WHITE PAPER

Exposure and Risk Assessment within the Framework of National Chemicals Management Policies: A Workable Solution to a Complex Problem

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I. INTRODUCTION

The intent of this paper is to propose the critical elements of a workable yet effective strategy for the hazard-based prioritization of exposure assessment within the context of national and international chemicals management policies being considered in the wake of the European Union's Registration, Evaluation, Authorization and Restriction of Chemicals ("REACH") regulation. It also provides valuable information for companies prioritizing exposure assessments for their internal product risk assessments such as those required under the American Chemistry Council Responsible Care® Product Safety Code of Management Practices. It is built upon the premise that it is not necessary to assess all exposures / risks to all chemicals placed on the market; only those uses of chemicals for which the need for risk management measures (RMM) is unclear or the types of RMM are unclear.

The focus is on direct human exposure, but indirect exposure via the persistent presence of a substance in the environment is also briefly addressed. Furthermore, the assessment of releases / exposures to the environment are intentionally not addressed here.

This White Paper is not intended to be a fully formed strategy or a critical review of REACH. Instead, it should be regarded as a stepping off point for a group of REACH-experienced exposure assessment professionals to work together to refine. The authors hope to generate a contemplative and in-depth dialog on this increasingly important and timely topic.

The proposed strategy is based on two assumptions: (1) that future chemicals management policies will, like REACH, rely more heavily on manufacturers and importers (M/I), rather than regulators, to assess exposures and risk to a large number of "new" and "existing" chemical substances so that they can gain regulatory approval to place these substances on the market, and (2) that there is a desire by all stakeholders for such assessments to be manageable, robust, and meaningful. These assumptions are consistent with the recommendations of the United Nations Environmental Programme (UNEP, 2012).

II. STATEMENT OF ISSUE

Following concerns that arose in the EU, in April of 1998, about the lack of information on chemicals, the European Commission (EC) launched a review of EU chemicals policy. This review resulted in a report, stakeholder brainstorming, and ultimately a White Paper from the EC on a strategy for a future chemicals policy. Through the legislative process, the EC's White Paper ultimately became what is known today as REACH. In the EC's White Paper, the following was noted:

> "Adequate knowledge about exposure is an absolute requirement for any reliable risk assessment. However, the process under Regulation 793/93 highlighted a general lack of knowledge on the exposure to the existing substances under review. Furthermore, in many cases, the Member State authorities responsible for the assessment were not able to establish all the relevant uses of these chemicals. This lack of knowledge and restricted access by authorities to these data hampers efficient surveillance of the chemical sector." (EC, 2001)

It was further concluded that:

> "The general shortage of exposure data must be addressed. Exposure estimates or, if appropriate, analytical determination of the exposure should be obligatory for manufacturers and downstream users (formulators and industrial users) of chemicals."

Prior to REACH, detailed risk assessments were carried out by the European Commission, with stakeholder involvement, on a relatively small set of priority substances and classical approaches to risk assessment were used. This same approach was simply accepted as the way forward under REACH except that the assessments would initially be carried out by the M/I:

> "Responsibility to generate knowledge about chemicals should be placed on industry. Industry should also ensure that only chemicals that are safe for the intended uses are produced and/or placed on the market. The Commission proposes to shift responsibility to enterprises, for generating and assessing data and assessing the risks of the use of the substances. The enterprises should also provide adequate information to downstream users." (EC, 2001)

One of the reasons for this shift in responsibility was that these kinds of detailed assessments placed too great a burden on the commission. However, there was little or no consideration of the feasibility of such an approach for industry, nor was there any serious consideration of alternative approaches.

Following the 2007 signing of REACH into law and with the first registration deadline more than 3 years away, one might have been quick to think that there was plenty of time for industry to gather the information they needed in order to complete the detailed risk assessments for the 2010 deadline, but the reality was much different. As those who were involved know very well, many things had to happen before the first exposure assessment and risk characterization could be made. As a result, most assessments were not even begun until late in 2009 and some not until the latter parts of 2010. So, whereas prior to REACH a member state, working under the direction of the EC, may have had years to complete a single risk assessment, industry was now faced with completing a large number of assessments in a very short timeframe. This led to the development of generic exposure scenarios and other shortcuts to help streamline the process. Not surprisingly, the quality of some of these assessments, and possibly most of them, did not meet expectations.

In a recent report by the European Chemicals Agency (ECHA) detailing their evaluation of approximately 146 dossiers submitted for the 2010 deadline, a number of systemic deficiencies were noted with regards to improper selection of use descriptors, insufficient details pertaining to the conditions of use / exposure, inadequate estimates of exposure, and poor traceability between the exposure scenarios, exposure estimates, and risk management measures (ECHA, 2012). In drawing these conclusions, ECHA relied on the following:

> "The objective of the exposure assessment is to "estimate … the dose / concentration of the substance to which humans and the environment … may be exposed" (Annex I Section 5.0). This estimate for the dose or the exposure concentration is then to be used for demonstrating the control of risks by comparison with the estimated no effect level or no effect concentration. The proper exposure assessment is therefore paramount to the safe use of a substance." (ECHA, 2012)

While some of the problems noted above may have been avoidable if it had not been for the mad rush to complete the registrations by the 2010 deadline, we decided to step back and asked a more fundamental question. Is the agency's assertion correct that "*the proper exposure assessment is therefore paramount to the safe use of a substance"*?

In the hopes of generating some serious dialog on the matter, it is our assertion that exposure assessment is NOT paramount to the safe use of a substance but rather should be judiciously reserved for determining if safe handling / use is possible, given the RMM available to the users, when such a conclusion cannot otherwise be made. After all, many chemicals are safely handled every day without ever knowing the level of exposure and, conversely, unsafe handling occurs despite a wealth of knowledge. It is this very subtle but very important distinction (i.e. the role of exposure assessment) that led us to the strategy being proposed here. This is not to say that more information isn't always preferred or that there is no need to understand and to register all product uses, but rather only to say that there is room for a prioritized process, without jeopardizing human health, where only certain high-priority uses / exposures need a rigorous exposure assessment. **To that end, the key issue being considered in this paper is the question of "when" is appropriate for the M/I to perform a rigorous exposure assessment to determine RMM and, consequently, to gain regulatory approval to place their substances on the market.**

III. PROPOSED STRATEGY - WHEN TO CONDUCT EXPOSURE ASSESSMENTS

Under REACH, all uses / exposures of nearly all substances are assessed so that appropriate RMM can be specified. The only exceptions are substances classified as onsite isolated intermediates that were handled under strictly controlled conditions, substances that were not classified as hazardous, and uses covered by other equivalent regulations (e.g. biocides and use as a cosmetic ingredient). In theory, requiring the M/I to assess nearly all product uses may seem appropriate and reasonable but, in practice, such a regulatory requirement burdens the system with unnecessary, and highly suspect, information. It is unrealistic to assume that the M/I has the means and capability to work so closely with the end-users and to have the capability and resources to fully assess all exposures with sufficient precision and accuracy so as to be able to establish definitive RMM.

For an alternative approach, one need not look further than the U.N. Globally Harmonized System of Classification and Labeling (GHS) for the basis of a strategy. GHS was developed to provide criteria and a consistent approach for hazard classification of chemicals. Our proposal is to combine GHS with the relevant physical-chemical properties of the substance being considered in order to prioritize the need for exposure assessment and risk characterization across the industrial, professional, and consumer use sectors.

By combining GHS with the relevant physical-chemical properties of the substance, the following matrices are proposed; with those cells in **RED** requiring an exposure assessment while those in **GREEN** would not. This is not to say that those uses falling in a **GREEN** zone are excluded completely from the M/I's responsibility, but rather to say that reasonable and appropriate RMM

for these substances can be described on the safety data sheet and/or product warning labels without the need for robust exposure assessment.

The strategy is divided according to the type(s) of uses / exposures, with **Industrial** in Table 1, followed by **Professional** in Table 2 and **Consumer** in Table 3.

Table 1: Proposed Exposure Assessment Strategy for Industrial Uses and Workers

Industrial Uses / Exposures (Workers):

GHS Classification		Closed-Continuous Process[A]	Other Than Closed-Continuous Process[A]							
			Volatility / Dustiness[B]				Dermal Penetrability[C]			
			High	Med	Low	Not	High	Med	Low	Not
Acute Toxicity	1									
	2									
	3									
	4									
	5									
Respiratory Sensitization	1A									
	1B									
Germ Cell Mutagenicity	1A									
	1B									
	2									
Carcinogenicity	1A									
	1B									
	2									
Toxicity to Reproduction	1A									
	1B									
	2									
	Lact.									
STOT-SE	1									
	2									
	3									
STOT-RE	1									
	2									

[A] A closed-continuous process is one in which the substance is contained during all stages of manufacturing, processing, and/or handling within tanks, piping, reactors, tanks, or other equipment with little or no opportunity for direct contact by workers or release to workplace air. This includes being able to sufficiently clear lines / equipment to prevent / minimize exposure before breaching the system for maintenance or repair. The term "strictly controlled" was the corollary term used under REACH. Batch processes can be regarded as closed-continuous processes if the equipment can be thoroughly cleaned between batches without breaching containment. Equipment that is "enclosed" by means of only a ventilation system is generally not considered a closed process because the ventilation equipment may not perform as intended and eliminate emissions to the workplace environment because of technical limitations and/or mechanical reliability.

[B] Volatility / Dustiness categories are consistent with those defined in ECETOC TRA. **These definitions apply to the substance at the temperature and pressure conditions of the process.**

Vapor Pressure (kPa)	Dustiness	Rating
<0.00001	e.g., Sticky or waxy granules or flakes, and particles >100 µm that are not easily ground or abraded to smaller particles.	None

Vapor Pressure (kPa)	Dustiness	Rating
≥0.00001 to <0.5	e.g., Plastic granules, pelletized fertilizers; dry garden peat, sugar, salt	Low
0.5 to 10	e.g., Talc, graphite	Medium
>10	e.g., Cement dust, milled powders, plaster, flour, lyophilized powders, and process-generated fumes	High

[C] Dermal penetrability as defined according to Schuhmacher-Wolz, U., et. al., 2003.

Dermal Permeability Coefficient (*Kp*)	Rating
< 10^{-5} cm/hr	None
< 10^{-4} to ≥ 10^{-5} cm/hr	Low
< 10^{-2} to ≥ 10^{-4} cm/hr	Med
≥ 10^{-2} cm/hr	High

Table 2: Proposed Exposure Assessment Strategy for Professional Uses and Workers

Professional Uses / Exposures (Workers):

GHS Classification		Dispersive Handling / Use[D]								Limited & Non-Dispersive Handling / Use[4]							
		Volatility / Dustiness[2]				Dermal Penetrability[3]				Volatility / Dustiness[2]				Dermal Penetrability[3]			
		High	Med	Low	Not	High	Med	Low	Not	High	Med	Low	Not	High	Med	Low	Not
Acute Toxicity	1																
	2																
	3																
	4																
	5																
Respiratory Sensitization	1A																
	1B																
Germ Cell Mutagenicity	1A																
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	2																
Carcinogenicity	1A																
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	2																
Toxicity to Reproduction	1A																
	1B																
	2																
	Lact.																
STOT-SE	1																
	2																
	3																
STOT-RE	1																
	2																

[D] Dispersive and Limited / Non-dispersive uses are defined according to the table below:

Dispersive Handling / Use	Limited & Non-Dispersive Handling / Use
Spraying, rolling, brushing, spreading, wiping, troweling, pouring, pumping / siphoning into open containers, dumping, shoveling, high-speed cutting, burning, grinding, welding, brazing, arc gauging, melting, paving, gluing (unless limited to outdoors), etc.	Greasing, oiling, caulking, hand sanding and scraping, drilling (hand-tool), etc.

[B] Volatility - see industrial handling / uses above.

[C] Dermal permeability - see industrial handling / uses above.

Table 3: Proposed Exposure Assessment Strategy for Consumer Uses and Consumers

Consumer Uses / Exposures (Consumers)

GHS Classification		Dispersive Handling / Use[D]	Non-Dispersive Handling / Use[E]
Acute Toxicity	1	Not Recommended in these consumer products	
	2		
	3		
	4		
	5		
Respiratory Sensitization	1A		
	1B		
Germ Cell Mutagenicity	1A	Not Recommended in these consumer products	
	1B	Not Recommended in these consumer products	
	2		
Carcinogenicity	1A	Not Recommended in these consumer products	
	1B	Not Recommended in these consumer products	
	2		
Toxicity to Reproduction	1A	Not Recommended in these consumer products	
	1B	Not Recommended in these consumer products	
	2		
	Lact.		
STOT-SE	1		
	2		
	3		
STOT-RE	1		
	2		

[E] Non-dispersive uses are those where the substance is tightly bound within an article or formulation such that it cannot physically become airborne or absorbed through the skin, or the substance is packaged in such small quantities making it impossible to release a sufficient quantity to cause adverse health effects. All other types of handling / uses are considered dispersive.

In cases where an exposure assessment is triggered for only one route of exposure but not the other, both routes (dermal and inhalation) should be assessed to account for the total exposure unless the substance is “not” volatile / dusty or is “not” capable of significantly penetrating the skin. In addition, substances which are persistent, bioaccumulative, and toxic (PBT), or are very persistent and very bioaccumulative (vPvB), warrant special consideration. For these substances, it is important to also consider the nature and extent of releases to the environment from all sources and how the substance is distributed in the environment, and to assess the resultant “indirect” exposures that may occur in combination with the direct exposures noted above. The details of these types of assessments is outside the scope of this paper but may be addressed separately in the future.

IV. DISCUSSION

There are, in general, four entities that play key roles in the supply and use of chemicals in the marketplace; the regulators, the manufacturers / importers, downstream processors / formulators and distributors, and the users (workers / consumers). By examining more closely each group's role within the [chemicals management] regulatory framework, an opportunity to establish clear responsibilities and expectations for exposure assessment was revealed. Consider the following typical responsibilities / expectations that can exist within a simple supply chain (Table 4).

Table 4: Supply Chain Responsibilities

Entity	Responsibilities in the Supply Chain / Regulatory Framework
Agency / Regulators	To ensure a regulatory framework is established and enforced that facilitates the safe manufacturing, supply, and use of chemicals in the marketplace.
Manufacturers / Importers (M/I)	To produce and supply chemicals that, based on available information, can be used safely and to ensure other entities in the supply chain are provided with sufficient information to use them safely.
Downstream Processors / Formulators and Distributors	To provide a safe workplace using the information provided by the M/I, to communicate appropriate safety information down the supply chain, and to ensure use and exposure information is communicated up the supply chain.
Users (Workers & Consumers)	To take responsibility for their own safety when handling hazardous chemicals by following the safe handling procedures as established by the employer (workers), or as established on product labels or other supplemental data sheets (workers and consumers).

As defined above, the roles / responsibilities of the M/I include assuring that the products they place on the market can be used safely, but not assuring that they are, in fact, actually being used safely. This would be accomplished by identifying and communicating appropriate / feasible RMM through, among other things, the prudent use of exposure assessment. While this is consistent with the recommendations put forth by the United Nations Environmental Programme (UNEP) in their "Global Chemicals Outlook Towards Sound Management of Chemicals Synthesis Report for Decision-Makers" (UNEP, 2012), those recommendations can be interpreted to mean that the M/I has an obligation to visit customer sites to verify safe handling. While this may be necessary and appropriate in some cases for some highly hazardous chemicals, it is largely impractical and unnecessary in most cases. Instead, the downstream processors, formulators, distributors, and end-users should be held accountable for actual safe handling and use when given appropriate RMM to follow.

In addition to clarifying the role of the M/I, the strategy we have outlined above was formed out of the rationale presented in Table 5, below.

Table 5: Proposed Exposure Assessment Rationale

Rule #	Rule / Description
General:	
1	All uses of / exposures to the substance must be considered, but only those uses / exposures that meet certain criteria will need special attention in terms of RMMs and/or exposure assessment.
2	An exposure assessment would not be warranted for substances that are aspiration hazards, corrosive or irritating to skin or eyes, or that cause allergic skin sensitization. The RMMs for these types of hazards can be determined without regard to the quantity and frequency of exposure and can be readily implemented by workers and consumers alike.
Industrial Uses / Exposures:	
3	An exposure assessment would not be warranted regardless of hazard for substances used only in industrial settings in closed continuous processes. Adequate RMMs can be developed by the M/I and communicated on the safety data sheet without knowing the level of exposure. Likewise, the downstream processor / formulator has (or should have) the capabilities to interpret and apply the information supplied by the M/I and is in the best position to ensure the safety of the exposed worker population.
4	For substances used only in industrial settings where the process is not a closed continuous one, an exposure assessment would not be warranted for substances that pose a slight to moderate health hazard. Adequate RMMs can be developed by the M/I and communicated on the safety data sheet without knowing the level of exposure. Likewise, the downstream processor / formulator has (or should have) the capabilities to interpret and apply the information supplied by the M/I and is in the best position to ensure the safety of the exposed worker population.
5	For substances used only in industrial settings but in other than closed continuous processes, an exposure assessment would generally be necessary for all substances that are highly hazardous to human health.
Professional Products / Uses:	
6	For substances used in professional products, an exposure assessment would not be warranted for substances that pose only a slight health hazard. Adequate RMMs can be developed and communicated by the M/I or formulator on the safety data sheet and product labels without knowing the precise level of worker exposure. Likewise, users are (or should be) sufficiently trained to handle these types of substances / products safely without having to apply extraordinary measures.
7	For substances used in professional products, an exposure assessment may be warranted for some substances that pose a slight to moderate health hazard depending on the type of hazard and type of product / use. An assessment is generally necessary for all substances that are highly hazardous to human health. Exceptions to these rules are when some physical-chemical property precludes release of the substance from the product or when the product is packaged in such a way (i.e. small quantities) as to preclude sufficient exposure.

Consumer Products / Uses:	
8	For substances used in consumer products, an exposure assessment would be necessary for any substances hazardous to human health except when some physical-chemical property precludes release of the substance from the product or when the product is packaged in such a manner (e.g. small quantities or as an article) so as to preclude sufficient exposure to result in toxicity. Substances that cause allergic skin sensitization should not be used in certain types of consumer products.

These underlying principles are rooted in a commonly accepted belief that access to, and the effectiveness of, exposure controls among the various user groups is not equal. Whether it is engineering controls, personal protective equipment, and/or procedures/administrative controls; industrial users have greater access than professional users, and consumers are least likely to have access to or will use such controls. Although industrial users will likely work with the greatest volumes of substances, this does not translate to greater exposure or risk.

While our strategy shares some common features with the various control banding approaches, it is tailored to fit within a chemicals management regulatory framework where the M/I is made to be responsible for performing the exposure assessments. Control banding approaches are either offered as a substitute for professional expertise or are used in industrial workplaces that handle potent pharmaceutical drugs for which there are no exposure limits. They are of little value for consumer products.

Our strategy also shares some common features with the priority setting system that has recently been proposed by the U.S. Chemical Industry (ACC, 2011), however, the context of this system was given as: "*to determine which chemicals should receive full safety assessments so EPA can focus its resources where they are most needed*". In other words, it was given for EPA to prioritize its focus. It is surprising to us that industry would propose such an approach since it can create a so-called "hit list" of chemicals. In addition, this type of approach can be expected to result in an abundantly large number of chemicals that fall into some gray category of not quite making the hit list but also not making the low risk group. Instead, our focus is on specific uses or exposures of concern rather than on the chemicals of concern.

V. CONCLUSIONS

Simply put, we believe that the *indiscriminate* use of exposure assessment within a chemical registration framework is unnecessary and has little chance of yielding the desired outcome. Instead, exposure assessment should be reserved for those situations where the path forward is unclear, either because the need for risk management measures is unclear or because the types of risk management measures are unclear. In this paper, we've begun outlining a process by which exposure assessments can be reserved for those situations where they are needed the most, without jeopardizing safety, so that they can be performed in a more thoughtful and rigorous manner. We believe this strategy can not only be incorporated into national and international

chemicals management programs, but can also be used voluntarily by industry to help prioritize the use of exposure assessment as part of their ongoing product stewardship efforts.

References

ACC (2011). American Chemistry Council (ACC). Testimony of The Honorable Cal Dooley, President and CEO American Chemistry Council, Before the Senate Committee on Environment and Public Works and the Subcommittee on Superfund, Toxics & Environmental Health, "Legislative Hearing on the Safe Chemicals Act". November 17, 2011.

EC (2001). Commission of the European Communities (EC). WHITE PAPER. Strategy for a future Chemicals Policy. COM (2001) 88 final. Brussels, 27.2.2001. Available online at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2001:0088:FIN:en:PDF

ECHA (2012). European Chemicals Agency (ECHA). Evaluation under REACH. Progress Report 2011. ECHA-12-R-02-EN. ISSN: 978-92-9217-643-3. ISBN-13: 1831-6506. 27-Feburary-2012. Available online at: http://echa.europa.eu/documents/10162/17221/evaluation_report_en.pdf

Schuhmacher-Wolz, U., et. al. (2003). U. Schumacher-Wolz, F. Kalberlah, R. Oppl, and J. J. Van Hemmen. A Toolkit for Dermal Risk Assessment: Toxicological Approach for Hazard Characterization. Ann. occup. Hyg. Vol. 47, No. 8, pp. 641-652, 2003.

UNEP (2012). Global Chemicals Outlook: Towards Sound Chemicals Management. Chapter III: Instruments and Approaches for the Sound Management of Chemicals. Ken Geiser and Sally Edwards, UNEP 2012. Available online at: http://clients.criticalimpact.com/go.cfm?a=1&b=173982&c=24360&f=c702c32e485829b4ce9765d727bee285322a70e5742bfe1d