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Advancing Safer Alternatives Through Functional Substitution

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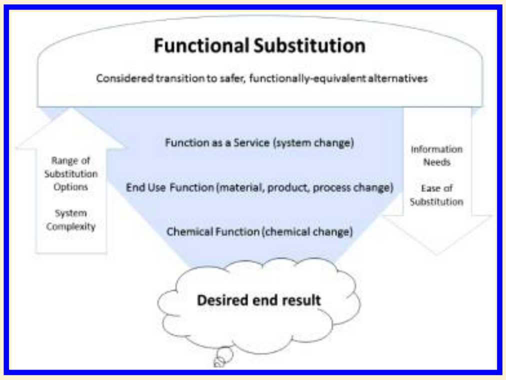
ABSTRACT: To achieve the ultimate goal of sustainable chemicals management policy—the transition to safer chemicals, materials, products, and processes—current chemicals management approaches could benefit from a broader perspective. Starting with considerations of function, rather than characterizing and managing risks associated with a particular chemical, may provide a different, solutions-oriented lens to reduce risk associated with the uses of chemicals. It may also offer an efficient means, complementing existing tools, to reorient chemicals management approaches from time-intensive risk assessment and risk management based on single chemicals to comparative evaluation of the best options to fulfill a specific function. This article describes a functional approach to chemicals management we call "functional substitution" that encourages decision-makers to look beyond chemical by chemical substitution to find a range of alternatives to meet product performance. We define functional substitution, outline a rationale for greater use of this concept when considering risks posed by uses of chemicals, and provide examples of how functional approaches have been applied toward the identification of alternatives. We also discuss next steps for implementing functional substitution in chemical assessment and policy development.



There is increasing scientific, policy, marketplace, and consumer attention on chemicals that may pose risks in various production processes and products. Target and Walmart recently convened their major suppliers of personal care products to encourage companies to design safer, more sustainable products.[1] Traditional approaches to chemicals management have been to collect information on chemical hazards, uses, and exposures, evaluate risks, and determine appropriate risk management measures, such as use restrictions or exposure controls. While providing an important foundation for decision-making, this process can be time-intensive due to the large number of chemicals and associated uses that could be assessed and, on its own, may only slowly spur innovation in safer chemicals. As a panel of the National Academy of Sciences noted, "the focus on problem identification sometimes occurs at the expense of efforts to use scientific tools to develop safer technologies and solutions. Defining problems without a comparable effort to find solutions can diminish the value of applied research efforts."[2]

In response to these challenges, there has been significant attention to the concept of chemical alternatives assessment in chemicals management decision-making. Alternatives assessment has been defined as "a process for identifying, comparing and selecting safer alternatives to chemicals of concern (including those in materials, processes or technologies) on the basis of their hazards, performance, and economic viability".[3] Alternatives assessment builds on existing tools by focusing scientific attention on informed substitution, the considered transition from chemicals that may pose risks in production processes or products to less hazardous alternatives.

The concept of chemical "function" or "functional use," that is to say how and why a chemical is used, is an underappreciated element in both traditional chemicals policy frameworks and alternatives assessment frameworks. Chemicals serve important functions in processes and products (e.g., impart flexibility to plastics, provide fire protection in homes, or prevent bacteria from building up in cosmetic products), and the chemicals currently used to perform a particular function may not be the safest option or the only way to achieve them. When potential hazards, exposures, or risks are considered for a particular chemical, knowledge on chemical function can be used to frame chemical assessments. For example, in risk assessment, chemical function and application or product use provides critical information on potential exposure. In alternatives assessment, function and application not only are generally used as a baseline for assumptions regarding exposure to a chemical but also are important for identifying the universe of potential alternatives

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and narrowing the scope of the assessment, in the case of multifunctional chemicals. Although function has been used to frame chemical assessments in both contexts, it has not traditionally been used as a starting point for chemicals policy and risk management decision-making.

Starting with considerations of function, rather than characterizing and managing a particular risk associated with the use of a chemical (e.g., solvents, lead in gasoline, ozone-depleting chemicals), may provide a different, solutions-oriented, lens to reduce risk associated with various chemical uses. It may also offer an efficient means, complementing existing tools, to reorient chemicals management approaches from time-intensive risk assessment and risk management based on single chemical substances to comparative evaluation of the best options to fulfill a specific function (e.g., options to achieve flame retardancy rather than risk assessment and risk management for a single flame retardant or structurally similar chemicals). While the concept of function may not be a key consideration in chemicals assessment and management today, chemists and designers regularly focus on function when identifying cost-effective, high performing options for a particular product or manufacturing process.

This paper describes an approach to chemicals management that combines the way that chemists and designers think about function with typical risk assessment and alternative assessment considerations of health, safety, and environment and, in doing so, provides a new narrative for addressing chemical problems that focuses on health and innovation. We call this functional approach to chemicals management "functional substitution". Approaching chemical assessment through the lens of functional substitution allows for broad thinking about alternative chemicals, materials, products, processes, and systems for achieving a particular chemical function, beyond simply drop-in chemical substitutes (that may have similar toxicity profiles as the substituted chemical) and, as a result, supports a considered transition to safer, functionally equivalent alternatives.

■ DEFINING FUNCTIONAL SUBSTITUTION

Functional substitution describes the application of information on function to identify, evaluate, and select safer alternatives that achieve a particular result. While traditional approaches to chemical design have historically begun with consideration of function and application, the toolbox of design alternatives for a chemist consists primarily of other chemical structures. Functional substitution, however, employs a wider lens that can be useful to chemical users and policy makers by focusing attention on the simultaneous consideration of three distinct conceptual levels of substitution—chemical function, end use function, and function as service. These are described below.

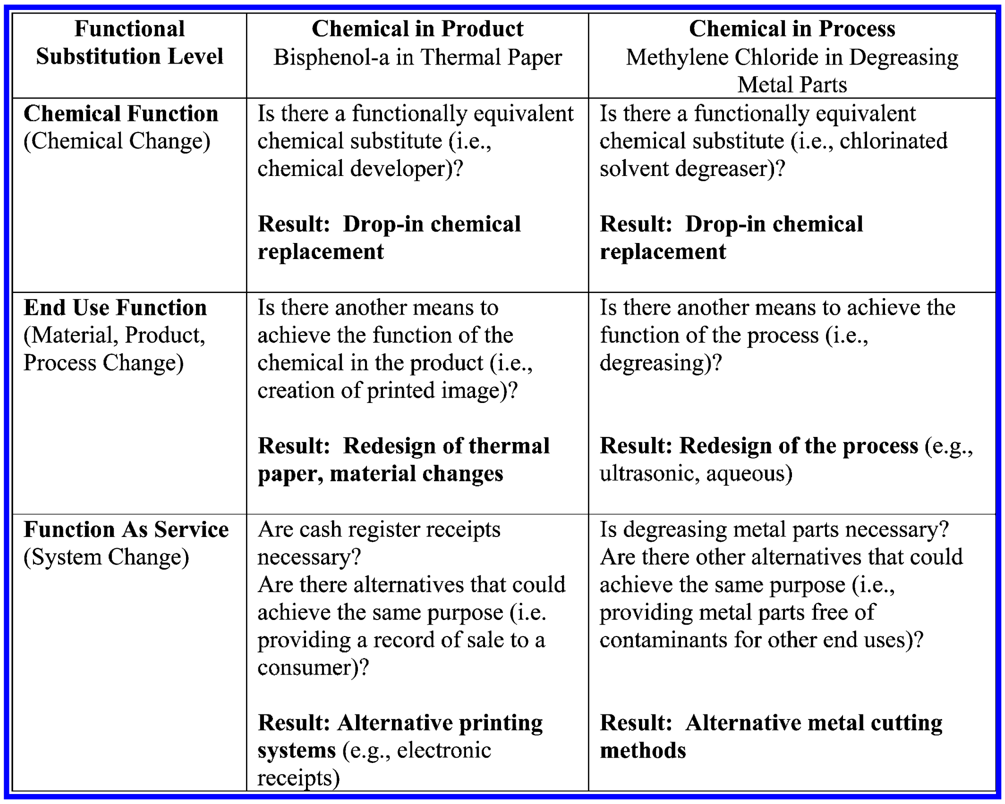
Chemical Function. At the level of basic chemistry, the potential function of a chemical is driven by the chemical's structure (functional groups, size, shape, geometry, electron distribution, etc.) and its physiochemical properties. Chemists think about the interconnection between function, physiochemical properties, and molecular structure in designing a chemical, what they call structure/function relationships.[4] Chemists design a chemical to have specific properties that will relate to its final potential functions (e.g., to impart color - dye, to reduce surface tension–surfactant, or provide corrosion resistance - reactive coating). A specific chemical may serve multiple functions, and, in some cases, there may be many different types of chemicals with diverse structures that can provide a specific function. In other cases, specific functions may be integrally linked to very specific chemical structures which may be inherently hazardous, and safer alternatives may not be readily available. For example, the predominant way to synthesize polyurethanes requires reaction of isocyanates with polyols. One newer approach, which may be an alternative for certain applications, involves the reaction of oligomeric cyclocarbonates with aliphatic amines (hybrid nonisocyanate polyurethanes).[5] In this case it may be possible to reduce the inherent toxicity of the molecule by making changes to the molecular design; however, this can be a time-intensive and expensive process. In some cases, there may be alternative ways to achieve the functionality in a less hazardous manner, such as by changing the chemistry required to make the molecule or material (alternative synthesis pathways or process chemistries).

When a chemist is given instructions to not use a particular chemical (e.g., because it is on a list of restricted chemicals or it is not available), it is reasonable to expect that the most likely alternatives that will be identified would be similar in structure. The focus, nonetheless, is on the chemical properties (and related chemical structures) needed to achieve a particular chemical function. For example, in looking at alternatives to bisphenol-a (BPA) as a developer in thermal paper, one might consider the chemical function of BPA, which is to transfer protons to the dye, triggering a conformational change that exhibits color,[6] but, structurally similar compounds, such as bisphenol-s (BPS), are also most likely to exhibit similar biochemical functions, indicating that estrogenic activity may be of comparable potency.[7] A better, but likely more challenging way to address the issue of BPA in thermal paper at a chemical function level would be to ask, "are there other potential proton donors with proton configurations similar to BPA that are unlikely to bind to estrogen?". Often those asked to find replacements are not necessarily chemical designers but formulators or product designers who look for readily available drop-in alternatives. This results in the isolation of stakeholders and overlooks a potentially useful dialogue between chemical designer and chemical user that could result in a more favorable substitution.

End Use Function. At the end use level, function relates to the specific purpose that a chemical serves in a product or process. In this instance, the particular end use of the chemical is known, including product/process properties and performance characteristics for which a chemical is needed. There may, however, be a limited number of options due to very specific technical or manufacturing requirements of the application in a specific firm (such as flame retardancy or cleaning requirements), but at the product/process end use level, there may be a broader range of possibilities to achieve the particular function, including alternative materials or process redesign changes. For example, an alternative to the use of phthalates in polyvinylidine chloride food wrap, where the end use is a flexible film that protects food with specific properties, could include a different material that does not need plasticizer additives, such as low density polyethylene. Another example of this is the use of high-density polyethylene instead of polyurethane for some applications.[8] Further, by looking at the end use, a product formulator or engineer is less wedded to a particular chemical structure but rather considers how that chemistry affects performance in a process or product.

Function As Service. At the design level, function relates to the broad "service" (function as service) that a chemical provides or is desired in a material, product, or process (e.g., microbial resistance, flame retardancy, impact resistance, lubrication, or

Table 1. Functional Substitution for Chemicals in Products, Chemicals in Processes



Functional Substitution Level	**Chemical in Product** Bisphenol-a in Thermal Paper	**Chemical in Process** Methylene Chloride in Degreasing Metal Parts
Chemical Function (Chemical Change)	Is there a functionally equivalent chemical substitute (i.e., chemical developer)? **Result: Drop-in chemical replacement**	Is there a functionally equivalent chemical substitute (i.e., chlorinated solvent degreaser)? **Result: Drop-in chemical replacement**
End Use Function (Material, Product, Process Change)	Is there another means to achieve the function of the chemical in the product (i.e., creation of printed image)? **Result: Redesign of thermal paper, material changes**	Is there another means to achieve the function of the process (i.e., degreasing)? **Result: Redesign of the process** (e.g., ultrasonic, aqueous)
Function As Service (System Change)	Are cash register receipts necessary? Are there alternatives that could achieve the same purpose (i.e. providing a record of sale to a consumer)? **Result: Alternative printing systems** (e.g., electronic receipts)	Is degreasing metal parts necessary? Are there other alternatives that could achieve the same purpose (i.e., providing metal parts free of contaminants for other end uses)? **Result: Alternative metal cutting methods**

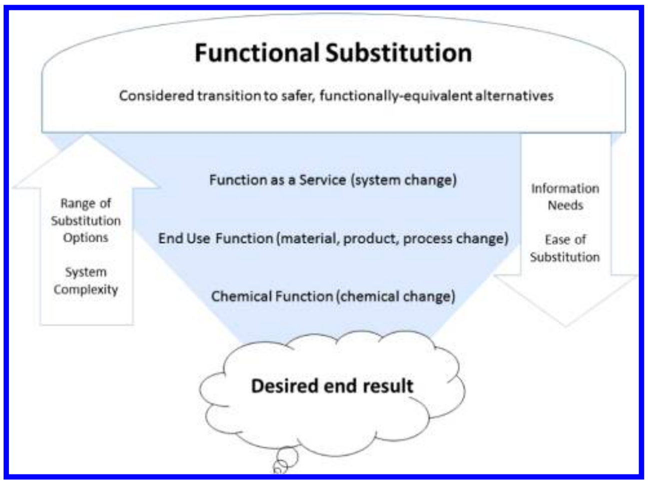


Figure 1. Relationship between chemical function, end use function, and function as service in functional substitution.

flexibility). That service may be provided through chemical, material, or product/process design changes, which are not necessarily dependent on specific chemistries. Importantly, at the function as service level, the question of the need for the function or the specificity of functional requirements (is specific functionality necessary?) can also be considered. For example, data indicate that antimicrobials, like triclosan, in handsoap may not be necessary in most applications. Hand washing with soap and water may provide similar functionality.[9] Another example, currently being debated, is the necessity for flame retardants in certain types of products, such as baby products and toys. In this case, the rigidity of flame retardant standards that require added chemical flame retardants is being discussed as well as other options to address fire safety, from barrier materials to alternative inherently flame retardant materials to safer flame retardant materials (such as nanoclays) to increased use of smoke detectors.[10]

Two examples, illustrated in Table 1, can help elucidate the differences between functional substitution at the chemical, end use, and service levels. While these three distinct levels can be readily distinguished in some examples, in others, the distinctions may be less clear. Although some ambiguity between these levels as defined may exist, they nonetheless provide a framework that can support dialogue around formulation of questions related to functional substitution for various chemical uses.

The relationship between the three conceptual levels of functional substitution—chemical function, end use function, and function as service—is outlined in Figure 1. As shown in the figure, taken together, the levels of functional substitution provide a broader lens with which to consider potential alternatives to achieve a desired end result. Moving from chemical function to function as service not only can serve to increase the range of substitution options available and help to more readily identify design change alternatives but also can increase the complexity of the evaluation (more difficult questions of trade-offs including cost, energy, and resource questions, evaluation of different chemical components of alternative materials, etc.). The narrower framing of chemical function may identify alternatives that can be more easily implemented, allow for greater predictability of potential exposures and health impacts given the expectation of similar use patterns, and can result in the design of novel, green chemistry alternatives. However, this framing may also result in "drop-in" structurally similar alternatives being chosen (with similar toxicity profiles).

It is also important to consider how moving from chemical function to end use function to function as service changes the focus of an evaluation of alternatives. At the chemical function level, the range of alternative options relates to the specific properties needed in a chemical, which are often related to structure. At the end use function level, information on the specific application and performance needs of a product/process (or component of a product/process) or formulation is needed. These performance needs (that may be defined by government policies or end users) may be very specific (such as requirements for fire retardancy in computer housings or for the use of hexavalent chromium metal coating of military vessels). In this case, there is a smaller range of options to meet that particular product or process performance need. At the function as service level, function is often described broadly—such as fire retardancy or antimicrobial action. In doing so, this spurs the consideration of systems changes and other nonchemical alternatives to meet that service.

THE VALUE OF FUNCTIONAL SUBSTITUTION

Chemicals are generally selected for the functions they provide in a particular production process, product, or product component. Some chemicals serve narrow niche functions while others serve a wide range of functions in different applications (multifunctional chemicals). Chemicals are chosen or designed to impart specific properties based on a range of chemical structures. Chemical users, who are on the front-lines of efforts to substitute safer chemicals in products and processes, select substances largely on their ability to perform a particular function in a specific application in a cost-effective manner. They are not looking for particular chemicals or chemistries but rather the functions those chemicals provide. Policy makers are often focused on eliminating the use of hazardous chemicals and are better able to achieve this goal where there is a wide range of safer, equally effective alternatives that can perform the same functions or where evidence indicates the functionality may not be necessary.

Functional substitution provides a useful lens to think about and compare potentially safer alternatives to meet a particular functional need, while reducing chemical hazards. It also provides an approach to guide the design of new options. While current approaches to chemicals management play an important role in characterizing the risk of specific chemicals on a case-by-case basis, functional substitution adds value by incorporating the identification and evaluation of a greater number of chemical, material, or product/process design options to meet a specific function. The availability of potentially safer options may facilitate decision-making when scientific evidence on the risks of an individual option is uncertain. Specifically, this approach has six main benefits:

It Provides a Framework To Efficiently Screen and Compare a Broader Range of Chemical and Design Alternatives, To Identify Best-in-Class for a Specific Function. While current regulatory and market policies will continue to focus on identifying and characterizing chemical risks, refocusing attention on achieving a desired result or function can help move toward the comparative evaluation of a broad set of solutions rather than detailed evaluation of the safety of specific chemicals. In this way, the functional substitution framework provides an approach to grouping chemicals and other alternatives based on specific performance needs for that function. Once alternatives are grouped by function, it becomes possible to comparatively evaluate options with regards to their hazards and potential exposures, based on a range of human health, environmental, and structural attributes. Specific minimum toxicity or hazard criteria for defining a safer alternative can provide important signals to designers developing additional options and can help with screening out unacceptable alternatives.

As an example, EPA's Safer Chemical Ingredient List (SCIL) includes chemicals that meet EPA's minimum toxicological criteria for different functional uses of chemicals in formulated products (e.g., biobased 1,3-propanediol as safer solvent ingredient).[11,12] Such "positive listing" type processes could be expanded beyond chemical for chemical substitutes to material and design change options.

It Helps Avoid Regrettable Substitutions. Market and regulatory pressures are leading many companies to seek out alternatives to chemicals that may pose risks. As noted, in traditional chemicals management approaches, when a specific chemical is restricted, a logical response of the chemist/chemical user/formulator/product designer is to find another structurally similar chemical drop-in substitute, which may lead to substitutions with alternatives that have similar toxicity profiles. On the other hand, a functional substitution approach shifts the focus from drop-in substitutes to a comparative evaluation of a broad range of options (chemical, product, material, process, systems alternatives) that can achieve the desired end result. The application of this approach opens up the possibility of identifying a range of potentially superior options that can be used by decision-makers, thus decreasing the chance of regrettable substitution.

Alternatives to chlorinated solvents in degreasing operations provide a case in point. When environmental and occupational health regulations came into effect restricting the use of some chlorinated solvents due to toxicity concerns, users of these materials (usually small and medium sized companies) sought chemical replacements that performed equally at similar cost. Many of these alternatives have similar toxicity profiles as the chlorinated solvent being substituted. On the other hand, by focusing on the function of the solvent in a manufacturing operation (removing grease from metal parts), the Massachusetts Toxics Use Reduction Institute (TURI) was able to explore a range of options to meet that function, including ultrasonic cleaning, water based cleaning, and removing the need for degreasing altogether through alternative metal cutting methods.[13] Similarly, EPA Region IX developed information on aqueous alternatives to solvents in auto repair and fleet maintenance.[14]

It Provides a Way To Make Data More Useful and Sortable to Different Users. Over time, more chemical hazard information has become available to governments, manufacturers, and the general public through public and private databases. This information is useful for understanding the hazards associated with individual chemicals but does not provide useful information to understand available alternatives. By grouping chemical information by function, product, and process use, different users can gain a better understanding of which functions have more problematic chemistries as well as the range of options available for a particular end use. This would also allow for cross-fertilization of different sectors that have the same functional needs.

For example, formaldehyde serves very different functions in its various applications (such as an adhesive in building products, a tissue preservative in medical laboratories, and a thickener in nail polish formulations) requiring more specific functional use categorization in order to find appropriate alternatives. Such categorization can help businesses compare options and governments to prioritize particular functions with limited safer alternatives for design challenges that could explore structurally different chemical options or product redesign possibilities. The EPA's SCIL list is a model for such categorization that provides a type of ranking system for chemicals that have been reviewed according to the Design for the Environment Program's functional use criteria.[11]

It Helps Guide the Design of Safer Chemicals. Understanding how chemical properties and structures relate to function also provides an important tool in green chemistry, the design of new chemicals that are less hazardous throughout their lifecycles. Green chemistry plays a particularly important role at the chemical and end use function levels of Figure 1. If the chemical options for a particular function are all similar and/or have similar toxicity profiles, this provides a signal to develop new, safer chemistries. By defining critical properties needed in a chemical substitute, chemists can explore a range of structures to meet a particular function, evaluating and reducing toxicity at the design stage. While identifying green chemistry alternatives may not always be possible, collaboration between chemists, end users, and toxicologists increases the potential to create inherently safer chemicals and materials.[4]

For example, in the case of chemical flame retardants, most research on alternatives has focused on functional replacements or ones that minimize exposure (encapsulation or binding to polymer), but a green chemistry approach to molecular design may look at a different set of options including natural antioxidants or nonpetroleum based material replacements that are inherently less flammable.

It Provides a More Robust Narrative To Enhance Traditional Regulatory Approaches. Knowledge of a broader range of substitutes for the function of a chemical can provide important input into risk management decisions, opening additional regulatory and discretionary options for policy makers.

For example, the functional substitution approach could enhance the ability of the EPA's Pollution Prevention (P2) Recognition Project, part of the New Chemicals Program, to incentivize the development of safer chemicals and technologies by more clearly targeting functions where safer alternatives are needed.[15] Similarly, examining data collected through the Toxics Release Inventory Program through a functional substitution lens could open up new opportunities for pollution prevention that significantly reduce or eliminate emissions and waste.[16]

It Creates a Cooperative Environment for the Development and Application of Safer Alternatives. At its heart, functional substitution connects design and health and safety considerations. This can cause a convergence of interests around innovation in safer chemicals and materials, as compared to the traditional chemicals management approach, which can entail extended debates about the safety of a particular chemical or of a small range of similar substitutes. At the chemical function and end use function level, a functional substitution approach encourages chemists to speak with product and production engineers about specific properties and performance needs of a chemical alternative in a product or process and to think about the toxicity profile associated with particular chemical structures or functions, thereby allowing signals of specific hazard criteria that define a safer option to be passed to chemists and designers. Defining function at the highest level—product, material, or service change—requires a broader range of perspectives from chemists, product designers, materials scientists, etc.—in identifying and evaluating design and systems alternatives, including consideration of the need for a particular function.

For example, many personal care product manufacturers are faced with a shrinking palette of preservatives, due to regulatory and market pressures.[17,18] Yet, keeping products safe from microbial contamination is an important function. The broad focus on the preservative function—rather than a focus on substitutes for parabens—opens up collaborative, precompetitive opportunities to identify and evaluate a range of innovative, safer and effective options, including alternative preservative formulations, as well as packaging and dispensing options that control or reduce the probability of contamination.[19] The traditional tools of risk assessment and risk management (including toxicology) play an important role in comparing options and assessing the safety of the chosen options.

■ EXAMPLES OF FUNCTIONAL SUBSTITUTION IN PRACTICE

A number of government efforts, emerging from increased attention to pollution prevention, toxics use reduction, and green chemistry in the 1990s,[20] apply considerations of functional substitution in the evaluation of alternatives to identified chemicals of interest. Three examples provide some context:

Use Cluster Scoring. In 1993, EPA created the Use Cluster Scoring System, a tool to systematically identify and screen chemicals in commerce. This system centered around the creation of chemical use clusters, that is to say a set of related chemicals and technologies for a functional use (e.g., adhesives, coloring agents, intermediates, solvents) in a particular industry (e.g., pharmaceuticals production, degreasing operations). Clusters were assembled for each relevant functional use category within each identified industrial sector category. For example, rubber chemical production included nine clusters with functions such as stabilizers, vulcanizing agents, and process regulators. EPA then evaluated information on hazard, exposure, pollution prevention potential, and past EPA regulatory interest to rank individual chemicals within clusters and to identify high priority clusters.[21]

Five Chemical Alternatives Assessment in Massachusetts. In 2005, the Massachusetts Legislature requested that the Massachusetts Toxics Use Reduction Institute (TURI) conduct a study to assess the feasibility of adopting safer alternatives for five chemicals of concern. After prioritizing the functions of greatest importance in Massachusetts for each chemical, TURI identified a range of chemical, process change, and systems alternatives for each. An alternatives assessment was then conducted for each of the high priority uses of the five chemicals of concern (16 different use categories in total), which compared existing alternatives based on technical feasibility, financial feasibility, and environmental and human health parameters. Ultimately, the assessments identified numerous promising alternatives to chemicals of concern in high priority uses and, in doing so, served to promote the adoption of these safer alternatives.[22]

EPA's Design for the Environment Alternatives Assessment Processes. EPA's Design for the Environment (DfE) Program takes a functional approach in its two major partnership programs: (1) the Alternatives Assessment Program, which compares alternatives for specific functional uses of chemicals (e.g., bisphenol-a in thermal paper; flame retardants in electronic housings) to support informed substitution processes, and (2) the Safer Product Labeling Program, which establishes criteria for safer chemistries for particular functional uses in formulated products (such as surfactants and solvents) to identify "best in class" products.[23]

These examples show that a focus on the thoughtful evaluation of alternatives to achieve a particular function can play a significant role in spurring the informed transition to safer alternatives. For instance, the Massachusetts' Five Chemical Alternatives Assessment illustrates how a functional substitution approach can identify safer options for a particular function, obviate the need for detailed safety assessments on each individual chemical, and, ultimately, provide companies with a broader set of evaluated options to consider as alternatives to hazardous chemicals. EPA DfE's Safer Products Labeling Program shows how the approach can support large purchasers by identifying best in class options for a particular chemical function. Further, the Use Clusters Scoring System demonstrates how, in a policy setting, the approach can help expedite chemical prioritization, screening, assessment, and risk management processes, given that there are significantly fewer combinations of functional use categories for various use applications to prioritize and screen, compared with the tens of thousands of chemicals in commerce.

Nonetheless, despite its utility, the functional substitution approach outlined in these examples has not been employed in a coherent or systematic fashion, nor has it been integrated into regulatory policy. Transforming functional substitution from a few illustrative, discretionary examples into an approach that is consistently applied to chemical problems will require the consideration of a number of challenges and needs.

IMPLEMENTING FUNCTIONAL SUBSTITUTION

In order for the functional substitution approach to be applied more broadly, we will need the following:

- A system for consistent, clear, and robust categorization of functional uses.
- More comprehensive and actionable chemical hazard data, including methods to evaluate the link between structure, function, and potential health impacts; predictive methods for evaluating toxicity when experimental data are lacking; and tools to combine toxicity data from multiple sources into hazard classifications.
- Scientific tools to compare chemical and design or systems alternatives for particular functions.
- Models for translating a functional substitution approach into existing policy frameworks.

Classifying and Characterizing Functions. To implement a functional substitution approach it is necessary to identify the universe of possible functions. In doing so, there are two fundamental questions to consider: (1) how broadly or narrowly functions ought to be defined and (2) who is the audience for the information.

Many existing approaches to categorize product uses and functional uses include categories which are broad or general in nature.[24−26] While a range of systems to categorize functional uses exist, they were constructed with a different purpose in mind—characterizing exposure rather than identifying alternatives for particular functions. Thus, there is a need to evaluate whether current classification systems are appropriate in the functional substitution context or, if not, identify nomenclature that works for this application. Creating categories for the different levels of functional substitution will require the appropriate balance between broad categories that could capture the function across many industries, sectors, and products and highly specific definitions that focus on a particular application in a particular product or industrial process.

There is an inherent tension in the level of specificity involved in characterizing function that needs to be acknowledged. The functional substitution approach encourages designers, manufacturers, and policy makers to understand why a chemical is used in a product or process and also to consider what other chemical, material, or design changes can be employed to achieve a particular function, but options may be limited due to the specific performance criteria for a chemical in a particular application. For example, a food can manufacturer only has a limited range of options for BPA replacements for lining the cans. A broader look at alternative packaging materials may not be an option for the can manufacturer but may be an option for the food processor.

While having clear definitions of functional use is important, there is also a critical need for data collection systems to compile information on chemical functions, linked to information on chemical structures and properties and use volumes, which would allow a more thoughtful comparison of alternatives. Such systems have been constrained to date due to concerns about protection of confidential business information. While it is important that such information be protected, overuse of confidential business information can hinder the ability of governments to collect and make publicly available data to support safer chemistry.

More Comprehensive and Useable Chemical Hazard Data. There are still far too many data gaps for the chemicals that are in commerce to effectively manage them under any type of framework. It is impossible to transition to safer chemicals and products without data to determine which chemicals and materials are indeed safer. While focused on identification of a range of alternatives to achieve a particular function, the functional substitution approach still requires information in order to evaluate and compare alternatives. A number of efforts are underway to evaluate chemical toxicity data. These include chemical assessment programs, such as those under the European Union's REACH Program, the Canadian Chemicals Management Plan, and the EPA's TSCA Work Plan Chemicals Program.[27−29] Additionally, efforts are underway to use nontraditional data streams, such as in silico modeling and high throughput in vitro screens to rapidly understand chemical toxicity. Many of these newer programs are incorporating increasing knowledge about the links between particular chemical structures and toxicological impact.[30]

For example, in response to limited toxicity testing requirements for new chemicals under the Toxic Substances Control Act, the EPA has developed significant expertise in toxicity prediction based on structure−activity relationships. The Agency established its chemical categories list for new chemicals more than 20 years ago to provide signals to chemical manufacturers on classes of chemical structures that were likely to result in toxicological impacts and for which additional testing is needed. These chemical categories help identify potential "structural alerts" or red flags defined in terms of physiochemical properties or structural attributes. Such toxicological prediction approaches have also existed in the pharmaceutical sector for decades but may be of limited use due to their proprietary nature.[31−33]

Chemical structure can be a good predictor of certain hazard end points (based on understanding specific binding and reactivity), but knowledge generally depends on the availability of toxicity data for closely related chemical structures. New high throughput testing models being developed under the EPA's ToxCAST program are likely to yield significant information on the links between specific chemical structures, properties, and toxicity.[2] Hence, predictive toxicology will provide significant input to understanding the relationship between chemical structures, physiochemical properties, and toxicological impacts. However, Voutchkova et al. note that these predictive tools are not fully useful for informing the design of molecules with specific functions linked to specific physiochemical properties for performance.[34]

To support the design and evaluation of safer chemistries, there is a need for more effective characterization and understanding of how chemical properties and structure affect toxicity. Better and more accessible methods, tools, and data to link chemical toxicity to specific chemical structures and properties can more effectively translate design criteria for chemists to potentially modify chemical structures and better incorporate knowledge of the relationship between toxicity, chemical mode of action, and physiochemical properties. With such information, chemists can then understand which types of chemical structures with specific properties would be the safest means to meet a particular chemical function.[4]

Additionally, there is a need for tools to combine toxicity data from multiple sources (*in vitro*, *in vivo*, and modeling) into actionable hazard classifications that product and process designers can use in evaluating substitutes. Tools such as the Globally Harmonized System of Classification and Labeling and Clean Production Action's Green Screen for Safer Chemicals (Green Screen) take chemical toxicity data and classify or benchmark it based on hazard criteria, making comparison between chemical options easier for the end user.[35]

Comparing Chemical, Material, and Design Alternatives. As discussed, defining functional substitution at the end use function and function as service levels opens up a broader range of options to meet a particular chemical or product/process function. This also increases systems complexity in terms of comparing options. At the chemical function level, chemicals can be compared on the basis of their intrinsic hazards and exposures. A number of well-established frameworks have been developed to compare chemical alternatives for particular functional uses. These include the EPA's DfE Chemical Alternatives Assessment Framework and the Green Screen for Safer Chemicals.[23,36] At the material or product/process level, such assessments get more complex. An alternative material or process design may involve a different set of chemistries or work structures that significantly change hazards—from toxicological to physical or lifecycle hazards. While lifecycle assessment (LCA) has been promoted as a tool for comparing product materials and product designs, it tends to be limited in its comparison of toxicological attributes and other attributes, such as worker health and safety. A number of efforts have been undertaken to rank and compare materials outside of a formal LCA, such as the Clean Production Action Plastics Scorecard, among others.[37−39]

Model Policy Frameworks. Traditional regulatory frameworks for chemicals management are focused on a chemical-by-chemical approach whereby data are collected on chemical hazards and exposures, risks are characterized, and risk management (sometimes involving evaluation of alternatives) is implemented to control exposures. Some newer policies, such as the European Union's REACH Authorization Process, the California Safer Consumer Product regulations, and safer children's products laws in Maine, Minnesota, and Washington, specifically call for safer alternatives to chemicals of concern.[40] In March 2014, the State of California produced its first categorized list of product/chemical combinations of priority concern for alternatives assessment requirements. In the case of Washington's law, the state has collected data on the use of priority chemicals in children's products, searchable by functional use and product classification. Under REACH, alternatives assessments are required in order to seek authorization for continued use of Substances of Very High Concern (SVHC), and the European Chemicals Agency has produced guidance on how to perform such assessments. Such authorizations are only permitted for specific uses of an SVHC.

At the present time, the functional substitution approach has worked as a discretionary complement to traditional regulatory chemicals risk management approaches. As noted, efforts such as the EPA's DfE initiatives apply a functional substitution approach in evaluating alternatives to priority chemicals. Nonetheless, this approach has not been systematically integrated into any chemicals management policy.

There is a need to develop model policy frameworks that both build on existing discretionary applications of the functional substitution approach and find ways to integrate it into more traditional regulatory chemicals management policies. Such model policies could facilitate a more systematic prioritization and comparison of chemicals for particular functions as well as prioritize chemical functions of highest interest due to chemical hazards, exposure potential, or substitution potential. Policies would need to be adaptable to different agency mandates and regulations. For example, a functional substitution approach would work differently in agencies that evaluate product safety, regulate chemical use, or set exposure limits. In all cases there will be needs for information on functions and uses, processes to "bin" and prioritize functions, processes to evaluate and determine what makes a "safer" substitute for a specific function, and ultimately information on safer alternatives for specific functions of chemicals.

Model frameworks not only are necessary in the regulatory context but also should be considered in the business decision-making context. Given the increasing marketplace and supply chain pressure to substitute chemicals that may pose risks in various production processes and products, functional substitution may provide chemical users, retailers, and brands with an effective approach that allows a collaborative, supply chain exploration of a broader range of options that meet consumer needs, achieving desired results through significantly changed and safer product designs, beyond chemical avoidance.

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Notes

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