APPENDIX B
Review of Methods for Conducting Uncertainty Analyses

As part of the TRIM model development process, the Agency has conducted and will continue to conduct uncertainty and variability analyses. To ensure that the most appropriate methods were selected for use in this effort, EPA conducted a literature search to identify the full range of the available methods and developed a set of selection criteria against which to compare those methods. This appendix describes the selection criteria and the review of available methods for use in connection with uncertainty and variability analyses for TRIM. The method that was selected is a two-stage approach consisting of a sensitivity/screening analysis followed by a detailed analysis of uncertainty and variability, as described in Chapter 3 and Section 4.7 of this report and in Chapter 6 of the TRIM.FaTE TSD Volume I.

B.1 CRITERIA FOR METHOD SELECTION

The primary objectives for the overall approach for TRIM uncertainty and variability analyses were articulated as detailed criteria that characterize the desirable and undesirable features of the candidate uncertainty and variability analysis methods. These criteria were used to distinguish the available methods according to how well they might serve the objectives. Most of the criteria described below are necessary or highly desirable to support the analysis of uncertainty and variability for TRIM. The required criteria for a method to be used are listed first, followed by additional criteria that are desirable but not absolutely necessary for a method to be used in TRIM uncertainty and variability analyses.

B.1.1 REQUIRED CRITERIA

- **Estimate uncertainty and variability separately, and maintain this separation throughout risk characterization and across module interfaces.** Uncertainty and variability have different meanings, and uncertainty may be reducible, while variability is not. The method should follow the distributions of both uncertainty and variability through the model, yielding uncertainty and variability distributions of the model outputs. The modular design of TRIM poses challenges for the propagation and analysis of uncertainty and variability, and it is important that the selected method be able to fit smoothly and accurately within the modular design and be able to transfer information between connected TRIM modules.

- **Evaluate sensitivity of both specific model inputs and model components.** In addition to the changes in the results which occur when the values of input variables are changed, it is useful to examine the changes in the results which occur when different algorithms are used in the mechanistic model.

- **Evaluate uncertainty and variability importance.** One of the key functions of the analysis methodology is to evaluate the importance, in terms of both uncertainty and variability, of specific model inputs and model components in relation to other inputs and components. This type of analysis provides insight into priorities for reducing uncertainty and allocating resources to the improved representation of uncertain and variable inputs. The ability to rank input parameters in order of their influence on the uncertainty of the model results is an important component of this function.

- **Identify and represent correlations and other interdependencies.** Physical processes or relationships can dictate that certain variable values change in concert with other variable values. The correlations can be weak or strong and can be negative or positive. Ignoring these relationships can introduce error into the risk assessment effort. Tracking these relationships can add substantial complexity and increase the computational resources necessary for the risk assessment effort. These correlations can exist between model input parameters or can be introduced within the model. The selected method should represent the input parameter correlations and follow these through the model with the structural correlations introduced by the model. It also should be able to identify correlations between sets of model inputs and outputs and between sets of intermediate variables.

- **Treat tails of distributions.** Some methods focus more on the central region of probability distributions and are less accurate in their treatment of extreme values. For risk assessment applications, accuracy in the tails of the probability distributions is very important. Therefore, the selected method should adequately treat infrequent but important events.

- **Evaluate relevant temporal and spatial scales.** The selected method should facilitate comparison of the results when different temporal or spatial scales are used, as the appropriate scale to use for modeling can directly impact model uncertainties.

- **Limit computational requirements.** The method should be computationally efficient and should not require excessive effort to set up or run.

- **Handle complex mathematical relationships.** Some available methods are designed for and more suited to models with simple mathematical constructs and cannot feasiblely handle more complex models. Other methods are designed to handle very mathematically complex models. The selected method for TRIM must be able to handle complex models.

- **Be easily automated.** Propagation and analysis of uncertainty and variability can require considerable effort, often in the form of large numbers of repetitions of model runs for numerical techniques and large numbers of algebraic manipulations for analytical techniques. The ability to automate the procedures is highly desirable to minimize effort and can provide the added advantage of reducing human errors.

B.1.2 DESIRABLE CRITERIA

- **Use input distributions directly without further approximations or need to fit input distributions to standard analytical forms.** When the values for the input variables arise from certain specific types of physical processes or have certain natural properties, they may be accurately represented by standard analytical forms (*e.g.*, normal or lognormal probability density functions). When conditions are less than ideal, fitting the values to such distributions can introduce unnecessary error into the risk assessment effort, and the use of nonparametric representations may be preferable. Some of the methods evaluated assume analytical forms, while other methods handle a wide variety of representations of probability distributions. Some available methods require discretization of continuous distributions to be applied. The selected method should be able to handle the basic types of distributions that will be encountered.

- **Increase the level of precision in a simple manner.** Most of the uncertainty methodologies have some means of increasing the precision of uncertainty analysis results. For some methods, however, the procedures for doing so are substantially more difficult or require substantially more effort. The method selected for TRIM needs to provide a balance between precision and necessary effort.

- **Support investigation of model behavior and changes to the model.** Insight into the structure of the model can reveal the effects of model changes and why changes affect uncertainty as they do. Obtaining this insight typically involves analysis of the intermediate calculations performed within the model and keeping track of the uncertainties of the intermediate values calculated.

- **Reduce opportunities for human error in the uncertainty and variability analysis.** Complex models, large numbers of variables, significant amounts of hand processing for data entry, debugging, and programming of transfers across modules among other processes all create significant opportunities for error. A desirable method for uncertainty analysis will not increase the opportunities for error and, ideally, will expose errors of this type.

- **Maintain ability to track causal links and support auditing.** This feature involves maintaining an audit trail of processing within the model, keeping track of where significant changes occur through the model data flow. Primarily useful during the development of an application, this ability supports the interpretation of the meaning of results as well as the need to check for errors. This desired characteristic can be partially fulfilled by retaining intermediate results (*e.g.*, input and output distributions) and tracking linkages within the model.

- **Provide capabilities for additional analysis.** A single method may not be able to perform all of the envisioned types of uncertainty analyses, and other methods might be used to perform specific analyses in conjunction with the primary method selected. It is desirable for a method to be able to interface with other analysis tools.

- **Support model evaluation efforts.** A major effort during the development of TRIM is model evaluation (see Chapter 6 of this report), and it would be advantageous for the method to be capable of supporting this effort.

- **Build a reduced form model.** While not a method for analysis of uncertainty *per se*, some methods used in connection with uncertainty analyses are able to produce a "reduced form model" (an approximation to the simulation model which runs much faster while giving results reasonably consistent with the results of the full simulation model). This can be advantageous when the uncertainty method requires thousands of simulations by using the reduced form model for some of the simulations.

B.2 DESCRIPTION OF AVAILABLE METHODS

Table B-1 presents descriptions of a number of available methods for analysis of model uncertainty and variability that were identified by EPA in its literature review. For each method, the strengths, weaknesses, and applicability for TRIM uncertainty analysis are summarized, with particular focus on TRIM.FaTE. The recommended uses of the methods reviewed, which are appropriate for a TRIM uncertainty and variability analysis, are summarized in Table B-2 and are described below.

B.2.1 THE CORE UNCERTAINTY ANALYSIS METHOD

The core uncertainty analysis method selected for use in TRIM must be able to handle propagation of uncertainty and variability of the model input parameters, taking into account distributions of parameter uncertainty and variability and parameter dependencies. The method will be used to provide uncertainties of model outputs in terms of distributions of model outputs, joint distributions of model inputs and outputs, and summary scalar measures.

For performing a thorough uncertainty and variability analysis, the Monte Carlo method has a number of advantages over other methods described in Table B-1, and therefore it has been selected as the core uncertainty analysis method for TRIM. The primary advantages of this method are the reduction of the number of simulations required, the ability to use different ways of specifying parameter distributions, the ability to handle very complex models, and the propagation of variability, uncertainty, and parameter dependencies through the model that are reflected in the distributions of model outputs. The Monte Carlo method is a widely used method, with numerous papers and other publications describing the method and how to apply it (Frey and Rhodes 1996, Morgan and Henrion 1990, Thompson et al. 1992, U.S. EPA 1997, Vose 1996, SRA 1993).

Table B-1
Available Methods for Analysis of Model Uncertainty and Variability

Method	Technique	Assumptions	Strengths	Weaknesses	Applicability to TRIM
Monte Carlo	Monte Carlo uses multiple iterations of random samples from model input distributions. Four sampling techniques include: • Simple Monte Carlo; • Latin Hypercube Sampling (LHS); • Midpoint LHS; and • Importance sampling.	• There are no specific assumptions; it works with any reasonable data set and does not require distributional assumptions other than reasonably complete distributions and correlations.	• Varied parameter distributions can be specified. • It can handle correlations, dependencies, and complex model algorithms. • Complexity is linear with the number of parameters. • It can find confidence bounds for estimates of output distributions. • Additional iterations increase precision. • It provides insight into behavior of the model. • It is widely used and accepted by the scientific community.	• Large numbers of parameters and correlations between parameters can require many iterations and large computing time requirements. (Note: a reduced form of the model can be used for some applications that significantly reduces the required computing time.)	Highly applicable: listed strengths are all desirable for TRIM.FaTE uncertainty analysis, and any of the four Monte Carlo techniques described would be applicable to TRIM requirements.
Method of Moments (Taylor Series Expansion)	The method of moments calculates partial derivatives of the mathematical expressions in the model and uses these to calculate effects of perturbing the data. The Taylor series expansion is a case of this method involving only first order derivatives. Analytical expressions for partial derivatives for each equation are coded into the model as a companion set of equations. Distributions of interest can be propagated through the model using derivatives to transform input distribution parameters to output distribution parameters.	• Distributions can be adequately parameterized by their means, variances, and other moments; distribution type/shape known *a priori*. • All parameters are independent of each other. • Mathematical expressions in the model are continuously differentiable.	• A well-known method, it has been extensively applied to a variety of applications. • It can be effective for models where analytic expressions for all derivatives can be derived and coded.	• Techniques are usually very complex. • Errors can be easily introduced when coding expressions for calculating derivatives. • Computation of derivatives can be intractable for all but fairly simple models. • Methods are not appropriate for some normality assumptions and distributional forms.	Not easily applicable: TRIM.FaTE algorithms are too complex to apply this method feasiblely.

Method	Technique	Assumptions	Strengths	Weaknesses	Applicability to TRIM
Differential Sensitivity Analysis (DSA)	DSA calculates partial derivatives of the mathematical expressions in the model (like method of moments, but uses additional techniques to reduce intractability of computing derivatives in complex models). Two classes of DSA methods exist: (1) specialized numerical procedures to efficiently calculate derivatives, and (2) symbolic differentiation methods to obtain derivatives through the use of computer programs that also generate code.	• Functions in model are continuously differentiable. • Output distributions and the distributions propagated throughout the model are normal.	• It can be a powerful tool for local model sensitivity analysis when coupled with automated procedures for generating code required to calculate derivatives • It can obtain derivatives even for complex models	• Procedures for calculating derivatives can be difficult and time-consuming to implement • Smoothness assumptions may be violated by step-functions or discrete distributions used in risk assessment • May not be able to integrate correlations unless DSA method is nested within a method that can	Not easily applicable for all cases; additional code would need to be developed to handle any discrete distributions due to the smoothness assumptions of DSA.
Classification and Regression Trees (CART)	CART uses a nonparametric, binary tree method to simultaneously treat ordered and categorical data in the same problem. It produces tree structures rather than predictive algorithms.	• No specific assumptions; it works with any reasonable data set and does not require distributional assumptions other than reasonably complete distributions and correlations	• It is applicable to large, high-dimensional data sets, non-homogeneous data, and sets with missing data. • It can account for masking of variables in ranking parameters according to their influence on the classification of outcomes. • It is robust with respect toward outliers. • It uses conditional information and dependencies in the data • Graphical tree structure produced can be relatively easy to understand and interpret.	• Complexity of results for complex models can hinder interpretation of analysis.	Possibly applicable through three uses: • Reduced-form model that allows for faster simulations; • A tool to examine model sensitivity to individual parameters; or • A method that provides initial importance-ranking of parameters, taking into account dependencies.

Method	Technique	Assumptions	Strengths	Weaknesses	Applicability to TRIM
Bootstrap Method	Bootstrap uses Monte Carlo algorithms to sample the data for multiple replications in order to obtain a confidence interval or other measure of accuracy for an estimated statistic. It is used primarily to assess the accuracy of estimated parameters and model predictions.	• Sufficient data are available to generate distributions (specific amount of data required depends on the particular application).	• It can be used to assess accuracy for complex procedures relatively easily. • It can be applied parametrically or nonparametrically • It can use importance sampling methods to improve efficiency of estimating tail probabilities. • With careful setup, it can be used with data having dependencies.	• It can give incorrect results if the nonparametric empirical distribution function deviates from the true distribution function in the tails • It can give downwardly biased estimates when used for assessment of model prediction accuracy. (Note: modified bootstrap methods can help to alleviate this problem.)	Possibly applicable: it can be used for estimating statistics of the input parameters (*e.g.*, mean, variance, distributions, and confidence intervals).
Response Surface Estimation	Response Surface Estimation uses sets of inputs and outputs from numerous model runs in a general regression model to produce a sample response surface that functions as an estimate of the actual model response surface. The fitted response surface can be used to predict outcomes of the model given values of the input parameters. Usually, factorial-type designs are used to specify the model runs used to fit the surface. Model inputs can be sampled carefully to give higher importance to more influential parameters and to ensure full representation of distribution tails.	• Simulations performed to develop the surface will provide adequate coverage of the parameter-outcome space at resolutions that will capture variability and dependencies. • Continuity and boundedness of response surface function exists. • Response surface should not be extended beyond the region represented by the simulations.	• It is widely used, well understood, and simple to interpret. • It is useful as an approximation of a reduced form of a complex model. • It provides an overview of how a model responds to variations in the input values.	• It requires a very large number of model runs to estimate the fitted response surface, particularly if there are many correlated parameters. • It can be tedious to estimate the accuracy of the sample response surface with respect to the full model response surface; this usually requires a second set of simulations .	It can serve as a reduced form replacement for TRIM.FaTE for fast simulations. Also, it could be used for sensitivity analyses in the initial ranking of model inputs according to contributions to model variability.

Method	Technique	Assumptions	Strengths	Weaknesses	Applicability to TRIM
Combinatorial Scenarios / Discrete Probability Trees	It produces *combinatorial scenarios* by selecting a small set of values for each input parameter and then running the model for all physically possible combinations of these parameters to form a grid on the response surface of the model. A *discrete probability tree* then analyzes results of these scenarios by using information about each parameter's probability.	• Chosen scenarios are representative of a range of scenarios.	• For models with few parameters, it provides insight into the structure of the influence of parameter uncertainty and variability on the model outcomes. • Tree diagrams present results relatively clearly for models with few parameters.	• Number of combinatorial scenarios increases exponentially with the number of parameters, leading to extremely long analysis times for models with many variables	Not applicable: the large number of uncertain parameters and the complexity inherent to TRIM.FaTE renders the use of these methods computationally infeasible.
Generalized Linear Models (GLM)	This class of classical linear models includes the use of techniques like analysis of variance (ANOVA), linear regression, logit/probit, log-linear, and multinomial response models. These models can calculate an uncertainty partitioning based on deviance or the generalized Pearson chi-squared statistic.	• It uses second-order moment assumptions, primarily on how moments vary with respect to each other.	• Restrictive assumptions on the form of distributions are not needed. • It handles both discrete and continuous covariates. • It is relatively easy to apply.	• As a parametric method, it does not have the flexibility of nonparametric methods like classification and regression tree methods.	May be applicable as a first-order type analysis of importance of parameters, taking into account interactions between pairs of parameters.
Neural Networks (artificial)	Neural Networks consist of a collection of techniques for estimating functions. Networks are composed of a large number of simple processing elements and connections between the elements. Elements operate only on local information and store information via a training process where the network "learns" about the data using observed data. The trained network can then make predictions of model outputs.	• For neural networks without smoothing, no assumptions made regarding parameter distributions or complexity of the model. Networks with smoothing limit the complexity of the fitted model.	• It provides models that are flexible and non-linear. • With sufficient training data, it can approximate any reasonable function of any degree of complexity. • Complexity of the network can be controlled. • As the number of model input parameters increases, computational complexity of the network does not increase exponentially.	• It has a tendency to overfit by using too many parameters. • There are high time requirements for the analyst to properly apply the appropriate neural network techniques. • For many applications, it offers no advantage over more simple standard statistical methods. • Poor model performance results if a small amount of data is available for training the network.	Applicability uncertain: probably not enough data to make use of neural networks directly for TRIM.FaTE uncertainty procedures. Method may be applicable for developing a reduced model that would execute faster than TRIM.FaTE; however, other approaches may be more favorable for the analysis due to the weaknesses.

Table B-2
Recommended Uses of Applicable Methods

Method	Uncertainty Analysis Methods	Sensitivity Analysis Methods	Supplementary Analysis Methods	Reduced Form Models
Direct Sensitivity Calculations		✔		
Monte Carlo	✔	✔		
Classification and Regression Trees			✔	✔
Response Surfaces			✔	
Combinatorial Methods			✔	
Generalized Linear Models			✔	

Compared to the Monte Carlo approach, the other methods reviewed in Table B-1 would not function as well for the core uncertainty analysis method for TRIM.FaTE, for different reasons. Taylor series expansion and methods of moments only treat local sensitivity analyses and are not feasible for this application due to the complexity of the TRIM.FaTE algorithms. The number of uncertain parameters and the complexity of TRIM.FaTE also make the use of combinatorial methods (*e.g.*, discrete probability trees) computationally infeasible for a full analysis. Neural network approaches require more simulations than Monte Carlo and operate on an approximation to the model. Treatment of parameter and model dependencies in a neural network approach is not straightforward and would entail development of additional techniques, as would the use of differential sensitivity analysis. The remaining methods reviewed (*i.e.*, response surface estimation, bootstrap, generalized linear models, and classification and regression trees (CART)) do not adequately address the primary requirements for uncertainty analysis (*e.g.*, propagation of uncertainty).

B.2.2 SENSITIVITY ANALYSIS METHODS

Sensitivity analysis and screening analysis are fast techniques for measuring changes in model results relative to changes in input parameters. These analyses provide a first-order determination of the influential parameters that will need to be included in the detailed uncertainty analysis. Sensitivity analyses often are conducted not only for the full model, but also for each modular component within the model. They also can be employed to uncover anomalies and verify that the model is performing as expected.

In addition to directly calculating parameter sensitivities (*e.g.*, elasticity and normalized sensitivity scores), response surface estimation and generalized linear models (GLM) can be used to characterize model sensitivity. These approaches require that a set of model simulations be performed that vary the parameter values according to some experimental design. Response surfaces involving many parameters are difficult to display and interpret and require more

simulations than direct calculation and therefore are not appropriate for TRIM sensitivity analysis. Measures of parameter importance are the primary result of sensitivity analysis and can be presented visually using graphs.

B.2.3 SUPPLEMENTARY ANALYSIS METHODS

Much of the uncertainty and variability analysis will involve direct computation of measures of uncertainty and variability and summaries of relationships between different input parameter variability/uncertainty distributions as well as dependencies of the input distributions with model output distributions. Some of the methods described in Table B-1 can be used to perform supplementary analyses of results of the Monte Carlo simulations. The use of these methods can provide a better understanding of the uncertainty and variability process and can provide additional measures. These methods include response surface estimation, combinatorial scenarios, discrete probability trees, GLM, and CART.

B.2.4 REDUCED FORM MODELS

Some of the available methods can be used to construct reduced form models (*i.e.*, simplified "models of the model") that, in the context of an uncertainty analysis, could be used for uncertainty propagation simulations. By substantially reducing the computational burden of model runs, the use of a reduced form model allows for a larger number of parameters to be treated and for more detailed results to be generated. This analysis would only need to be performed if the computational requirements for the detailed analysis using the full model are excessive. Reduced form models can be built using a variety of non-linear regression methods. CART could be used for this because it typically produces good models of non-linear systems, it is relatively easy to implement, it provides insight into the model itself, and the way that CART functions is not difficult to conceptualize and explain.

References for Appendix B

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