Probabilistic and Multi-criteria Operations Research Nanomanufacturing Risk Assessment Models

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ABSTRACT

Although the rapidly developing nanotechnology field holds enormous societal promise across a range of energy, medicine, electronics, and consumer product applications, significant uncertainty also exists about occupational, consumer, and environmental, health, and safety (EHS) risks associated with many nanomaterials, uses, and processes. Since better toxicology data are unlikely to be available for several years, modeling relative risks is very important to help compare materials and processes, inform decision making, and prioritize EHS research. Many decisions additionally involve multiple criteria, such as balancing exposure, production yield, product reliability, and cost. Yet researchers, policy makers, and businesses working with engineered nanomaterials often have little guidance for how to best manage such processes. We develop and illustrate several operations research risk modeling approaches (Monte Carlo, goal programming, stochastic programming, and desirability function models) for a range of nanotechnology research, laboratory, and production contexts – spanning the continuum from fume hood design to production optimization to regulatory policy. The utility of these methods is demonstrated for helping to develop better understandings of the relative risks, benefits, and tradeoffs necessary to maximize nanotechnology’s great potential.

Key words: Carbon nanotubes, nanomaterials, EHS, occupational health, multi-criteria, uncertainty
1. INTRODUCTION

Nanotechnology holds enormous promise in energy, technology, medicine, electronics, consumer products, and other applications – with over $12 billion spent in 2006 alone on technology and commercialization research and with 800+ consumer goods already on the market\(^{(1)}\). In parallel, however, significant uncertainty and concerns exist regarding occupational and public health risks of nanomanufacturing processes and engineered nanomaterials, and in turn significant uncertainty about appropriate workplace safeguards and commercialization regulations. Of the toxicity studies to date, several suggest that engineered nanomaterials may pose potential human health risks, due to their small size and large surface area allowing them to penetrate dermal barriers, cross cell membranes, breach gas exchange regions in lungs, travel throughout the body, and interact at the molecular level\(^{(2)}\). By example, critical reviews of single wall carbon nanotubes (SWNTs) toxicity found damage to mice lung tissue\(^{(3,4)}\), although further research is necessary to understand any translational risks to humans. In response, several authors and regulatory bodies have advocated more research on nanotechnology environmental, health, and safety (EHS) implications\(^{(5)}\), including the U.S. Environmental Protection Agency, National Institute for Occupational Safety and Health, and National Nanotechnology Initiative\(^{(6,7,8,9,10)}\).

Published nanotoxicology studies have increased nearly 600% since 2000, with over 1,900 articles focused on human and ecological risks\(^{(11)}\). One of the most studied eco-concerns is the potential effects and risks of nanoscale materials (fullerenes\(^{(12,13)}\), carbon nanotubes\(^{(14)}\), silver nanoparticles\(^{(15,16)}\), and others\(^{(17)}\) to aquatic ecosystems. Human health concerns focus mainly on nanomaterials used in consumer products and cosmetics, such as studies of carbon nanotube toxicity\(^{(3)}\) and of human skin penetration of sunscreen zinc oxide\(^{(18)}\) and titanium dioxide\(^{(19)}\). Such toxicity and exposure studies, combined with categorization\(^{(20)}\) and characterization\(^{(21)}\) of nanomaterials, are beginning to shape EHS nanotechnology risk assessment and regulation, yet development of more precise understandings of these risks likely will take several years. For example, although carbon nanotubes are among the most studied nanomaterials, the behavioral differences between single and multi-wall carbon nanotubes remain unclear. Recent nanomaterial and nanotechnology assessment studies discuss possible benefits, potential risks, and knowledge gaps\(^{(22,23)}\), the potential applicability of past experiences with other technologies to nanotechnology issues\(^{(24,25)}\), and efforts to address EHS concerns\(^{(26,27)}\). Until proposed studies develop better understandings of these issues, however, nanomaterial researchers, policy makers, and businesses have little guidance to inform safe handling of engineered nanomaterials.

Despite the above concerns, very limited work has been conducted to develop nanotechnology risk models, with only a few published studies appearing recently. These include Monte Carlo models to
compare alternate SWNT workplace safeguards\textsuperscript{(28)}, multi criteria decision analysis methods to prioritize hypothetical alternate nanomaterials\textsuperscript{(29)}, expert elicitation to develop exposure-response functions for nanomaterials\textsuperscript{(30)}, and scenario-based life-cycle risk analysis for a particular nano-product (an air freshener spray)\textsuperscript{(31)}. Although life cycle assessment (LCA) and related cost modeling techniques are increasingly used in materials assessment\textsuperscript{(32)} and have been used to study economic and environmental impacts of carbon nanotube manufacturing\textsuperscript{(33)}, limited information about exposure, costs, and effectiveness of various EHS protections limits their ability to inform nanotechnology decisions in meaningful ways.

Several risk assessment methods, however, that are used in a variety of other industries (nuclear power, aerospace, chemical processes, transportation, military, and financial management)\textsuperscript{(34)} could be similarly useful in nanomanufacturing, including Monte Carlo models\textsuperscript{(35,36)}, Bayesian approaches, tree analyses, and multi criteria decision analysis tools\textsuperscript{(37)}. Bayesian methods are gaining wider acceptance to quantify uncertainties, with decision tree risk analysis and its various extensions such as multi-objective\textsuperscript{(38)} or Markov-cycle decision trees\textsuperscript{(39)} also increasingly being used in probabilistic risk assessment.

Table I summarizes possible operations research modeling approaches for studying and managing nanotechnology risks - differing in the manner by which they handle uncertainty and multiple criteria tradeoffs - along with potential applications, strengths, and limitations for each. Some of the most promising approaches include Monte Carlo, multi-criteria, stochastic programming, and desirability function models, with the applicability of each depending on the problem setting and decision needs. Each of these approaches is illustrated in the following sections, using a variety of nanomanufacturing process as examples. More broadly, until more is known about the spectrum of possible risks of any
nanotechnology or nanomaterial, these types of models can help provide manufacturers, researchers, and policy makers with better frameworks for managing these risks, costs, and inherent trade-offs.

2. RISK ASSESSMENT MODELING APPROACHES

2.1. Monte Carlo Models

Monte Carlo (MC) simulation models are widely used in risk assessment because they are straightforward and can realistically capture process complexities, chance events, and probabilistic outcomes, with Table II summarizing some potential nanomanufacturing applications. MC results are computed from randomly generated data that emulate model input uncertainty (e.g., exposure amount, impact, regulatory requirements, associated costs), with results re-computed a large number of times in order to develop distributions and ranges of true (one-time) outcomes. These models can be run on a wide range of assumptions, help identify optimal decisions, and provide other useful information, such as identifying inputs for which further research would be the most useful in order to minimize uncertainty in results and make better decisions.

<table>
<thead>
<tr>
<th>Problem Type</th>
<th>Potential Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human health risk assessment</td>
<td>Exposure assessment of occupational health protection strategies</td>
</tr>
<tr>
<td></td>
<td>Modeling of a dose-response curve of a specific engineered nanomaterial</td>
</tr>
<tr>
<td>Ecological risk assessment</td>
<td>Estimation of nanomaterial accumulation in ecosystem</td>
</tr>
<tr>
<td></td>
<td>Risk modeling for environmental policy issues</td>
</tr>
</tbody>
</table>

As one example, Ok, Benneyan, and Isaacs\(^{(28)}\) developed a MC risk model to assess cost-exposure trade-offs in high pressure carbon monoxide (HiPco) processes, a common SWNT production process. Uncertainties associated with the process (e.g., costs and occupational health risks) and regulatory environment (e.g., EHS standards timing, requirements, and costs) are modeled as probabilistic events, with the produced results being in the form of distributions, probability intervals, confidence intervals, expected values, and standards deviations of production costs, occupational health exposure, or other important measures. As the MC model executes, it generates manufacturing costs, occupational exposure, and regulatory requirements according to context logic, computing total \(N\)-year costs and exposure amounts and repeating these \(N\)-year cycle computations some large number \(R\) times in order to obtain accurate results. For example, Figure 1 illustrates (top graph) the joint distribution of production cost and exposure for a given scenario and (bottom graph) the resultant total (production and exposure)
cost distribution under four difference sets of process, regulatory, and cost scenarios (10-year cycle; 10,000 replications). As shown, production costs and exposure are highly correlated, whereas the total costs (computed as in Ok, Benneyan, and Isaacs\cite{28}) illustrate interesting multi-modality, presumably due to discrete step-changes in EHS levels.

Note that the high amount of uncertainty in model inputs - costs, exposure, dose response, and regulatory environments - translates to excessive variability in results and at times significantly overlapping distributions. From a decision-making perspective, this exacerbates the ability to determine which EHS
policies would be best, since the true total cost of any given scenario might fall anywhere under its respective density function. A helpful framework in such cases, however, may be to identify conditions, processes, or decisions under which various types of stochastic ordering (or majorizing) exist\(^{(40,41)}\), concepts that have been used a bit in other risk contexts\(^{(42,43)}\). For example, the cumulative distributions in Figure 2 illustrate that costs and exposures under some scenarios are ordered stochastically; that is, given two decisions A and B, \(X_A\) is stochastically larger than \(X_B\) (written \(X_A \geq_s X_B\)) if \(P(X_A \leq d) \leq P(X_B \leq d)\) for all values of \(d\), where \(X_i\) is the true cost or exposure under decision \(i\).

In practical terms, the implication is that the probability that total cost exceeds some value \(d\) always is smaller for one scenario than all other scenarios, for all possible values of \(d\), and in this sense is always better (i.e., having less financial risk). By this criteria, scenario 4 in Figure 2 is dominantly the least preferable in terms of manufacturing costs, dominantly the most preferable in terms of exposure, and nearly preferable in terms of total cost. Scenario 3, however, is slightly preferred over scenario 4 across roughly 85% of the total cost probability space, despite not being dominant in production costs nor exposure individually, illustrating how this approach might lead to the discovery of non-obvious decisions.

2.2. Multi-criteria Methods

While the above approach helps analyze tradeoffs and optimize single-objective problems (or aggregate objective functions), multi-criteria decision making (MCDM) methods can help directly optimize decisions with multiple conflicting objectives (cost, yield, exposure, et cetera). Because all criteria usually cannot be optimized simultaneously, trade-off solutions that somehow balance all objectives are computed or identified. Many MCDM methods exist to address situations having either a continuous or discrete number of solutions (i.e., identifying optimal decision variable values or selecting between particular alternatives). Discrete methods most commonly include multi-attribute utility\(^{44}\), analytic hierarchy process (AHP)\(^{45}\), and outranking models\(^{46}\), whereas continuous methods most commonly include weighted-sum\(^{47}\), vector maximum\(^{48}\), and goal programming\(^{49}\) approaches. Each of these methods might be applicable to a wide range of nanomanufacturing applications, with some summarized in Table III.
Figure 2. HiPco cumulative probability distributions and full or partial stochastic orderings of SWNT manufacturing costs (top), exposure (center), total manufacturing-plus-exposure costs (bottom).
Table III. Potential nano applications for multi-criteria decision making methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Alternatives</th>
<th>Potential Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-attribute utility theory</td>
<td>Discrete</td>
<td>- Comparison of environmental risks of candidate nanotechnologies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Choice among business strategies for commercialization of nanotechnology</td>
</tr>
<tr>
<td>Analytic hierarchy process</td>
<td>Discrete</td>
<td>- Material selection for a nanomanufacturing application</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Ranking of environmental and health practices for safe nanotechnology</td>
</tr>
<tr>
<td>Outranking methods</td>
<td>Discrete</td>
<td>- Selection of a fume hood for a nanotechnology research lab from a set of alternatives</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Prioritization of nanomaterials used in nanotechnology research labs</td>
</tr>
<tr>
<td>Weighted-sums methods</td>
<td>Continuous</td>
<td>- Balance of engineering objectives in the nanomanufacturing process development</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Choice of specific process settings for a nanomanufacturing process</td>
</tr>
<tr>
<td>Vector maximum approach</td>
<td>Continuous</td>
<td>- Development of responsible nanomanufacturing processes by balancing benefits and risks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Design of nanotechnology research lab conditions to avoid nanoparticle exposure</td>
</tr>
<tr>
<td>Goal programming</td>
<td>Continuous</td>
<td>- Balance of reliability, exposure, and throughput in a nanomanufacturing process</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Production planning for a nanomanufacturing plant</td>
</tr>
</tbody>
</table>

The following example illustrates a potential use of goal programming (GP) to balance three criteria in a SWNT electrophoretic assembly nanomanufacturing process – reliability, throughput, and occupational safety – with goals and priorities for each factor summarized in Table IV. The overall GP objective here is to identify values of the three decision variables pH ($x_1$), conductivity ($x_2$), and temperature ($x_3$) that minimize total deviation from these goals. Here, the highest priority is given to maintaining a 90% reliability goal, with the two remaining goals (production, exposure) being secondary priorities. Of course, these goals and priorities can be updated as knowledge about emerging technologies evolves, since solutions are likely to be sensitive to these values.

Table IV. Inputs for electrophoretic assembly nanomanufacturing process goal programming example

<table>
<thead>
<tr>
<th>Priority Level</th>
<th>Factor</th>
<th>Goal</th>
<th>Penalty Weights</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-priority</td>
<td>Reliability rate</td>
<td>$\geq 90%$</td>
<td>$M$</td>
</tr>
<tr>
<td>Second-priority</td>
<td>Production rate</td>
<td>$\geq 10$ grams/hr</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Exposure level</td>
<td>$\leq 5$ units (on 1-10 scale)</td>
<td>3</td>
</tr>
</tbody>
</table>

Under the GP method, the highest priority goal is considered infinitely more important than others and a large penalty weight $M$ is assigned for deviations from this goal so that it definitely is met. Positive or
negative deviations from any goal $i$ are denoted by $d_i^-$ or $d_i^+$ (respectively corresponding to less-than and greater-than constraints), with the general GP formulation being

$$\text{lex} \min \{d_i^-, d_i^+, d_j^+\} \text{ is equivalent to }$$  
$$\min \ M d_i^- + 5d_j^- + 3d_j^+ \tag{1}$$

$$\text{s.t. } c^j x + d_i^- \geq 90\% \tag{2}$$

$$c^2 x + d_j^- \geq 10 \tag{3}$$

$$c^3 x - d_j^+ \leq 5 \tag{4}$$

$$x \in S \tag{5}$$

$$\text{all } d_i^\pm \geq 0 \tag{6}$$

where the $c^j$ terms are constraint vectors and $x$ is the decision variables vector. These models can be solved using Excel’s Solver or any standard linear programming software such as LINGOTM, GAMS™, CPLEX™, or others. Constraint relationships might be developed from first principles or designed experiments, as illustrated in section 2.4, although for the sake of illustration the example in Table IV using purely hypothetical constraints becomes

$$\text{lex} \min \{d_i^-, d_i^+, d_j^+\} \text{ is equivalent to }$$  
$$\min \ M d_i^- + 5d_j^- + 3d_j^+ \tag{7}$$

$$\text{s.t. } 0.098x_1 + 0.00014x_2 - 0.0004x_3 + d_i^- \geq 90\% \tag{8}$$

$$0.27x_1 - 0.0167x_2 + 0.058x_3 + d_j^- \geq 10 \tag{9}$$

$$- 0.01x_2 + 0.047x_3 - d_j^+ \leq 5 \tag{10}$$

$$7 \leq x_1 \leq 11, 100 \leq x_2 \leq 1000, 50 \leq x_3 \leq 200 \tag{11}$$

$$\text{all } d_i^\pm \geq 0 \tag{12}$$

example is illustrated here. Results of model indicate that the optimal solution in this case is $x_1^*$(pH) = 10.68, $x_2^*$ (conductivity) = 100 S/cm, and $x_3^*$ (temperature) = 151.49° F, satisfying the first two goals (reliability, production) but not the third (exposure) – but none-the-less optimal – and thereby resulting in optimal goal deviations of $d_j^- = 0$, $d_j^+ = 0$, and $d_j^{++} = 1.12$. Table V, however, illustrates the solution’s sensitivity to weights and constraints, which typically are somewhat arbitrary or include estimation error, with the weights varied between which criteria is most important in each example (inner rows) and with the pH, conductivity, and temperature model equations containing different amounts of experimental error (outer rows). The results indicated by “10% random error” and “20% random error” correspond to cases where the coefficients in equations (10) – (12) were randomly increased or decreased by 10% and 20% of their given values, respectively. In this example, the optimal value for temperature ($x_3^*$) appears most sensitive to penalty weight and model equation assumptions, in turn affecting whether the reliability, production, and exposure goals are satisfied (denoted with a check in Table V).
Table V. Sensitivity of goal programming example to weight selection and constraint model equation estimates

<table>
<thead>
<tr>
<th>Penalty Weights</th>
<th>Model Equations</th>
<th>Obj fn</th>
<th>Decision Variables</th>
<th>Deviations</th>
<th>Criteria (( \sqrt{\cdot} ) = goal satisfied)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( p_1 ) ( p_2 ) ( p_3 )</td>
<td>( M ) 5 3</td>
<td>3.36 10.68 100 151.49</td>
<td>0 0 1.12</td>
<td>1 ( \sqrt{\cdot} ) 10 ( \sqrt{\cdot} ) 6.12</td>
<td></td>
</tr>
<tr>
<td>( 5 ) ( M ) 3</td>
<td>as above</td>
<td>3.36 10.68 100 151.49</td>
<td>0 0 1.12</td>
<td>1 ( \sqrt{\cdot} ) 10 ( \sqrt{\cdot} ) 6.12</td>
<td></td>
</tr>
<tr>
<td>( 5 ) ( 3 ) ( M )</td>
<td>4.23 10.58 100 127.66</td>
<td>0 1.41 0</td>
<td>0.99 ( \sqrt{\cdot} ) 8.59 5 ( \sqrt{\cdot} )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( M ) ( 5 ) ( 3 )</td>
<td>10% random error</td>
<td>3.78 11 100 169.16</td>
<td>0 0 1.26</td>
<td>0.92 ( \sqrt{\cdot} ) 10 ( \sqrt{\cdot} ) 6.26</td>
<td></td>
</tr>
<tr>
<td>( 5 ) ( M ) 3</td>
<td>3.78 11 100 169.16</td>
<td>0 0 1.26</td>
<td>0.92 ( \sqrt{\cdot} ) 10 ( \sqrt{\cdot} ) 6.26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( 5 ) ( 3 ) ( M )</td>
<td>4.65 11 100 139.48</td>
<td>0 1.55 0</td>
<td>0.93 ( \sqrt{\cdot} ) 8.45 5 ( \sqrt{\cdot} )</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A related type of multi-objective optimization model uses one criteria (e.g., maximize production rate) in a (univariate) objective function subject to constraints that all other criteria meet some thresholds (e.g., exposure \( \leq \) threshold). By iterating across a range of values for these constraint thresholds, the optimal tradeoff frontier can be mapped out (e.g., the lowest exposure can be identified to achieve any desired production rate). For the electrophoretic assembly example, Figure 3 illustrates these trade-off frontiers for two and three criteria, leaving it to decision makers to determine exactly where they want to locate on this optimized surface.

On the top graph in Figure 3, for example, the maximum possible production rates at 2, 6, and 8 units of exposure are roughly 5 g/hr, 9.9 g/hr, and 12.4 g/hr, respectively, with the corresponding values of the pH, conductivity, and temperature decision variables in order to achieve these optima (different for each point on the frontier) noted on the graph. The dashed lines indicate the tradeoff frontiers if the response equation coefficients are randomly changed by 10%, again reflecting the sensitivity of results to experimental error. The bottom figure in Figure 3 similarly illustrates the tradeoff surface using all three criteria, e.g. the minimum exposure level possible to achieve specified production and reliability rates. Again, the optimal values of the decision variables may be different to achieve any given point on this surface, with the decision-maker first specifying which of these possible optimal tuple values (exposure, production, reliability) is desirable.
2.3. Stochastic Programming Models

Stochastic programming (SP) models include either probabilistic objective functions (such as to minimize expected exposure or the probability that cost exceeds some amount) or probabilistic constraints (such as not allowing total exposure to exceed some value with some probability), often with uncertainty represented by probability distributions or treating secondary objectives as probabilistic constraints (somewhat extending the above frontier idea). Two standard types of SP models are recourse\(^{(50,51)}\) and chance-constrained\(^{(52)}\) models, with Table VI summarizing potential nano applications of each.
Table VI. Potential nano stochastic programming applications

<table>
<thead>
<tr>
<th>Problem Type</th>
<th>Potential Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-period recourse models</td>
<td>- Investment planning for a nanomanufacturing plant</td>
</tr>
<tr>
<td></td>
<td>- Technology choices for a nanomanufacturing process</td>
</tr>
<tr>
<td></td>
<td>- Capacity planning for a small start-up company</td>
</tr>
<tr>
<td>Chance-constrained models</td>
<td>- Selection of optimal EHS strategy</td>
</tr>
<tr>
<td></td>
<td>- Yield/cost optimization for a nanomanufacturing process</td>
</tr>
<tr>
<td></td>
<td>- Material selection for a nanomanufacturing application</td>
</tr>
</tbody>
</table>

Recourse models often are used when sequential decisions over multiple time periods are possible, producing a schedule of optimal decisions for the present and next several time periods in the form of optimal corrective (recourse) actions, depending on which specific random events occur in the interim. An example might be a capacity planning problem in a nanomanufacturing facility under uncertain market, technology, and production conditions, adapting as the future unfolds and starting with an optimal capacity selected so as to be best positioned for possible recourse actions.

Chance-constrained programs are used to make decisions that ensure certain constraints will be satisfied with some specified probability, such as an investment portfolio selection example that ensures a loss greater than some value will occur with less than some specified probability. These models can be written in the general form

\[
\begin{align*}
\text{Minimize} & \quad f(x_1, x_2, x_3, x_4) \\
\text{subject to} & \quad P(c_1'x \geq b_1) \geq \alpha_1 \\
& \quad P(c_2'x \geq b_2) \geq \alpha_2 \\
& \quad P(c_3'x \leq b_3) \geq \alpha_3 \\
& \quad x \geq 0 \\
\text{where} & \quad 0 < \alpha < 1
\end{align*}
\]

where the \(c_i\) terms are constraint vectors, \(x\) is the decision variables vector, and \(\alpha_1\), \(\alpha_2\), and \(\alpha_3\) are user-specified probabilities of satisfying each constraint. To illustrate, an example of a chance-constrained model for the reliability of a nanomanufacturing process is
Minimize $6.5x_1 + 0.7x_2 + 3.25x_3 + 10x_4$

subject to

\[ P(0.137x_1 + 0.007x_2 - 0.0023x_3 + 0.033x_4 \geq 60\%) \geq 0.95 \]  

\[ P(1.82x_1 - 2.34x_2 + 7.1x_3 - 1x_4 \geq 10) \geq 0.90 \]  

\[ P(0.94x_1 - 0.0043x_2 + 0.13x_3 - 10x_4 \leq 2) \geq 0.95 \]  

\[ 7 \leq x_1 \leq 11, \quad 100 \leq x_2 \leq 1000, \quad 50 \leq x_3 \leq 200, \quad 1 \leq x_4 \leq 4 \]  

\[ x_1, x_2, x_3, x_4 \geq 0, \text{ and } x_4 \text{ integer} \]

where the objective function finds the values of four decision variables – pH \((x_1)\), conductivity \((x_2)\), temperature \((x_3)\), and occupational health protection level \((x_4)\) – that minimize cost while maintaining a yield rate of 60% with at least 95% probability, a production rate of 10 grams per hour with at least 90% probability, and cumulative exposure less than the “no observable effect” level with at least 95% probability (i.e., \(\alpha_{\text{Yield}} = 0.95, \alpha_{\text{Prod}} = 0.90, \text{ and } \alpha_{\text{Exp}} = 0.95\)).

As previously noted, constraint relationships, appropriate probability distributions, means, and standard deviations might be developed experimentally, however for illustration purposes a normal distribution and a coefficient of variation of 0.5 are assumed for all responses (where the polynomials inside each probability constraint define both the mean and standard deviation of the response), producing optimal decision variable values of \(x_1^*\) (pH) = 11, \(x_2^*\) (conductivity) = 292.5 S/cm, \(x_3^*\) (temperature) = 97.9° F, \(x_4^*\) (occupational health protection level) = 3, and a minimum cost of $624.57. As new technologies are developed, initially some processes might be extremely costly and tolerances might be relaxed to reduce costs but still be able to meet a reliability target with some probability.

Alternately, a stochastic programming recourse (SPR) model can be formulated to develop a schedule of optimal decisions for a multistage planning problem, such as for a nanomanufacturing plant, where decisions are dependent not only on random variables in the traditional SPR sense (such as future regulatory occupational health and safety requirements) but possibly also on “degrees of belief” or “probabilistic knowledge” such as true health risks. The idea is to produce a schedule of present and future decisions in the form of optimal corrective (recourse) actions dependent on specific outcomes or risk knowledge that develop over time. The following example illustrates a two-stage workplace safeguard investment decision problem for a SWNT nanomanufacturing workplace to minimize expected total costs over future time periods, where EHS requirements and associated costs are represented as random variables. Note that in this example the nanomanufacturing decision-maker considers one period into the future to plan investments and productions, although the example can be extended to include more time periods.
Figure 4 summarizes six hypothetical possible future scenarios for regulatory occupational health and safety requirements (levels 1-6), with associated costs per “unit” of safeguards ($C_1$-$C_6$) and equal probabilities of $p_1 = p_2 = \ldots = 1/6$ for sake of illustration. The nanomanufacturer can invest $X$ amount of safeguards in the current period with a cost of $100$ per unit. Due to uncertainty in the occupational health risks of engineered nanomaterials, however, future regulatory requirements are unknown. To satisfy these eventual possible requirements, if not currently met by the current level, recourse actions would be taken in subsequent periods with additional (usually higher) costs of $C_i \geq 100$ per unit to increase the amount of EHS safeguards to the required level.

The general formulation of this type of problem, where the objective function seeks to minimize the total expected cost (i.e., the cost of the first-stage decisions, $f_1(x)$, plus the expected recourse cost of the second-stage problem, $E[f_2(x,w)]$), is

\[
\text{Minimize} \quad f_1(x) + E_w[f_2(x,w)] \\
\text{subject to} \quad Ax \geq b \quad (28) \\
\quad \quad \quad x \geq 0 \quad (29) \\
\text{where} \quad f_2(x,w) = \min \left\{ f(y,w) \middle| W(w)y \geq h(w) - T(w)x, y \geq 0 \right\} \quad (30)
\]

where $x$ is the first-stage decision (here the initial level of safeguards) and the second period recourse variable $y$ depends on the outcome of the random event vector $w$ (here the various safeguards that might be required in the future and their associated costs). Equation (30) solves the second-stage recourse problem for any given initial decision $x$ and random outcome $w$, minimizing the recourse cost, $f(y,w)$, across all possible recourse values for $y$. The right-hand term in the objective function finds the expected
value of this cost over all possible \( w \) outcomes for any given \( x \), with the total objective function then minimizing the total cost over all \( x \) (and \( y \)). Using the example in Figure 4, this model becomes

\[
\text{Minimize} \quad 100x + \left( 16.67y_{2,1} + 23.33y_{2,2} + 30y_{2,3} + 36.67y_{2,4} + 43.33y_{2,5} + 50y_{2,6} \right) \\
\text{subject to} \quad \begin{align*}
  x + y_{2,1} & \geq 0 \\
  x + y_{2,2} & \geq 1 \\
  x + y_{2,3} & \geq 2 \\
  x + y_{2,4} & \geq 3 \\
  x + y_{2,5} & \geq 4 \\
  x + y_{2,6} & \geq 5 \\
  x, y_{2,1}, y_{2,2}, y_{2,3}, y_{2,4}, y_{2,5}, y_{2,6} & \geq 0
\end{align*}
\]

where \( x \) is the initial amount of occupational safety investment at the first stage and \( y_{i,j} \) is the recourse action at stage \( i \) for scenario \( j \). The objective function is the sum of the initial costs for the first stage (100\( x \)) plus the expected cost for the optimal second stage decisions (\( p_1C_{1y_{2,1}} + p_2C_{2y_{2,2}} + \ldots = 16.67y_{2,1} + 23.33y_{2,2} + \ldots \)). In this example, the optimal (minimum) value of the objective function (total two-year expected cost) is $443.33, with decision variables \( x^* = 3, y_{2,1}^* = 0, y_{2,2}^* = 0, y_{2,3}^* = 0, y_{2,4}^* = 0, y_{2,5}^* = 1, \) and \( y_{2,6}^* = 2 \). Thus to minimize total expected cost, the decision maker should initially invest in 3 occupational safety units, with no additional investment if scenarios 1-4 occur, 1 additional unit at a cost of $260 if scenario 5 occurs, and 2 additional units at $300 each if scenario 6 occurs. Figure 5 summarizes the change in the minimal possible total expected cost depending on the initial occupational safety investment level, \( x \).

![Figure 5. Effect of initial occupational safety investment level on total expected cost](image-url)
2.4. Desirability Functions

A less-familiar multi-criteria approach based on desirability functions\(^{(53)}\) also can be used either to choose between a finite number of alternatives\(^{(54)}\) (e.g., fume hood selection) or to identify the optimal settings of continuous process variables (e.g., flow rate, hood height, solution concentration), similar to multi-attribute methods and GP or SP models, respectively. Each criteria’s value, \(Y_i\), (which depends on the alternative selected or process variable settings) is transformed to a dimensionless desirability value \(d_i\) where \(0 \leq d_i \leq 1\), the value of \(d_i\) increases as the desirability of the corresponding \(Y_i\) increases, and \(d_i = 0\) and \(d_i = 1\) correspond to completely unacceptable (undesirable) and acceptable (desirable, ideal) results, respectively. These individual \(d_i\) values then are combined into an overall desirability value \(D\) associated with each possible combination of results for the \(K\) criteria of interest, and the optimum solution is found as that which maximizes \(D\). Sensitivity and what-if analysis can be conducted by examining plots of the desirability surface, providing practical process improvement insights (e.g., moving in steepest ascent directions).

Table VII. Potential nano applications of desirability functions

<table>
<thead>
<tr>
<th>Problem Type</th>
<th>Potential Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discrete problems</td>
<td>- Selection among distinct workplace safeguards</td>
</tr>
<tr>
<td>(selecting among several alternatives)</td>
<td>- Determination of the most preferred process from alternate nanomanufacturing processes</td>
</tr>
<tr>
<td></td>
<td>- Material selection for a nanomanufacturing application</td>
</tr>
<tr>
<td>Continuous problems</td>
<td>- Balance among reliability, exposure, and throughput in the development of a nanomanufacturing process</td>
</tr>
<tr>
<td>(finding optimum variable values)</td>
<td>- Development of specific nanomanufacturing processes by balancing benefits and risks</td>
</tr>
</tbody>
</table>

The following two examples illustrate discrete and continuous uses of desirability functions to select nanotechnology laboratory equipment and to optimize fume hood effectiveness against engineered nanomaterials, with other possible nano applications summarized in Table VII. In the first (discrete) case, three criteria are important for an effective fume hood – air flow \(Y_1\), cost \(Y_2\), and ease of use \(Y_3\). Figure 6 illustrates desirability curves for each criteria, here using standard Derringer and Suich\(^{(55)}\) one-sided (larger-is better (Equation (39)), smaller-is-better (Equation (40))), and two-sided (nominal-is-best (Equation (41))) transformations, with shape parameters \(P = 1\), \(R = 2\), and \(S = T = 1\). For any criteria value, a zero-to-one desirability value can be found from the corresponding curve, where \(Y_{i\text{-min}}\), \(\tau_i\), and \(Y_{i\text{-max}}\) are the minimum, target, and maximum values of the criteria response \(Y_i\).
Figure 6. Fume hood desirability curves for cost (top), air flow (center), ease of use (bottom).

\[
d_i = \begin{cases} 
0 & Y_j \leq Y_{i_{\text{min}}} \\
\left( \frac{(Y_j - Y_{i_{\text{min}}})}{(Y_{i_{\text{max}}} - Y_{i_{\text{min}}})} \right) & Y_{i_{\text{min}}} \leq Y_j \leq Y_{i_{\text{max}}} \\
1 & Y_j \geq Y_{i_{\text{max}}} 
\end{cases}
\]  

(39)
In addition to the desirability curves, each criteria \( i \) has an associated importance weight \( w_i \), usually based on expert judgment, that are used to compute the overall desirability \( D \). Table VIII summarizes individual criteria desirabilities and the overall desirability \( D \) of each candidate fume hood, typically calculated as a weighted geometric mean

\[
D = (d_1^{w_1} d_2^{w_2} d_3^{w_3})^{1/\sum w_i},
\]

for 3 different \((w_1, w_2, w_3)\) weight combinations. In the first case (i.e., \( w_1 = 2, w_2 = 4, w_3 = 1 \)), fume hood F2 has the largest \( D \) value and this is the best selection in terms of balancing effectiveness, cost, and ease of use, although as shown different weights (or mathematical forms for \( d_i \) and \( D \)) can change the results, underscoring the importance of sensitivity analysis.

Table VIII. Individual desirability values and overall desirability for each candidate fume hood (shaded cells indicate optima)

<table>
<thead>
<tr>
<th>Candidate Fume Hood</th>
<th>Cost</th>
<th>Individual criteria and desirabilities ( (d_i) )</th>
<th>Overall Desirability ( D ) ( (w_1, w_2, w_3) )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cost ( d_1 )</td>
<td>Effectiveness ( d_2 )</td>
</tr>
<tr>
<td>F1</td>
<td>$7,500</td>
<td>0.56</td>
<td>145</td>
</tr>
<tr>
<td>F2</td>
<td>$9,500</td>
<td>0.30</td>
<td>120</td>
</tr>
<tr>
<td>F3</td>
<td>$6,000</td>
<td>0.81</td>
<td>110</td>
</tr>
</tbody>
</table>

Alternately, the following example of a continuous problem seeks to find the values of three continuous decision variables – fume hood height \((x_1)\), sash position \((x_2)\), and volume flow rate \((x_3)\) – that optimize fume hood effectiveness against exposure to nanomaterials. The overall desirability \( D \) is maximized based on four criteria that are important for fume hood performance – face velocity \((Y_1)\), turbulence \((Y_2)\), particle size distribution \((Y_3)\), and particle number concentration \((Y_4)\) – across all possible values of the
controllable factors (i.e., \(x_1, x_2, \) and \(x_3\)). For \(Y_1\) and \(Y_2\) the two-sided transformation (where \(Y_{1\text{min}} = 100, Y_{1\text{max}} = 150, \tau_1 = 125, Y_{3\text{min}} = 10, Y_{3\text{max}} = 100, \) and \(\tau_3 = 30\)) and for \(Y_3\) and \(Y_4\) the one-sided transformations (where \(Y_{2\text{max}} = 10\%\) and \(Y_{4\text{max}} = 100\)) are used. For this example, it is assumed that desirability changes in a linear manner (i.e., shape parameters \(R = S = T = 1\)) and that all criteria are equally important (i.e., \(w_1 = w_2 = w_3\)), although in practice this need not always be the case.

Table IX. Example of experimental design used to develop responses for desirability function example

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Fume Hood Height</th>
<th>Sash Position</th>
<th>Value Flow Rate</th>
<th>Face Velocity</th>
<th>Turbulence</th>
<th>Particle Size</th>
<th>Particle Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-1</td>
<td>-1</td>
<td>+1</td>
<td>118</td>
<td>14</td>
<td>55</td>
<td>133</td>
</tr>
<tr>
<td>2</td>
<td>+1</td>
<td>-1</td>
<td>-1</td>
<td>103</td>
<td>10</td>
<td>40</td>
<td>147</td>
</tr>
<tr>
<td>3</td>
<td>-1</td>
<td>+1</td>
<td>-1</td>
<td>143</td>
<td>11</td>
<td>115</td>
<td>167</td>
</tr>
<tr>
<td>4</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td>60</td>
<td>0</td>
<td>97</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>160</td>
<td>13</td>
<td>25</td>
<td>270</td>
</tr>
<tr>
<td>6</td>
<td>+1</td>
<td>-1</td>
<td>+1</td>
<td>68</td>
<td>8</td>
<td>52</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>-1</td>
<td>+1</td>
<td>+1</td>
<td>103</td>
<td>8</td>
<td>118</td>
<td>10</td>
</tr>
<tr>
<td>8</td>
<td>+1</td>
<td>+1</td>
<td>-1</td>
<td>95</td>
<td>6</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>9</td>
<td>-1.633</td>
<td>0</td>
<td>0</td>
<td>148</td>
<td>14</td>
<td>106</td>
<td>177</td>
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<tr>
<td>10</td>
<td>+1.633</td>
<td>0</td>
<td>0</td>
<td>65</td>
<td>3</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>-1.633</td>
<td>0</td>
<td>130</td>
<td>15</td>
<td>28</td>
<td>200</td>
</tr>
<tr>
<td>12</td>
<td>0</td>
<td>+1.633</td>
<td>0</td>
<td>95</td>
<td>1</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>0</td>
<td>0</td>
<td>-1.633</td>
<td>130</td>
<td>11</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td>0</td>
<td>+1.633</td>
<td>73</td>
<td>3</td>
<td>76</td>
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<tr>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>95</td>
<td>7</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>16</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>95</td>
<td>7</td>
<td>61</td>
<td>0</td>
</tr>
<tr>
<td>17</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>108</td>
<td>6</td>
<td>58</td>
<td>52</td>
</tr>
<tr>
<td>18</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>108</td>
<td>6</td>
<td>58</td>
<td>70</td>
</tr>
<tr>
<td>19</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>98</td>
<td>5</td>
<td>64</td>
<td>13</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>98</td>
<td>6</td>
<td>70</td>
<td>0</td>
</tr>
</tbody>
</table>

Again, the mathematical relationships between the decision variables and response values might be developed experimentally. For illustration purposes, a three-factor rotatable central composite experimental design (Table IX) was used to fit empirical models for each response, producing

\[
\hat{Y}_1 = 105.0 - 25.0x_1 - 7.89x_2 - 18.4x_3, \quad (42)
\]

\[
\hat{Y}_2 = 7.70 - 3.00x_1 - 3.21x_2 - 1.73x_3, \quad (43)
\]

\[
\hat{Y}_3 = 68.7 - 8.46x_1 + 25.9x_2 + 9.81x_3, \quad \text{and} \quad (44)
\]

\[
\hat{Y}_4 = 65.7 - 48.6x_1 - 47.5x_2 - 38.0x_3. \quad (45)
\]

In general, we have had very successful experience developing accurate response models via design experiments. In this example, the optimum values of the decision variables are \(x_1^* = 0.57, x_2^* = 1.05, \) and \(x_3^* = -1.633\) resulting in \(Y_1^* = 112.6, Y_2^* = 5.46, Y_3^* = 75.09, Y_4^* = 50.40, d_1^* = 0.51, d_2^* = 0.45, d_3^* = 0.36, \)
\[ d_1^* = 0.49, \text{ and } D^* = 0.449. \] Again, sensitivity analysis could be conducted on the weights, response equations (especially since they may contain experimental error), and functional forms of \( d \) and \( D \).

3. CONCLUSIONS

Assessing tradeoffs among nanomanufacturing safety, production, and cost is both difficult and important due to the significant promise of nanotechnology and the significant uncertainty that exists about exposure effects, future regulatory environments, production capability, and all associated costs. Sufficient toxicology and other studies, moreover, are expected to take many years to develop actionable information, leaving nanomaterial researchers, businesses, and policy makers with little guidance in the foreseeable future for important decisions and safe operating practices. This paper illustrates several operations research risk assessment models – including Monte Carlo, goal programming, stochastic programming, and desirability function methods – that can be further developed and used to help inform the difficult tasks of identifying appropriate or optimal process design, equipment selection, and regulatory decisions across a wide range of research, laboratory, and production contexts. As more becomes known about nanomaterial exposure risks, these models can be updated to reflect the current knowledge base, suggesting optimal decisions likely will change over time, in turn underscoring the value of stochastic programming and other multi-period models.
REFERENCES


2 NIOSH, Progress toward safe nanotechnology in the workplace. 2007, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health: Washington, DC.


