Guest Editorial

Introduction to Special Section on Sensitivity Analysis and Summary of NCSU/USDA Workshop on Sensitivity Analysis

by

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Abbreviated Title: Sensitivity Analysis

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Abstract
This guest editorial is a summary of the NCSU/USDA Workshop on Sensitivity Analysis held June 11-12, 2001 at North Carolina State University and sponsored by the U.S. Department of Agricuture's Office of Risk Assessment and Cost Benefit Analysis. The objective of the workshop was to learn across disciplines in identifying, evaluating, and recommending sensitivity analysis methods and practices for application to food safety process risk models. The workshop included presentations regarding the Hazard Assessment and Critical Control Points (HACCP) framework used in food safety risk assessment, a survey of sensitivity analysis methods, invited white papers on sensitivity analysis, and invited case studies regarding risk assessment of microbial pathogens in food. Based upon the sharing of interdisciplinary information represented by the presentations, the workhop participants divided into breakout sessions responded to three trigger questions: What are the key criteria for sensitivity analysis methods applied to food safety risk assessment?; What sensitivity analysis methods are most promising for application to food safety and risk assessment?; and What are the key needs for implementation and demonstration of such methods? The workshop produced agreement regarding key criteria for sensitivity analysis methods and the need to use two or more methods to try to obtain robust insights. Recommendations were made regarding a guideline document to assist practitioners in selecting, applying, interpreting, and reporting the results of sensitivity analysis.

Key Words: Sensitivity Analysis, Food Safety, Uncertainty, Variability, Modeling

Introduction

On June 11-12, 2001, NC State University hosted a Workshop on Sensitivity Analysis, sponsored by the U.S. Department of Agriculture's Office of Risk Assessment and Cost Benefit Analysis (USDA/ORACBA). This special section of Risk Analysis is based upon several papers originally developed for and presented at the workshop. The workshop is part of a project whose objective is to transfer, apply, and adapt sensitivity analysis methods developed in other disciplines (e.g., complex engineered systems, others) to food safety risk assessment. Sensitivity analysis of process risk models of microbial pathogens in food is hypothesized to be a means for identifying potential "critical control points" and key uncertainties in the farm-to-table continuum.

Papers in the Special Section

An accompanying guest editorial by Hulebak and Schlosser describes the Hazard Assessment and Critical Control Point (HACCP) concept that underlies risk assessment and risk management pertaining to food safety.[1] Because the workshop was comprised of participants with different disciplinary backgrounds, it was important to introduce everyone to a similar conceptual framework. The workshop participants are listed in Table 1.

In order to learn from different disciplines, and in preparation for the workshop, NCSU prepared a literature review and report regarding sensitivity analysis methods, including the strengths and limitations of selected methods that merit consideration for possible application to food safety risk assessment.[2] The paper presents a brief overview of the risk assessment framework pertaining to food safety risk assessment and then reviews some key issues in food safety risk modeling, including the purpose of the model, complexity, verification, validation, extrapolation, and the role of sensitivity analysis. Sensitivity analysis methods are classified as mathematical, statistical, and graphical. Ten specific methods are reviewed, including nominal range sensitivity analysis, difference in log-odds ratio, break-even analysis, automatic differentiation, regression analysis, analysis of variance, response surface methods, Fourier amplitude sensitivity test, mutual information index, and scatter plots. For each method, a description, example, advantages, and disadvantages are addressed. The methods are compared with respect to applicability to different types of models, computational issues, ease and clarity in representation of results, and purpose of the sensitivity analysis. Some methods are model-free and global in nature, and may be better able to deal with non-linear models that contain thresholds and discrete inputs than can other methods. However, because each sensitivity analysis method is based upon different measures of sensitivity, two or more methods can in general produce dissimilar results. Therefore, as a practical matter, it is advisable to explore two or more techniques in order to make a robust identification of the most sensitive inputs.

Selected experts were invited to write and present "white papers" reviewing the application of sensitivity and/or uncertainty analysis to complex engineered and/or environmental systems. The purpose of these white papers was to: (1) summarize the

development of sensitivity and uncertainty analysis of complex simulation methods in order to synthesize lessons learned in the field; (2) provide a state-of-the-art review and critique of selected applied methods and approaches; and (3) identify the most promising methods and approaches for application to large, complex food safety process risk models. The invited authors were Dr. Jon Helton, Sandia National Laboratory; Dr. Michael Kohn, National Institute of Environmental Health and Safety; Dr. Elisabeth Pate-Cornell, Stanford University; Dr. Andrea Saltelli, The European Commission; and Dr. Kimberly Thompson, Harvard School of Public Health. The white papers prepared by these authors were peer reviewed and revised for this special section of *Risk Analysis*.[3-7]

Dr. Saltelli's paper highlighted important criteria for sensitivity analysis methods.[3] These included the need to properly specify a model output that is directly relevant to a decision, as well as identification of desirable properties in sensitivity analysis methods. The latter includes ability to cope with the scale of inputs and the shape of distributions assigned to inputs; global methods that can deal with the simultaneous effects of variation in multiple inputs; model independent methods that work regardless of the functional form of the model; and an ability to group inputs as if they were a single factor. A distinction was made between prognostic (forecast) and diagnositic (estimation) models. Variance-based methods, such as variations of Sobol's method, are described and illustrated with an example using a prognostic model.

Dr. Helton's paper, co-authored with F.J. Davis, illustrates the use of Latin Hypercube sampling combined with statistical and regression techniques in an overall approach for first propagating probability distributions through a model and then analyzing the results to identify the most sensitive inputs.[4] The performance of selected sensitivity analysis methods with respect to linear test problems, monotonic nonlinear test problems, and non-monotonic test problems is addressed. The different test problems illustrate the strengths and weaknesses of specific sensitivity analysis methods. For example, regression techniques based upon linear measures, such as sample correlations, perform well on linear models. Rank-based regression techniques perform well on monotonic models. Common means, common locations, common medians, and statistical independence approaches performed well on non-monotonic test problems. With 150 cited references, the Helton and Davis paper also provides the reader with an introduction to a large supporting literature.

Dr. Kohn's paper discusses the reliability of a model, which in his view is related to the testability of the model.[5] If a model is not sensitive to variation in the inputs that exceeds the range of experimental error in the inputs, then the model would generate similar predictions regardless of the input parameter values specified within this range. If such behavior was not expected, then the credibility of the model may be in question. Conversely, if the model is highly sensitive to an input when varied within its range of experimental error, then it may be difficult to validate the model. The author introduces sensitivity analysis techniques based upon system sensitivity theory, with applications to empirical models and to metabolic networks. Examples of the application of such methods to physiological modeling are reviewed, illustrating the dynamic nature of

sensitivities. In one case study, it was possible to identify a relatively small number of inputs to which the model results were most sensitive, while in another case study the model output was sensitive to a larger portion of the inputs. Of significance is that the techniques discussed by the author support evaluation of the sensitivity of a dynamic system and can be applied to models of varying complexity. Sensitivity analysis was shown to provide insight into the apportionment of the model response to various inputs in a manner that can be explained based upon understanding of the biological processes being modeled.

Dr. Pate-Cornell's paper places risk analysis and sensitivity analysis more squarely in the context of government decision-making, including the process of formulating hypotheses and bounding of the risk analysis problem.[6] A probabilistic framework based upon Bayesian methods is described. This approach is motivated because "expert judgment is simply unavoidable" in most risk assessment problems. A brief discussion of key motivating questions, risk assessment frameworks, and modeling approaches is followed by a discussion of the difficulty of ranking risks when "conservative" assumptions are built into an assessment. Examples of three risk assessment case studies are given which feature decomposition of a problem into subsystems and identification of the weakest points in the systems. The overall risks estimated in each case were attributed to specific subsystems or triggering events. The quantitative analyses often produced surprises that were contradictory to conventional wisdom but that could be explained clearly and convincingly based upon the assessment. Some key issues regarding the role of stakeholders in risk assessment and management are reviewed, followed by a conceptual framework for dealing with epistemic and aleatory uncertainties. Different risk analysis methods may substantially complicate or preclude the ability to compare and rank risks, because different methods may be fundamentally incommensurate. Another challenge in risk assessments is conditionality predicated on key assumptions regarding scenarios or conservatism in inputs. Thus, this paper places the need for and interpretation of sensitivity analyses in the context of the formulation of a risk problem, including both the scenarios and the model, the source of information for developing model inputs, and the specific methods used to model the risk problem.

Dr. Thompson's paper addresses the risk management implications of the trend from point-estimate risk analysis to analyses that explicitly address both variability and uncertainty.[7] Using two example case studies, one based upon ground fatalities attributable to airline crashes, and the other based upon the risks and benefits of airbags, Thompson illustrates the importance of explicitly accounting for variability in risks. In the former case, risk is a function of distance from an airport, and in the latter case, risk varies with age, weight, size, and other factors. An understanding of variability aids in both risk communication and risk management by identifying opportunities to reduce risk for those who face the highest risks. An understanding of key sources of uncertainty can assist in identifying opportunities to seek better information in an effort to reduce uncertainty. With the growing role of probabilistic risk assessments pertaining to food safety, as reflected by recent examples for foodborne *Listeria monocytogenes*, *Vibrio parahaemolyticus* in raw molluscan shellfish, *Campylobacter* in chicken, *E. coli* O157:H7 in beef, and *Salmonella* Enteritidis in shell eggs and egg products, there will be

a need for risk managers to take into account both variability and uncertainty when developing risk management strategies.

Challenges for Sensitivity Analysis Applied to Food Safety Risk Assessment

To attune the workshop participants to the needs of and challenges faced by food safety risk modeling practitioners, case studies of food safety risk assessment models were presented by Greg Paoli of Decisionalysis Risk Consultants, Mark Walderhaug of the Center for Food Safety and Applied Nutrition (CFSAN) at the U.S. Food and Drug Administration (FDA), and Eric Ebel of the Food Safety and Inspection Service (FSIS) of USDA.

After all of the presentations were completed regarding HACCP, sensitivity analysis methods, the invited white papers, and the invited case studies, the participants were divided into working groups to formulate recommendations in response to specific trigger questions:

- What are the key criteria for sensitivity analysis methods applied to food safety risk assessment?
- What sensitivity analysis methods are most promising for application to food safety risk assessment?
- What are the key needs for implementation and demonstration of such methods?

The first question addresses the key challenges associated with sensitivity analysis applied to food safety risk assessment, while the latter two questions pertain to recommendations for identification, evaluation, and selection of methods and for transferring results into the hands of practitioners. The first question is addressed here, and the last two questions are addressed in the section on recommendations. Each point here represents, more or less, a consensus position of the workshop.

A key criteria for sensitivity analysis, and for the risk model and analysis in general, is that it must be relevant to a decision. This means that the model output of interest must be directly related to the decision. Using a highly stylized example, if a decision is informed by whether risk is above or below a threshold, then the model output should be a variable indicating the probability that the estimated risk is above or below the threshold. The sensitivity analysis should pertain to variation in inputs that causes a change in the value of this output that would lead to a different decision.

Technical requirements of a sensitivity analysis method are manifold and may differ from one application to another, and from one decision application to another. The ideal sensitivity analysis method would be applicable to models that have the following characteristics, which are typical of food safety risk models:

- nonlinearities
- thresholds (e.g., below which there is no growth of a microbial pathogen)

- discrete inputs (e.g., integer numbers of animals or herds, yes or no indicators of contamination)
- incorporation of measurement error
- variation in the scale (units and range) and shape of distributions of model inputs
- temporal and spatial dimensions, including dynamics, seasonality, or inter-annual variability

An ideal sensitivity analysis method would be model independent. Specifically, the sensitivity analysis method should not require the introduction of any assumptions regarding the functional form of the risk model and, therefore, should be applicable to a wide range of different model formulations. Although sensitivity analysis methods that are based upon linear formulations and additivity are relatively convenient and easy to apply, it is important that methods be used that take into account the simultaneous interaction among multiple inputs, especially for nonlinear models that contain thresholds.

The method should provide not just a rank ordering of key inputs, but also some quantitative measure of the sensitivity of each input so that it is possible to distinguish the most strongly sensitive inputs from those with weaker influence on the selected model output. For example, is the most sensitive of the inputs substantially more important than the second ranked input, or do the top two inputs have approximately equal influence on the model output?

While there was general acceptance of the potential importance of distinguishing variability and uncertainty where appropriate, there was also discussion that such a distinction could be useful but not essential in every case. Thus, it may or may not be necessary, in a particular assessment, to distinguish between variability and uncertainty when doing the sensitivity analysis. There was some discussion of trying to distinguish key sources of uncertainty that are based upon data analysis from key sources of uncertainty that are based upon expert judgment.

The results of both the risk analysis and the sensitivity analysis should be interpreted in terms of plausibility with respect to governing biological, physical, chemical, and other processes. The results should be explainable to key target audiences, such as risk managers and stakeholders.

There was discussion regarding the need to identify critical points in a model, even if the critical point is a fixed point estimate that represents a scenario or policy assumption. Some inputs to the model might be treated as fixed points because of lack of information regarding variability and/or uncertainty for those inputs.

There was much discussion about the different types of decisions that might be informed by sensitivity analysis, and whether the selection of sensitivity analysis methods should be motivated by the anticipated decision application of the analysis. Several different types of model applications and decision problems were discussed, including forecasting or prediction versus empirical, diagnostic or descriptive models. Some analyses are

intended to be predictive in the sense of forecasting the response of a system to specific policy options. Such analyses typically involve evaluation of future scenarios that cannot be directly validated. In contrast, in a diagnostic or descriptive case study, the intent may be to reconstruct a past scenario, and there may be opportunities to compare model predictions with observed data. Sensitivity analysis methods should be applicable to the type of model used and should be feasible to implement. In the modeling process, sensitivity analysis is typically done post hoc. Instead, there is a need to anticipate sensitivity analysis in the process of formulating the model so that sensitivity analysis may be more easily accommodated.

Because it is unlikely that one sensitivity analysis method will meet all of the criteria for an ideal method, the group agreed that it would be necessary to apply two or more sensitivity analysis methods in a given context in pursuit of obtaining robust insight regarding key sensitivities based upon different sensitivity analysis measures. Methods that have been peer reviewed, have been clearly demonstrated, and that are readily available will be more readily accepted by practitioners.

Because food safety risk assessment has implications for international trade, there was some discussion of the level of expertise needed to perform the risk assessment as well as the sensitivity analysis, the human resource problem these requirements might pose, the software and hardware requirements, and the capability of developing countries to produce or make use of such analyses. It was also pointed out that resource requirements should be identified up front, regardless of the organization or country that is sponsoring or conducting the assessment.

Recommendations Regarding Sensitivity Analysis and Food Safety Risk Assessment Modeling

In response to the second trigger question:

- What sensitivity analysis methods are most promising for application to food safety risk assessment?

the group did not identify specific methods. Instead, the group emphasized the key criteria that were generated in response to the first question. For example, methods that can deal with interactions, nonlinearities, discontinuities, and discrete inputs would be preferred over methods that cannot.

Methods that are global or generic, such as ANOVA, are likely to be more promising than other types of methods, although ANOVA also has some limitations. However, techniques are also needed that can identify not just the effect of variance in the inputs with respect to variance in the outputs, but also shifts in central tendency or position of the output associated with skewness of distributions assigned to inputs.

Before applying a sensitivity analysis method, it may help to reduce the computational burden by narrowing down the search space among the input parameters. For example, if

adverse consequences do not occur unless a temperature exceeds a threshold above which microbial growth becomes significant, it may not be necessary or important to analyze model behavior when the temperature is below the threshold. Thus, the search space could be narrowed to cases where the temperature is above the threshold in order to reduce computational time.

One participant suggested that it would be valuable to have examples of where erroneous sensitivity analyses lead to incorrect insights.

In response to the third trigger question,

- What are the key needs for implementation and demonstration of such methods?

The group agreed that there was a need to explore multiple sensitivity analysis methods and apply them to more than one food safety risk model. The methods should be tested at research institutes and efforts should be made to confirm or validate the results. The process of testing methods will help in establishing a track record for specific methods applied to food safety process risk models.

Based upon experience with sensitivity analysis methods and representative food safety process risk models, practitioners indicated that it would be useful to have a guideline regarding the use of sensitivity analysis methods. The guideline should not be too prescriptive, but should provide useful boundaries and principles for selecting, using, and interpreting sensitivity analysis methods, as well as in reporting results. A comparison of methods, taking into account real life constraints, should be part of the guideline. The guideline should outline a tiered approach to sensitivity analysis.

The guideline could make a useful contribution by clearly defining terminology. Because of the interdisciplinary nature of risk assessment and of sensitivity analysis, terms may be defined differently by different experts or practitioners. Therefore, a common reference regarding such definitions is important.

A need for training of practitioners was expressed in order to help practitioners learn about methods and to learn from other disciplines in using such methods.

The interpretation of sensitivity analysis results in terms of biological, physical, chemical, or other plausibility was mentioned repeatedly during the discussion. A potential concern is the possibility that a model is mis-specified. Because sensitivity analysis is conditional on the assumption that the model formulation is acceptable, it is important to have prior comfort with the plausibility of the model, and to examine the sensitivity analysis results to determine if any of the model responses are inconsistent with plausible expectations regarding the relationship between the model output and the model inputs. If the model is giving responses that appear to be in error, then the sensitivity analysis may have value as a tool for diagnosing problems with the model but cannot be used for predictive purposes.

Overall, the workshop resulted in identification of key criteria for sensitivity analysis methods and recommendation for work needed to further evaluate and specify appropriate sensitivity analysis approaches in the context of food safety risk assessment. This special section represents the first step in an ongoing process to explore sensitivity analysis methods and their application in food safety risk assessment. Future work to be performed at NC State based upon the results of this workshop includes the application of selected methods to two food safety risk process models and the development of a guideline along the lines suggested here.

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REFERENCES

1. Hulebak, K.L, and W.Schlosser, "Hazard Analysis and Critical Control Point (HACCP) History and Conceptual Overview," *Risk Analysis*, … (submitted)
2. Frey, H.C., and S.R. Patil, "Identification and Review of Sensitivity Analysis Methods," *Risk Analysis*, … (submitted)
3. Saltelli, A., "Sensitivity Analysis for Importance Assessment," *Risk Analysis*, … (submitted)
4. Helton, J.C., and F.J. Davis, "Illustration of Sampling-Based Methods for Uncertainty and Sensitivity Analysis," *Risk Analysis*, …. (submitted)
5. Kohn, M.C., "Use of Sensitivity Analysis to Assess Reliablity of Metabolic and Physiological Models," *Risk Analysis*, … (submitted)
6. Pate-Cornell, E., "Risk and Uncertainty Analysis in Government Safety Decisions," *Risk Analysis*, … (submitted)
7. Thompson, K.M., "Variability and Uncertainty Meet Risk Management and Risk Communication," Risk Analysis, … (submitted)

[NOTE to editor: all of the above references are other papers that are part of the same special section that this guest editorial will be part of.]

Table 1. Participants of the NCSU/USDA Workshop on Sensitivity Analysis, June 11-12, 2001, Raleigh, NC

Dr. Timothy Barry U.S. Environmental Protection Agency
Dr. Clark Carrington U.S. Food and Drug Administration
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Dr. Eric Ebel U.S. Department of Agriculture
Dr. H. Christopher Frey North Carolina State University
Dr. Tsegaye Habtemariam Tuskegee University
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Dr. Wayne Schlosser U.S. Department of Agriculture
Dr. Kimberly Thompson Harvard School of Public Health
Dr. Mark Walderhaug Food and Drug Administration