

# High Production Volume Challenge Program → Data Use

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# Overview

- HPV Submissions
- HPVIS
- NPPTAC Guidance
- Tier I and Tier II Review
- Tier II == Implementation and Production
  - Hazard Characterization Documents
  - Risk Characterizations (next phase)

# Tier I - Screening Criteria

Based upon: Data Summaries

Human Health Effects

Environmental Effects (Ecotoxicity)

Log Kow (>4) and Biodegradation

The final group assignment is the highest ranking achieved for any or all endpoints selected by NPPTAC guidance

1 is higher than 3

# Tier I Criteria → Human Health

- Primary endpoint is Repeated-Dose Toxicity
- Modifying endpoints include:
  - Genetic toxicity (gene mutation and chromosomal aberrations)
  - Reproductive toxicity
  - Developmental toxicity

# Tier I Screening Process

## Health Effects

### Primary Endpoint → Repeated-Dose Toxicity

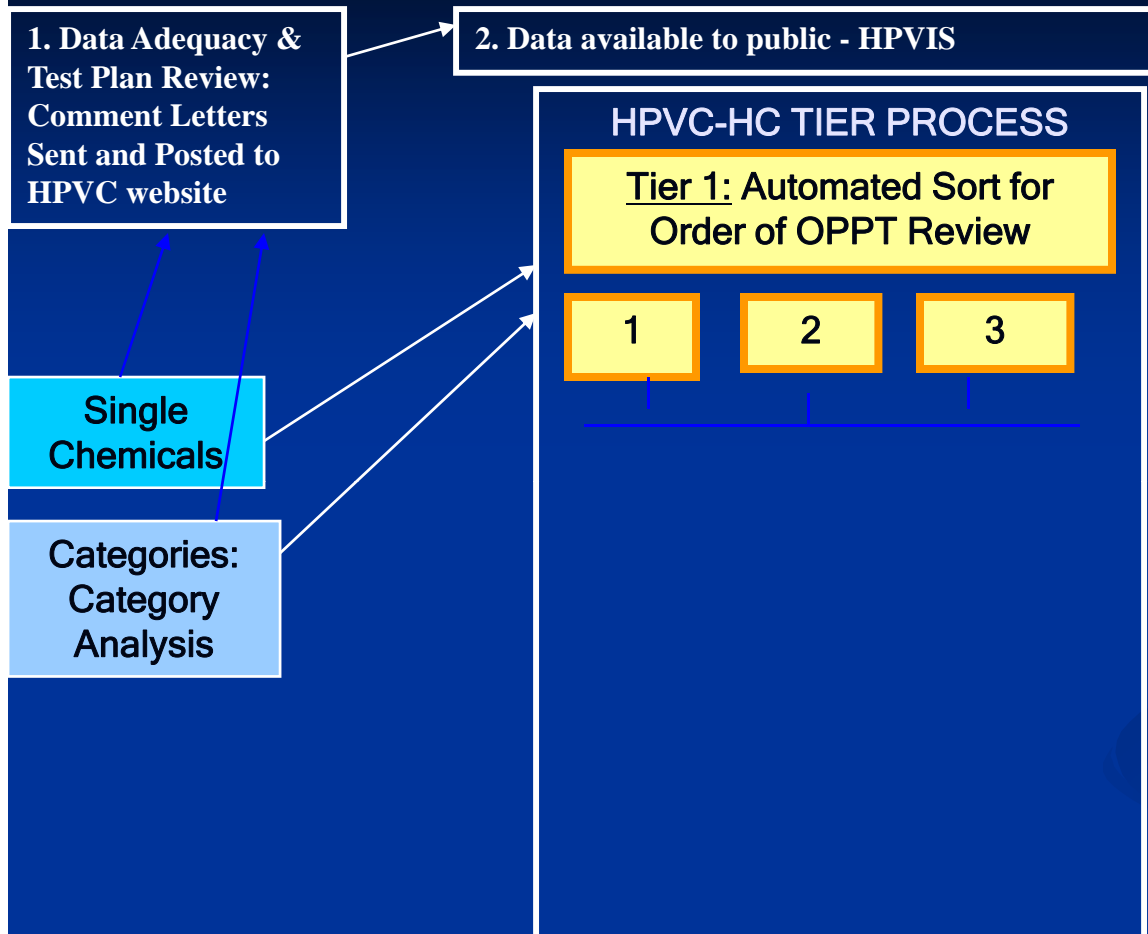
ROUTE OF EXPOSURE	UNITS	Group 1	Group 2
Oral (rat)	mg / kg body weight/ day	≤10	10-100
Dermal (rat or rabbit)	mg / kg body weight/ day	≤ 20	20-200
Inhalation (rat) gas	ppm / 6h / day	≤ 50	50-250
Inhalation (rat) vapour	mg / litre / 6h /day	≤ 0.2	0.2-1.0
Inhalation (rat) dust/mist/fume	mg / litre / 6h / day	≤ 0.02	0.02-0.2

Group 1 and 2 are the lowest effects levels (LOAEL) obtained in 90-day repeated-dose toxicity studies (criteria values triple for 28-day studies)

Chemicals that exceed the Group 2 criteria are placed into Group 3.

# HPV Chemical Screening Process and Key Outputs

## The Vision



# Tier I → Tier II

- Based on a recommendation from the National Pollution Prevention and Toxic Advisory Committee – NPPTAC
- Tier I - prioritization by applying screening criteria to a subset of SIDS data—largely based on criteria from OECD's Globally Harmonized System (GHS) for Classification and Labeling of Hazardous Substances; it is an automated Process
  - Data in HPVIS not reviewed at this point
  - Not part of a classification and labeling effort
- Tier I - **roughly** sorts HPV chemicals into Three Groups based on submitted data for human health and environmental effects (ecotoxicity)
  - Environmental fate data are used to further modify group assignments
    - **Persistence or Bioaccumulation**

# Current Status – HPVIS & SUBMISSIONS

- As of September 2007:
  - Majority of Sponsored Chemicals have completed the Test Plan Review Phase of the program
  - Small percentage of chemicals in Test Plan stage
    - Complex cases and recent submissions
    - Chemicals with testing in progress
  - Many Submissions are now FINAL and available for review by Public and EPA
    - More than 800 chemicals are loaded into HPVIS
      - Many as category members



National Pollution Prevention and Toxics Advisory Committee (NPPTAC)  
Recommendation to the U.S. Environmental Protection Agency on the  
High Production Volume Challenge Program:  
HPV Chemical Screening Process

February 10, 2005

**Manual Review and Characterization:** In Tier II OPPT would conduct a more in-depth review of the data in the Challenge Program submissions for quality and completeness; develop a screening level hazard assessment based on SIDS and non-SIDS hazard data provided by the sponsors; and inform the sponsors and the public of its findings. Tier II review could potentially include additional or updated hazard information of which EPA and/or sponsors or other parties have become aware. Any use and exposure information in the submission should be described to assist in any further information gathering, assessment, or management activities that OPPT deems appropriate. **However, Tier II is not an evaluation of the exposure potential or risks of a chemical.** Finally, the hazard assessment should note situations where the Tier II review has revealed that a chemical is potentially persistent or potentially bioaccumulative.

# “Test Run” of the Algorithm → 508 sorted

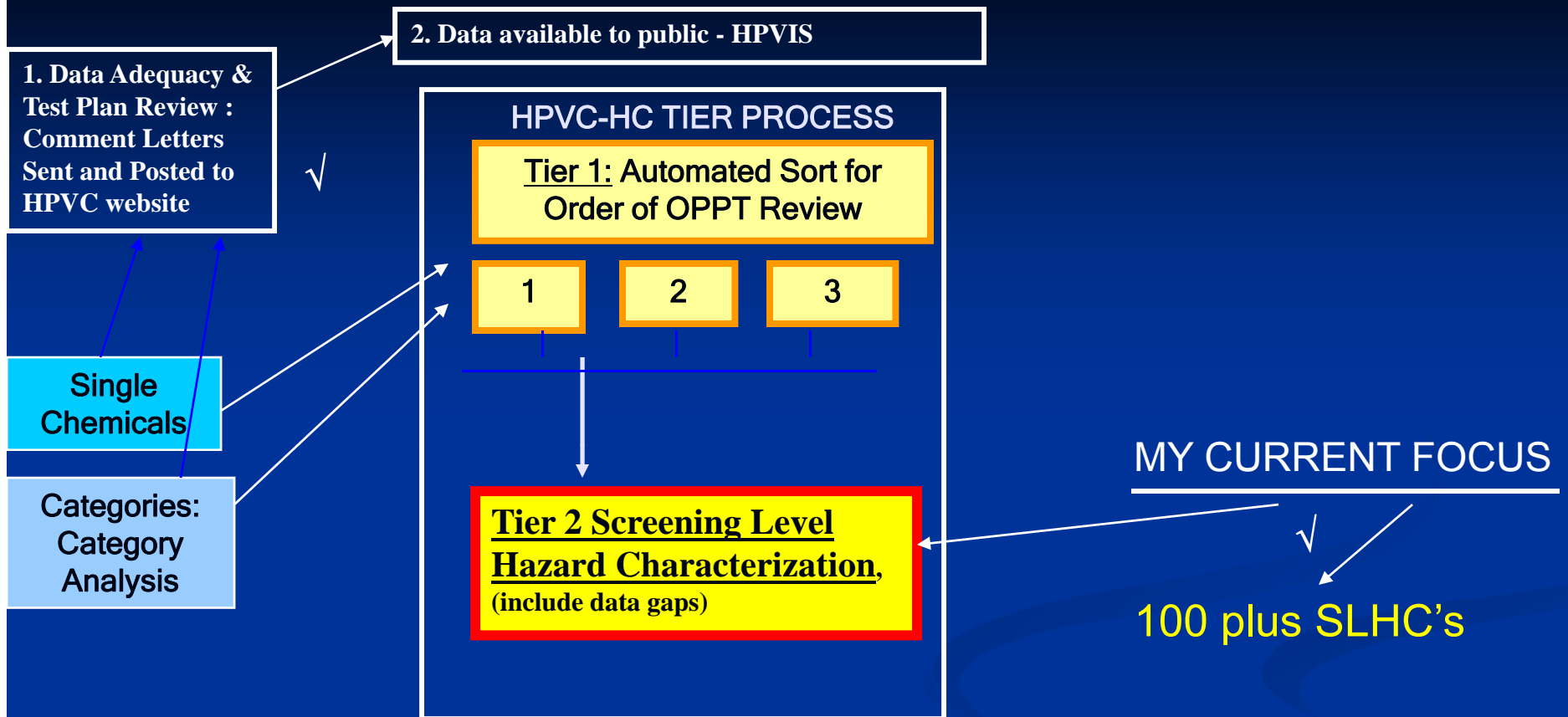
- Group 1
  - 240 chemicals identified
    - 88 single chemicals
    - 152 category chemicals selected 82 categories
- Group 2
  - 123 chemicals
    - 52 singles
- Group 3
  - 145 chemicals
    - 58 singles

# Grouping Example

101-96-2891,4-Benzenediamine, N,N'-bis(1-methylpropyl) → 111N1

- 1 = Initial Repeat Dose Toxicity Group
- 1 = Final Health Effect Group
- 1 = Ecotoxicity Group
- N = Environmental Fate Modification
- 1 = Final Value or Prioritization Group

# HPV Chemical Screening Process and Key Outputs



# http://iaspub.epa.gov/oppphpv/hpv\_hc\_characterization.get\_report

High Production Volume Information System (HPVIS) | OPPT | US EPA - Netscape Navigator

U.S. Environmental Protection Agency

## High Production Volume Information System (HPVIS)

Contact Us Search:  All EPA  This Area

You are here: [EPA Home](#) » [Prevention, Pesticides & Toxic Substances](#) » [Pollution Prevention & Toxics](#) » [High Production Volume Information System](#) » HPV Chemical Hazard Characterizations

### HPV Chemical Hazard Characterizations

These "characterizations" are evaluations conducted by EPA of the hazard (toxicity) data submitted on selected chemicals through the [High Production Volume Challenge](#). [Read more about how EPA selected these chemicals and conducts the review.](#) To search for hazard characterizations by CAS Number, use the search box on the [HPVIS home page](#).

*\*Sort columns by clicking on the arrows beneath the column title*

You will need Adobe Acrobat Reader to view some of the files on this page. See [EPA's page](#) to learn more about PDF, and for the link to the free Acrobat Reader.

Submission Name	Posted Date	View HPVIS Data
<ul style="list-style-type: none"> <li><a href="#">1,3-Dioxolane (PDF)</a> (10 pp, 81 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">1,4-Cyclohexanedimethanol (PDF)</a> (10 pp, 120 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">2,3-Dihydro-2,2-dimethyl-7-benzofuranol (PDF)</a> (10 pp, 83 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">2,4,7,9-Tetramethyl-5-decylne-4,7-diol (PDF)</a> (10 pp, 128 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">2,4,8,10-Tetraoxa-3,9-diphosphaspiro[5.5]undecane, 3,9-diphenoxy- (PDF)</a> (7 pp, 59 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">2-Propanol, 2-methyl- (PDF)</a> (13 pp, 103 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">2-Propen-1-ol (PDF)</a> (11 pp, 130 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">Acetyl chloride, dichloro- (PDF)</a> (14 pp, 115 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">Alkaryl Sulfonate Category (PDF)</a> (26 pp, 254 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">Alkylphenols Category (PDF)</a> (37 pp, 351 KB) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">Aluminum Alkyls Category (PDF)</a> (10 pp, 76 kb) <a href="#">List Chemical(s)</a></li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>
<ul style="list-style-type: none"> <li><a href="#">Butanoic acid, 3-oxo-, methyl ester (PDF)</a> (9 pp, 125 KB)</li> </ul>	SEPTEMBER 2007	<a href="#">View Chemical Data</a>

# Hazard Characterization

- Goals for 2007
  - Initial “Focus” on Group 1 chemicals:
    - Single Chemicals and Categories
  - Share sample reviews ✓
  - Gather feedback ✓
  - Improve program ✓
  - Increase rate of review & production ✓
  - Post products to the web ✓

# THE PROCESS PLAN

2006

- Develop format and distribute draft model documents for review and feedback
  - Kick off in late 2006
    - Preliminary model Hazard Characterizations for two chemicals distributed at Data Use Conference (Austin, Texas: Dec 2006)
      - Available through the NEWMOA site

# THE PROCESS PLAN

## 2007

- Dissemination
  - Comments and Feedback posted -- Submitter/Sponsor comments
    - Public/NGO comments
    - Comments addressed
  - Web site links to Test Plans, comments on test plans from all sources, and FINAL submissions (HPVIS is primary resource for searching)
  - Begin posting reviewed submissions
    - Hazard Characterizations to the HPV web pages
- [http://iaspub.epa.gov/oppthpv/hpv\\_hc\\_characterization.get\\_report](http://iaspub.epa.gov/oppthpv/hpv_hc_characterization.get_report)



# Development of Tier II Screening-level Hazard Characterizations

## Key Outputs

- Determine quality and completeness of submitted data
- Assess significance of hazard and environmental fate data
- Make information and initial scientific assessment publicly available:
  - Technical review primarily based on submitted data
- Tier II assessment is roughly comparable to level of analysis conducted under the Organization for Economic Cooperation and Development's HPV Program and as such informs need for and the nature of next steps

# SCREENING LEVEL HAZARD CHARACTERIZATION:

- **Background**
- **History of the chemical in the program**
- **Summary Conclusion for the Case**
- **Summary of Critical Studies**
  - **Health Effects**
  - **Environmental Effects**
- **Overall Conclusion**
  - **Data Gaps, Next steps – If needed**
- **Summary Data Table**

# For Example:

## Introduction

The sponsor, The Dioxolane Manufacturers Consortium, submitted a Test Plan and Robust Summaries to EPA for 1,3-dioxolane (CAS No. 646-06-0; 9th CI name: 1,3-dioxolane) on November 20, 2000. EPA posted the submission on the ChemRTK HPV Challenge Website on December 19, 2000 (<http://www.epa.gov/chemrtk/pubs/summaries/dioxlne/dioxtc.htm>). EPA comments on the original submission were posted on April 18, 2001.

Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on June 12, 2001, which were posted to the ChemRTK HPV Challenge website on April 3, 2002.

# For Example:

## Summary - Conclusion

- The log K<sub>ow</sub> indicates that the potential of 1,3-dioxolane to bioaccumulate is expected to be low. 1,3-Dioxolane is not readily biodegradable, indicating that it has the potential to persist in the environment.
- The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of 1,3-dioxolane to aquatic organisms are low.

# For Example:

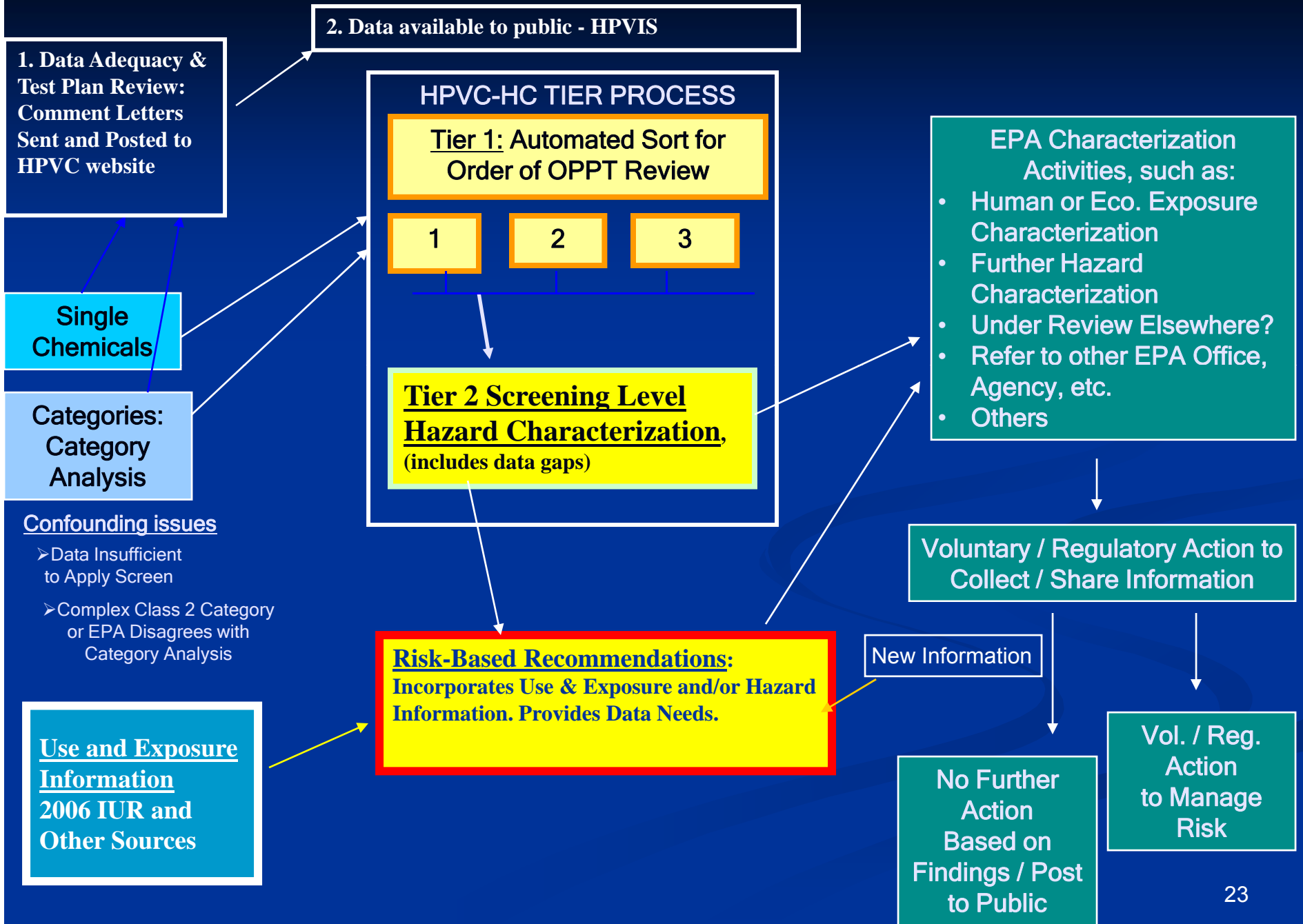
## Summary – Conclusion (continued)

- The potential health hazard of 1,3-dioxolane is high based on repeated-dose, reproductive and developmental toxicity.
- No data gaps were identified under the HPV Challenge Program.

# Summary Table of the Screening Information Data Set as submitted under the U.S. HPV Challenge Program

- **Endpoints SPONSORED CHEMICAL 1,3-Dioxolane (646-06-0)**
  - **Repeated-Dose Toxicity**
    - **NOAEL/LOAEL (mg/kg-bw/day)**
      - LOAEL (male) = 0.9
      - LOAEL (inhalation; female) = 3.03
  - **Reproductive Toxicity**
    - **NOAEL/LOAEL (mg/kg-bw/day)**
      - LOAEL ~ 500 (0.5%)
      - NOAEL = Not established
  - **Developmental Toxicity**
    - **NOAEL/LOAEL (mg/kg-bw/day)**
      - (maternal toxicity)
      - (developmental toxicity)
      - NOAEL = 250

# HPV Chemical Screening Process and Key Outputs



## Development of Tier II Screening-Level Hazard Characterization

- **Conduct a Screening-Level scientific/critical review of the data (quality and completeness) with main focus on potential hazard**
- **Develop a Screening-Level Hazard Characterization**
  - **Does not make determination about risk to human health or environment but may make recommendations for further post-Tier II work**
- **Inform sponsors and public by posting these Screening Level Hazard Characterizations on the HPV Challenge website**



## Post-Tier II Activities

- **Where the Tier II evaluation raises specific questions or identifies further information needs, there exists a range of potential follow-up actions:**
  - **Information gathering**
    - consider exposure information obtained under Inventory Update Rule which may yield preliminary risk characterization which can inform:
      - need for higher level test data
      - need for more detailed exposure information

## Post-Tier II Activities (Cont.)

- **Identify need for consideration of early risk reduction steps**
- **Indicate need for more detailed risk assessment**
- **Provide information/recommendations for referral to other EPA program offices or Federal agencies**

# In Summary: NEXT STEPS

- Consider comments on Posted Screening Level Hazard Characterizations
- Develop Screening Level Hazard Characterizations for all HPV Challenge Chemicals/Chemical Categories
- Base need for further work activities on Screening Level Risk Characterizations

# High Production Volume Challenge Program → Data Use

Please send your comments to:  
**[townsend.mark@epa.gov](mailto:townsend.mark@epa.gov)**



# Questions?

- Save postage – ask me now



# THE CHALLENGE

- Goal is to characterize hazard potential of ALL HPV chemicals by the end of December 2009
  - EPA to complete processing of all TEST PLANS
  - SPONSORS must submit FINAL documentation
  - Chemicals loaded in HPVIS