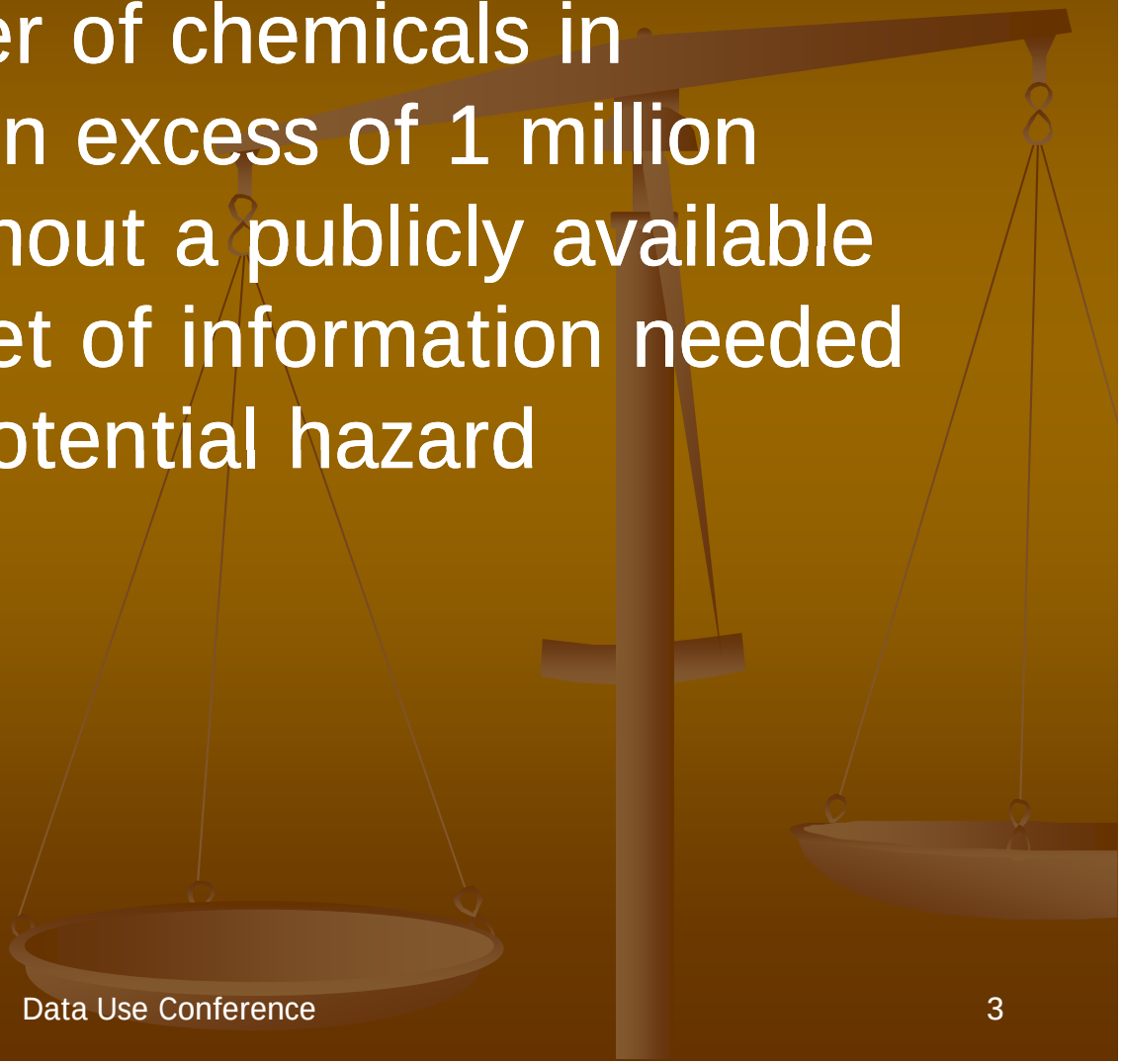
Prioritization Process and Development of the Hazard Characterization Documents

Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, DC

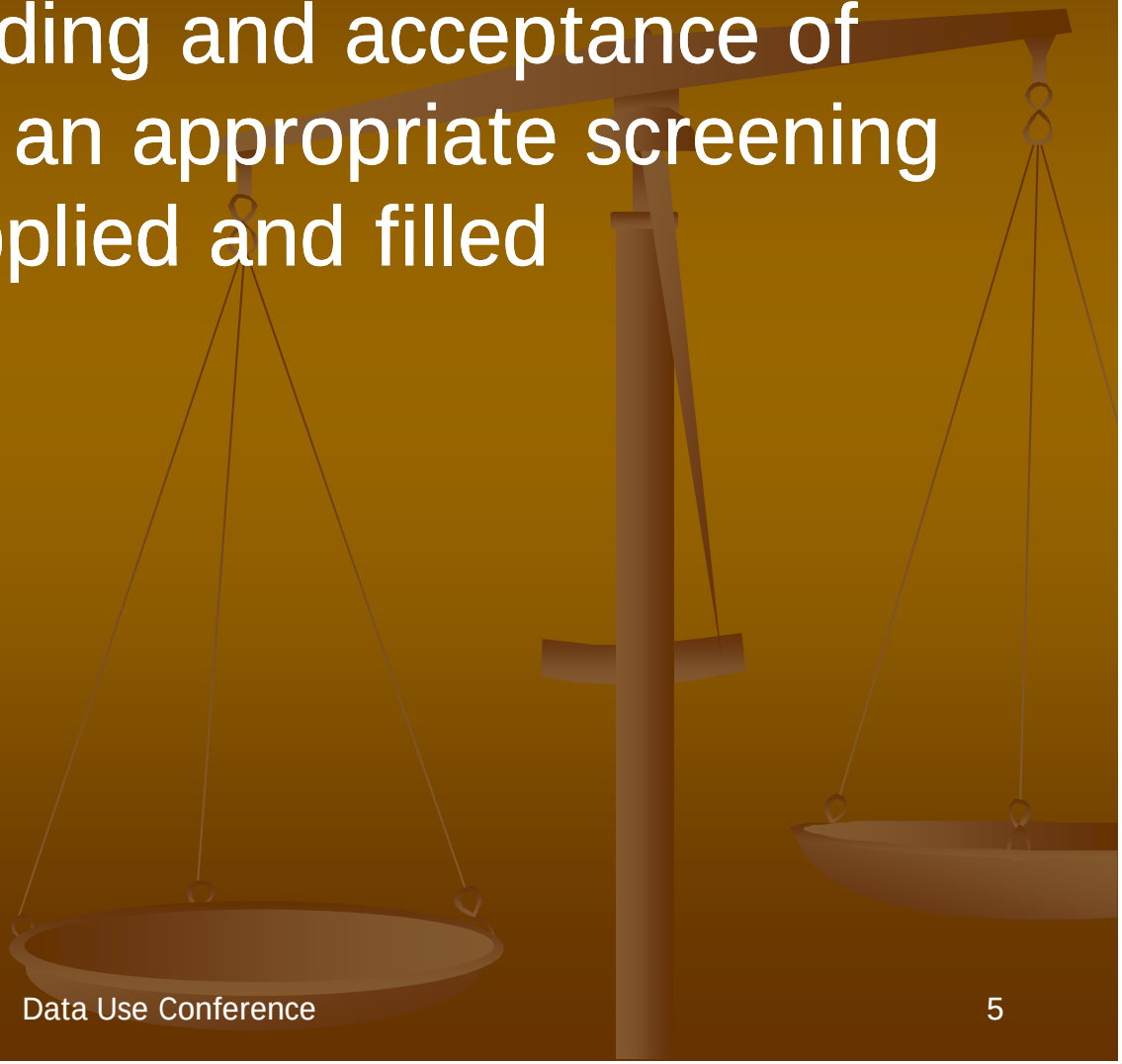
An Overview

Large number of chemicals in commerce in excess of 1 million pounds without a publicly available minimum set of information needed to assess potential hazard

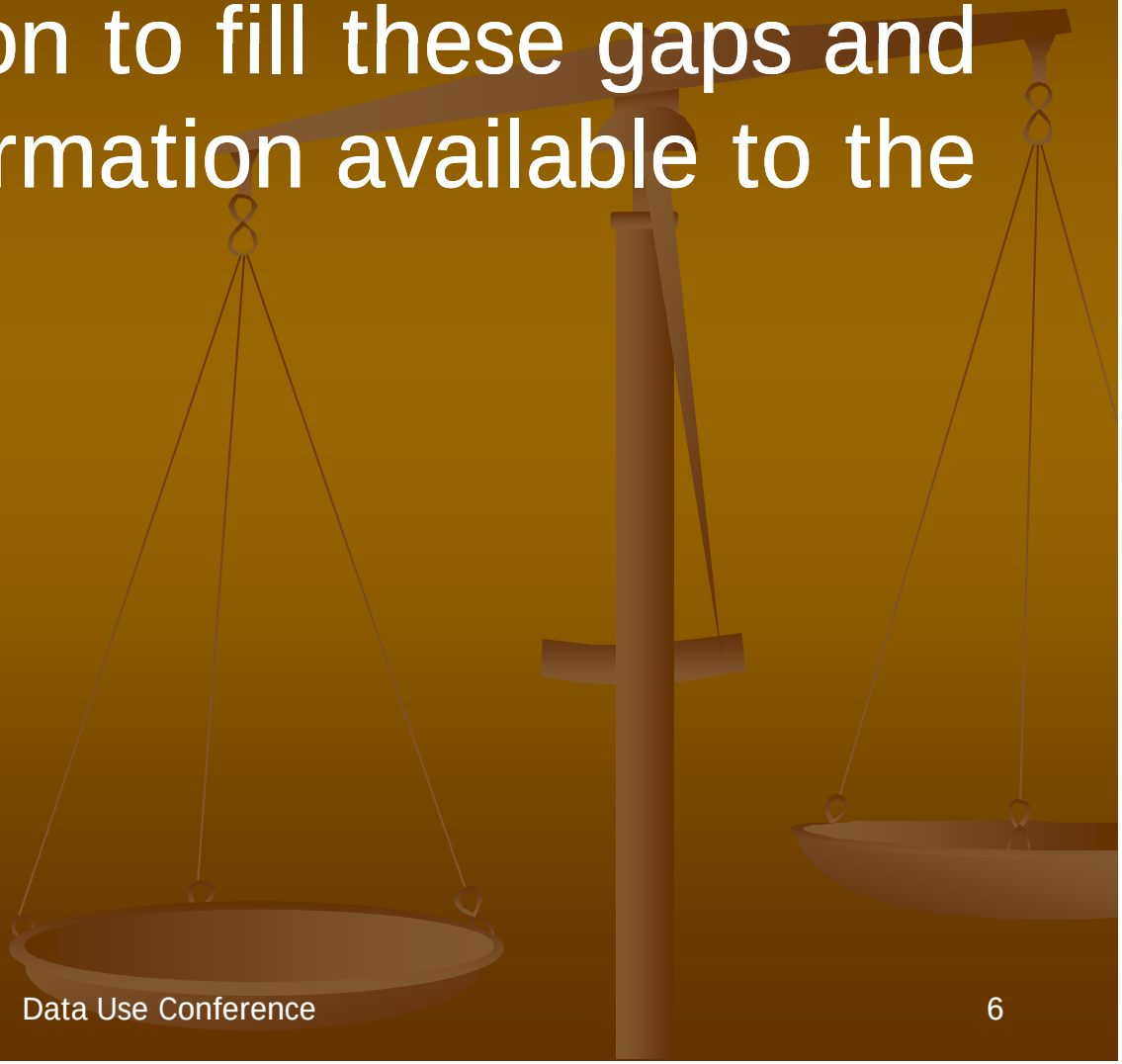


- Shared recognition that data gaps should be filled in a responsible and thoughtful manner – including consideration for animal welfare and avoidance of un-needed testing
- An open opportunity for comments on Test Plan proposals – comments that were used by EPA reviewers and by Sponsors as they worked towards Final submissions

Shared understanding and acceptance of SIDS battery as an appropriate screening battery to be applied and filled



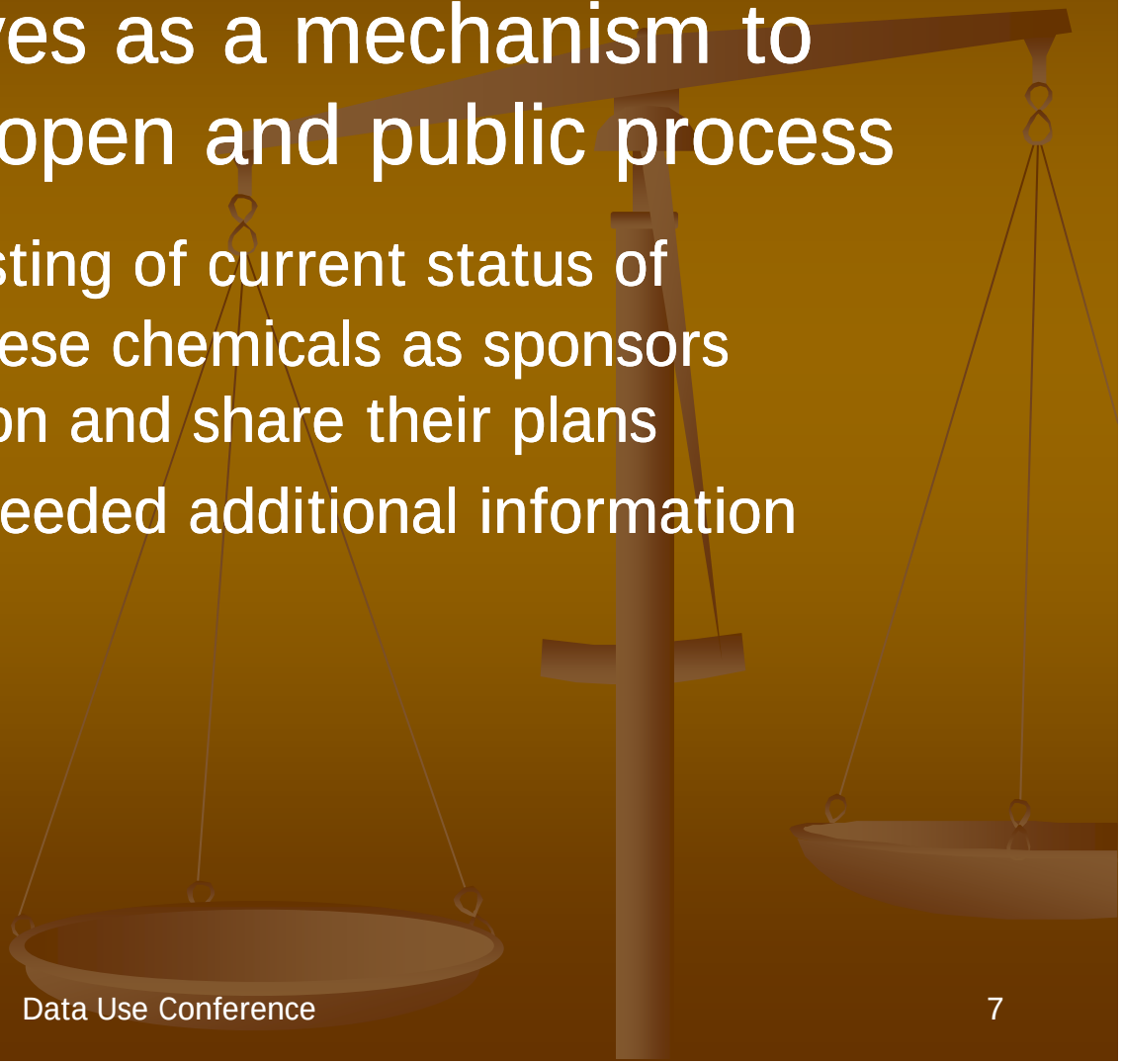
Collaboration to fill these gaps and make information available to the Public



The WWW serves as a mechanism to make this an open and public process

Allows posting of current status of knowledge for these chemicals as sponsors submit information and share their plans

for posting any needed additional information



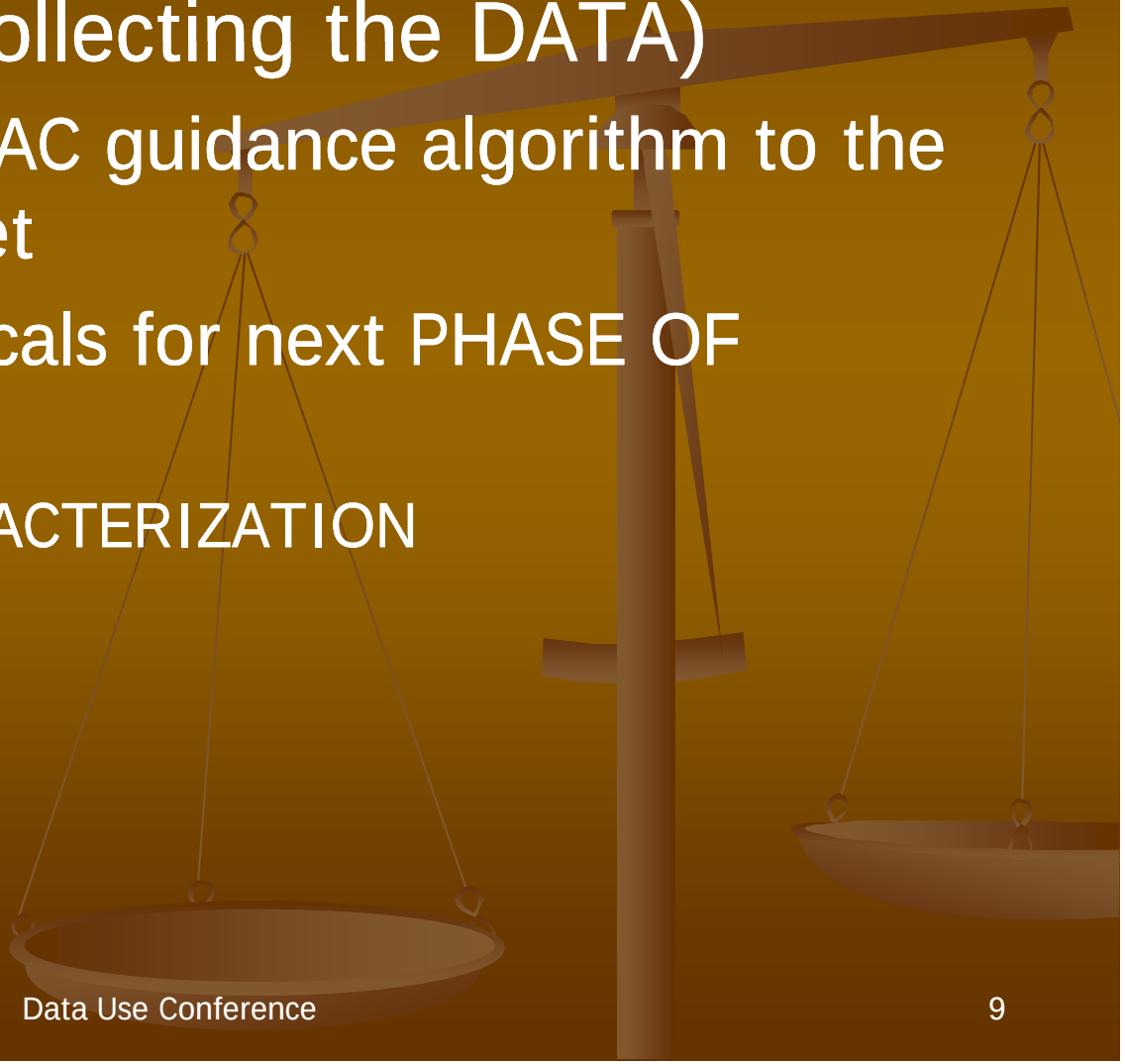
The evolution of a web based information system to receive, index, and facilitate access – HPVIS

- A browser based set of PDF'S and guidance
- A modern database tool with sorting capabilities

EPA Use of HPVIS

STEP one (after collecting the DATA)

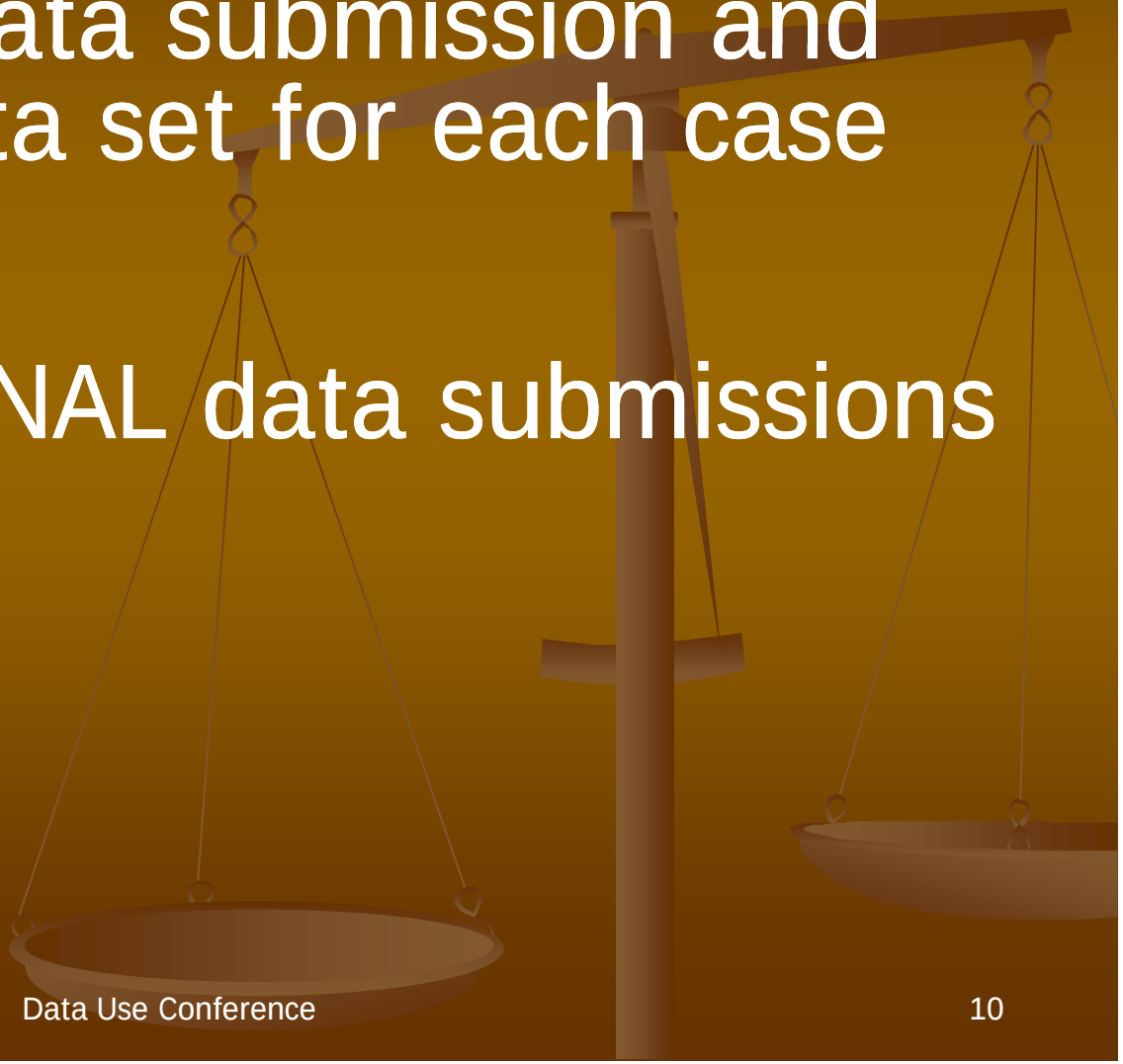
- Apply the NPPTAC guidance algorithm to the available dataset
- Prioritize chemicals for next PHASE OF PROGRAM
  - HAZARD CHARACTERIZATION



Challenges to NEXT STEP

Lack of final data submission and complete data set for each case

=> Need FINAL data submissions



Challenges to NEXT STEP

- Complex chemical categories
  - Mixtures
  - Process streams
  - Both combined

  - READ ACROSS

Mixtures

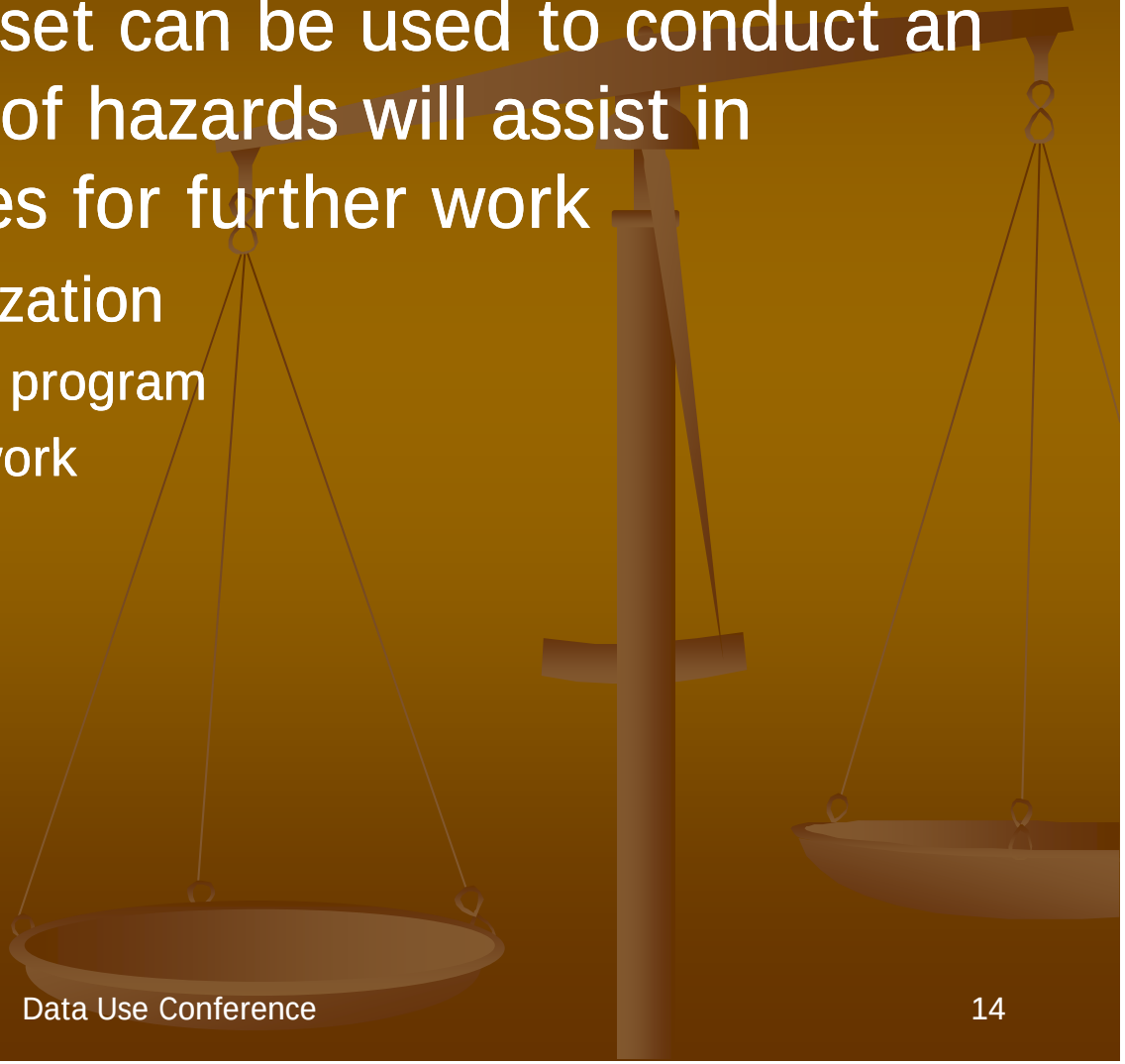
- Lack of adequate substance characterization can make studies hard to evaluate; must characterize in adequate detail
- Can be helpful to reviewer to understand how mixtures are manufactured
- Category members may have single or multiple CAS numbers (process streams)
- Identity may be variable or relatively constant
- Constituents of related mixtures often overlap

Challenge Submissions: Some Numbers

- As of 12/1/06:
- 404 Original (cases) submissions on the website as PDF file sets*
  - 280 individual substances
  - 124 categories
  - Substances in categories represent the majority (75-80%) of the submissions

The FINAL Submission

- A completed data set can be used to conduct an initial assessment of hazards will assist in identifying priorities for further work
  - Hazard characterization
    - Data adequate for program
    - Need for further work



LACK of FINAL SUBMISSION

- The Tier 1 Screening Process can not be finalized
  - Screening effort intended to be inclusive of the HPV Challenge listed chemicals
  - Interim screens must be updated as with new submissions

➔ NEED ALL FINAL DATA SUBMISSIONS

PROGRESS

- Submitted data is publicly available, easily accessed, and searchable via HPVIS
- PRIORITIZATION FOR FURTHER WORK IS BEGINNING IN EARNEST
  - Of approximately 800 chemicals in the system Oct 2006, 537 were sort able
  - Final submissions sort – NOT Test Plans

Guidance Documents and Recognition

- U.S. HPV Category Guidance Document is essentially the same as OECD SIDS Manual Category document
- New OECD Category guidance is in preparation and EPA is actively participating
- SIDS Program reviews involve a considerable collaborative international effort
  - 58 US cases and 94 non-US cases in the last year

HPV Data Process Flow and Screen

- Tier I Screening Criteria
  - Use Subset of SIDS data
  - Automated Process (has been tested and is being used “in house”)
- Tier I Criteria based on OECD’s Globally Harmonized System (GHS) for Classification and Labeling of Hazardous Substances

EPA Tier I Screening Process

Tier I Screening Criteria Application

- Prioritization sorts HPV chemicals into THREE GROUPs based on Sponsor's data submitted for human health and environmental effects (ecotoxicity)
  - Environmental fate data are used to further modify group assignments
- Grouping denotes priority for Tier II review; i.e., Group 1 chemicals have highest priority

HPV Data Process Flow and Screen

Health Effects

Primary Endpoint → Repeat Dose Toxicity

ROUTE OF EXPOSURE	UNITS	First Group	Second Group
Oral (rat)	mg / kg body weight/ day	≤10	10-100
Dermal(rat or rabbit)	mg / kg body weight/ day	≤ 20	20-200
Inhalation (rat) gas	ppm / 6h / day	≤ 50	50-250
Inhalation (rat) vapour	mg / litre / 6h /day	≤ 0.2	0.2-1.0
Inhalation (rat) dust/mist/fume	mg / litre / 6h / day	≤ 0.02	0.02-0.2

Hazard Group Assignment Flow Chart

Adequate Repeated Dose Toxicity or Systemic (Parental) Toxicity LOAEL values available

Yes

No

Initial Health Assignment 1 2 3

Group according to the table on previous slide

Yes

Yes

Positive Chromosomal Aberration, Gene Mutation, Reproductive or Developmental Toxicity Studies

Valid Reproductive or Developmental Toxicity Studies with Cat 1 LOAEL

No

No

Valid studies present for the four endpoints stated above

Yes

Yes

Positive Chromosomal Aberration, Gene Mutation, Reproductive or Developmental Toxicity Studies

No

Valid studies present for the four endpoints stated above

No

Yes

Final Health Assignment 1 2 3 I/D N/D

GHS Criteria for Aquatic Effects Assignment	Group 1	Group 2	Group 3	(N/D)
	< 1 mg/L	1 – 10 mg/L	>10 mg/L	No Data
	Values refer to 96-h Fish, 48-h Daphnia,& 72-h algae studies			

I/D – Insufficient Data. Although study data exist, there are insufficient values to determine a final Group. Retain the initial classification and add a footnote that the classification may increase after additional details/studies are supplied.

Compare the final health classification Group and ecological toxicity Group. If they differ, use the more severe classification for the next step of the flow chart.

1 2 3 N/D

Yes

Log Kow ≥ 4 and/or 28-day Biodeg < 70%

Log Kow ≥ 4

No Yes

No

Yes

28-day Biodeg < 70%

No

No

28-day Biodeg < 70%

* * Yes*

Final Assignment according to NPPTAC Criteria 1 2 3 N/D

*** Note:** If an item with a Group 3 Health/Aquatic assignment fails both 28-day Biodegredation and Log Kow Criteria, it is designated 'Group 1 or 2.'

N/D – No Data. There are no data for the endpoint that are sufficient to assign the chemical to a Hazard Group.