Environmental Impact Assessment of Semiconductor Effluents: Toxicity Data and QSAR Methods in Life Cycle Assessment

Prof. David Dornfeld
Sarah Boyd

Problem Statement

There is a dearth of toxicity data for semiconductor materials and process effluents.

No basic human health or environmental toxicity information is publicly available for 43% of US high production volume (HPV) chemicals

A full set of basic toxicity information is available for only 7% of HPV chemicals. [1]

Out of a representative set of 130 chemicals used in electronics manufacturing[2] :

11 are tracked through High Production Volume Challenge (of > 2,800 HPV Chemicals)

17 are profiled in the Hazardous Substances Databank (HSDB)

35 are profiled in the Registry of Toxic Effects of Chemical Substances (RTECS)

6 are profiled in the Carcinogenic Potency Database

17 are profiled in the Integrated Risk Information System (IRIS)

[1] United States. Environmental Protection Agency. Chemical Hazard Data Availability Study. Washington DC: Office of Pollution Prevention and Toxics, 1998.

[2] A Misra, JD Hogan, R Chorush. Handbook of Chemicals and Gases for the Semiconductor Industry Wiley-VCH, 2002.

Problem Statement (continued)

There is also a need for *faster* assessment of toxicity in life cycle assessment (LCA) methods.

In order for environmental impacts to contribute to manufacturing decision-making, LCA must:

- have as short a "turn-around" time as possible.
- be practicable as early as possible in process and equipment design.

Objectives

The objective of this work is to improve environmental and human health impact assessment as it is conducted in semiconductor life cycle assessment by:

- conforming these methods with current and emerging assessment procedures in government and industry.
- filling in data gaps by using additional resources and tools for toxicity assessment.
- tracking data quality and data uncertainty.
- focusing on transparency, such that decision-making can make use of discrete information as well as aggregated data.

Objectives (continued)

Faster assessment of toxicity in life cycle assessment (LCA) methods can be achieved through :

- automation of data aggregation from available databases, e.g. HSDB, IRIS.
- integration of toxicity assessment tools and software.

Automation and software integration must be done with care, by:

- assessing/monitoring data quality
- tracking uncertainty
- ensuring applicability of each toxicity assessment tool to its subject

Human Health Impact: Current Assessment Methods

The Multi-Criteria Health Hazard metric is a measure of potential worker health and safety impacts.

- Calibrated to reference chemicals.
- Calculated on log scale.
- Designed to use robust set of endpoints describing acute, systemic, developmental and reproductive toxicity, carcinogenicity, mutagenicity, and genotoxicity, as well as physical hazards and standards and regulations.

…However, many of these endpoints or classifications are not available.

Streamlined MCH, based on:

acute effects, physical hazards, and standards and regulations.

Environmental Impacts: Current Assessment Methods

Environmental impacts are evaluated using a number of metrics:

- Resource depletion: electricity, fuel, public water, process cooling water, and overall material use.
- GWP
- HAPS loading
- NOx
- CO
- Flammable emissions
- Liquid waste: total, HF and hazardous and non-hazardous solid waste volumes.

Toxicity Assessment in the Chemical Industry

Commonly used tools among toxicologists in the chemical industry:

Ecological Structure Activity Relationships (ECOSAR):

EPA-developed QSAR software tool for ecological toxicity assessment

National Toxicological Program (NTP) Reports

DIALOG: directed search engine for licensed publications including:

- Environmental Chemistry Health and Safety, Royal Society of Chemistry
- Hazardous Substances Databank (HSDB), National Library of Medicine
- National Institute for Occupational Safety and Health Technical Information (NIOSHTIC), NIOSH
- MEDLINE

SARs and QSARs in US Environmental Regulation

SARs have been a part of US environmental regulation since 1976, with passage of the Toxic Substances Control Act (TSCA).

In 1976 the Interagency Testing Committee (ITC) was mandated by Section 4(e) of TSCA to use SARs and QSARs as factors to consider in the recommendation of chemical testing:

Factor 5: "[consider] the extent to which the substance or mixture is closely related to a chemical substance or mixture which is known to present unreasonable risk to health or the environment."

Factor 7: "[consider] the extent to which testing of the substance or mixture may result in the development of data upon which the effects of the substance or mixture on health or the environment can be reasonably determined or predicted."

QSARs in US Environmental Regulation

Substantial efforts have been made to make the evaluation of toxicity more accessible to the public, resulting in a broad set of publicly available tools and guidelines.

> 7 Regulatory Applications

Agency for Toxic Substances and Disease Registry (ATSDR): Uses 2 commercial software QSAR packages to predict toxicity

EPA: Screening Premanufacturing notices, Prioritization for risk assessments, predicting estrogen receptor binding affinities

FDA: uses commercial software for drug toxicity evaluation

>10 Tools

ASTER
AQUIRE
COREPA
SIDS
ECOSAR
ECOTOX
EDPSD2
SuCCSES
DEBITS
WMPT

General QSAR Method

A QSAR is most commonly a statistical model of test data.

$$\Phi = f(C)$$

1. Create bin of comparable compounds (training set) based on the target chemical's structure.

2. Choose sets of chemical descriptors (C) according to method (e.g. number of substructures or bonds and their configuration, molecular weight, pKa, hydrophobicity, steric and electronic properties)

3. Choose f to best model the set (test through cross-validation)
   - multiple regression analysis
   - principle component and factor analysis
   - partial least squares
   - discriminant analysis

Other types of QSAR models include neural nets and expert systems.

QSARs in EU Environmental Regulation

Registration, Evaluation and Authorization of Chemicals (REACH) Draft Legislation

It is anticipated that QSARs will be used more extensively under new legislation for screening and testing prioritization.

"(Q)SARs are likely to play an important role in the assessment of chemicals produced or imported in quantities between 1 and 10 tonnes" [3]

Joint Research Council (JRC) in collaboration with European Centre for the Validation of Alternative Methods (ECVAM) has established a working group for validation of new and existing QSAR models under REACH.

[3] EU, the European Commission, REACH White Paper: Strategy for a Future Chemicals Policy, Brussels, COM (2001) 88 final, 2001.

QSARs in Environmental Regulation in Japan

QSARs are not part of the regulatory process in Japan, but the Japanese Ministry of the Environment is considering future use of QSAR methods. [4]

[4] Walker JD, Carlsen L, Hulzebos E, Simon-Hettich B. 2002. Global government applications of analogues, SARs and QSARs to predict aquatic toxicity, chemical or physical properties, environmental fate parameters and health effects of organic chemicals. SAR QSAR Environ Res 13:607-616.

ECOSAR

ECOSAR: Ecological Structure Activity Relationships, an EPA-developed software tool

- Used by the EPA to screen Pre-Manufacturing Notices.
- Models toxicity to fish, invertebrates and algae.
- Based on over 70 property-activity equations.
- Good model and data transparency.
- Under continuous review and subject to public criticism.

Limitations of ECOSAR

ECOSAR is appropriate for use with:

- Neutral organics that are non-reactive and non-ionizable
- Organics that are reactive and ionizable
- Surface-active organic compounds such as surfactants and polycationic polymers
- Inorganic compounds including organometallics

Sizes of data sets for models vary:

- the neutral organic 96-hour fish LC50 SAR was based on toxicity values for over 60 chemicals
- 96-hour LC50 SAR for propargyl alcohols was based on only one toxicity value.

However, the transparency of data is good, and uncertainty values can be assigned in cases of smaller data sets or less accurate models.

Integration of ECOSAR

Analysis could be integrated into other LCA software. ECOSAR requires SMILES chemical formula, Kow, and molecular weight:

- Online SMILECAS DB (>103,000 entries) from Syracuse Research applies to some molecules, others will have to be manually entered.
- Molecular weight can be calculated automatically.
- Kow may be determined using KowWin, given CAS or SMILES notation.

ECOSAR is available through the EPA; SMILECAS and KowWin are owned by Syracuse Research.

Some SARs require other physical data, such as number of ethoxylates or percent amine nitrogen.

Conclusions

In summary:

- Some information is better than no information
- LCA toxicity assessment methods are best aligned with those of government and industry
- QSARs are advantageous as a predictive tool, there are many well-established models, and QSAR methods are being continuously refined and evaluated in the US and abroad.

Future Work:

ECOSAR can be used as a toxicity assessment tool, and may be integrated into LCA tools, providing for the following limitations:

- Subjects of analysis must be screened by chemical group.
- ECOSAR does not assess toxicity of mixtures.
- ECOSAR does not evaluate compound effects.
- ECOSAR assesses aquatic toxicity, and is not representative of human environmental exposure.

Questions?

Contact:
Sarah Boyd
sboyd@me.berkeley.edu
(510)643-5114

Example QSAR: Henry's Law Constant

$$\log H = \Sigma\, n_i\, h_i + \Sigma\, n_j\, c_j$$

1. The Meylan and Howard method was built from a training set of 345 compounds

2. The descriptors are based on free energy of binding (Hansch analysis)

3. Regression analysis resulted in the function above, composed of bond contributions factors (h_i) times number of bonds (n_i) and a correction factor (c_j) for each substituent group j