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Relative Risk Analysis of Several Manufactured Nanomaterials: An Insurance Industry Context

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A relative risk assessment is presented for the industrial fabrication of several nanomaterials. The production processes for five nanomaterials were selected for this analysis, based on their current or near-term potential for large-scale production and commercialization: single-walled carbon nanotubes, bucky balls (C_{60}), one variety of quantum dots, alumoxane nanoparticles, and nano-titanium dioxide. The assessment focused on the activities surrounding the fabrication of nanomaterials, exclusive of any impacts or risks with the nanomaterials themselves. A representative synthesis method was selected for each nanomaterial based on its potential for scaleup. A list of input materials, output materials, and waste streams for each step of fabrication was developed and entered into a database that included key process characteristics such as temperature and pressure. The physical-chemical properties and quantities of the inventoried materials were used to assess relative risk based on factors such as volatility, carcinogenicity, flammability, toxicity, and persistence. These factors were first used to qualitatively rank risk, then combined using an actuarial protocol developed by the insurance industry for the purpose of calculating insurance premiums for chemical manufacturers. This protocol ranks three categories of risk relative to a 100 point scale (where 100 represents maximum risk): incident risk, normal operations risk, and latent contamination risk. Results from this analysis determined that relative environmental risk from manufacturing each of these five materials was comparatively low in relation to other common industrial manufacturing processes.

Introduction

The production of significant quantities of anthropogenically derived nanomaterials will inevitably result in the introduction of these materials to the atmosphere, hydrosphere, and biosphere. The composition of engineered nanomaterials may closely resemble materials for which there is considerable information on health and environmental impact. In the absence of data, material safety data sheets (MSDSs) treat nanomaterials like their bulk counterparts despite their unique properties. Such is the case for C_{60}, which is often represented by the carbon black MSDS. Nanomaterials are engineered to have distinctive properties based on their size, shape, surface functionality relative to mass, and uniformity of the material. These differences may produce responses in organisms that differ from those of compositionally similar larger materials (*1*). Although many studies are beginning to appear in the published literature addressing the toxicity of nanomaterials (*2*−*8*) and their potential for exposure (*9*, *10*), statements regarding the impacts of nanomaterials on human health and the environment remain largely speculative.

While there are many unknowns surrounding the fate of nanomaterials in the environment and their impacts on human health and ecosystems, there is a great deal known about the properties and impacts of the materials used to produce nanomaterials. As in any industry, an important goal for the emerging nanomaterials industries is to ensure that the risks to human health and the environment due to nanomaterial fabrication are minimal. Indeed, the nanomaterials industry has a tremendous opportunity to evolve as a "green" industry, benefiting from the experience of previous industrial enterprises.

The objective of this study is to assess relative risk associated with the production of five specific nanomaterials, thereby producing a baseline of information concerning hazards posed by this new industry. The assessment decouples risks associated with handling inputs and wastes in the nanomaterials production process from the issues surrounding possible direct risks posed by nanomaterials. Although calculated under conditions of great uncertainty, we are able to arrive at relative risk scores regarding the manufacturing process by focusing on known activities and substances. We also compare our calculated relative risks of nanomaterial production with those arising from other industrial activities.

Methods

The production processes for five different nanomaterials were considered in this work: single-walled carbon nanotubes, bucky balls (C_{60}), quantum dots composed of zinc selenide, alumoxane nanoparticles, and nano-titanium dioxide. These materials were selected based on a current or anticipated near-term potential for commercialization and production beyond a laboratory scale. In each case, a potentially scalable published synthesis method for the nanomaterial was articulated as a process flowchart. The processes deemed appropriate for use in this study had the most available data and utilized constituent materials and processes that could most likely be scaled to industrial levels of production based on cost and availability. Energy use and other considerations of a full life-cycle assessment were omitted from the assessment; instead we narrowed our risk focus to factors considered from an insurer's risk perspective: constituent materials, their properties, and overall process parameters. Risk can be conceptually represented as the product of hazard and exposure, so these materials, properties, and parameters were collected with the purpose of characterizing hazard and exposure probability. A detailed account of input materials, output materials, and waste streams for each step of fabrication was developed. The physical-chemical properties and quantities of the inventoried materials were used to assess relative risk based on factors such as toxicity, flammability, and persistence in the environment. These factors were first qualitatively assessed for each process, then combined using an actuarial protocol

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TABLE 1. Nanomaterial Fabrication Methods Chosen for Manufacturing Risk Analysis

nanomaterial	reference	description	commercial status
single-walled carbon nanotubes (SWNTs)	Bronikowski et al. (*12*)	gas-phase chemical-vapor-deposition process known as the HiPco process	currently in use for commercial production
C_{60}	Howard et al. (*13, 14*)	production of C_{60} and C_{70} fullerenes in premixed laminar benzene−oxygen−argon flame	proprietary process modified from the reference currently in use for mass production ~1500 ton/year
ZnSe quantum dots	Karanikolos et al. (*11*)	self-assembly of zinc selenide quantum dots in a microemulsion	recently published, this method utilizes less expensive input materials than predecessors; current commercial methods are unknown to the authors
alumoxane nanoparticles	Callender et al. (*15*)	aqueous synthesis and subsequent thermolysis of alumoxane	currently in use for commercial production
TiO_2 nanoparticles	Duyvesten et al. (*16*)	production of nanosized TiO_2 through hydrolysis and calcinations with chemical additives to control particle size	currently in use for commercial production

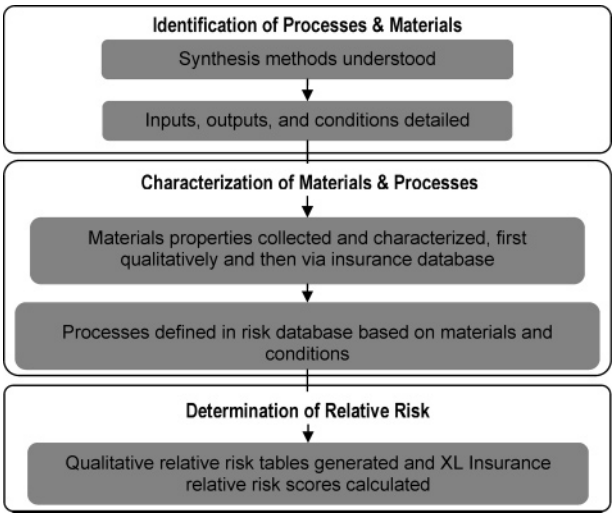

FIGURE 1. Schematic of the nanomaterial fabrication risk assessment methodology used in this study.

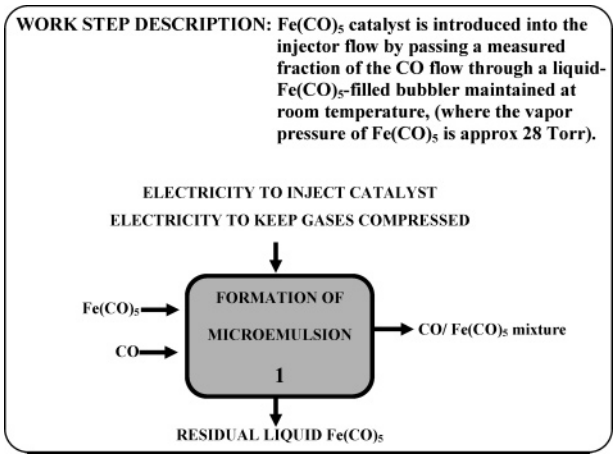

FIGURE 2. Example of a synthesis step from a single-walled nanotube process map.

developed by the insurance industry for the purpose of calculating insurance premiums for chemical manufacturers (*11*).

A schematic of the full process of adapting nanomaterial fabrication data to enable risk assessment is seen in Figure 1.

Identification of Processes and Materials: Synthesis Methods. To first understand the synthesis processes, published fabrication methods were reviewed with the goal of finding a representative production technique suitable for scaleup and likely to be used in the industry. The processes chosen for this study are summarized in Table 1.

Identification of Processes and Materials: Inputs, Outputs, and Conditions Detailed. The chosen synthesis processes were expressed in simplified building block steps as part of a flow diagram. Defining substance and process characteristics for each synthesis step were articulated in a detailed process map based on the method reported by Pojasek (*17*). Each fabrication step was further described by its process characteristics as reported in the literature, and expected material input streams, output streams, and waste streams were recorded. A portion of the HiPco method of fabricating single-walled carbon nanotubes (SWNTs) is represented in Figure 2; the full process flows for all five nanomaterial production methods are available in the Supporting Information.

Characterization of Materials and Processes: Materials Properties Collected and Characterized, First Qualitatively and Then via Insurance Database. The collected and fabrication data were then organized qualitatively to characterize and compare the relative risks. This representation of the data focused on the relative risk posed by five key properties for each constituent material of each nanomaterial fabrication process. We collected data regarding each substance's toxicity (LC_{50} and LD_{50}), water solubility, log K_{ow}, flammability, and expected emissions. After the characteristics for the qualitative assessment were assembled, additional data were compiled for each substance for use in the XL Insurance database to prepare for calculating relative risk scores. Adapting our information to the requirements of the system was an iterative process, resulting in the definition of each chemical and process according to the chemical and physical properties required by the insurance company's algorithm in determining its relative risk. The substance characteristics utilized in the database to rank relative substance risk are detailed in Figure 3. It should be noted that the numerical values for each of the substance data fields are mapped to relative risk classes. These risk classes group levels of risk posed by orders of magnitude. For example, the entire spectrum of possible values for any given substance in the category of LC_{50} is represented in a scale of 1 through 4. In instances where a substance characteristic value was not known, typically in the case of persistence factors such as photolytic half-life, a relative risk class was directly assigned based on comparative substance research. The Supporting Information presents further details regarding the risk classes and scoring methods of the XL Insurance Database as well as a table as well as with a listing of all the material property data fields (Table SI-9).

Characterization of Materials and Processes: Processes Defined in a Risk Database Based on Materials and Conditions. Manufacturing processes were then defined within the database in terms of their constituent substances

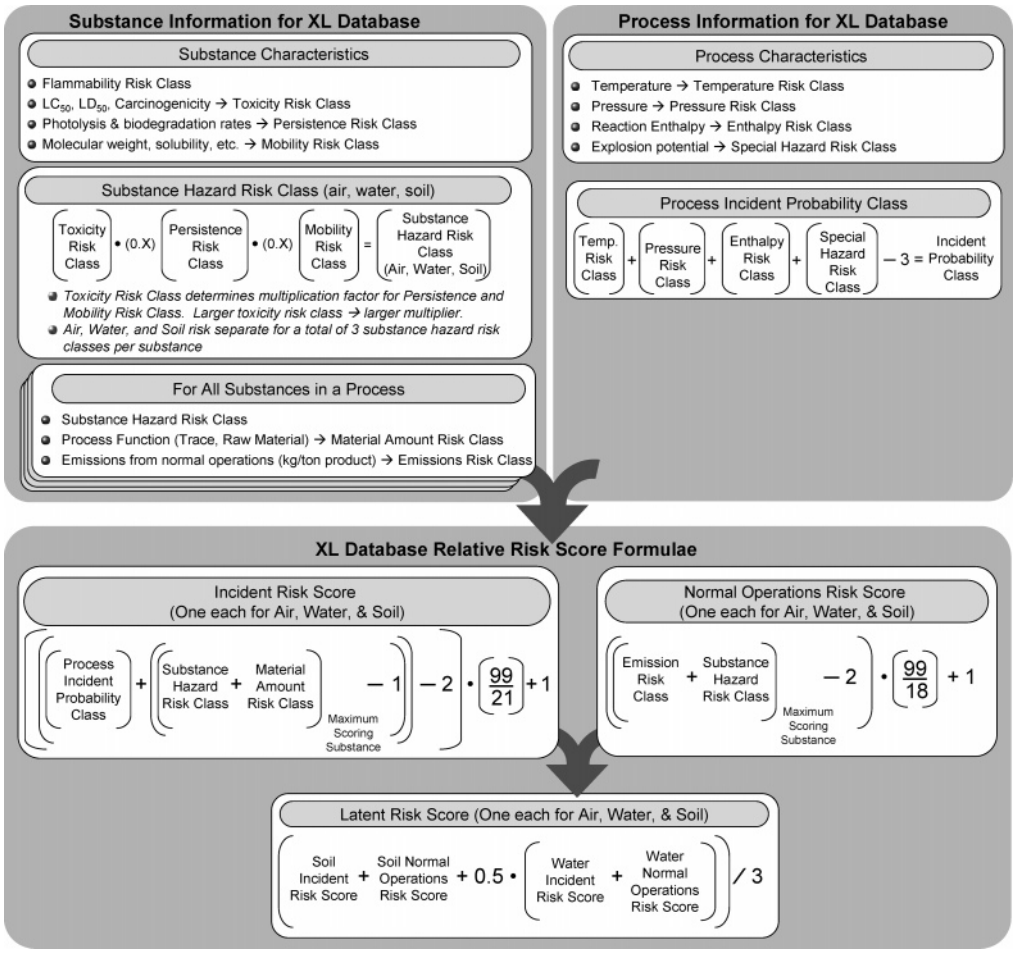

FIGURE 3. Schematic of the XL Insurance database and formulation of risk scores.

and conditions such as temperature, pressure, and enthalpy. Figure 3 depicts the process characteristics utilized in the insurance algorithm. Each substance involved in the process, with the exception of the final nanomaterial product, was defined within the particular fabrication process to quantify its contribution to risk. For each substance, the amount present, its role in the process, its physical phase at the temperature and pressure of the process, and any emissions were defined. Specifying the substance role allowed the model to incorporate the probability of exposure to each substance by denoting whether such exposure could only result from an in-process accident, if there would be emissions resulting from normal operations, or if exposure would be possible via both pathways. Information about which physical phase-(s) the substance would be in upon reaching the environment enabled the appropriate application of persistence and mobility data for the media of air, soil, and water. For any substances expected to be emitted during or after the process, an emission factor was determined describing the order of magnitude of substance released to the environment in kilograms per ton of product. These numerical emission factors were again mapped to a scale grouped by orders of magnitude, so that the spectrum of emissions from less than 0.00001 kg/ton to greater than 1000 kg/ton was represented in a set of emissions risk classes ranging from 1 to 10. Empirical emissions values were often challenging to determine due to the lack of experimental information regarding detailed mass balances of waste streams and due to the uncertainty involved with scaling up published processes to industrial fabrication proportions. In cases where the emission quantity was not known, an order of magnitude was estimated based on comparative process research within the existing database and on stoichiometric calculation of mass balance. Once substance contribution to risk was recorded, the process was defined in terms of conditions that contribute to potential hazard. A listing of every data field for processes in the XL Insurance Database is presented in the Supporting Information, in Table SI-10.

Determination of Relative Risk

Qualitative Methodology. Since risk can be represented as a combination of hazard and exposure, we incorporated both of these components in our qualitative risk assessment. Potential hazards of a substance were taken into account by the data fields for toxicity via LC_{50} and LD_{50} values, for mobility via water solubility values, for bioaccumulation tendencies via log K_{ow} values, and for flammability via Occupational Safety and Health Administration ratings. Exposure potential was also reflected in estimates for the emissions in kg/ton product. First, the values for each substance characteristic were translated to a qualitative scale, grouped by orders of magnitude. For instance, a water solubility value of less than 10 mg/L was placed in the lowest risk (least mobile) category, a value of greater than 1000 mg/L was placed into the highest risk (most mobile) category, and intermediate values were ranked in the middle. Water solubility qualitative scores are therefore either "low solubility", "medium solubility", or "high solubility". The accumulation of these substance characterizations for each material in each process was intended to impart a general indication of the magnitude of risk posed by the process.

XL Insurance Database Methodology. In addition to the qualitative review of the processes, the XL Insurance database was utilized to calculate relative risk scores for each of the

five nanomaterial manufacturing processes. The hazard of each process was defined based on constituent substance characteristics such as carcinogenicity or lethal dose in rats and on such relevant process characteristics as temperature, pressure, enthalpy, and fire hazard rating (*18*). The exposure portion was quantified by incorporating persistence and mobility of constituent substances and by scoring expected emissions of the substances during the manufacturing process. By applying an insurance database currently in commercial use, we were able to benchmark the risk of nanomaterials' fabrication processes against each other and against other non-nanomaterials from the perspective of an industrial insurer. This type of risk assessment, although not inclusive of all environmental impacts or life-cycle considerations, is representative of the type of risk assessment nanomaterials manufacturers will encounter as insurers grapple with qualifying the relative risk of these new processes. Figure 3 provides a schematic of the XL Database requirements and actuarial protocol, and it serves as a pictorial reference for the terminology used for different types of scores and risks within the system. As discussed earlier, the numerical values for each of the substance data fields are mapped to relative risk classes. These relative risk classes are then combined to determine the substance's substance hazard score.

The insurance protocol calculations provided three relative risk scores for each fabrication process: incident risk, normal operations risk, and latent contamination risk.

Incident risk represents the impact of an in-process accident, leading to accidental exposure. Normal operations risk refers to the risk posed by substances that are expected to be emitted during the course of the fabrication process. Latent contamination describes potential for long-term contamination of the operations site.

Risk scores corresponding to conditions such as temperature and pressure were combined to calculate the probability of an accident occurring during the process, expressed as a process incident probability class. An amount category was assigned to each substance based on the relative amount used in the process, wherein more of a substance enhances the level of risk posed. Risk scores corresponding to toxicity, persistence, and mobility data for each constituent substance were then combined to calculate the risk associated with that constituent's interaction with air, water, and soil; this cumulative risk score for each compound was denoted as its substance hazard risk class. The process incident probability class, amount hazard risk class, and substance hazard risk class then served as variables in computing final risk ratings for air, water, and soil pathways due to sudden release and due to normal emissions from a given process.

For incident risk, each pathway's risk ranking was determined as a function of the process' hazard rating, the amount hazard ratings for each substance, the substance hazard risk classes, and an actuarial adjustment coefficient that forced the final score into a 1−100 distribution. A schematic of all risk class calculations can be seen in Figure 3, and all adjustment coefficient values can be found in the Supporting Information. Normal operations risk was calculated for each pathway by combining the constituent substances' emission coefficient risk categories, their substance hazard risk classes, and an actuarial adjustment coefficient that forced the score into a 1−100 distribution. Latent risk was calculated by combining the final risk ratings calculated for soil and water, for both incident and normal operations. Air ratings are excluded from this calculation because in the time frame of latent contamination airborne contaminants will have settled into the water or soil.

In the XL Database, a final score in the incident risk and normal operations risk categories corresponds to the highest of the three scores out of air risk, water risk, and soil risk. For each of those transport-media-based risks, the score relates to that of the highest risk substance affecting that medium. This method of taking the highest risk medium based on its highest risk substance is appropriate for insurance premiums, because it is intended to approximate the relative order of magnitude of the risks. Admittedly, the practice of choosing only the highest scoring constituent material rather than accounting for multiple substances in use precludes differentiating processes that involve multiple hazardous substances. A process that includes benzene and toluene as main ingredients scores the same as one that uses only benzene, since benzene earns the highest substance hazard risk class. However, the database is focused on assessing differences in liability risk in terms of orders of magnitude. While adding toluene to a process does change the consequent risk, it does not change it by an order of magnitude from an insurance perspective.

Applying the XL Insurance Database Methodology. The five chosen nanomaterial production processes were each entered into the database for calculation of the three final risk scores. The data for each individual substance and for the manufacturing processes were determined based on published synthesis methods, by industry interview, by comparison with common similar manufacturing practices (*19*), or by stoichiometric predictions. The constituent substance characteristics were often already present in the database or were found in Material Safety Data Sheets and U. S. Environmental Protection Agency substance listings. Most of the required fields for substances and process characteristics were attainable, but due to the uncertain nature of predicting the final scaled-up manufacturing process the expected emissions during normal operations were not as clear. Three separate hypothetical cases are therefore defined, and three sets of scores are determined for each nanomaterial fabrication process. The cases are based on assumptions that represent a range of manufacturing scenarios, attempting to scope probable boundary conditions of "most materials emitted" and "least materials emitted". In processes for which the authors had mostly published information available, such as ZnSe quantum dots, we tried to vary the emission risk class by a few orders of magnitude between the low risk and high risk cases. In other processes for which more data were accessible, such as SWNT and alumoxane production, closer approximations could be made based on reaction stoichiometry or on known lab practices. Detailed assumptions for all the nanomaterials fabrication processes' scores, including case differences, are presented in the Supplimental Information in Tables SI-11 through SI-14.

Results

Utilizing the insurance protocol allowed comparison among the manufacturing processes for the nanomaterials, but perhaps more important, it allowed comparison with other common processes previously defined in the system for premium calculation purposes. For both our qualitative and insurance-based results, nanomaterial risk scores appear along with scores for six other commonplace processes: silicon wafer (semiconductor) production, wine production, high-density plastic (polyolefin) production, automotive lead-acid battery production, petroleum refining, and aspirin production. Silicon wafer production, key in the manufacture of computer parts, and automotive lead-acid battery production are both widespread manufacturing processes found in or near many communities. Polyolefin production and petroleum refining pervade petrochemical complexes in industrial cities, and more specifically, both are dominant manufacturing activities in Houston's ship channel. Wine production serves as an interesting benchmark comparison, as it would be considered by most a relatively benign process.

TABLE 2. Qualitative Risk Rankings for Single-Walled Carbon Nanotube Production

SWNT	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
carbon monoxide	●	●	○	●●	–○ – ●●
sodium hydroxide	●●	●●	○	○	●
iron pentacarbonyl	○	○	○	○	○ – ●●
carbon dioxide	○	●●	○	○	○ – ●●
water	○			○	●

TABLE 3. Qualitative Risk Rankings for C_{60} Production

C_{60}	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
benzene	●●●	●●	○	●●	
toluene	●●	●	●	●●	○ – ●
argon	○	●	○	○	○
nitrogen	○	●	○	○	○
oxygen	○	●	○	●	○ – ●●
soot	●●	○	●●	○	●●●
activated carbon	○	○	●●	●	
carbon dioxide	○	●●	○	○	●●
water	○			○	○

TABLE 4. Qualitative Risk Rankings for ZnSe Quantum Dot Production

ZnSe quantum dots	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
nitrogen	○	●	○	○	○
formamide	●●	●●	○	○	
heptane	●	○	●●	●●	● – ●●
poloxalene	●	●●	○	○	● – ●●
diethyl zinc	●	○	○	●●	
hydrogen selenide	●●●	●●	○	●●	● – ●●
carbon dioxide	○	●●	○	○	●●
carbon monoxide	●	●	○	●●	●●

TABLE 5. Qualitative Risk Rankings for Alumoxane Production

alumoxane	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
acetic acid	●●	●●	○	●	○ – ●
aluminum oxide	○	○	●●	○	○ – ●●●
water	○			○	

The scores producing aspirin are also included to represent the widespread pharmaceutical industry. As these comparison processes have been taken directly from current XL Insurance database entries, their underlying assumptions are not addressed. The sole change was the removal of all final products from the recipes for each of the non-nanoscale comparison materials, to consistently compare only the manufacturing processes' contribution to insurance risk.

Qualitative Risk Results. The qualitative tables show each manufacturing process with its constituent materials listed beneath. Each constituent material received scores for each of the five chosen fields: toxicity, solubility, log K_{ow}, flammability, and expected emissions. The five chosen characteristics for the non-nano comparison processes were ranked using the substance data from the XL database, wherein values for a characteristic were grouped by orders of magnitude to arrive at relative scores. In cases for which there were no available data, XL Insurance risk engineers assigned relative values by comparing the compound to other chemically similar compounds with known relative scores. The first four characteristics considered are properties of the substance irrespective of the process in which it is used, so they represent the hazard posed by the substance. The emissions category represents exposure, ranking the relative amount of the substance if any of it is expected to be emitted during normal operations specific for a process. Lower toxicity, flammability, and emissions are clearly less hazardous; low water solubility is less hazardous because the substance will not travel as far. A low log K_{ow} implies less potential for bioaccumulation. Tables 2–12 show the results of the qualitative review of the five nanomaterials manufacturing processes, followed by the six non-nano comparison processes. Relative risk is indicated by a white circle for low risk, a black circle for intermediate risk, two black circles for high risk, and three black circles for very high relative risk. The emissions scores for the nanomaterials fabrication processes are shown as a range of values, based on the three cases defined earlier and detailed in the Supporting Information assumptions in Tables SI-11 through SI-15.

As a group, nanomaterials fabrication processes appear to have fewer constituent materials and generally fewer toxic materials, but they also are projected to have higher emissions than their non-nano counterparts. These higher emissions projections could be in part due to the uncertainty in projecting how the scaled-up published processes will change at industrial-level production volumes. The established, non-

TABLE 6. Qualitative Risk Rankings Nano-Titanium Dioxide Production

nano-TiO_2	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
methane	○	●	○	●●	
hydrochloric acid	●●	●●	○	○	○ – ●●
phosphoric acid	●●●	●●	○	○	○ – ●●
titanium tetrachloride	●●●	○	○	○	○ – ●●
carbon dioxide	○	●●	○	○	●

TABLE 7. Qualitative Risk Rankings for Silicon Wafer Production

silicon wafers	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
sodium hydroxide	●●	●●	○	○	
hydrochloric acid	●●	●●	○	○	
phosphoric acid	●●●	●●	○	○	
hydrogen fluoride	●●	●●	○	○	○
sulfuric acid	●●●	●●	○	●	
N-methyl-2-pyrrolidone	●	●●	○	●	○
acetone	○	●●	○	●●	○
ethanol	○	●●	○	●●	○
nitrogen	○	●	○	○	
anhydrous ammonia	●●	●●	○	●●	●●
chlorine	●●●	●●	○	●	
hexafluoroethane	●	○	●●	○	●●
phosphine	●●●	●	●	●●	○
boron trifluoride	●●●	○	○	○	
hydrogen bromide	●●	●●	○	○	
silicon	○	○	●●	○	
diborane	●●●	○	○	●●	
germanium	●	○	●●	○	
arsine	●●●	●●	○	●●	●
oxygen	○	●	○	●	

TABLE 8. Qualitative Risk Rankings for Wine Production

wine	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
zineb	●●●	●	●	○	
maneb	●●●	○	●●	○	
copper oxychloride	●●	○	●●	○	
water	○			○	
glucose	●	●●	○	○	
sulfur	●	○	●●	○	
sulfur dioxide	●●	●●	○	○	○

nano industrial processes have so few emissions perhaps because they have become more streamlined with respect to recapture and recycle of the many hazardous materials that they employ. These non-nano processes may also involve the use of more materials because their scaled-up processes have been fully developed; as the nanomaterial production processes develop further and are analyzed in terms of their final production process, recycling, washing, and recapturing steps may require additional chemicals to be added to the process. Among the nano processes, SWNT and alumoxane production both appear to present lower risk, while ZnSe quantum dots, C_{60}, and nano-titanium dioxide appear to be associated with more risk. In these qualitative graphs, all of the nanomaterials production processes appear to be less risky than polyolefin production and petroleum refining.

Insurance-Based Quantitative Risk Results. Our insurance database results tables and graphs show incident risk, normal operations risk, and latent risk for each of the nano and non-nano manufacturing processes. As seen in Figure 4, the incident risk for most of the nanomaterial production processes score comparably or lower than the common non-nano processes. The relative risk of alumoxane particles and SWNTs are low in comparison to all of the non-nano products, falling near or below wine production. The low hazard ratings of constituent substances and the absence of extreme temperatures and pressures in the alumoxane and SWNT production processes are primarily responsible for these results. ZnSe quantum dots and nano-TiO_2 fall in a midrange incident risk, near silicon wafer production, automotive lead-acid battery production, petroleum refining, and aspirin production. The database incident ratings show C_{60} as the highest risk nanomaterial, close to the risk presented by polyolefin production. This is explained by the fact that our chosen method for producing C_{60} utilizes one very hazardous culprit material (benzene). As this risk category is defined based on all materials present and process conditions, the published synthesis methods provide enough information to allow a relatively confident characterization of the nanomaterials' risk in the incident risk category. For this reason, there are no error bars or ranges of risk scores included in the incident risk results.

Unlike the incident risk calculations, the normal operations scores include projected emissions of the constituent materials during the manufacturing process. A range of probable manufacturing scenarios is included by scoring the three different cases defined for each nanomaterial; the

TABLE 9. Qualitative Risk Rankings for High-Density Plastic (Polyolefin) Production

high-density plastics (polyolefins)	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
ethylene	○	●	○	●●	●●
butylene	●	●	○	●●	●●
n-hexane	●	●	●	●●	●●
propylene	○	●●	○	●●	●●
hydrogen	○	○	●●	●●	
hydrochloric acid	●●	●●	○	○	
vinyl acetate	●●	●●	○	●●	
polyethylene	○	○	●●	○	●●
styrene	●●●	●	●	●	
titanium tetrachloride	●●●	○	○	○	●●
alumina trihydrate	●	○	●●	○	●●
magnesium hydroxide	●	○	●●	○	
aluminum chloride	●	●●	○	○	
cyclohexane	●	●	●	●●	
triethyl aluminum	●●	○	○	●●	
polypropylene	○	○	●●	○	●●
acrylic acid	●●	●●	○	●	
methacrylic acid	●	●●	○	●	
methyl acrylate	●●	●●	○	●●	
methyl methacrylate	●	●●	○	●●	
polybutylene	○	○	●●	○	●●
isobutane	○	●	○	●●	
diethylaluminum chloride	●	○	○	●●	
diethyl aluminum hydride	●●	○	●●	●●	
titanium trichloride	●	○	○	●	●●
vanadium trichloride	●●	●	●●	●	○
magnesium ethylate	○	○	○	●	
2,6-di-*tert*-butyl-4-methylphenol	●	○	●●	○	
ethyl benzoate	●	●	●	●	
butyl alcohol	●	●●	○	●	●●
silicon dioxide	○	○	●●	○	○

TABLE 10. Qualitative Risk Rankings for Automotive Lead-Acid Battery Production

automotive lead battery	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
sulfuric acid	●●●	●●	○	●	●
calcium sulfate	○	●●	○	○	●●●
antimony	●●	○	●●	○	
arsenic	●●●	○	●●	○	
tin	●	○	●●	○	
soot	●●	○	●●	○	
lead	●●	○	●●	○	
lead oxide	●●	○	●●	○	
lead monoxide	●●	●	●●	○	●
lead dioxide	●●	●	●●	●	
sodium perchlorate	●	●●	○	●	
barium sulfate	●●	○	●●	○	
polyvinyl chloride	○	○	●●	○	
hydrochloric acid	●●	●●	○	○	

assumptions underlying each case result in different scores for the production of the material. Figure 5 shows the variability of the normal operations risk score as a range of values, with the midrange risk case appearing as the main data point. The non-nano production methods are scored with a single point because they have been previously established in the insurance database as fully scaled-up manufacturing processes, so variability in emissions data does not apply as it does with projecting the scaleup of nanomaterial production processes. In the case of ZnSe quantum dots, the different assumptions did not cause the final score to differ by orders of magnitude, so the range is very narrow. The normal operations risk scores show SWNTs and alumoxane production to be low again, on the order of the lowest scoring non-nanomaterial processes, wine and aspirin. Scores for C_{60}, ZnSe quantum dots, and nano-TiO_2 were again the highest three nanomaterials, scoring similarly to silicon wafers and automotive lead-acid batteries. Polyolefin production and petroleum refining scored higher than all of the nanomaterial production processes. To deal with the uncertainty involved with predicting industrial-scale manufacturing practices, the emissions values were chosen conservatively, erring on the side of more emitted materials and higher emissions levels. It is therefore likely that further development of the processes may contribute not only to reduced variability in the score but lower overall risk scores as well. For example, in the case of both SWNTs and alumoxane particles, the authors had access to more production information than the others; the normal operations risk scores for each of these prove to have narrow margins of error and lower overall values. Another illustration of the possible trend toward lower emissions for more developed processes is that mature processes with high incident risk, scores such as polyethylene production and silicon wafer production, have very low expected emissions and thus lower normal operations risk scores.

TABLE 11. Qualitative Risk Rankings for Refined Petroleum Production

refined petroleum	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
thiophene	●●●	●●	○	●●	
benzene	●●●	●●	○	●●	●●
ethylenediamine	●●	●●	○	●	
xylene	●●	●	●	●	
toluene	●●	●	●	●●	
paraffin oil	○	○	●●	●	
silica, crystalline	●●	○	●●	○	
methane	○	●	○	●●	●●●
ethylene	○	●	○	●●	
sulfur	●	○	●●	○	
butane	○	●	●	●●	
1,3-butadiene	●●●	●	○	●●	
sulfur dioxide	●●	●●	○	○	●●
hydrogen sulfide	●●	●●	○	○	
soot	●●	○	●●	○	
aluminum oxide	○	○	●●	○	
vanadium pentoxide	●●●	●●	●●	○	
chromic oxide	●●	●●	●●	○	
bitumen	●	○	●●	○	
anhydrous ammonia	●●	●●	○	●●	
carbon monoxide	●	●	○	●●	●
nitrogen dioxide	●●●	○	○	●	●●
phenol	●●	●●	○	●	●

TABLE 12. Qualitative Risk Rankings for Aspirin Production

asprin	toxicity	water solubility	log K_{ow} (bioaccumulation)	flammability	emissions
sodium phenolate	●●	●●	○	●	
phenol	●●	●●	○	●	○
toluene	●●	●	●	●●	
acetic acid	●●	●●	○	●	
salicylic acid	●	●●	○	○	○
sodium salicylate	●	●●	○	○	
acetic anhydride	●●	●●	○	●	
sulfuric acid	●●●	●●	○	●	
sodium sulfate	○	●●	○	○	○
carbon	○	○	●●	●	
carbon dioxide	○	●●	○	○	

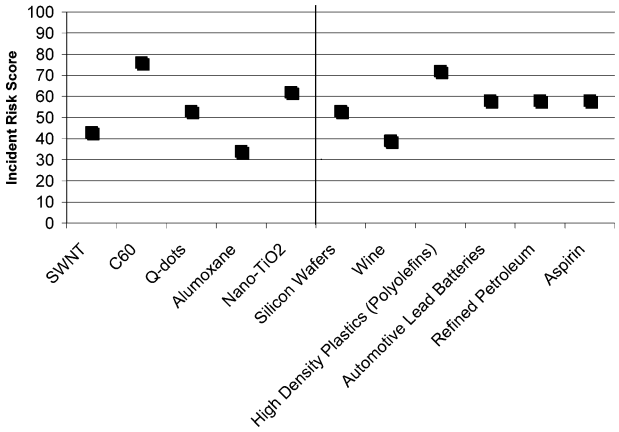

FIGURE 4. XL Database incident risk scores for nanomaterial and non-nanomaterial production processes.

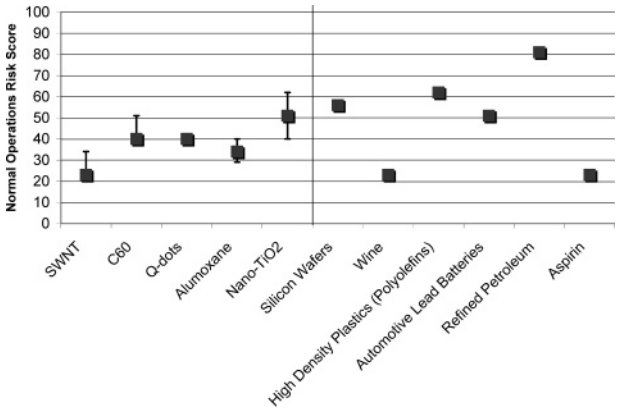

FIGURE 5. XL Database normal operations risk scores for nanomaterial and non-nanomaterial production processes.

Figure 6 shows similar rankings of the latent risks among the 11 compared processes; this is to be expected because latent risk is a function of the incident and normal operations risks with respect to soil and water. The results in this risk category show that all of the nanomaterials' fabrication processes with the exception of C_{60} compare similarly to silicon wafer, wine, and aspirin production and are lower than polyolefin, automotive lead-acid battery, and refined petroleum production. Although C_{60} production earns a markedly higher score than the other nanomaterials, it is comparable to the latent contamination score for polyolefin and automotive lead-acid battery production and is significantly lower than that of petroleum refining.

Numerical scores for all three risk categories are presented in Table 13 for all 11 processes, along with the culprit material or materials whose high score drove the incident risk or normal operations risk score.

TABLE 13. XL Insurance Database Risk Scores with Culprit Materials Responsible for the Risk Score

	incident risk		normal operations risk		latent risk
production process	score	culprit material(s)	score	culprit material(s)	score
single-walled nanotubes	43	carbon monoxide, iron pentacarbonyl	23−34	sodium hydroxide, carbon monoxide	25
C_{60}	76	benzene	40	soot, toluene	52−54
quantum dots	58	hydrogen selenide	40	hydrogen selenide, carbon monoxide, surfactant	24−31
alumoxane	34	acetic acid	29−40	acetic acid, aluminum oxide	11−26
nano-TiO_2	62	titanium tetrachloride	40−62	titanium tetrachloride	21−32
silicon wafers	53	sulfuric acid	56	arsine	19
wine	39	dithiocarbamate pesticides (zineb)	23	sulfur dioxide	12
high-density plastic (polyolefin)	72	titanium tetrachloride, vinyl acetate	62	titanium tetrachloride	51
automotive lead-acid batteries	58	lead dioxide	51	sulfuric acid, lead monoxide	50
refined petroleum	76	benzene, toluene	67	benzene, toluene, xylenes	42
aspirin	58	phenol, toluene	23	phenol	31

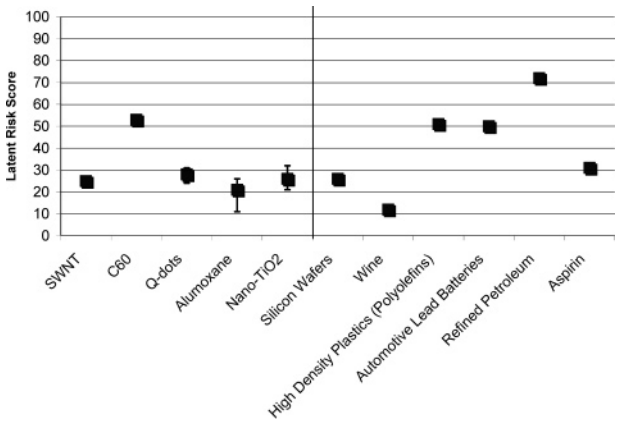

FIGURE 6. XL Database latent risk scores for nanomaterial and non-nanomaterial production processes.

Discussion

Our study in assimilating nanomaterials production into a risk assessment evaluation method concludes that there do not appear to be any unusual risks associated with the production of alumoxane, bucky balls (C_{60}), nano-titanium dioxide, ZnSe quantum dots, or single-walled carbon nanotubes. Although all of the processes used to make nanomaterials include processes and materials already in existence, understanding the relative risk of these combinations of substances and process characteristics is an important step in translating this emerging field into the language of risk assessment. Furthermore, it appears that according to the established methods of quantifying risk in the insurance and risk assessment communities, the fabrication of nanomaterials may present lower risks than those of current activities such as petroleum refining, polyethylene production, and synthetic pharmaceutical production.

Several objectives could be pursued to further examine and refine our conclusions. Empirical data regarding mass balances of waste streams and yield rates would help corroborate emissions values calculated theoretically based on reaction stoichiometry. Since the insurance protocol applied in this study scores process risks by orders of magnitude, it only accounts for the highest scoring material rather than accounting for multiple chemicals. A potential improvement would be the incorporation of a method for determining the cumulative contribution to risk of multiple substances and their interactions. Most significant would be the collection of more data regarding the industrial-scale operations for producing larger volumes of the materials than were produced under the conditions in publications of the methods. Narrowing the risk range seen in our normal operations scoring would be a primary benefit of these data. Our results from both the qualitative and insurance-based approaches suggest that, almost as much as constituent substances in a process, differences in handling operations could have a marked effect on the final risk scores. Recycling and successful recapture of materials play a key role in lowering normal operations risk scores. Although some materials conservation was assumed in the risk calculations, nanomaterial producers could greatly mitigate their risks through more rigorous process practices. Such a trend is likely as industrial-level production earns greater economies of scale on recycling infrastructure and delivers increased savings with recapture and reuse of more materials. The nanomaterials fabrication industry is presented with an opportunity to employ green chemistry principles as the onset of rapid growth occurs concurrently with new availability of risk information.

A 2004 preliminary risk assessment conducted by the Health and Consumer Protection Division of the European Commission included the suggestion that data collection on some of the particle characteristics that have been previously undocumented should begin and that a system of nomenclature for nanomaterials be developed (*20*). Moreover, the European Commission's report also stated that nanotechnology concepts should be integrated into our current insurance risk assessment methods so that "the risk assessment community can at least be speaking a common language when tackling this new challenge." Beyond the risk assessment community, the impact of understanding businesses' exposure to risk is also significant. To the many investors and entrepreneurs venturing into the burgeoning field of nanomaterials' manufacturing immediately, the financial benefits of estimating risk include cost avoidance, lower insurance premiums, reduced legal and regulatory costs, preferred loan rates, and significantly, avoidance of lost revenue due to consumer activist actions (*21*). Though toxicological studies are not adequate to fully assess the life-cycle impacts of these nanomaterials, our manufacturing risk information based on the current state of the field suggests that the in-plant processes and materials used in fabrication of these five nanomaterials pose moderate to relatively low risks from an insurer's perspective. By decoupling risks associated with handling inputs and wastes in the nanomaterial production process from any possible direct risks posed by nanomaterials, we can begin the processes of bringing nanomaterial fabrication into the risk assessment framework used to qualify industrial risks. Using this work as a baseline of information concerning hazards posed by manufacturing nanomaterials, the industry can focus on how to develop safely and responsibly.

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Supporting Information Available

A detailed explanation of the XL Insurance Database protocol, process maps depicting the nanomaterials production processes evaluated in this study, and assumptions behind entering the nanomaterials fabrication methods into the XL Insurance Database for ranking their relative risk. This information is provided free of charge via the Internet at http://pubs.acs.org.

Literature Cited

(1) Zhang, Z.; Kleinstreuer, C.; Donohue, J. F.; Kim, C. S. Comparison of micro- and nano-size particle depositions in a human upper airway model. *J. Aerosol Sci.* **2005**, *36* (2), 211−233.

(2) Lam, C.-W.; James, J. T.; McCluskey, R.; Hunter, R. L. Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation. *Toxicol. Sci.* **2004**, *77* (1), 126−134(9).

(3) Shvedova, A. A.; Castranova, V.; Kisin, E. R.; Schwegler-Berry, D.; Murray, A. R.; Gandelsman, V. Z.; Maynard, A.; Baron, P. Exposure to carbon nanotube material: Assessment of nanotube cytotoxicity using human keratinocyte cells. *J. Toxicol. Environ. Health, Part A* **2003**, *66*, 1909−1926.

(4) Warheit, D. B.; Laurence, B. R.; Reed, K. L.; Roach, D. H.; Reynolds, G. A. M.; Webb, T. R. Comparative pulmonary toxicity assessment of single-wall carbon nanotubes in rats. *Toxicol. Sci.* **2004**, *77*, (1), 117−125.

(5) Chen, L.; Yang, X.; Peng, K.; Cheng, F.; Zhu, H. Dynamic research of photo-induced toxicity against cell membrane by water-soluble C_{60} derivative. *Gaojishu Tongxin* **2001**, *11* (2), 17−20.

(6) Rajagopalan, P.; Wudl, F.; Schinazi, R. F.; Boudinot, F. D. Pharmacokinetics of a water-soluble fullerene in rats. *Antimicrob. Agents Chemother.* **1996**, *40* (10), 2262−2265.

(7) Oberdorster, E. Manufactured nanomaterials (fullerenes, C-60) induce oxidative stress in the brain of juvenile largemouth bass. *Environ. Health Perspect.* **2004**, *112* (10), 1058−1062.

(8) Oberdorster, G.; Beckett, W. S.; Chalupa, D. F.; Pauly-Brown, A.; Speers, D. M.; Stewart, J. C.; Frampton, M. W.; Utell, M. J.; Huang, L.-S.; Cox, C.; Zareba, W. Comparing inhaled ultrafine vs fine zinc oxide particles in healthy adults: A human inhalation study. *Am. J. Respir. Crit. Care Med.* **2005**, *171* (10), 1129−1135.

(9) Lecoanet, H. F.; Bottero, J.-Y.; Wiesner, M. R. Laboratory assessment of the mobility of nanomaterials in porous media. *Environ. Sci. Technol.* **2004**, *38* (19), 5164−5169.

(10) Lecoanet, H. F.; Wiesner, M. R. Velocity effects of fullerene and oxide nanoparticle deposition in porous media. *Environ. Sci. Technol.* **2004**, *38* (16), 4377−4382.

(11) Karanikolos, G. N.; Alexandridis, P.; Itskos, G.; Petrou, A.; Mountziaris, T. J. Synthesis and size control of luminescent ZnSe nanocrystals by a microemulsion-gas contacting technique. *Langmuir* **2004**, *20* (3), 550−553.

(12) Bronikowski, M. J.; Willis, P. A.; Colbert, D. T.; Smith, K. A.; Smalley, R. E. Gas-phase production of carbon single-walled nanotubes from carbon monoxide via the HiPco process: A parametric study. *J. Vac. Sci. Technol.* **2001**, *19* (4), 1800−1804.

(13) Zhennan, G.; Jiuxin, Q.; Xihuang, Z.; Yongqing, W. Buckminsterfullerine C_{60}: Synthesis, spectropic characterization, and structure analysis. *J. Phys. Chem.* **1991**, *95* (24), 9615−9618.

(14) Howard, J. B.; McKinnon, J. T.; Johnson, M. E.; Makarovsky, Y.; Lafleur, A. L. Production of C_{60} and C_{70} fullerenes in benzene−oxygen flames. *J. Phys. Chem.* **1992**, *96* (16), 6657−6662.

(15) Callender, R. L.; Harlan, J.; Shapiro, N. M.; Jones, C. D.; Callahan, D. L.; Wiesner, M. R.; MacQueen, D. B.; Cook, R.; Barron, A. R. Aqueous synthesis of water-soluble alumoxanes: Environmentally benign precursors to alumina and aluminum-based ceramics. *Chem. Mater.* **1997**, *9* (11), 2418−2433.

(16) Duyvesteyn, W. P. C.; Malcome, S. T.; Sabacky, B. J.; Prochazka, J. Processing aqueous titanium chloride solutions to ultrafine titanium dioxide. U. S. Patent 6,440,383, 2002.

(17) Pojasek, R. B. Understanding Processes with Process Mapping. *Pollut. Prev. Rev.* **1997**, (Summer), 91−101.

(18) *XL Pollution Index: The Scientific Basis*; XL Insurance Risk Engineering: Zurich, Switzerland, April 2004; pp 3−16.

(19) Tanzil, D.; Murphy, K.; Schwarz, J.; Restoske, M.; Beloff, B.; Beaver, E. *Incorporating Total Cost Assessment Methodology to Enhance Chemical Complex Optimization*; BRIDGES to Sustainability: Houston, TX, 2002; p 30.

(20) In *Nanotechnologies: A Preliminary Risk Analysis on the Basis of a Workshop*, Brussels, Belgium, March 2004; Community Health and Consumer Protection Directorate General of the European Commission: Brussels, Belgium 2004; pp 11−29.

(21) Willard, B., *The Sustainability Advantage: Seven Business Case Benefits of a Triple Bottom Line*; New Society Publishers: Gabriola Island, BC, Canada, 2002; p 135.

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