR methods offer the only non-testing alternative to fill data gaps and set priorities
- Most QSAR methods are computer-based but are viewed too complex for assessments
- A Toolbox will reduce complexity in the use of QSAR methods for reliable estimates



Goals for the Pilot Version of the QSAR Application Toolbox

-Proof-of-Concept-

- Demonstrate that the Toolbox concept will make most QSAR methods readily accessible
- Apply QSAR methods to the formation of chemical categories and filling data gaps
- Illustrate the importance of the domain of application in making reliable QSAR estimates
- Integrate existing data, expert knowledge and QSAR models to facilitate risk assessments





Outline of the QSAR Application Toolbox

- The QSAR Toolbox will house QSAR models, databases and regulatory application chassis
- The Toolbox chassis is a flexible simulator of the normal workflow of experts and specialists
- The chassis will link needed tools to speed information/options to the application experts
- User interfaces will be designed by the application experts to reduce complexity



Typical Queries included in the QSAR Application Toolbox

- Describe the chemical(s) of Interest
- Are the chemical(s) included in regulatory inventories or categories?
- Has the chemical already been assessed by other agencies/organisations?
- Would you like to search for available data on assessment endpoints for each chemical?



Typical Queries included in the QSAR Application Toolbox

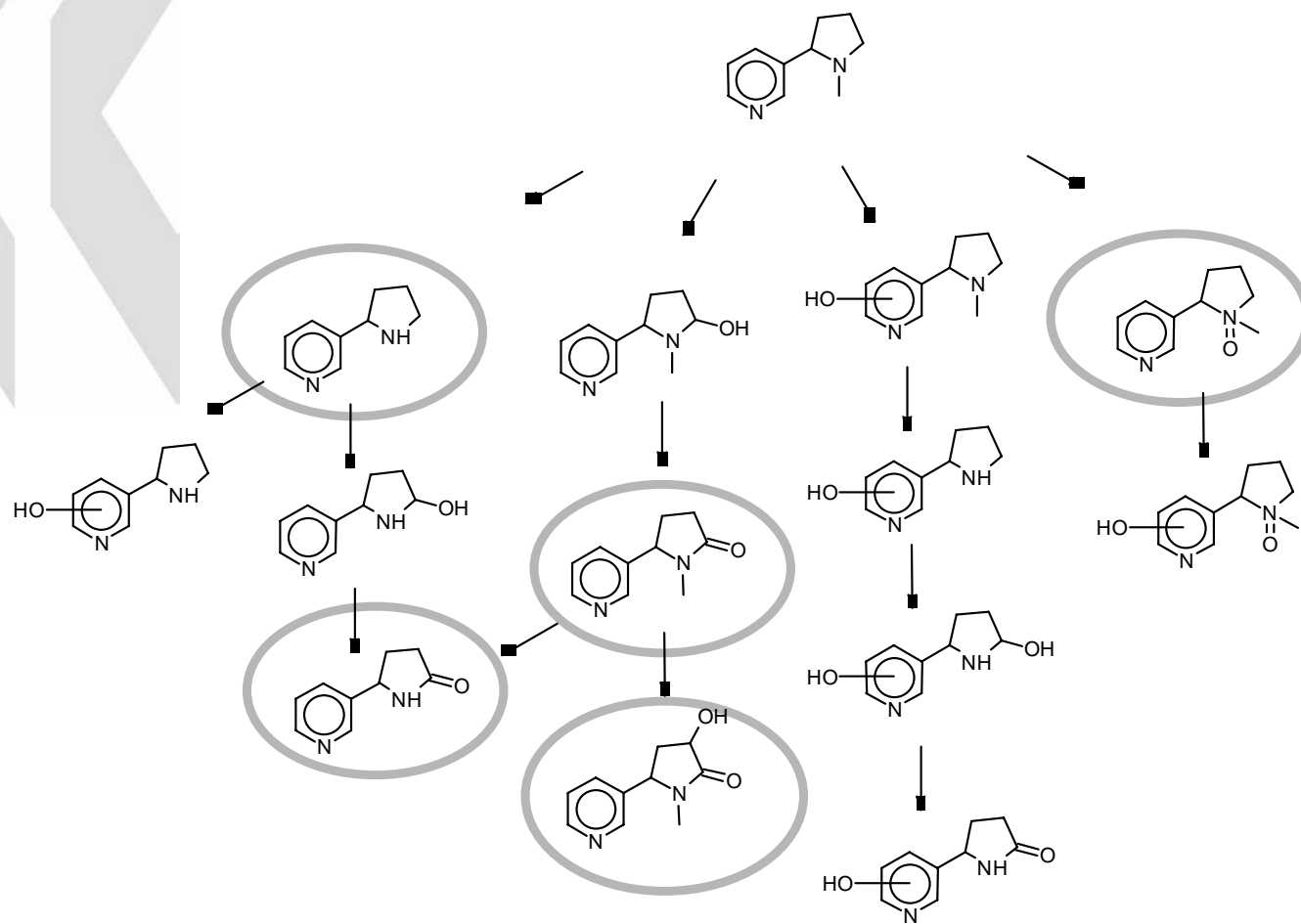
- Would you like structural alerts for each chemical?
- Examples:
 - Acetolactate Inhibitors (herbicides)
 - Acetylcholine analogs (spasmolytics)
 - Acyl-ureas (sedatives)
 - Anthroquinone,1,4-dihydroxy (intercalating anti-neoplastics)
 - Benzhydryl, alpha-hydroxy (anticholinergics)
 - Benzopyran,2,2-dimethyl (K channel openers)
 - Benzothiadiazine,dihydro,1,1-dioxide (diuretics)
 - Beta-blocker (oxime type)
 - Chrysanthemic acid esters (insecticides)
 - Formamido oxime (antifungal;antihypertensive)



Typical Queries included in the QSAR Application Toolbox

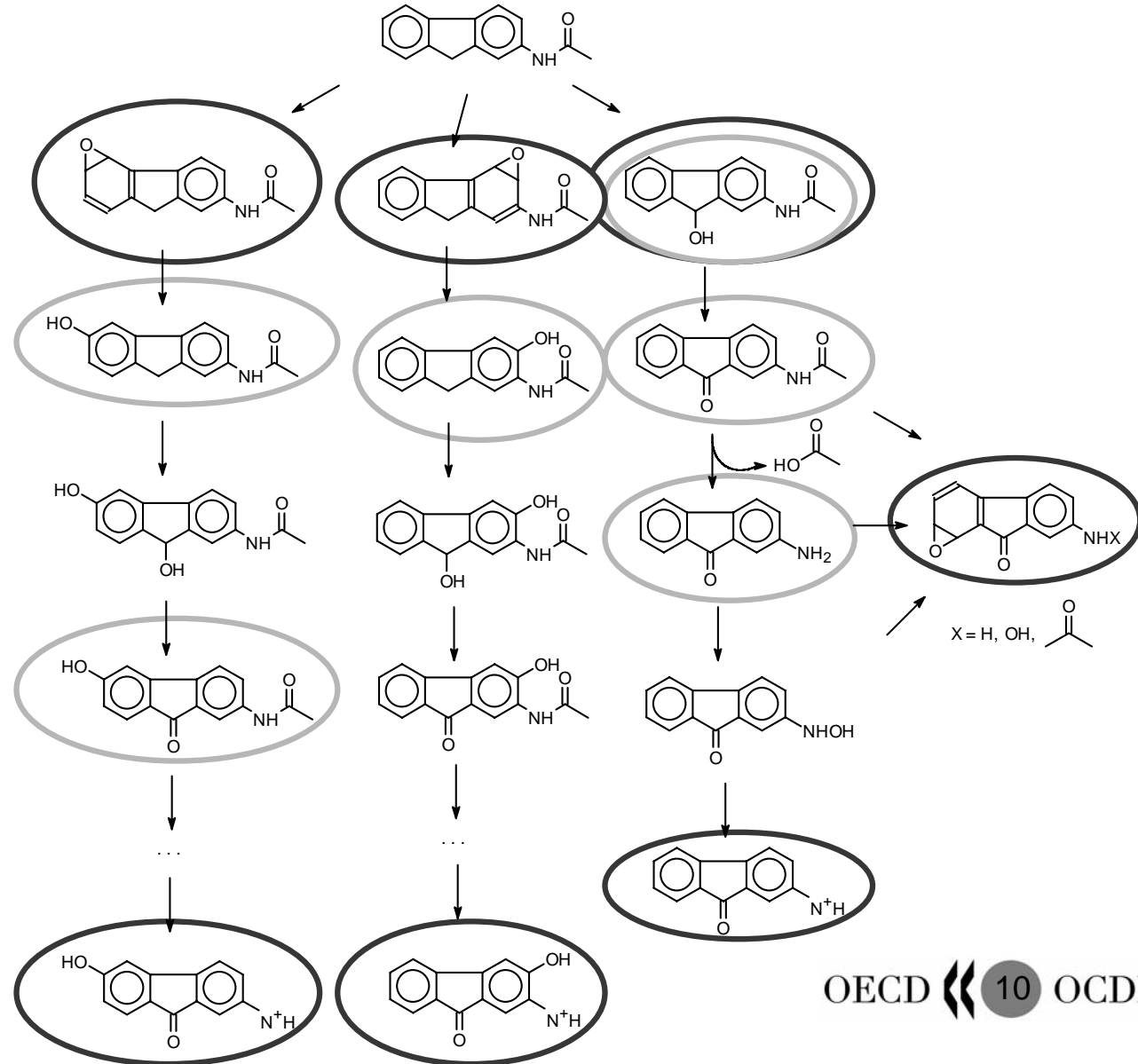
- Explore a chemical list for possible analogues for each chemical?
 - select analogue searches engines
 - customize chemical list of inventory
- Group chemicals based with molecular similarity analysis?
- Prune chemicals with anomalous metabolic pathways or toxicity mechanisms?

Computer Simulated Pathways



Indicates observed metabolites

Identifying Plausible Metabolic Activation

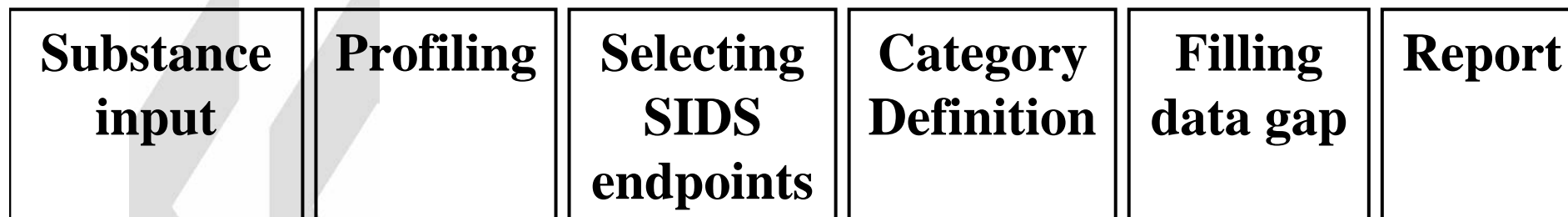




Typical Queries included in the QSAR Application Toolbox

- Include estimated values in the categories data matrix using read-across, trend analysis or QSAR models?
- Design the data matrix for printing/exporting results (harmonized templates default)

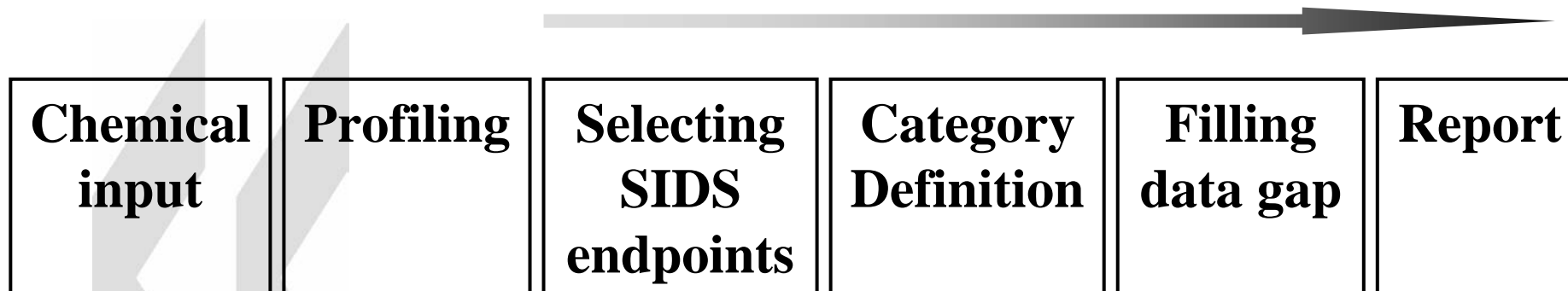
One Logical Workflow Sequence



User Alternatives for Chemical ID

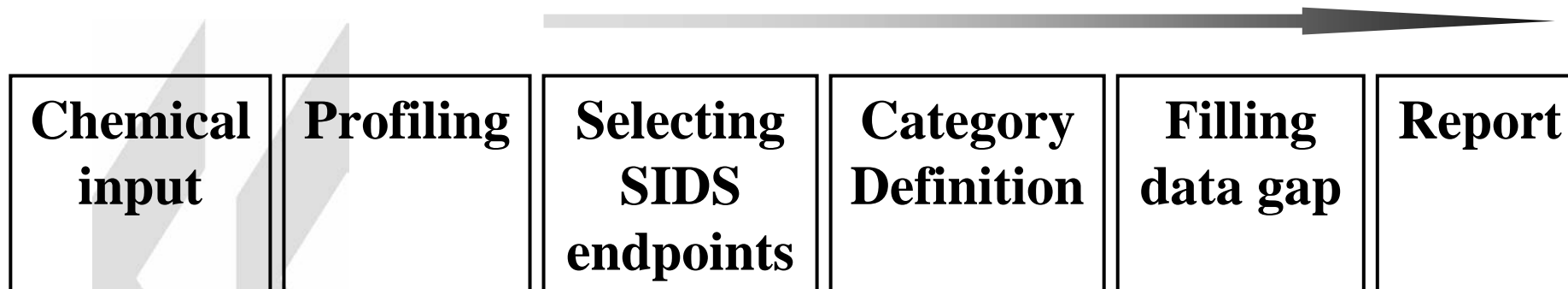
- Name
- CAS#
- SMILES
- Drawing

- Create List
- Use Existing List
- Use Entire Inventory



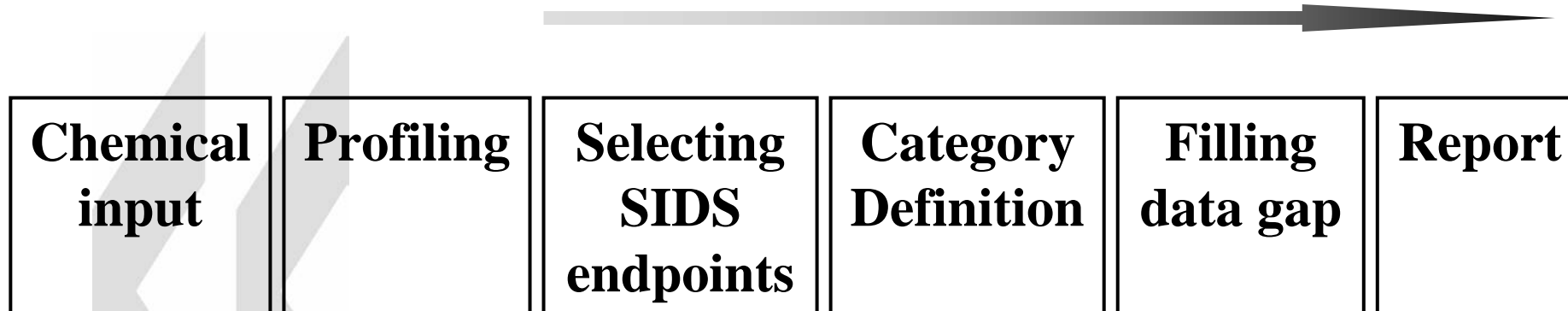
General characterization of chemical

- **Inventory Affiliation: HPVC, LPVC, TSCA, DSL, etc.**
- **Substance Type: inorganic/organic, discrete, mixture, polymers, hydrolyzing compound, etc.**
- **Chemical Class/Category nitro, aldehyde, phenol, etc.**
- **Hazard/Risk Assessments**
- **Profile from Structural Alerts**



Select SIDS and Other Properties

- **Toolbox Data Summary**
 - ✓ **Measured Data Summaries**
 - ✓ **Estimated Data Summaries**
- **Toolbox Links to High Quality Databases**
- **Metabolism Assessment Review**



Category formation

- **Grouping chemicals into categories:**
 - **OECD Categories**
 - **Other Established Categories**
 - **AIM (EPA)**
 - **Super-fragments (Al Leo)**
 - **Atom-centered fragments (AMBIT, etc.)**
- **Pruning chemicals with anomalous behaviour:**
 - **Mechanisms**
 - **Metabolism**

