Thought-starter on a Framework to Implement the Chemical Assessment and Management Program (ChAMP) under the Montebello Agreement

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1.0 Introduction

1.1 The Montebello Agreement

On August 20-21, 2007, United States President George Bush, Canadian Prime Minister Stephen Harper and Mexican President Felipe Calderon met in Montebello, Quebec, to discuss the Security and Prosperity Partnership of North America. Upon conclusion of the meeting the U.S. Environmental Protection Agency (EPA) announced, as part of a trilateral agreement (the Montebello Agreement; see www.tcata.org/montebellagreement103007.pdf and www.epa.gov/chemrtk/pubs/general/sppframework.htm), a major shift in how chemicals will be addressed and managed in the U.S. The Montebello Agreement sets out a plan to coordinate risk assessment and risk management activities across North America, building on work done under the Canadian Chemicals Management Plan (www.chemicalsubstanceschimiques.gc.c/plan/index_e.html) and the U.S. EPA High Production Volume (HPV) Chemical Challenge (www.epa.gov/chemrtk/index.htm). The goal of the agreement is to enhance trade among the three countries, while ensuring protection of human health and the environment and retaining sovereignty.

1.1.1 Current and Future Chemicals Management in North America

Under the Canadian Environmental Protection Act (CEPA see www.ec.gc.ca/ceparegistry) of 1999, the Canadian Parliament required Environment Canada to work with Health Canada to conduct screening-level risk characterizations on all chemicals in the Canadian marketplace. As part of an already close working relationship, Canadian authorities met with their colleagues at the U.S. EPA to discuss tools and methods used in the U.S. to evaluate new chemical substances. The mandate of CEPA 1999 led Canadian regulatory authorities to devise novel and workable approaches to risk evaluation, leading to a truly tiered, targeted and risk-based approach to chemical risk assessment and risk management, which is called the Canadian Chemicals Management Plan (CCMP). The initial tier makes use of conservative, predictive modeling and assimilates hazard data from chemicals with similar molecular structures—i.e., structure-activity relationship analysis, or SAR—to assist in the hazard characterization of the chemicals. Potential exposure to the substances, the other integral part of the risk equation, was characterized employing general use categories and production/import volumes. These methods allowed the Canadian authorities to evaluate 23,000 chemical substances quickly and focus scarce resources on those substances that require further study and possible risk management action.

In 1999 the U.S. EPA announced the HPV Challenge, a voluntary program in which chemical companies would sponsor toxicity and other testing on chemicals that were produced or imported at amounts greater than 1 million pounds per year in aggregate. Chemical companies responded and volunteered to provide information on over 2,100 HPV chemicals. The program has resulted in an unprecedented amount of hazard data being made available to the public. EPA has already posted initial hazard characterizations on the EPA web site (http://iaspub.epa.gov/oppthpv/hpv_hc_characterization.get_report).

The Agency plans to post several hundred more in 2008. To build upon this ongoing work and the work of the CCMP in Canada, EPA announced at GlobalChem 2008 its new Chemical Assessment and Management Program (ChAMP). Under ChAMP, the Agency stated it will screen out the low toxicity chemicals first, and then utilize production and use data from the 2006 Inventory Update Rule (IUR) reporting to characterize the risks of the remaining HPV chemicals that are categorized as moderately to highly toxic. After conducting risk characterizations of the HPV chemicals, EPA will turn its attention to moderate production volume (MPV) chemicals, those produced or imported in amounts between 25,000

and 1,000,000 pounds annually. The hazard and risk characterizations for HPV and MPV chemicals will provide the EPA with information necessary for their future risk assessments and risk management activities.

1.1.2 Potential Impact of the Montebello Agreement on International Chemicals Policy

Chemicals management policy, including the legislation and regulations that result from such policy deliberations, is one of the few types of law that can directly affect a company's ability to sell chemicals into the marketplace. For the past five years, chemicals management policy has been vigorously debated throughout the industrialized world. One of the primary factors leading to these discussions is the new European Union REACH legislation, a dramatically different chemicals management policy.

The chemicals policy debates in the U.S. accelerated several years ago when environmental groups saw the European REACH system (ec.europa.eu/environment/chemicals/reach/reach_intro.htm) as a model to achieve their goal of banning toxic chemicals. Work under the Montebello Agreement will provide a unique opportunity to affect the future of chemicals management policy both here and abroad. The ChAMP and CCMP approaches discussed under Montebello are the only current regional models that are truly tiered, targeted and risk-based. The conceptual foundation of ChAMP and CCMP can provide regions that do not currently have chemicals management policies a rational and workable approach to chemical risk management.

1.2 Proposed Framework for Implementation of ChAMP

This document lays out a proposed framework to consider when implementing ChAMP in the United States. The document addresses industry's perspective on hazard, exposure and risk, and then moves into the concepts of tiered approaches and targeted risk assessment. The framework outlined in this document reflects the consensus of a broad coalition of industry sectors, including automotive, aerospace, electronics, consumer products and chemicals, and seeks to institutionalize a tiered, targeted and risk-based approach to chemical risk assessment and risk management across North America. Industry believes that the U.S. EPA and its colleagues in Canada are already implementing the conceptual framework outlined in this document; however, to institutionalize this thinking requires a more formal documentation of the practices that will be used to implement ChAMP.

2.0 Chemical Risk and Risk Analysis Concepts

2.1 The Difference between Hazard and Risk

One of the more important methods used in scientific study is called the "weight-of-evidence" approach. The weight-of-evidence approach simply means that scientists consider all available information pertaining to a given subject. Looking at only part of the picture can lead to inaccurate or misleading conclusions. When analyzing a chemical and trying to determine whether or not it could cause harm, the hazards are not the only things that count. An additional component to the equation, which is just as important, is the likelihood that someone could come into contact with the material. If little chance exists that someone could come in contact with a chemical, how could harm occur? To put it simply: HAZARD ≠ RISK.

In general, risk can be described as the likelihood that an undesirable event will take place. In risk analysis, complex mathematical models are often used to characterize risk in terms of probability, which

is based on past history. For chemicals, however, risk analysis typically uses a different approach to characterize the probability component. Risk for a chemical is seen as a function of the intrinsic hazards possessed by the chemical (possibly producing the undesired event) and the potential to which someone or something could be exposed to those hazards (the likelihood). This is one of the most important concepts to remember when discussing chemical safety. Even if a chemical has hazardous properties, that does not mean it is likely to cause harm.

2.2 General Approaches to Chemical Risk Analysis

A chemical risk analysis may be qualitative, quantitative, or a combination of both approaches. The terms *analysis* and *characterization* are used frequently in this document because their meanings are more general than *assessment*, which has a quantitative connotation. No matter which approach is used, chemical risk analyses share a common trait: hazard and exposure must both be considered. This consideration does not have to involve a mathematical equation and produce a quantitative value; however, numerical values can be helpful for comparing different chemicals and prioritizing them for possible further work.

When analyzing chemicals for risk, it is important to remember that the potential for exposure is directly related to each chemical's use and the activities associated with each type of use. Therefore, analyzing chemicals for risk is usually done on a chemical-by-chemical and use-by-use basis. Cases exist, however, where chemicals can be grouped according to similar use and activity patterns. For example, if a company makes seven different substances that go into hand soap, shampoo or other products applied to the skin but washed off in less than a minute, the use and activity patterns for the seven chemicals would be similar. The analyst could feasibly group these chemicals and compare the constant use and activity pattern with the hazards of each substance. In fact, by keeping the use and activity pattern constant and organizing the group of chemicals according to their hazards, e.g. from high to low, a qualitative risk profile could be developed for the entire group. Because of a similar exposure pattern, the resulting risk profile would correspond directly to the hazards, so the chemicals would also be organized according to risk, i.e. from high to low. No matter what analysis method is chosen, it is important to remember that chemical risk analysis must consider both a chemical's hazards as well as its potential exposures.

2.3 Tiered Approach to Chemical Risk Analysis

Some chemical risk characterizations employ extensive laboratory testing for hazards and complex mathematical models and distribution functions for the exposure component, but most chemicals do not need such intensive scrutiny. Instead, a tiered approach to hazard, exposure and risk characterization is used, which saves time and resources, especially when analyzing the risks of many different chemicals. A tiered approach is nothing more than starting with a general look, then targeting and refining certain areas to bring about more clarity or certainty. It is an iterative process during which hazard and exposure are looked at simultaneously, throughout the entire process. To develop a complete hazard characterization and exposure characterization separately, before comparing the two, could result in wasted work, time and resources, because some areas may not require the same level of detail as others.

Conducting a full suite of toxicity testing is generally not necessary to begin a chemical's hazard characterization. Often, existing information is adequate to qualitatively or semi-quantitatively characterize the chemical with a simple analysis of hazards and potentials for exposure to yield a measure of risk. To begin, the analyst can look at the composition, chemical/physical properties, health effects information, hazard ratings, e.g., NFPA, HMIS, etc., and use information from the chemical's Material

Safety Data Sheet (MSDS) and other readily available sources of hazard information. If the analyst believes that there are gaps for certain endpoints, then conservative modeling, based on structure-activity relationships, can be conducted to fill in those gaps.

A tiered risk approach for chemicals can begin with a qualitative or semi-quantitative look at the known hazards and how the chemical is used. Often, a qualitative look at just a few factors will show that the risks posed by a particular chemical are adequately controlled and do not require more scrutiny. For some chemicals, however, this initial tier may not provide as clear a picture of risk as one would like.

The next step, and all subsequent steps in a tiered analysis, is to identify the area or areas in which more information could yield a clearer picture, including the methods to acquire that information. This could mean looking at the following:

- exposure controls, such as engineering or personal protective equipment
- physical properties that could exacerbate or mitigate exposures
- surrounding environments in which the chemical is used
- a larger portion of the life-cycle, including disposal of containers

Or, it could mean conducting a more definitive hazard study or doing some exposure modeling or monitoring. In practice, each subsequent tier should refine one or more areas of the hazard or exposure characterization, which will act to refine the overall risk profile.

One important thing to remember is that the decision to refine one part of the risk equation, e.g., hazard, may be dependent on the information in the other part, i.e. exposure. Another way to express this concept is that *hazard information should be driven by exposure information, and vice versa*. This is what makes risk analysis an iterative process. This is commonly referred to as a "targeted approach." For example, if a chemical is a known skin sensitizer, then the analyst may want to concentrate on certain exposures that are relevant to that endpoint, such as when the dermal exposures could occur. On the other hand, if a chemical is used in a consumer item and could be released in amounts that lead to the potential exposure of pregnant women, then the analyst would concentrate on toxicity endpoints that could affect that subpopulation, such as genetic, developmental and reproductive toxicity. Appendix A provides a detailed discussion of the components of a tiered, targeted and risk-based analysis.

3.0 Chemical Risk Screening and Prioritization

Chemical risk screening is not intended to be an exact science. Its primary use is for prioritizing what to address, in what order and to what initial level of detail. Risk screening allows the placement of resources where the efforts will be most beneficial. When the approach considers hazard and exposure, a general risk screening method should suffice for the first tier in a tiered risk analysis. If areas exist that require more information, spotting these areas in a tiered, step-wise approach will be easier than when a classic risk assessment approach is used.

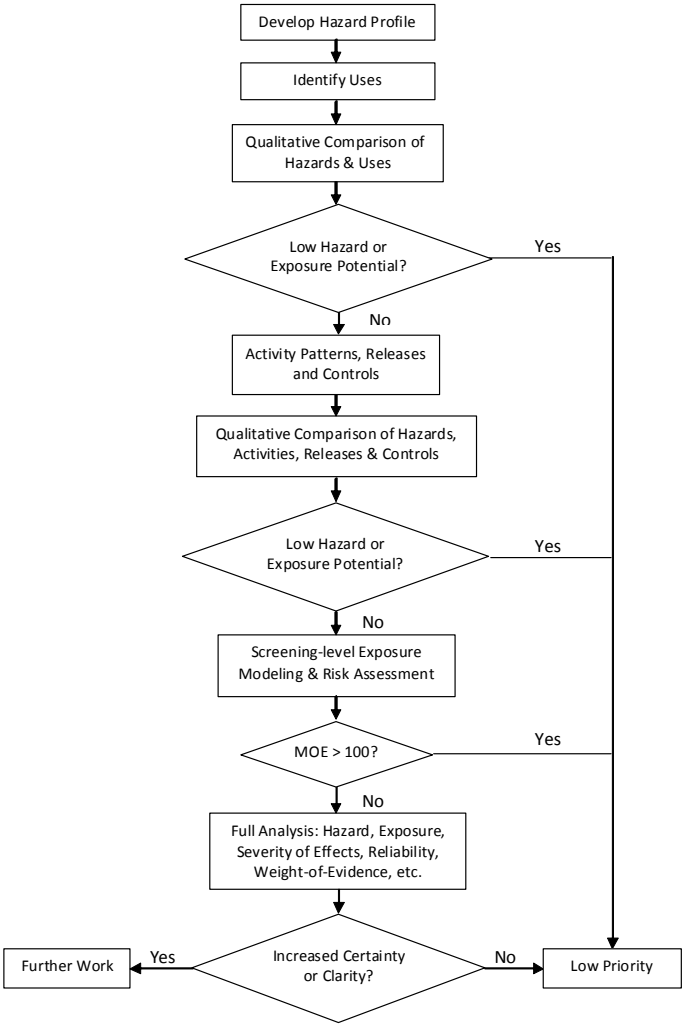
If a company decides to refine a screening-level analysis, starting over from scratch is not necessary. Typically, factors that can affect direct exposure are identified in the first step. The analyst decides whether more information is needed, e.g., disposal of residual materials, disposition of empty containers, cleaning of equipment, etc., or if the existing information needs to be further refined.

The classic approach to risk assessment is different and does not usually follow a tiered and targeted approach, primarily because the objectives are different from the goals of chemical risk screening, where the efficient use of time and resources are incorporated into the risk assessment process. The goal of both risk assessment processes is to reduce uncertainty; chemical risk screening expedites risk-based decision-making and allows for the handling of many different chemicals in a more efficient and effective manner. Both the classic risk assessment and chemical risk screening approaches provide adequate information for synthesizing risk management recommendations. However, the screening approach provides a means of prioritizing chemicals and assessing them in a rapid, practical and sustainable manner. Furthermore, this approach allows the allocation of limited resources so that the protection of human health and the environment are maximized. Appendix C contains an example of how a risk-based chemical screening and prioritization method could be conducted.

4.0 An Example Framework for a Tiered Risk Analysis Process

Information gathering is a pre-step in the risk analysis process. The process cannot begin without at least some hazard and exposure-related (use) information. The analytical process, see Figure 1, begins with the development of a hazard profile for the substance of interest, as well as similar materials when necessary, based on available information from the scientific literature that can include laboratory studies, structure-activity relationships and predictive models. During the hazard characterization process, care should be taken to distinguish between measured and modeled data, where measured data is given more weight. Generally, after a chemical is manufactured, it can be consumed on-site, sold into commerce as is, repackaged or blended into a product mixture. Tracking how the chemical flows through commerce can help identify how and where the chemical is ultimately used and what form the chemical is in at the point of use. For chemicals that are used in many different applications, it may be more practical to first look at the major uses that consume the majority of

Figure 1: Risk Analysis Process Flow Diagram



production and import volume. It is rarely necessary to track every molecule in commerce before one can gain a general understanding of risks associated with certain uses of a particular substance. Once the uses are identified, an initial qualitative review of the hazards and general exposure potential that is associated with each use, can give a rough indication of the associated risks. If low hazard or exposure potential cannot be readily demonstrated, the next step in the process focuses closely on the activity patterns associated with each use and potential release points throughout the lifecycle. After the release scenarios and activity patterns have been identified, a look at physical and chemical properties, exposure controls and other factors that can mitigate or exacerbate exposures will allow for a clearer picture regarding exposure potential. At this point, another qualitative review of the hazard and exposure information will help inform the decision for the next step. If, at this point, it can be demonstrated that there is a low hazard or exposure potential, then the chemical can be considered a low priority for further work. This is not a static process, however. As new information arises, such as new toxicity data or a new use is identified, then those new factors should be considered in the overall risk characterization.

If the risk picture is still uncertain after an initial qualitative review, then conservative estimates of exposure and another more intensive analysis with the known hazard values could be useful. Screening-level exposure estimates can be derived several different ways. One method is to use regulatory limits as conservative estimates. For instance, using the high-end value from a release permit and adding the amount of residue that could be washed down the drain would provide a conservative amount of chemical to which people could be exposed by way of background or environmental exposures. Similarly, a time-weighted exposure threshold, such as an OSHA occupational "Permissible Exposure Limit," could provide a conservative estimate for potential direct exposures at manufacturing or use sites.

Another conservative approach to generating exposure estimates is by using screening-level computer models. The U.S. EPA makes several exposure models available to the public free of charge (see Appendix B.1). Typically, these types of models are built around assumed activity patterns and employ default values for various factors that could affect exposure. The models do require some initial inputs, such as use categories and release information, but it is not so burdensome that a person fairly new to exposure assessment cannot figure it out. The outputs from the screening-level exposure models are usually in units of milligrams of chemical per day, which can be directly compared to a chemical's No Observable Adverse Effect Level (NOAEL) from toxicity studies. The numerical value that represents the ratio between the NOAEL level and the exposure level is referred to as a Margin of Exposure (MOE) and is calculated by dividing the NOAEL by the exposure estimate to yield the MOE. A value of 100 is generally considered to be conservatively safe in a screening-level assessment. Various other ratios use different toxicological values, but for simplicity the MOE is one of the more commonly used values for risk screening.

After estimating exposures and reviewing the MOE values, the analyst may decide that further work is required to reduce the uncertainty of a screening-level assessment. In that case, targeting which hazard and exposure information could be refined is often the next step in a tiered process. Professional judgment must be used to determine where and how to refine the information. An option could be to take some measurements to replace default values, such as residue left in empty containers or efficacy of water treatment at a water treatment facility, or it may mean conducting a more definitive toxicological study. Either way, it is up to analysts to decide what best suits their needs.

Moving to higher tiers in a risk analysis usually means considering more information to build a comprehensive picture of risk and reduce uncertainty, or refining existing information for clarity. Higher

tiers in the process can include aggregating all known potential exposure information, defining a representative hazard value, targeting specific toxicological endpoints and refining the risk analysis, conducting higher level exposure modeling or actual monitoring studies, or some other approach to reduce uncertainty about the risk.

5.0 Conclusion

The ChAMP and CCMP initiatives under the Montebello Agreement present a unique opportunity to institutionalize a truly tiered, targeted and risk-based approach to chemical risk management across North America. Further, a workable alternative can be provided for those regions that are seeking to develop a chemical risk management policy or augment an existing policy. This thought-starter can serve as a starting point for discussions on what that framework should look like.

APPENDIX A
Components of a Tiered, Targeted and Risk-based Analysis

A.1 Hazard Characterization and the Tiered Approach

The initial consideration of a chemical's hazards with uses could result in a conclusion that no further information is required. That is not always the case, however, and the review could lead the analyst to conclude that more work is needed. If that is the case, then a more extensive, but still focused, gathering of information on specific hazard endpoints and potential sources of exposure will further the analysis and may save valuable time and resources. For instance, if the greatest likelihood for exposure is through inhalation, then obtaining information on ingestion or dermal contact may not be the best way to refine a risk analysis for that particular chemical.

For more hazard data, the analyst can search the readily accessible, internet-based, scientific literature for a chemical's hazard information (see Section A.1.1 for suggestions). If significant gaps still exist, the analyst can focus on the hazards of materials with similar physical/chemical properties that are likely to have similar hazards, and fill the gaps by extrapolation. Further, the structure of the chemical can be used to make predictions on the chemical's potential hazards. The EPA and others employ models to predict certain hazards according to a substance's structure.

Under its Sustainable Futures Program, the EPA provides public access to the same "structural" models it uses when evaluating new chemicals that are about to enter into commerce. Most of these models are conservative in nature and are not intended to provide a definitive view of a chemical's hazards. Rather, the models conservatively predict certain hazards based on what is known about the activity of structurally similar substances.

The properties of substances may not always be predictable through modeling. Certain chemicals with complex molecular structures present unique challenges to many predictive models. If no appropriate surrogate data exist for a particular substance, and the molecular structure is not well-suited for modeling, significant data gaps may exist and a company may need to conduct laboratory testing.

To save time and preserve animal resources, the necessary testing can also be approached in a tiered fashion. Initial screening-level tests use isolated organisms, e.g. bacteria or cultured cells for the "*in vitro"* type of testing. This approach can give rapid answers to questions about the potential hazards of a chemical and reduces the need for animal resources. For general purposes, the following example may be useful to get acquainted with the tiered approach for hazard characterization.

Tier 1: General information regarding the hazards, e.g., NFPA, NIOSH, etc.

Tier 2: Specific published data regarding the hazards of the chemical and for structurally similar substances with similar chemical and physical properties

Tier 3: Data from predictive models, based on structure-activity relationships

Tier 4: Data from *in vitro* laboratory experiments to evaluate hazards

Tier 5: Data from *in vivo* laboratory experiments to identify and quantify hazards

Tier 6: Comprehensive in vivo experiments, e.g., multi-generational, dosing variation, etc.

Toxicologists use the results from these screening-level tests to help determine if a more definitive study is required to fully understand a chemical's potential hazards. This is commonly referred to as a "targeted or trigger-based approach" to hazard characterization. If the decision is made to advance to a higher-tiered program, the testing typically involves whole animals in an "*in vivo"* type of testing and generally looks at more sophisticated toxicity endpoints, e.g. reproduction, and is more complex to conduct.

Higher-tiered testing can be targeted to investigate the effects of different exposure periods, a specific toxicity endpoint or an area of health effects where more information is needed. As the testing moves up the tiers, longer periods of chemical dosing are typically employed or multiple generations of animals can be used. The tiered approach, beginning with non-animal methods, saves time and spares animals and, allows resources to be employed most efficiently and effectively.

A.1.1 Resources for Hazard Information and Analysis

There are several repositories for chemical information, including:

US EPA HPV Challenge web site:
www.epa.gov/chemrtk/index.htm

National Library of Medicine's TOXNET:
http://toxnet.nlm.nih.gov/

as well as a number of other sources. The U.S. EPA also provides guidance on how to go about reviewing and using structural similarities, i.e. structure-activity relationships, in hazard characterizations on their HPV Challenge web site:
www.epa.gov/chemrtk/pubs/general/guidocs.htm

Information on the Sustainable Futures Program and EPA's predictive models can be found at http://www.epa.gov/oppt/sf/ .

A.2 Exposure Analysis and the Tiered Approach

Similar to hazard analysis, a full quantification of all potential exposures is usually not necessary to conduct a risk characterization. Exposure analysis is particularly well-suited for a tiered approach, because even if a company wants to quantify some or all of the exposures for a chemical, known uses and associated activity patterns must first be qualitatively identified. The individual tiers that make up a tiered exposure analysis are not clearly defined in most guidance publications on the subject. For general purposes, the following example may be useful to get acquainted with the tiered approach for exposure analysis.

Tier 1: General use categories and production/import volumes

Tier 2: Consideration of exposure controls, e.g., engineering controls, PPE, etc., and other factors, e.g., confined spaces, substance properties, temperature, etc., that could mitigate or exacerbate exposures

Tier 3: Expansion to life-cycle factors, e.g., product disposal, disposition of empty containers, cleaning of equipment, releases into the environment, etc.

Tier 4: Screening-level modeling for conservative exposure estimates

Tier 5: Screening-level modeling with the same models as Tier 4 but with the incorporation of measured data to change default values and justification for these changes.

Tier 6: Use of measured data as primary source of estimates

Tier 7: Comprehensive aggregate exposure assessment

Tier 8: Cumulative exposure assessment, which usually requires sophisticated modeling.

Like hazard analysis, exposure can also be approached in a targeted manner. Several ways exist to target specific areas of exposure potential for examination. For instance, if a chemical has an endpoint that indicates a high hazard potential, then an effective approach could be to study potential exposures that would be directly related to that endpoint. Another way to target the analysis is to concentrate on specific uses with the greatest exposure potential. Some uses might be associated with direct potential exposures that are much higher than all other exposures combined. At a screening level, it is scientifically sound to concentrate on the highest exposures and not try to capture every possible exposure scenario.

When considering potential exposures, it is important to be as thorough as possible from the beginning. A life-cycle approach can be used to qualitatively identify potential sources of exposure. That does not mean that an analysis must account for every molecule or that all exposures must be considered at the same level of detail. Rather, the life-cycle approach can be used to ensure that a complete consideration was undertaken. This approach also provides the opportunity to communicate the completeness and transparency of the analysis. Appendix B provides examples of possible exposure analysis components.

Appendix B
Example Components of a Screening-level Exposure Analysis

Uses

A chemical's use(s) is arguably the most important piece of information for exposure analysis. Most uses can be generalized and binned into different categories (e.g., intermediates, cleaning agents, surfactants, etc.). Use descriptions can also be specific, such as an ingredient in a brand-name product, which is commonly used by a certain type of person in a specific setting.

Exposure Scenarios

Exposure scenarios are scenarios under which the chemicals are used. Most scenarios can be generalized and binned:

- cleaning sinks
- washing dishes
- sealing floors
- transferring chemicals to other containers
- Scenarios can also be specific:
- cleaning sinks in a hotel room versus a laboratory
- washing clothes by hand versus machine
- sealing floors with a sponge mop versus machine

Activity Patterns

Activity patterns contain the details of how chemicals are used in the exposure scenarios. Details, such as frequency, duration and the amount of chemical used in each application can help characterize the potential for exposure and associated risk from chemicals. These patterns can also be used as inputs for generating exposure estimates. Physical surroundings, such as space, temperature and other parameters can also be useful, because these factors may indicate the exacerbation or mitigation of a potential exposure. An important factor that serves to reduce exposures is exposure control which includes air-exchanges, i.e. ventilation, and personal protective equipment.

Factors that Mitigate or Exacerbate Exposures

Before getting too far into the analysis, a smart practice in the tiered and targeted approach is to explore factors that can mitigate or exacerbate certain exposures. For example, a substance could be an inhalation hazard; however, if that substance had the physical form of large granules versus much smaller respirable dust particles, one could reasonably conclude that the inhalation risk is lower. Other physical properties, such as boiling point and vapor pressure, can also affect the exposure potential and the associated risk from a chemical.

In addition to physical attributes of the chemical itself, the conditions and activities associated with how the chemical is used can have a bearing on risk. Temperature, engineering controls and personal protective equipment can all have an impact. In fact, understanding these factors is paramount to safety at chemical manufacturing and handling sites.

Background Exposures

Background exposures, also referred to as environmental exposures, are those human exposures that are encountered in everyday life that result from chemicals being released into the environment naturally, as a result of lifestyle choices, e.g. hobbies and smoking, or from manufacturing, use or disposal. Life-cycle analysis can be used to identify releases that could lead to exposures. For example, conservative exposure estimates can be derived using information from release permits. Quantifying background exposures is more complex and labor-intensive that quantifying direct exposures; and, background exposures are usually orders of magnitude less than direct exposures. The decision to look at background exposures is often driven by a substance being detected in an organism and the absence of apparent direct exposures.

B.1 Resources and Tools for Exposure Analysis

While chemical exposure analysis is still a fairly young science, plenty of guides and tools exist that are publicly available. The Alliance for Chemical Awareness (ACA), a consortium of chemical trade groups and companies, has developed a technical framework and guidance documents on how to analyze for potential exposures. The guidance is somewhat detailed and more appropriate for those who wish to quantify exposures in the upper tiers, but is a good starting point to learn about various approaches to exposure analysis. The guidance and tools are available at www.chemicalawareness.org .

The U.S. EPA has also developed a great deal of guidance for exposure analysis and makes their computer-based exposure models available to the public under the Sustainable Futures Program. The models are inherently conservative and use default values to generate estimates. The default values can be changed to yield a more accurate exposure estimate, but any deviation from the default values needs to be fully explained and justified in the analysis, e.g. using measured data instead of a default value. For information, visit the EPA web site at http://www.epa.gov/opptintr/exposure/ .

Appendix C
Example of a Risk-based Chemical Screening and Prioritization Method

The following is an example of one method for screening and evaluating chemicals, which uses risk-based principles and simultaneously looks at hazard and the potential for exposure. It is not necessarily a predictive or quantitative approach; rather, it is tiered, targeted and geared for decision-making. **Please note that the objective of this example is only to demonstrate the feasibility of tiered, targeted and risk-based approaches.**

Gather existing hazard information on the substance of interest. If toxicity ranges are used, then the same ranges should be applied to the other chemicals of interest as well. This allows for a qualitative comparison between chemicals and avoids comparing apples with oranges.

If hazard data do not exist for a particular chemical, then identify a chemical with a similar structure or one that is chemically related to the compound of interest. For example, acid chlorides generally hydrolyze to their corresponding acids, especially in an acidic environment, such as the stomach. It is reasonable, therefore, to use the hazard information from the acid as a surrogate for the acid chloride. It is also appropriate to use extrapolation if the chemical of interest can be grouped into a category of chemicals with known hazards and its structure follows the same general pattern as the category. For instance, if the chemical of interest is a secondary linear alcohol, then it is reasonable to use data from other secondary linear alcohols to predict the potential range of toxicity for the chemical of interest.

If an appropriate surrogate cannot be found or if there are no data for any similarly structured compounds, then using one of the Sustainable Futures or other comparable structural models may be in order.

The General Use Pattern Table below lists generic types of uses (e.g., consumer, commercial or industrial) and general circumstances surrounding each type of use (e.g., whether or not workers are directly supervised, closed versus open system, etc.). The left column of the table can be used to assign qualitative values for comparison with other chemicals of interest. For this particular example, a numerical ranking system of 1 – 4, with 4 representing potentially higher degrees of exposure, is employed to illustrate how the general uses can allow for a qualitative comparison of potential exposures between different substances.

Although the listed examples do not try to capture all of the different use scenarios, these uses help to identify the value that best fits the situation. Again, this is not a quantitative tool; professional judgment is expected and encouraged.

General Use Pattern Table:

Value	Use Description
4	Used in consumer item intended to be ingested or inhaled, or direct skin application Examples: Additive for skin lotion Additive in air freshener
4	Commercial, institutional or industrial item used by hand as regular part of an unsupervised job Examples: Cleanser used by a cleaning person

	Degreaser used by a mechanic
3	Commercial or institutional item applied by hand as regular part of a job under direct supervision (see examples above)
3	Consumer item that releases substance and contact is incidental, or dermal contact but is not intended to be left on skin Examples: Additive for dishwashing detergent Paint vapors
2	Industrial item applied by hand as regular part of a supervised job Examples: Solvent used on an assembly line Adhesive used on a construction site
2	Industrial item used in an open system on a regular basis Examples: Blending and formulation process Processing solvent in automated electronics operation
1	Consumer item that may release substance at a slow rate Examples: Performance additive for food-use plastic Stain resistance substance in textiles
1	Industrial item used in a closed system Example: Closed-system intermediate in chemical process Processing solvent in a closed manufacturing process

The same principle outlined above can be used to also look at other key factors that have a bearing on potential exposure. The following Concentration Table assigns the same values, i.e. 1 – 4, according to the percentage range of concentration at the point of use. Dilutions of concentrated materials should be accounted for when selecting the appropriate range. This value can be used to help get a rough idea of the potential magnitude of exposure.

Concentration Template:

Value	Concentration Range
4	80 – 100%
3	40 – 80%
2	10 – 40%
1	< 10%

The following Frequency Table assigns values, i.e. 1-4, according to the frequency at which a chemical, or item that contains the chemical, is used. This applies to an average individual who would use this item.

Frequency Table:

Value	Frequency of Use
4	Once a day or more
3	Less than 3 days a week

2	Once or twice a month
1	Less often than once a month

The following Duration Table assigns values, i.e. 1-4, according to the duration in which a chemical, or item that contains the chemical, is used. As with the frequency table, this assumes an average individual following the item's intended use.

Duration Table:

Value	Duration of Each Use
4	Ingested, inhaled for 1 hour or more, or left on skin
3	Used for 30 minutes to 1 hour
2	Used for 15 to 30 minutes
1	Used for less than 15 minutes

The following Total Volume Table assigns values, i.e. 1-4, according to the total average annual production or importation volume of the chemical that goes into a specific use.

Total Volume Table:

Value	Total Annual Production or Importation
4	> 1,000,000 pounds
3	300,000 – 1,000,000 pounds
2	25,000 – 300,000 pounds
1	Less than 25,000 pounds

This same approach can be used for any number of relevant factors, as long as the symbolic values are consistent. Because the same values, i.e. 1-4, are used for all of the tables, one can get a qualitative feel for the exposure component of the risk equation. Weighting systems can also be used in this type of approach to give some factors more weight than others. The idea with this type of approach is to begin with a simple, qualitative look at uses, then add other factors to help clarify and refine the information for decision-making.