ENVIRONMENTAL PROTECTION AGENCY

[OPPTS–42213; AR–201; FRL–6754–6]

Data Collection and Development on High Production Volume (HPV) Chemicals

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: Although HPV chemicals are produced or imported in large quantities in the United States, there is little or no publicly available information regarding the potential hazards associated with most HPV chemicals. In order to obtain such information, EPA has established a data collection and development program for existing HPV chemicals. Through the HPV Initiative, which includes the voluntary HPV Challenge Program, certain international efforts, and potential rulemaking under the Toxic Substances Control Act (TSCA), basic screening level hazard data necessary to provide critical information about the environmental fate and potential hazards associated with HPV chemicals will be collected or, where necessary, developed. A primary component of this HPV Initiative is the voluntary HPV Challenge Program, which was created in cooperation with industry, environmental groups, and other interested parties, and is designed to assemble basic screening level test data on the potential hazards of HPV chemicals while avoiding unnecessary or duplicative testing. Data needs which remain unmet in the voluntary HPV Challenge Program, may be addressed through the international efforts or rulemaking. Data collected and/or developed under the HPV Initiative will provide critical basic information about the environmental fate and potential hazards associated with these chemicals which, when combined with information about exposure and uses, will allow the Agency and others to evaluate and prioritize potential health and environmental effects and take appropriate follow up action. EPA has taken steps, as described in this document, to consider animal welfare and to provide instructions on ways to reduce or in some cases eliminate animal testing, while at the same time ensuring that the public health is protected.

FOR FURTHER INFORMATION CONTACT: *For general information contact:* Barbara Cunningham, Acting Director, Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: (202) 554–1404; e-mail address: TSCAHotline@epa.gov.

For technical information contact: Barbara Leczynski, Existing Chemicals Branch, Chemical Control Division (7405), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: (202) 260–3945; fax number: (202) 260–1096; e-mail address: chem.rtk@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Document Apply to Me?

This document applies to the public in general and, in particular, those companies that manufacture (defined by statute to include import) industrial chemicals for which the aggregate U.S. production/importation volumes meet or exceed 1 million pounds per year. Those chemicals that meet these criteria are referred to as HPV chemicals. The HPV chemicals that are included in the voluntary HPV Challenge Program are listed in *ChemRTK HPV Challenge Program Chemical List* (Ref. 1). If you have any questions regarding the applicability of this action to a particular entity, consult the technical person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Get Additional Information, Including Copies of this Document and Support Documents?

1. *Electronically*. You may obtain copies of this document, and certain other related documents that might be available electronically, from the EPA Internet Home Page at http://www.epa.gov/. To access this document, on the Home Page select ''Laws and Regulations,'' ''Regulations and Proposed Rules,'' then look up the entry for this document under the ''**Federal Register**—Environmental Documents.'' You can also go directly to the **Federal Register** listings at http://www.epa.gov/fedrgstr/. To access the OPPTS Harmonized Guidelines referenced in this document, go directly to the guidelines at http://www.epa.gov/opptsfrs/home/guidelin.htm.

You may also access additional information about the Chemical Right-to-Know Program at http://www.epa.gov/chemrtk/ or about the TSCA testing program at http://www.epa.gov/opptintr/chemtest/sct4main.htm.

For your convenience, EPA has also provided some non-EPA internet addresses. In doing so, the Agency has verified the accuracy of these addresses at the time of signature. However, since EPA is not responsible for these non-EPA sites, the Agency does not exercise any control over these addresses. A paper copy of any document referenced in this way has been included in the public version of the official record for this document as described in Unit I.B.2.

2. *In person*. The official record for this document, which includes the public version, has been established under docket control number OPPTS–42213 and administrative record number AR–201. This official record consists of the documents referenced in this document, as well as any comments received, and other information related to this document, including information claimed as Confidential Business Information (CBI). This official record includes the documents that are physically located in the docket, as well as all documents that are referenced in those documents. The public version of the official record does not include any information claimed as CBI. The public version of the official record, which includes printed, paper versions of any electronic comments that may be submitted, is available for inspection in the TSCA Nonconfidential Information Center, Northeast Mall, Rm. NE B–607, Waterside Mall, 401 M St., SW., Washington, DC. The Center is open to the public from noon to 4 p.m., Monday through Friday, excluding legal holidays. The telephone number of the Center is (202) 260–7099.

C. Can I Submit Comments Under the Voluntary HPV Challenge Program?

Yes. Although this document does not establish a specific comment period, you may submit comments at various times throughout the voluntary HPV Challenge Program. This document describes the various opportunities that are available for you to submit comments under the voluntary HPV Challenge Program. In addition, specific information about the voluntary HPV Challenge Program and the opportunities for you to submit comments is provided on the Agency's web site identified in Unit I.B.1.

In general, you may submit comments under the voluntary HPV Challenge Program via the following methods: The mail, in person, or electronically. To ensure proper receipt by EPA, please identify the docket control number OPPTS–42213 and the administrative record number AR–201 in the subject line on the first page of your response. In addition, Challenge Program sponsors should reference the unique seven-digit registration number they were assigned

when the Agency verified the information presented in their original commitment letters. Sponsors who need to confirm their registration numbers should call (202) 260–6199.

1. *By mail*. Submit your comments to: Carol Browner, Administrator, Environmental Protection Agency, P.O. Box 1473, Merrifield, VA 22116, Attention: Chemical Right-to-Know Program.

2. *In person or by courier*. Deliver your comments to: OPPT Document Control Office (DCO) in East Tower Rm. G–099, Waterside Mall, 401 M St., SW., Washington, DC. The DCO is open from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The telephone number for the DCO is (202) 260–7093.

3. *Electronically*. Submit your comments electronically by e-mail to oppt.ncic@epa.gov, hpv.crtk@epa.gov, and chem.rtk@epa.gov (please be sure to send your e-mail to all three addresses). (Note: To submit comments on a test plan, please go to http://www.epa.gov/chemrtk/viewsrch.htm.) Do not submit any information electronically that you consider to be CBI. Electronic comments must be submitted as an ASCII file avoiding the use of special characters and any form of encryption. Comments will also be accepted on standard computer disks in WordPerfect 6.1/8 or ASCII file format, mailed or delivered to the address identified in Unit I.C. All comments in electronic form must be identified by docket control number OPPTS–42213 and administrative record number AR–201. Electronic comments may also be filed online at many Federal Depository Libraries.

D. How Should I Handle CBI Comments that I Want to Submit to the Agency?

Considering that one of the goals of the HPV Initiative is to provide information needed to meet the public's right-to-know about the hazards that may be posed by exposure to HPV chemicals, EPA encourages companies and other interested parties not to make CBI claims in submitted comments. If you do choose to submit CBI in your comments, adhere to the following procedures. Do not submit any information electronically that you consider to be CBI. You may claim information that you submit to EPA in response to this document as CBI by marking any part or all of that information as CBI. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. In addition to one complete version of the comment that includes any information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public version of the official record. Information not marked confidential will be included in the public version of the official record without prior notice. If you have any questions about CBI or the procedures for claiming CBI, consult the technical person listed under **FOR FURTHER INFORMATION CONTACT**.

II. Background

A. Why is EPA Pursuing Hazard Information on HPV Chemicals?

EPA found that, of those non-polymeric organic substances produced or imported in amounts equal to or greater than 1 million pounds per year based on 1990 reporting for EPA's Inventory Update Rule (IUR) (40 CFR part 710), only 7% have a full set of publicly available internationally recognized basic health and environmental fate/effects screening test data (Ref. 2). Of the over 2,800 HPV chemicals based on 1990 data, 43% have no publicly available basic hazard data. For the remaining chemicals, limited amounts of the data are available. This lack of available hazard data compromises EPA's and others' ability to determine whether these HPV chemicals pose potential risks to human health or the environment, as well as the public's right-to-know about the hazards of chemicals that are found in their environment, their homes, their workplaces, and the products that they buy. It is EPA's intent to close this knowledge gap. EPA believes that for most of the HPV chemicals, insufficient data are readily available to reasonably determine or predict the effects on health or the environment from the manufacture (including importation), distribution in commerce, processing, use, or disposal of the chemicals, or any combination of these activities. EPA has concluded that a program to collect and, where needed, develop basic screening level toxicity data is necessary and appropriate to provide information in order to assess the potential hazards/risks that may be posed by exposure to HPV chemicals.

On April 21, 1998, a national initiative, known as the ''Chemical Right-To-Know'' Program, was announced in order to empower citizens with knowledge about the most widespread chemicals in commerce—chemicals that people may be exposed to in the places where they live, work, study, and play. EPA's Chemical Right-To-Know (ChemRTK) initiative is being designed in such a way as to make certain basic information about HPV chemicals available to the public.

EPA plans to make available to the public the summarized data obtained on HPV chemicals. In addition, any subsequent information that EPA receives will be shared with the public, other Federal agencies, and any other interested parties. As appropriate, this information will be used to ensure a scientifically sound basis for risk assessment/management actions. This initiative will serve to further the Agency's goal of identifying and controlling human and environmental risks as well as providing greater protection and knowledge to the public. In addition, EPA and other parties agreed to work with other nations and international groups to ensure commensurate increases in the pace of complementary voluntary international data collection and development efforts on HPV chemicals.

This ChemRTK initiative is consistent with the U.S. policy as presented in section 2(b)(1) of TSCA, 15 U.S.C. 2601(b)(1), which states that it is the policy of the United States that ''adequate data should be developed with respect to the effect of chemical substances and mixtures on health and the environment and that the development of such data should be the responsibility of those who manufacture and those who process such chemical substances and mixtures.''

B. What do we Currently Know about the Basic Health and Environmental Hazards of HPV Chemicals?

The information relevant to understanding the basic health and environmental hazards of HPV chemicals is derived from a battery of tests agreed upon by the international community as appropriate for screening international HPV chemical substances for toxicity. Six basic testing endpoints have been adopted by the Organization for Economic Cooperation and Development (OECD) as the minimum required to screen international HPV chemical substances for toxicity (Ref. 3). The agreed-upon testing endpoints, known as the OECD's ''Screening Information Data Set'' (SIDS) include: Acute toxicity; repeat dose toxicity; developmental and reproductive toxicity; mutagenicity (gene mutation and chromosomal aberration/damage assays); ecotoxicity (studies in fish, invertebrates, and algae); and environmental fate (including physical/chemical properties [melting point, boiling point, vapor pressure, *n*-octanol/water partition coefficient, and water solubility], photolysis, hydrolysis, transport/distribution, and

biodegradation). As conceived by the OECD, the ''SIDS battery'' of tests can be used by governments to conduct an initial assessment of the hazards and risks posed by HPV chemical substances and prioritize HPV chemicals to identify those in need of additional, more in-depth testing and assessment.

A need for basic screening level data on HPV chemicals has been identified and supported by various data availability studies conducted by EPA and others. *Toxic Ignorance*, which was prepared by Environmental Defense (formerly the Environmental Defense Fund), raised a variety of concerns about the untested chemicals that are produced and/or imported into the United States (Ref. 4). Environmental Defense found that baseline data on health effects were not publicly available for a selected set of 100 HPV chemicals.

In April 1998, EPA completed a study entitled *Chemical Hazard Data Availability Study: What Do We Really Know About the Safety of High Production Volume Chemicals?* (Ref. 2) that evaluated the ''public availability'' of health hazard data and environmental hazard/fate data on HPV chemicals. EPA's study found major gaps in the basic information on HPV chemicals that is readily available to EPA and to the public, and reinforced the need for governmental leadership on this issue. The study analyzed the availability of test data for 2,863 HPV chemicals (defined as those organic substances produced in or imported into the United States in amounts equal to or greater than 1 million pounds per year based on 1990 reporting for EPA's IUR). EPA searched for publicly available data on these chemicals and learned that most of them may never have been tested for any or most of the SIDS endpoints. The search strategy used a total of 11 publicly accessible databases in its analysis. Details of the search strategy can be found in the report (Ref. 2). The major conclusions of EPA's study are described in Unit II.A.

In June 1998, the American Chemistry Council (ACC, formerly the Chemical Manufacturers Association (CMA)) issued a report (Ref. 5) regarding public data availability for HPV chemicals based on a study conducted with 11 main data sources, including data sources other than those searched by EPA for its study. The ACC report, entitled *Public Availability of SIDS-Related Testing Data for U.S. High Production Volume Chemicals* (Ref. 5), reached conclusions similar to EPA, that is, that only limited toxicity and environmental fate testing data appear to exist in the public domain for many HPV substances. Details of the search strategy used can be found in the ACC report (Ref. 5).

EPA recognizes that additional data may exist beyond those identified through either the EPA, ACC, or Environmental Defense studies. To the extent that additional relevant data are known to exist, EPA is particularly interested in receiving this information as part of the HPV Initiative, including, where possible, a full citation for publications and ''robust'' (i.e., detailed) summaries of pertinent published and unpublished studies. Guidance on the preparation of robust summaries is available on EPA's ChemRTK web site (Ref. 6). In developing the testing requirements for chemicals contained in the HPV Initiative, EPA is utilizing information and sources in EPA's study, the *Chemical Hazard Data Availability Study* (Ref. 2), and ACC's report, i.e, *Public Availability of SIDS-Related Testing Data for U.S. High Production Volume Chemicals* (Ref. 5), to determine whether screening level data for characterizing the hazards of these HPV chemicals are publicly available. Under the voluntary HPV Challenge Program, EPA is utilizing the 120 day comment period for test plans to allow for further identification of existing data. If no data are available for a SIDS testing endpoint, there cannot be sufficient data to characterize the potential hazards/risks associated with the chemical. As the Agency found in its study, insufficient data are available to characterize many of the HPV chemicals with respect to the internationally accepted SIDS testing endpoints, including acute toxicity, repeat dose toxicity, developmental and reproductive toxicity, mutagenicity (gene mutation and chromosomal aberration assays), ecotoxicity (tests in fish, Daphnia, and algae), and for environmental fate (including five tests for physical chemical properties [melting point, boiling point, vapor pressure, *n*-octanol/water partition coefficient, and water solubility], and biodegradation). As a result, EPA and others cannot reasonably determine or predict the human health and environmental effects resulting from manufacture, processing, and use of these chemical substances.

EPA solicits comment concerning the availability of SIDS data on the chemicals included in the HPV Initiative and encourages industry and other interested parties to identify and provide any additional existing data which are relevant to the hazard characterization to avoid any unnecessary or duplicative testing. Furthermore, anyone may provide any relevant information to the Agency that indicates that certain endpoints need not be tested. If EPA judges the available data to be adequate, the data gap identified in the HPV Initiative will be considered to be filled. To the extent that additional data relevant to the HPV chemicals are known to exist, EPA is interested in receiving this information under the voluntary HPV Challenge Program, including a full citation for publications and full copies of unpublished studies. Although the Agency encourages anyone with such information to submit it to EPA during the early stages of this initiative in order to avoid any unnecessary testing, such submissions may be made at any time. Commenters are also encouraged to prepare a robust summary (Ref. 6) for each study to facilitate EPA's review of the full-study report or publication. It is important to note that EPA does not intend to include any chemicals which are Generally Recognized as Safe (GRAS) for a particular use by the Food and Drug Administration (FDA) in its initial TSCA section 4 HPV SIDS rulemaking for certain HPV chemicals. However, such chemicals may be included in a future TSCA section 4 HPV SIDS rulemaking where SIDS data needs remain unmet.

C. Why is EPA Focusing on HPV Chemicals?

It is generally accepted that chemicals having a high level of production have an increased potential for exposure in comparison to low production volume chemicals. The HPV focus of the HPV Initiative is derived from the experience gained over the past 15 years by EPA and the OECD. The OECD is an intergovernmental organization consisting of 29 developed countries, including the United States, with advanced worldwide market economies. The OECD is helping coordinate a cooperative, international effort to secure basic toxicity information on HPV chemicals in use worldwide.

The OECD, after considering a variety of priority-setting approaches, concluded in 1990 that consideration of HPV status provided a useful and effective organizing focus for a voluntary testing and assessment effort to screen and thereby identify priorities among international HPV chemicals.

III. HPV Chemical Data Collection and Development Initiative

A. What is the HPV Initiative?

Through the HPV Initiative, which includes the voluntary HPV Challenge Program, certain international efforts, and potential rulemaking under TSCA,

basic screening level hazard data necessary to provide critical information about the environmental fate and potential hazards associated with HPV chemicals will be collected or, where necessary, developed. These data, when combined with information about exposure and uses, will allow the Agency and others to evaluate and prioritize potential health and environmental effects and take appropriate follow up. Created in cooperation with industry, environmental groups, and other interested parties, a primary component of this initiative is the voluntary HPV Challenge Program. To fill any data gaps not addressed as part of the voluntary HPV Challenge Program, EPA is continuing to participate in the international efforts coordinated by the OECD to secure basic hazard information on HPV chemicals in use worldwide, including some of those on the HPV chemicals list. The voluntary HPV Challenge Program and the international efforts will be supplemented by rulemaking under TSCA, which the Agency intends to use to collect or develop data on those HPV chemical substances for which data needs remain unmet in the voluntary HPV Challenge Program, or as part of the international efforts.

Although an important component of the HPV Initiative is the potential for TSCA rulemaking to address any data needs identified that are not met by either the voluntary HPV Challenge Program or international efforts, the focus of this document is the voluntary HPV Challenge Program. The specific requirements for any associated TSCA section 4 HPV SIDS rulemaking will be addressed in that rulemaking.

The voluntary HPV Challenge Program and any associated rulemaking, will generally be carried out in a manner consistent with the OECD HPV SIDS Program to ensure that the data and information generated can be contributed to the international efforts and, conversely, that international SIDS testing and assessments can be used to fulfill the data gaps identified as part of the voluntary HPV Challenge Program or in related TSCA section 4 HPV SIDS rulemaking thus avoiding unnecessary or duplicative testing and its associated costs. The elements of this strategy and the overall approach that EPA is using to address data collection needs for HPV chemicals are discussed in this document, along with the components of the voluntary HPV Challenge Program.

B. Which Industrial Chemicals are Covered in this HPV Initiative?

1. *How were chemicals identified for inclusion in the HPV Initiative?* The industrial chemicals covered by the HPV Initiative are those non-polymeric organic chemicals that are produced in, or imported into, the United States in amounts equal to, or greater than, 1 million pounds per year according to the 1990 IUR. This list of HPV chemicals can be viewed at EPA's ChemRTK web site (Ref. 1).

2. *How will chemicals that are solely produced as closed system intermediates be included in the HPV Initiative?* Chemicals which meet the requirements for ''closed system intermediates'' as described in an available guidance document (Ref. 7 and Unit IV.B.1.) on this topic, will be eligible for a reduced SIDS testing battery. For further information you should check EPA's ChemRTK web site (Ref. 7) to obtain a copy of this document. EPA's guidance is based on section 3.6 of the *Screening Information Data Set (SIDS) Manual* which concerns ''intermediates contained in closed systems.'' The requirements for classification as a closed system intermediate must be met by all U.S. manufacturers (including importers) for a chemical to be eligible for a reduced level of testing. Under the voluntary HPV Challenge Program, EPA asked that participants in that program observe certain principles laid out in an October 14, 1999, letter (Ref. 8). One principle is that participants shall not develop sub-chronic or reproductive toxicity data for the HPV chemicals that are solely closed system intermediates as defined by the OECD/SIDS guidelines, and that testing of closed system intermediates shall be deferred until 2003.

3. *Are HPV Chemicals that are no longer produced or imported included in this HPV Initiative?* EPA previously issued guidance for verifying that a chemical is ''no longer HPV'' (based on national aggregate production/importation volume) and is not likely to become HPV in the future. This guidance document can be found on the Agency's ChemRTK web site (Ref. 9).

For EPA to conclude that a ''no longer HPV'' claim is valid, a chemical cannot be produced by any company or group of companies at a total aggregate production volume of 1 million pounds per year or greater, and the chemical must be shown as not likely to become an HPV chemical in the future, based on business plans, past production patterns, and credible trends in the market. These conditions are intended to satisfy the terms of the voluntary HPV Challenge Program Framework Document, as quoted on the EPA Chemical Right-to-Know web site: ''Substances that sponsors verify are no longer ''HPV'' and are not likely to become HPV again will not require testing and will be removed from the list.''

In accordance with the policy announced in the guidance document (Ref. 9), EPA has set the minimum criteria for identifying chemicals as no longer HPV as a total annual aggregate production volume below 1 million pounds for the last two IUR reporting cycles (i.e., 1994 and 1998).

Written documentation demonstrating that the current aggregate U.S. production/importation volume of a chemical was substantially less than 1 million pounds per year and was likely to remain so was required as described in the guidance document (Ref. 9). This justification had to have been provided for all U.S. producers and importers of the chemical. Once it has been established via specific requests received before the end of the voluntary HPV Challenge Program sign up period that a chemical is ''no longer HPV'' and is not likely to become an HPV chemical again, EPA would remove the chemical from the HPV Initiative.

4. *How will EPA handle HPV chemicals that do not warrant any further SIDS testing?* As of November 9, 2000, EPA has determined that for 44 HPV chemicals, SIDS level testing is not warranted. These chemicals are identified on the Agency's web site at http://www.epa.gov/chemrtk/hpv_1990.htm. EPA's preliminary review of these chemicals indicates that testing using the SIDS base set would not further our understanding of the chemicals' properties. These chemicals are identified on the voluntary HPV Challenge Program Chemical List (Ref. 1) with an indicator value of ''1.'' EPA has invited, and continues to invite, industry and other interested parties to identify additional chemicals that might be appropriate for this designation. This identification process would take the form of a review of the available information which shows that, for a given chemical, conducting the SIDS battery of tests would not be of value in furthering an understanding of the chemical's properties including physical/chemical, environmental fate, environmental toxicity, and mammalian toxicity endpoints. Alternatively, for well-tested chemicals, companies are encouraged to provide the information in a ''no test'' test plan along with robust summaries of the existing data which indicate that no testing is required. In addition, as part of EPA's

efforts under the OECD HPV SIDS Program, the Agency will be working with other OECD member countries to identify chemicals for which adequate data may have been produced in the context of foreign regulatory or testing regimes.

C. What Information is Being Collected on HPV Chemicals?

The OECD member countries reached consensus in 1990 on a set of basic screening-level tests deemed needed for all international HPV chemicals. This OECD understanding was captured in a formal 1991 OECD decision (Ref. 10) with which the United States concurred. This decision resulted in the OECD HPV SIDS Program, which is part of the OECD overall program on existing chemicals. The OECD HPV SIDS review process includes information on the identity of each chemical, its uses, sources and extent of exposure; physical and chemical properties; environmental fate; and certain limited toxicity data for humans and the environment. The SIDS data set is not intended to describe a chemical thoroughly, but rather is intended to provide enough information to support an initial (or screening level) assessment and to assign a priority for further work, if necessary. To date, the OECD has initiated or completed work on over 350 HPV chemicals. The OECD HPV SIDS Program seeks the development of test data, if such data are not already available, related to six health and environmental effects endpoints for international HPV chemicals (see Unit II.B.). The SIDS test guidelines are regarded as the minimum data set required to make an informed preliminary judgment about the hazards of a given HPV chemical.

EPA is implementing the HPV Initiative as part of its domestic industrial chemical screening efforts, in a manner that is consistent with OECD efforts. The information to be gathered under EPA's HPV Initiative comes from the same battery of tests agreed upon by the OECD member countries as being appropriate for screening international HPV chemicals for toxicity and environmental fate (Ref. 3). As conceived by the OECD, the SIDS data set can be used by governments and others worldwide to conduct an initial assessment of the hazards and risks posed by HPV chemical substances and to prioritize chemicals to identify those which are in need of additional, more in-depth testing and assessment, as well as those of lesser concern.

In addition to addressing the six basic screening endpoints, basic exposure information including general and occupational use patterns, and sources and levels of exposure, can be submitted under the HPV Initiative. The basic exposure information could be similar to that gathered as part of the OECD HPV SIDS Program. EPA encourages companies to provide exposure information to help place the hazard information into an appropriate context. Additional guidance may be made available at EPA's ChemRTK web site or through other means. In the interim, the voluntary HPV Challenge Program sponsors are encouraged to consult Annex 5 of the SIDS Manual (Ref. 3) which presents the exposure information recommendations developed by the Use and Exposure Information Project (UEIP) in the United States.

The OECD HPV SIDS Program includes the step of preparing an initial assessment of the SIDS data. Although this step is not formally included as an element in the voluntary HPV Challenge Program commitment, EPA encourages sponsors to prepare an initial assessment using the OECD's procedure for preparing a SIDS Initial Assessment Report (SIAR) that can be subsequently reviewed through the OECD HPV SIDS Program. The International Council of Chemical Associations' (ICCA) (Ref. 11) HPV Initiative, which complements the OECD's HPV SIDS Program, has committed to completing the full SIDS battery and preparing a SIAR.

D. What Role do Existing Data Play Under the HPV Initiative?

The HPV Initiative is designed to make maximum use of scientifically adequate existing test data and to avoid unnecessary, duplicative testing, thereby avoiding the excessive use of animal testing. Opportunities to comment on identified data gaps or submit any available adequate data are being provided during the voluntary HPV Challenge Program, in response to this document, and in response to any future proposed TSCA section 4 HPV SIDS rulemaking. EPA will also post the test plans submitted under the voluntary Program to allow for a 120 day review period before testing begins. It is also EPA's intention for the comment period in the associated TSCA section 4 HPV SIDS rulemaking to run for 120 days to allow for an equivalent review to occur before the rulemaking requirements are finalized. If at any time the Agency receives adequate existing data that fulfill a specific data gap, EPA will ensure that unnecessary testing is not conducted.

During the continued development of the HPV Initiative, EPA was encouraged to consider the relationship between existing data submitted under the HPV Initiative and reporting requirements under TSCA section 8(e). In response to these concerns, and as part of the Agency's efforts to encourage the fullest use of existing test data, EPA intends to consider existing data submissions under the voluntary HPV Challenge Program in the manner described in an October 14, 1999, letter to program participants (herein after ''the October 14, 1999, letter'') (Ref. 8). EPA's voluntary HPV Challenge Program guidance document on literature searches deals with part of this issue (Ref. 18). EPA believes that it is in the economic best interest of companies to identify and make publicly available all relevant existing data in order to reduce possible testing costs. To the extent that data exist which address any SIDS endpoints, the voluntary HPV Challenge Program is designed to ensure that sponsors identify and use such data to fill the related data gap(s) identified. In addition, EPA plans to post an announcement on its ChemRTK web site for incoming test plans. Many of these test plans will also be submitted electronically by sponsors to the ''US HPV Chemical Tracking System'' (Ref. 19).

Studies that have been conducted as specified in appropriate OECD test guidelines (as noted in the SIDS Manual (Ref. 3) or comparable EPA test guidelines (such as the OPPTS Harmonized Guidelines (http://www.epa.gov/opptsfrs/home/guidelin.htm)), and appropriate Good Laboratory Practice Standards (GLPS) (e.g., see the TSCA GLPS at 40 CFR part 792) consistently generate data adequate to fulfill the HPV Initiative needs. Data from studies that did not follow these procedures, however, may not be adequate.

As indicated in the October 14, 1999, letter to the voluntary HPV Challenge Program participants, in analyzing the adequacy of existing data, EPA encouraged participants to conduct a thoughtful and qualitative analysis rather than using a rote checklist approach. If EPA judges the available data to be adequate, the data gap identified in the HPV Initiative will be considered to be filled. In addition, participants in the voluntary HPV Challenge Program may conclude that certain endpoints need not be tested if, given the totality of what is known about a chemical, including human experience, there is sufficient existing data that is consistent with the Agency's guidance on determining the data adequacy. EPA has developed a guidance document on determining data adequacy which is available on EPA's ChemRTK web site (Ref. 12). This

guidance document is useful in assessing whether a study design used in generating existing data is sufficient to meet the needs of the HPV Initiative. For example, summary information, such as that taken from Material Safety Data Sheets (MSDSs), is not considered adequate to meet the needs of the HPV Initiative. Where relevant existing studies are identified, companies should provide information at the level of a ''robust summary'' for each study (Ref. 6).

E. How are Animal Welfare Issues Being Considered in this Initiative?

EPA recognizes the concerns that have been expressed about test procedures that require the use of animals. EPA is making every effort to ensure that as the HPV Initiative is implemented, unnecessary or duplicative testing is avoided and the use of animals is minimized. As a general matter, EPA does not require that tests on animals be conducted if an alternative scientifically validated method is found acceptable and practically available for use. Where testing must be conducted to develop adequate data, the Agency is committed to reducing the number of animals used for testing, to replacing test methods requiring animals with alternative test methods when acceptable alternative methods are available, and to refining existing test methods to optimize animal use when there is no substitute for animal testing. EPA believes that these reduction, replacement, and refinement objectives are all important elements in the overall consideration of alternative testing methods.

The governmental and non-governmental scientific community is working to design, validate, and employ new methods of toxicity testing that are more accurate, less costly, and that reduce the need to use live animals. Over the years, significant research has been pursued to develop and validate non-animal test methods. United States scientists in academia, government, and industry have participated in both domestic and international efforts to develop alternative, non-animal tests. As part of the enterprise, the National Institute for Environmental Health Science (NIEHS) established a Federal interagency committee, the Interagency Coordinating Committee on Validation of Alternative Methods (ICCVAM), to review the status and validation of toxicological test methods including those that are performed *in vitro*. EPA scientists have contributed significantly to this body of knowledge and are continuing to play a vital role by developing test methods for consideration. Many test methods have begun the process of validation and several have completed the steps leading to government-wide regulatory acceptance. Within the SIDS battery of tests, a number of *in vitro* genotoxicity tests, such as the Ames test for gene mutations in bacteria, have received uniform acceptance among regulatory agencies.

In addition, as part of the voluntary HPV Challenge Program, EPA asked participants in that Program to observe certain principles laid out in the October 14, 1999, letter. In its letter, EPA also indicated that it is the intention of the Agency that the HPV Initiative, including the voluntary HPV Challenge Program and any associated TSCA section 4 HPV SIDS rulemaking, proceed in a manner consistent with these principles and concerns. One of the principles in the October 14, 1999, letter to participants in the voluntary HPV Challenge Program, is that participants shall conduct a thoughtful, qualitative analysis of existing data before testing and that all animal testing on individual chemicals (as opposed to testing of categories of chemicals) under the voluntary HPV Challenge Program or under an associated rule(s) be deferred until November 2001 and that testing of chemicals solely manufactured as closed system intermediates be deferred until 2003.

Under the voluntary HPV Challenge Program structure, alternatives to help further reduce animal testing are available. For example, under the OECD HPV SIDS Program, some instances have been identified where, using chemical category approaches, less than a full set of SIDS data for every chemical in the category has been judged sufficient for screening purposes. In addition, the OECD HPV SIDS Program allows some use of structure activity relationships (SAR) analysis for individual chemicals. These strategies have the potential to reduce the time required to complete the program, the number of tests actually conducted, and the number of test animals needed. One of the principles in the October 14, 1999, letter is that participants in the voluntary HPV Challenge Program shall maximize the use of scientifically appropriate categories of related chemicals and SAR. Those who wish to use these alternative approaches should seriously consider handling the chemical voluntarily, by submitting a viable commitment as described in Unit IV.C. A viable commitment involving these alternate approaches can still be submitted during the regulatory phase of the HPV Initiative, but submission in the earlier phases of this initiative will best avoid unnecessary or duplicative testing.

F. How Will Data Collected on HPV Chemicals be Used?

The availability of hazard information on individual chemicals is fundamental to EPA's ability to accomplish its mission of environmental protection—risk assessment based on sound science, risk management, safeguarding children's health, transparency, expanding the public's right-to-know, and promoting the pollution prevention ethic. Activities to ensure the availability of basic hazard information on HPV chemicals are an integral part of meeting these objectives.

The approach to collection of information and conducting testing for identified needs on HPV chemicals is essentially identical in scope and applicability to the OECD HPV SIDS Program that has been internationally agreed upon by the 29 OECD member countries as providing the minimum data set needed to screen HPV chemicals and identify priorities for additional testing or assessment. While the SIDS data set does not fully measure a chemical's toxicity, it does provide a consistent minimum set of information that can be used to assess the relative hazards and risks of chemicals and to judge if additional testing or assessment is necessary or if a chemical may be considered of lesser concern. EPA and others will use the data obtained from this program to support the development of preliminary risk assessments for these HPV chemicals. Data in addition to those provided through the SIDS battery of tests may be needed to provide sufficient understanding to adequately assess the hazards and risks presented by some HPV chemicals. The data obtained on HPV chemicals under the HPV Initiative will be used to develop initial risk assessments that will allow EPA, other Federal agencies, the public, industry, and others to set priorities for further data collection/development and to identify chemicals of lesser concern. EPA has used data from previous data collection/development activities to support a variety of EPA and other Federal agency programs and actions including the development of water quality criteria, Toxics Release Inventory listings, chemical advisories, and reduction of workplace exposures.

G. Are There Other Voluntary Means to Address the Data Needs for HPV Chemicals?

Yes. These approaches include agreements to sponsor a HPV chemical under either the OECD HPV SIDS

Program, including sponsorship by OECD member countries beyond the United States, or the international HPV Initiative that is being organized by the ICCA. The OECD HPV SIDS Program has already been described in Unit II.B. The ICCA consists of representatives of chemical industry trade associations from the Argentina, Australia, Brazil, Canada, Europe, Japan, Mexico, New Zealand, and United States. The ICCA HPV Initiative calls for the testing and screening-level assessment of 1,000 ''high priority'' chemicals by the end of the year 2004. Most of the chemicals on the ICCA working list (Ref. 11) are also HPV chemicals. The ICCA testing/assessment work will be tied directly to that under the OECD HPV SIDS Program.

Sponsorship under either the OECD HPV SIDS Program or the ICCA HPV Initiative also includes the step of preparing the SIAR that provides a screening level assessment of chemical hazards and includes the reporting of limited exposure information on each HPV chemical. While the submission of exposure information and the preparation of the SIAR are not required elements under the voluntary HPV Challenge Program, EPA encourages industry sponsors to include these elements in their submissions under the voluntary HPV Challenge Program.

Any HPV chemicals that are handled under the OECD HPV SIDS Program or the ICCA HPV Initiative are considered by EPA to be ''sponsored'' and are not intended to be addressed in either the voluntary HPV Challenge Program or in any associated TSCA section 4 HPV SIDS rulemaking unless the international commitments are not met.

IV. Voluntary HPV Challenge Program

A. What is the Voluntary HPV Challenge Program?

As a part of the Chemical Right-to-Know initiative that was announced in April, 1998, EPA, in partnership with industry and environmental groups, announced a voluntary chemical data collection effort called the HPV Challenge Program. This program challenges industry to make publicly available a complete set of baseline health and environmental effects data (i.e., the SIDS data set) on HPV chemicals. Under the voluntary HPV Challenge Program, data are to be collected for each chemical on EPA's list of 1990 U.S. HPV chemicals. For the voluntary HPV Challenge Program, production volumes were derived from reporting under the 1990 IUR (Ref. 2). Testing will be necessary only when data do not exist or when existing data are not adequate.

The voluntary HPV Challenge Program will generally be carried out in a manner consistent with the OECD HPV SIDS Program to ensure that the data and information generated can be contributed to the international effort and, conversely, that international SIDS testing and assessments can be used to fulfill the data gaps identified as part of the HPV Initiative. (See also Refs. 1 and 3). Robust summaries of all of the data collected through the voluntary HPV Challenge Program will be made available by EPA to the public via the Internet in a timely manner, fulfilling the Agency's commitment to the public's right-to-know about chemical hazard information. The collected data will also be used to support efforts by EPA and others to evaluate and prioritize potential HPV chemical risks.

On October 9, 1998, the voluntary HPV Challenge Program was announced as a major new effort to close a gap in the public's right-to-know about possible risks related to HPV chemicals, prompting companies to make more informed and sensible decisions about chemical use. In this announcement, EPA was joined by the American Petroleum Institute (API), ACC, and Environmental Defense. The following three elements comprise the voluntary HPV Challenge Program:

1. *Fixed timetable and fixed list of chemicals*. Information gathering for the chemicals in the voluntary HPV Challenge Program will begin in 2000, with voluntary participants indicating commitments to provide the needed data for specific HPV chemicals. After relevant existing data have been identified, and EPA has judged their adequacy, participants will analyze the status of existing data fulfilling the SIDS data set and prepare a test plan which identifies needed testing based on this analysis. The test plans that are submitted by the voluntary participants will be posted for 120 days before any testing is initiated, providing an opportunity for interested parties to review and provide comments on the test plans, including technical comments regarding alterations to the proposed test plans. EPA will also review the test plans during the 120 day period, and will judge the adequacy of any existing data submitted with the test plan. In addition, as indicated in the October 14, 1999, letter, because validated non-animal tests for some SIDS endpoints may be available soon, participants in the voluntary HPV Challenge Program shall make the following revisions to the sequence of testing:

i. Testing of closed system intermediates (as described in Unit III.B.2.), which present less risk of exposure, shall be deferred until 2003; and

ii. Individual chemicals (i.e., those HPV chemicals not proposed for testing in a category) that require further testing on animals shall be deferred until November 2001.

The Agency also stated in the October 14, 1999, letter that these revisions should not be construed to suggest that delay or deferral is appropriate with respect to testing of scientifically appropriate categories of related chemicals.

If adequate existing data are submitted to EPA during the 120 day test plan review period under the voluntary HPV Challenge Program, or at any other time before testing has begun, such that EPA can determine that certain endpoints need not be tested, EPA will consider the specific data gap to be filled. As indicated previously, the Agency strongly encourages participants and any other interested parties to maximize the use of existing and scientifically adequate data by submitting such data in the early stages of the voluntary HPV Challenge Program so that the Program does not lead to the unnecessary use of animals in tests, and in order to minimize testing costs.

2. *Continuous public access to program status and results*. The public will be able to follow the status and progress of the chemicals in the voluntary HPV Challenge Program over time. This will be done by making information publicly available on the Internet. EPA and other parties have committed to help the public stay informed about progress in the voluntary HPV Challenge Program, with an emphasis on the status of data collection and testing efforts. EPA will have responsibility for making the data available in ways which are useful to diverse stakeholders.

3. *International sharing of testing responsibility*. A significant increase in the pace of information gathering and testing by chemical manufacturers in other countries is needed. To encourage this, EPA and other parties agreed to work with other nations and international groups to assure commensurate increases in the rate of these efforts on HPV chemicals.

B. What are the Goals and Principles for the Voluntary HPV Challenge Program?

1. *HPV Challenge Program goals*. The original goals established for the voluntary HPV Challenge Program are as follows:

i. Ensure full public availability of screening level data on HPV chemicals.

ii. Determine the adequacy of existing published and unpublished data to maximize its use for HPV chemicals in order to avoid repeat testing.

iii. Conduct needed testing to ensure the availability of screening level data on HPV chemicals.

EPA intends to make available to the public all the summarized data obtained on HPV chemicals. In addition, any subsequent information that EPA receives on HPV chemicals would be shared with the public, other Federal agencies, and any other interested parties.

The voluntary HPV Challenge Program is designed to make maximum use of scientifically adequate existing test data and to avoid unnecessary, duplicative testing, thereby avoiding the excessive use of animal testing. EPA encourages industry in general and other interested parties to identify and provide any additional adequate existing data about these HPV chemicals that are relevant to the hazard characterization. If at any time, the Agency receives adequate existing data that fulfill a specific data gap, EPA will ensure that unnecessary testing is not conducted.

The Agency will provide additional opportunities in the voluntary HPV Challenge Program to minimize the participant's burden where there is a need to develop new test data. These opportunities will include:

- Providing guidance for the use of SAR.
- Encouraging the maximum use of category approaches to handle groups of HPV chemicals with similar structures or functionalities.
- Identifying those HPV chemicals that do not need further screening level testing because additional testing will not enhance understanding of the potential health or environmental hazards/risks.
- Allowing reduced data sets for closed system intermediates.
- Allowing parties to identify and substantiate that certain chemicals are ''no longer HPV.''

Guidance documents have been developed for:

- *The Use of Structure Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program* (Ref. 13).
- *Development of Chemical Categories in the HPV Challenge Program* (Ref. 14).
- *Determining the Adequacy of Existing Data* (Ref. 12).
- *Guidance for Testing Closed System Intermediates for the HPV Challenge Program* (Ref. 7).
- *Procedures for Removing Chemicals that are No Longer HPV and are not Likely to Become HPV Again from the HPV List* (Ref. 9).

2. *HPV Challenge Program principles.* EPA supplemented these goals in the October 14, 1999, letter to the companies participating in the voluntary HPV Challenge Program (Ref. 11), by asking the participants to observe several principles as they proceed with the program. These principles, which were developed after consultation with the organizations involved in developing the framework for the program, are intended to address concerns raised by certain animal advocacy organizations who wish to ensure that the HPV Initiative not lead to the excessive use of animals in tests and that attention is paid to existing information and alternative testing methods that do not require animals as test subjects. A copy of the October 14, 1999, letter is available on the ChemRTK web site (Ref. 8) and the public version of the official record for this document. As indicated in the letter, animal experiments should not be performed if another validated method—not involving the use of animals—is reasonably and practically available for use.

The October 14, 1999, letter to participants in the voluntary HPV Challenge Program, indicates that participants shall maximize the use of existing and scientifically adequate data to minimize further testing. EPA also stated that participants, in analyzing the adequacy of existing data, shall conduct a thoughtful and qualitative analysis rather than use a rote checklist approach. The letter also indicated that participants may conclude that there are sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested, and that participants shall maximize the use of SAR analysis and scientifically appropriate category approaches where feasible to address the data needs under the voluntary HPV Challenge Program. The letter further suggests that participants reviewing the adequacy of existing data for GRAS chemicals should specifically consider whether the information available makes it unnecessary to proceed with further testing involving animals.

As discussed in Unit IV.H., the letter states that participants in the voluntary HPV Challenge Program shall not conduct any terrestrial toxicity testing, and should generally not develop any new dermal toxicity data. In the letter and as discussed in Unit IV.F.5., EPA also encourages participants to use *in vitro* genetic toxicity testing to generate any needed genetic toxicity screening data, unless known chemical properties preclude its use.

In addition, as indicated in Unit IV.A., the letter states that individual chemicals (i.e., those HPV chemicals not proposed for testing in a category) that require further testing on animals shall be deferred until November 2001. The October 14, 1999, letter also indicates that testing of chemicals which are determined to meet the requirements of closed system intermediates shall be deferred until 2003, and that participants shall not develop sub-chronic or reproductive toxicity data for the HPV chemicals that are solely closed system intermediates, as defined by OECD/SIDS Guidelines.

As indicated in Unit IV.A., and discussed in more detail in Unit IV.C.2., the letter indicates that participating companies shall allow 120 days between the posting of test plans and the implementation of any testing plans.

C. What Does Participation in the Voluntary HPV Challenge Program Specifically Involve?

The voluntary HPV Challenge Program contained two phases during which sponsors made commitments. The first phase ended on March 15, 1999, and the second commitment phase ended on December 1, 1999. EPA is not currently planning to include in a TSCA section 4 HPV SIDS rulemaking any chemicals which were sponsored during these first two phases. EPA, however, intends to issue proposed TSCA section 4 HPV SIDS rulemaking to address unmet data needs for a portion of those chemicals which were not sponsored during these phases. Although the commitment phase of the voluntary HPV Challenge Program has ended, EPA can accept viable commitments to sponsor additional chemicals, even though the chemical may have been included in a proposed rule. Such commitments must be consistent with the ''viable commitment'' guidance available on the EPA's ChemRTK web site (Ref. 15). EPA does not intend to include a chemical covered by a viable commitment in a final TSCA section 4 HPV SIDS rulemaking, if, during the regulatory phase of the Program, the sponsor, in addition to agreeing to meeting all of the commitments that would have been necessary under the voluntary phase of the Program, provides the following additional information:

- Evidence that work is underway and proceeding in a timely manner.

• Data required to complete the SIDS battery are developed within the time frame set by EPA in the proposed rule.

• Robust summaries and full copies of all study reports from new studies and existing data are submitted to EPA in a timely manner.

Viable commitments can include categories and SAR consistent with the available guidance (Refs. 13 and 14). If a viable commitment is made and fulfilled, and the information is deemed adequate, EPA would not include that chemical in a multi-chemical HPV TSCA rulemaking for SIDS testing.

The following are expected to be provided by those wishing to participate as viable commitment sponsors in the voluntary HPV Challenge Program:

1. *A simple commitment letter*. The letter lists those HPV chemicals, including those included in categories, for which SIDS data will be supplied by the company(s). The letter identifies chemicals by CAS numbers and chemical names, proposes a ''start year'' for evaluation of each chemical, and identifies a technical contact (including name and phone number) with whom EPA can consult. Full commitments under the voluntary HPV Challenge Program must specify the names and CAS numbers of the chemicals to be sponsored, the year test plans will be submitted, and the name and other contact data for the technical person within the company who should be reached for more information. Commitment letters under the voluntary HPV Challenge Program were due to the Agency by December 1, 1999. EPA has posted the voluntary HPV Challenge Program commitment letters on its ChemRTK web site (http://www.epa.gov/chemrtk/smrestbl.htm). EPA anticipates that many companies will also submit their commitments electronically to a third-party Internet database, the ''US HPV Chemical Tracking System'' (Ref. 19), the initial development of which was supported by the ACC. For more information on making commitments to the voluntary HPV Challenge Program, consult the EPA web site (Ref. 15).

2. *Test plans*. Test plans submitted electronically at a pace that is specified in the commitment letter. The test plans and accompanying robust summaries will be submitted in the year indicated, will identify existing adequate test data on the SIDS endpoints, and will propose the tests deemed necessary to complete the SIDS testing requirements. For those chemicals for which the sponsor determines that existing test data are inadequate, needed tests included in the test plan will be conducted in accordance with OECD guidelines. The Agency anticipates that test plans will be submitted electronically to the ''US HPV Chemical Tracking System'' (Ref. 19). To ensure adequate public notice about the proposed test plan, a principle in the October 14, 1999, letter is that sponsors shall allow 120 days between the posting of a test plan and the implementation of any testing plans. EPA will post specific reference as to the public availability of the submitted test plan and robust summary information on the ChemRTK web site.

3. *A ''Robust Summary.''* A ''robust summary'' prepared in a standardized electronic format for each existing and new study. These summaries will be submitted to EPA and will be posted on the Agency's ChemRTK web site to ensure public access to detailed synopses of the studies for the SIDS endpoints. Guidance on the content/format of a ''robust'' summary can be found on the ChemRTK web site (Ref. 6).

D. How Will the Test Data Collected Under the Voluntary HPV Challenge Program be Managed?

Most information associated with the voluntary HPV Challenge Program will be submitted electronically in order to better allow both efficient analysis of the data by EPA and real-time public access to the collected data. Many submissions will be made electronically via the Internet. EPA intends to post the information on the Internet immediately following a simple quality control check to ensure the information is complete and in a form that can be uploaded on the web, and will note that it has not been critically reviewed for adequacy by EPA. The web posting will be updated following the Agency's review of the information. EPA will provide the public with more complete and detailed information via its web site (http://www.epa.gov/chemrtk/elecsubm.htm) about EPA's approach to data management as the voluntary HPV Challenge Program progresses.

E. How Many HPV Chemicals Have Been Sponsored Thus Far Under the Voluntary HPV Challenge Program?

As of November 9, 2000, EPA has received full or provisional commitments from 469 companies, individually or as part of 187 consortia (see Unit III.G.) to sponsor 2,155 chemicals under the voluntary HPV Challenge Program. A provisional commitment is one that is lacking one or more of the specific elements (e.g., name and phone number of a technical contact) required for a commitment to be considered a ''full'' commitment to sponsor a chemical under the voluntary HPV Challenge Program. EPA anticipates that most, if not all, of the provisional commitments received thus far will be upgraded to full commitments upon the Agency's receipt of the needed additional information. Continually updated information regarding the chemicals being sponsored under the voluntary HPV Challenge Program and the names of company sponsors and consortia can be found on EPA's ChemRTK web site (http://www.epa.gov/chemrtk/sumresp.htm), and on the ''US HPV Chemical Tracking System'' (Ref. 19).

F. What Specific Testing Endpoints are Called for in the Voluntary HPV Challenge Program?

Definitive test guidance can be found in the third edition of the *Screening Information Data Set Manual of the OECD Programme on the Co-operative Investigation of High Production Volume Chemicals*, published in July 1997 (Ref. 3). The SIDS basic screening-level endpoints are listed in section 2.2 of the SIDS Manual (Ref. 3). Because terrestrial toxicity testing will normally be considered to belong to the OECD post-SIDS tier, terrestrial toxicity testing (including avian toxicity) is not included in the voluntary HPV Challenge Program. The actual OECD test guideline for each of the SIDS tests can be found at http://www.oecd.org/ehs/guide/index.htm. The EPA-recommended screening level tests (with their OECD test guideline numbers) under the voluntary HPV Challenge Program are as follows:

1. *Physical/chemical property tests*:

• Melting Point (OECD 102).

• Boiling Point (OECD 103).

• Vapor Pressure (OECD 104).

• *n*-Octanol/Water Partition Coefficient Method (OECD 107 or OECD 117).

• Water Solubility (OECD 105 and OECD 112, if applicable).

2. *Environmental fate tests*:

• Photodegradation (determined via estimation, see guidance document on data adequacy at EPA's ChemRTK web site (Ref. 12).

• Hydrolysis-Stability in Water (OECD 111).

• Transport/Distribution (determined via modeling, see guidance document on data adequacy at EPA's ChemRTK web site (Ref. 12).

• Biodegradation (OECD 301 or OECD 302).

3. *Ecotoxicity tests*:

• Acute Toxicity to Fish (OECD 203).

• Acute Toxicity to Daphnia (OECD 202).

• Toxicity to Plants (Algae) (OECD 201).

• Chronic Toxicity to Daphnia, when appropriate (OECD 211).

4. *Mammalian toxicity—acute*:

• Acute Oral Toxicity Test (rat)(OECD 425).

• Acute Inhalation Toxicity Test (OECD 403).

For the ''Mammalian Toxicity—Acute'' endpoint, certain ''Special Conditions'' in the form of a chemical substance's physical/chemical properties or physical state should be considered in determining the appropriate test method that would be used from among those included for this endpoint. The OECD HPV SIDS Program recognizes that for most chemical substances, the oral route of administration will suffice for this endpoint. Under the voluntary HPV Challenge Program, for test substances that are gases at room temperature (25°C), the acute mammalian toxicity study should be conducted using inhalation as the exposure method. In the case of a potentially explosive test substance, care should be taken to avoid the generation of explosive concentrations. For all other chemicals (i.e., those that are either liquids or solids at room temperature), acute toxicity testing should be conducted via oral administration. Dermal toxicity testing is not included in the voluntary HPV Challenge Program.

5. *Mammalian toxicity—genotoxicity*:

i. Gene mutations.

• Bacterial Reverse Mutation Test: (OECD 471) [or use the *In Vitro* Mammalian Cell Mutation Test (OECD 476)].

ii. *Chromosomal damage*.

• *In Vitro* Mammalian Chromosomal Aberration Test (OECD 473) [or use either the *In Vivo* Mammalian Bone Marrow Chromosomal Aberration Test (rodents: mouse (preferred species), rat, or Chinese hamster) (OECD 475), or the *In Vivo* Mammalian Erythrocyte Micronucleus Test (sampled in bone marrow) (rodents: mouse (preferred species), rat, or Chinese hamster) (OECD 474)].

Persons who conduct testing for chromosomal damage are encouraged to use *in vitro* genetic toxicity testing (Mammalian Chromosomal Aberration Test) to generate needed genetic toxicity screening data, unless known chemical properties preclude its use. These could include, for example, physical properties or chemical class characteristics. With regard to such cases, test sponsors are asked to submit to EPA the rationale for conducting one of these alternative tests (OECD 474 or OECD 475) as part of the test plan. A primary focus of the voluntary HPV Challenge Program is to implement this program in a manner consistent with the OECD HPV SIDS Program and as part of a larger international activity with global involvement. This approach provides the same degree of flexibility as that which currently exists under the OECD HPV SIDS Program (Ref. 2).

6. *Mammalian toxicity—repeated dose/reproductive/developmental*:

• Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422) [or use these two tests: Reproduction/Developmental Toxicity Screening Test (OECD 421) and Repeated Dose 28-Day Oral Toxicity Screen (OECD 407)].

For ''Mammalian Toxicity—Repeated Dose/Reproductive/Developmental,'' EPA recommends the use of the Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422). EPA recognizes, however, that there may be reasons to test a particular chemical using both the Reproduction/Developmental Toxicity Screening Test (OECD 421) test guideline and the Repeated Dose 28-Day Oral Toxicity Screen (OECD 407) test guideline instead of the OECD 422 test guideline. With regard to such cases, test sponsors are asked to submit to EPA the rationale for conducting these alternative tests as part of the test plan.

Certain of the chemicals for which Mammalian Toxicity—Repeated Dose/Reproductive/Developmental data are needed may be used solely as ''closed system intermediates,'' as described in the EPA guidance document developed for the voluntary HPV Challenge Program (Ref. 7). As described in this guidance document, such chemicals may be eligible for a reduced testing battery which substitutes a developmental toxicity study for the SIDS requirement to address repeated dose, reproductive, and developmental toxicity. At the present time, EPA does not have sufficient information to know with any degree of certainty which if any of the chemicals that are included in the voluntary HPV Challenge Program are solely closed system intermediates as defined by the OECD/SIDS guidelines. Persons who believe that a chemical fully satisfies the terms outlined in the guidance document are encouraged to submit appropriate information which substantiates this belief. If, based on submitted information and other information available to EPA, the Agency believes that a chemical substance is considered likely to meet the requirements for use solely as a closed system intermediate, EPA will handle that chemical substance in accordance with the existing OECD procedures. A principle in the October 14, 1999, letter to participants in the voluntary HPV Challenge Program is that participants shall not develop sub-chronic or reproductive toxicity data for the HPV chemicals that are solely closed system intermediates as defined by the OECD/SIDS guidelines. Actual initiation of testing for chemicals that are solely closed system intermediates would be deferred until 2003, if adequate existing data are not otherwise available.

G. Are Acute Aquatic Toxicity Studies Always Needed Under the Voluntary HPV Challenge Program?

No, acute aquatic toxicity studies are not always needed under the voluntary HPV Challenge Program. For ''Ecotoxicity Tests,'' the OECD HPV SIDS Program recognizes that, for certain HPV chemicals, acute toxicity studies are of limited value in assessing the substances' aquatic toxicity. This issue arises when considering chemicals with higher *n*-octanol/water partition coefficients (log K_{ow} or log P) values. In such cases, toxicity is less likely to be observed over the duration of acute toxicity studies because of the reduced uptake and the extended amount of time required for such substances to reach toxic concentrations in the test organism. For such situations, the OECD HPV SIDS Program recommends use of chronic toxicity testing in Daphnia (OECD 211) in place of acute toxicity testing in fish (OECD 203) and Daphnia (OECD 202). For the purposes of the voluntary HPV Challenge Program, EPA recommends that the need for longer term tests be judged based on log K_{ow} and other factors. In general, EPA believes that for chemicals determined to have a log K_{ow} equal to or greater than 4.2 (which corresponds to a fish bioconcentration factor (BCF) of approximately 1,000), the following tests should be conducted: Chronic Toxicity to Daphnia study (in place of the acute toxicity tests in fish and Daphnia) and Toxicity to Plants (Algae; OECD 201). For chemicals determined to have a log K_{ow} less than 4.2, EPA believes that Acute Toxicity to Fish, Acute Toxicity to Daphnia and Toxicity to Plants (Algae) testing should be conducted. EPA recognizes that in some circumstances, however, acute aquatic toxicity testing may be relevant for certain chemical substances having high log K_{ow} values. For example, chemical substances that are dispersible in water (e.g., surfactants, detergents, aliphatic amines, and cationic dyes) may have high log Kow values and yet may still be acutely toxic to aquatic organisms. Sponsors under the voluntary HPV

Challenge Program are encouraged to consider these factors in developing test plans. Thus, a sponsor who believes that acute aquatic testing is appropriate for an HPV chemical with a high log K_{ow} should provide in its submitted test plan the rationale for conducting such testing. Public comments on test plans relating to this issue will be considered on a chemical by chemical basis.

The OECD HPV SIDS Program includes testing on terrestrial organisms if ''significant exposure is expected in the terrestrial environment.'' Under the voluntary HPV Challenge Program, exposure information need not be collected/submitted on each HPV chemical as is done under the OECD HPV SIDS Program. In addition, OECD is limiting the collection of exposure information to that obtained from the sponsor country/countries; in the past, each OECD member country was expected to provide this exposure information. In recognition of the changing role of exposure information in the OECD HPV SIDS process, EPA raised the issue of changing the OECD's approach to terrestrial toxicity testing at the 8th Meeting of the OECD's workgroup on existing chemicals (October 25–28, 1999, Paris). EPA proposed that the OECD move consideration of the need for terrestrial toxicity testing to a subsequent step in its process (known as ''post-SIDS'' testing). This proposal was accepted in part by the OECD. Avian toxicity testing was moved to the post-SIDS tier but the OECD retained the element of considering the need for soil toxicity testing (earthworms and plants) based on the potential for terrestrial exposure. For the purposes of the voluntary HPV Challenge Program, EPA is not asking sponsors to include consideration of soil toxicity testing. This aspect, however, will need to be considered for HPV chemicals which enter the OECD HPV SIDS Program.

H. Are Dermal Toxicity or Terrestrial Toxicity Testing Required Under the Voluntary HPV Challenge Program?

No. Another principle in the October 14, 1999, letter, is that participants in the voluntary HPV Challenge Program shall not conduct any terrestrial toxicity testing and generally should not develop any new dermal toxicity data. See also Unit IV.F. Dermal toxicity testing is not included in the voluntary HPV Challenge Program.

I. Are Acute LD_{50} Tests Always Needed for Mammalian Acute Toxicity Testing Under the Voluntary HPV Challenge Program?

No, acute LD_{50} tests are not always needed for mammalian acute toxicity testing under the voluntary HPV Challenge Program. In fact, as was discussed in the proposal (Ref. 16) which was submitted by the United States to the February 1999, meeting of the OECD workgroup on existing chemicals, EPA recommends the use of the ''Up and Down Procedure'' (OECD 425) in the voluntary HPV Challenge Program for those chemicals in need of acute toxicity testing. This particular test greatly reduces the number of test animals required and provides a point estimate of the lethal dose that is adequate for screening assessments on industrial chemicals. The OECD's Joint Meeting, at its 29th Session in June 1999, agreed with the general approach to use alternative methods for acute oral toxicity testing on industrial chemicals and ''specifically encourages this for work under the OECD's Existing Chemicals [(i.e., SIDS)] Program'' (Ref. 17).

As this topic is discussed in section 3.4 of the OECD HPV SIDS Manual, ''All substances, except gases and vapors, should be tested by the oral route. . . .Gases should be tested by the inhalation route alone'' (Ref. 3). The SIDS Manual also notes that ''dependent upon the physical-chemical properties . . . and the most important route of human exposure, the dermal or the inhalation route could also be considered.'' EPA raised a question regarding this guidance for consideration by the OECD at the October 1999, meeting of the OECD's workgroup on existing chemicals. As originally presented, the United States proposed to delete the reference to dermal testing in the SIDS data set; however, comments indicated that this would not be accepted by other countries. The United States modified its proposal, based on comments from other countries, to indicate that acute testing need be done by one route of exposure only, such that, where appropriate, dermal testing could be done as an alternative to oral testing. This revision also failed to gain the needed support. The basis for rejection of the revised proposal was that oral testing is necessary to satisfy hazard classification requirements and that if dermal exposure (or inhalation exposure) was an issue, countries should still consider the need for testing by an additional route at the SIDS level. Thus, the OECD workgroup did not agree to modify the SIDS battery requirements for acute toxicity. As indicated in Unit IV.H., dermal toxicity testing is not included in the voluntary HPV Challenge Program.

Recognizing that exposure information need not be collected/submitted under the voluntary HPV Challenge Program, and the contingent nature of the need for acute toxicity testing by a second route of exposure, EPA recommends that acute toxicity testing conducted under the voluntary HPV Challenge Program be limited to a single route of exposure. Decisions regarding the need for acute toxicity testing by a second route would be need to be considered for HPV chemicals which enter the OECD HPV SIDS Program.

J. Are Both In Vitro and In Vivo Genotoxicity Tests Needed Under the Voluntary HPV Challenge Program?

Sponsors are encouraged to use *in vitro* testing unless there are chemical properties (including chemical class considerations) or other aspects which may call its use into question. EPA has recommended certain *in vitro* protocols, and, as appropriate and to the extent possible, will review test plans submitted by sponsors of HPV chemicals to promote use of such protocols. Participants in the voluntary HPV Challenge Program are encouraged to use *in vitro* genetic toxicity testing to generate any needed genetic toxicity screening data, unless known chemical properties preclude its use.

In February 1999, at the meeting of the OECD workgroup on existing chemicals, EPA made a proposal (Ref. 16) for the use of the male rats from the combined repeated dose/reproductive/developmental toxicity screen (OECD 422) for the purpose of running the mammalian erythrocyte micronucleus test (OECD 474). This would reduce the number of animals needed, and, if the protocol can be successfully developed, would also increase the amount of information which would be received from this single study. Initial consideration of this approach suggested that while this strategy might be acceptable with mice, the use of this approach with rats (the species typically used in SIDS testing) appeared to present technical issues. Because there seemed to be technical problems with this modification of the *in vitro* micronucleus protocol, EPA initiated a review of its approach to this SIDS endpoint under the voluntary HPV Challenge Program. Following this review, EPA has decided to remove its preference for the use of the *in vivo* chromosomal effects test and to accept

either *in vitro* or *in vivo* studies, as is allowed under the OECD procedure for this endpoint. Sponsors are encouraged to use *in vitro* testing unless there are chemical properties (including chemical class considerations) or other aspects which may call its use into question.

K. Can Some of the Mammalian Toxicity Protocols Included in the Voluntary HPV Challenge Program be Combined?

For the purposes of the voluntary HPV Challenge Program, EPA strongly recommends the use of the combined protocol for repeat dose, reproductive, and developmental toxicity (OECD 422) for chemicals where data are needed for these endpoints (see Unit IV.F.6.). This particular test guideline was initially developed by the United States in the late 1980's and early 1990's for use in the OECD HPV SIDS Program. This screening test guideline provides limited information on systemic toxicity following repeated exposure over a limited time period. In addition, it provides initial information on developmental and reproductive toxicity. The United States has been and remains one of its strongest supporters within the OECD and strongly recommends its use. Historically, EPA has relied on this combined protocol for HPV chemicals needing this type of testing under the OECD HPV SIDS effort.

EPA also recognizes that the OECD HPV SIDS Program allows for other approaches that can be used to meet the repeat dose, reproductive and developmental toxicity endpoint needs covered by the combined protocol. EPA can also envision circumstances where other such approaches might make sense. These can include, for example, situations concerning existing data wherein only certain of these endpoints require testing or in cases where there is a particular need identified by a sponsor (e.g., high-exposure potential) such that a different testing approach is indicated. In these cases, voluntary HPV Challenge Program sponsors are asked to provide the rationale for conducting such testing in their submitted test plans. EPA, as appropriate and to the extent possible, plans to follow up with sponsors who propose in their test plans to use approaches other than OECD 422 to ensure that their decision to do so is an informed one.

In those cases for which adequate data are available for reproductive and developmental toxicity but not for repeat dose toxicity, EPA recommends that the 28-day repeated dose toxicity test (OECD 407) be used by sponsors to meet the repeat dose data need for the voluntary HPV Challenge Program.

In cases for which adequate data are available for the repeat dose endpoint, but not for reproductive and/or developmental toxicity, EPA recommends that the combined reproductive and developmental toxicity guideline (OECD 421) be used in lieu of separate testing for reproductive toxicity (OECD 415) and/or developmental toxicity (OECD 414) unless there is information indicating that separate testing may be advisable. This point was raised by the United States at the February 1999 meeting of the OECD's Working Party on Existing Chemicals and further discussions will be pursued in that forum.

L. How do the Rulemaking Efforts Relate to the Voluntary HPV Challenge Program?

In the October 14, 1999, letter to participants in the voluntary HPV Challenge Program, EPA stated that it was the intention of the Agency that the TSCA section 4 HPV SIDS rulemaking proceed in a manner that is consistent with the principles and concerns outlined in the letter for the participants in the voluntary program. As such, EPA would incorporate in the TSCA section 4 HPV SIDS rulemaking the criteria established under the voluntary HPV Challenge Program to the extent possible in the context of a rulemaking, and would also consider improvements based on experiences with implementing that program. The specific requirements of any associated TSCA section 4 HPV SIDS rulemaking will be addressed in future proposed rulemaking.

V. Administrative Requirements

As indicated previously, this action describes the HPV Initiative, focusing on the Agency's strategy and overall approach to addressing data collection needs for HPV chemicals, along with the components of the voluntary HPV Challenge Program. Although the Agency has indicated that the HPV Initiative may also involve rulemaking under TSCA, any TSCA rulemaking associated with the HPV Initiative will be addressed in that rulemaking, rather than in this document. Since this action is not a regulatory action and does not impose any requirements, the regulatory assessment requirements that apply when an agency imposes requirements do not apply to this action.

A. Was this Action Reviewed by the Office of Management and Budget?

Yes. The Agency submitted this action to the Office of Management and Budget (OMB) for review under Executive Order 12866, entitled *Regulatory Planning and Review* (58 FR 51735, October 4, 1993), because OMB determined that this document may result in a ''significant regulatory action'' subject to review by OMB. Any comments or changes made during that review have been documented in the public version of the official record.

B. Does the Agency Have Approval for this Information Collection Activity?

Yes. Pursuant to the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.*, an agency may not conduct or sponsor, and a person is not required to respond to, an information collection request unless it displays a currently valid OMB control number. In general, the OMB control numbers for EPA's regulations, after appearing in the preamble of a final rule, are listed in 40 CFR part 9, and included on the related collection instrument. The information collection activities related to chemical testing under TSCA section 4(a), which includes activities related to chemical testing under a consent order, a voluntary program, or a TSCA rulemaking, have already been approved under OMB control number 2070–0033 (EPA ICR No.1139). This action does not contain any new information collection activities requiring additional OMB review and approval.

As described in this document, the voluntary HPV Challenge Program involves the submission of a commitment letter, study or testing plans, and a final report. In general, the average annual per chemical burden estimate approved under OMB Control number 2070–0033 is about 488 hours per response, including time for preparing letter of intent and study plans, conducting laboratory testing, submitting progress reports (if applicable), and preparing final reports on each study. For recordkeeping, the average burden is estimated to be 330 hours per recordkeeper. As defined by the PRA and 5 CFR 1320.3(b), ''burden'' means the total time, effort, or financial resources expended by persons to generate, maintain, retain, or disclose or provide information to or for a Federal agency. This includes the time needed to: Review instructions; develop, acquire, install, and utilize technology and systems for the purposes of collecting, validating, and verifying information, processing and maintaining information, and disclosing and providing information; adjust the existing ways to comply with any previously applicable instructions and requirements; train personnel to be able to respond to a collection of information; search data sources; complete and review the collection of

information; and transmit or otherwise disclose the information.

VI. Materials in the Public Docket

As indicated in Unit I.B.2., the official record for this document has been established under docket control number OPPTS–42213 and the administrative record number AR–201. The following is a listing of documents that are specifically referenced in this document and which have already been placed in the public version of the official record for this action. For your convenience, EPA has also provided some non-EPA internet addresses to allow you to access the electronic version of the referenced document. In doing so, the Agency has verified the accuracy of these addresses at the time of signature. However, since EPA is not responsible for these non-EPA sites, the Agency does not exercise any control over these addresses. A paper copy of any document referenced in this way has been included in the public version of the official record for this document as described in Unit I.B.2.

1. EPA, Office of Pollution Prevention and Toxics (OPPT). ChemRTK HPV Challenge Program Chemical List. (May 1999) (This list is updated periodically and is available electronically at http://www.epa.gov/chemrtk/hpvchmlt.htm).

2. EPA, OPPT. Chemical Hazard Data Availability Study: What Do We Really Know About the Safety of High Production Volume Chemicals? (April 1998) (http://www.epa.gov/opptintr/chemtest/hazchem.htm).

3. OECD Secretariat. *SIDS Manual*. Third Ed. Screening Information Data Set Manual of the OECD Programme on the Co-Operative Investigation of High Production Volume Chemicals. Paris, France; July 1997. Copies this Manual can be obtained by accessing EPA's web site at http://www.epa.gov/chemrtk/sidsappb.htm, as well as directly from OECD at http://www.oecd.org/ehs/sidsman.htm (non-EPA site).

4. Environmental Defense. *Toxic Ignorance*. New York, New York, (Summer 1997). Copies of ''Toxic Ignorance'' can be obtained by accessing ED's web site (non-EPA site) at http://www.edf.org/pubs/reports/toxic ignorance/ or by calling 1–800–684–3322.

5. ACC. Public Availability of SIDS-Related Testing Data for U.S. High Production Volume Chemicals (June 12, 1998). Copies of ACC's report can be obtained by writing to ACC at 1300 Wilson Blvd., Arlington, VA 22209 or by calling ACC at (703) 741–5226.

6. EPA, OPPT. Draft Guidance on Developing Robust Summaries (October 22, 1999) (http://www.epa.gov/chemrtk/robsumgd.htm).

7. EPA, OPPT. Guidance for Testing Closed System Intermediates for the HPV Challenge Program (Draft, March 17, 1999) (http://www.epa.gov/chemrtk/closed9.htm).

8. EPA, Office of Prevention, Pesticides and Toxic Substances (OPPTS). Letter from Susan H. Wayland, Deputy Assistant Administrator, to participants in the voluntary High Production Volume Challenge Program (October 14, 1999) (http://www.epa.gov/chemrtk/ceoltr2.htm).

9. EPA, OPPT. Procedures for Removing Chemicals that are No longer HPV and Not Likely to Become HPV Again from the HPV List (Draft, March 17, 1999) (http://www.epa.gov/chemrtk/nolohpt8.htm).

10. OECD. Decision-Recommendation of the Council on the Cooperative Investigation and Risk Reduction of Existing Chemicals (January 31, 1991).

11. ICCA. ICCA HPV Working List (July 1, 2000). Copies of this List can be obtained by accessing ICCA's web site (non-EPA site): http://www.icca-chem.org/hpv.

12. EPA, OPPT. Determining the Adequacy of Existing Data (May 17, 2000) (http://www.epa.gov/chemrtk/datadfin.htm).

13. EPA, OPPT. The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program (August 26, 1999) (http://www.epa.gov/chemrtk/sarfinl1.htm).

14. EPA. OPPT. Development of Chemical Categories in the HPV Challenge Program (Draft, August 25, 1999) (http://www.epa.gov/chemrtk/categuid.htm).

15. EPA, OPPT. ChemRTK HPV Challenge Program Making Commitments (June 29, 2000) (http://www.epa.gov/chemrtk/makecom.htm).

16. EPA. Proposal Made at the Organization for Economic Cooperation and Development (OECD) Working Party Meeting on Existing Chemicals (February 1999).

17. OECD. Acute Oral Toxicity Testing: Data Needs and Animal Welfare Considerations Agreement Reached by the 29th Joint Meeting of the Chemicals Committee and the Working Party on Chemicals (ENV/JM/HCL/RD(99)6; June 1999).

18. EPA, OPPT. Draft Guidance on Searching for Chemical Information and Data (April 1999, rev. May 1999) (http://www.epa.gov/chemrtk/srchguid.htm).

19. ACC. U.S. HPV Chemical Tracking System. Non-EPA site: http://www.hpvchallenge.com.

List of Subjects

Environmental protection, Hazardous chemicals, Reporting and recordkeeping.

Dated: December 14, 2000.

Susan H. Wayland,

Acting Assistant Administrator for Prevention, Pesticides and Toxic Substances.

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