Final Report

Use of the HPVIS to identify Chemicals that may pose a Threat to the Great Lakes Fishery

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Abstract

The purpose of this research was to evaluate the use of data from the HPVIS to rank high production volume chemicals based on their toxicity, persistence and bioaccumulative properties in an attempt to identify substances that have the potential to impact the Great Lakes fishery. These PBT chemicals would be candidates for environmental monitoring and potentially for replacement in commerce with less persistent or less toxic substitutes. As of October 2006, the HPVIS database contained entries for 879 chemicals. Data for the seven endpoints used in our research was available for 55 chemicals and 5 of these chemicals were identified as potential threats to the Great Lakes. Locating and retrieving data from the HPVIS was somewhat difficult. Web links didn't work consistently and some of the numeric fields had been created as text fields and could not be sorted. Many of the field names were vague making it difficult to find data for the endpoints of interest. When data entry is completed the HPVIS will have the potential to provide a valuable tool for public health and environmental protection agencies. However, this potential will not be reached unless more work is done to make this internet-accessible database more user-friendly. Specific problems and recommendations are outlined in our report.

I. Background information and purpose of the project, including specific questions to be addressed

The five Great Lakes make up the most important fresh water fishery in North America. Annual revenue from commercial and sport fishing on the lakes has been estimated at more than $4 billion. These lakes are also an important source of drinking water for many major Canadian and US cities. Each year, millions of families boat on these lakes, swim on their beaches or enjoy a walk along their shores. Eagles, osprey, seagulls and other fish-eating animals that live near these lakes also depend on them as a source of food.

These deep lakes are easily contaminated by atmospheric pollutants or toxins that enter the lakes directly through wastewater effluent or contaminated rivers and streams. Once contaminated, the lakes are not easily cleaned up. Turnover of the water in the Great Lakes system takes several decades. Toxic pollutants that break down slowly and bioconcentrate in the aquatic food chain pose the greatest environmental and human health hazards. Toxic substances can have adverse impacts on a fishery by reducing the amount of food available to fish, by altering the life cycle of the fish, or by making the fish unsafe for human consumption. To ensure protection of the Great Lakes fishery, it is essential that we identify tools that can be used to screen chemicals for these effects and take steps to prevent them from entering this fragile ecosystem.

When it is fully populated, the HPVIS database will provide a publicly-accessible, internet-based source of toxicity and environmental fate data for more than 1,200 chemicals that are produced or imported in quantities exceeding 1 million pounds per year. Many of the chemicals included in this database are released into the environment as a component of a consumer product or as industrial waste. Once chemicals enter the environment they will either degrade completely; degrade to form new substances that may be more toxic, equally toxic, or less toxic; or persist without significant degradation.

Toxic chemicals that persist for long periods or degrade to form toxic metabolites pose a risk to the environment as well as to public health. This problem is exacerbated if the chemical is also able to bioaccumulate in the food chain. Examples of chemicals that are known to be persistent and bioaccumulative include chlorinated insecticides - such as dieldrin and DDT, polychlorinated biphenyls, and mercury. All of these chemicals have been detected in fish and pose health risks such as cancer and reproductive problems to humans and fish-consuming wildlife. Recently, we have learned that perfluorochemicals (PFCs) that have been used for several years as fabric stain repellants, fire-fighting foams and non-stick cookware finishes, are resistant to degradation and can persist in the environment for decades. Perfluoro-octane sulfonate (PFOS) has been detected in surface water and fish forcing the state of Minnesota to restrict consumption of bluegill, sunfish and small mouth bass from a section of the Mississippi River. PFCs have recently been detected in the Great Lakes and in the blood of eagles and other fish-eating birds. The potential for these toxic chemicals to resist biodegradation and enter the aquatic food chain was not appreciated until they were detected in human and animal tissues many years after they were put into commercial use.

There is a pressing need to be able to predict the impact of high production volume chemicals on the natural environment and on public health before problems are discovered. Toxicity and fate data provided by the HPVIS offers a unique opportunity to screen more than 1,200 high production volume chemicals for their potential impacts on the environment. Such screening should be able to identify toxic chemicals that resist degradation and have bioaccumulative properties. If additional assessment indicates problems, these substances could be regulated or replaced with safer alternatives thereby preventing widespread contamination and human exposure.

Project Purpose: The purpose of this project was to evaluate the use of the HPVIS as a tool that could be used to screen high production volume chemicals for their potential to pose a threat to the Great Lakes Fishery**.** Data from the HPVIS was used to identify chemicals that were resistant to degradation, had high octanol/water partition coefficients, and were toxic to aquatic organisms or mammalian systems.

Research Questions:

1. Can the HPVIS database be used to create a list of chemicals that are toxic and likely to be bioaccumulative and environmentally-persistent?
2. Are data in the HPVIS stored in a format that supports numeric sorting?
3. Are data available for the endpoints of interest for most HPV chemicals?
4. Are read-across and estimated values easy to distinguish from measured values?
5. How much time is required to identify chemicals that meet study criteria?

II. Methods Used

HPVIS was queried individually for three fate and four toxicity endpoints. Using the tabular selection form, data for each endpoint was downloaded into an MS Excel database. Typically, the fields selected for download were limited to the test chemical CAS no., the result value, the result units and the result type. The resulting Excel worksheets were edited as needed to ensure that data were reported with uniform units of measurement. For example, water concentrations for aquatic toxicity tests were converted from ug/L or ppb to mg/L and half-lives were converted from minutes, hours, months or years to days. Data from animal feeding studies were frequently provided in units of ppm in feed or mg/L in water. Unless conversions were provided in the robust summaries, we did not attempt to convert these units to mg/kg/day which was the standard unit for this data and the data were not used in our analysis.

Following conversions to standard units, MS Excel work sheets were imported into an MS Access database to facilitate queries. MS Access tables were reformatted to ensure that numeric data was stored in numeric fields. Because most CAS numbers had multiple values for each endpoint, queries were used to create a table for each endpoint that contained the ‘worst-case’ maximum or minimum value for each endpoint. These tables were then joined using CAS numbers for matching. Queries were used to provide a list of chemicals that met our study criteria.

III. General Findings and Discussion

As of October 20 2006, the HPVIS database contained data for 879 chemicals. However, data sets were incomplete for most of these chemicals. Data for all seven endpoints used in our research was available for only 55 (6%) of the chemicals in the HPVIS.

Table 1. Availability of data in HPVIS

Endpoints of interest	# of CAS nos. (% of total)
One or more endpoints	879
Log Kow	339 (38%)
Aquatic Half Life	375 (43%)
Ready Biodegradation	127 (14%)
Genetic toxicity	254 (29%)
Reproductive NOAEL	233 (26%)
Repeated Dose NOAEL	335 (38%)
Aquatic NOEC/LOEC/LC/EC	354 (40%)
All endpoints	55 (6%)

We were able to identify five chemicals that met our criteria as toxic in one or more biological systems, resistant to degradation, and potentially bioaccumulative based on its octanol/water partition coefficient. Because more than one value was available for most endpoints, minimum or maximum values were used to represent 'worst case' values for each endpoint. The use of worst-case values is a conservative approach and more be over-predictive of a substance's hazard potential.

Table 2. No. of HPVIS chemicals that met study criteria

Endpoints of interest	Study criteria value	Units	No chemicals
Log Kow	Max >4	Unitless	106
Aquatic Half Life	Max >30	Days	265
Biodegradation	Min < 68% at 28 days	Percent	83
Genetic toxicity	Positive	Unitless	144
Reproductive NOAEL	Min < 10	Mg/kg/day	21
Repeated Dose NOAEL	Min < 10	Mg/kg/day	96
Aquatic NOAEL	Min < 10	Mg/L	148
All fate & one or more toxicity value			5

Results

Using the MS Access tables that were created, nine chemicals initially met study criteria for Log Kow, biodegradation and aquatic half-life. However, further evaluation determined that test methods for one of these did not meet our criteria. One substance had a biodegradation value of 5% from a 2-day incubation, but degradation was nearly complete at 28 days. The remaining 8 chemicals are listed in Table 3 along with toxicity values for four endpoints. Five chemicals were highly toxic in one or more test systems and are highlighted in blue.

Chemical selection tree

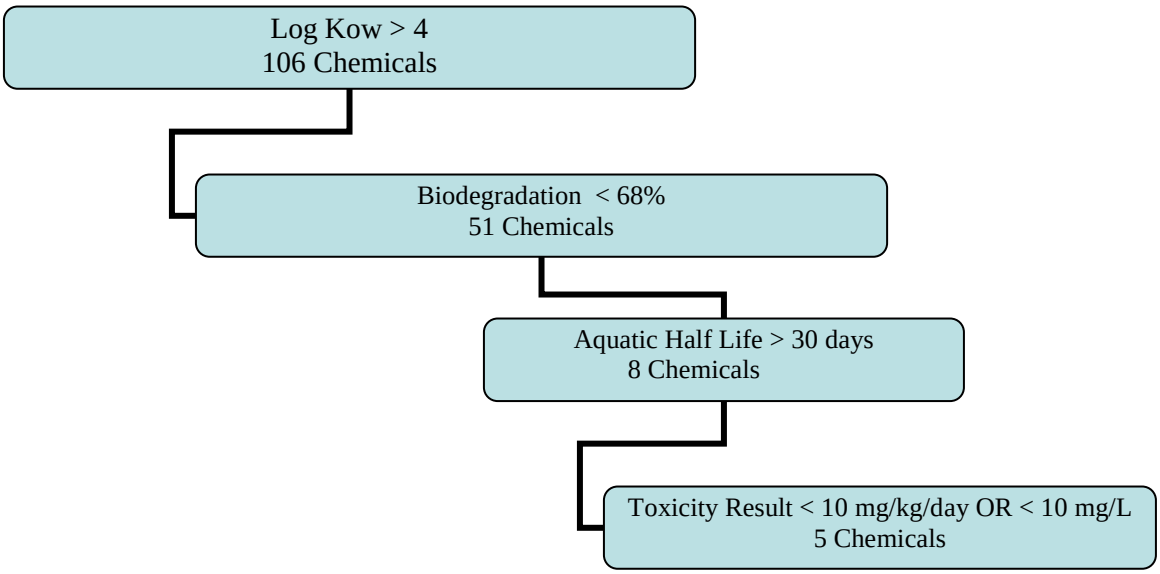

Table 3. Chemicals that met criteria for fate endpoints

CAS Number	Chemical Name	Max Log Kow	Min Biodeg % at 28 Days	Max Aquatic Half Life in Days	Genetic Toxicity	Min Rep Dose NOAEL Mg/kg/day	Min Repro NOAEL Mg/kg/day	Min Aquatic NOEC Mg/L
101-20-2	Triclocarban	4.9	0	365	Neg	25		0.00006
118-58-1	Benzyl salicylate	4.31	62	620.5	Pos			0.84
2050-08-0	Amyl salicylate	4.57	29	2518.5		500		0.9
2082-79-3	Antioxidant 1076	13.4	21	2628	Neg			30
32687-78-8	Antioxidant 1024	7.79	6	365				1.23
35074-77-2	Benzenepropanoic acid, 3,5-bis(1,1-dimethylethyl)-4-hydroxy-, 1,6-hexanediyl ester	11.74	1	584				33
6683-19-8	Antioxidant 1010	23	4	766.5			10,000	100
68526-82-9	Alkenes, C6-C10	4.11	21	365		100		0.1

Research Question Responses

1. Can the HPVIS database be used to create a list of chemicals that are toxic and likely to be bioaccumulative and environmentally-persistent?

   Yes, however very few HPV chemicals can be screened at this time due to incomplete datasets. Because much of the data contained in the HPVIS was entered as text and because field names are vague and difficult to recognize, a substantial amount of time was required to extract data from the HPVIS and reformat it to support numeric sorting

2. Are data in the HPVIS stored in a format that supports a numeric sort?

   Not always. Some data fields were created as text fields and entries often contain text notes along with numeric data. Log Kow is an example of a field that should be numeric was created to allow text entries. Many numeric values in this field are followed by text notes such as (calculated by model) or (KOWWIN program). In order to sort chemicals by Log Kow, these notes were deleted and the field was converted to a numeric field using MS Access. MS Excel was unable to convert this field from text to numeric.

3. Are data available for the endpoints of interest for most HPV chemicals?

   Not at this time. As of October 2006, only 6% of the chemical entries were complete for the seven endpoints we used.

4. Are read-across values easy to distinguish from measured values?

   No. We were unable to distinguish read across from measured values without reading the robust summaries.

5. How much time is required to identify chemicals that meet study criteria?

   It took us approximately six weeks to complete our research. However, future searches of the HPVIS could be accomplished much more quickly now that we are familiar with the database and have established methods for editing, reformatting and querying downloaded data.

Discussion

Creation and population of the HPVIS continue to be a work in progress. As of October 2006, 879 of approximately 1,200 HPV chemicals had data entered into the system. Data are incomplete for the majority of these, however.

The HPVIS is a large database and is somewhat user unfriendly. The web portals don't work consistently, numeric data often appear as text and cannot be sorted, field names are vague and not linked to a particular endpoint (see appendix A). The process of becoming familiar with the data field names, learning to use the query functions, extracting data, editing data and creating a database in MS Access that was capable of numerical sorts took several weeks.

Specific problems we encountered with the database include:

1. We were unable to locate a description of study methods or requirements for endpoints listed in the HPVIS. Our sporadic review of Robust Summaries identified a variety of experimental conditions and laboratory animal species. Some studies were completed as early as the 1970s and likely do not conform to current GLP requirements.
2. Some query functions don't work (see Figure 1).
3. Many fields that contain numeric data were created as text fields (see Figure 2). These fields often include notes and cannot be sorted or ranked without being edited to remove text and converted to numeric fields.
4. Units are not uniform and are sometimes missing even though they can often be found in the robust summaries. Some endpoints have as many as 7 different units reported, e.g. seconds, minutes, hours, days, weeks, months, and years (see Figure 3). In the case of animal studies, units should be reported in terms of mg/kg/day which is the unit used in risk assessment. Approximately half of the mammalian toxicity values in the HPVIS have been entered in units of ppm, mg/L, or % diet.
5. Two or more CAS numbers (CAS no., Test Substance CAS no and Category Chemical CAS no) are listed for some endpoints. This is apparently for read across values and created some confusion as to which chemical the data represented.
6. Each data value is entered as a separate record for each CAS number. This structure makes automated sorting very difficult and results in very large datasets.
7. Database entries aren't always consistent with robust summaries in that the units are sometimes different.
8. Many chemicals have multiple results entered for a single endpoint.
9. Field names are often vague and confusing (see Appendix A).
10. Some data entries don't include a CAS number or a chemical name.
11. Comparison for the chemicals that met our study criteria found that data from the HPVIS did not match data in the PBT Profiler. As shown in tables 4 and 5, log Kow values from the HPVIS were not predictive of BCF values provided by PBT Profiler for several chemicals. Significant differences were also found in aquatic toxicity values and aquatic half-lives for some chemicals. Since the PBT profiler doesn't provide study references, it's impossible to know which database is more accurate.
12. Data for aquatic toxicity were split among three fields. Initially, it was thought that all data would be found in the NOEC and LOEC fields. However, LC50 and EC50 values were listed under a field named 'concentration value.'

Problems we encountered with the data included:

1. When multiple result values were entered for a single endpoint and chemical, it was difficult to know which value to use in our analysis.
2. Result values are listed in many different units. These values cannot be compared without converting them to common units.

IV. Lessons learned and recommendations concerning the database.

When data entry is complete, the HPVIS will be a valuable tool for public health and environmental protection agencies. It will provide environmental fate and short-term toxicity data for nearly 1,200 high production volume chemicals. We found it relatively easy to learn how to access data via the HPVIS website, however, data often needed to be edited and verified before it could be used to screen chemicals for their persistence, tendency to bioconcentrate, and toxicity. The following recommendations are intended to make the database easier to use and understand.

1. Ideally, the HPVIS should contain one record per CAS no. Each record should contain one entry per cell. For endpoints that have more than one result, data should be entered into fields designated as min, max and mean, or otherwise prioritized.
2. Each data field should be limited to a single unit of measure. Appropriate conversions should be made prior to entry of data into HPVIS.
3. To the extent possible, data for a given endpoint should be from studies of similar quality, exposure duration and test systems.
4. All field names should be unique and easily linked to an endpoint.
5. Numeric data fields should be formatted to exclude text entries.
6. Read across and estimated values should be clearly distinguished from measured values, but should appear in the same field.
7. Once data entry is completed, a metadata section should be added to the HPVIS website. This would include an explanation of the testing methods for each endpoint as well as a summary of the number of chemicals that have data values for each endpoint.

V. Lessons learned and recommendations concerning the data.

While our study was not intended to evaluate the accuracy or representativeness of the HPVIS, we identified numerous data gaps as well as data that did not match data found in the PBT Profiler. Until data can be validated, it should be used cautiously with appropriate comparisons to data from other sources. Much of the data in the HPVIS could not be used for comparison purposes due to non-standard units of measure. Examples of problems we encountered are provided in the figures below.

Users of the HPVIS should be aware that data made available through this website have not been reviewed or approved by EPA. This is especially important since HPVIS is accessed via EPA's website and will likely be used by people who are familiar with IRIS and similar databases that provide EPA risk assessment information. They may assume that the HPVIS data they download has been verified by the agency or approved for risk assessment.

Figure 1. Query sub-index appears off-screen.

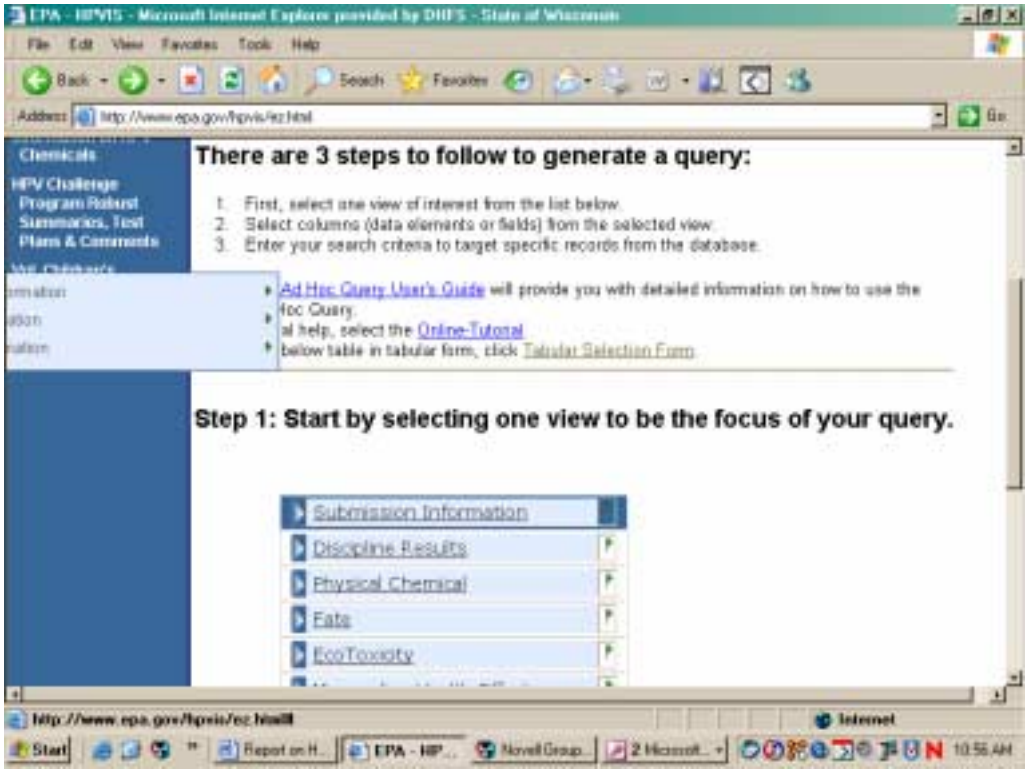

Figure 2. Results field cannot be sorted due to unnecessary text in a field that should be numeric.

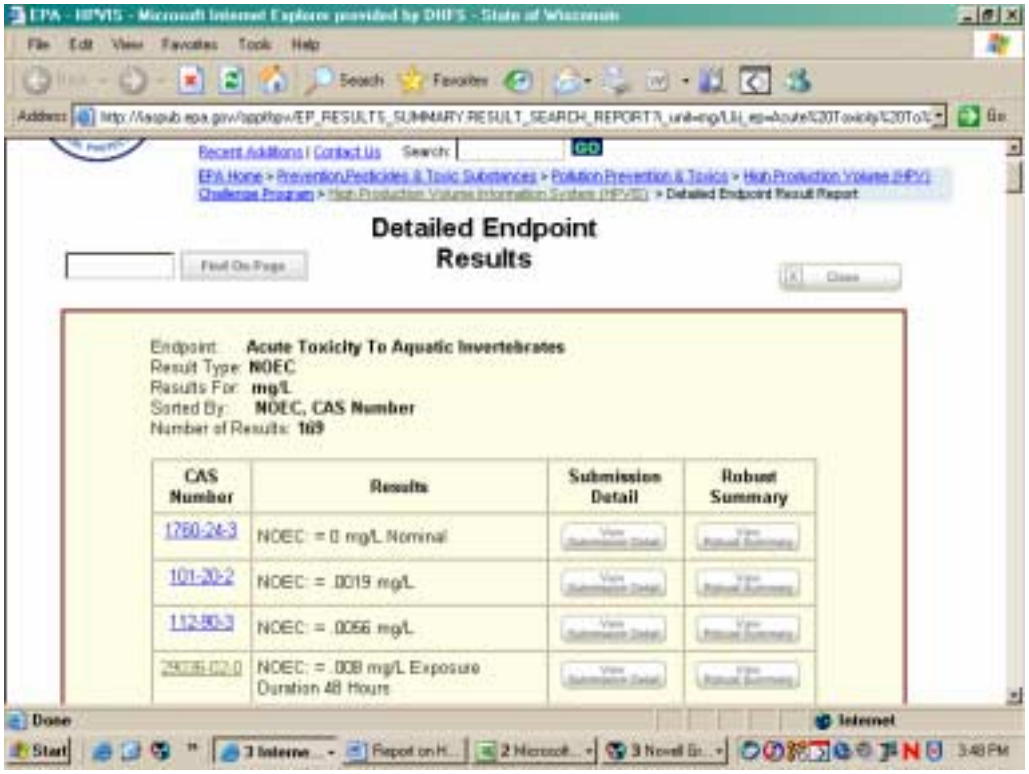

Figure 3. Example of an endpoint that has multiple reporting units. This requires conversion of data to a standard unit prior to sorting.

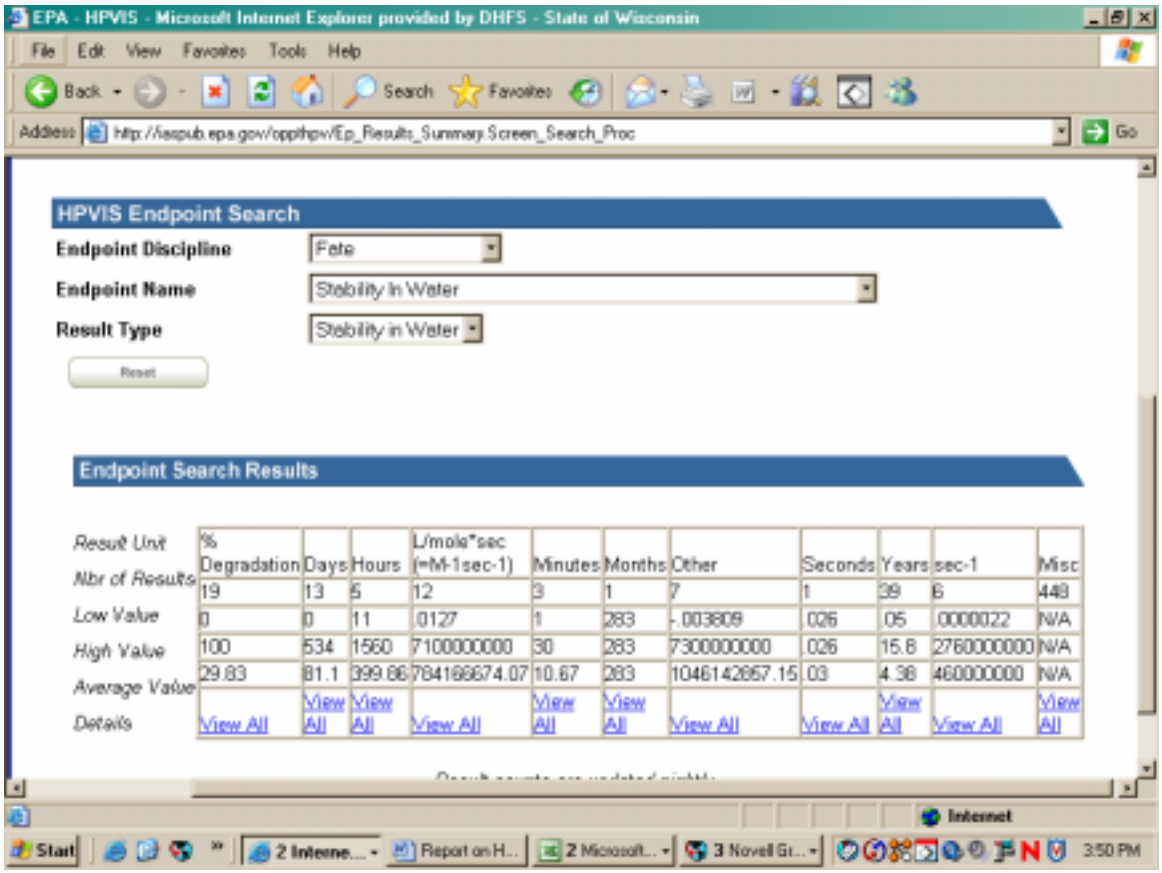

Figure 4. Comparison of HPVIS and PBT Profiler data

HPVIS Data							
CAS Number	Max Log Kow	Min Biodeg Value In %	Max Aquatic Half Life in Days	Genetic Toxicity	Min Repeated Dose Mg/kg/day	Min Repro NOAEL Mg/kg/day	Min Aquatic NOEC Mg/L
101-20-2	4.9	0	365	Neg	25		0.00006
118-58-1	4.31	62	620.5	Pos			0.84
2050-08-0	4.57	29	2518.5		500		0.9
2082-79-3	13.4	21	2628	Neg			30
32687-78-8	7.79	1	365				1.23
35074-77-2	11.74	1	584				33
6683-19-8	23	4	766.5			10,000	100
68526-82-9	4.11	10	365		100		0.1

PBT Profiler Data							
CAS Number	BCF	Soil Half-life Days	Water Half-life Days	Genetic Toxicity	Min Repeated Dose Mg/kg/day	Min Repro Toxicity Mg/kg/day	Fish Chronic Toxicity Mg/L
101-20-2	1,200	120	60				0.09
118-58-1	420	30	15				0.025
2050-08-0	660	30	15				0.018
2082-79-3	3.2	120	60				
32687-78-8	1,900	360	180				0.00063
35074-77-2	3.2	360	180				
6683-19-8							
68526-82-9							

Orange cells contain PBT Profiler values that differ by more than an order of magnitude from values found in the HPVIS (assuming log Kow is an estimate of the log of the BCF).

Table 4. Chemicals of identified as potentially toxic, persistent and bioaccumulative

CAS No.	Chemical Name	Uses
101-20-2	Triclocarban	Antimicrobial in soaps
118-58-1	Benzyl salicylate	Flavor/fragrance Naturally-occurring
2050-08-0	Amyl salicylate	Flavor/fragrance Naturally-occurring?
32687-78-8	Antioxidant 1024	Rubber additive
68526-82-9	EP-290, C6-C10 Alkenes	Defoamer, lubricant