The U.S. High Production Volume (HPV) Challenge Program

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Topics Covered

- HPV Challenge Program
- Participating in the Program
- HPV Guidance Issued by EPA
- Current OPPT Initiatives
  - Coming OECD Guidance on Exposure Information
  - HPV Challenge Database

U.S. HPV Challenge Program

- History
  - Goals
  - Modeled after OECD SIDS Program
  - The beginning…

THE HPV CHALLENGE PROGRAM

- HPV – High Production Volume chemicals (manufactured/imported into U.S. in quantities of one million lbs or more per yr)
- Goal of the HPV Challenge Program:

Have basic hazard information on all HPVs available to the public through the internet

MODELED AFTER OECD HPV SIDS

- OECD HPV SIDS = Organization for Economic Cooperation and Development (OECD), Screening Information Data Set (SIDS)
- OECD: International organization with 29 member countries
- SIDS: A number of elements/endpoints that make up a basic set of hazard information

The Basis for OECD Work
(1990 Council Decision/Recommendation)

- Members countries shall cooperatively investigate HPV chemicals to identify those which are potentially hazardous
- Member countries shall cooperatively select the HPV chemicals (…) agree upon basic data .. and co-operatively make an initial assessment

OECD HPV Chemicals

- HPV chemicals are produced in quantities greater than 1000 tonnes (2.2 million lbs)*
- HPV chemicals account for over 98% of total chemical volume
- Over 4000 chemicals on OECD HPV List
- Basic screening level information (i.e. SIDS) should be available for all HPV chemicals…

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* U.S. definition of HPV chemical is one million pounds….

Screening Information Data Set (SIDS) = Minimum Hazard Data Set

Physicochemical properties: melting & boiling pts., vapor pressure, water solubility, partition coeff.

Environmental fate: photodegradation, stability in water, biodegradation, transport/distribution (model)

Environmental effects: acute toxicity in fish, aquatic invertebrates and aquatic plants

Health effects: acute and subchronic toxicity, genetic toxicity, reproductive and developmental toxicity

U.S. HPV CHALLENGE PROGRAM HISTORY

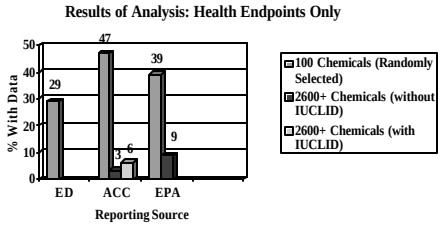
- Three separate studies….
- The Earth Day, 1998 Announcement
  - Cooperative effort among industry, government, and environmental groups
- Two Components
  - Voluntary and Regulatory

Three Separate Studies…

- *Toxic Ignorance* 1997 (Environmental Defense, or ED – formerly EDF)
- *Data Availability Study* 1998 (EPA)
- *Data Availability Study* 1998 (American Chemistry Council, or ACC – formerly CMA)

All Concluded……..

"Most" HPVs Do Not Have Basic Hazard Information (SIDS)



HVP Challenge: Two Components

- October 1998 formal announcement of the Challenge Program: EPA, ACC, ED, API
  - Voluntary Component (65 FR 81686—12/26/2000)
  - Regulatory Component (65 FR 81658—12/26/2000)
    - Proposed Test Rule on some chemicals not sponsored by industry

Voluntary Component

- Companies asked to volunteer ("commit") to sponsor one or more HPV chemicals
- Commitment consists of naming the chemical(s), CAS number and the year the test plan and existing information will be made publicly available
- December 1, 1999, was the deadline for voluntary component

Regulatory Component

- HPV Chemicals not sponsored in the Voluntary Component are subject to the Regulatory Component of the program
- "HPV Test Rule" published December 26, 2000 as a proposed rule – expected to be finalized in early 2004)
  - Will include about 30 chemicals
- Work on a test rule for additional HPV substances is underway

Participating in the Program

- What is a submission?
  - Test Plans
  - Robust Summaries
- Posting of a submission
- Status
  - Sponsored chemicals/number submissions posted
- Categories

An HPV Submission:

- *Robust Summaries* of scientifically adequate existing studies showing that new testing is not necessary

AND

- A *Test Plan* (what you plan to do* if there are no existing data for a given endpoint)

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* Are options available without actual testing: SAR, category analysis, difficult-to-test, wt-of-evidence, etc.

POSTING DATA & COMMENTS

- EPA posts submitted data no later than 10 days from its receipt
- The public has 120 days to comment on the information

HPV Challenge Commitments

- ~2,800 HPV chemicals covered in Challenge.
- As of 2/2004:
  - 2,238 sponsored chemicals.
  - 411 companies and 113 consortia participating.
- List of sponsored chemicals can be found at:

http://www.epa.gov/chemrtk/spnchems.htm

HPV Challenge Test Plans (As of 2/2004)

- 335 Test Plans submitted covering 1,249 chemicals.
  - 110 are for categories.
  - 225 are for individual chemicals.
- All Test Plans are posted to the EPA website at: http://www.epa.gov/chemrtk/viewsrch.htm

Robust Summaries

A Robust Summary is ***"…sufficient information to allow a technically qualified person to make an independent assessment of a given study report without having to go back to the full study report.."***

AND

will bring the most important and relevant information forward in an electronic format that can be manipulated, studied, and compared with other data

Robust Summary Template: Repeat Dose (14-90 days) Toxicity Study

- Company, CAS No.
- Chemical name
- Test substance ***remarks***
- Chemical Category
- Method, GLP, Study year
- Method ***remarks***
- Species, strain, sex, #
- Route of administration
- Exposure period, frequency

- Doses, controls, post-exposure observations
- Statistical methods
- NOEL, LOEL, Type of effect
- Toxic response
- Statistical results
- Results ***remarks***
- Concluding ***remarks***
- Reliability, General ***remarks***, References.

Robust Summaries Submitted (Early Fall, 2003)

- >8,000
- Health Effects—4,984
- Environmental Effects—1,370
- Environmental Fate—638
- Physicochemical Properties—1,434

Health Effects

Endpoint	Published	Unpublished	Total
Acute	414	1,245	1,659
Repeat Dose	419	495	914
Gene Tox	874	850	1,724
Repro/Dev	337	314	651

Environmental Effects/Fate

Endpoint	Published	Unpublished	Total
Fish	148	473	621
Dphnid	97	348	445
Algae	65	239	304
Biodeg	196	442	638

How SIDS Endpoints are Met in the HPV Challenge Program

Human Health		Environmental Effects	
Adequate studies	50%	Adequate studies	58%
Estimation	44%	Estimation	35%
Testing	6%	Testing	7%

Categories

"a group of chemicals whose properties are likely to be similar or follow a pattern as a result of structural similarity"

"These structural similarities may create a predictable pattern in any or all of the following parameters: physicochemical properties, environmental fate, environmental effects, and/or human health effects."

Why Use Categories?

- To assess the effects of chemicals on human health and the environment
- Faster and more efficient than chemical by chemical approach
- Results in reduced costs and animal usage

A category may be based on:

- A common functional group (e.g., aldehyde, epoxide, ester, etc.)
- The likelihood of common precursors and/or breakdown products (e.g., acid/ester/salt)
- An incremental and constant change across the category (e.g., CH_2 for alpha olefins)
- A series of chemical reaction products/mixtures (e.g., petroleum streams, surfactant mixtures)

Types of Categories

- Traditional
  --Common functional group
  --Incremental change in chain length
- Production streams
  --Petroleum products
  --Sequential change in composition
- Mixture families
  --Family of similar substances

Categories in the HPV Challenge Program

- About 82% of the chemicals submitted to date in the U.S. HPV Challenge Program are members of a category….

110 categories (1024 chemicals)*

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* As of 2/2004

Categories in the U.S. HPV Challenge Program

- Submitter proposes a category in the Challenge Program
- EPA provides comments
  - EPA does not "approve" Category Test Plans
- Once proposed testing is completed, an evaluation of the results - and how it applies to the rest ("untested" members) of the category - needs to be made *(Category Analysis Document)*

U.S. HPV Challenge Guidance Documents

http://www.epa.gov/chemrtk/guidocs.htm

EXAMPLES:

- Data Adequacy
- Developing Robust Summaries
- Developing Categories
- Use of Structure-Activity Relationships (SAR)
- Exposure Templates
- Closed System Intermediates
- No Longer HPV

Some Current OPPT Initiatives

- Coming OECD guidance on exposure…
- HPV Information Database

OECD Summary Exposure Reporting Format

- Internationally agreed upon format for summarizing exposure data and information
- Comparable to the hazard robust summary
- Flexible format, yet comprehensive in scope
- Covers workers, environmental exposures, and consumer exposures; Monitoring and modeling
- Undergoing final approval through OECD

Consistency in Reporting Information

- Consistent reporting format: allows reviewers to know where to look for information such as:
  - Completeness of the overall assessment
  - Summary of release and exposure information by activity (mfg/processing/uses)
  - Discussion of objective and elements of quality of individual exposure estimates

Incorporates Important Basic Principles

- Characterize Transparency:
  - Describe underlying data, assumptions, uncertainties & data gaps
- Characterize Data Quality:
  - Describe objective and study design, sampling methods, analytical methods, QA/QC, uncertainty
  - Describe model objective, key inputs, assumptions, uncertainty, scenario, model evaluation/model peer review
- Characterize Completeness:
  - Describe scope of assessment, what exposures were assessed, what were not assessed, why they were not assessed

HPV Challenge Database

- Currently Test Plans/Robust Summaries available only on HPV Website

  --Submission date ordered/Not searchable
- Searchable Webpage end of March
- OPPT has been involved in development of an HPV information system for the past few years

HPVIS: High Production Volume Information System

- The purpose of the system is to store and manage submitted data, and to facilitate access to information via the program's website
- In the Summer of 2003, OPPT held meetings with stakeholders and customers to understand their expectations

HPVIS: Data Management and Accessibility

- Based on stakeholder and customer input, OPPT has prioritized its efforts
- Focus will be on:
  - re-designing the information system to meet needs
  - improved search capabilities on the website
- Other desirable features for future enhancements:
  - more focus on accessing endpoint/toxicity data
  - public access using system data
  - integrate with other agency systems