USE OF READ-ACROSS OF EXISTING HAZARD DATA TO FULFILL HPV CHEMICAL PROGRAM REQUIREMENTS SIGNIFICANTLY REDUCES CHEMICAL TESTING

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ABSTRACT

The American Cleaning Institute® (ACI) 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. ACI'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. Sponsored chemicals include surfactants and other substances relevant to the cleaning products industry. The chemical categories represented by these consortia include: aliphatic acids, aliphatic alcohols, alkoxides, alkyl sulfates, amine oxides, glycerides, hydrotropes, LAS/ABS, and methyl esters. Due to the structural similarity of the chemicals within a category, their environmental fate, 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 needs for other chemicals within the same category that lack data. ACI has found read-across to be especially useful in assigning data for physicochemical, ecotoxicity and human health endpoints to many chemicals among its 143 completed chemical commitments to date. It has greatly reduced the need for chemical testing while allowing ACI consortia to fulfill data requirements. The ACI-managed chemical consortia have realized significant benefits by using read-across. By applying this process the use of thousands of test animals has been avoided, and millions of euros in testing and administrative expenses have been saved.

INTRODUCTION

The American Cleaning Institute (ACI) 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 (ACI 2011a). Since 1999 ACI 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 presentation provides an overview of the impacts of read-across on testing requirements to meet commitments under the voluntary programs for six chemical categories and provides a break out for impacts related to eight SIDS endpoints that rely upon vertebrate animal testing.

TABLE 2 - THE ACI HPV CHEMICAL PROGRAM

ACI has to date managed ten industry HPV consortia each based upon an 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 cateroies of chemicals for which ICCA commitments or HPV submissions to the US EPA have been completed. 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 reviewed 142 sponsored chemicals and compiled hundreds of supporting chemical data sets, only six new aquatic toxicity tests were necessary to fulfill SIDS requirements.

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. ACI's consortia have taken advantage of Read-Across to significantly reduce the numbers of tests required to complete their SIDS for sponsored chemicals.

TABLE 3 - BENEFITS OF READ-ACROSS

The benefits arising from the use of Read-Across within the six chemical data sets of ACI-managed HPV consortia have been significant. Among the SIDS endpoints that require the use of vertebrate animals, 900 tests, or 79.2%, were avoided by applying Read-Across. Forgoing these tests translates to the replacement of 109,456 vertebrate test animals. The animal test numbers for this assessment were derived from the OECD Guidance Manual for HPV Chemicals (OECD 2009a). The estimated costs of the actual animal testing that was avoided calculated to be a savings of € 60,789,000 or $ 87,202,000. When all of the SIDS endpoints were evaluated for the availability of test data, to include mammalian toxicity, ecotoxicity, environmental fate and physico-chemical properties, a total of 2057 tests, or 69.0%, were avoided by applying Read-Across. The estimated costs of the chemical testing that were avoided calculated to be a savings of €66,923,000 or $96,001,000. 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). Furthermore, the savings of additional resources by not conducting these tests is amplified since the administrative costs of managing these testing efforts were also avoided (not calculated here). It is anticipated that the future completion of HPV commitments by three additional ACI-managed HPV chemical consortia will result in similar benefits.

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CONCLUSIONS

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

2) The application of Read-Across to fulfill the SIDS data requirements of 142 chemicals by six ACI-managed HPV chemical consortia has resulted in the replacement of 109,456 test animals and the savings of € 66,923,000.

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

	ENDPOINT[a,b]
Physico-chemical Properties	Melting Point Boiling Point Partition Coefficient Vapor Pressure Water Solubility
Environmental Fate	Biodegradation Photodegredation (Photolysis) Stability in Water (Hydrolysis) Transport and Distribution (Fugacity)
Ecotoxicity	Acute Toxicity to Fish[c] Acute Toxicity to Aquatic Invertebrates Acute Toxicity to Aquatic Plants Chronic Toxicity to Aquatic Invertebrates
Mammalian Toxicity	Acute Toxicity[c] Repeated Dose Toxicity[c] Reproductive Toxicity[c] Developmental Effects[c] Mutagenicity *in vitro* Mutagenicity *in vivo*[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 ACI-managed HPV consortia to replace new animal testing, as reported here

Table 2 - Status of Sponsored Chemical Categories within the ACI 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	Final to EPA May 2006
Aliphatic acids	ICCA	86	> 1000	0	Fall 2011 SIAM (projected)
Glycerides	ICCA	31	275	0	Spring 2012 SIAM (projected)
Methyl esters	ICCA	33	> 500	0	Spring 2012 SIAM (projected)

a. The application of read-across to reduce chemical testing within this data set is 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 - Status of Benefits from Using Read-Across within Chemical Data Sets of Six ACI-Managed HPV Consortia

SIDS Test Endpoint[a]	OECD Test Guideline # [b]	Total Tests Needed per Test Type	Tests Total # Avoided By Read Across	Cost per Test[c] (Euro)	Cost Total Saved (Euro) / (US Dollar)[d]	Animals # per Test[e]	Animals Total # Replaced
Acute Oral Toxicity (rat)	423[f]	142	77	1474	113,498 / 162,813	12	924
Acute Dermal Toxicity (rat)	402[g]	142	109	2,011	219,199 / 314,441	50	5,450
Acute Inhalation Toxicity (rat)	403[g]	142	116	11,734	1,361,144 / 1,952,560	80	9,280
Repeated Dose 28-day Oral Toxicity (rat)	407[h]	142	123	49,390	6,074,970 / 8,714,540	80	9,840
Prenatal Developmental Toxicity (rat)	414[h]	142	130	63,100	8,203,000 / 11,767,200	160	20,800
Two-Generation Reproduction Toxicity (rat)	416[h]	142	131	327,975	42,964,725 / 61,632,900	320	41,920
Mouse Erythrocyte Micronucleus Assay (*in vivo* mutagenicity)	474[i]	142	135	11,268	1,521,180 / 2,182,130	100	13,500
Fish, Acute Toxicity	203	142	79	4,193	331,247 / 475,174	98	7,742
TOTAL BENEFITS OF REDUCED VERTEBRATE ANIMAL TESTING			**900 (79.2%) Vertebrate Animal Tests Avoided**		**€ 60,789,000 / $ 87,202,000 [j] Saved**		**109,456 Vertebrate Animals Replaced**
Aquatic Invertebrate, Acute Toxicity	202	142	76	3,742	284,392 / 407,960		
Aquatic Plant, Acute Toxicity	201	142	104	4,510	469,040 / 672,838		
Aquatic Invertebrate, Chronic Toxicity	211	142	117	13,426	1,570,842 / 2,253370		
Mammalian Cell Gene Mutation Assay (*in vitro* mutagenicity)	476	142	104	17,283	1,797,432 / 2,578,430		
Melting Point	102	142	103	674	69,422 / 99,586		
Boiling Point	103	142	98	719	70,462 / 101,078		
Partition Coefficient	107, 117	142	104	3,248	337,792 / 484,563		
Vapor Pressure	104	142	99	2,779	274,121 / 394,661		
Water Solubility	105	142	105	3,813	400,365 / 574,324		
Biodegradation	301	142	85	3,901	331,585 / 475,659		
Photodegradation (Photolysis)	316	142	45	3,901 [k]	175,545 / 251,819		
Stability in Water (Hydrolysis)	111	142	50	6,573	328,650 / 471,448		
Transport and Distribution (Fugacity)	Level III Model [l]	142	67	350 [m]	23,450 / 33,639		
TOTAL BENEFITS OF REDUCED CHEMICAL TESTING			**2057 (69 %) Tests Avoided**		**€ 66,923,000 / $ 96,001,000 [j] Saved**		

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. Values represent 2004 average prices based upon a survey of 28 independent and corporate testing laboratories. (Fleischer 2007)
d. Based on the Euro-US Dollar exchange rate as of May 12, 2011 (1 Euro = 1.43450 US Dollar)
e. Values were derived from respective test protocols within the OECD Guidelines for the Testing of Chemicals (OECD 2009a)
f. Since the data were compiled, use of OECD Test Guideline # 425 is recommended
g. Acute Dermal and Acute Inhalation tests are generally not required in the SIDS unless indicated, but data for these endpoints were included since they were relevant to these chemical categories,
h. While these data were available at the time of ACI data set compilation, it should be noted that alternate and less costly means to fulfill data requirements for these endpoints may be through the use of combined test protocols such as Test # 421 (Reproduction/Developmental Toxicity Screening Test) and Test # 422 (Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test)
i. US-EPA accepts OECD Test 474, but OECD SIDS specifies OECD Test 475, Mouse Bone Marrow Chromosome Aberration
j. Values rounded to the nearest 1,000
k. Cost is an estimate based on Test # 301 as a comparative.
l. EQC Level III model is downloadable from Trent University web site (http://www.trentu.ca/envmodel)
m. Cost is an estimate.

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