

## Appendix B: The HPV October Agreement

October 14, 1999

Company name

Street

City, State, Zip

Dear Company Contact:

On behalf of the Environmental Protection Agency (EPA), I would like to thank you for your commitment to participate in the voluntary High Production Volume Challenge (HPV) program. We look forward to working with you over the coming years as we achieve our goals for this important program.

As you may be aware, a number of animal protection organizations and the public have raised concerns that the HPV Challenge program may lead to the excessive use of animals in tests and to inadequate attention to existing information and alternative testing methods that do not require animals as test subjects. As a general matter, animal experiments should not be performed if another validated method—not involving the use of animals—is reasonably and practically available for use in the HPV Challenge program. To respond to these concerns, and after consultation with the organizations involved in developing the framework for this initiative, I am asking you and your fellow HPV Challenge participants to observe the following principles as we proceed with the program:

1. In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested.
2. Participants shall maximize the use of existing and scientifically adequate data to minimize further testing. To reinforce this approach, EPA will consider information contained in the databases identified in the enclosure, or in databases maintained by the organizations identified in the enclosure, to have been known to the Agency within the meaning of Section 8(e) of the Toxic Substances Control Act (TSCA), 42 U.S.C. 2607(e). This policy is limited to information reported by participants under the HPV Challenge program and generated for or contained in these databases as of the date of this letter. In addition, any other potential liability under TSCA Section 8(e) for existing data on HPV Challenge program chemicals will be limited according to the terms of the “Registration Agreement for TSCA Section 8(e) Compliance Audit Program (56 Fed. Reg. 4128, Feb. 1, 1991).” This policy does not affect prior 8(e) enforcement actions.
3. Participants shall maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships.
4. Consistent with the Screening Information Data Set (SIDS) program of the Organization for Economic Cooperation and Development (OECD), participants shall not conduct any terrestrial toxicity testing.
5. Participants are encouraged to use in vitro genetic toxicity testing to generate any needed genetic toxicity screening data, unless known chemical properties preclude its use.
6. Consistent with the OECD/SIDS program, participants generally should not develop any new dermal toxicity data.
7. 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.

8. In analyzing the adequacy of screening data for chemicals that are substances Generally Recognized as Safe (GRAS) for a particular use by the Food and Drug Administration (FDA), participants should consider all relevant and available information supporting the FDA's conclusions. Participants reviewing the adequacy of existing data for these chemicals should specifically consider whether the information available makes it unnecessary to proceed with further testing involving animals. As with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant.
9. Because validated non-animal tests for some SIDS endpoints may be available soon, participants shall make the following revisions to the sequence of testing:
  - (a) Testing of closed system intermediates, which present less risk of exposure, shall be deferred until 2003;
  - (b) 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.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.
10. Companies shall allow 120 days between the posting of test plans and the implementation of any testing plans.

To promote the availability and use of alternatives to tests involving animals, the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP) will commit at least \$1.5 million in FY 2000, and \$3 Million in FY 2001, and any further funds appropriated by Congress, to the development and validation of non-animal alternative test methods and protocols. EPA will provide an additional \$250,000 this year and will seek to provide a similar amount next year to these efforts. The Multicenter Evaluation of In Vitro Cytotoxicity (MEIC), on the agenda for the October 14 meeting of NTP's Advisory Committee on Alternative Toxicological Methods, will be given priority attention. EPA will promptly incorporate, as appropriate, the work of NIEHS and NTP into the HPV Challenge program.

EPA recognizes that the HPV Challenge is a voluntary program that includes substantial public review and involvement. The successful implementation of the changes described in this letter will depend upon the good faith effort and cooperation of all parties. We appreciate the spirit of cooperation and commitment that has characterized this initiative to date. The changes to the HPV Challenge program outlined above present the opportunity to advance our shared goals of expanding the basic health data available to the public, while incorporating certain animal welfare concerns and scientific principles. It is the intention of the Agency that the HPV Challenge program, including the test rule(s), should proceed in a manner that is consistent with these principles and concerns.

Again, I thank you for your commitment to participate in the HPV Challenge program. If you need further clarification or assistance with this program, please contact Barbara Leczynski at 202-260-3749 or visit the website at [www.epa.gov/chemrtk](http://www.epa.gov/chemrtk).

Sincerely,

/s/

Susan H. Wayland  
Deputy Assistant Administrator