USE OF READ-ACROSS OF EXISTING HAZARD DATA TO FULFILL HPV CHEMICAL PROGRAM REQUIREMENTS WITHOUT THE NEED FOR NEW ANIMAL TESTING

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ABSTRACT

The Soap and Detergent Association (SDA) is a leading manager of chemical consortia fulfilling commitments to the voluntary global International Council of Chemical Associations (ICCA) and U.S. Environmental Protection Agency (EPA) high production volume (HPV) chemical programs. SDA's commitment to compile and make publicly available a baseline set of health and environmental effects data covers 291 chemicals sponsored by 62 companies within ten chemical consortia. The chemical categories represented by these consortia include: aliphatic acids, alkoxides, alkyl sulfates, amine oxides, glycerides, hydrotropes, LAS/ABS, long chain alcohols, methyl esters, and triclocarban. Due to the structural similarity of the chemicals within a category their physiochemical and toxicological properties are likely to be similar. This has allowed the utilization of the read-across technique where the data available for some substances satisfy the data need for member chemicals without data. SDA has found read-across to be especially useful in assigning data for ecotoxicity and human health endpoints to many chemicals among its 143 completed chemical commitments to date. Consequently, the use of read-across has eliminated the need for new animal testing while allowing SDA consortia to meet those data requirements. The use of thousands of test animals has been avoided. SDA anticipates additional reductions in animal testing by utilizing read-across in ongoing efforts to complete the data sets for the balance of its sponsored chemicals.

INTRODUCTION

SDA is a U.S. National Trade Association representing the formulators of household, institutional and industrial cleaning products and the manufacturers of the ingredients and finished packaging used to bring these products to the marketplace (SDA 2009a). Since 1999 SDA has managed chemical consortia fulfilling commitments to the voluntary U.S. Environmental Protection Agency (EPA) and International Council of Chemical Associations (ICCA) high production volume (HPV) chemical programs (SDA 2008, US EPA 2009, ICCA 2009). These programs are focused efforts to provide assessments of baseline sets of hazard data for chemicals that are manufactured or imported in amounts of one million pounds or greater per year, and to make these assessments publically available. The benefits of these programs include providing a sound basis for future industry and government chemical risk assessments, eliminating duplicative testing and assessment efforts, minimizing costs for the industry, and reducing the numbers of animals for testing.

Table 1 – SIDS Endpoints

An initiative of the chemical industry working through the ICCA in partnership with the OECD HPV program has led to the global harmonization of baseline hazard data sets and their initial assessment. Here sponsoring countries along with industry partners cooperatively select chemicals and collect a set of baseline hazard and exposure data for them from governmental, industrial and public sources. The guidelines on the composition of the baseline hazard data dossier known as the Screening Information Data Set (SIDS) is provided by the OECD (OECD 2009a). The specific test endpoints comprising the SIDS include those in Table 1. The SIDS dossier provides the basis for the initial hazard assessment of the chemical. The sponsoring country will prepare this information as a SIDS Initial Assessment Report (SIAR) for submission to OECD who will subsequently review it for its completeness and finalization at a SIDS Initial Assessment Meeting (SIAM) (ICCA 2009). It is noteworthy that the requirements of the EPA HPV program can be indirectly met through the OECD SIDS program. This report will consider only the eight SIDS endpoints that rely upon vertebrate animal testing.

Table 2 – SDA HPV Program

The SDA has to date managed ten industry HPV consortia each based upon a HPV chemical category, and as a whole representing a total of 291 chemicals. Consortia are generally formed by companies that produce HPV chemicals, and they have proven to be efficient mechanisms for sharing the resources necessary to support data gathering, testing and the preparation of initial hazard assessments. SDA's consortia are comprised of 62 companies who also serve as sponsors for the chemicals assessed. This report focuses on those six SDA-managed consortia that have completed their ICCA commitment or have completely finalized their HPV submission to the US EPA. These include: aluminum alkoxides, alkyl sulfates, amine oxides, hydrotropes, LAS/ABS, and long chain alcohols. OECD assessments that have been reviewed at a SIAM are available either on the OECD or United Nations Environment Program (UNEP) websites. Final HPV submissions to the US EPA can be accessed on the USA EPA website (US EPA 2009). Data sharing is an important advantage from participation in consortia, since a frequent outcome is that the SIDS can be fulfilled with a minimum of new testing, both for non-animal and animal tests. Demonstrative of this point is that after SDA consortia compiled and reviewed 142 sponsored chemicals and hundreds of supporting chemical data sets only six new aquatic toxicity tests were necessary to fulfill SIDS requirements.

Table 3 – Application of Read-Across

The management of HPV chemicals as chemical categories has greatly facilitated the fulfillment of program commitments. A chemical category is a group of chemicals whose physicochemical, environmental fate, and human health and eco-toxicological properties are likely to be similar as the result of their structural similarity or functionality (OECD 2009b). These similarities may be based upon common functional groups, chemical class, carbon chain length, or on their common precursors or breakdown products. A very beneficial consequence is that data gap filling in a chemical category may be accomplished by either Trend Analysis, QSARs, or Read-Across. Read-Across is a process where endpoint information for one chemical may be used to predict the same endpoint for another chemical based upon similarities in their chemical structure or functionality. SDAs consortia have taken advantage of Read-Across to significantly reduce the numbers of tests and vertebrate animals used to complete their SIDS. Here, of the 1136 tests required to fulfill SIDS for all of the chemicals in the six categories, 212 were met by available test data but 924 were avoided by applying Read-Across. Overall, the application of Read-Across by SDA consortia for 142 chemicals has allowed the replacement of 81.3% of those SIDS tests requiring the use of vertebrate animals.

Table 4 – Example of Read-Across

An example of the application of Read-Across is represented by the fulfillment of the SIDS for the Amine Oxides category. All of the chemicals in this category are surfactants whose molecular structure is represented by a polar, amine group "head" and a hydrophobic long alkyl "tail", and they share specific structural variations that relate to their amine group substituents, alkyl chain length, and extent of double bonds. Within the data for the 15 chemicals in this category, for each of the endpoints that require vertebrate animal use there was an acceptable test data set that could be referenced to apply Read-Across to the other members of the category that were without data (Sanderson et al. 2006).

Table 5 – Benefits of Read-Across

The benefits arising from the use of Read-Across within the six chemical data sets of SDA-managed HPV consortia have been significant. Among all of the SIDS endpoints that require the use of vertebrate animals 924 tests were avoided by applying Read-Across. Forgoing these tests translates to the replacement of 112,788 vertebrate test animals. Furthermore, the savings of additional resources by not conducting these tests is noteworthy. Not only were the administrative costs of managing these test avoided but the estimated costs of the actual testing calculates to be a savings of € 60,932,000 or $ 86,397,000. The animal test numbers for this assessment were derived from the OECD Guidance Manual for HPV Chemicals (OECD 2009a). The estimated costs for this assessment were based upon average test price data derived from a published 2004 survey of 28 independent and corporate testing laboratories (Fleischer 2007). It is anticipated that the future completion of HPV commitments by three additional SDA-managed HPV chemical consortia will result in similar benefits.

REFERENCES

Fleischer, M. (2007) Testing Costs and Testing Capacity According to the REACH Requirements – Results of a Survey of Independent and Corporate GLP Laboratories in the EU and Switzerland. *Journal of Business Chemistry*, Vol. 4, Issue 3, pp. 96-114.

ICCA High Production Volume (HPV) Chemical Program 2009. http://www.cefic.org/activities/hse/mgt/hpv/hpvinit.htm

OECD (Organization for Economic Co-Operation and Development) Guidance Manual for HPV Chemicals 2009a. http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html

OECD Guidance on Chemical Categories and Read-Across 2009b. http://www.oecd.org/document/6/0,3343,en_2649_34379_43087494_1_1_1_1,00.html

Sanderson, H., Counts, J.L., Stanton, K.L., and Sedlak, R.I. (2006) Exposure and Prioritization — Human Screening Data and Methods for High Production Volume Chemicals in Consumer Products: Amine Oxides a Case Study. *Risk Analysis*, Vol. 26, Issue 6, pp. 1637-1657.

The Soap and Detergent Association (2008) Meeting the Challenge: Progress Report on The Soap and Detergent Association Commitments under Voluntary High Production Volume Chemical Programs.

The Soap and Detergent Association (SDA) 2009a. http://www.cleaning101.com

SDA 2009b. http://www.sdascience.org

US EPA High Production Volume Challenge 2009. http://www.epa.gov/chemrtk/index.htm

Table 1 - Baseline Data for HPV Programs - Endpoints from OECD Screening Information Data Sets (SIDS)

ENDPOINT [a,b]		
Physico-chemical Properties	Melting Point Boiling Point Water Solubility Partition Coefficient Vapor Pressure	
Environmental Fate	Photodegredation Fugacity Biodegradation Hydrolysis	
Environmental Effects	Acute Toxicity to Fish Acute Toxicity to Aquatic Invertebrates Acute Toxicity to Aquatic Plants	[c]
Mammalian Toxicity	Acute Toxicity Repeated Dose Toxicity Reproductive Toxicity Developmental Effects Bacterial Mutagenicity Mammalian Mutagenicity	[c] [c] [c] [c] [c]

[a] SIDS endpoints are accepted by both ICCA and US-EPA HPV programs
[b] A SIDS endpoint can often be fulfilled by different specified test protocols
[c] Read-Across was used in data sets by SDA-managed HPV consortia to replace new animal testing, as reported here

Table 2 - Status of Sponsored Chemical Categories within the SDA HPV Chemical Program

Category	Program	Number of Chemicals	No. of Robust Summaries [c]	Number of New Studies Conducted	Completion Status
Aluminum alkoxides [a]	US EPA	17	1195	0	Final to EPA April 2008
Alkyl sulfates [a]	ICCA	61	> 1300	0	Finished / SIAM October 2007
Amine oxides [a]	ICCA	15	180	0	Finished / SIAM April 2006
Hydrotropes [a]	ICCA	10	125	1 vapor pressure test	Finished / SIAM October 2005
LAS/ABS [a,b]	US EPA	9	192	0	Final to EPA April 2008
Long chain alcohols [a]	ICCA	30	< 1400	6 acute and chronic aquatic toxicity tests	Finished / SIAM April 2006
Triclocarban	US EPA	1	102	1 vapor pressure test	Finished / May 2006
Aliphatic acids	ICCA	86	> 1000	0	Spring 2010 SIAM (projected)
Glycerides	ICCA	31	275	0	Fall 2010 SIAM (projected)
Methyl esters	ICCA	33	> 500	0	Fall 2010 SIAM (projected)

[a] The application of read-across to replace animal testing within this data set was evaluated in this presentation
[b] Linear (LAS) and branched (ABS) alkylbenzene sulfonates
[c] A robust summary is a compilation of data in IUCLID format with sufficient information to permit an assessment of study quality

Table 3 - Extent of Read-Across Used as Replacement to Vertebrate Animal Testing in Fulfilling HPV Data Sets

Number of Tests Avoided by Using Read-Across per Category (No. of chemicals)

Animal Test	Aluminum alkoxides (17)	Alkyl sulfates (61)	Amine oxides (15)	Hydrotropes (10)	LAS/ABS (9)	Long chain alcohols (30)	Total Tests Avoided by Read-Across per test type	Total Tests Needed per test type	Percent of Tests Avoided by Read-Across
Acute Oral toxicity	17	32	11	7	3	7	77	142	54.2
Acute Dermal toxicity	17	56	14	9	8	5	109	142	76.8
Acute Inhalation toxicity	17	61	14	10	9	5	116	142	81.7
Repeat Dose toxicity	17	54	13	8	8	23	123	142	86.6
Developmental toxicity	17	54	13	9	8	29	130	142	91.5
Reproductive toxicity	17	58	13	10	8	25	131	142	92.2
Mutagenicity (mammal)	17	57	15	8	9	29	135	142	95.1
Fish, Acute toxicity	17	47	5	7	7	20	103	142	72.5
TOTAL per all categories							**924**	**1136**	**81.3 %**

Table 4 - Example of Read-Across Application: Amine Oxide Category Fulfillment of SIDS for Vertebrate Animal Tests

AMINE OXIDES by CAS NUMBER	1643-20-5	70592-80-2	68955-55-5	3332-27-2	2605-79-0	61788-90-7	85408-48-6	85408-49-7	7128-91-8	2571-88-2	2530-44-1	61791-47-7	61791-46-6	14048-77-2	93962-62-0
MAMMALIAN TOXICITY DATA															
Acute Oral toxicity	A	A	R	R	R	A	R	R	R	R	R	R	R	R	R
Acute Dermal toxicity	R	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Acute Inhalation toxicity	A	R	R	R	R	R	R	R	R	R	R	R	R	R	R
Repeated Dose toxicity	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Developmental toxicity	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Reproductive toxicity	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Mutagenicity [a]	A-	R	R	R	R	R	R	R	R	R	R	R	R	R	R
ENVIRONMENTAL EFFECTS DATA															
Fish, Acute toxicity	A	A-	A	A	R	A	R	A-	A	A	A	A	A	R	A

A = Reliable study data available
A- = Data available, considered inadequate
R = Read across from other category members or supporting substance
[a] – Supporting substance used to support Read-Across was CAS No. 60729-78-4

Table 5 - Status of Benefits from Using Read-Across within the Chemical Data Sets of SDA-Managed HPV Consortia

Animal Test Endpoint [a]	OECD Test Guideline # [b]	Tests Total # Avoided	Cost per Test [e] (Euro)	Cost Total Saved (Euro) / (US Dollar) [f]	Animals # per Test [d]	Animals Total # Replaced
Acute Oral Toxicity - Acute Toxic Class (rat)	423	77	1474	113,498 / 160,932	12	924
Acute Dermal Toxicity (rat)	402	109	2,011	219,199 / 310,808	50	5,450
Acute Inhalation Toxicity (rat)	403	116	11,734	1,361,144 / 1,930,006	80	9,280
Repeated Dose 28-day Oral Toxicity (rat)	407	123	49,390	6,074,970 / 8,613,882	80	9,840
Prenatal Developmental Toxicity (rat)	414	130	63,100	8,203,000 / 11,631,279	160	20,800
Two-Generation Reproduction Toxicity (rat)	416	131	327,975	42,964,725 / 60,920,972	320	41,920
Mouse Erythrocyte Micronucleus Assay (mutagenicity)	474 [c]	135	11,268	1,521,180 / 2,156,926	100	13,500
Fish, Acute Toxicity	203	113	4,193	473,809 / 671,827	98	11,074
TOTAL BENEFITS		**924 Tests avoided**		**€ 60,932,000 / $ 86,397,000 [g] Saved**		**112,788 Animals replaced**

[a] Protocols are linked to published test price data (Fleischer 2007)
[b] OECD Guidelines for the Testing of Chemicals (OECD 2009a); protocols are generally acceptable to both ICCA and US-EPA
[c] US-EPA accepts OECD Test 474, but OECD SIDS specifies OECD Test 475, Mouse Bone Marrow Chromosome Aberration
[d] Values were derived from respective test protocols within the OECD Guidelines for the Testing of Chemicals (OECD 2009a)
[e] Values represent 2004 average prices based upon a survey of 28 independent and corporate testing laboratories.(Fleischer 2007)
[f] Based on the Euro-US Dollar exchange rate as of August 11, 2009 (1 Euro = 1.41793 US Dollar)
[g] Values rounded to the nearest 1,000

CONCLUSIONS

1) Data sharing within HPV Chemical Consortia facilitates chemical assessments, saves resources, and reduces chemical testing based on both non-animal and animal methods.

2) The application of Read-Across to fulfill the SIDS data requirements of 142 chemicals by six SDA-managed HPV chemical consortia has resulted in the avoidance of 924 animal tests, the savings of € 60,932,000, and the replacement of 112,788 vertebrate test animals.