ABSTRACT

Title of Dissertation: ENGINEERING-BASED PROBABILISTIC RISK ASSESSMENT FOR FOOD SAFETY WITH APPLICATION TO *ESCHERICHIA COLI* O157:H7 CONTAMINATION IN CHEESE

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A new methodology is introduced in which engineering-based tools and techniques are adapted to quantitative microbial risk assessment (QMRA) in order to offer a more systematic solution to food safety problems. By integrating available microbial data and adapted engineering techniques within the traditional QMRA framework, this new methodology addresses some of the deficiencies of traditional approaches. Through the use of a hierarchical structure, the system is decomposed into its most basic elements so that the interrelationships and interdependences of these basic elements are captured. This hierarchical structure also identifies variability throughout the process, resulting in a risk model in which multiple scenarios can be analyzed. In addition, the engineering approach adapts methods for characterizing and propagating uncertainties. Unlike the traditional approaches in food safety, the engineering-based methodology relies on mathematical models; the uncertainties about these models (both aleatory and epistemic), as well as the

uncertainties about the model parameters, are formally quantified and properly considered. This separation and characterization of uncertainties results in a more powerful risk model, so that assessments can be made as to whether additional information or changes to the physical system will reduce the total uncertainty. Finally, this research characterizes the validity of the various dose-response models. Comparison of actual outbreak observations to model predictions lends credibility and assesses uncertainty of the developed dose-response models. Thus, the results of the risk model can be used both as an absolute assessment of risk and as a relative measurement of mitigation and control strategies.

As a case study, the engineering-based methodology is applied to the problem of *Escherichia coli* O157:H7 contamination in cheese. While it has been assumed that pathogenic microorganisms in raw milk die during cheese-making, several studies on the survival of *E. coli* O157:H7 in cheese have demonstrated growth during cheese manufacturing. Furthermore, *E. coli* O157:H7 has been linked to several outbreaks involving cheese, thereby establishing the need to investigate this route of transmission. The successful application of the engineering-based approach to the problem of *E. coli* O157:H7 contamination in cheese suggests that this new methodology can be applied to other food safety problems.

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by

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List of Abbreviations

AHP	Analytical Hierarchy Process
CAC	Codex Alimentarius Commission
CDC	Centers for Disease Control
CFSAN	Center for Food Safety and Applied Nutrition
CFU	Colony-Forming Unit
DAEC	Diffuse-Adhering *Escherichia coli*
DML	Dynamic Master Logic
EaggEC	Enteraggregative *Escherichia coli*
EHEC	Enterohemorrhagic *Escherichia coli*
EIEC	Enteroinvasive *Escherichia coli*
EIP	Emerging Infections Program
EPEC	Enteropathogenic *Escherichia coli*
ERS	Economic Research Service
ETEC	Enterotoxigenic *Escherichia coli*
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
FSIS	Food Safety and Inspection Service
HTST	High-Temperature, Short-Time
HUS	Hemolytic Uremic Syndrome
IDF	International Dairy Federation
IFST	Institute of Food Science and Technology
LAB	Lactic Acid Bacteria
MCMC	Markov Chain Monte Carlo
MF	Multiplicative Factor
MLE	Maximum Likelihood Estimate
NSLAB	Non-Starter Lactic Acid Bacteria
PMO	Pasteurized Milk Ordinance
PRA	Probabilistic Risk Assessment
PRAEC	Probabilistic Risk Assessment of *E. coli* O157:H7 in Cheese
PRM	Process Risk Model
QMRA	Quantitative Microbial Risk Assessment
STEC	Shiga-toxin *Escherichia coli*
TTP	Thrombotic Thrombocytopenic Purpura
USDA	United States Department of Agriculture
VBA	Visual Basic for Applications
WHO	World Health Organization

1. INTRODUCTION

1.1 Dissertation Overview

Foodborne disease is a serious cause of illness in the United States and is estimated to affect over 76 million people each year and cost the economy several billion dollars. While many different pathogens can cause foodborne illness, *Escherichia coli* O157:H7 has emerged as a primary food safety concern in recent years. Many estimates of the severity of *E. coli* O157:H7 cases have been made over the last decade. While these figures vary, an estimated 62,000 cases of symptomatic *E. coli* O157:H7 infections occur annually in the United States due to foodborne exposures. These infections result in approximately 1,800 hospitalizations and 52 deaths (Mead et al., 1999). In addition, the annual cost to the United States economy for foodborne *E. coli* O157:H7 cases has been estimated to be as high as $659 million (Buzby, 2002). Thus, *E. coli* O157:H7 has emerged as a foodborne pathogen with major public health significance in the United States.

E. coli O157:H7 was first isolated by the Centers for Disease Control (CDC) in 1975; however, it was identified as a cause of human illness in 1982, after it was associated with a severe outbreak of hemorrhagic colitis in Oregon and Michigan that was traced back to undercooked ground beef (Riley et al., 1983). Since that time, numerous outbreaks of *E. coli* O157:H7 infections associated with beef products have been reported, establishing cattle as the primary reservoir of *E. coli* O157:H7 (Griffin and Tauxe, 1991). These ground beef related outbreaks prompted the Food Safety and Inspection Service (FSIS) and others to conduct risk assessments of *E. coli*

O157:H7 in ground beef (Cassin et al., 1998; FSIS, 2001; Ebel et al., 2004). Although fecal contamination of carcasses during slaughter and processing of beef has been established as route of transmission, investigations have shown that fecal contamination of milk is an important route of transmission as well (Marek et al., 2004). Multiple outbreaks of *E. coli* O157:H7 linked to the ingestion of both raw and pasteurized milk have been reported (Keene et al., 1997; Martin et al., 1986; Upton and Coia, 1994), and this association with milk raises the possibility of *E. coli* O157:H7 survival in other dairy products such as cheese.

Cheese was originally developed as a means of preserving raw milk in times of excess production, and has generally been considered a relatively "safe" food. Traditionally, it has been assumed that pathogenic microorganisms in raw milk die during the cheese manufacturing process due to the production of high acidity (i.e., low pH value) and competition from starter cultures (Fox, 1993). However, studies on the survival of *E. coli* O157:H7 in hard cheese indicate that the pathogen can grow during the cheese manufacturing process and survive for up to 70 days post-manufacturing (Hudson et al., 1997; Maher et al., 2001; Reitsma et al., 1996; Teo et al., 2000). Therefore, the indications are that the additional hurdles imposed during the cheese manufacture are insufficient to prevent the growth and survival of the pathogen in cheese produced from milk contaminated with the pathogen.

In recent years, several outbreaks of *E. coli* O157:H7 infection have been linked to cheese. Five cases of gastroenteritis in Wyre, England were linked with the consumption of cheese made from unpasteurized milk in November 1997 (Strachan et al., 2005). In 1998, an outbreak affecting 55 people in Wisconsin was linked with the

consumption of fresh Cheddar cheese curds contaminated with *E. coli* O157:H7 (CDC, 2000). Finally, 13 cases of *E. coli* O157:H7 infection associated with the consumption of Gouda cheese were identified in Alberta, Canada in 2003. Two of these cases involved children who later developed hemolytic uremic syndrome (HUS) as a result of infection (Hornish et al., 2005).

Not only has *E. coli* O157:H7 been shown to survive the cheese manufacturing and ripening process, but it has also been linked to several outbreaks involving cheese, thereby establishing the need to investigate this route of transmission. This research develops a risk model using probabilistic-based engineering tools and techniques in order to describe the behavior of *E. coli* O157:H7 in cheese during production, distribution, and consumption and estimate the overall human health risk. The framework upon which the model is based organizes and links the data to a user-interface, allowing for scenario development and sensitivity analysis. In addition, the inclusion and recognition of variation within the process and data, parameter, and model uncertainty allows for the consideration of both aleatory and epistemic uncertainty when assessing the societal impacts, identifying control strategies, and weighing risk management options.

Despite the introduction of engineering tools and techniques, the risk assessment described herein is consistent with other food safety risk assessments (Cassin et al., 1998; Bemrah et al., 1998; FSIS, 2001; Ebel et al., 2004). These risk assessments follow the basic guidelines set forth in the "Application of Risk Analysis to Food Standards Issues" prepared by the Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Consultation at the request of the Codes

Executive Committee during the 41st Session of the Codex Alimentarius Commission (CAC) (WHO, 1995). Although risk assessment terminology varies slightly among the various regulatory agencies and organizations, the key elements of a risk assessment are the same (Buchanan, 1997; Hoornstra and Notermans, 2001; Potter, 1996). This research uses a framework consisting of four components, as outlined by Buchanan (1997), to establish the risks associated with *E. coli* O157:H7:

(1) Hazard Identification: Identification of known or potential health effects associated with a particular agent in food.

(2) Exposure Assessment: Evaluation of the degree of intake likely to occur.

(3) Dose-Response Assessment: Determination of the relationship between the quantity of the biological agent consumed and the magnitude and frequency of adverse health effects.

(4) Risk Characterization: Integration of the results from the exposure and dose-response assessments to provide an overall estimate of the likelihood and magnitude of the hazard; includes aleatory and epistemic uncertainties associated with the assessment.

1.2 Risk Assessment Overview

1.2.1 History of Risk Assessment in Food Safety

Risk analysis is a process composed of three elements: risk assessment, risk management, and risk communication. Risk assessment is the use of scientific information to describe the likelihood and magnitude of harm attributed to a specific

hazard. Risk management consists of all activities undertaken to control a hazard. Risk communication is the exchange of information and opinions about a hazard among concerned parties (Dennis et al., 2001). Thus, risk analysis may be described as a framework to analyze, manage, and communicate any activity that may have negative consequences (Lindqvist et al., 2002), and is accomplished through the efforts of separate but integrated assessment, management, and communication teams (Dennis et al., 2001).

The concept of risk analysis has been applied to many areas including transportation, energy, aerospace, chemical processing, etc. In addition, the Food and Drug Administration (FDA) has more than 30 years experience conducting and using safety and risk assessments for food additives and chemical contaminants. However, only recently have these techniques been applied to microbial food safety issues (Dennis et al., 2001). With the emergence of newly identified human pathogens, such as *E. coli* O157:H7, risk analysis has become an increasingly important activity in the area of microbial food safety. A joint consultation of the WHO/FAO was held in 1995 to address the application of risk analysis to food standards issues. This consultation was convened at the request of the 41st Session of the CAC Executive Committee which recognized the need to promote consistency and transparency in the establishment of Codex standards, guidelines, and recommendations. The main objective of the joint WHO/FAO consultation was to provide FAO, WHO, CAC, and member countries with advice on practical approaches for the application of risk analysis, with a focus on risk assessment, to food standards issues (WHO, 1995). Since that time, WHO, FAO, and CAC have developed an international strategy and

identified mechanisms required to support risk assessment of microbial hazards in foods. Additionally, several risk assessments for different food-pathogen combinations have been undertaken, thus advancing microbial risk assessment as an important discipline for addressing complex food safety issues.

1.2.2 Components of Microbial Risk Assessment

Although there are some differences in risk assessment terminology among various regulatory and international agencies/organizations, the framework used to accomplish the task of microbial risk assessment generally includes four components: hazard identification, exposure assessment, dose-response assessment, and risk characterization (Buchanan, 1997; Hoornstra and Notermans, 2001; Potter, M.E., 1996). This framework is consistent with elements adopted by CAC and defined in the FAO/WHO report (FAO/WHO, 1995). These four steps provide a systematic process for identifying and evaluating the significance of microbial hazards in the food of concern, with the outcome of this process being an estimate of risk (i.e., the measure of the magnitude of the risk), based on current scientific knowledge and understanding (Lammerding and Fazil, 2000). These four components are often combined with problem statement that describes the purpose and scope of the assessment and establishes the key assumptions and goals. The four main components of a microbial risk assessment are described in detail in the following sections.

1.2.2.1 Hazard Identification

Epidemiological, biological, and other information about the pathogen, the food, and the adverse health outcomes associated with the consumption of

contaminated foods is gathered in the hazard identification step (Dennis et al., 2001). In many cases, the hazard is well established and information about the pathogen and food can be found in biological surveillance, process evaluations, epidemiological surveillance, and epidemiological investigations (Buchanan, 1997).

1.2.2.2 Exposure Assessment

The exposure assessment provides an estimate of the levels of the pathogen consumed. This requires estimation of the probability that the pathogen will be present in the food, the levels of the pathogen in the food consumed, the impact of food handling, processing, and storage conditions on the pathogen, and the duration and frequency of exposure (Dennis et al., 2001). In addition, host population demographics, consumption patterns, consumer handling practices, pathogen distributions, and predictive models for estimating the effects of processing, distribution, and preparation may need to be considered (Buchanan, 1997).

1.2.2.3 Dose-Response Assessment

Also known as hazard characterization, the dose-response assessment estimates the relationship between the exposure level (i.e., dose) and the frequency of illness or other adverse health effect (i.e., response). In addition, the severity of the health effect, squelae, and secondary infections must also be considered (Dennis et al., 2001). The information used to develop the dose-response relationship includes human volunteer feeding studies, epidemiological data, and animal model data (Buchanan, 1997).

1.2.2.4 Risk Characterization

Risk characterization mathematically integrates the results from the exposure and dose-response assessments to determine the likelihood of the adverse health outcomes from exposure to the pathogen. This step also involves the determination of the degree of uncertainty in relation to the results and distinguishes this from the inherent biological variation (Dennis et al., 2001). In addition, an effort should be made in this step to identify areas in which additional data could enhance the accuracy of the model (Buchanan, 1997).

1.2.3 Quantitative Microbial Risk Assessment (QMRA)

While there are two general approaches to risk assessment, qualitative and quantitative, this research focuses on quantitative microbial risk assessment (QMRA). Dennis et al. (2001) define the QMRA approach as the combination of existing laboratory and surveillance databases with computational techniques to yield models that predict public health outcomes. This approach takes the microbial aspect of the process into account, as it evaluates the likelihood of adverse human health effects due to exposure to a pathogenic microorganism; however, it also takes the quantitative aspect into consideration, as the magnitude of the risk is expressed as a mathematical statement. According to Lammerding and Fazil (2000), quantitative risk assessment can be divided into two categories: deterministic and stochastic. The deterministic, or point-estimate, approach uses single values such as the average or worst-case as inputs to the risk assessment, while the stochastic, or probabilistic, approach considers all of the available data and uses probability distributions to describe the parameters that contribute to the risk. Thus, the probabilistic approach

produces a distribution of risk that characterizes the range of risk that might be experienced by an individual or population (Lammerding and Fazil, 2000).

1.2.3.1 Probabilistic Approach to QMRA

Although the probabilistic approach is more complex than point-estimate calculations, it is becoming the choice for quantitative risk assessments. This is partially due to the recommendations of the 1994 National Research Council that wrote "Science and Judgment in Risk Assessment" emphasizing the need to address both the variability and uncertainty of risks (Thompson, 2002). Variability, or aleatory uncertainty, refers to the real and identifiable differences in nature, represents the diversity in a well-characterized population or parameter, and is irreducible (Lammerding and Fazil, 2000). In contrast, epistemic uncertainty arises from a lack of knowledge and may be related to the model used to characterize the risk, the parameters used to provide values for the model, or both (Thompson, 2002). In some cases, epistemic uncertainty can be reduced through the attainment of better information, but this is not always possible. Thus, there is a clear distinction between aleatory and epistemic uncertainty. Recognizing and characterizing both aleatory and epistemic uncertainty in a risk assessment is important, as these uncertainties have different implications in the risk assessment results, and therefore, the risk management decisions (Lammerding and Fazil, 2000).

A quantitative risk assessment uses mathematical models to estimate risk as a function of several inputs. A point-estimate assessment largely ignores aleatory and epistemic uncertainties, as a single point-estimate or worst-case value is used to represent a given data set for an input. In contrast, a probabilistic assessment

substitutes probability distributions for the single point-estimate values to describe the inputs. The probability distributions assigned to input values are based on empirical data, knowledge of underlying biological phenomena, or derived from expert opinion (Vose, 1998). Thus, in the probabilistic assessment, a range of values is used and the frequency with which different values occur is also characterized (Lammerding and Fazil, 2000). As stated by Lammerding and Fazil (2000), the importance of acknowledging the range of possible values is emphasized by the recognition that it is unlikely that microbial risks to human health are uniformly distributed, nor that "average" occurrences of events are likely to cause significant problems.

Probabilistic risk assessments (PRA) can be evaluated using analytical techniques such as the method of moments or exact algebraic solutions; however, these techniques have limitations and can be quite tedious (Vose, 2000). An alternative to analytical techniques is Monte Carlo simulation, which offers a powerful and precise method for incorporating both the aleatory and epistemic uncertainty of a problem (Vose, 2000). In Monte Carlo simulation, a single value is randomly selected from each of the probability distributions assigned to each input parameter involving epistemic uncertainty. These randomly selected single values are then used to calculate a mathematical solution, as defined by the risk assessment model. This result is stored, and this sequence is repeated several thousand times (i.e., iterations). During each iteration, a different set of values for the inputs is selected with values that are more likely to occur, as defined by the probability distribution, selected more frequently. The end result is a probability distribution for

the output of interest, represented by the combination of ranges and frequencies of the input parameters (Lammerding and Fazil, 2000).

1.2.3.2 Examples of Previous Probabilistic QMRAs

The number of published quantitative microbial risk assessments, examining a variety of different food-pathogen combinations, has increased in recent years due in part to the proliferation of personal computers and availability of commercial software modeling tools (Dennis et al., 2001). Much work has been done to characterize and quantify the factors contributing to exposure to various foodborne pathogens. Duffy and Schaffner (2002) have developed a model to examine the risk of contamination of apples with *E. coli* O157:H7. Lindqvist et al. (2002) performed a quantitative risk assessment of *Staphlyococcus aureus* in unripened cheese made from raw milk. In addition, several studies have examined the contamination of milk with various bacterium (Peeler and Bunning, 1994; Zwietering et al., 1996; Notermans et al., 1997; Nauta and van der Giessen, 1998). However, these risk assessments have not attempted to quantify the associated human health risk. In fact, there are relatively few published comprehensive quantitative microbial risk assessments. Table 1.1 contains references of recent QMRAs, along with the food and pathogen of interest.

Table 1.1: Summary of Food-Pathogen QMRAs

Reference	Food	Pathogen
Cassin et al., 1998 Marks et al., 1998 FSIS, 2001 Ebel et al., 2004	Ground Beef	*E. coli* O157:H7
Nauta et al., 2001	Steak Tartare	*E. coli* O157:H7
Baker et al., 1998 Whiting and Buchanan, 1997	Shell/Liquid Eggs	*Salmonella enteritidis*
Bemrah et al., 1998 Sanaa et al., 2004	Soft Cheese	*Listeria monocytogenes*

The references listed in Table 1.1 take similar approaches to quantitative microbial risk assessment in that all include the major components of a formal quantitative microbial risk assessment; however, these risk assessments differ in the approach used to address the aleatory and epistemic uncertainty associated with the process investigated. A brief literature review of three of these risk assessments follows.

1.2.3.2.1 *Salmonella enteritidis* in Shell Eggs and Egg Products

Baker et al. (1998), under the direction of FSIS, develop a comprehensive quantitative model to characterize the public health effects associated with the consumption of *Salmonella enteritidis* infected shell eggs and egg products; this research is prompted by the increasing number of human illnesses attributed to the consumption of shell eggs. Baker et al. (1998) present the risk assessment in the farm-to-table context, and follow the guidelines for microbial risk assessments (i.e., hazard identification, exposure assessment, dose-response assessment, and risk characterization). Finally, the main objectives of the risk assessment are identified: establish the unmitigated risk of foodborne illness from *S. enteritidis*, identify and evaluate potential risk reduction strategies, identify data needs, and prioritize future data collection efforts (Baker et al., 1998).

Baker et al. (1998) provide an explanation of the evidence, the expected value, and the distribution for each influencing factor in the model. In addition, the output of the model is a prediction of various health effects given the simulated number of eggs contaminated with *S. enteritidis.* Aleatory and epistemic uncertainty are separated within the risk assessment. This enables the identification of data gaps and

future research needs when the risk estimate is driven by epistemic uncertainty, and the identification of areas needing better process control when the risk estimate is driven by aleatory uncertainty. This research also attempts to validate the risk assessment model by comparing the simulated distribution of the number of illnesses due to *S. enteritidis* positive eggs with a distribution of illnesses from *S. enteritidis* positive eggs prediction from national public health surveillance data; the result is a substantial overlap between these distributions. Finally, a number of input variables are reduced in order to investigate how changes in module variables affect the model output (Baker et al., 1998). However, it should be noted that there are limitations to the scope, resulting in important restrictions in terms of the overall conclusions of the model (Schlundt, 2000). For example, only *S. enteritidis* contamination from egg contents is included even though it is stated that *S. enteritidis* contamination from external sources (i.e., shell contamination) would significantly change the outcome.

1.2.3.2.2 *Listeria monocytogenes* in Soft Cheese

Bemrah et al. (1998) study the risk of listeriosis from the consumption of soft cheese made from raw milk by modeling the process from milking to consumption. Again, this risk assessment takes a farm-to-table approach and considers the four components of a comprehensive microbial risk assessment. The scope of this work is limited to analyzing the risk created only by the raw milk itself. To this end, the probability of temperature abuse is not considered during the various phases of the model and the model is "limited to what is good hygienic practice" (Bemrah, et al., 1998). These assumptions have important implications on the results, as many risk-contributing factors are potentially ignored or overlooked (Schlundt, 2000).

The results of the model are given in terms of the annual cumulative risk of listeriosis based on estimates of the number of servings/capita/year with the premise that only a proportion of the *Listeria monocytogenes* strains in the cheese are virulent; however, these results are not compared to epidemiological evidence. In addition, while attempts are made to address the aleatory and epistemic uncertainty of the input parameters, it is unclear as to whether the uncertainty and variability have been separated in the risk estimates. Finally, no risk management options/mitigation strategies are explored.

1.2.3.2.3 *Escherichia coli* O157:H7 in Ground Beef

Cassin et al. (1998) apply quantitative risk assessment techniques to *E. coli* O157:H7 contamination in ground beef in order to calculate the human health risk. Again, like Baker et al. (1998) and Bemrah et al. (1998) this study follows the guidelines for microbial risk assessments; however, this risk assessment differs in that it uses scenario analysis and predictive microbiology to assess the hygienic characteristics of a manufacturing process as well. This work introduces the idea of a process risk model (PRM) that integrates the application of the quantitative risk assessment methodology with scenario analysis and predictive microbiology to provide an assessment of a process (Cassin et al., 1998). This results in a prediction of the probability of illness attributable to *E. coli* O157:H7 in a particular ground beef manufacturing scenario. Because this model is limited to a particular food production system, the annual number of illness is not estimated.

Another aspect of the model developed by Cassin et al. (1998) is that it incorporates two mathematical sub-models. The first described the behavior of the

pathogen through the various phases of processing, handling, and consumption in order to predict human exposure. This exposure estimate is then used as an input to the second sub-model, the dose-response model, in order to estimate the health risk associated with consumption. In addition, this risk assessment also investigates and identifies intervention procedures that potentially mitigate the risk. Three strategies for controlling contamination and their influence on the final outcome of human health risk are examined, demonstrating how the PRM concept can be useful to risk managers (Cassin et al., 1998). Finally, this research acknowledges that confidence limits and uncertainty bounds cannot be put on the expected value of risk, as the final distribution represents both aleatory and epistemic uncertainty. Treatment of aleatory and epistemic uncertainty separately would be necessary to estimate uncertainty bounds on the risk estimate, and this would require a more sophisticated simulation technique (Cassin et al., 1998).

1.3 Engineering-Based Approach to QMRA

The model developed in this research has similarities to previous QMRAs, and builds upon many of the ideas introduced in Bemrah et al. (1998), Cassin et al. (1998), and Baker et al. (1998). However, this work differs significantly in that it is performed from an engineering perspective with the main goal being the adaptation of probabilistic-based engineering risk assessment techniques to a food safety project. As a case study, this research develops a probabilistic risk assessment model to study *E. coli* O157:H7 contamination in cheese using tools and techniques adapted from various engineering disciplines.

1.3.1 Similarities: Traditional QMRAs vs. Engineering Approach

As stated, the engineering-based approach to QMRA has similarities to the traditional approach used in prior works (Bemrah et al., 1998, Cassin et al., 1998; Baker et al., 1998). First, the engineering approach taken in this research works within the framework of traditional quantitative microbial risk assessments in that it employs the four components of a risk assessment (i.e., hazard identification, exposure assessment, dose-response assessment, and risk characterization) in the development of the model. Second, the goals of the engineering approach remain the same as those of traditional QMRA: 1) quantitatively model and account for the uncertainty of *E. coli* O157:H7 contamination in cheese, 2) estimate the likelihood and magnitude of *E. coli* O157:H7 contamination occurring at various locations along the exposure pathway, 3) estimate various adverse human health effects due to *E. coli* O157:H7 exposure, 4) determine risk-significant contributors/activities, 5) identify possible control and/or mitigation strategies, and 6) identify data gaps and future research needs to reduce uncertainty. Finally, while difficult to implement, both approaches recognize the need for the separation of aleatory and epistemic uncertainty within the model, and attempt to accomplish this separation through the use of Monte Carlo methods to simulate the output distributions of interest.

1.3.2 Differences: Traditional QMRAs vs. Engineering Approach

The differences between the engineering approach employed in this research and traditional QMRA approach are significant. Obviously, the most important difference between these approaches is the adaptation of probabilistic model-based engineering tools and techniques to a food-pathogen combination. The use of

methods, such as Dynamic Master Logic (DML), Multiplicative Factors (MF), and Analytical Hierarchy Process (AHP), allow for consideration of data, parameter, and model uncertainty, as well as variability, generally not accounted for in traditional QMRAs. Thus, this research has the additional goal of adapting non-traditional models and methods to a quantitative microbial risk assessment. The utilization of these methods is briefly described below; however, a detailed discussion of these methods is reserved for Chapters 2 and 3.

1.3.2.1 Dynamic Master Logic (DML) method

The DML methodology is the main technique by which the decomposition, or "reduction", of the problem is performed. It is used not only to structure the overall cheese model, but also to develop the Probabilistic Risk Assessment of *E. coli* O157:H7 in Cheese (PRAEC) software interface. The DML modeling concept is a knowledge management methodology, relying on the fact that complex systems can generally be decomposed hierarchically. Once the system is broken down into its basic elements, it is easier to understand how and why those basic elements exist and are interrelated. This hierarchy structure then lends itself to the development of the user-interface which, in turn, allows for the consideration of process variability and model uncertainty.

For example, in terms of cheese production, there are several key steps in the production of cheese; however, there are many different cheese types and each variety is produced differently. The DML methodology not only identifies the various steps of the cheese-making process and establishes the interdependencies, but also identifies basic elements for each step and the various options for each basic

element in order to account for the variability within the cheese-making process. It should be noted that this decomposition approach can be applied to the exposure assessment, dose-response assessment, and risk characterization elements of the problem. By using this same concept to develop the PRAEC interface, any number of different scenarios can be analyzed. Thus, the DML concept builds on the idea of the PRM introduced by Cassin et al. (1998) by integrating the quantitative microbial risk assessment methodology with scenario analysis. However, while PRM investigates one specific scenario, the DML model is structured to examine any number of different scenarios.

In addition to identifying the variability throughout the model, the DML structure also considers model uncertainty. Developing a dose-response model for *E. coli* O157:H7 is a difficult task and presents a number of challenges due to both model and data uncertainty. There are a number of different dose-response models that describe the relationship between the level of microbial exposure and the likelihood of occurrence of an adverse health consequence. However, within the literature there is no consensus on which specific model is most applicable to *E. coli* O157:H7. Furthermore, due to the severe nature of *E. coli* O157:H7, volunteer human dose-response studies are not possible resulting in much uncertainty about the data used for parameter estimation of the dose-response model. The DML structure recognizes this uncertainty and identifies various options for both the dose-response model and the data sets from which the parameters of the model are estimated. Consequently, the results from various dose-response models or data sets can be compared.

1.3.2.2 Multiplicative Factors (MF)

The multiplicative factor is a mathematical predictive model that allows contamination to propagate through production phase of the DML-structured model. As the model for *E. coli* O157:H7 contamination in cheese is based solely on information and data available in the open literature, the MF concept attempts to address data gaps and data inconsistencies among the available experimental research. Furthermore, due to the assortment of cheeses, the variability in the cheese-making process, and the number of influencing factors (i.e., pH, temperature, salt content, moisture content, fat content, starter cultures, etc.) on microbial growth, data relating to the kinetics of *E. coli* O157:H7 throughout the cheese-making process is somewhat limited. Since there is not enough data available to develop microbial predictive models based on all of these influencing factors, the DML method is used to identify which of these influencing factors are most critical to the growth and survival of *E. coli* O157:H7. MFs are then developed for the critical factors at each step in order to propagate the contamination through the cheese-making process.

The MF is essentially a "multiplier" that allows the contamination to be increased or decreased throughout the production phase. A distribution is created for each MF by calculating the multiplier based on the contamination level at the input and output of a step. Hence, if a selection increases the contamination, the multiplier will be greater than 1; if a selection decreases the contamination, the multiplier will be between 0 and 1. Bayesian updating is used not only to develop the distributions for the MF, but also to account for the parameter uncertainty.

1.3.2.3 Analytical Hierarchy Process (AHP)

The AHP method is a powerful and flexible decision making process that helps set priorities and compares alternative concepts when both qualitative and quantitative aspects of a decision need to be considered. It is a comprehensive, logical, and structured framework that helps to improve the understanding of complex decisions by decomposing the problem in a hierarchical structure. Again, developing a dose-response model for *E. coli* O157:H7 is difficult as there is both model and data uncertainty. The AHP methodology is extended to the dose-response model to account for the data uncertainty.

The AHP method is used to develop a weighted-average dose-response model by comparing alternative data sets on several criteria. A pair-wise comparison of the various criteria is completed for each alternative and the comparisons are synthesized to get the absolute weights of the alternatives with respect to each criterion. The weights of each criterion with respect to the goal are obtained from a matrix operation, with the end result being the overall priority of each alternative. Thus, by developing a weight for each data set, a new "weighted-average" model is developed which accounts for the uncertainty associated with the *E. coli* O157:H7 dose-response data. The model uncertainty is then addressed through the DML structure, which allows for selection among three previously proposed dose-response models as well as AHP weighted-average model developed in this research.

1.4 Contributions of Engineering-Based Approach to QMRA

Traditional QMRAs have focused on identifying various steps in the exposure assessment of a pathogen; these steps are typically quantified with either a point estimate or a distribution representing the best-case, most-likely, and worst-case values. The dose-response data judged most relevant is selected in order to determine the parameters of a single dose-response model. Finally, based on the results of the exposure and dose-response assessments, risks are characterized using point-estimates of adverse health outcomes. This research differs in several ways and provides a number of advancements to the area of food safety risk assessment. Three main contributions are summarized below.

First, the engineering approach proposed is a decomposition, or reductionist, approach to risk assessment. This approach offers a more systematic solution to food safety problems. A hierarchy, in this case, encompasses important elements (i.e., constituents) of the exposure assessment, dose-response assessment, risk characterization, and their relationships. The hierarchy is divided into multiple levels of interrelated constituents, each of which can be studied in relative isolation from the rest. These constituents can be a combination of diverse entities involving human activities, processes, events, equipment, software errors, etc. Thus, a "systems" approach to a food safety problem, which captures the interdependencies and interrelationships of the entire problem, is attained through the decomposition process. Because the traditional PRA techniques applied to engineering systems are not directly applicable to food safety problems, a major advancement of this research

is the adaptation of the reductionist thinking of engineering PRAs resulting in a new modeling paradigm.

Second, the proposed engineering food safety assessment approach relies on mathematical models. Unlike the traditional approaches in food safety, the uncertainties about these models (both aleatory and epistemic), as well as the uncertainties about the model parameters, are formally quantified and properly considered in the risk assessment. The methods used for characterizing and propagating these uncertainties are adapted to the proposed engineering-based risk assessment methodology, resulting in another advancement. Again, the traditional risk assessments use either point estimates or simplified distributions representing the minimum and maximum values or the best-case, most-likely, and worst-case values. This results in conservative models that do not represent epistemic uncertainty. The engineering approach uses the large amount of experimental data available in order to develop mathematical models for the constituents of the risk model. In addition, the uncertainty associated with these mathematical models is also accounted for, resulting in a model that avoids conservatism and characterizes uncertainty.

Finally, this research characterizes the validity of the various dose-response models. Traditional QMRAs have been performed to determine the risk of pathogenic infection from various foods, but the dose-response models used in these risk assessments have yet to be fully validated. Comparison of actual observations in outbreak data to the predicted observation lends credibility, ensures accuracy, and assesses uncertainty of the developed dose-response models. Previous risk assessments have provided worst-case estimates of risk or been most useful as

relative assessments of risk. By validating the dose-response models developed in this research, the results of the risk model can be used both as an absolute assessment of the risk and as a relative measurement of mitigation and control strategies.

2. METHODOLOGY AND BACKGROUND

2.1 Overview of Methodology and Background

This research adapts probabilistic-based engineering tools and techniques to a food safety problem. While this research uses *E. coli* O157:H7 contamination in cheese for the application of this approach, it should be noted that the methodology developed in this research can be applied to any food-pathogen combination of interest. This chapter provides a general overview of the engineering risk assessment methodology developed in this research. In addition, a statement of the problem is given, as applied to *E. coli* O157:H7 in cheese; this statement includes the purpose, structure, scope/assumptions, and goals of the application. Finally, in order to better understand the application of the methodology, background information on cheese-making is provided.

2.2 Engineering-Based Probabilistic Risk Assessment Methodology

The Dynamic Master Logic (DML) modeling concept is used to create the risk model which consists of the exposure assessment, dose-response assessment, and risk characterization. The DML modeling concept is a knowledge management methodology, and relies on the fact that complex systems can generally be decomposed into hierarchies based on functions, structures, behaviors, goals, etc. This hierarchy model is primarily used to explain and simulate system behavior, by modeling system elements and the relationships between those elements. The system is decomposed until the basic elements are discovered. Once the system is broken

down into the basic elements, it is easier to understand how and why these basic elements exist and are interrelated. Thus, the mathematical model developed in this research to describe the process by which contamination is propagated through the system is based upon the conceptual model created with the DML concept. It should also be noted that the DML modeling concept is instrumental in developing the Probabilistic Risk Assessment of *E. coli* O157:H7 in Cheese (PRAEC) software interface that accompanies this project, as the PRAEC interface is based on the conceptual DML model as well. The PRAEC tool is discussed in detail in Appendix I.

In order to apply the DML concept to a food safety problem, a top-level model is established in order to model the system elements and their interactions in a systematic manner. Although this methodology can be applied to any food safety problem, it is discussed in terms of *E. coli* O157:H7 contamination in cheese. Figure 2.1 shows this top-level conceptual DML model in which the relationship between the system elements of the exposure assessment (i.e., production, distribution, and consumption phases) are modeled, with each phase dependent on the previous phase. The initial input into this model is the distribution of *E. coli* O157:H7 contamination in milk. This distribution of contamination enters the production phase, where contamination is increased or decreased. The end result of the production phase is a distribution of *E. coli* O157:H7 contamination in the final cheese product. This distribution is the input to the distribution phase where, again, the contamination of *E. coli* O157:H7 in cheese is increased or decreased. The end result of the distribution phase is a distribution of *E. coli* O157:H7 contamination in cheese, and this

distribution becomes the input for the consumption phase. Propagating the contamination through the model results in an estimate of the distribution of *E. coli* O157:H7 contamination in the cheese at the consumer level. A number of risks can then be characterized by combining the result of the consumption phase with the dose-response assessment and the adverse health consequences. Thus, the end societal risk is calculated by multiplication of the distribution of contamination per serving, the distribution of consumption, the distribution of tolerance level, and the distribution of the adverse health outcome of interest. The dose-response relationship is represented by the area of overlap between the distribution of dose (i.e., resulting from the multiplication of the distribution of contamination per serving and the distribution of consumption) and the distribution of tolerance.

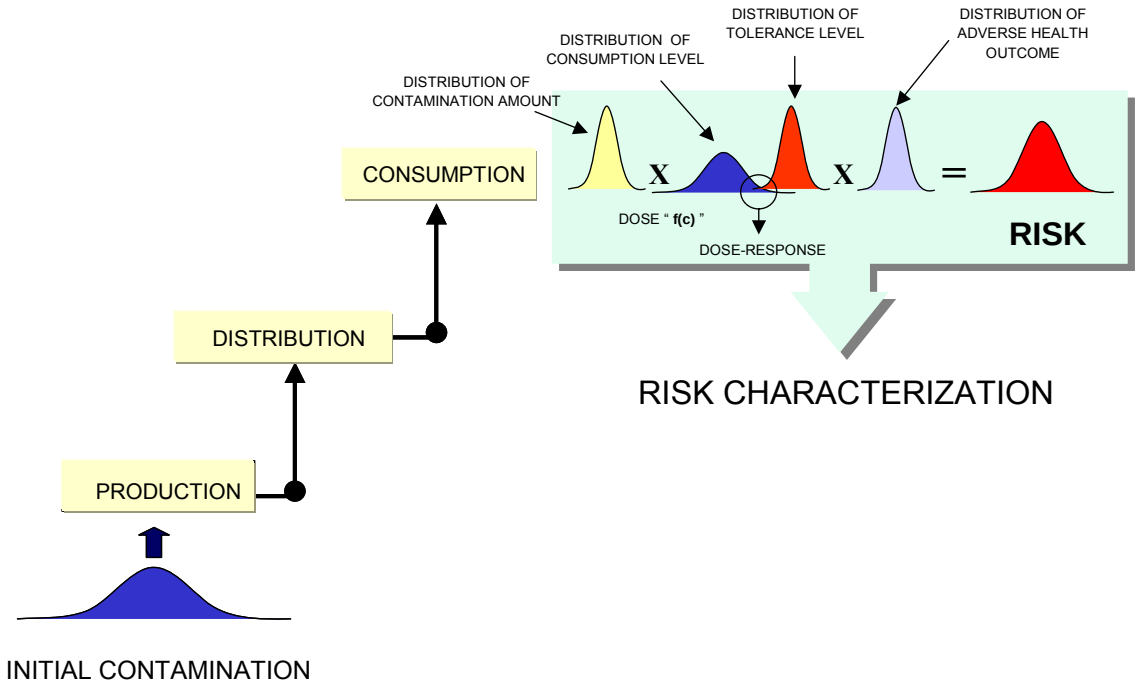


Figure 2.1: Top-Level Conceptual Food Safety Risk Assessment Approach

Next, the DML modeling concept is applied to each of the phases identified in the top-level model in order to further refine the phase. If the production, distribution, and consumption phases are thought of as system elements, then each of these systems can be decomposed into sub-system elements. The sub-system elements of each phase represent various steps that can increase or decrease the *E. coli* O157:H7 contamination, and the DML method models the dependencies and interrelationships between these sub-system elements. Figure 2.2 demonstrates how this concept is abstractly applied to the system elements. The system element, or phase, is broken down into its sub-system elements so that the model for this phase represents all the major process steps and events that affect contamination, as well as the dependencies and relationships between these steps (represented by the nodes). For example, step 3 directly depends on the contamination level of both steps 1 and 2; in addition, step 3 indirectly depends on step 1 through its direct dependence on step 2. In contrast, step 6 directly depends only on step 5. The contamination at the start of the phase can be increased or decreased at each particular step. Thus, the initial contamination is propagated through the various steps (i.e., sub-system elements) of the phase, and results in a distribution of contamination at the end of the phase.

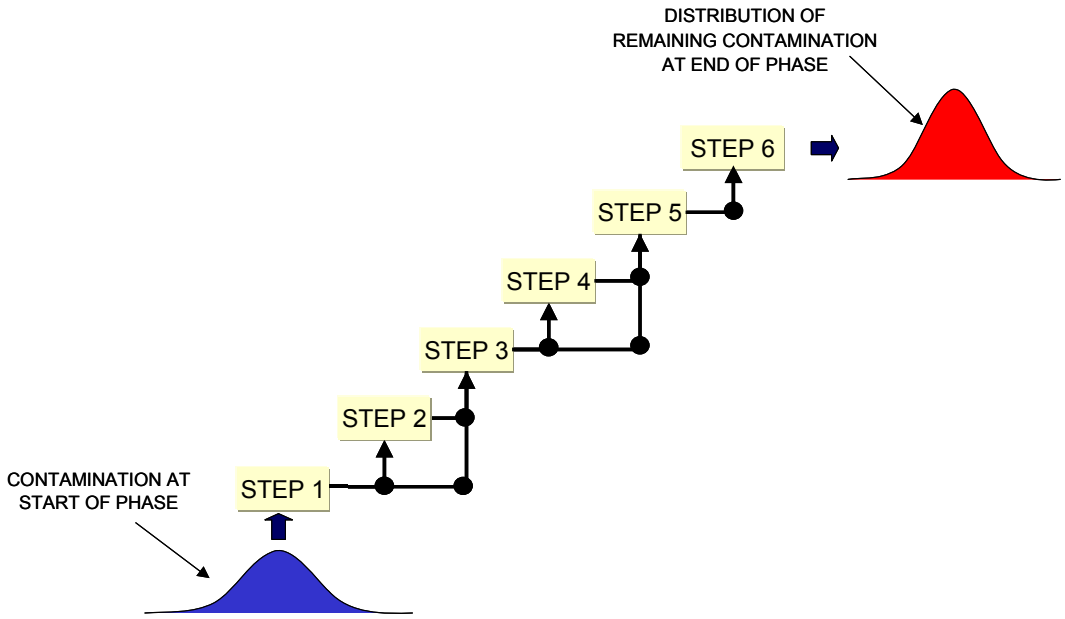


Figure 2.2: Example DML Modeling Approach to Sub-System Element

Finally, each sub-system element in a particular phase can be further decomposed depending on the practices and/or physical conditions (i.e., time, temperature, etc.) at that particular step. Figure 2.3 demonstrates how the DML concept is abstractly applied to a step in order to identify the various basic elements at each step. These basic elements represent the physical conditions, manufacturing practices, distribution practices, consumer practices, etc. that influence bacterial growth or inactivation during that particular step. In addition, the DML concept is used to identify the sub-conditions, or options, for the physical conditions and various practices.

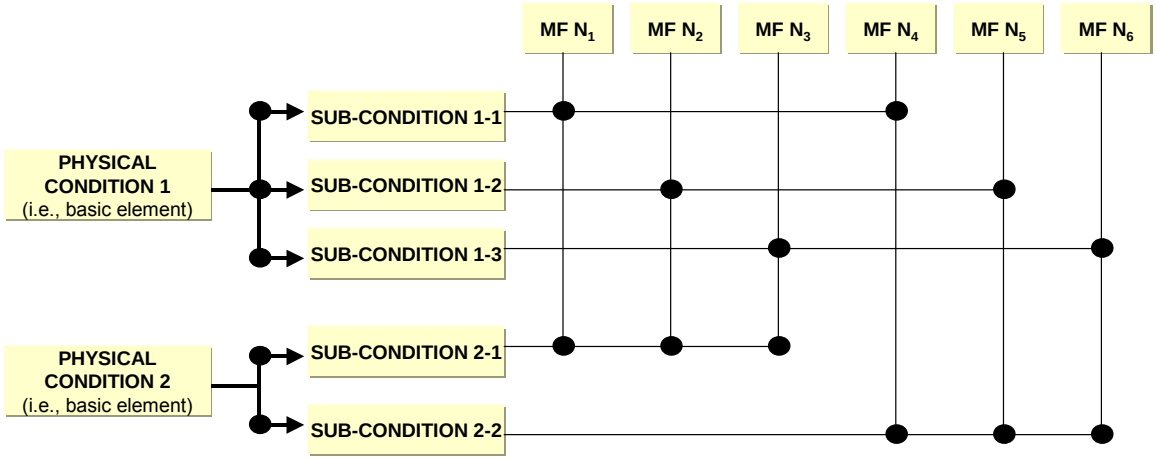


Figure 2.3: Example DML Modeling Approach to Basic Elements

Figure 2.3 is representative of a production phase step and shows a particular step "N" with two physical conditions that influence the contamination level; physical condition 1 has three sub-conditions and physical condition 2 has two sub-conditions. The influence on contamination level is dependent on which sub-condition is selected for each physical condition. A mathematical model called a Multiplicative Factor (MF) is developed to propagate the contamination through the production phase based on the selected sub-conditions at each step. For step "N" represented in Figure 2.3, there are six possible combinations of sub-conditions, and each combination has an associated MF. Thus, if sub-condition 1-1 is selected for physical condition 1, and sub-condition 2-2 is selected for physical condition 2, then MF "N_4" is the multiplicative factor used to propagate the contamination at this particular step.

Each step in the production phase has a MF associated with it, based on the selected sub-conditions. The contamination is propagated through the production phase by multiplying the selected MFs for each step; the following equation represents this concept:

$$C_{FINAL} = C_{INITIAL} * \prod_{i=1}^{n} \mathbf{MF}_i \quad (2.1)$$

MF_i represents the multiplicative factor at step *i*, and *n* represents the number of steps in the production phase. Thus, the final contamination in the production phase is calculated by multiplying the initial contamination by the product of the MFs. It should be noted that other mathematical models are used in the risk model, such as the Gompertz model in the distribution phase; however, regardless of the particular mathematical model used for a system element, the same decomposition approach is applied throughout the model.

In terms of the exposure assessment, the DML concept reduces the system to a number of system elements, or phases. The system elements are then reduced to sub-system elements, or the steps of the phase that influence contamination. The sub-system elements are then reduced to the physical conditions or practices at that particular step that influence contamination. Finally, the various sub-conditions for the physical conditions or practices are identified. By accounting for the various options, or sub-conditions, of the basic elements at each step within the phase, the DML concept takes variability into account throughout the exposure assessment. More specifically, the DML concept takes the variability of industry practices into account during the production phase, the variability of physical conditions into account during the distribution phase, and the variability of the consequences into account during the consumption phase. In this way, the DML methodology not only identifies the various steps throughout the phases of the exposure assessment and establishes the interdependencies, but also identifies the sub-conditions for each

physical condition or practice at each step in order to account for the variability within the entire process.

The DML decomposition approach is not just applicable to the exposure assessment; this reductionist, approach is applied to the dose-response assessment and risk characterization portions of the risk model. In addition, by using this concept to develop the PRAEC interface, any number of different scenarios can be analyzed. Thus, the DML methodology concept builds on the idea of the process risk model (PRM) introduced by Cassin et al. (1998) by integrating the quantitative microbial risk assessment methodology with scenario analysis. However, while PRM investigates one specific scenario, the DML concept structures the PRAEC tool in such a way that multiple scenarios can be examined.

2.3 Risk Assessment Problem Statement

2.3.1 Purpose

Not only has *E. coli* O157:H7 been shown to survive the cheese manufacturing and ripening process, but it has also been linked to several outbreaks involving cheese, thereby establishing the need for a quantitative microbial risk assessment (QMRA) on this particular food-pathogen combination. This research proposes the adaptation of probabilistic-based engineering risk assessment tools and techniques in order to study *E. coli* O157:H7 contamination in cheese. The use of methods, such as Dynamic Master Logic (DML), Multiplicative Factors (MF), and Analytical Hierarchy Process (AHP), allow for consideration of data, parameter, and model uncertainty, as well as variability, generally not accounted for in traditional

QMRAs. In addition, by accounting for the variability throughout the process with the DML modeling concept, this research builds on the idea of the PRM by allowing multiple scenarios to be examined.

2.3.2 Structure

Although this research introduces engineering techniques to QMRA, the risk assessment to study *E. coli* O157:H7 in cheese still follows the traditional four-component structure for quantitative microbial risk assessments: hazard identification, exposure assessment, dose-response assessment, and risk characterization. In this research, the hazard identification includes information about *E. coli* O157:H7, its presence in cheese, and the adverse health outcomes associated with the consumption of *E. coli* O157:H7. The exposure assessment is the quantitative evaluation of the probability that *E. coli* O157:H7 will be present in the cheese and the level of *E. coli* O157:H7 consumed through cheese; the exposure assessment accounts for the impact of production, distribution, and storage on the overall potential exposure. The dose-response assessment determines the relationship between the quantity of *E. coli* O157:H7 consumed and the magnitude and frequency of the adverse health effects. Finally, risk characterization involves the integration of the results from the exposure and dose-response assessments to provide an overall estimate of the likelihood and magnitude of adverse health outcomes from exposure to *E. coli* O157:H7 in cheese; in addition, this step includes the scientific and statistical uncertainties associated with the assessment.

The information and data collected for the risk assessment of *E. coli* O157:H7 in cheese are obtained from the literature. The database and user-interface are

developed within Microsoft Excel (Microsoft Corp., CA) and linked using Visual Basic for Applications (VBA). The interface allows for the development of any number of different scenarios in terms of the distributions attributed to the various options throughout the process. Developing the risk model in this way lends itself to Monte Carlo simulation, in which the simulation represents not only the variability throughout the cheese manufacturing process, but also the uncertainty in the mathematical model of the process. The final outcome is the human health risk of the population represented as a probability density function. The simulations are run on an Intel Pentium 1500 MHz based PC with the @RISK software package, version 4.5.5 (Palisade, Newfield, NY), as an add-in for Microsoft Excel. Due to computer limitations and time constraints, one thousand iterations are performed for 100 simulations.

2.3.3 Scope/Assumptions

The scope of this risk assessment is confined to rennet-coagulated cheeses made with cow's milk, with the exception of Feta cheese. In addition, the scope is restricted to the cheese production, distribution, and consumption phases, and does not consider the on-farm processes associated with milk production or consumer handling before consumption. Finally, the model only considers contamination from the milk and does not account for contamination from sources such as the production facility and machinery.

The model is based solely on information and data available in the open literature through 2005. Therefore, the model developed for this research should be considered a baseline risk assessment, in that it reflects to the extent possible, a full

range of current practices, behaviors, and conditions of the cheese-making process. In addition, while each cheese variety is produced differently, there are basic steps involved in the production of most cheeses (Fox, 1993, Law, 1999). An effort is made to identify all major process steps or events affecting contamination during cheese production, distribution, and consumption.

2.3.4 Goals

The goals of the engineering QMRA approach remain the same as those of traditional QMRA:

1) Quantitatively model and account for the uncertainty of *E. coli* O157:H7 contamination in cheese
2) Estimate the likelihood and magnitude of *E. coli* O157:H7 contamination occurring at various locations along the exposure pathway
3) Estimate various adverse human health effects due to *E. coli* O157:H7 exposure
4) Determine risk-significant contributors/activities
5) Identify possible control and/or mitigation strategies
6) Identify data gaps and future research needs to reduce uncertainty

Furthermore, this research has the additional goal of adapting non-traditional models and methods to a quantitative microbial risk assessment. Probabilistic-based engineering tools and techniques are adapted and then applied to a microbial risk assessment studying *E. coli* O157:H7 contamination in cheese, with the expectation of the following advancements:

1) Development of a framework that identifies the variability throughout the process, organizes the data, and links these with a user-interface
2) Development of methods within the framework to account for data deficiencies and data uncertainty, as well as parameter uncertainty
3) Development of a process risk model in which multiple scenarios can be created, sensitivity analyses can be performed, and dose-response model uncertainty is addressed

2.4 Cheese-Making Background Information

2.4.1 Cheese-Making Overview

2.4.1.1 Origins of Cheese-Making

In the most generic sense, cheese is the name for a group of fermented milk-based food products that are produced in a great range of flavors and forms throughout the world. Cheese manufacture is one of the classic examples of food preservation, dating from 6000-8000 BC (Fox, 1993; Davis, 1965). Early on, it was recognized that cheese possessed much better keeping qualities than milk and provided a suitable food for journeys. Thus, cheese-making was a convenient method of converting a considerable part of the constituents of milk (i.e., fat and protein) into a product that kept well; in addition, cheese was more compact than milk because it contained much less water, was of high nutritive value, and was both palatable and readily digestible (Davis, 1965). Although the origins of cheese-making will never be known with absolute certainty, cheese existed during ancient Egyptian, Greek, and Roman times. Despite the uncertainty about the origins of cheese-making, it is

commonly believed that cheese evolved in the Fertile Crescent between the Tigris and Euphrates, in today's Iraq, during the Agricultural Revolution with the domestication of plants and animals. It is probable that the first fermented dairy products were made by accident, with an unexpected combination of events occurring in order to produce either isoelectic or enzymatic coagulation.

While the nutritive value of milk was realized very early on, it was also discovered that these nutrients provided a rich food source for the bacteria that contaminate the milk. Bacterial growth and acid production would have occurred during attempts at storage in the warm, dry climate. These bacteria utilized the natural sugar of the milk, or lactose, as a source of energy, producing lactic acid as a by-product. Once the level of acid passed a certain point, the milk protein (i.e., casein) would separate from the watery content of milk, yielding solid curds and liquid whey (Battistotti et al., 1983). The acidity of the naturally curdled milk was refreshing, but another important advantage was also discovered. Few dangerous germs could live in this high-acid environment, and thus acid-curd cheese was safer to consume than milk directly from an animal (Battistotti et al., 1983). Thus, isoelectric coagulation involves the growth of bacteria (now known as lactic acid bacteria) in milk, producing just enough acid to reduce the pH of milk to the isoelectric point of the caseins, resulting in coagulation of these proteins (Fox, 1993).

While this explains the evolution of the acid cheeses, which include cottage cheese, cream cheese, quarg, and quesco blanco, an alternative mechanism to lactic acid coagulation was also recognized from an early date. It was soon discovered that milk could be solidified more quickly by the addition of an acid, rather than letting

the milk sit to form acid-curd. Adding a citrus juice or vinegar, for example, would speed up the process; however, this resulted in a sharp-tasting product (Battistotti et al., 1993). Many proteolytic enzymes can modify the milk protein system, causing it to coagulate under certain circumstances. Enzymes capable of causing this transformation are widespread in nature and include bacteria, molds, plant and animal tissues. However, the most obvious source would have been animal stomachs, with the best known medium being rennet, which is made from the fourth stomach of young, cud-chewing animals (Battistotti et al., 1983). Before the development of pottery (c. 5000 BC), storage of milk in bags made from animal stomachs was a common practice, as stomachs provide ready-made, easily sealed containers. Under these circumstances, milk would extract coagulating enzymes from the stomach tissue, leading to coagulation during storage (Fox, 1993). Thus, enzymatic coagulation also evolved by accident through the carrying of milk in the stomachs of animals, with the milk-clotting enzymes of the stomach eventually converting the souring milk into a solid mass (Davis, 1965).

Once cheese could be made with the choice of either acidic or sweet curd there was no limit to the possibilities. Every year scientists and historians find new evidence of the extraordinarily long history and early importance of cheese (Battistotti et al., 1983). Although cheese-making was discovered as a convenient method of preserving the most important constituents of milk, it has evolved into a booming industry. Current technology has smoothed out many of the once variable steps of cheese-making; however, due to the complex chemical and physical

phenomenon involved in the process, cheese-making remains an "art" even today (Law, 1999).

2.4.1.2 Cheese Classification

Today, there are thousands of named varieties of cheese, as cheese may differ in size, shape, color, hardness, texture, odor, and taste. The literature suggests that there are somewhere between 400-1000 different varieties of cheese, depending on the classification system (Fox, 1993). The wide assortment of cheese and the variability in manufacturing make the classification of cheese difficult. A number of attempts have been made to develop a classification scheme for cheese, with Fox (1993) providing a summary of these schemes. One classification system proposed is based primarily on moisture content. This scheme consists of five groups: dried (<40%), grated (40-49.9%), hard (50-59.9%), soft (60-69.9%), and fresh (70-82%). Four of these groups (i.e., fresh, soft, hard, and grated) are further sub-divided into two subgroups based on whether or not the cheese is pressed and/or cooked. Another scheme proposes cheese be classified by moisture into very-hard, hard, semi-hard, and soft, and then subdivided on the basis of the principal characteristic microflora, for example, normal lactic starter, surface mold, interior mold, etc. (Fox, 1993). However, it should be noted that these schemes can only be applied to rennet cheese. To address this limitation, Fox (1993) proposes a classification of cheese by super-families, based on the coagulation agent: rennet, acid, heat/acid, and concentration/crystallization. Fox et al. (2000) expand on the concept of super-families by further classifying rennet cheese based on the principal ripening agents

and/or characteristic technology. Figure 2.4 represents the classification scheme proposed by Fox et al. (2000).

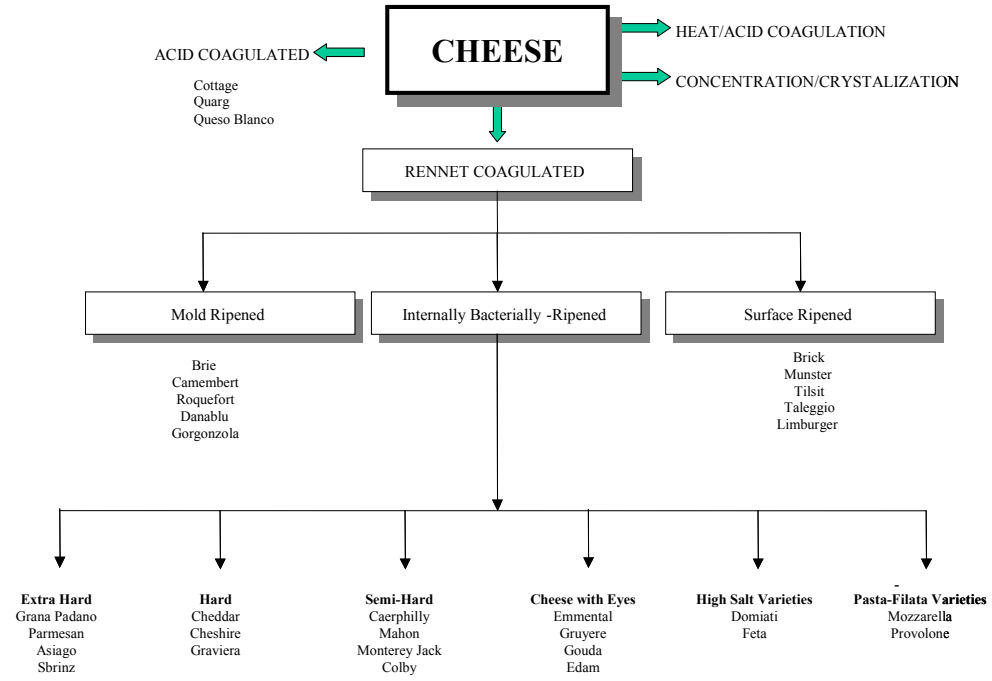


Figure 2.4: Cheese Classification by Super-Family

2.4.2 Modern Cheese Technology

There are two main goals of modern cheese-making technology. First, the parameters such as flavor, body, texture, melt, and stretch properties that make a given cheese desirable must be established. Second, a manufacturing and ripening protocol that will routinely reproduce these parameters every time cheese is made must be developed (Law, 1999). Modern cheese technology has been credited to Joseph Harding, an English innovator of the nineteenth century, who perfected various stages of making Cheddar cheese. Harding asserted that the crucial part of cheese-making depended on how the procedure was handled in the dairy and

promoted the strictest standards of hygiene. Each process was considered to be of equal importance needing to be carried out correctly and under controlled conditions; this scientific approach to the production of cheese represented a great step forward (Battistotti et al., 1983).

Today, the production of the vast majority of cheese varieties can be sub-divided into two well-defined phases: manufacturing and ripening. Essentially, cheese-making is a concentration, or dehydration, process, beginning with the gelation of the casein via isoelectric (acid) or enzymatic (rennet) coagulation (Law, 1999). Depending on the variety, the fat and casein in milk are concentrated 6-12 fold. The degree of dehydration is regulated not only by the extent and combination of a number of steps but also the chemical composition of the milk (Fox, 1993). In turn, the moisture level, salt level, pH, and microflora regulate and control the biochemical changes that occur during ripening, and therefore determine the flavor, aroma, and texture of the finished product. Thus, the nature and quality of the finished cheese are determined to a very large extent by the manufacturing steps, with each step serving a clearly defined purpose. However, it is during the ripening phase that the characteristic flavor and texture of the individual cheese varieties develop (Fox, 1993).

The manufacturing phase can be defined as those operations performed during the first 24 hours, although some of these operations (i.e., salting and dehydration) may continue over a longer period (Fox, 1993). The manufacturing protocols for individual varieties of cheese differ in detail; however, a review of the literature (Kosikowski, 1977; Davies and Law, 1984; Fox, 1993; Varnam and Sutherland,

1994; Law, 1999; Fox et al., 2000) reveals that there are basic steps necessary and common among most cheeses. The transformation of milk into cheese generally involves the following series of separate steps: Milk Selection and Pre-Treatment, Addition of Starter Bacteria, Addition of Coagulant, Cutting, Cooking, Separating and Draining, Milling, Salting, Hooping and Pressing, and Packaging and Ripening. Figure 2.5 depicts a flow diagram from Law (1999), representing the main steps in cheese-making. This diagram also shows possible variations of the process which are used to make different varieties of cheese.

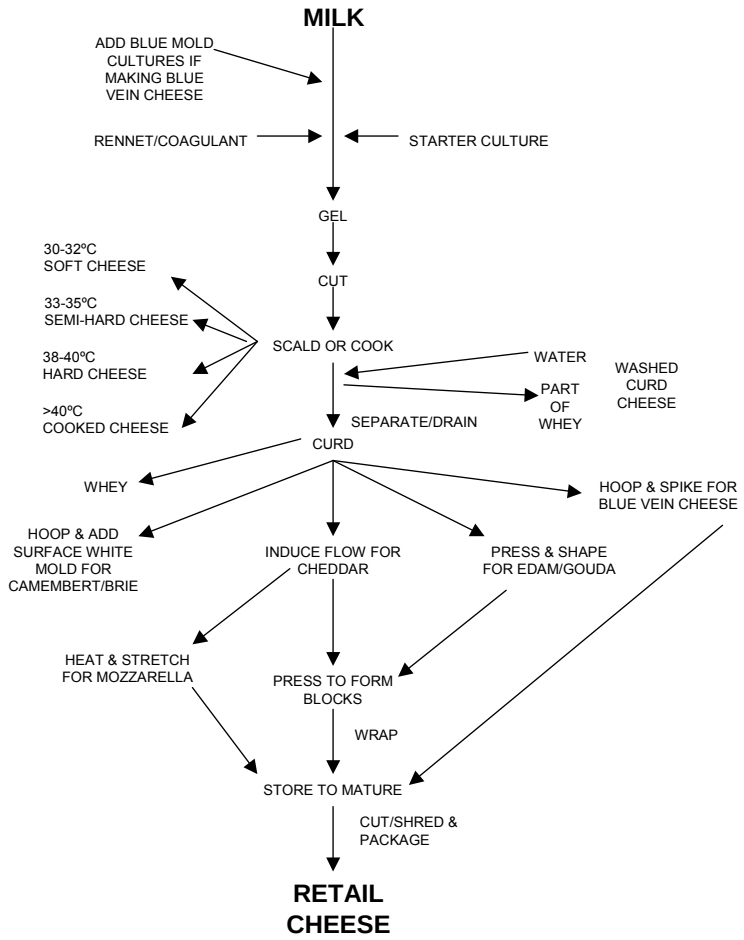


Figure 2.5: Flow Diagram of Cheese-making Process

While these steps are common to all cheese, the conditions of manufacture vary considerably. The differences in the final cheese product are due to the following main factors: the type of milk used, the degree of souring and the type of souring organisms added, the temperature of renneting and subsequent cooking or scalding of the curd in the whey (not applied to all varieties), the method and fineness of cutting or breaking up the curd, the treatment of the curd after separation from the whey, the milling and salting of the curd before placing in the hoop or mold (not applied to all varieties), the pressure applied to the green cheese (not applied to all varieties), the time, temperature and relatively humidity of ripening, and special treatments such as pricking or stabbing the cheese (not applied to all varieties), bathing in brine (not applied to all varieties), and surface treatment to produce a certain type coat (Law, 1999).

All of these variables are under the control of the cheese-maker and influence the physical, chemical, and microbiological changes taking place in the milk, coagulum, curd, and cheese. While scientists and microbiologists understand the important changes, there are still many mechanisms and interactions between factors that are not completely known (Davis, 1965). Of all dairy products, cheese is the most diverse group due to its biological, biochemical, and chemical instability. The manufacturing and ripening processes represent a series of consecutive and associated biochemical events. This series of biochemical events results in a flavorful cheese when synchronized and balanced; however, when unbalanced, this series of steps can result in off-flavors, odors, and allows for the growth of undesirable bacteria (Fox, 1993).

While it has traditionally been assumed that pathogenic microorganisms in raw milk die during the cheese manufacturing process, it is now understood that pathogens can survive and grow during both the manufacturing and ripening phases. The following sections provide a detailed description of the main steps in the cheese-making process, the possible manufacturing conditions at each step, and the influence of these manufacturing conditions on the survival of pathogenic microorganisms in the final cheese product.

2.4.2.1 Milk Selection and Pre-Treatment

Cheese manufacture begins with the selection of milk, which should be of high microbiological and chemical quality. Depending on the type of cheese being made, cow, sheep, goat, or buffalo milk may be selected. It is recommended that milk for cheese be cooled to 4˚C immediately after milking and it may be held at this temperature for several days at the farm or factory (Fox, 1993). However, the USDA/CFSAN Grade "A" Pasteurized Milk Ordinance (PMO), 2001 Revision states that all raw milk and milk products shall be maintained at 7°C or less until processed (USDA, 2001). The type of milk used for cheese-making can be raw, pasteurized, or heat treated (i.e., thermization or sub-pasteurization). Although raw milk can still be used both in commercial and farmhouse cheese-making, most cheese-milk is now pasteurized.

Milk used for cheese-making is usually pasteurized immediately before use. The pasteurization process alters the indigenous microflora of the milk and facilitates the manufacture of cheese of a uniform quality. However, proponents of raw milk cheese argue that cheese made from pasteurized milk develops a less intense flavor

and ripens more slowly than raw milk cheese (Fox, 1993). Raw milk proponents also argue that pathogens that are present will die during the ripening process, and that pathogens can be introduced during cheese production after the milk is pasteurized (Law, 1999). Proponents of pasteurization contend that by starting with milk free of pathogens and producing cheese in an environment free of pathogens, the end product will remain free of pathogens. In addition, proponents of pasteurization claim that any difference in flavor is inconsequential as compared to the public health issues caused by some pathogens (Law, 1999).

In this case, pasteurization is the process of heating the milk to a specific temperature for a specific period of time in order to kill all the naturally occurring pathogens. The process is based on the thermal destruction of *Coxiella burnetti*, the most heat resistant organism found in milk. Table 2.1 table gives the minimum time-temperature combinations that are recommended for the pasteurization process according to the PMO Revision 2001 (USDA, 2001).

Table 2.1: Time-Temperature Combinations Recommended for Milk Pasteurization

Temperature	Time
63 °C (145°F)*	30 minutes
72 °C (161°F)*	15 seconds
89 °C (191°F)	1.0 seconds
90 °C (194°F)	0.5 seconds
94 °C (201°F)	0.1 seconds
96 °C (204°F)	0.05 seconds
100 °C (212°F)	0.01 seconds

*If the fat content of the milk product is ten percent (10%) or more, or if it contains added sweeteners, the specified temperature shall be increased by 3ºC (5ºF).

In the United States, most cheese production employs the pasteurization process. Legislation in most countries requires that cheese be made from high-temperature, short-time (HTST) pasteurized milk, that cheese be aged for 60 days which allows food-poisoning and pathogenic bacteria to die, or the cheese itself should be pasteurized (i.e., converted to processed cheese) (Fox et al., 2000). However, in many other countries a significant amount of cheese is made from milk that has received either a lesser heat treatment or no heat treatment at all.

Sub-pasteurization heat treatments, also known as thermization, encompass a wide range of time-temperature combinations; however, one typical time-temperature combination used in thermization involves heating the milk to 63°C for 10-15 seconds (Fox et al., 2000). This treatment results in less inactivation of enzymes and nonstarter lactic acid bacteria (NSLAB) that are important in developing cheese flavor. There is some controversy over using thermalized milk for cheese-making. Fox et al. (2000) state that depending on the time and temperature used, thermization may not kill all of the pathogenic and food-poisoning microorganisms. However, cheese made from heat-treated raw milk can be microbiologically safe; Johnson et al. (1990) report that a heat treatment of 65-65.6ºC for 16-18 seconds will destroy almost all pathogenic microorganisms that pose a treat to a safe cheese product. In addition, studies by D'Aoust et al. (1988) show heating of raw milk at 65ºC for a mean holding time of 17.6 seconds destroyed all strains of *E. coli* O157:H7. Therefore, temperatures higher than 63ºC are generally recommended for thermization (D'Aoust et al., 1988; Blackburn et al., 1997); however, some studies have investigated temperatures as low as 50ºC (Read et al., 1960).

Cheese made with milk receiving no heat treatment (i.e., raw milk cheese) is still made in many countries, including the United States. However, raw milk used for cheese-making should be of good bacteriological quality (Fox, 1993). According to the PMO Revision 2001 it is illegal to sell raw milk cheese across state lines, and raw milk cheese must be ripened for at least 60 days (USDA, 2001). In addition, raw milk cheese should be cooked to a high temperature (>50 °C) for up to one hour during the cheese-making process, thereby killing some of the bacteria originating from the raw milk (Fox et al., 2000). The influence of the cooking step in the cheese-making process is further explained in section 2.2.5.

2.4.2.2 Addition of Starter Bacteria

Carefully selected strains of different species of lactic acid bacteria (LAB), or starter cultures, are added to the milk shortly before renneting. The purpose of these bacteria is to produce lactic acid, with this acid production having three main functions: 1) promote rennet activity through the reduction of pH, 2) aid the expulsion of whey from the curd, which reduces the moisture content of the cheese, and 3) help prevent the growth of undesirable bacteria in the cheese (Fox et al., 2000). Although starter cultures can influence the taste, aroma, and texture of the cheese, other bacteria are typically added to influence these properties (Law, 1999). The selection of starter bacteria in cheese-making is based not only on tradition, but also the flavor, rate and extent of acid development desired in the finished cheese. Starter cultures differ in their sensitivity to salt, temperature, and pH, and exploitation of these characteristics during the cheese-making process influences the end product (Law, 1999). Thus, the starter culture plays a crucial role in both manufacturing and ripening.

Starter cultures are commonly divided into two main groups: mesophilic and thermophilic cultures. Mesophilic cultures are typically used with cheese requiring an optimal temperature of 30˚C during the cooking step, while thermophilic cultures have an optimal cooking temperature of 42˚C or above (Fox et al., 2000). Examples of mesophilic cultures include *Lactococcus lactis* subspp. c*remoris* and *Lactococcus lactis* subspp. *lactis*. Typically, mesophilic cultures are used in the production of Cheddar, Gouda, Edam, Blue, and Camembert cheeses. Swiss and Italian varieties of cheese typically use thermophilic starter cultures. Examples of thermophilic cultures include *Streptococcus salivarius* subspp. *thermophilus* and several species of *Lactobacillus* (i.e., *Lactobacillus helveticus, Lactobacillus delbrueckii* subspp. *lactis,* and *Lactobacillus delbrueckii* subspp. *bulgaricus*) (Fox et al., 2000).

Each group of starters can be further subdivided into defined- and mixed-strain cultures. Mixed-strain cultures contain unknown numbers of strains of the same species and are typically used by small-scale producers. Defined-strain cultures are pure cultures, with known and identifiable physical characteristics, and are typically used by large-scale producers. However, it should be noted that defined cultures are rarely used as pure cultures or single strains, but rather as mixtures of 2 to 6 known strains (Fox et al., 2000). Table 2.2 provides a short list common mesophilic and thermophilic starter cultures used to manufacture various types of cheese; various starter cultures can be used to manufacture the same cheese.

Table 2.2: Starter Cultures Used in the Manufacture of Different Cheeses

Culture Type	Species Name	Cheese Type
Mesophilic	*Lactococcus lactis* subspp. *lactis*	Cheddar, Gouda
	Lactococcus lactis subspp. *cremoris*	Tilsiter, Camembert
	Leuconosoc lactis	Gouda
Thermophilic	*Streptococcus thermophilus*	Mozzarella, Brie
	Lactobaccilus helveticus	Swiss, Gruyere, Emmental
	Lactobaccilus delbrueckii subspp. *lactis*	Emmental

2.4.2.3 Addition of Coagulant

The purpose of a coagulant in cheese-making is to convert the liquid milk to a gel. All cheese varieties have this essential manufacturing step in which the casein component of the milk protein coagulates to form a gel which entraps the fat. According to Fox (1993), coagulation may be achieved by: 1) limiting proteolysis through selected proteinases, 2) acidification to pH ~4.6, or 3) acidification to pH values >4.6, in combination with heating. Cheeses produced either by acid or heat/acid are usually consumed fresh, and are not very interesting from a biochemical viewpoint (Fox, 1993). The majority of cheeses are produced by enzymatic (i.e., rennet) coagulations, with aspartic proteinases being the active milk-clotting enzyme. Rennet cheeses are almost always ripened, or matured, before consumption through the action of a complex battery of enzymes and are consequently in a dynamic state (Fox, 1993). The properties of rennet curds are very different from those produced by isoelectric precipitation. Rennet curds have better syneresis properties making it possible to produce low-moisture cheese curd without hardening; therefore, rennet curd can be converted to a more stable product than acid curds. Rennet coagulation has become predominant in cheese manufacture and is the starting material for the vast majority of modern cheese varieties.

Typically, rennet refers to enzyme preparations from the lining of the fourth stomach of calves, with chymosin being the most important enzyme in rennet. Chymosin is considered nature's enzyme for coagulating milk; thus, calf rennet is regarded as the ideal enzyme for cheese-making because of its high chymosin content (Law, 1999). However, the increasing trend to slaughter calves at an older age and the increase in cheese production, has led to a shortage of calf rennet. Due to this shortage rennet substitutes (usually bovine or porcine pepsins) are widely used in cheese-making (Fox, 1993). The International Dairy Federation (IDF) has stated that the term rennet should be reserved for enzyme preparations from ruminant stomachs, whereas other milk-clotting enzymes should be named coagulants (Law, 1999).

2.4.2.4 Cutting

Cutting occurs after the milk has clotted, and the coagulum is cut into pieces called grains or curd. Cutting facilitates the removal of whey from the coagulated casein by increasing the surface area (Battistotti et al., 1983). It is during cutting that the differentiation of the individual cheese varieties really begins, with the firmness and size of the cut coagulum being the two main influencing factors (Law, 1999).

The smaller the coagulum is cut, the greater the surface area exposed and the more fat lost (Law, 1999). The increased surface area of a small curd also results in the curd particle shrinking rapidly and expelling a larger amount of whey. Therefore, low-moisture cheeses are made from a coagulum in which the curd is cut small and soft, while high-moisture cheeses are made from a coagulum in which the curd is cut large and firm (Law, 1999).

2.4.2.5 Cooking

After the curd is cut, it is typically cooked, or heated, and stirred. Cooking not only influences the curd texture, but also gains time for lactic acid development and suppresses spoilage and pathogenic microorganisms. The combination of stirring and heating, in addition to continued acid production by the starter, affect the final level of moisture in the cheese (Law, 1999). However, the main objective of cooking is to contract the curd particles and drive out the free whey (Kosikowski, 1977). Internally, casein molecules are rearranging and tightening, in a process called syneresis, resulting in the squeezing out of the whey from the casein network (Law, 1999). The rate and extent of syneresis are influenced by milk composition, pH of the whey, cooking temperature, rate of stirring of the curd-whey mixture, and time (Fox, 1993). The composition of the finished cheese is largely influenced by the extent of syneresis, and is under the control of the cheese-maker (Fox, 1993).

Cooking is a thermal application which takes on many forms, ranging from direct steam to jacketed water; the choice is usually dictated by cheese type. Depending on the cheese variety, the maximum cooking temperature varies widely. The cooking of the curds must be conducted slowly and gently in the early stages, otherwise shattering of the curd results. In addition, rennet formed curds are never heated beyond the generally accepted maximum temperature because of the danger of curtailing the lactic acid fermentation (Kosikowski, 1977). Curds are heated at such a rate that the temperature rises to 32ºC in about 15 minutes and then to the maximum scalding temperature (35-43ºC) at the rate of 1ºC every four minutes (Davis, 1965). Typically, the curds for harder cheeses with lower moisture contents are heated to

between 46-56ºC, allowing more whey to be expelled. In contrast, low scalding temperatures leave more moisture in the curd resulting in a softer cheese (Battistotti et al., 1983).

2.4.2.6 Separating and Draining

At a carefully chosen point in the manufacturing process, the curd grains are separated from the whey. Whey is the separated watery portion of the milk left over from the coagulation process (Kosikowski, 1977). The method by which the whey and curd are separated plays an important role in not only the texture of the cheese, but also the color and flavor (Law, 1999).

There are several methods for draining the whey. With soft cheese, whey is typically drained from the perforations in the cheese molds. In hard and semi-hard cheese, whey is drained from the vat, with the curds being held back with a screen and a channel is made in the curd mat to allow the whey to flow out. Finally, in large-scale productions, the whey and curd are pumped into a vat with a perforated screen at the bottom. The whey is able to flow through the screen, while the curd is held back. Regardless of the draining technique, the curd is allowed to mat together as the whey is drained and the mat is then cut into slabs (Law, 1999).

2.4.2.7 Milling

After draining the curd from the whey, the curds are allowed to mat together and form a slab, and as the layer of curd compacts, more whey is released from the curd (Fox, 1993). With certain cheeses, such as Cheddar, the compression is allowed to continue for a considerable amount of time, after which the curd mass is cut, or milled, into small pieces. Milling is the mechanical shredding and reduction of the

curd blocks to a size suitable for salting. Other varieties of cheese allow for a short compression period, after which the blocks of curds are cut from the slabs and then subject to molding and pressing (Fox, 1993).

2.4.2.8 Salting

The salting step consists of spreading coarse salt over the curd surfaces in a variety of ways: manually, mechanically, or by immersing the pressed curd under brine. Dry salting may be applied either to the loose curds or to the compact wheels (Kosikowski, 1977). In some varieties of cheese, salting is dependent on when the milling occurs (Davis, 1965). For example, the Cheddar cheese curd blocks are first milled to a suitable size and then salted (Kosikowski, 1977). If salt is not added to the curd before pressing, it may be added by soaking the cheese in brine (i.e., a sodium chloride solution). The brine is usually a saturated salt solution (ca. 23% salt; but some are only 15%), at or near the pH of the cheese and at 40-50ºC (Law, 1999). Examples of cheeses that use a brine solution include Edam, Gouda, and Provolone. Salting may also be accomplished through rubbing dry salt onto the surface of the molded curds as in Blue-type cheeses.

The salting of cheese not only improves its flavor, texture, and appearance, but also serves a variety of other functions. First, salting helps control bacterial activity and the rate of ripening by suppressing the growth of some types of microorganisms. In addition, salting also results in the immediate release of further whey from the curd. However, while salting contributes to syneresis, it should not be used as a means of controlling the moisture content. Finally, salting also assists in the matting of the curd (Davis, 1965). Although salting should be a very simple

operation, quite frequently it is not performed properly, with adverse effects on cheese quality (Fox, 1993). Cheeses made without salt or improperly salted often ripen too quickly and develop unpleasant flavors (Davis, 1965). In addition, salting of the curd should be uniform otherwise the cheese may take on a mottled appearance (Kosikowski, 1977). The curd should be uniformly salted at the rate of about one ounce to three pounds of curd in order to obtain a quality cheese (Davis, 1965).

2.4.2.9 Hooping and Pressing

The term hoop is typically used in America (while mold is used in Britain), to refer to the containers used to receive the milled curd and shape the cheese (Davis, 1965). After the curd is placed in the hoop, the curd mass is pressed with the aim of obtaining a coherent mass. The act of pressing accomplishes three main objectives: 1) the curd is formed into its characteristic shape and compact texture; 2) whey is forced out; and 3) the curds knit together more quickly (Law, 1999). There are various ways and means of pressing the curd, with Kosikowski (1977) stating that confining the wet, warm curds (salted or unsalted) in a constricted wooden or metal form or cloth bag, with or without external weights or allowing the piled up curd to rest on itself in a vat for fixed periods of time constitutes pressing. Typically, the time, pressure, and efficiency of pressing depends on the condition of the curd at the time of pressing and the decrease in pH during pressing (Law, 1999).

A substantial amount of whey is released during the time the curd is being consolidated to form cheese. The higher the moisture content of the curd (i.e., softer curd), the greater the amount of whey and rate of release of the whey from the curd. In order to accommodate the release of whey, hoops and molds are designed for the

escape of whey. This may be accomplished by using detachable bottoms or no bottom, with the mold simply resting on a draining table. Other designs involve small holes, perforations, slits, or other openings in the molds (Davis, 1965).

2.4.2.10 Packaging and Ripening

Some cheeses are consumed fresh; however, most cheese varieties, including rennet coagulated, are not ready for consumption at the end of manufacturing and undergo a period of ripening. Before the cheese is ripened, it is packaged. Typically, packaging occurs after the curd has been pressed. The cheese may be surface dried, parafinned (i.e., wrapped in a plastic film), or it may be left untouched, except for oiling of its surfaces (Kosikowski, 1977). The shaped and packaged cheese is then allowed to ripen by placing the cheese in a temperature and humidity controlled room for a specified period of time. Times for ripening (i.e. curing, maturation, aging) may vary from a few weeks to more than two years, depending on the variety of cheese; typically, the duration of ripening is inversely related to the moisture content of the cheese (Fox, 1993). The temperature for ripening varies from 2-16ºC (Kosikowski, 1977).

The ripening step is one of the most important in the cheese-making process because during this time both physical and chemical changes are taking place that define the flavor, aroma, texture, and appearance of the final cheese. Cheese ripens into distinct varieties because, according to Law (1999), cheeses are made physically different by the technology in the cheese plant and the microbial cultures. Curds for different cheese varieties are noticeably different at the end of manufacture; however, the unique characteristics of the individual cheeses develop during ripening.

Therefore, the biochemical changes resulting in characteristics such as flavor, aroma, and texture that typically occur during ripening, are largely predetermined by the manufacturing process (Fox, 1993).

The development of these characteristics in cheese is due to various types of chemical breakdowns involving the microorganisms in the milk and starter and the enzymes in the rennet and milk (Davis, 1965). In addition, there are secondary microflora that also influence these characteristics; these secondary microflora arise from several sources. Sometimes secondary microflora survive pasteurization, but more often they are added purposely depending on the type of cheese being manufactured. For example, some microorganisms are added as a secondary starter, such as a blue or while mold during ripening or a surface smear of bacteria.

Cheese ripening gives these microorganisms and enzymes in the cheese curd an opportunity to hydrolyze fat, protein, lactose, and other compounds. According to Kosikowski (1977), the breakdown produces a softer, pliable body, and a more aromatic flavor, as the rigid insoluble protein changes to soluble nitrogenous forms and the neutral fat splits partially into free fatty acids and glycerol. Thus, ripening catalyzes the production of a great variety of water-soluble, flavorful components: peptides, amino acids, amines, fatty acids, and carbonyls. Presumably, in properly balanced ratios, these form the typical flavor of a ripened cheese (Kosikowski, 1977).

3. APPLICATION OF ENGINEERING-BASED PROBABILSTIC RISK ASSESSMENT

3.1 Application Overview

The engineering-based risk assessment methodology developed in this research differs from traditional quantitative microbial risk assessment (QMRA); however, the engineering approach still works within the traditional QMRA framework of hazard identification, exposure assessment, dose-response assessment, and risk characterization. The application of this approach to a particular food-pathogen combination, *E. coli* O157:H7 contamination in cheese, demonstrates the engineering risk assessment methodology within the traditional QMRA framework. In addition, the adaptation of other engineering tools and techniques, such as Multiplicative Factors (MF) and Analytical Hierarchy Process (AHP), are explained throughout the risk model.

3.2 Hazard Identification

3.2.1 Foodborne Disease

Infectious diseases spread through food are a common, and sometimes life-threatening, problem for millions of people in the United States and around the world. In the United States alone, foodborne diseases have been estimated to cause 76 million illnesses, 325,000 hospitalizations, and 5,000 deaths each year (Mead et al., 1999). There are more than 250 known foodborne diseases that can be caused by bacteria, parasites, viruses, or fungi; however, over 90% of confirmed foodborne human illness reported to the Centers for Disease Control (CDC) are attributed to

bacteria (Buzby et al., 1996). In addition to the societal impact, the economic burden of foodborne illness is estimated to be approximately $6.9 billion annually for the five most common bacterial pathogens (ERS, 2004).

Most bacteria do not cause human illness, with over 400 species of bacteria living harmlessly in the gastrointestinal tracts and skin of humans. However, bacteria causing foodborne illness may be found in soil, water, plants, and animals (including humans) and may cause illness by direct killing of cells or through the production of toxins. Some bacteria infect both animals and humans, while others can be harmless to animals but cause infection in humans. Further, only certain strains of a bacterium may cause illness (Buzby et al., 1996). One such bacterium, and the focus of this research, is *Escherichia coli* O157:H7, as this particular pathogen lives innocuously in the intestinal tract of some cattle, but can cause severe illness if ingested by humans.

3.2.2 *Escherichia coli*

At the very basic level, *Escherichia coli* is a species of gram-negative, facultatively anaerobic, rod-shaped bacteria. Many *E. coli* strains are normal inhabitants of the gastrointestinal tract of humans and other warm-blooded animals, and do not cause disease in humans (Buzby et al., 1996). Prior to identification of specific virulence factors in diarrheal *E. coli* strains, serotypic analysis was used to differentiate pathogenic strains. *E. coli* are serotyped on the basis of three major surface antigens: O (somatic), H (flagellar), and K (capsular). Specific combinations of O and H antigens define the "serotype" of an isolate. *E. coli* of specific serogroups can be associated with certain clinical syndromes, but it is not the serologic antigens

themselves that determine virulence. Rather, the serotypes and serogroups serve as readily identifiable chromosomal markers that correlate with specific virulence factors (Nataro and Kaper, 1998).

Although serotypic markers correlate with certain clinical syndromes, *E. coli* strains that cause diarrheal illness are categorized into specific groups based on several characteristics: virulence properties, pathogenic mechanisms, clinical syndromes, and distinct O:H serogroups (Nataro and Kaper, 1998). The categories of diarrheal *E. coli* strains include: enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enteroinvasive *E. coli* (EIEC), diffuse-adhering *E. coli* (DAEC), enteroaggregative *E. coli* (EaggEC), and enterohemorrhagic *E. coli* (EHEC) (LeBlanc, 2003).

3.2.3 *E. coli* O157:H7

E. coli O157:H7 belongs to the EHEC group; however, for an organism to be considered EHEC it must have two virulence factors that are necessary to cause disease. *E. coli* that produce Shiga-like toxins are referred to as Shiga-toxin producing *E. coli* (STEC); however, production of Shiga-like toxins does not necessarily cause disease. In addition to these toxins, some strains of *E. coli* have adherence factors (i.e., *eaeA* gene) that attach and damage intestinal tract cells causing attaching and effacing lesions (Nataro and Kaper, 1998). Thus, EHEC is a distinct subgroup of STEC strains that appear to cause serious disease by both adherence to intestinal cells and the release of Shiga-toxins.

3.2.3.1 Emergence of *E. coli* O157:H7

Although *E. coli* O157:H7 was first isolated by the CDC in 1975, it was not identified as a cause of human illness until 1982, after it was associated with two outbreaks of hemorrhagic colitis in Oregon and Michigan. Investigation of these two outbreaks linked the illness to the consumption of contaminated hamburgers (Riley et al., 1983). The widespread occurrence of outbreaks and the increased incidence of reported cases resulted in designation of *E. coli* O157:H7 as an emerging pathogen. In 1994, *E. coli* O157:H7 was officially designated as a nationally notifiable disease by the Council of State and Territorial Epidemiologists. And, in 1996, the Foodborne Diseases Active Surveillance Network (FoodNet), as a part of the CDC's Emerging Infections Program (EIP), began a program of active surveillance of clinical laboratories for *E. coli* O157:H7 infections (Mead et al., 1999). Based this surveillance data, Mead et al. (1999) estimate 62,000 annual cases of symptomatic *E. coli* O157:H7 infections in the United States related to foodborne exposure. These infections result in approximately 1,800 hospitalizations and 52 deaths (Mead et al., 1999).

3.2.3.2 Adverse Health Outcomes Associated with *E. coli* O157:H7

Ingestion of food contaminated with *E. coli* O157:H7 results in a wide range of possible outcomes from asymptomatic infection to death. In order to cause disease, *E. coli* O157:H7 must survive the acidic conditions of the stomach and move to the gastrointestinal tract. The incubation period, or time from ingestion to the onset of symptoms, ranges from 1 to 8 days (Mead and Griffin, 1998). The most common symptoms of illness include non-bloody diarrhea, hemorrhagic colitis (i.e.,

bloody diarrhea), hemolytic uremic syndrome (HUS), and thrombotic thrombocytopenic purpura (TTP).

Typically, illness due to *E. coli* O157:H7 infection begins with abdominal cramping and non-bloody diarrhea, with as many as 70% of patients developing hemorrhagic colitis after 1-2 days (Mead and Griffin, 1998). The symptoms of hemorrhagic colitis include severe abdominal cramping, bloody diarrhea, and swelling, erosion and hemorrhage of the mucosal lining of the colon (Su and Brandt, 1995). While severe cases of hemorrhagic colitis can result in hospitalization (30 – 45%), most patients with hemorrhagic colitis recover within 7 days (Mead and Griffin, 1998; Slutsker et al., 1998; Bell et al., 1994).

Hemorrhagic colitis may be the only clinical manifestation of *E. coli* O157:H7 infection, or it may precede other life-threatening complications such as HUS and TTP. The onset of HUS is approximately a week after the onset of hemorrhagic colitis and is a severe form of kidney disease. HUS is characterized by red blood cell destruction, lack of urine formation, kidney failure, and neurological complications, such as seizures and strokes (Buzby et al., 1996). HUS occurs most often in children under the age of ten years and is the leading cause of acute renal failure in children (Duncan and Hackney, 1994). Estimates of the number of hemorrhagic colitis cases progressing to HUS vary, with Mead and Griffin (1998) estimating 3-7% of sporadic cases and 20% or more of outbreak-related cases progress to HUS. Bleem (1994) estimates up to 10% of hemorrhagic colitis cases progress to HUS while Duncan and Hackney (1994) estimate 15% of hemorrhagic colitis cases develop into HUS. In addition, many patients with HUS die, with Mead and Griffin (1998) estimating the

mortality rate between 3-5% and Su and Brandt (1995) estimating the mortality rate to be as high as 10%.

TTP is another condition which may follow hemorrhagic colitis, and typically affects the elderly (Buzby et al., 1996). TTP is a condition that is similar to HUS, but with more prominent neurological symptoms and fewer renal symptoms; essentially, TTP is thought to represent a more extensive form of the clinical spectrum of vascular diseases that produces HUS (Su and Brandt, 1995). It should be noted that there is some debate as to whether TTP and HUS are distinct syndromes. In fact, Mead and Griffin (1998) believe when associated with *E. coli* O157:H7, TTP is probably the same disorder as HUS. TTP related data is sparse, but Su and Brandt (1995) estimate as many as 8% of patients with *E. coli* O157:H7 associated hemorrhagic colitis progress to TTP. The mortality rate for TTP varies widely among outbreaks. Griffin and Tauxe (1991) give the combined case-fatality rate of four nursing home outbreaks as 18%, while Duncan and Hackney (1994) report that the incidence of death in the elderly from TTP is reported to be as high as 50%.

The case-fatality rate of those suffering hemorrhagic colitis, without progression to HUS or TTP, is thought to be less than 1% (Ryan et al., 1986; Boyce et al., 1995). However, Su and Brandt (1995) estimate the case-fatality rate for *E. coli* O157:H7 infection from 3% to 36% among the elderly and Gerba et al. (1996) speculate that case-fatality rate can be 10-100 times greater in the elderly than in the general population. Therefore, age and immune system status appear to be the greatest risk factors for the development of *E. coli* O157:H7 related illness. Persons at extremes of age are at an increased risk for *E. coli* O157:H7 associated diarrhea as

well as for HUS, TTP, and death (Su and Brandt, 1995). According to Gerba et al. (1996) infectious diseases are a major problem in the elderly because the immune function declines with age, antibiotic treatment is less effective because of a decrease in physiological function, and malnutrition is more common. Consequently, outbreaks of gastroenteritis in nursing homes can be devastating and result in a significantly higher mortality rate than the general population.

Table 3.1, from Su and Brandt (1995), gives a summary of statistics relating to *E. coli* O157:H7 associated diarrhea, hemorrhagic colitis, and HUS. However, it should be noted that these statistics vary greatly from source to source and that the actual incidence rates are impossible to determine. Information on the incidence of foodborne disease is obtained through surveillance systems, which collects outbreak data from state and local health departments. The reporting of outbreaks is dependent on patient and physician recognition, motivation to contact local health officials, and resources of laboratories to identify the pathogen. For these reasons, it is thought that only a small fraction of foodborne disease outbreaks are actually reported to the CDC and outbreak data seriously under-represents the prevalence of foodborne illness in the United States (Steahr, 1994).

Table 3.1: Statistics on the Association of *E. coli* O157:H7 Infection with Diarrhea, Hemorrhagic Colitis, and HUS

Variable	Percentage
Incidence of *E. coli* O157:H7 in all cases of diarrhea	0.6-2.4
Incidence of *E. coli* O157:H7 in bloody diarrhea of hemorrhagic colitis	15-36
Development of hemorrhagic colitis in *E. coli* O157:H7 infection	38-61
Incidence of *E. coli* O157:H7 in HUS	46-58
Progression of *E. coli* O157:H7 infection to HUS	2-7

3.2.3.3 Sources of *E. coli* O157:H7

While *E. coli* O157:H7 may be transmitted through water or person-to-person contact, foodborne transmission is the most important means of infection and the focus of this research; Mead et al. (1999) estimate that 85% of *E. coli* O157:H7 illnesses are foodborne. *E. coli* O157:H7 have been isolated from a variety of animals including pigs, horses, dogs, cats, birds, and rodents (Duffy et al., 2001); however, healthy cattle are the primary reservoir for human infection with *E. coli* O157:H7 (Mead and Griffin, 1998). *E. coli* O157:H7 lives innocuously in the intestinal tracts of some cattle and is excreted through the feces (Buzby et al., 1996), with most foodborne outbreaks being traced to foods derived from cattle, especially ground beef and raw milk (Mead and Griffin, 1998). Contamination of foods generally occurs in one of three ways: 1) through fecal contamination of food crops when untreated or poorly treated manure is used for fertilizer, 2) fecal contamination of carcasses through poor hygienic practices during slaughter and evisceration processes, and 3) consumption of fecally contaminated raw milk or products made from such milk (Bell and Kyriakides, 1998).

The principle food vehicle implicated in many *E. coli* O157:H7 outbreaks has been ground beef (Riley et al., 1993; Ryan et al., 1986; Ostroff et al., 1990; Bell et al., 1994; CDC, 1993); however, E. coli O157:H7 outbreaks have also been associated with raw milk, apple cider, mayonnaise, and vegetables (Olsen et al., 2000). Fresh-pressed, unpreserved apple cider has been implicated in two outbreaks of *E. coli* O157:H7 infection, with the transmission possibly occurring through the pressing of apples contaminated on the ground (Besser et al., 1993; CDC, 1997). Multiple

outbreaks of *E. coli* O157:H7 linked to the ingestion of milk have been reported (Keene et al., 1997; Martin et al., 1986; Upton and Coia, 1994). In addition, an outbreak of *E. coli* O157:H7 infection associated with eating fresh cheese curds has also been documented (CDC, 2000). *E. coli* O157:H7 has been associated with numerous outbreaks involving ground beef and milk, and the pathogen has been isolated from milk and the feces of healthy cattle (Martin et al., 1986; Wells et al., 1991). Thus, it appears that cattle are an important reservoir for *E. coli* O157:H7.

3.2.3.4 Survival and Growth Factors of *E. coli* O157:H7

E. coli O157:H7 presents a serious food safety issue not only in terms of the severe health outcomes it causes, but also because it is an extremely virulent organism. A number of studies have investigated the effects of temperature, pH, salt, and water activity on the survival and growth of *E. coli* O157:H7 (Buchanan and Bagi, 1997; Sutherland et al., 1995; Buchanan et al., 1993; Buchanan and Klawitter, 1992). First, *E. coli* O157:H7 is capable of surviving at low temperatures and resists freezing. The organism will not typically grow below 8°C - 10°C or above 45°C, with optimal growth occurring at 37°C (Doyle and Schoeni, 1984; Buchanan and Doyle, 1997). *E. coli* O157:H7 has no unusual resistance to heat, and thorough cooking of foods or pasteurization will kill the organism (Doyle et al., 1997). Second, unlike many foodborne disease-causing organisms, *E. coli* O157:H7 is tolerant of acidic environments, and it can survive the high acidity of the stomach (Buzby et al., 1996); Duncan and Hackney (1994) state that *E. coli* O157:H7 can survive pH as low as 3.7. Third, *E. coli* O157:H7 is a facultative anaerobe, meaning it can grow in environments where oxygen is present, low, or absent. Therefore,

modified-atmosphere packaging, which is commonly used to prevent bacterial growth in packaging fresh foods, has little effect on the growth and survival of the organism (Hao and Brackett, 1993; Duffy et al., 2001). Finally, while *E. coli* O157:H7 does not tolerate high salt conditions, the organism is able to survive for extended periods under conditions of reduced water activity (Buchanan and Doyle, 1997).

3.2.3.5 Low Infectious Dose

Although the precise infectious dose for *E. coli* O157:H7 is unknown, it is thought to be extremely low. The literature reveals an infectious dose of between 10-1000 cells. CAST (1994) estimates between 10-1000 cells are required to cause infection, while the Institute of Food Science & Technology (2004) estimate between 10-100 cells can cause infection. Dennis (2000) estimates that fewer than 100 cells are required to cause infection, while Duncan and Hackney (1994) estimate as few as 10 cells could cause infection. Regardless of the true infectious dose, *E. coli* O157:H7 presents a serious food safety concern due to the low infectious dose and ability to survive the acidic conditions of the stomach.

3.2.4 *E. coli* O157:H7 Relevance to Cheese

Multiple outbreaks of *E. coli* O157:H7 have been linked to the ingestion of both raw and pasteurized milk (Keene et al., 1997; Martin et al., 1986; Upton and Coia, 1994). Contamination with cattle fecal material has been implicated in the infections of *E. coli* O157:H7 associated with raw milk. Outbreaks related to pasteurized milk have occurred due to inadequate pasteurization or post-process contamination (Duffy et al., 2001). Wang et al. (1997) showed that *E. coli* O157:H7 was able to grow in both pasteurized and unpasteurized milk stored at 8ºC, 15ºC, and

22ºC; however, while *E. coli* O157:H7 failed to grow at 5ºC, it did survive with only a small population decrease after 28 days of storage. Studies performed by Mamani et al. (2003), Massa et al. (1999), Palumbo et al. (1997), and Altieri et al. (1997) were consistent with the results of Wang et al. (1997).

The association of milk with *E. coli* O157:H7 outbreaks and the previous studies on the growth of *E. coli* O157:H7 in milk raises the possibility of *E. coli* O157:H7 survival in other dairy products such as cheese. Traditionally, it has been assumed that pathogenic microorganisms in raw milk die during the cheese manufacturing process due to the production of high acidity (i.e., low pH value) and competition from starter cultures (Fox, 1993). However, studies on the survival of *E. coli* O157:H7 in hard cheese indicate that the pathogen can grow during the cheese manufacturing process and survive for up to 70 days post-manufacturing (Hudson et al., 1997; Maher et al., 2001; Reitsma et al., 1996; Teo et al., 2000). Therefore, the indications are that the additional hurdles imposed during cheese manufacturing are insufficient to prevent the growth and survival of the pathogen in cheese produced from milk contaminated with the pathogen.

Not only has *E. coli* O157:H7 been shown to survive the cheese manufacturing process, but it has also been linked to several outbreaks involving cheese, thereby establishing cheese as a viable route of transmission for *E. coli* O157:H7. Table 3.2 presents a summary of these cheese related *E. coli* O157:H7 outbreaks. Although cheese related *E. coli* O157:H7 outbreaks do not represent a large proportion of all *E. coli* O157:H7 outbreaks, on some occasions the health

consequences have been particularly severe, resulting in serious infections, long-term sequelae, and even death (IFST, 1998).

Table 3.2: Summary of Reported Cheese Related *E. coli* O157:H7 Outbreaks

Reference	Outbreak	Cheese Type	Milk Type	Number of Illnesses	Number of HUS	Number of Deaths
MacDonald, 1983; Nooitgedagt and Hartog, 1988	1983, Netherlands, Denmark, Sweden, and USA	Brie	Unpasteurized	>3000	NR[1]	NR
Anon., 1994a	1992, France	Fromage frais	Unpasteurized	NR	NR	1
Anon, 1994b	1994, Scotland	Farm cheese	Unpasteurized	20	1	0
Anon, 1997	1997, Wyre, England	Lancashire	Unpasteurized	2	0	0
CDC, 2000	1998, Wisconsin, USA	Fresh cheese curds	Pasteurized[2]	55	0	0
Hornish et al., 2005	2002, Alberta, Canada	Gouda	Unpasteurized	13	2	0

[1]Not Reported
[2]Post-process contamination

In the majority of these outbreaks, the cheese was made with unpasteurized milk. In the outbreak associated with cheese made from pasteurized milk, post-pasteurization contamination occurred. While it is recognized that post-pasteurization contamination can occur whether or not the milk is pasteurized, the data in Table 3.2 indicate that outbreaks are more likely to arise from cheese made from unpasteurized milk even if the starting material is of exceptionally high microbiological quality and the manufacturing conditions are the most hygienic possible (IFST, 1998).

3.3 Exposure Assessment

3.3.1 Production

3.3.1.1 Production Overview

In order to estimate the extent to which cheese may become contaminated with *E. coli* O157:H7 during the production phase, the steps (i.e., sub-system elements) in the cheese-making process where *E. coli* O157:H7 contamination may be increased or decreased are identified; in addition, the mechanisms affecting the growth or inactivation of *E. coli* O157:H7 contamination at each step (i.e., the basic elements) are identified as well; the basic elements are further reduced into options in order to account for the variability of the process. The significant steps in the production of cheese have been identified as: milk storage, milk heat treatment, addition of coagulant, cutting the curd, cooking the curd, separation of whey and curd, salting, hooping and pressing, and ripening. These steps and their relationships are depicted in the sub-system DML model shown in Figure 3.1.

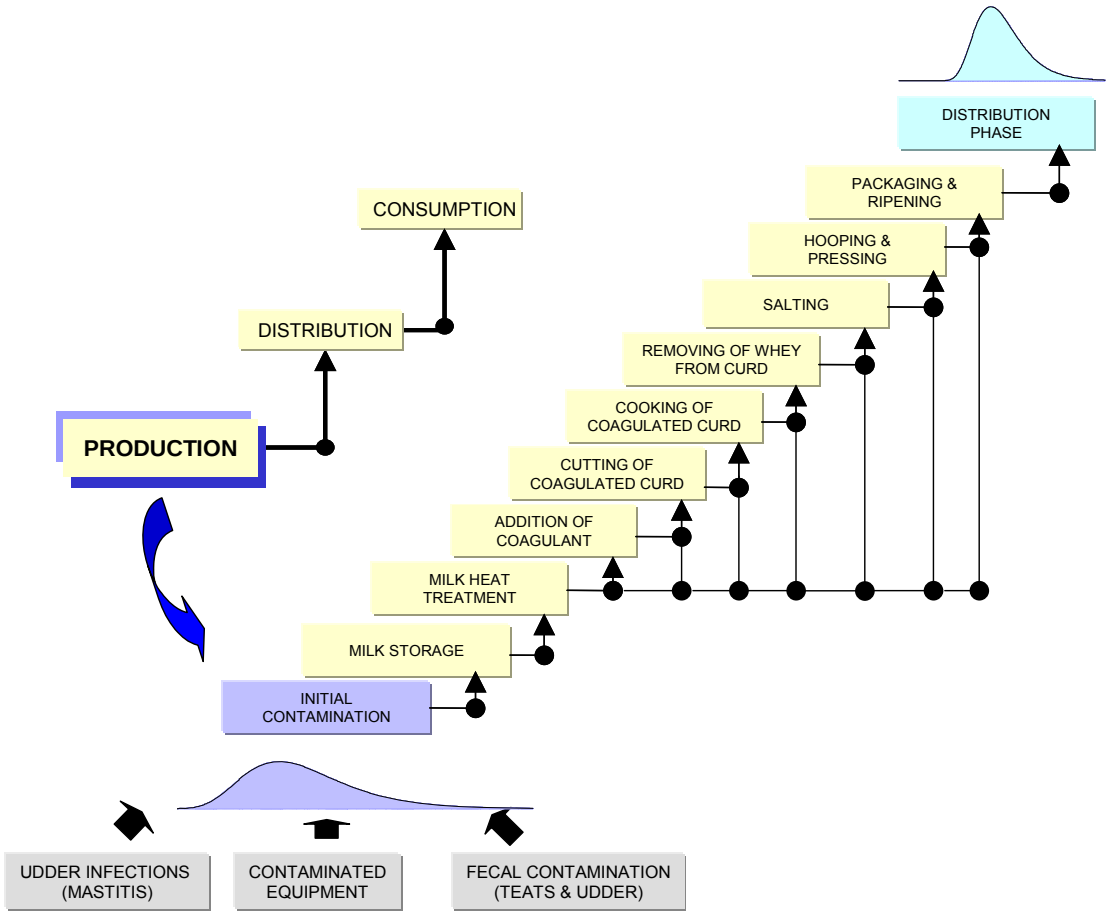


Figure 3.1: DML Model of Cheese Production Phase

The input to the production model is the initial contamination of *E. coli* O157:H7; this contamination may come from various sources such as fecal contamination of the teats and udder, udder infections (i.e., mastitis), or contaminated equipment. The contamination is propagated through the production phase, with the contamination level at each step dependent on the contamination at the previous step. In addition, the milk heat treatment step influences the contamination at all of the subsequent steps. The end result of the production phase is the level of *E. coli* O157:H7 contamination in 1 kilogram of cheese which serves as the input to the distribution phase.

3.3.1.2 Multiplicative Factor Approach

As previously stated, the DML model represents the conceptual model upon which the mathematical model is based. The mathematical predictive model used to propagate the contamination through the production phase is the Multiplicative Factor (MF). The MF is essentially a "multiplier" that allows the contamination to be propagated through the model. If a selection increases the contamination, the multiplier will be greater than 1; if a selection decreases the contamination, the multiplier will be between 0 and 1. These multipliers can be calculated by obtaining the contamination level at the input and output of the step from the experimental data in the literature. Figure 3.2 demonstrates how the MF is used to propagate the contamination at a particular step. The distribution of contamination before step "N" is multiplied by the MF in order to obtain the distribution of contamination after step "N".

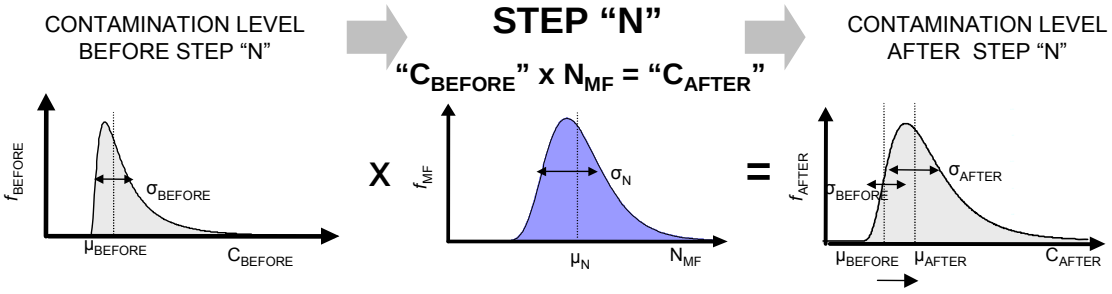


Figure 3.2: Multiplicative Factors Approach

In order to consider the uncertainty associated with the MFs, the MFs are also shown in the form of a distribution. The distribution of the MFs is assumed to be lognormal for several reasons. First, the lognormal distribution is often used to model bacterial survival and the MFs represent the survival of *E. coli* O157:H7 from one step to the next. In addition, the range of the multipliers can be from more than 0 to

infinity, depending on whether a particular option increases or decreases the contamination, and are positively skewed. Since the MF can vary by orders of magnitude, the lognormal distribution is a natural choice. Finally, the contamination at the end of the production phase is calculated by multiplying the initial contamination by the various MFs for each step. The Central Limit theorem shows that the product of a large number of probability distributions is lognormally distributed, therefore, it seems reasonable to assume the MFs are lognormally distributed (Vose, 2000).

Although the MFs are assumed to be lognormally distributed in the Bayesian analysis for describing the distribution of the MF, no prior knowledge of the parameters of the distribution is assumed. For each MF distribution, non-informative uniform prior distributions are assumed for both the mean and standard deviation. Using data from the literature, multipliers are calculated for each option from the level of contamination at the input and output of a step. These multipliers are the "observed" data and used as evidence for developing the likelihood function in the Bayesian updating process. The Bayesian updating results in posterior distributions of the mean and standard deviation of the MF distribution. Figure 3.3 illustrates this approach; the MF parameter distributions, and the data used to develop these distributions, are given in Appendix II.

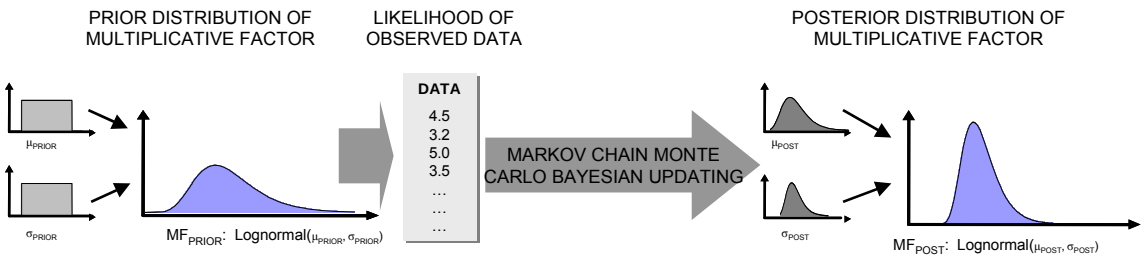


Figure 3.3: Bayesian Approach for Developing Multiplicative Factor Distribution

The Bayesian updating process illustrated in Figure 3.3 is accomplished using the WinBUGS (Bayesian Inference Using Gibbs Sampling) software, version 1.4.1. This software allows for the Bayesian analysis of complex statistical models using Markov Chain Monte Carlo (MCMC) methods. WinBUGS allows a model to be specified, and then updated with the observed data using MCMC methods. The final output is posterior distributions for the parameters of interest.

3.3.1.3 Production Phase Decomposition

Again, the production phase is reduced to a series of sub-system elements (i.e., steps), basic elements (i.e., physical conditions and/or manufacturing practices), and options (i.e., variations within the physical conditions and/or manufacturing practices) using the DML concept. MF distributions exist for the various combinations of options for the basic elements of a step. However, only one MF distribution is applied to each step, based on the options selected for that particular step. Thus, the DML decomposition aids in the identification of the selected MF distribution. The following sections discuss the basic elements and options for each step of the production phase. In addition, the MF distributions available for each step are identified.

3.3.1.3.1 Production Step A0: Initial Contamination

The input to the production model is the initial contamination of *E. coli* O157:H7, which may come from a variety of sources. The initial contamination is a variable in the form of the lognormal distribution, as the bacterial concentration is positively skewed in the range from 0 to infinity. Any mean and standard deviation of contamination may be used and is in the form of colony-forming units per milliliter (CFU/ml). This analyst-defined contamination level is assumed for a 1,000 L vat of milk, an amount representative of smaller scale cheese production (Bemrah et al., 1998). Thus, the remaining steps in the production phase influence the *E. coli* O157:H7 contamination in the entire vat of milk used to produce the cheese. Figure 3.4 illustrates the calculation for the initial *E. coli* O157:H7 contamination in a 1,000 L vat of milk using the basic elements for step A0.

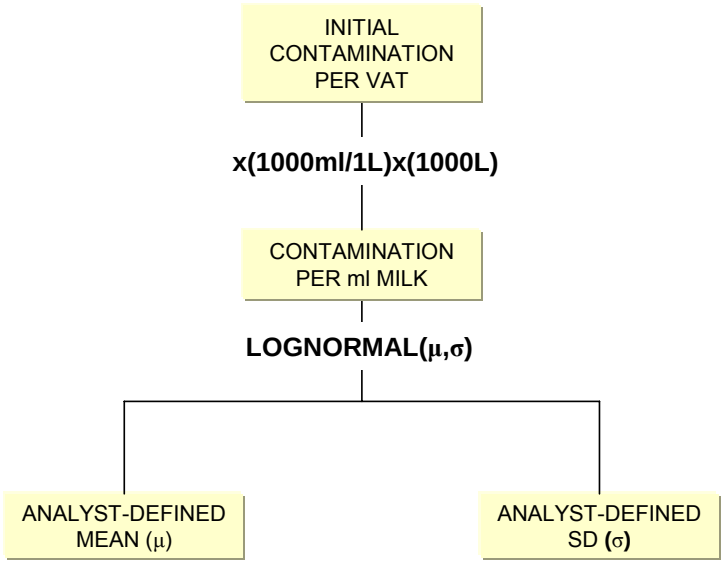


Figure 3.4: DML Representation of Step A0 (Initial Contamination) Calculation

3.3.1.3.2 Production Step A1: Milk Storage

Step A1 determines the level of *E. coli* O157:H7 contamination after milk storage. Time and temperature are identified as the two factors contributing to the growth or inactivation of the pathogen. Although the literature reveals that milk should be stored at less than 5ºC (Law, 1999), the PMO Revision 2001 states that milk should be maintained at 7ºC or less (USDA, 2001). Four temperature options are available for milk storage temperature: $T \leq 5$ºC, 5ºC < T < 8ºC, T = 8ºC, or T > 8ºC. Milk may be stored for several days prior to cheese-making (Law, 1999); Fox et al. (2000) state that raw milk may be stored on the farm for 3-4 days and stored an additional 1-2 days at the factory prior to use in cheese-making. In this analysis, five options are available for milk storage time: 1, 2, 3, 4, or 5 days. The various combinations of both milk storage time and temperature result in the development of 20 MF distributions. Figure 3.5 shows how the DML concept is applied to step A1 in order to model the variability.

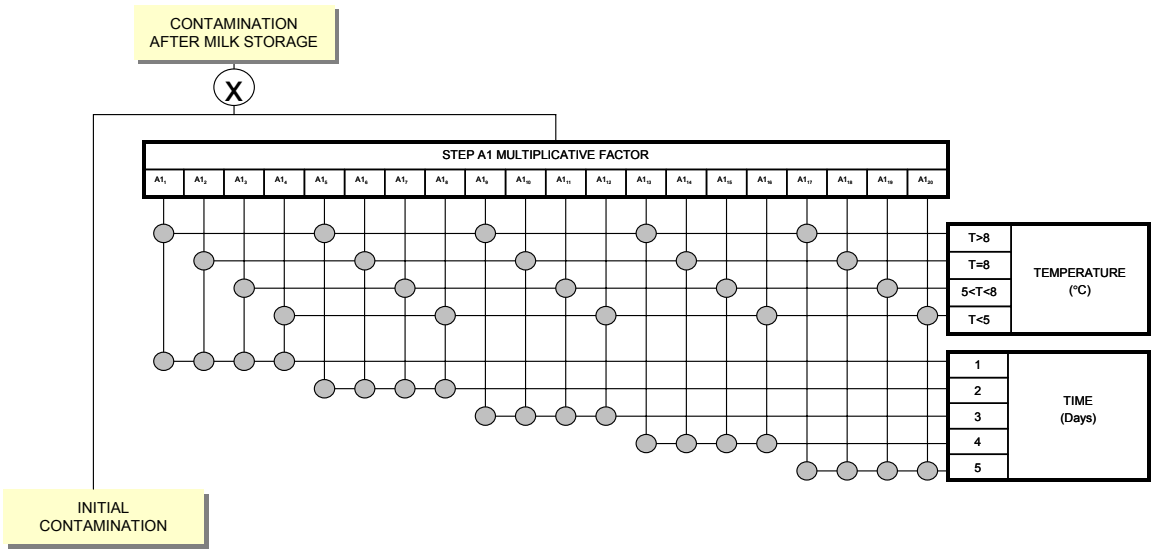


Figure 3.5: DML Decomposition of Production Step A1 (Milk Storage)

3.3.1.3.3 Production Step A2: Milk Heat Treatment

Step A2 determines the level of *E. coli* O157:H7 contamination after milk heat treatment. It should also be noted that the milk treatment step is an influencing factor in all the subsequent production steps, as shown in Figure 3.4. While a study by Wang et al. (1997) showed no significant difference in the survival and growth of *E. coli* O157:H7 in pasteurized milk, Marek et al. (2004) found that *E. coli* O157:H7 persisted longer in pasteurized whey versus unpasteurized whey, indicating that there might be a difference in *E. coli* O157:H7 survival in cheese made from pasteurized milk versus unpasteurized milk.

Three categories of heat treatment for cheese-milk are identified for step A2: 1) cheese made from raw milk (i.e., no heat treatment), 2) cheese made from thermalized, or sub-pasteurized milk, and 3) cheese made from pasteurized milk. For cheese made from raw milk, the milk heat treatment step has no influence on the level of *E. coli* O157:H7 contamination. For the thermalized milk option, the effect of time

and temperature are taken into account, so increasing the time at a particular temperature will decrease the multiplicative factor. The time used for thermalization is defined by the analyst, and temperature options range from 50-100ºC. In addition, the thermalized milk option may be used to account for an inadequate pasteurization process. Finally, the pasteurization of milk will have the most significant impact on the reduction of bacterial contamination. According to Fox et al. (2000), pasteurization is the single most important step in cheese-making in terms of reducing bacterial contamination, as it kills the majority of pathogens found in raw milk. Figure 3.6 illustrates the DML decomposition for step A2.

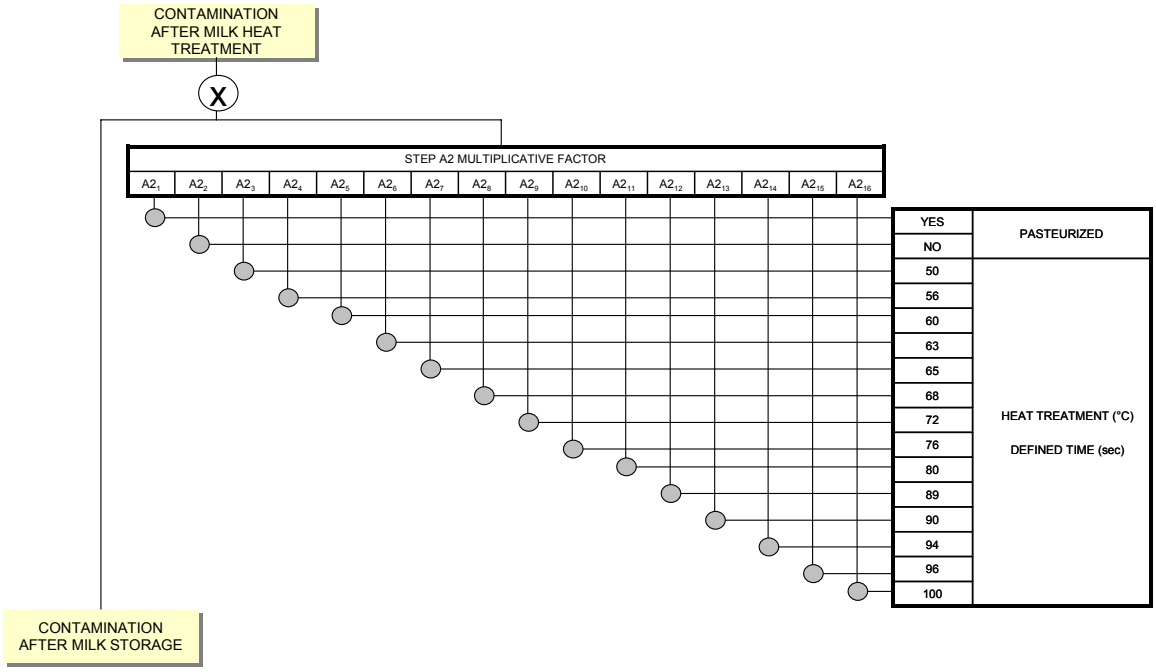


Figure 3.6: DML Decomposition of Production Step A2 (Milk Heat Treatment)

3.3.1.3.4 Production Step A3: Addition of Coagulant

Step A3 determines the level of *E. coli* O157:H7 contamination after the coagulant has been added to the milk. Dennis (2000) states that the more rapid the

development of acidity, the more rapid the death of *E. coli* O157:H7; starter cultures that are able to obtain a higher level of acidity appear to have more influence on the survival of *E. coli* O157:H7. Dennis (2000) identifies several mesophilic cultures as being more effective in controlling *E. coli* O157:H7 contamination. Therefore, step A3 considers the influence of mesophilic and thermophilic starter cultures. As stated previously, the influence of the milk heat treatment is also considered. Figure 3.7 shows the DML decomposition of these influencing factors for step A3.

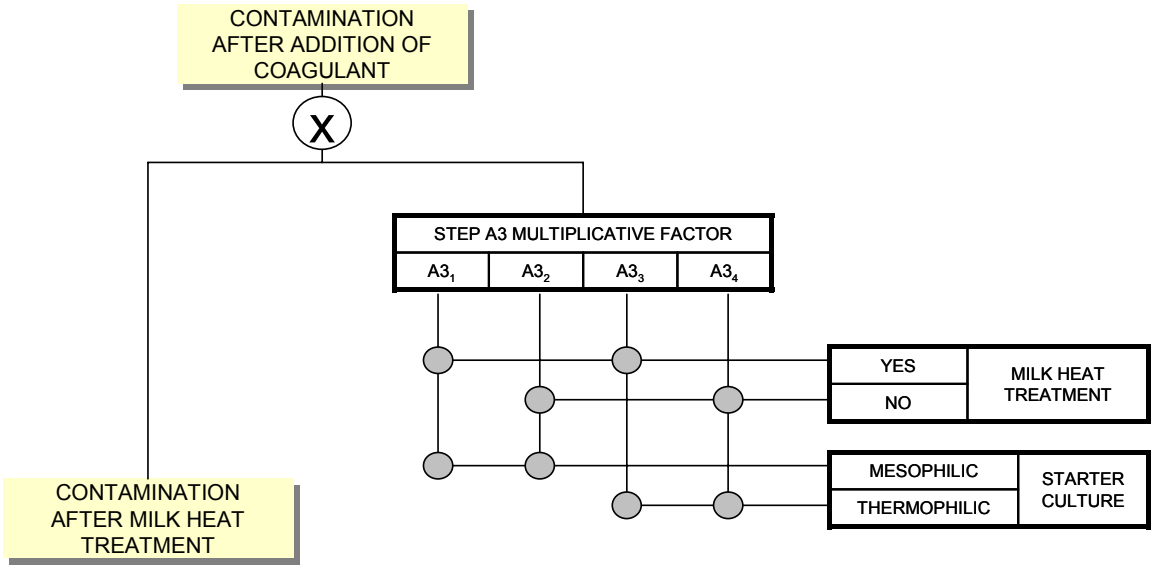


Figure 3.7: DML Decomposition of Production Step A3 (Addition of Coagulant)

3.3.1.3.5 Production Step A4: Cutting of Curd

Step A4 determines the level of *E. coli* O157:H7 contamination after the curd has been cut. No manufacturing variations have been identified at this step that would influence the level of contamination; therefore, the only influencing factor considered is the heat treatment of the milk. Figure 3.8 shows the DML decomposition for step A4.

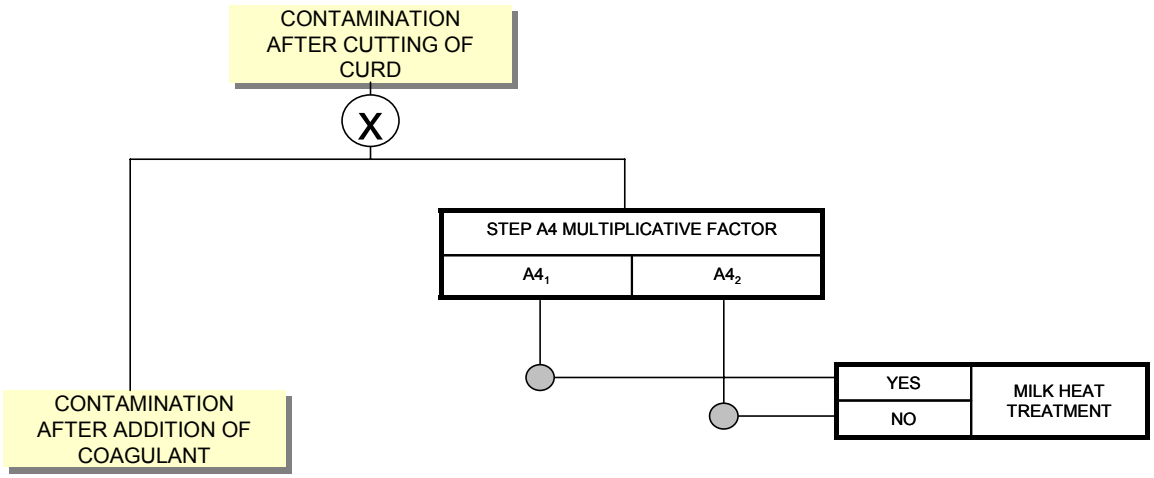


Figure 3.8: DML Decomposition of Production Step A4 (Cutting of Curd)

3.3.1.3.6 Production Step A5: Cooking of Curd

Step A5 determines the level of *E. coli* O157:H7 contamination after the curd has been cooked. The cooking temperature is dependent on the type of cheese being manufactured. Typically, softer cheeses are cooked at a lower temperature and harder cheeses are cooked at a higher temperature. Law (1999) identifies four cooking temperature ranges: $30^{\circ}C \leq T \leq 32^{\circ}C$, $33^{\circ}C \leq T \leq 35^{\circ}C$, $36^{\circ}C \leq T \leq 40^{\circ}C$, or $T > 40^{\circ}C$. Therefore, step A5 considers the influence of cooking temperature, with higher temperatures being more likely to thermally inactivate *E. coli* O157:H7. Again, the influence of the milk heat treatment is also considered. Figure 3.9 shows the DML decomposition of these influencing factors for step A5.

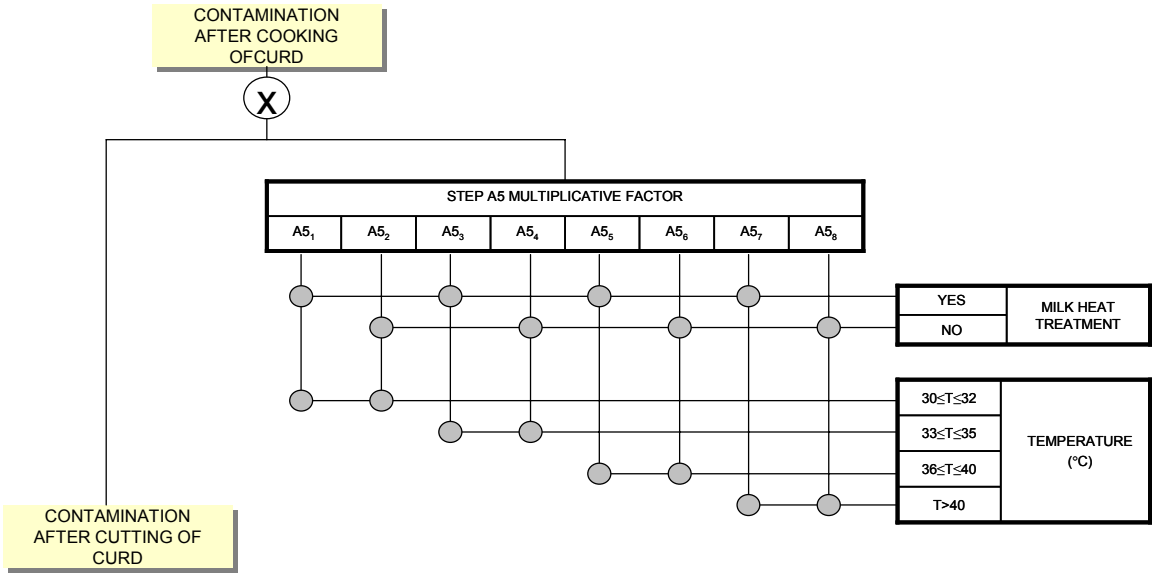


Figure 3.9: DML Decomposition of Production Step A5 (Cooking of Curd)

3.3.1.3.7 Production Step A6: Separation of Curd and Whey

Step A6 determines the level of *E. coli* O157:H7 contamination after the curd has been separated from the whey. No manufacturing variations have been identified at this step that would influence the contamination level; therefore, the only influencing factor considered is the heat treatment of the milk. While *E. coli* O157:H7 growth can occur during this step, it is also important to account for the percentage of bacteria remaining in the curd versus the bacteria transferred to the whey. Based on Bemrah et al. (1998), it is assumed that 90% of the bacteria resides in the curd and continues through the rest of the production phase; the remaining 10% of the bacteria is transferred to the whey. Figure 3.10 shows the DML decomposition for step A6, and accounts for 90% of the bacteria continuing through to the next step in production.

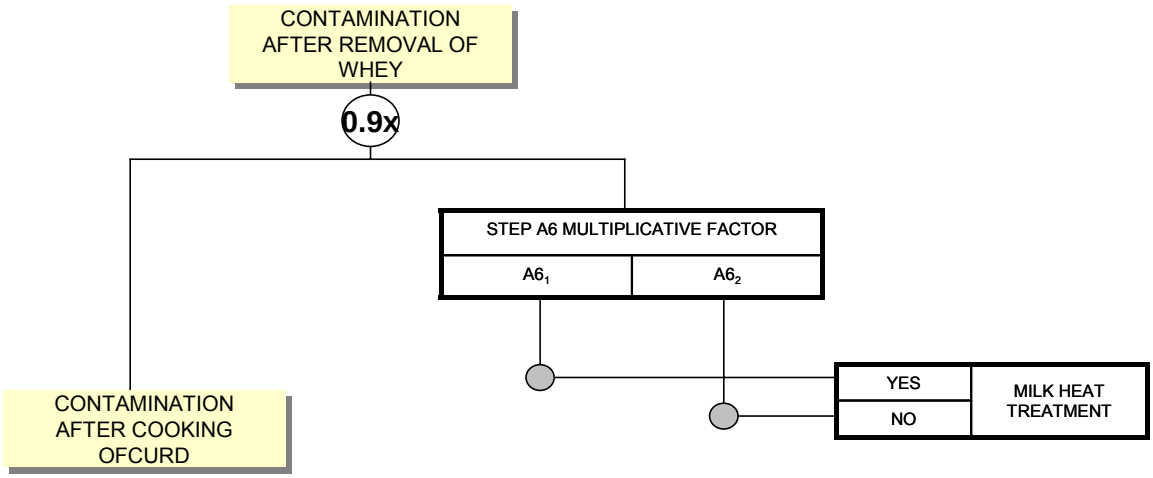


Figure 3.10: DML Decomposition of Production Step A6 (Separation of Curd and Whey)

3.3.1.3.8 Production Step A7: Salting

Step A7 determines the level of *E. coli* O157:H7 contamination after salting. The salting step can help control bacterial activity and the rate of ripening by suppressing the growth of some types of microorganisms (Davis, 1965). The type of salting varies depending on the type of cheese being manufactured. Two types of salting are considered in step A7: dry and brine. Therefore, step A7 considers the influence of salting on *E. coli* O157:H7 contamination in combination with milk heat treatment. Figure 3.11 shows the DML decomposition of these influencing factors for step A7.

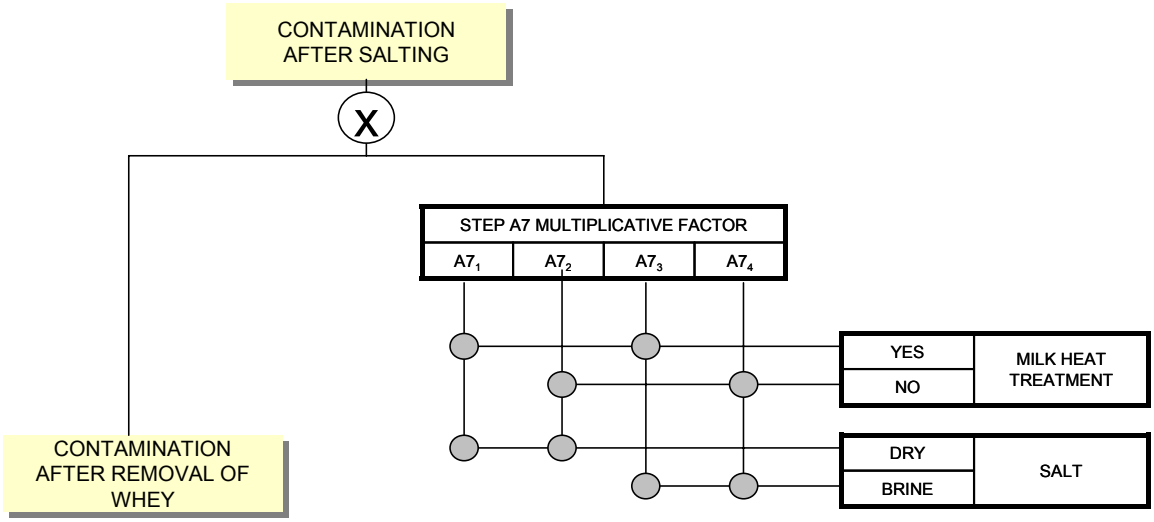


Figure 3.11: DML Decomposition of Production Step A7 (Salting)

3.3.1.3.9 Production Step A8: Hooping and Pressing

Step A8 determines the level of *E. coli* O157:H7 contamination after hooping and pressing. No manufacturing variations have been identified at this step that would influence the *E. coli* O157:H7 contamination level; therefore, the only influencing factor considered is the heat treatment of the milk. Figure 3.12 shows the DML decomposition for step A8.

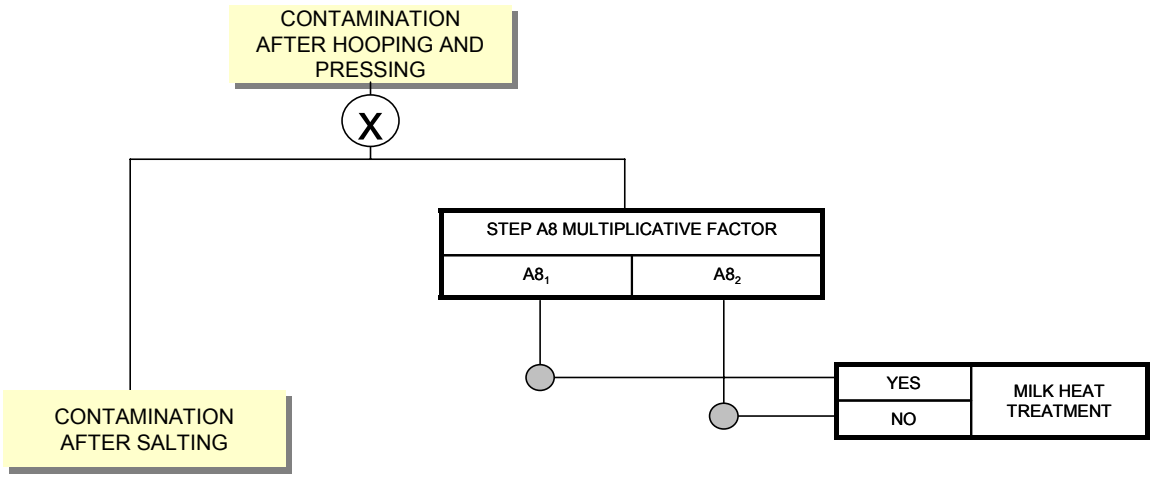


Figure 3.12: DML Decomposition of Production Step A8 (Hooping and Pressing)

3.3.1.3.10 Production Step A9: Packaging and Ripening

Step A9 determines the level of *E. coli* O157:H7 contamination after packaging and ripening. The previous steps have determined the level of *E. coli* O157:H7 contamination in the entire cheese vat; step A9 assumes that the vat is packaged into 1 kg portions of cheese. Several calculations are needed in order to determine the amount of cheese per 1,000 L vat of milk. The amount of cheese produced from a given amount of milk varies depending on the type of cheese, typically, it takes 8-15 units of milk to produce 1 unit of cheese (Battistotti et al., 1983). The 1,000 L vat of milk assumed at the start of the production phase should yield 67-125 kg of cheese; a uniform distribution is used to represent this variability. Thus, in order to determine the amount of contamination per kilogram cheese, the amount of contamination in the entire cheese vat is divided by the uniform distribution representing the amount of cheese produced from 1,000 L of milk.

Once the cheese is packaged into 1 kg portions, step A9 determines the level of contamination after ripening. Previously, it was assumed that any pathogenic microorganisms surviving the cheese-making process would die during cheese ripening, resulting in the PMO Revision 2001 stipulation that raw milk cheese must be ripened for at least 60 days. However, numerous studies have shown that *E. coli* O157:H7 can survive the ripening period (Hudson et al., 1997; Maher et al., 2001; Reitsma et al., 1996; Teo et al., 2000). Time has been identified as the main influencing factor on the survival of *E. coli* O157:H7 during the ripening period. The ripening time is dependent on the type of cheese being manufactured, and may vary from a few weeks to more than two years; typically, the duration of ripening is inversely related to the moisture content of the cheese (Fox, 1993). From the literature, a number of different ripening times have been identified for step A9: 14, 27, 45, 75, 90, 104, and 150 days. Therefore, step A9 considers the influence of ripening time, in combination with milk treatment, with longer ripening times resulting in a more significant decrease in *E. coli* O157:H7 contamination. Figure 3.13 shows the DML decomposition of these influencing factors for step A9.

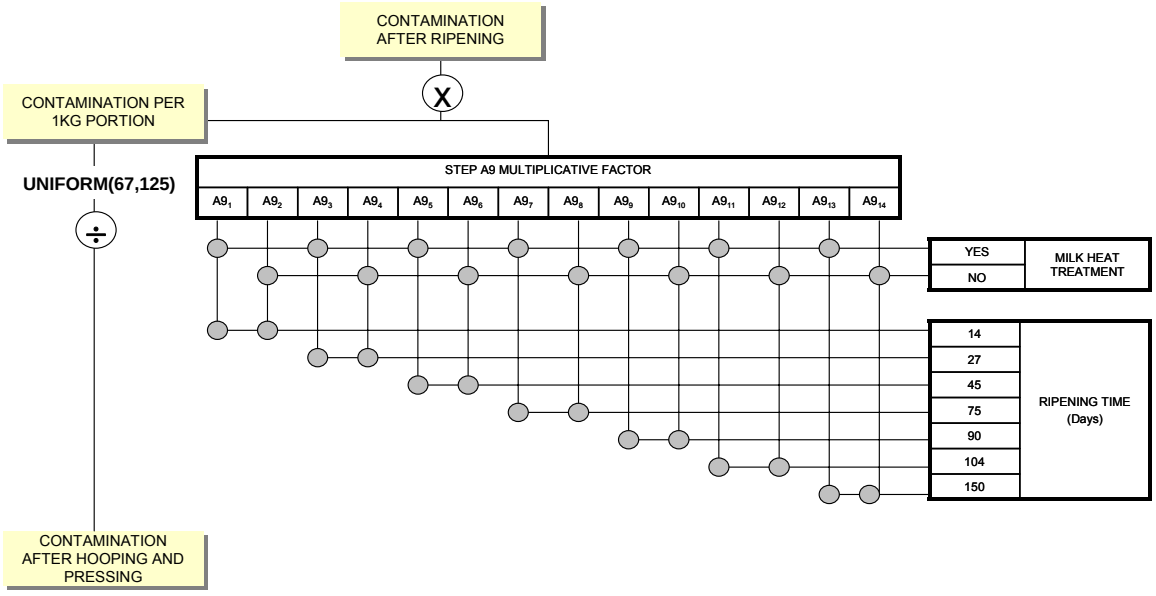


Figure 3.13: DML Decomposition of Production Step A9 (Packaging and Ripening)

3.3.1.4 Production Calculation Summary

After entering the initial *E. coli* O157:H7 contamination, this contamination is propagated through the production phase. The contamination is increased or decreased by the multiplicative factor for each step; the multiplicative factor varies based on the options selected for the basic elements of that step. The end result of the production phase is an estimation of *E. coli* O157:H7 contamination in 1 kg of cheese; this level of contamination is also used as the initial contamination in the distribution phase. A summary of the production phase calculations is given in Table 3.3.

Table 3.3: Production Phase Calculations

Step	Description	Distribution/Model	Calculation	Unit
A0	Initial *E. coli* O157:H7 Contamination (CFU/ml)	Lognormal[a]	Lognormal(μ,σ)*(1000ml/1L)*1000L	CFU/vat
A1	Contamination after Milk Storage	MF A1*i*[b] (*i* = 1-20)	A0*(A1*i*)	CFU/vat
A2	Contamination after Milk Heat Treatment	MF A2*i* (*i* = 1-16)	A1*(A2*i*)	CFU/vat
A3	Contamination after Addition of Coagulant	MF A3*i* (*i* = 1-4)	A2*(A3*i*)	CFU/vat
A4	Contamination after Cutting of Curd	MF A4*i* (*i* = 1-2)	A3*(A4*i*)	CFU/vat
A5	Contamination after Cooking of Curd	MF A5*i* (*i* = 1-8)	A4*(A5*i*)	CFU/vat
A6	Contamination after Separation of Curd and Whey	MF A6*i* (*i* = 1-2)	0.9[c]*A5*(A6*i*)	CFU/vat
A7	Contamination after Salting	MF A7*i* (*i* = 1-4)	A6*(A7*i*)	CFU/vat
A8	Contamination after Hooping and Pressing	MF A8*i* (*i* = 1-2)	A7*(A8*i*)	CFU/vat
A9	Contamination after Packaging and Ripening	MF A9*i* (*i* = 1-14)	Uniform(67,125)[d]*A8*(A9*i*)	CFU/kg

[a]Analyst-defined mean and standard deviation
[b]Multiplicative Factor model for step A1; the MF used is based on user selections, with 20 options available for step A1
[c]Multiplication by 0.9 accounts for 90% of bacteria being transferred to curd
[d]Uniform distribution accounts for variability in amount of cheese produced from 1,000 L milk

3.3.2 Distribution

3.3.2.1 Distribution Overview

The distribution phase begins after cheese ripening and uses the distribution of *E. coli* O157:H7 contamination after cheese ripening as the input (i.e., step A9). The distribution phase identifies the steps (i.e., sub-system elements) along the path from cheese production to the end consumer. In addition, the mechanisms (i.e., the basic elements) affecting growth of *E. coli* O157:H7 contamination at each step are identified as well, with these basic elements being further reduced into options. The significant steps that affect the growth of *E. coli* O157:H7 in the distribution phase are identified as: storage before transportation, transportation to retail, retail storage, transportation to consumers, and consumer storage. Figure 3.14 shows the sub-system decomposition developed with the DML approach.

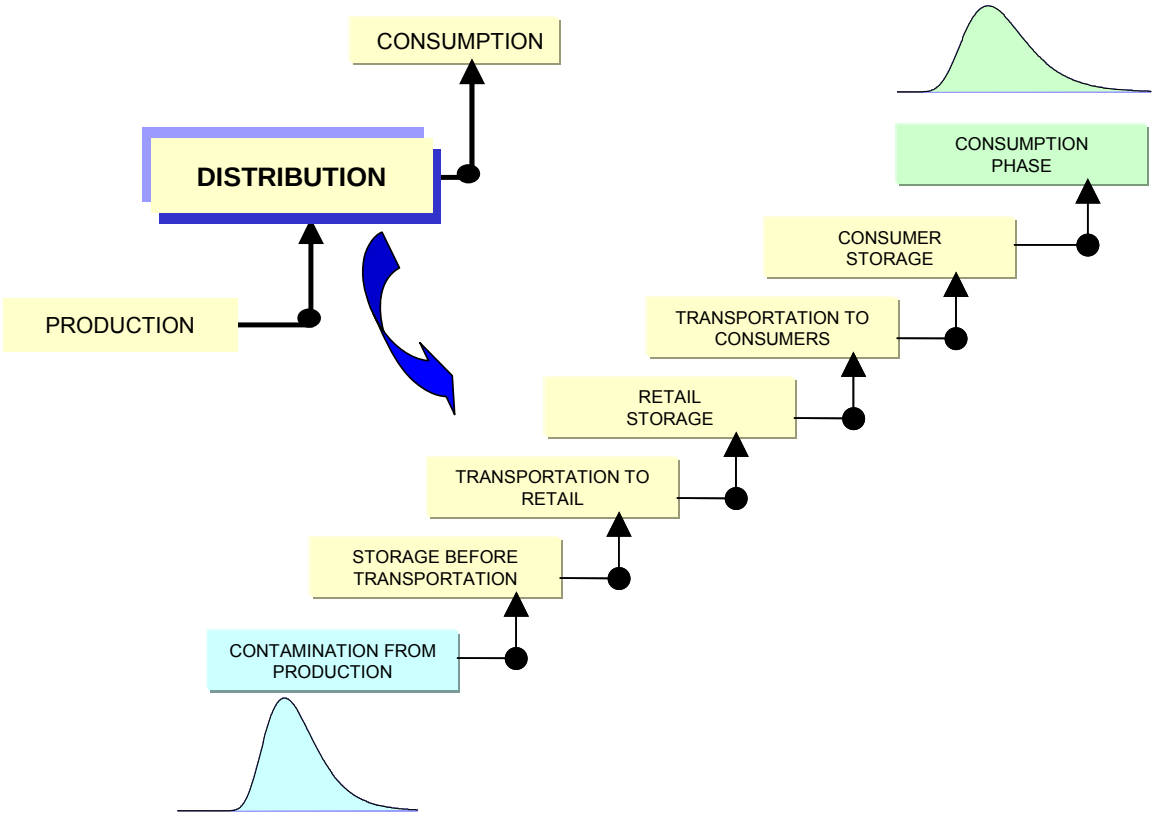


Figure 3.14: DML Model of Cheese Distribution Phase

Using the distribution of *E. coli* O157:H7 contamination from the production phase as the input, the distribution phase accounts for the growth of microorganisms between the time of production and the time of consumption. Loss of temperature control as the cheese is being transported and stored may result in microbial growth. The amount of bacterial growth is dependent on the nature of the cheese, with pH, sodium chloride concentration, and water activity being the most influential. In addition, the behavior of the organism is also influenced by conditions such as the temperature and length of storage time. The end result of the distribution phase is the distribution of contamination in 1 kg cheese, accounting for the increase or decrease

in contamination along the distribution pathway. This distribution is then used as the input to the consumption phase.

3.3.2.2 Gompertz Model Approach

Several mathematical models have been proposed in the literature to represent the dynamic growth behavior of microorganisms in food, including the Gompertz, Baranyi, logistic, and exponential (Buchanan et al., 1997). The literature search reveals a number of experiments in which growth curves of *E. coli* O157:H7 are successfully fit to the Gompertz equation. These experiments use the Gompertz equation to describe the effect of a number of different variables, such as temperature, pH, sodium chloride concentration, and water activity on the growth of *E. coli* O157:H7 (Buchanan et al., 1993; Duffy et al., 1999; Sutherland et al., 1995). Due to its wide acceptance in the literature and the availability of data to define the Gompertz equation parameters, the Gompertz model is selected to describe the growth of *E. coli* O157:H7 during the distribution phase.

The Gompertz equation is a commonly used mathematical model that predicts the log increase in microorganism concentration at a constant temperature. The growth curve is sigmoidal with two shoulders and a period of exponential growth, with the shape of the curve controlled by three parameters: B, M, and C. Table 3.4 gives the Gompertz equation, defines the Gompertz parameters, and derives the growth kinetics (Rajkowski and Marmer, 1995).

Table 3.4: Gompertz Equation and Parameters

The Gompertz Equation:

$L(t) = A + C * \exp[-\exp(-B (t - M))]$

Where:

L(t) = log count of bacteria (log CFU/ml) at time (t) (in hours);
A = asymptotic log count of initial bacteria as time decreases indefinitely, (log CFU/ml);
C = asymptotic amount of bacteria growth that occurs as T increases (number of log cycles of growth (log CFU/ml));
B = relative growth rate at M, [log (CFU/ml)/h], where
M = the time at which the absolute growth rate is maximal (h)

Derived growth kinetic values:

Name	Definition	Value	Unit
Exponential Growth Rate (EGR)	The time cells divide at a constant rate	BC/2.71818	[log (CFU/ml)]/h
Generation Time (GT)	The time cells take to double in number	[(log 2)*2.71818]/BC	hours
Lag Phase Duration (LPD)	The time before cells start to grow at a constant rate	(M - 1)/B	hours
Maximum Population Density (MPD)	The final count at the end of growth study	A + C	[log (CFU/ml)]/h
Time one-thousand (T_{1000})	The time to obtain a 3-log increase in cell numbers	10.1155GT + LPD	hours

Based on the data obtained from the literature, distributions for the Gompertz equation parameters B, M, and C are estimated using a Bayesian approach similar to the one described for the multiplicative factors. Again, a lognormal distribution is assumed for each of the Gompertz parameters (i.e., B, M, and C), as these parameters describe bacterial survival. However, no prior knowledge of the parameters (i.e., mean and standard deviation) of the lognormal distribution describing the Gompertz parameters is assumed; therefore, uniform prior distributions are assumed for both the mean and the standard deviation. Data for B, M, and C are obtained from the literature, and this data serves as the likelihood in the Bayesian updating process. The Bayesian updating results in posterior distributions of the mean and standard deviation of the Gompertz parameters, thereby addressing the parameter uncertainty of the distributions describing B, M, and C. The parameter distributions for B, M, and C, and the data used to develop these distributions, are given in Appendix III.

For each of the steps in the distribution phase, the DML concept is used to identify the physical conditions (i.e., basic elements) that affect the growth or

inactivation of *E. coli* O157:H7. In this research, temperature and pH are presumed to be the determining factors in the magnitude of microbial growth, and the distributions of the Gompertz parameters are developed for the various combinations of temperature and pH. Sodium chloride concentration has also been identified as a factor that affects *E. coli* O157:H7 growth (Buchanan and Klawitter, 1992; Sutherland et al., 1995); however, this factor is not considered in this research as there is insufficient data to develop distributions for the Gompertz parameters based combinations of temperature, pH, and sodium chloride concentration.

In addition, the DML concept is used to identify the various temperature and pH options that might be observed during distribution. A number of different temperatures options are available at each of the steps in the distribution phase; these temperature options allow both proper cheese storage and severe temperature abuse to be considered. The temperature options available for the steps in the distribution phase are: 5, 8, 10, 12, 19, 28, 37, and 42ºC. A number of different pH options are available as well in order to account for the variation in pH among cheeses (USDA, 2003). The pH options available in the distribution phase are: 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, and 8.5. Although the pH of cheese is dynamic during the ripening phase, it is assumed that once the cheese enters the distribution phase, the pH remains constant. Therefore, the pH selection is made only in the first step of the distribution phase (i.e., storage before transportation step). Figure 3.15 illustrates how each of the Gompertz parameters are represented by a distribution based on a specified pH and temperature; the initial bacterial count is also represented by a distribution. The end result is a distribution of the final bacterial count at the end of the step.

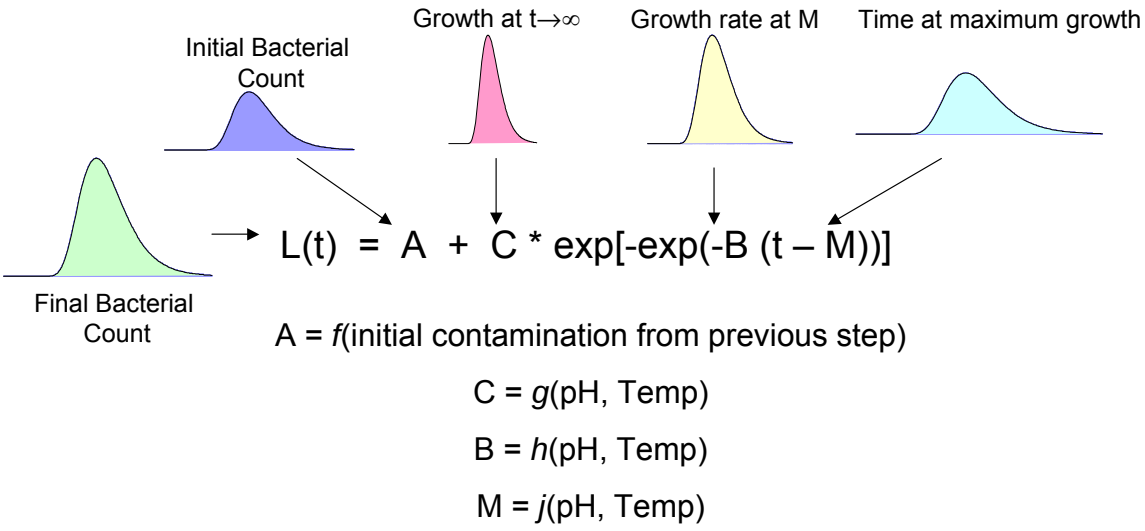


Figure 3.15: Dynamic Growth Represented by Gompertz Equation

3.3.2.3 Distribution Phase Decomposition

The distribution phase resembles the production phase in that the phase is reduced to a series of sub-system elements (i.e., steps), basic elements (i.e., physical conditions), and options (i.e., variations within the physical conditions) using the DML concept. In the distribution phase, temperature and pH have been identified as the basic elements for each step. Based on the pH and temperature selection for a step, a distribution exists for each of the Gompertz equation parameters. Therefore, based on the distribution of the *E. coli* O157:H7 contamination from the previous step, the distributions for the Gompertz parameters (determined by the pH and temperature selections), and a uniform distribution for time, the final distribution of *E. coli* O157:H7 contamination for a particular step is calculated. The following sections discuss each of the distribution steps in detail and demonstrate how the DML concept is applied to the Gompertz equation.

3.3.2.3.1 Distribution Step B1: Storage Before Transportation

Step B1 describes the level of *E. coli* O157:H7 contamination after storage, before transportation to retail. The level of contamination after step A9 (i.e., the contamination after cheese ripening in the production phase) is the initial distribution of *E. coli* O157:H7 contamination for step B1. In this step, the pH of the cheese is selected, as is the storage temperature of the cheese. Based on the options for pH and temperature, there are 72 pH/temperature combinations. Figure 3.16 shows a simplified example of the pH/temperature combinations identified with the DML concept for parameter B for step B1; a distribution exists for each of these pH/temperature combinations. In addition, distributions exist for these pH/temperature combinations for parameters M and C.

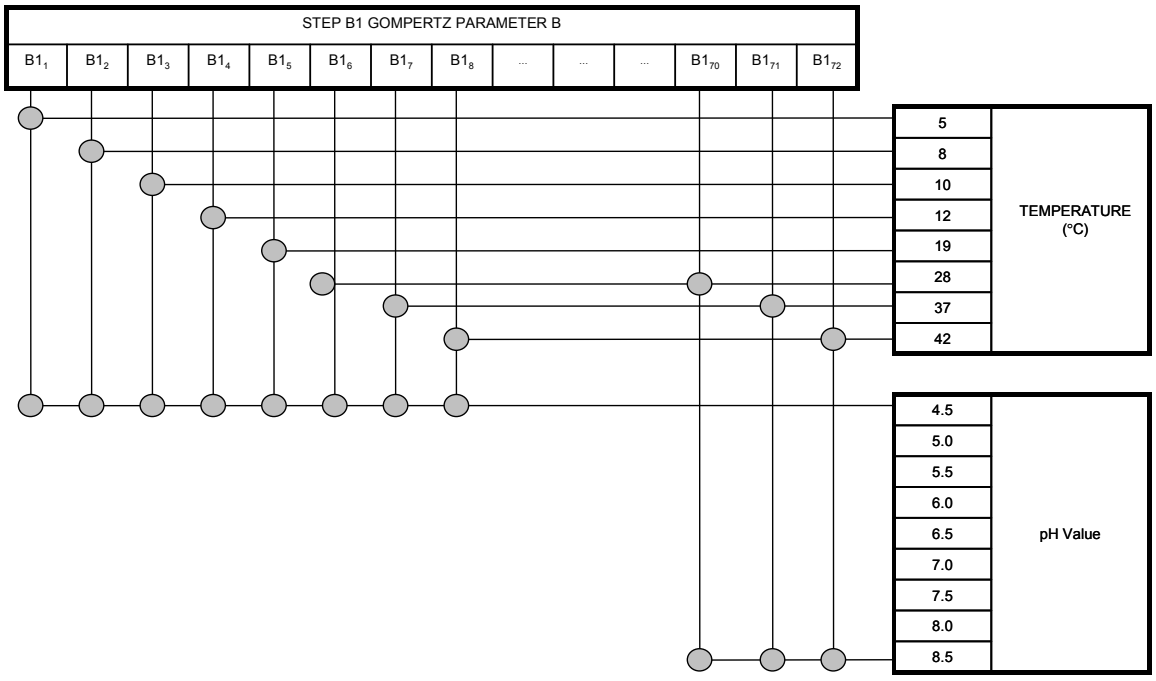


Figure 3.16: Example of Possible pH/temperature Combinations for Gompertz Parameters

Figure 3.17 shows how the DML concept is applied to step B1 using the Gompertz equation. The contamination after the production phase represents the initial bacterial count, A, in the Gompertz equation. This is added to the remainder of the equation which includes the parameters B, M, and C, as well as the time. A selection is made for pH and temperature, and the distributions for B, M, and C are all based on these selections, with 72 available pH/temperature combinations for each parameter; the time is represented by a uniform distribution. The end result is the distribution of *E. coli* O157:H7 contamination after storage, before transportation to retail. It should be noted that the pH value selected in step B1 is used as the pH value for all the remaining steps in the distribution phase.

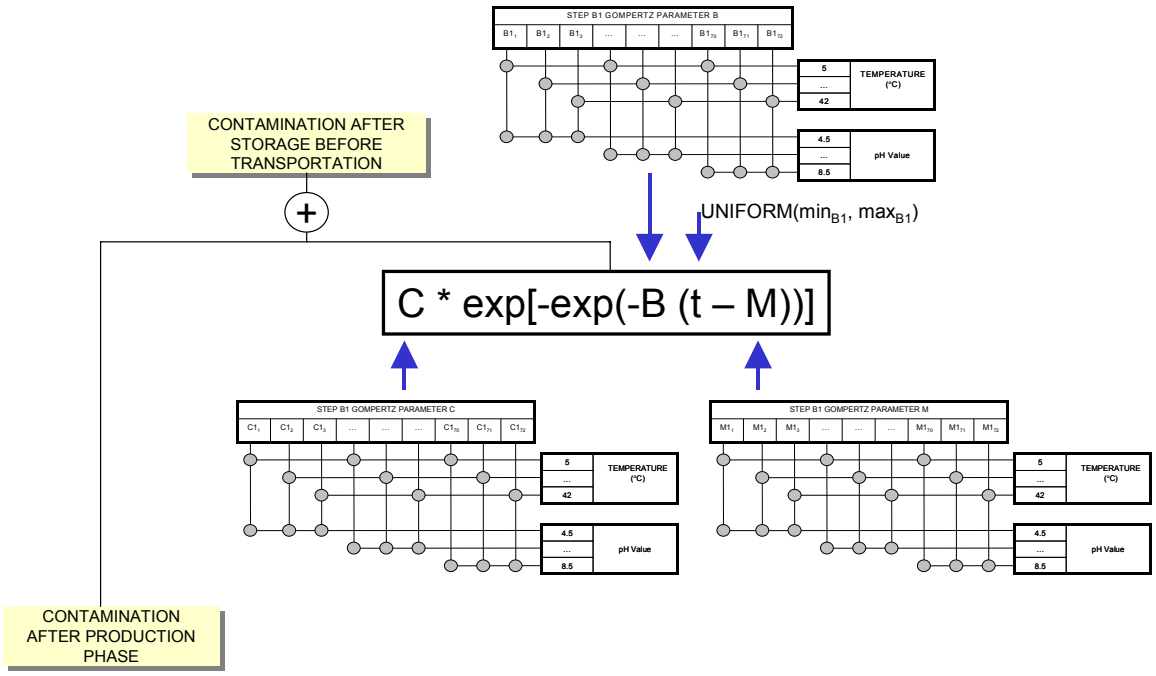


Figure 3.17: DML Decomposition of Distribution Step B1 (Storage Before Transportation)

3.3.2.3.2 Distribution Step B2: Transportation to Retail

Step B2 describes the level of *E. coli* O157:H7 contamination after transportation to retail. The level of *E. coli* O157:H7 contamination after step B1 represents the initial distribution of *E. coli* O157:H7 contamination for step B2 (i.e., parameter A in the Gompertz equation). In this step, only the temperature of the cheese during transportation to retail is selected; the pH value for step B2 remains the same as the value used in step B1. The time is represented as a uniform distribution. The DML representation of the basic elements (i.e., options) for step B2 is shown in Figure 3.18.

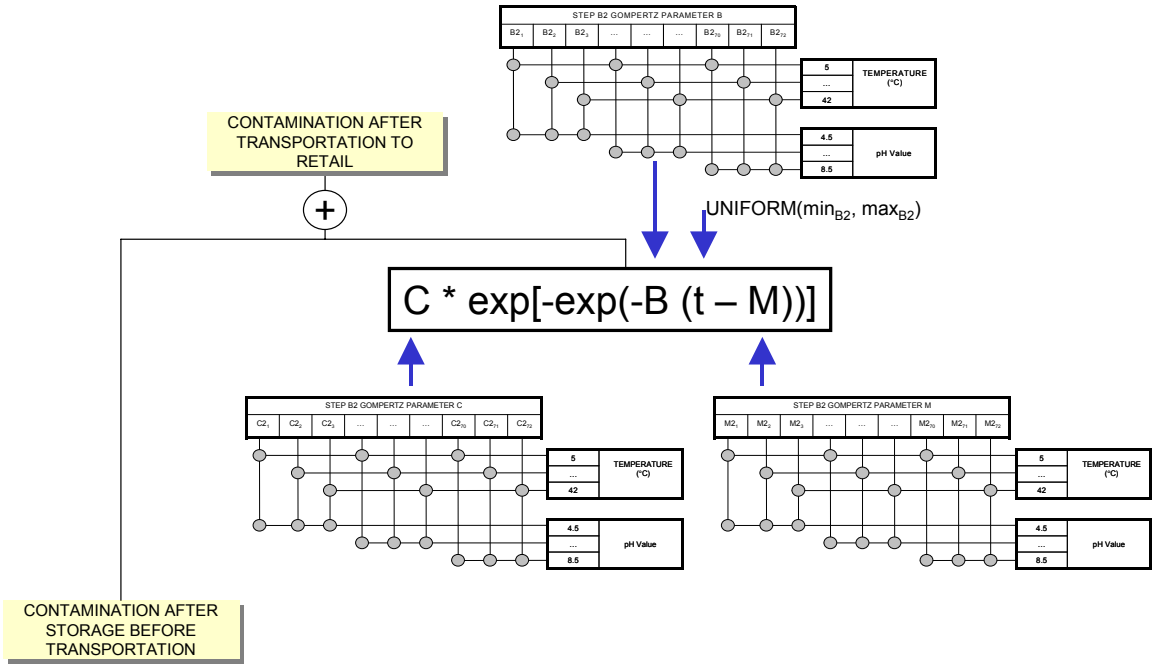


Figure 3.18: DML Decomposition of Distribution Step B2 (Transportation to Retail)

3.3.2.3.3 Distribution Step B3: Retail Storage

Step B3 describes the level of *E. coli* O157:H7 contamination after retail storage. The level of *E. coli* O157:H7 contamination after step B2 represents the

initial distribution of *E. coli* O157:H7 contamination for step B3. In this step, only the temperature of the cheese during retail storage is selected; the pH value for step B3 remains the same as the value used in step B1. The time is represented by a uniform distribution. The DML representation of the basic elements for step B3 is shown in Figure 3.19.

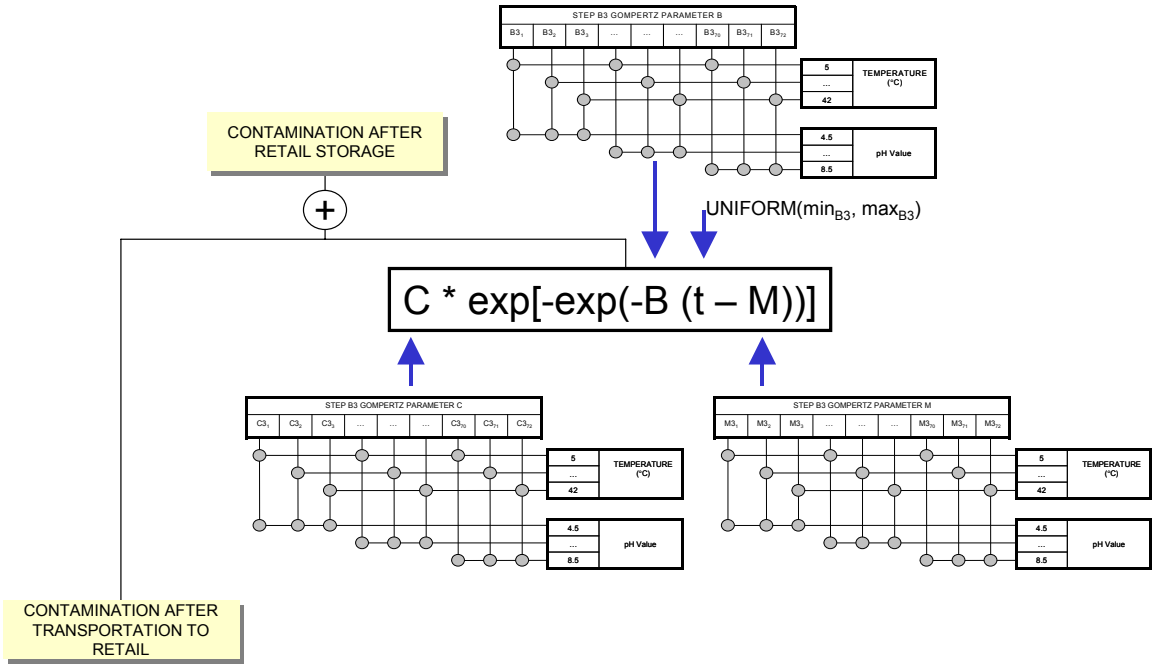


Figure 3.19: DML Decomposition of Distribution Step B3 (Retail Storage)

3.3.2.3.4 Distribution Step B4: Transportation to Consumers

Step B4 describes the level of *E. coli* O157:H7 contamination after transportation to consumers. The level of *E. coli* O157:H7 contamination after step B3 represents the initial distribution of *E. coli* O157:H7 contamination for step B4. Again, only the temperature of the cheese during transportation to consumers is selected, the pH value for step B4 remains the same as the value used in step B1. The

time is represented by a uniform distribution. The DML representation of the basic elements for step B4 is shown in Figure 3.20.

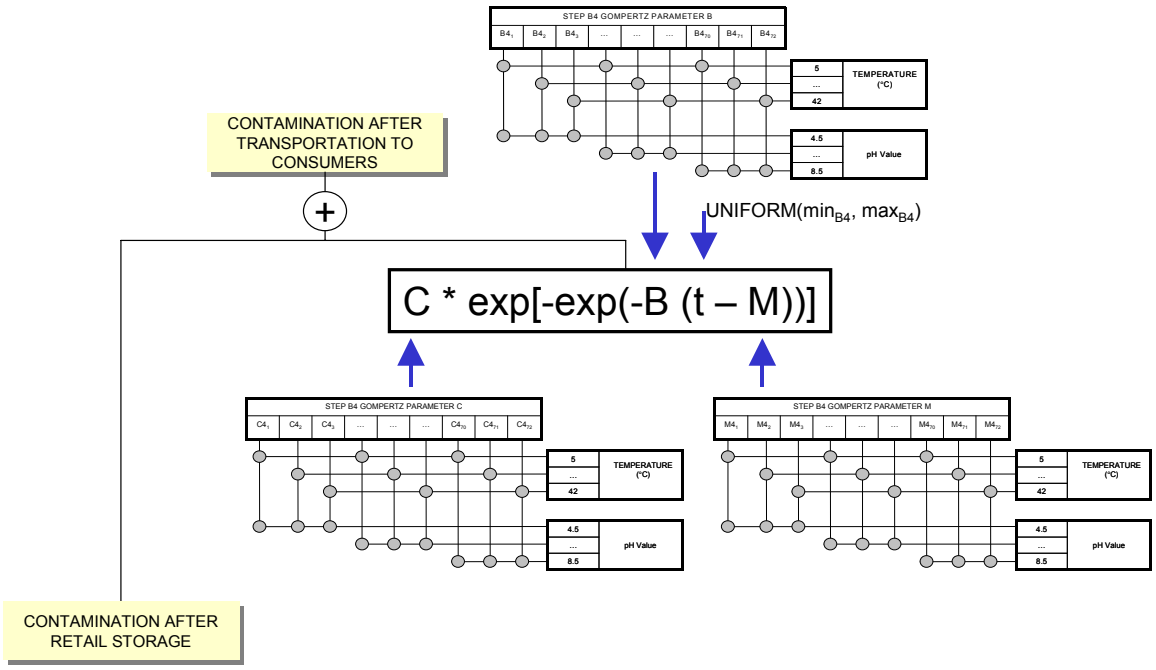


Figure 3.20: DML Decomposition of Distribution Step B4 (Transportation to Consumers)

3.3.2.3.5 Distribution Step B5: Consumer Storage

Finally, step B5 describes the level of *E. coli* O157:H7 contamination after consumer storage. The level of *E. coli* O157:H7 contamination after step B4 represents the initial distribution of *E. coli* O157:H7 contamination for step B5. The temperature of the cheese during consumer storage is selected, with the pH value for step B5 being the same as the value used in step B1. The time is represented by a uniform distribution. The DML representation of the basic elements for step B5 is shown in Figure 3.21.

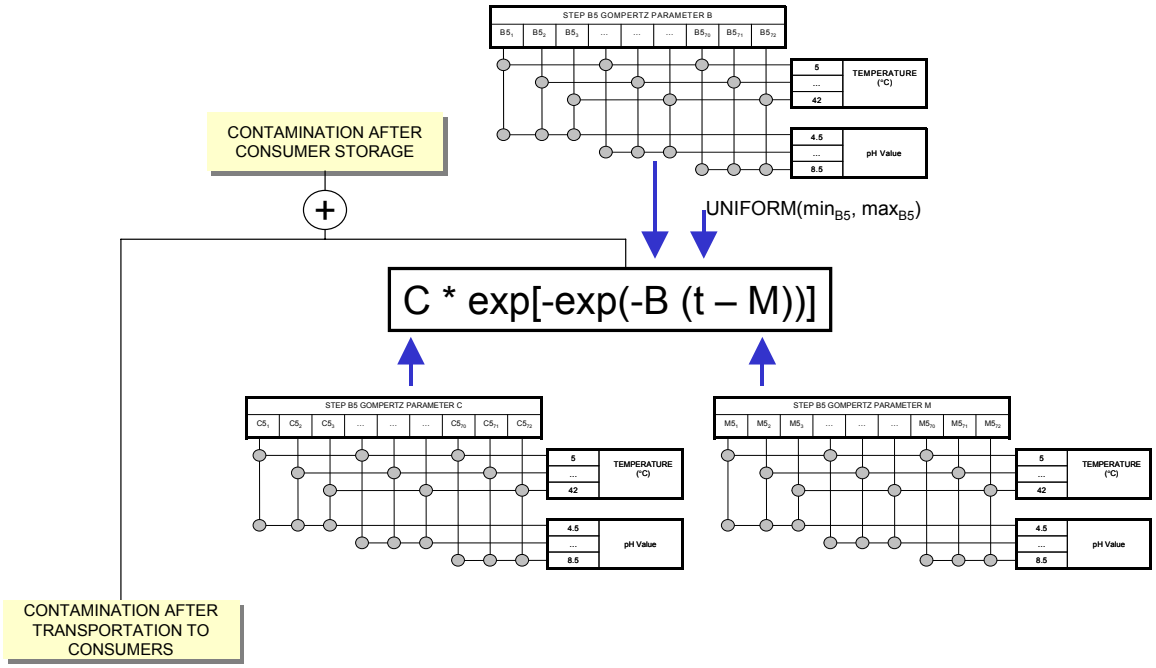


Figure 3.21: DML Decomposition of Distribution Step B5 (Consumer Storage)

3.3.2.4 Distribution Calculation Summary

The distribution phase uses the distribution of *E. coli* O157:H7 contamination after cheese ripening (i.e., step A9) as the initial contamination for the phase. The level of contamination is calculated at each step of the distribution phase using the Gompertz equation. The distributions for the Gompertz parameters are determined by the pH/temperature selection for the step, with pH remaining constant after the initial selection is made in step B1, the initial contamination for each step is the distribution of contamination from the previous step, and time is entered as a user-defined uniform distribution. The end result of the distribution phase is an estimation of *E. coli* O157:H7 contamination in 1 kg of cheese. A summary of the distribution phase calculations is given in Table 3.5.

Table 3.5: Distribution Phase Calculations

Step	Description	Distribution/Model	Calculation	Unit
B1	Contamination after Storage, before Transportation	Gompertz	$A9 + C_{B1} \cdot \exp[-\exp(-B_{B1}(t_{B1}-M_{B1}))]$ [a]	CFU/kg
B2	Contamination after Transportation to Retail	Gompertz	$B1 + C_{B2} \cdot \exp[-\exp(-B_{B2}(t_{B2}-M_{B2}))]$ [b]	CFU/kg
B3	Contamination after Retail Storage	Gompertz	$B2 + C_{B3} \cdot \exp[-\exp(-B_{B3}(t_{B3}-M_{B3}))]$	CFU/kg
B4	Contamination after Transportation to Consumer	Gompertz	$B3 + C_{B4} \cdot \exp[-\exp(-B_{B4}(t_{B4}-M_{B4}))]$	CFU/kg
B5	Contamination after Consumer Storage	Gompertz	$B4 + C_{B5} \cdot \exp[-\exp(-B_{B5}(t_{B5}-M_{B5}))]$	CFU/kg

[a] C_{B1}, B_{B1}, and M_{B1} are lognormal distributions based on pH and temperature selections for Step B1; t_{B1} is a user-defined uniform distribution for Step B1

[b] Parameters for remaining steps are lognormal distributions based on pH selected in Step B1 and temperature based on selection for given step; time is a user-defined uniform distribution for given step

3.3.3 Consumption

3.3.3.1 Consumption Overview

In order to estimate the amount of *E. coli* O157:H7 ingested by the consumer, a number of steps (i.e., sub-system elements) are identified in the consumption phase. The distribution of *E. coli* O157:H7 in cheese after the distribution phase is used as an input to the consumption phase. The dose ingested by the consumer is calculated as a function of the amount of *E. coli* O157:H7 in a serving of cheese and the number of servings of cheese ingested. The distribution of dose then becomes an input to the dose-response assessment in the risk characterization portion of the model. The DML decomposition of the consumption sub-system elements is shown in Figure 3.22.

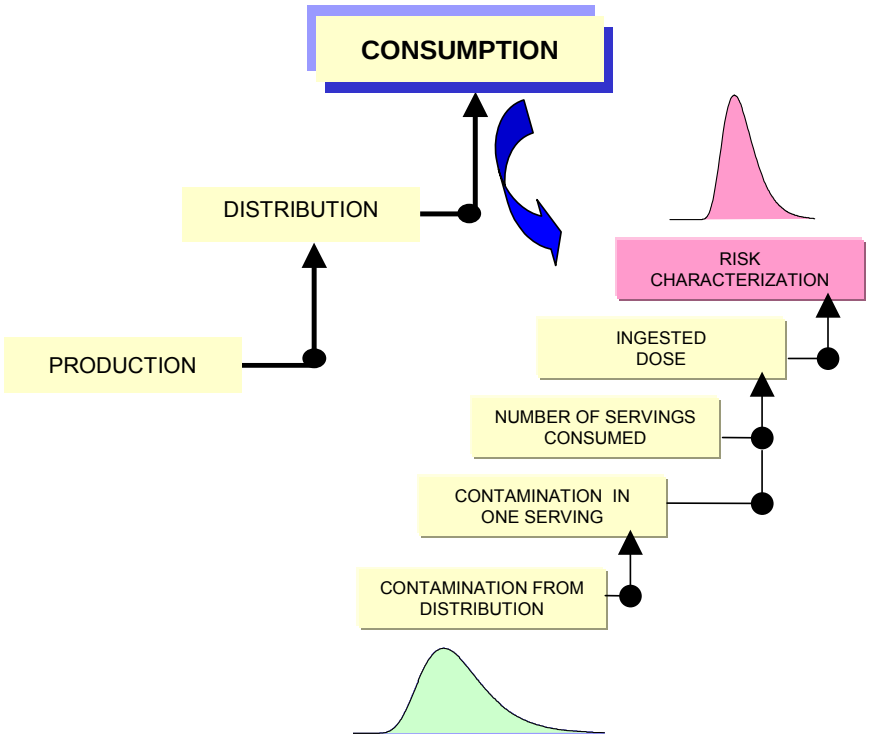


Figure 3.22: DML Model of Cheese Consumption Phase

3.3.3.2 Consumption Phase Decomposition

The consumption phase is further refined into sub-system elements, basic elements, and options using the DML concept. A number of calculations are made during the consumption phase in order to determine the amount of *E. coli* O157:H7 ingested by the consumer. The following sections provide a detailed discussion of each of the steps identified in the consumption phase, as well as the DML decomposition of the step.

3.3.3.2.1 Consumption Step C1: Contamination in One Serving

The input to the consumption model is the distribution of *E. coli* O157:H7 contamination after the distribution phase (i.e., step B5); the contamination is given for a 1 kilogram portion of cheese. Step C1 determines the level of *E. coli* O157:H7

per serving of cheese, assuming that a serving size is 1 ounce. Thus, the contamination per serving is determined by dividing the contamination in 1 kilogram of cheese by the number of ounces in a kilogram (35.274 ounces/kg). Figure 3.23 illustrates this calculation using the DML concept.

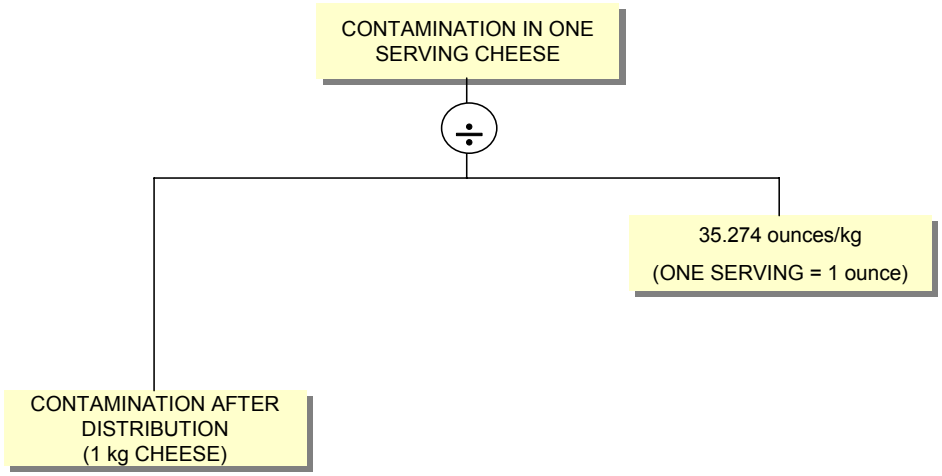


Figure 3.23: DML Decomposition of Consumption Step C1 (Contamination in One Serving)

3.3.3.2.2 Consumption Step C2: Number of Servings Consumed

Step C2 represents the number of 1 ounce servings consumed. The number of servings is entered as a user-defined variable; the number of servings consumed is represented by a uniform distribution in which the user enters the minimum and maximum values. Figure 3.24 illustrates the calculation for the number of servings consumed.

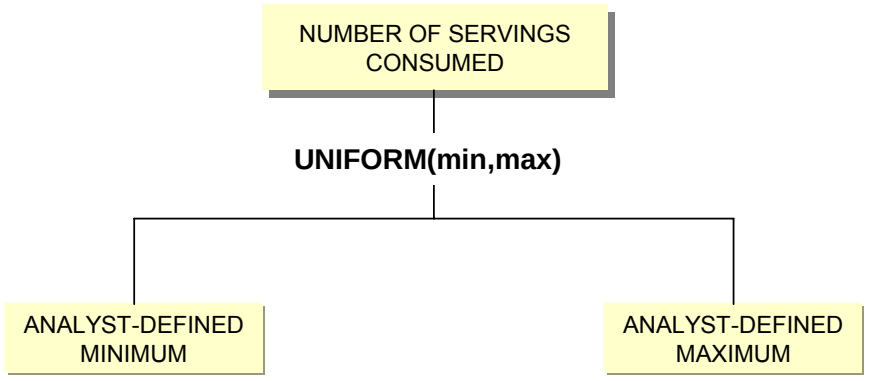


Figure 3.24: DML Decomposition of Consumption Step C2 (Number of Servings Consumed)

3.3.3.2.3 Consumption Step C3: Ingested Dose

Step C3 determines the distribution of *E. coli* O157:H7 contamination ingested by the consumer. The ingested dose is a function of the contamination per serving and the number of servings consumed, as depicted in Figure 3.25. Figure 3.28 illustrates the calculation of the ingested dose using the DML concept.

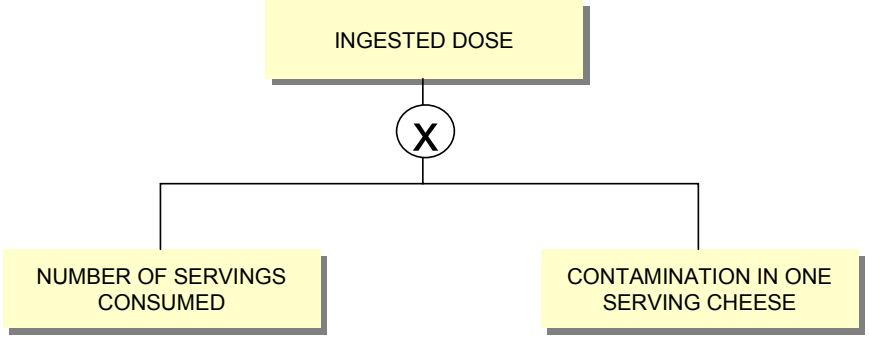


Figure 3.25: DML Decomposition of Consumption Step C3 (Ingested Dose)

3.3.3.3 Consumption Calculation Summary

The consumption phase uses the distribution of *E. coli* O157:H7 contamination after consumer storage (i.e., step B5) as the contamination level for several calculations. Using the end result from step B5, the distribution of *E. coli* O157:H7 in one serving is calculated. In addition, based on the number of servings consumed, the ingested dose is calculated. A summary of the consumption phase calculations is given in Table 3.6.

Table 3.6: Consumption Phase Calculations

Step	Description	Distribution/Model	Calculation	Unit
C1	Contamination in One Serving	---	B5/35.274	CFU/ounce
C2	Number of Servings Consumed	Uniform[a]	Uniform(min, max)	Ounce
C3	Ingested Dose	---	C1*C2	CFU/serving

[a]Analyst-defined minimum and maximum number of servings

3.4 Dose-Response Assessment

3.4.1 Dose-Response Assessment Overview

An important part of the quantitative risk assessment is the dose-response assessment, as it provides the connection between the amount of *E. coli* O157:H7 ingested in the consumption phase and the adverse health outcomes associated with *E. coli* O157:H7, which are estimated in the risk characterization component of the quantitative microbial risk assessment. Thus, the dose-response model predicts the relationship between the level of microbial exposure and the likelihood of occurrence of an adverse health outcome (i.e., illness).

Developing the dose-response assessment for *E. coli* O157:H7 is a difficult task and presents a number of challenges due to model uncertainty, data uncertainty,

and lack of model validation. First, the literature review demonstrates that there is no consensus on which specific model is most applicable to microbial dose-response, as a number of dose-response models have been proposed in quantitative microbiology to describe the relationship between the level of microbial exposure and the likelihood of illness. Second, there is a lack of *E. coli* O157:H7 dose-response data; due to ethical considerations, adequate human dose-response data is not available for highly infectious agents, like *E. coli* O157:H7. Third, the *E. coli* O157:H7 dose-response assessments that have been performed have not been validated.

3.4.1.1 Dose-Response Assessment Challenges

3.4.1.1.1 Model Uncertainty

In terms of the model used for microbial dose-response, Holcomb et al. (1999) suggest that model applicability should include properties such as: 1) adequacy in how well the model fits available data, 2) simplicity in model formulation including parsimony in the number of parameters in the model without sacrificing the quality of adequacy, and 3) the range of conditions over which the model gives good predictions. The models that have been used to describe microbial dose-response data include: log-logistic, lognormal, exponential, beta-Poisson, and Weibull-Gamma. The log-logistic and lognormal models have commonly been used to describe quantal bioassay data, though not necessarily microbial dose-response data.

The exponential model is considered to be the simplest form of the single-hit model in which only one ingested organism is required to cause infection even though the probability of this occurring may be very small (Haas et al., 1999). Thus, this model assumes that the host-pathogen interaction probability is constant for a

population, although this is unlikely because there is variability in microorganism infectivity and host susceptibility (Holcomb et al., 1999). The exponential model has been successfully used for microbial dose-response by Sanaa et al. (2004) to describe the dose-response of *Listeria monocytogenes*.

The beta-Poisson model is derived from the single-hit exponential model. However, while the exponential model assumes a discrete value for the host-pathogen interaction probability, the beta-Poisson model assumes a beta distribution for the host-pathogen interaction. In most cases, the beta-Poisson provides a statistically significant improvement in fit over the exponential model (Strachan et al., 2005). The beta-Poisson model is most widely associated with microbial dose-response and has been used to model data from several foodborne pathogens including *Shigella* spp., *Campylobacter jejuni*, and *E. coli* O157:H7 (Crockett et al., 1996; Haas et al., 2000; Holcomb et al., 1999; Powell et al., 2000).

Finally, the Weibull-Gamma model is an example of an empirical model. Although empirical models lack biological plausibility, this type of model can be especially useful when there is no direct dose-response data available (Haas et al., 1999). As with the beta-Poisson model, the host-pathogen heterogeneity in the Weibull-Gamma model is described with a distribution rather than a constant. Parameter estimation with the Weibull-Gamma model can be more difficult, but research has shown that it is a more flexible and powerful model (Powell et al., 2000). Farber et al. (1996) have successfully estimated infectious doses for *Listeria monocytogenes* with this model.

3.4.1.1.2 Data Uncertainty

The lack of dose-response data for *E. coli* O157:H7 makes parameter estimation for the dose-response model challenging as well. One obvious alternative to human data is the use of animal models; however, animal models must be carefully reviewed for applicability to humans, because of the inherent variability in host-pathogen interaction (Strachan et al., 2005). Another alternative has been to use human dose-response relationships of surrogate pathogens, such as *Shigella dysenteriae*, *Shigella flexneri*, infant diarrheal *E. coli* strains, and enteropathogenic *E. coli* (EPEC) strains, to estimate the dose-response of *E. coli* O157:H7 (Marks et al., 1998; Powell et al, 2000; Crockett et al., 1996; Haas et al., 1999). Studies have shown that *E. coli* O157:H7 produces shiga-like toxins similar to *S. dysenteriae* and it has been suggested that *Shigella* can be used as a surrogate for *E. coli* O157:H7, since their mechanisms of infection are quite similar (Hass et al., 2000). EPEC stains share the attaching and effacing gene with *E. coli* O157:H7 and have also been proposed as a surrogate pathogen (Powell et al., 2000).

Previous *E. coli* O157:H7 dose-response models include several beta-Poisson models based on feeding studies in humans and animal data. Marks et al. (1998) proposed pooling strains of *S. dysenteriae* and *S. flexneri* as possible surrogates for *E. coli* O157:H7. Strachan et al. (2001) demonstrated that the surrogate *Shigella* model gave the closest fit to data obtained from an environmental outbreak. A model by Crockett et al. (1996) pooled experimental data from both *S. flexneri* and *S. dysenteriae* strains as well, and was shown to be statistically indistinguishable from separate dose response models of each species, suggesting its potential to represent

the *Shigella* species. Powell et al. (2000) proposed a dose-response envelope for *E. coli* O157:H7 with bounding values of the dose-response defined by two separate beta-Poisson dose-response curves fitted to human clinical trial data for two surrogate pathogens (i.e., *S. dysenteriae* and EPEC). Marks et al. (1998) also proposed infant diarrheal *E. coli* as a possible surrogate as these strains are part of the STEC group. Finally, Haas et al. (2000) proposed a dose-response model for *E. coli* O157:H7 based on data from rabbits inoculated with *E. coli* O157:H7.

3.4.1.1.3 Model Validation

Lastly, quantitative microbiological risk assessments have been performed to determine the risk of *E. coli* O157:H7 infection from various foods, but the dose-response models used in these risk assessments have yet to be fully validated. Quantitative microbial risk assessments are extremely useful in proposing mitigation strategies for reducing risk of infection; however, to ensure accuracy and assess uncertainty, a risk assessment requires a validated dose-response model (Strachan et al., 2005). Dose-response models should be validated with outbreak data using both the attack rate and likely dose. However, this information is often difficult to obtain, making model validation another difficult task in dose-response assessment.

3.4.1.2 Dose-Response Assessment Approach

This research uses the DML concept to decompose the dose-response assessment into its basic elements. In order to address the model uncertainty, the DML method identifies several dose-response models, previously used in other QMRAs, as possibilities for describing the dose-response relationship for *E. coli* O157:H7. In addition, the DML method also addresses the data uncertainty by

identifying several data sets from which the various dose-response model parameters can be estimated. Finally, this research also proposes a new method for developing a "weighted-average" dose-response for the various models investigated. These weights are developed using the Analytical Hierarchy Process (AHP) method in which alternative data sets are compared on several criteria defined in this research as data relevance, data quality, data quantity, and data extrapolation/fit. The weighted average dose-response models developed in this research offer an alternative way to account for the data uncertainty associated with the dose-response relationship for *E. coli* O157:H7. A detailed explanation of the dose-response models, data and methodology used for parameter estimation, development of the weighted-average model, and validation follows.

3.4.2 Development of Dose-Response Models

3.4.2.1 Traditional Dose-Response Model Approach

3.4.2.1.1 Dose-Response Models

A number of different microbial dose-response models have been derived in order to describe the relationship between the level of exposure (i.e., dose or number of organisms ingested) and the likelihood of occurrence of an adverse consequence (i.e., illness). Prior work has shown that the exponential, beta-Poisson, and Weibull-Gamma provide good fits for microbial dose-response data (Haas et al., 2000). Table 3.7 provides a summary of these models, followed by a discussion of the derivation.

Table 3.7: Dose-Response Models and Parameter Definition

Model Name	Function	Where
Exponential	$P_I(d) = 1 - \exp(-rd)$	r = constant host-pathogen interaction probability, Denotes the fraction of microorganisms ingested that survive to initiate infection
Beta-Poisson	$P_I(d) = 1 - \left(1 + \frac{d}{\beta}\right)^{-\alpha}$	α, β = shape parameters, Beta-Poisson derived from exponential, assumes beta distribution for host-pathogen interaction instead of constant
Weibull-Gamma	$P_I(d) = 1 - \left[1 + \left(\frac{d^x}{\beta}\right)\right]^{-\alpha}$	α, β, x = shape parameters, Weibull-Gamma reduces to beta-Poisson if x = 1 Assumes Gamma distribution for host-pathogen interaction

Haas et al. (1999) state that the process of infection requires two sequential, but independent, subprocesses to occur: 1) the human host must ingest one or more organisms that are capable of causing disease and 2) the organisms undergo decay or are impaired from multiplying to cause infection by host responses, and only a fraction of the ingested organisms reach a site where infection can begin. Infection occurs when at least some critical number of organisms survive to initiate infection. This minimum number, $k_{\min}$, is the probability of infection, or the fraction of individuals who are exposed to an average dose d and become infected, and may be written as:

$$P_I(d) = \sum_{k=k_{\min}}^{\infty} \sum_{j=k}^{\infty} P_1(j \mid d) P_2(k \mid j) \tag{3.1}$$

Here, the probability of ingesting j organisms from an exposure to a dose, d, is written as $P_1(j|d)$. The function P_1 includes the individual-to-individual variation in the actual number of organisms ingested or exposed. The probability of k organisms ($\leq j$) surviving to initiate an infection is written as $P_2(k|j)$. The function P_2 addresses the host-pathogen interaction that allows some organisms to survive to initiate infection. Thus, by specifying functional forms for P_1 and P_2, as well as numerical

value of $k_{\min,}$ a number of dose-response relationships can be derived (Haas et al., 1999).

The exponential dose-response model is the simplest model that can be formulated. This model assumes that the distribution of organisms is random (modeled by a Poisson distribution), each organism has an independent and identical survival probability, r, and $k_{\min}$ equals 1. Thus, by substituting the Poisson distribution for $P_1(j|d)$ and the binomial distribution for $P_2(k|j)$ in equation (3.1), Haas et al. (1999) derive the exact exponential dose-response relationship. However, the following approximation is generally used for the exponential dose-response model:

$$P_I(d) = 1 - \exp(-rd) \tag{3.2}$$

Thus, the exponential dose-response model defines the probability of infection given a dose, d, in terms of one parameter, r, which characterizes the process.

While the exponential model assumes a constant value for the host-pathogen survival probability, r, there may be variation in this success rate. This variation may be attributed to diversity in human responses, diversity in pathogen competence, or both. The beta-Poisson model is derived from the exponential model and addresses this variation by allowing r to be governed by a probability distribution (Haas et al., 1999). The beta-Poisson model still assumes that $P_1(j|d)$ is a Poisson distribution; however, the beta-Poisson model characterizes the probability of an ingested organism surviving to infect the host as following a beta distribution (i.e., $P_2(k|j)$) (Powell et al., 2000). Haas et al. (1999) derive the exact solution of the beta-Poisson; however, the following approximation is used in this research:

$$P_I(d) = 1 - \left(1 + \frac{d}{\beta}\right)^{-\alpha} \tag{3.3}$$

Thus, in the beta-Poisson model, the average probability of infection, $P_I(d)$, when exposed to a dose, *d*, is described by two parameters, α and β. It should be noted that α is nonnegative, resulting in a slope which is less than the respective exponential model; however, when α approaches infinity, the beta-Poisson model approaches the exponential model. The parameter β describes the shape of the dose-response curve (Haas et al., 1999)

In contrast to the exponential and beta-Poisson models which are developed from mechanistic assumptions, the Weibull-Gamma is an empirical model in that it lacks biological plausibility (Haas et al., 1999); however, empirical models can be especially useful when there is no direct dose-response data available. These models are flexible enough to accommodate all qualitative information and adaptable to both healthy and high risk groups (Farber et al., 1996). The Weibull model is one such model that has been proposed as a flexible dose-response model (Haas et al., 1999; Farber et al., 1996), and defined by Farber et al. (1996) as:

$$P_I(d) = 1 - \exp\left(-ad^x\right) \tag{3.4}$$

Where $P_I(d)$ denotes the probability of illness for an individual exposed to a dose, *d*, of a pathogen. The properties of this relationship are determined by the parameters *a* and *x*. The parameter *x* determines the shape of the individual dose-response curve. The parameter *a* is related to the probability of illness given exposure to a single pathogen. The host-pathogen heterogeneity can be described by specifying a probability distribution for the Weibull parameter *a*; in this case, a Gamma

distribution with parameters α and β is specified. As a result, the Weibull-Gamma dose-response model for the average probability of illness for a given dose, *d,* can be derived and is approximated by Farber et al. (1996) as:

$$P_I(d) = 1 - \left[1 + \left(\frac{d^x}{\beta}\right)\right]^{-\alpha} \tag{3.5}$$

Hence, the Weibull-Gamma dose-response model defines the probability of infection, $P_I(d)$, when exposed to a dose, *d*, in terms of three parameters, α, β, and *x*. It should be noted that the Weibull-Gamma dose-response model reduces to the beta-Poisson dose-response relationship when $x = 1$. In addition, the Weibull-Gamma dose-response model reduces to the log-logistic model when $\alpha = 1$ (Farber et al., 1996).

3.4.2.1.2 Parameter Estimation

After selecting the three dose-response models for study, a method for estimating the parameters of the models must be established. In this work, the parameters of the three models described above are estimated by the method of maximum likelihood. Prior work (Crockett et al., 1996; Haas et al., 2000; Powell et al., 2000) has shown that the fit of the dose-response model can be determined using a binomial likelihood function, as derived by Strachan et al. (2005). This prior work has also shown that by minimizing the deviance of the binomial likelihood function, the maximum likelihood estimates (MLE) of the dose-response parameters can be obtained. The deviance, *Y*, has been derived by Strachan et al. (2005) as:

$$\min Y = -2\sum_{i=1}^{j}\left[P_i \ln\left(\frac{p_i}{p_i^o}\right) + (T_i - P_i)\ln\left(\frac{1-p_i}{1-p_i^o}\right)\right] \tag{3.6}$$

Where $p_i = P_I(d;\theta)$ is the predicted response, with P_I representing the dose-response relationship and θ representing the set of dose-response parameters. The observed response is represented by $p_i^o = P_i / T_i$ where P_i is the observed number of positive responses at the *i*th dose group and T_i is the total number of subjects in the *i*th dose group. Thus, the maximum likelihood estimates are obtained by finding the values of θ that through their influence on p_i, minimize Y (Haas et al., 1999). No model should be accepted for use without examination of goodness of fit. In order to test the goodness of fit, Y is compared to the χ^2 value at $j - q$ degrees of freedom, where j is the number of doses and q is the number of parameters in the dose-response model of interest (Haas et al., 2000). For example, the null hypothesis of fit acceptability may be rejected (i.e., the dose-response model is rejected) if Y exceeds the 5th percentile of the χ^2 distribution.

The parameter estimates and goodness of fit calculations are obtained using a spreadsheet procedure described by Haas (1994). An advantage of this spreadsheet routine is that it facilitates analysis of the effect of differing the starting values (i.e., initial estimates) for the parameters to confirm that the maximum likelihood estimates of the parameters obtained are unique and stable (Powell et al., 2000). Optimizations are performed using Microsoft Excel (2000) loaded with the Solver add-in tool. Thus, the parameters of the three dose-response models are calculated using this method for each of the data sets examined and then tested for goodness of fit.

3.4.2.1.3 Clinical Trial Data for Parameter Estimation

Table 3.8 presents the data used to develop the parameters of the exponential, beta-Poisson, and Weibull-Gamma dose-response models. This data includes feeding

study data for *Shigella* spp. in healthy male human adults, *E. coli* O157:H7 in infant New Zealand white rabbits, and EPEC and infant diarrheal *E. coli* strains fed at different doses to adult male human volunteers.

Table 3.8: Dose-Response Data from Human and Animal Feeding Studies

S. flexneri		***S. dysenteriae***		***E. coli* O157:H7 Rabbit**[a]		**EPEC**		**Infant Diarrheal *E. coli***	
Dose[b]	**+/Total**[c]	**Dose**	**+/Total**	**Dose**	**+/Total**	**Dose**	**+/Total**	**Dose**	**+/Total**
[d]10	1/10	[e]10^4	1/4	Control	0/7	[g]10^6	0/4	[j]$5x10^8$	3/5
[d]200	2/4	[e]10^5	3/4	10^5	1/3	[g]10^{10}	3/5	[j]$2.5x10^9$	6/6
[d]2000	7/10	[e]10^6	7/8	10^6	2/5	[h]10^8	0/5	[j]$2x10^{10}$	2/2
[d]10^4	5/6	[e]10^7	13/19	10^7	5/5	[i]10^6	1/5	[k]$7x10^6$	7/11
[d]200	1/4	[e]10^8	7/8	10^8	12/13	[i]10^8	1/5	[k]$5.3x10^8$	8/12
[d]10^4	2/6	[f]180	6/36	10^9	5/5	[i]10^{10}	5/5	[k]$6.5x10^9$	11/11
		[f]5000	33/49	$3x10^9$	2/2			[k]$9x10^9$	12/12
		[f]10^4	66/87	10^{10}	6/6			[k]$1.4x10^8$	6/8
		[f]10^5	15/24					[k]$1.7x10^9$	5/7
								[k]$5.3x10^9$	6/8
								[k]$1.6x10^{10}$	7/8

[a] *E. coli* O157:H7 rabbit data (Pai et al., 1986)
[b] Dose is the number of colony forming units ingested
[c] +/Total is the number of subjects infected with symptoms of disease divided by the total number exposed
[d] *S. dysneteriae* data (Levine et al., 1973)
[e] *S. flexneri* data (Dupont et al., 1969)
[f] *S. flexneri* data (Dupont et al., 1972)
[g] *E. coli* O127 data (Levine et al., 1978)
[h] *E. coli* O128 data (Levine et al., 1978)
[i] *E. coli* O142 data (Levine et al., 1978)
[j] *E. coli* B-171-8 data (Levine et al., 1978)
[k] *E. coli* 55, B_5 and 111, B_4 data (June et al., 1953)

The data in Table 3.8 is analyzed in a number of different ways; in addition to analyzing the data individually (i.e., *S. dysenteriae*, *S. flexneri*, *E. coli* O157:H7 rabbit, EPEC, and infant diarrheal *E. coli*), the data sets are also combined and analyzed (i.e., all data, all human data, all *E. coli* data, all human *E. coli* data, all *Shigella* data). In all, ten data sets are considered in this study: all data, all human data, all *E. coli* data, all human *E. coli* data, EPEC data, infant diarrheal *E. coli* data, *E. coli* O157:H7 rabbit data, all *Shigella* spp. data, *S. dysenteriae* data, and *S. flexneri* data. These data sets are referred to as data sets 1-10, respectively. The data included in each of the ten data sets evaluated in this research is documented in Table 3.9.

Table 3.9: Data Sets for Evaluation with the Exponential, Beta-Poisson, and Weibull-Gamma Dose-Response Models

Data Set Name	Data Set Number	Data Included (reference)
All Data	1	*E. coli* O157:H7 rabbit (Pai et al., 1986)
		S. dysneteriae (Levine et al., 1973)
		S. flexneri (Dupont et al., 1969)
		S. flexneri (Dupont et al., 1972)
		E. coli O127 (Levine et al., 1978)
		E. coli O128 (Levine et al., 1978)
		E. coli O142 (Levine et al., 1978)
		E. coli B-171-8 (Levine et al., 1978)
		E. coli 55, B_5 and 111, B_4 (June et al., 1953)
All Human Data	2	*S. dysneteriae* (Levine et al., 1973)
		S. flexneri (Dupont et al., 1969)
		S. flexneri (Dupont et al., 1972)
		E. coli O127 (Levine et al., 1978)
		E. coli O128 (Levine et al., 1978)
		E. coli O142 (Levine et al., 1978)
		E. coli B-171-8 (Levine et al., 1978)
		E. coli 55, B_5 and 111, B_4 (June et al., 1953)
All *E. coli* Data	3	*E. coli* O157:H7 rabbit (Pai et al., 1986)
		E. coli O127 (Levine et al., 1978)
		E. coli O128 (Levine et al., 1978)
		E. coli O142 (Levine et al., 1978)
		E. coli B-171-8 (Levine et al., 1978)
		E. coli 55, B_5 and 111, B_4 (June et al., 1953)
All Human *E. coli* Data	4	*E. coli* O127 (Levine et al., 1978)
		E. coli O128 (Levine et al., 1978)
		E. coli O142 (Levine et al., 1978)
		E. coli B-171-8 (Levine et al., 1978)
		E. coli 55, B_5 and 111, B_4 (June et al., 1953)
EPEC Data	5	*E. coli* O127 (Levine et al., 1978)
		E. coli O128 (Levine et al., 1978)
		E. coli O142 (Levine et al., 1978)
Infant diarrheal *E. coli* Data	6	*E. coli* B-171-8 (Levine et al., 1978)
		E. coli 55, B_5 and 111, B_4 (June et al., 1953)
E. coli O157:H7 rabbit Data	7	*E. coli* O157:H7 rabbit (Pai et al., 1986)
Shigella spp. Data	8	*S. dysneteriae* (Levine et al., 1973)
		S. flexneri (Dupont et al., 1969)
		S. flexneri (Dupont et al., 1972)
S. dysenteriae Data	9	*S. dysneteriae* (Levine et al., 1973)
S. flexneri Data	10	*S. flexneri* (Dupont et al., 1969)
		S. flexneri (Dupont et al., 1972)

3.4.2.1.4 Dose-Response Model Parameter Estimation Results

The parameter estimates for the exponential, beta-Poisson, and Weibull-Gamma dose-response models are obtained for each of the data sets evaluated. The

parameters, along with the residual deviance and goodness of fit are summarized in Table 3.10.

Table 3.10: Results of Exponential, Beta-Poisson, Weibull-Gamma Dose-Response Analysis based on Data Sets 1-10

Data Set[a]	Model	Parameters	Residual Deviance (Y)	P (goodness of fit)
1	Exponential	r = 2.08E-09	3366.10	~0
	Beta-Poisson	α = 0.094	94.82	5.67E-07
		β = 1.24		
	Weibull-Gamma	α = 0.020	94.70	3.56E-07
		β = 4.09		
		x = 4.65		
2	Exponential	r = 2.10E-09	3272.96	~0
	Beta-Poisson	α = 0.087	78.69	1.81E-06
		β = 0.61		
	Weibull-Gamma	α = 0.013	78.61	1.07E-06
		β = 0.078		
		x = 6.52		
3	Exponential	r = 9.11E-10	278.38	1.04E-45
	Beta-Poisson	α = 0.23	39.12	0.01
		β = 279603.34		
	Weibull-Gamma	α = 0.028	38.40	0.01
		β = 1.38E+42		
		x = 7.87		
4	Exponential	r = 5.91E-10	143.95	3.83E-23
	Beta-Poisson	α = 0.22	23.75	0.049
		β = 643283.44		
	Weibull-Gamma	α = 100.67	23.19	0.057
		β = 6627.039		
		x = 0.22		
5	Exponential	r = 4.07E-10	31.83	4.37E-05
	Beta-Poisson	α = 0.22	11.24	0.081
		β = 3112329.52		
	Weibull-Gamma	α = 1.94	9.57	0.088
		β = 7408.83		
		x = 0.42		
6	Exponential	r = 7.10E-10	109.19	1.35E-20
	Beta-Poisson	α = 0.17	8.95	0.18
		β = 48284.30		
	Weibull-Gamma	α = 1064.55	8.17	0.15
		β = 11847.74		
		x = 0.14		
7	Exponential	r = 5.70	17.98	0.012
	Beta-Poisson	α = 0.49	3.12	0.79
		β = 189343.32		
	Weibull-Gamma	α = 0.090	2.18	0.82
		β = 9.611E+36		
		x = 6.62		
8	Exponential	r = 3.74-07	1487.57	~0

	Beta-Poisson	α = 0.16 β = 16.86	26.54	0.014
	Weibull-Gamma	α = 0.14 β = 21.89 *x* = 1.12	26.51	0.01
9	Exponential	*r* = 0.00021	30.45	1.21E-05
	Beta-Poisson	α = 0.16 β = 9.17	4.88	0.30
	Weibull-Gamma	α = 0.022 β = 19456.03 *x* = 6.40	4.82	0.19
10	Exponential	*r* = 3.74-07	1268.25	~0
	Beta-Poisson	α = 0.17 β = 29.16	21.02	0.0037
	Weibull-Gamma	α = 0.029 β = 6.77E+09 *x* = 6.31	20.24	0.0025

[a] Data sets 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 refer to all data, all human data, all *E. coli* data, all human *E.* coli data, *E. coli* EPEC data, infant diarrheal *E. coli* data, E. *coli* O157:H7 rabbit data, all *Shigella* spp. data, *S. dysenteriae* data, and *S. flexneri* data

From the data in Table 3.10, it is clear that the beta-Poisson and Weibull-Gamma models provide good fits for data sets 4, 5, 6, 7, and 9 (all human *E.* coli, EPEC, infant diarrheal *E. coli*, *E. coli* O157:H7 rabbit data, and *S. dysenteriae* data); however, these models do not provide good fits to data sets 1, 2, 3, 8, and 10 (all data, all human data, and all *E. coli*, *Shigella* spp., and *S. flex*neri data). This suggests that there is too much variance among the data sets from multiple sources. In addition, Table 3.10 shows that the exponential dose-response model fails the goodness of fit test ($P<0.05$) for all of the data sets investigated. Therefore, the exponential model does not provide a good estimate for the dose-response of *E. coli* O157:H7 and is excluded as a potential dose-response model for *E. coli* O157:H7.

A graphical comparison of the dose-response models for the various data sets is given in the Figures 3.26-3.28. Although the fits are undesirable, Figure 3.26 shows the exponential dose-response model for the ten data sets evaluated.

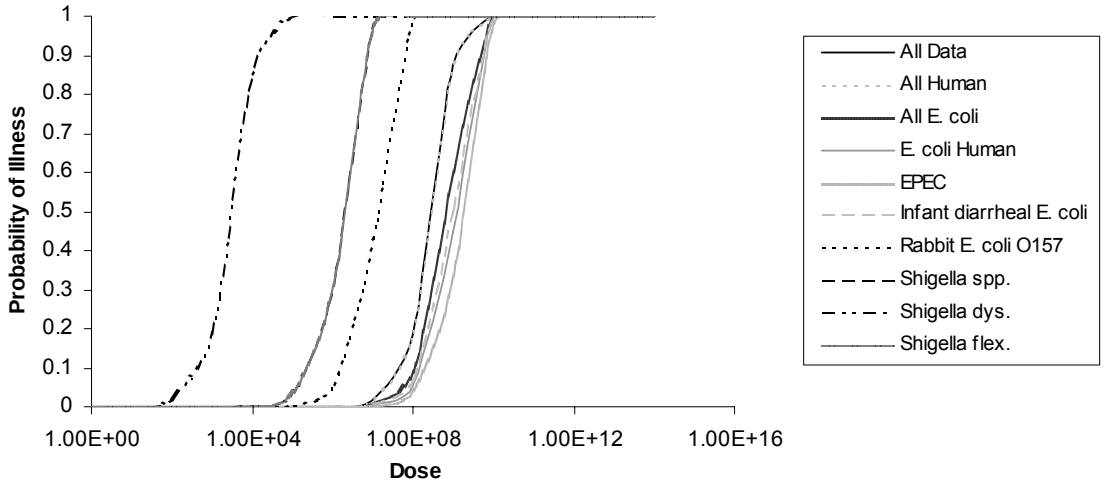


Figure 3.26: Exponential Dose-Response Curves for Data Sets 1-10

Figures 3.27 and 3.28 show the beta-Poisson and Weibull-Gamma dose-response models for the ten data sets investigated, respectively. The bold lines represent the data sets that have a significant fit (P>0.05); those data sets include all human *E.* coli, EPEC, infant diarrheal *E. coli*, *E. coli* O157:H7 rabbit data, and *S.* dysenteriae data.

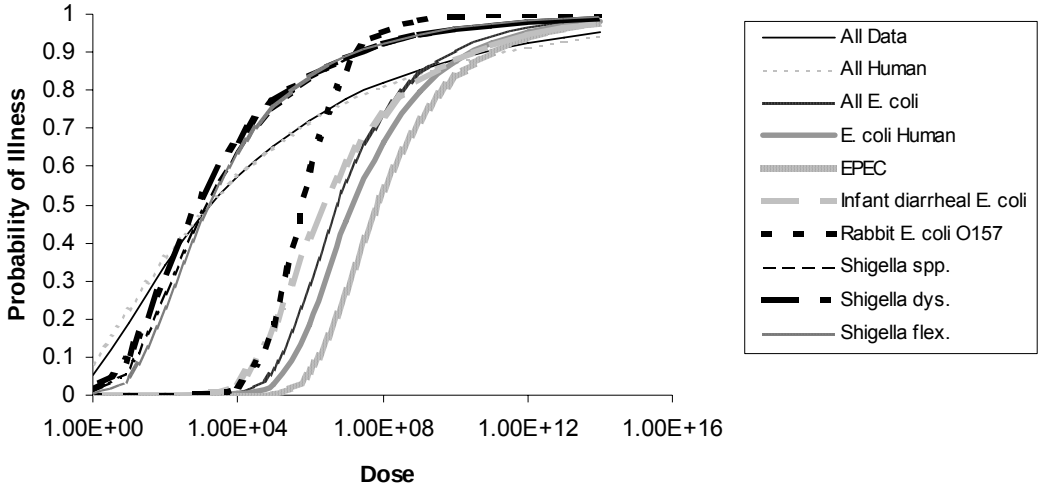


Figure 3.27: Beta-Poisson Dose-Response Curves for Data Sets 1-10

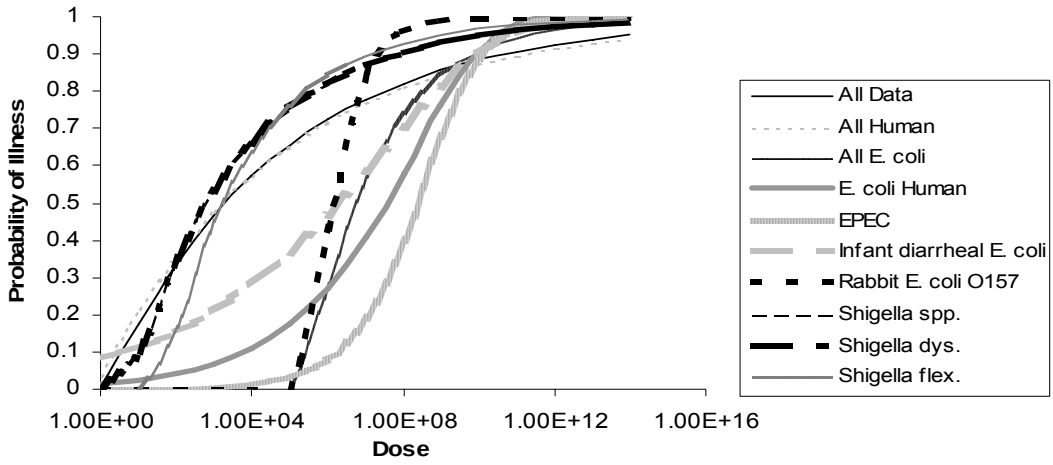


Figure 3.28: Weibull-Gamma Dose-Response Curves for Data Sets 1-10

3.4.2.2 AHP Dose-Response Model Approach

3.4.2.2.1 AHP Methodology

Within the literature, there is some disagreement as to which of the data listed in Table 3.8 is most appropriate for estimating the dose-response of *E. coli* O157:H7. To address this data uncertainty issue, this research proposes a method for weighting the dose-response results on a number of criteria in order to obtain a "weighted-average" for the most common dose-response models (i.e., exponential, beta-Poisson, and Weibull-Gamma). These weighted-average models are developed using the Analytical Hierarchy Process (AHP) method. The AHP method is a powerful and flexible decision making process that helps set priorities and compare alternative concepts when both qualitative and quantitative aspects of a decision need to be considered. It is a comprehensive, logical, and structured framework that helps to improve the understanding of complex decisions by decomposing the problem in a hierarchical structure. The incorporation of all relevant decision criteria, and their pair-wise comparison allows the decision maker to determine the trade-offs among

objectives. Thus, by reducing complex decisions to a series of one-on-one comparisons, then synthesizing the results, the AHP method not only helps decision makers arrive at the best decision, but also provides a clear rationale that it is the best (Measurement Methods, 2005).

The AHP method is based on three principles: decomposition of the decision problem, comparative judgment of the elements, and synthesis of the priorities. The first step is to decompose the problem by determining the goal of the analysis, identifying the criteria relevant for this goal, and identifying the alternatives to be evaluated. The second step is the comparison of the alternatives and the criteria. A pair-wise comparison of the various criteria is completed for each alternative; the scale in Table 3.11 is used for this relative comparison. This allows the comparisons to be expressed in verbal terms which are then translated into the corresponding numbers. The last step synthesizes the comparisons to get the priorities of the alternatives with respect to each criterion and the weights of each criterion with respect to the goal. The local priorities are then multiplied by the weights of the respective criterion. The results are summed up to get the overall priority of each alternative (Measurement Methods, 2005).

Table 3.11: Fundamental Scale for Pair-Wise Comparisons for the AHP Method

Verbal Scale	Numerical Values
Equally important, likely or preferred	1
Moderately more important, likely or preferred	3
Strongly more important, likely or preferred	5
Very strongly more important, likely or preferred	7
Extremely more important, likely or preferred	9
Intermediate values to reflect compromise	2, 4, 6, 8

The AHP method is used to compare the data sets resulting in significant fits for the dose-response models examined. The data sets are compared using four criteria: relevance, quality, quantity, and extrapolation/fit. These four characteristics are selected as the criteria because they provide ways to judge and measure the uncertainty of the data. Data relevance is important due to the disagreement within the literature as to which pathogens should be used to describe the dose-response of *E. coli* O157:H7. The quality criterion is used to judge how much information is available about the experiment and how tightly that experiment is controlled. The quantity characteristic is used to judge the number and size of the administered doses, as it is problematic to make realistic estimates based on only a few doses. Finally, most experiments and clinical trials administer dose levels that are much higher than what would be expected to be ingested; therefore, the extrapolation/fit criteria judges how well the data could be extrapolated from high to low doses. After establishing the alternatives and criteria of the problem, the pair-wise comparisons of the various criteria are completed for each alternative.

3.4.2.2.2 AHP Weighted-Average Model Results

The AHP method compares the data sets on the relevance, quality, quantity, and extrapolation/fit criteria and is used to develop weights for the data sets considered. Only the data sets resulting in a significant fit with the beta-Poisson and Weibull-Gamma models are considered in the AHP method; the AHP method is not applied to the exponential dose-response model, as this model did not result in a significant fit for any of the data sets investigated. Since the all human *E. coli* data set includes the data in the EPEC and infant diarrheal *E. coli* data sets, only the all

human *E. coli*, *E. coli* O157:H7 rabbit, and *S. dysenteriae* data sets are used in the development of the weighted-average dose-response models for the beta-Poisson and Weibull-Gamma models. The pair-wise comparison of each criterion is completed for the three significant data set alternatives using expert judgment. The comparisons are then synthesized to get the absolute weights of the alternatives with respect to each criterion. Table 3.12 shows this pair-wise comparison of the alternatives for each of the criterion; in addition, the absolute weight, with respect to the criterion, is also given for each alternative. Table 3.13 gives the pair-wise and absolute weights of the criteria with respect to the goal.

Table 3.12: AHP Pair-Wise and Absolute Weights of Alternatives for each Criterion

	Pair-wise Weights with Respect to Relevance		
	***E. coli* Human**	**O157:H7 Rabbit**	***S. dysenteriae***
***E. coli* Human**	1.000	0.500	0.250
O157:H7 Rabbit	2.000	1.000	0.500
S. dysenteriae	4.000	2.000	1.000
Absolute Weights with Respect to Relevance	**0.143**	**0.286**	**0.571**
	Pair-wise Weights with Respect to Quality		
	***E. coli* Human**	**O157:H7 Rabbit**	***S. dysenteriae***
***E. coli* Human**	1.000	0.500	1.000
O157:H7 Rabbit	2.000	1.000	3.000
S. dysenteriae	1.000	0.333	1.000
Absolute Weights with Respect to Quality	**0.240**	**0.550**	**0.210**
	Pair-wise Weights with Respect to Quantity		
	***E. coli* Human**	**O157:H7 Rabbit**	***E. coli* Human**
***E. coli* Human**	1.000	2.000	1.000
O157:H7 Rabbit	0.500	1.000	0.333
S. dysenteriae	1.000	3.000	1.000
Absolute Weights with Respect to Quantity	**0.387**	**0.169**	**0.444**
	Pair-wise Weights with Respect to Fit/Extrapolation		
	***E. coli* Human**	**O157:H7 Rabbit**	***S. dysenteriae***
***E. coli* Human**	1.000	2.000	0.250
O157:H7 Rabbit	0.500	1.000	0.333
S. dysenteriae	4.000	3.000	1.000
Absolute Weights with Respect to Fit/Extrapolation	**0.218**	**0.151**	**0.630**

Table 3.13: AHP Pair-Wise and Absolute Weights of the Criteria

	Pair-wise Weights of the Criteria			
	Relevance	**Quality**	**Quantity**	**Fit/Extrapolation**
Relevance	1.000	6.000	4.000	1.000
Quality	0.167	1.000	3.000	0.167
Quantity	0.250	0.333	1.000	0.143
Fit/Extrapolation	1.000	6.000	7.000	1.000
Absolute Weights of the Criteria	**0.393**	**0.095**	**0.059**	**0.453**

Finally, the overall priority of each alternative is obtained from a matrix operation involving the absolute weights of the alternatives with respect to the criteria and the absolute weights of the criteria with respect to the goal. Equation (3.7) shows this matrix operation and the resulting priority of each alternative. The *S. dysenteriae* data has the highest weight of the alternatives examined, followed by the *E. coli* O157:H7 rabbit and the all human *E. coli* data sets.

$$\begin{bmatrix} 0.143 & 0.240 & 0.387 & 0.218 \\ 0.286 & 0.550 & 0.169 & 0.151 \\ 0.571 & 0.210 & 0.444 & 0.630 \end{bmatrix} \begin{bmatrix} 0.393 \\ 0.095 \\ 0.059 \\ 0.453 \end{bmatrix} = \begin{bmatrix} 0.201 & 0.243 & 0.556 \end{bmatrix} \quad (3.7)$$

Using these weights, a weighted-average dose-response model can be developed. For the beta-Poisson model, the form of the AHP weighted-average dose-response model is:

$$P_I(d) = 0.201 * \left[1 - \left(1 + \frac{d}{643283.44}\right)^{-0.220}\right] + 0.243 * \left[1 - \left(1 + \frac{d}{189343.32}\right)^{-0.487}\right] + 0.556 * \left[1 - \left(1 + \frac{d}{9.168}\right)^{-0.157}\right] \quad (3.8)$$

The AHP weighted-average Weibull-Gamma dose-response model, therefore, has the following form:

$$P_I(d) = 0.201 * \left[1 - \left[1 + \left(\frac{d^{0.219}}{6627.04}\right)\right]^{-100.67}\right] + 0.243 * \left[1 - \left[1 + \left(\frac{d^{6.622}}{9.613 * 10^{36}}\right)\right]^{-0.0896}\right] + 0.556 * \left[1 - \left[1 + \left(\frac{d^{6.40}}{19456.03}\right)\right]^{-0.022}\right] \quad (3.9)$$

Figures 3.29 and 3.30 show the AHP weighted-average dose-response curves for the beta-Poisson and Weibull-Gamma models, respectively. The three data sets used to develop the AHP weighted-average model are shown for comparison purposes.

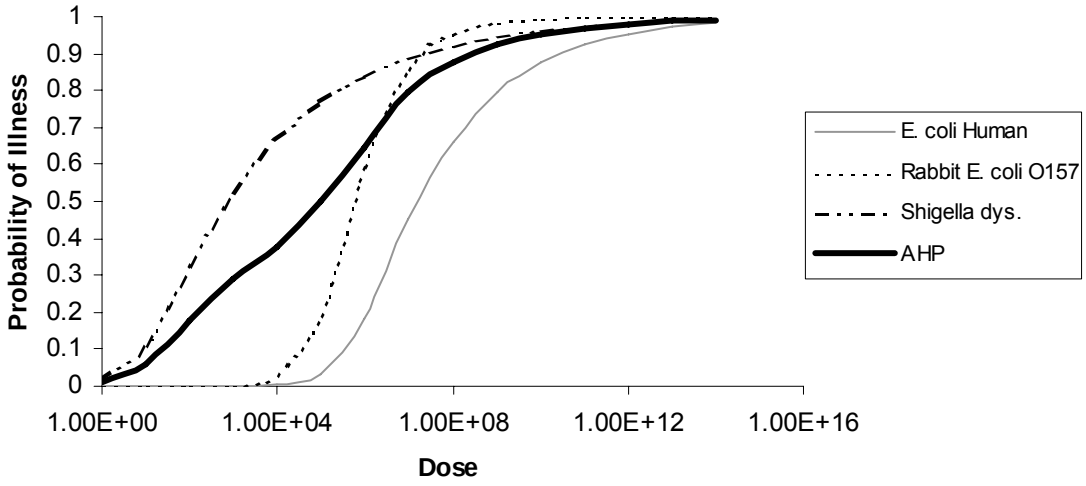


Figure 3.29: Beta-Poisson Dose-Response Curves (for data sets 4,7, & 9) with AHP Weighted-Average

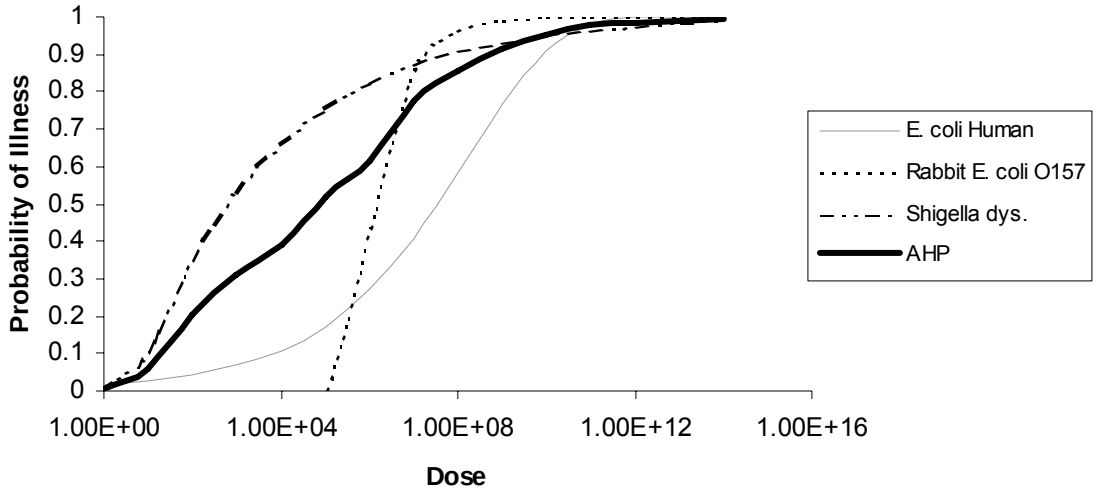


Figure 3.30: Weibull-Gamma Dose-Response Curves (for data sets 4, 7, & 9) with AHP Weighted-Average

3.4.3 Validation of Dose-Response Models

3.4.3.1 Validation Method Overview

It is desirable to validate dose-response models with human epidemiological information; this is especially important in the case of *E. coli* O157:H7 since the underlying data here are based on animal studies and surrogate pathogens. Especially in the case of the animal data, there is little experience with interspecies dose-response extrapolation from animals to humans (Haas et al., 2000). Furthermore, dose-response experiments are frequently, and of necessity, conducted at higher doses and levels of risk than may be encountered in an actual exposure situation.

Comparing actual observations in outbreak data to the predicted observation lends credence to the developed dose-response models. Thus, this research attempts to characterize the validity of the various dose-response models developed using the clinical trial data as well as validate the AHP weighted-average dose-response relationships by comparing the model estimates with actual human outbreak information. This characterization is achieved by obtaining *E. coli* O157:H7 outbreak data from Strachan et al. (2005), in which the attack rate and duration of exposure are used to determine the likely dose of the pathogen in the incriminated source. Using the attack rate and likely dose, the predicted response for each model is calculated and then compared with the levels observed during the outbreak (Haas et al., 2000). In addition, a comparison of the clinical trial data to the dose-response curves is also performed. Each model is developed from a subset of all of the relevant clinical trial data, by comparing the each model to all of the clinical trial data it can be determined if one model provides an overall best fit.

The maximum likelihood method is used to quantitatively assess which model best fits the observed data. Using the dose and attack rates in Table 3.14, equation 3.6 is solved for each of the dose-response models developed. The dose-response model producing the minimum deviance provides the best fit to the outbreak data. Next equation 3.6 is solved using the dose and attack rate information in Table 3.8 for the clinical trial data. The dose-response model producing the minimum deviance provides the best fit to the clinical trial data.

3.4.3.2 *E. coli* O157:H7 Outbreak Data for Model Validation

In order to validate a dose-response model, it is necessary to obtain outbreak information with the following well-documented characteristics: (1) vehicles of infection, (2) attack rates, and (3) measurements of bacteria levels in the incriminated sources. While it is difficult to obtain outbreak data that has these characteristics accurately determined, Strachan et al. (2005) have identified eight *E. coli* O157:H7 outbreaks in which enough information is known to estimate the dose and the attack rate (i.e., response). Table 3.14, taken from Strachan et al. (2005), summarizes these outbreaks.

Table 3.14: *E. coli* O157:H7 Outbreak Data

Outbreak number and reference	Outbreak site	Vehicle	Estimated dose	Total number of subjects	Number of subjects infected	Attack Rate
1 (Strachan et al., 2001)	UK, New Deer	Sheep feces/soil	14	228	20	8.77%
2 (Nauta et al., 2001; Shinagawa et al., 1997)	Japan, Morioka	Salad/ seafood sauce	31	871	215	24.68%
3 (Keene and Sazie, 1997)	USA, Oregon	Deer jerky	10000	12	10	83.33%
4 (Uchimura et al., 1997)	Japan, Kashiwa	Melon	1100	71	32	45.07%
5 (Bell et al., 1994; Tuttle et al., 1999)	USA, Washington	Hamburger	23	5634	398	15.11%
6 (Tilden et al., 1996)	USA, Washington/ California	Salami	23	2778	17	0.61%
7 (Warrner et al., 1995)	USA, Illinois	Water	75	2350	12	0.51%
8 (Anon., 1997)	UK, Wyre	Cheese	380	360	2	0.56%

3.4.3.3 Validation Results: Traditional vs. AHP Weighted-Average

To validate the AHP weighted-average dose-response models, the data from the outbreaks documented in Table 3.14 is superimposed on the graphs for each of the dose-response models investigated. Figures 3.31 and 3.32 display the beta-Poisson and Weibull-Gamma dose-response curves and AHP weighted-average models, respectively, with the data points from the eight outbreaks. Both of the AHP weighted-average models appear to provide a good fit for the low dose outbreak data.

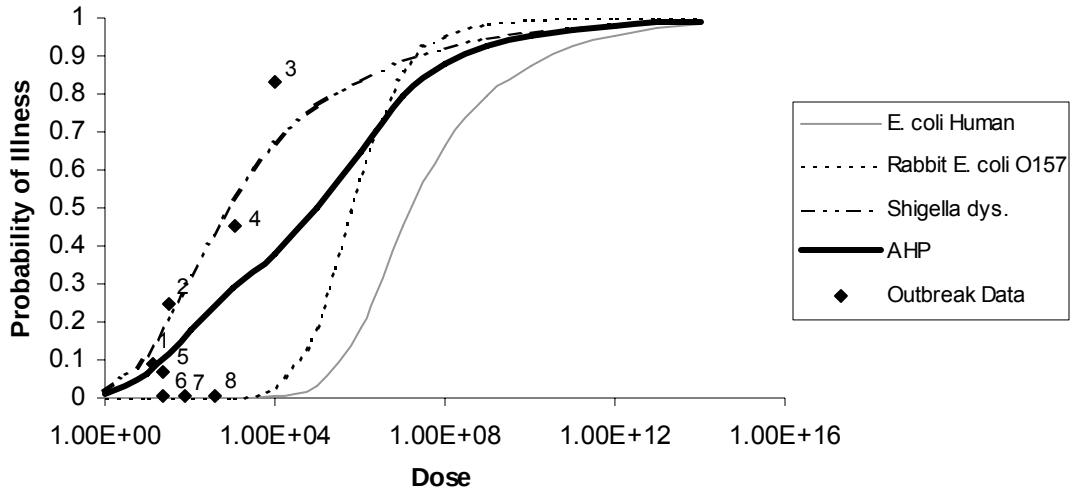


Figure 3.31: Beta-Poisson Dose-Response Curves (for data sets 4, 7, & 9) with AHP Weighted-Average Superimposed with Outbreak Data

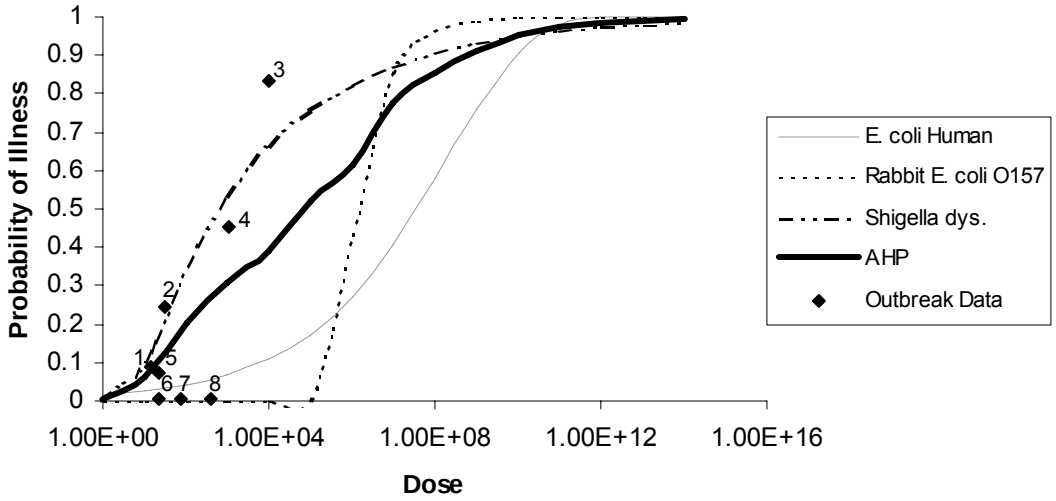


Figure 3.32: Weibull-Gamma Dose-Response Curves (for data sets 4, 7, & 9) with AHP Weighted Average Superimposed with Outbreak Data

Visual inspection of the beta-Poisson models in Figure 3.31, show that the *S. dysenteriae* model provides a good fit to data points 1, 2, 3, 4, and 5; however, this model does not appear to fit data points 6, 7, or 8. The all human *E. coli* and *E. coli*

O157:H7 rabbit models appear to fit data points 6, 7, and 8, but not 1, 2, 3, 4, or 5. Although each of these models appears to fit a few of the outbreak data points, none of these models provide a good fit to all of the outbreak data points. While the AHP model does not fit all of the data points either, it does appear to provide a good fit to data points 1, 2, 4, 5, 6, and 7. Again, visual inspection of the various Weibull-Gamma models in Figure 3.32 show that neither the all human *E. coli* nor *E. coli* O157:H7 rabbit Weibull-Gamma model appear to be a good approximation for *E. coli* O157:H7 as these models appear to only fit data points 6, 7, and 8, but not 1, 2, 3, 4, or 5. However, the *S. dysenteriae* Weibull-Gamma model does provide a good fit to data points 1, 2, 3, 4, and 5. The AHP Weibull-Gamma model provides a good fit to data points 1, 2, 4, 5, and 6. These results suggest that either the *S. dysenteriae* Weibull-Gamma model or the AHP Weibull-Gamma model may provide a good approximation for the dose-response of *E. coli* O157:H7.

Figures 3.33 and 3.34 show the AHP weighted-average dose-response curves for the beta-Poisson and Weibull-Gamma models, respectively. The three data sets used to develop the AHP weighted-average model are shown for comparison purposes along with the actual clinical trial data from which the dose-response curves are generated. While the all human *E. coli*, *E. coli* O157:H7 rabbit, and *S. dysenteriae* dose-response models fit their respective data points well, both the AHP weighted-average beta-Poisson and Weibull-Gamma models visually provide the best fit to all of the clinical trial data.

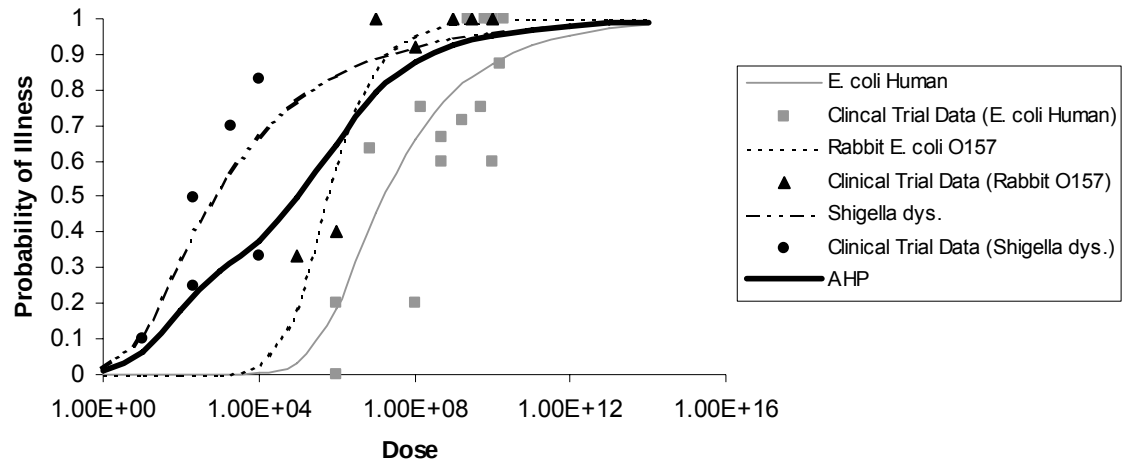


Figure 3.33: Beta-Poisson Dose-Response Curves and Clinical Trial Data Points (for data sets 4,7, & 9) with AHP Weighted-Average

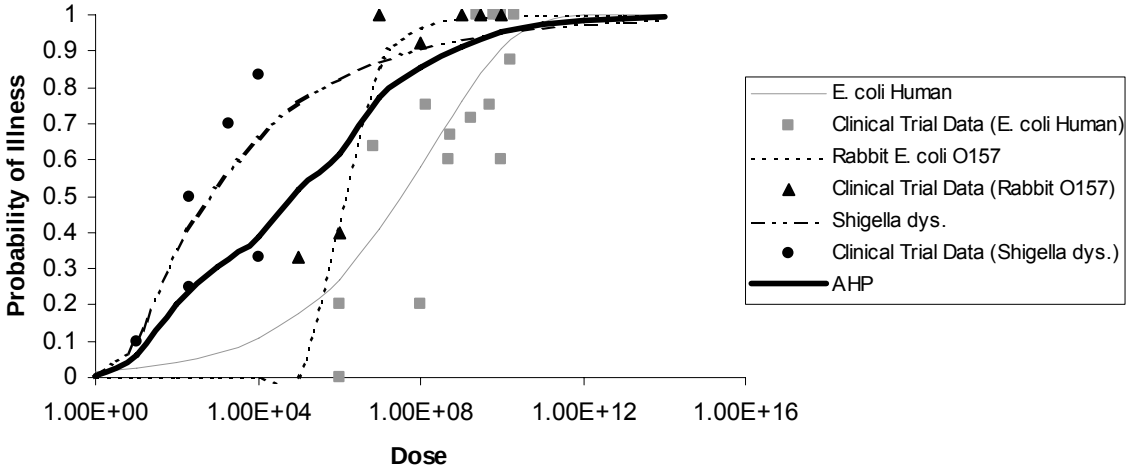


Figure 3.34: Weibull-Gamma Dose-Response Curves and Clinical Trial Data Points (for data sets 4, 7, & 9) with AHP Weighted-Average

As seen in Figures 3.31-3.34, there is wide dispersion amongst the clinical trial and outbreak data, and graphically, none of the beta-Poisson or Weibull-Gamma models alone appear to provide a good estimate to all of the available data. However, by comparing these data points to the AHP weighted-average dose-response curves for the beta-Poisson and Weibull-Gamma models, it visually appears that the AHP

method provides a reasonable fit to all of the available data. The results in Figures 3.31-3.34 are quantitatively verified by examining the deviance calculations for the various models; the model that minimizes the deviance statistic (i.e., Equation 6) best fits the outbreak data. The deviance statistic is calculated for the outbreak data, the clinical trial data, and the outbreak and clinical trial data combined. As seen in Table 3.15, the *S. dysenteriae* beta-Poisson model results in the minimum deviance for the outbreak data. However, the AHP model results in the minimum deviance for the clinical trial data and the outbreak and clinical trial data combined. While these results are not significant when the deviance is compared to the critical values of the χ^2 distribution, the AHP weighted-average model considerably reduces the deviance compared to the other models for both the clinical trial data and the clinical trial and outbreak data combined. In the case of the outbreak data, both the *S. dysenteriae* and AHP weighted-average model reduce the deviance as compared to the all human *E. coli* and *E. coli* O157:H7 rabbit models.

The results for the Weibull-Gamma model show slightly different results in that the all human *E. coli* model results in the minimum deviance for the outbreak data and the outbreak and clinical trial data combined. However, the AHP model results in the minimum deviance for the clinical trial data. Again, these results are not significant when the deviance is compared to the critical values of the χ^2 distribution; however, the AHP weighted-average model considerably reduces the deviance compared to the other models in the case of the clinical trial data. Although the all human *E. coli* model produces the minimum deviance for the outbreak and the

outbreak and clinical data combined, the AHP weighted-average model still noticeably reduces the deviance as compared to the *S. dysenteriae* model.

Table 3.15: Deviance Calculation for Dose-Response Models

		Deviance, Y			
		All human *E. coli*	***E. coli* O157 rabbit**	***S. dysenteriae***	**AHP**
Model	**Validation data**				
beta-Poisson	Outbreak Data	11622.11	26547.97	8753.08	9023.10
	Clinical Trial Data	269.05	255.70	90.66	73.22
	Outbreak & Clinical Trial Data	11891.16	9008.77	4468.70	2303.95
Weibull-Gamma	Outbreak Data	1356.00	No solution	6432.20	3085.91
	Clinical Trial Data	98.60	No solution	85.14	66.12
	Outbreak & Clinical Trial Data	1454.60	No solution	6517.34	3152.03

3.5 Risk Characterization

3.5.1 Overview of Risk Characterization

The final component in the quantitative microbial risk assessment framework is the risk characterization. The risk characterization involves the integration of the results from the consumption phase of the exposure assessment with the dose-response assessment in order to provide an overall estimate of the likelihood and magnitude of the adverse health outcomes from exposure to *E. coli* O157:H7 in cheese; in addition, this step includes aleatory and epistemic uncertainties associated with the assessment. Another important aspect of the risk characterization includes sensitivity analysis which identifies the steps and the physical conditions and/or practices at those steps (i.e., sub-system elements and basic elements) that influence the occurrence and magnitude of *E. coli* O157:H7 contamination in cheese, and therefore, the risk to consumers.

Risk may be estimated in a variety of ways. The estimated risk of an adverse health outcome may vary depending on the level at which the risk is focused and the duration of the exposure. First, the risk of an adverse health outcome may be focused on an individual consuming a single serving of cheese, the risk adverse health outcomes for a group of individuals consuming cheese from the same production lot, or the risk of an adverse health outcome across the entire United States population. Second, the risk of an adverse health outcome may be calculated per serving, per annum, or per lifetime. The decomposition of the cheese manufacturing and distribution process using the DML concept results in a model that lends itself to scenario development, thereby making the model helpful in calculating the adverse health outcomes associated with cheese-related outbreaks of *E. coli* O157:H7. Thus, this research focuses on calculating the risk of adverse health outcomes associated with exposure to *E. coli* O157:H7 in cheese for a group of individuals consuming cheese made from the same vat of milk, and is calculated on a per serving basis.

While the output of the dose-response assessment is a probability of illness (i.e., response) given exposure to *E. coli* O157:H7 (i.e., dose), several other adverse health outcomes may be assessed with a QMRA. As indicated in the hazard identification, *E. coli* O157:H7 infection can lead to many other severe health risks including: hospitalization, HUS/TTP, and death. In order to identify the adverse health outcomes to be assessed, the DML concept is applied to the risk characterization. Figure 3.35 decomposes the risk characterization into a number of adverse health outcomes to be assessed and indicates the dependencies.

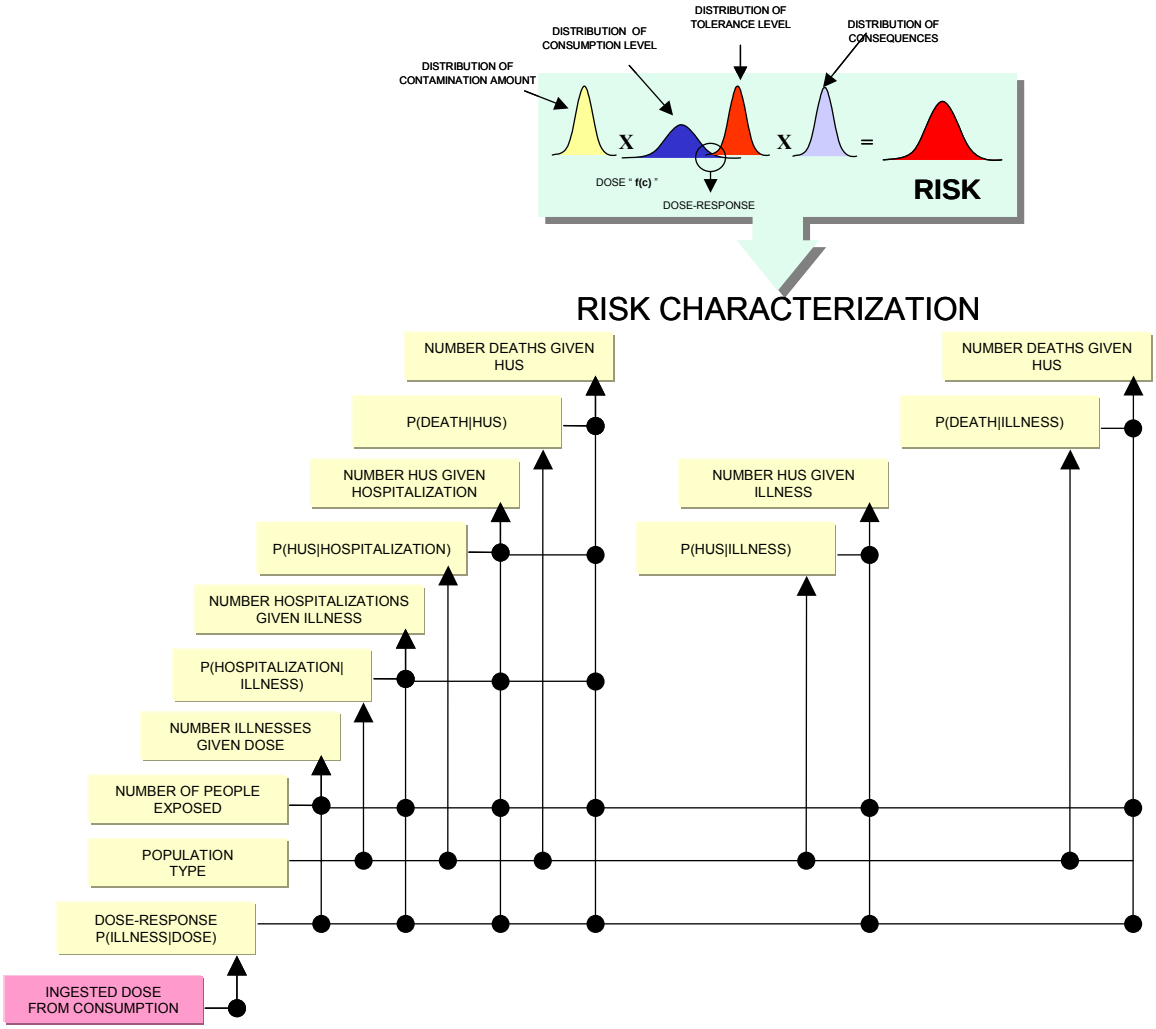


Figure 3.35: DML Model of Risk Characterization

For a particular scenario, the dose-response assessment results in a probability of illness given the ingested dose from the consumption phase. The probability of illness given the ingested dose, in combination with the number of people exposed, results in an estimated distribution of the number of illnesses for a specific outbreak scenario. As shown in Figure 3.35, the remaining risk calculations are based on the number of people exposed, the probability of a specific consequence, and the influence of the population type on the consequence of interest.

Since population type influences the proportion of illnesses progressing to adverse health outcomes, it is an important step in the risk characterization. According to Gerba et al. (1996), approximately 20% of the population in the United States is more susceptible to serious illness and mortality from foodborne pathogens. The susceptible population is comprised of the very young, the elderly, pregnant women, and the immunocompromised. Thus, the type of population affected determines the severity of the adverse health outcomes, with the susceptible population facing the most severe outcomes. However, as illustrated in Figure 3.35, the dose-response models for the normal and susceptible population are the same, with the distinction between population type accounted for in the consequence distributions. This is a similar approach to that used by Cassin et al. (1998) in which the normal and susceptible populations are assumed to have a similar vulnerability to illness following the ingestion of *E. coli* O157:H7, but the susceptible population has an increase propensity for severe health outcomes progressing from illness.

The end result of the risk characterization is an estimated distribution of the number of people affected by an adverse health outcome based on the number of people exposed, the probability of a specific consequence, and the influence of population type on consequence of interest. The risk calculations considered include: the number of hospitalizations given illness, the number of HUS/TTP cases given hospitalization, the number of deaths given HUS/TTP, the number of HUS/TTP cases given illness, and the number of deaths given illness. It should be noted that the all of the risks characterized are in the form of a distribution, as all the inputs (i.e.,

contamination/serving, consumption, tolerance, and consequences) to the risk calculation are distributions.

3.5.2 Methodology for Consequence Distributions

Although the dose-response assessment is used to calculate the probability of illness given *E. coli* O157:H7 exposure, the probability of *E. coli* O157:H7-related illnesses progressing to other severe health outcomes needs to be determined for both the normal and susceptible populations. Surveillance data provides the best estimate of the incidence of various adverse health outcomes due to *E. coli* O157:H7 infection. Typically, surveillance data for foodborne outbreaks is given in terms of the number of illnesses, hospitalizations, HUS/TTP, and deaths. This data is utilized to determine the proportion of *E. coli* O157:H7 illnesses that progress to more severe outcomes such as hospitalization, HUS/TPP, and death. Probability distributions are used to describe the outbreak data and updated using Bayesian inference to account for the uncertainty about the proportion of illnesses progressing to severe adverse health outcomes.

Previous research has also accounted for the uncertainty associated with the underreporting of outbreaks (Powell et al., 2000; Powell et al., 2001); however, these previous analyses focused on estimating the annual risk due to *E. coli* O157:H7 exposure for the entire United States population. Since this research focuses on calculating the adverse health outcomes of a specific *E. coli* O157:H7 outbreak scenario, it is assumed that all cases associated with the outbreak are reported. Therefore, the risk characterization does not account for the underreporting of cases.

3.5.2.1 *E. coli* O157:H7 Surveillance Data

3.5.2.1.1 Normal Population

Epidemiological data for *E. coli* O157:H7 foodborne outbreaks is collected from several sources for the normal population in order to determine the proportion of *E. coli* O157:H7 illnesses that progress to more severe adverse health outcomes. First, FoodNet (Foodborne Diseases Active Surveillance Network), publishes annual reports containing a summary of *E. coli* O157:H7 outbreaks collected through active surveillance. FoodNet obtains this surveillance data from laboratories in several states including Connecticut, Georgia, Maryland, Minnesota, Oregon, and Tennessee and select counties in California, Colorado, and New York. Second, the CDC's Foodborne Outbreak Response and Surveillance Unit collects data on *E. coli* O157:H7 outbreaks and clusters due to foodborne, waterborne, and person-to-person transmission reported to CDC by the states or regulatory agencies; the Foodborne Outbreak Response and Surveillance Unit also provides annual summaries of these *E. coli* O157:H7 outbreaks. Finally, unpublished *E. coli* O157:H7 foodborne outbreak data from the CDC is obtained from Powell et al. (2001). The outbreak data collected includes information on the number of illnesses and the number of hospitalizations, HUS/TTP cases, and deaths resulting from *E. coli* O157:H7 illness. Based on the *E. coli* O157:H7 foodborne outbreak data collected between 1982-2003 there are 8,894 cases of illness. Of these 8,894 illnesses, 2,430 cases resulted in hospitalization, 488 cases progressed to HUS/TTP, and 58 cases resulted in death. Table 3.16 provides a summary of this data in terms of the adverse health outcomes for the normal population.

Table 3.16: Summary of Surveillance Data used for Consequence Determination of Normal Population

Reference	Year	Ill	Hospitalized	HUS/TTP	Deaths
Powell et al., 2001	1982-1998	4478	968	228	28
FoodNet Annual Report, 1999	1999	510	199	37	7
FoodNet Annual Report, 2000	2000	626	262	58	7
FoodNet Annual Report, 2001	2001	560	214	56	3
FoodNet Annual Report, 2002	2002	636	249	58	4
FoodNet Annual Report, 2003	2003	444	173	---	4
CDC, 1999	1998	377	73	8	1
CDC, 2000	1999	659	96	15	2
CDC, 2001	2000	206	70	10	1
CDC, 2002	2001	131	53	8	0
CDC, 2003	2002	267	63	10	1
TOTAL		**8894**	**2420**	**488**	**58**

It should be noted that for the normal population, an effort has been made so as not to duplicate any of the outbreak data, include non-foodborne related *E. coli* O157:H7 outbreak data, or include data specifically related to the susceptible population. First, the unpublished foodborne *E. coli* O157:H7 outbreak data from Powell et al. (2001) encompasses data from 1982-1998. For this reason, data from the FoodNet Annual Reports from 1996, 1997, and 1998 is omitted. The Foodborne Outbreak Response and Surveillance Unit annual reports provide information on the vehicle of transmission, the setting, and the state in which the outbreak occurred. Data relating to non-foodborne *E. coli* O157:H7 outbreaks, settings which include the susceptible population, and outbreaks occurring in any of the states (i.e., CT, GA, MD, MN, OR, TN, CA, CO, and NY) monitored by FoodNet are eliminated.

3.5.2.1.2 Susceptible Population

The epidemiological data for determining the proportion of *E. coli* O157:H7 illnesses progressing to more severe adverse health outcomes for the susceptible population is collected from reported cases in the literature and the Foodborne Outbreak Response and Surveillance Unit annual summaries. In addition to providing information on the various health outcomes and the vehicle of infection for a particular *E. coli* O157:H7 outbreak, the Foodborne Outbreak Response and Surveillance Unit annual summaries also provide information on the setting in which the outbreak occurred. Settings involving day care, schools, and retirement communities are utilized in order to determine the proportion of *E. coli* O157:H7 illnesses progressing to severe outcomes for the susceptible population. For each *E. coli* O157:H7 outbreak, the data collected for the susceptible population includes not only the number of illnesses, but also the number of hospitalizations, HUS/TTP cases, and deaths resulting from those illnesses. Based on the *E. coli* O157:H7 outbreak data collected from various sources between 1980-2002 there are 495 cases of illness. Of these 495 *E. coli* O157:H7 illnesses among the susceptible population, 126 resulted in hospitalization, 34 progressed to HUS/TTP, and 30 resulted in death. Table 3.17 provides a summary of this data in terms of the adverse health outcomes for the susceptible population.

Table 3.17: Summary of Surveillance Data used for Consequence Determination of Susceptible Population

Reference	Year	Ill	Hospitalized	HUS/TTP	Deaths
Griffin et al., 1988	1980-1986	178	69	20	30
Griffin et al., 1991	1988-1990	125	8	1	0
CDC, 1999	1998	21	7	2	0
CDC, 2000	1999	45	9	2	0
CDC, 2001	2000	43	10	4	0
CDC, 2002	2001	40	18	5	0
CDC, 2003	2002	43	5	1	0
TOTAL		**495**	**126**	**34**	**30**

3.5.2.2 Characterization of Consequence Uncertainty

Although proportions of *E. coli* O157:H7 illnesses progressing to severe adverse health outcomes can be developed from the surveillance data collected, there is uncertainty about these proportions. This research accounts for the uncertainty regarding the number of illnesses that progress to more severe health outcomes (i.e., hospitalization, HUS/TTP, and death) through Bayesian inference. By selecting a distribution to represent the prior state of knowledge about a particular adverse health consequence, and updating the prior with the observed surveillance data (i.e., the likelihood), a posterior distribution which accounts for the uncertainty about the surveillance data can be obtained. Thus, knowledge of Bayes' theorem is needed in order to understand the selection of the prior distribution and likelihood function for developing the posterior distribution to characterize the uncertainty. Bayes' theorem may be written as:

$$f(\theta \mid X) = \frac{\pi(\theta) l(X \mid \theta)}{\int \pi(\theta) l(X \mid \theta) d\theta} \tag{3.10}$$

Where the prior distribution is represented by $\pi(\theta)$, the likelihood function is represented by $l(X \mid \theta)$, and the posterior distribution is represented by $f(\theta \mid X)$. The

prior distribution is the density function of the prior belief about the parameter θ before the observed data, X, is obtained. In other words, the prior distribution is not a probability distribution of θ but rather an uncertainty distribution, as it represents the state of knowledge about θ before the data X is observed. The likelihood function is the calculated probability of randomly observing the data X for a given value of θ, with the shape of the likelihood function embodying the amount of information contained in the data. Finally, the posterior distribution is the description of the state of knowledge of θ after the observed data X is obtained, given the prior belief of the value of θ before X is observed (Vose, 2000).

In terms of Bayesian inference, the *E. coli* O157:H7 outbreak surveillance data represents the likelihood, or observed data, and a probability distribution is needed to describe this data. The surveillance data collected represents a binomial process, where the probability of the consequence of interest, p, can be estimated from the number of observations, n, resulting in s consequences of interest. Selection of the conjugate prior for the binomial likelihood results in a posterior distribution belonging to the same distribution family as the prior, thus avoiding complicated mathematics (Vose, 2000).

By selecting the Beta-binomial conjugate pair, the resulting posterior distribution will be in the form of a Beta distribution. This posterior Beta distribution represents the uncertainty about the binomial distribution representing the surveillance data and can be derived as follows. The prior distribution is represented by Beta (α_1, α_2) and has a probability density function $f(\theta)$ given by:

$$f(\theta) = \frac{\theta^{\alpha_1 - 1}(1-\theta)^{\alpha_2 - 1}}{\int_0^1 t^{\alpha_1 - 1}(1-t)^{\alpha_2 - 1}\,dt} \tag{3.11}$$

The likelihood function represents the surveillance data and is in the form of a binomial distribution. Thus, the likelihood function $l(s,n;\theta)$ is given by:

$$l(s,n;\theta) = \binom{n}{s}\theta^s(1-\theta)^{n-s} \tag{3.12}$$

Where θ represents the parameter *p*, or the probability of the consequence of interest, and $\binom{n}{s}$ is constant for the given data set. Thus, the Beta distribution and the binomial likelihood function have the same functional form in θ, that is $\theta^a(1-\theta)^b$, where *a* and *b* are constants (Vose, 2000).

Since the posterior distribution is a product of the prior and likelihood functions, it will have the same functional form; the resulting posterior distribution is:

$$f(\theta \mid s,n) = \frac{\theta^{\alpha_1 - 1 + s}(1-\theta)^{\alpha_2 - 1 + n - s}}{\int_0^1 t^{\alpha_1 - 1 + s}(1-t)^{\alpha_2 - 1 + n - s}\,dt} \tag{3.13}$$

Where $f(\theta \mid s, n)$ is the Beta($\alpha_1 + s$, $\alpha_2 + n - s$) distribution.

3.5.2.3 Consequence Distribution Results

No prior information about the proportion of illnesses progressing to adverse health outcomes is known for either population; therefore, an uninformed distribution should be used for the prior distribution as it adds no information to the Bayesian inference. A Uniform(0,1) distribution is considered an uninformed prior for estimating a binomial probability because it states that prior to collection of any data, every possible value for the true probability is equally likely. According to Vose (2000), the Beta(1,1) distribution is equivalent to the Uniform(0,1) distribution.

Therefore, using the uninformed Beta(1,1) distribution as the prior distribution for the binomial likelihood function, the posterior distribution, Beta($\alpha_1 + s$, $\alpha_2 + n - s$), becomes Beta($s + 1$, $n - s + 1$). Using the surveillance data from Table 3.16 for the normal population, the proportion of illnesses progressing to adverse health consequences, with uncertainty, can be derived. These distributions are given in Table 3.18.

Table 3.18: Uncertainty Characterization about Proportion of Severe Outcomes for Normal Population

Description of Adverse Health Consequence	Likelihood Function	Prior Distribution	Posterior Distribution
Proportion of illnesses progressing to hospitalization	$\binom{8894}{2420}\theta^{2420}(1-\theta)^{8894-2420}$	Beta(1,1)	Beta(2420+1, 8894-2420+1)
Proportion of hospitalizations progressing to HUS/TTP	$\binom{2420}{448}\theta^{448}(1-\theta)^{2420-448}$	Beta(1,1)	Beta(448+1, 2420–448+1)
Proportion of HUS/TTP progressing to death	$\binom{448}{58}\theta^{58}(1-\theta)^{448-58}$	Beta(1,1)	Beta(58+1, 448–58+1)
Proportion illnesses progressing to HUS/TTP	$\binom{8894}{448}\theta^{448}(1-\theta)^{8894-448}$	Beta(1,1)	Beta(448+1 8894–448+1)
Proportion illnesses progressing to death	$\binom{8894}{58}\theta^{58}(1-\theta)^{8894-58}$	Beta(1,1)	Beta(58+1, 8894–58+1)

Using the surveillance data from Table 3.17 for the susceptible population, the proportion of illnesses progressing to adverse health consequences, with uncertainty, can be derived. These distributions are given in Table 3.19.

Table 3.19: Uncertainty Characterization about Proportion of Severe Outcomes for Susceptible Population

Description of Adverse Health Consequence	Likelihood Function	Prior Distribution	Posterior Distribution
Proportion of illnesses progressing to hospitalization	$\binom{495}{125}\theta^{126}(1-\theta)^{495-126}$	Beta(1,1)	Beta(126+1, 495-126+1)
Proportion of hospitalizations progressing to HUS/TTP	$\binom{126}{34}\theta^{34}(1-\theta)^{126-34}$	Beta(1,1)	Beta(34+1, 126–34+1)
Proportion of HUS/TTP progressing to death	$\binom{34}{30}\theta^{30}(1-\theta)^{34-30}$	Beta(1,1)	Beta(30+1, 34–30+1)
Proportion illnesses progressing to HUS/TTP	$\binom{495}{34}\theta^{34}(1-\theta)^{495-34}$	Beta(1,1)	Beta(34+1 495–34+1)
Proportion illnesses progressing to death	$\binom{495}{30}\theta^{30}(1-\theta)^{495-30}$	Beta(1,1)	Beta(30+1, 495–30+1)

3.5.3 Risk Characterization Decomposition

In terms of the DML method, the risk characterization may be thought of as a system element of the quantitative microbial risk assessment. As such, the risk characterization can be decomposed into sub-system elements as well. The end result of the consumption phase (i.e., the distribution of the ingested dose of *E. coli* O157:H7) is an input to the dose-response model, and based on the population type and number of people exposed, a number of different risk distributions can be estimated. Section 3.5.2 explained the methodology for determining the probability distributions that describe the various adverse health consequences resulting from illness. The following sections provide a detailed discussion of how these consequence distributions are used in the various risk calculations.

3.5.3.1 Risk Characterization Step D1: Dose-Response Model

Step D1 in the DML decomposition of the risk characterization of *E. coli* O157:H7 represents the dose-response assessment, as discussed in section 3.4. Step D1 determines the dose-response model used to calculate the probability of illness given the ingested dose, and thereby influences the remaining adverse health outcomes in the risk characterization. Developing a dose-response model for *E. coli* O157:H7 is a difficult task due to both model and data uncertainty. Although there are a number of different dose-response models that describe the relationship between the level of microbial exposure and the likelihood of occurrence of an adverse health consequence, there is no consensus on which specific model is most applicable to *E. coli* O157:H7. In addition, due to the severe nature of *E. coli* O157:H7, volunteer human dose-response studies are not possible, resulting in much uncertainty about the

data used for parameter estimation of the dose-response model. The DML concept is used in step D1 to identify various dose-response models, as well as various data sets from which the model parameters can be calculated. Figure 3.36 gives the DML decomposition for step D1.

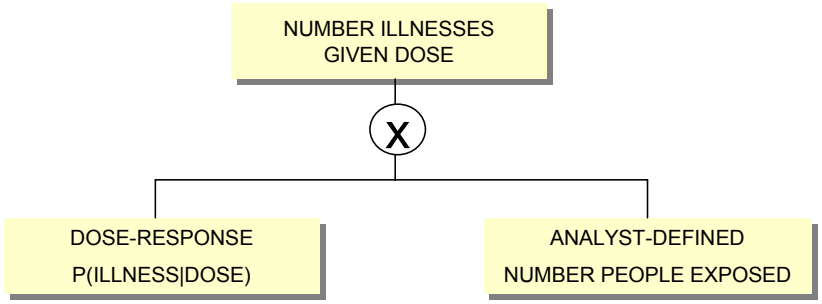


Figure 3.36: DML Decomposition of Consumption Step D1 (Dose-Response Model)

3.5.3.2 Risk Characterization Step D2: Number of Illnesses Given Dose

Step D2 estimates the distribution of the number of illnesses in the exposed population given the ingested dose. The inputs to this calculation are the probability of illness given the ingested dose, calculated from the dose-response model in step D1, and the number of people in the exposed population. The number of people in the exposed population is a user-defined input. Again, for this calculation, the population type is not an input, as the normal and susceptible populations are assumed to have a similar vulnerability to illness following the ingestion of *E. coli* O157:H7. The susceptible population's increased propensity for severe health outcomes progressing from illness is accounted for in the remaining risk calculations. Figure 3.37 represents the DML decomposition for step D2.

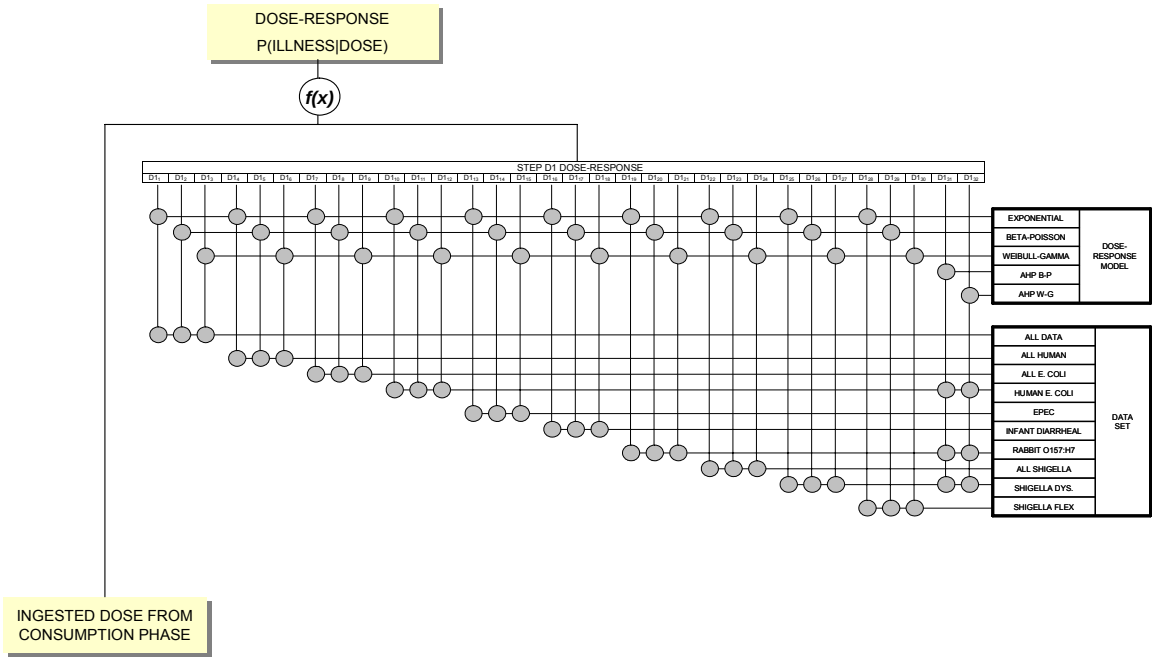


Figure 3.37: DML Decomposition of Consumption Step D2 (Number of Illnesses Given Dose)

3.5.3.3 Risk Characterization Step D3: Number of Hospitalizations Given Illness

Step D3 estimates the distribution of the number of hospitalizations in the exposed population given the illness. The inputs to this calculation are the probability of illness given the ingested dose, calculated from the dose-response model in step D1, the number of people in the exposed population, and the population specific probability of hospitalization given illness. Figure 3.38 represents the DML decomposition for step D3.

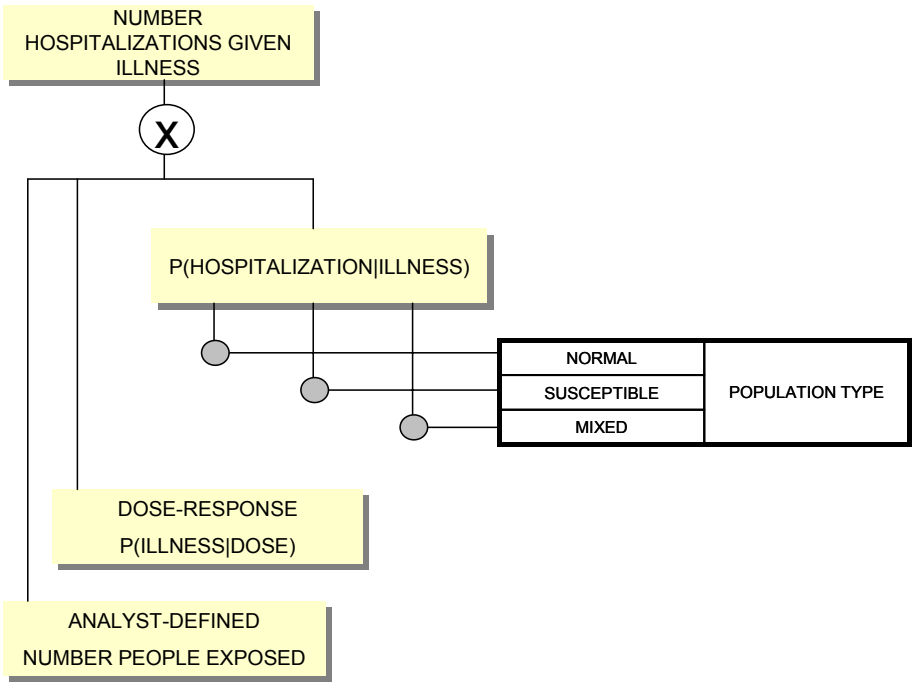


Figure 3.38: DML Decomposition of Consumption Step D3 (Number of Hospitalizations Given Illness)

3.5.3.4 Risk Characterization Step D4: Number of HUS/TTP Cases Given Hospitalization

Step D4 estimates the distribution of the number of HUS/TTP cases in the exposed population given hospitalization. The inputs to this calculation are the probability of illness given the ingested dose, calculated from the dose-response model in step D1, the number of people in the exposed population, and the population specific adverse health consequences of the probability of hospitalization given illness and the probability of HUS/TTP given hospitalization. Figure 3.39 represents the DML decomposition for Step D4.

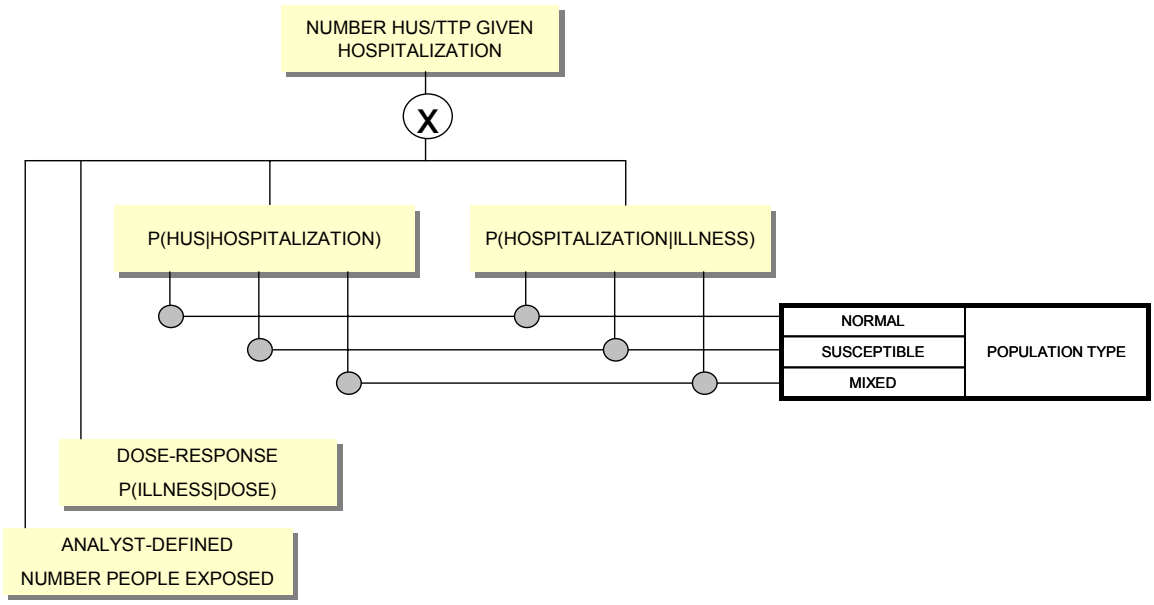


Figure 3.39: DML Decomposition of Consumption Step D4 (Number of HUS/TTP Cases Given Hospitalization)

3.5.3.5 Risk Characterization Step D5: Number of Deaths Given HUS/TTP

Step D5 estimates the distribution of the number of deaths in the exposed population given HUS/TTP. The inputs to this calculation are the probability of illness given the ingested dose, calculated from the dose-response model in step D1, the number of people in the exposed population, and the population specific adverse health consequences of the probability of hospitalization given illness, the probability of HUS/TTP given hospitalization, and the probability of death given HUS/TTP. Figure 3.40 represents the DML decomposition for Step D5.

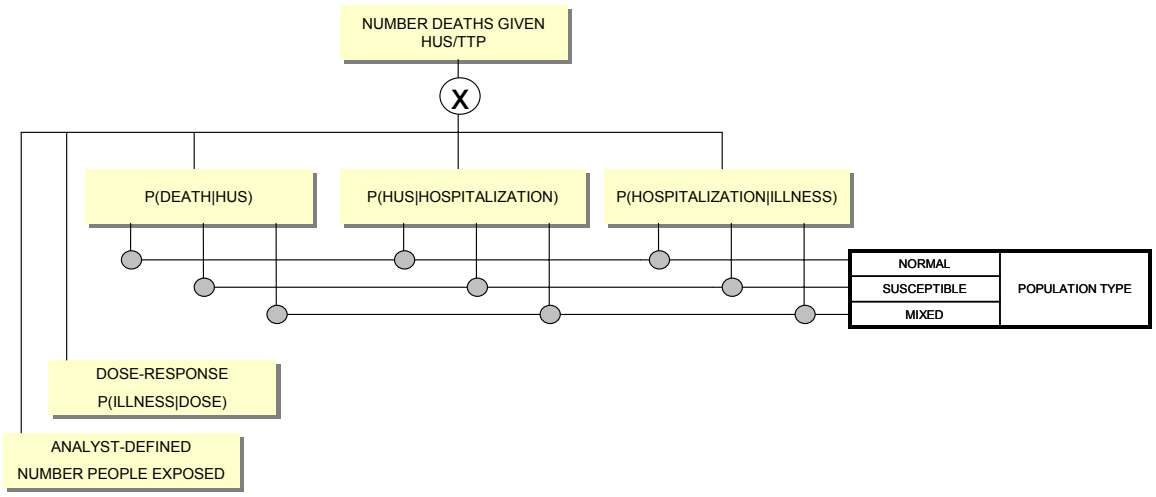


Figure 3.40: DML Decomposition of Consumption Step D5 (Number of Deaths Given HUS/TTP)

3.5.3.6 Risk Characterization Step D6: Number of HUS/TTP Cases Given Illness

Step D6 estimates the distribution of the number of HUS/TTP cases in the exposed population given illness. The inputs to this calculation are the probability of illness given the ingested dose, calculated from the dose-response model in step D1, the number of people in the exposed population, and the population specific probability of HUS/TTP given illness. Figure 3.41 represents the DML decomposition for Step D6.

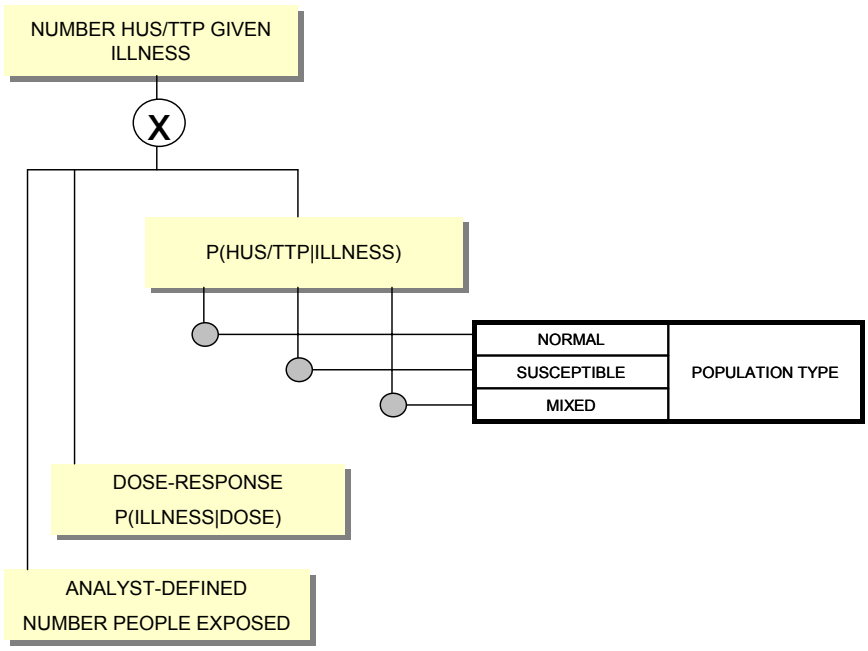


Figure 3.41: DML Decomposition of Consumption Step D6 (Number of HUS/TTP Cases Given Illness)

3.5.3.7 Risk Characterization Step D7: Number of Deaths Given Illness

Step D7 estimates the distribution of the number of deaths in the exposed population given illness. The inputs to this calculation are the probability of illness given the ingested dose, calculated from the dose-response model in step D1, the number of people in the exposed population, and the population specific probability of death given illness. Figure 3.42 represents the DML decomposition for Step D7.

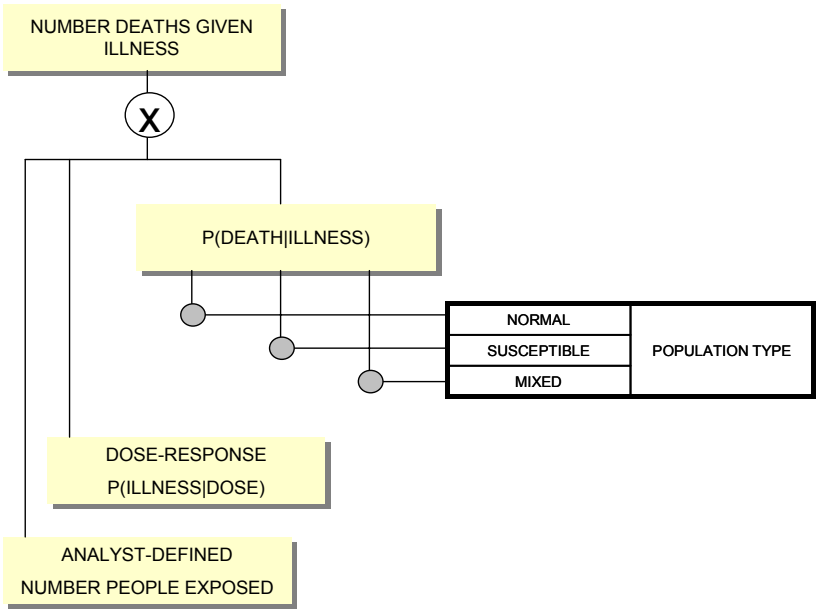


Figure 3.42: DML Decomposition of Consumption Step D7 (Number of Deaths Given Illness)

3.5.4 Risk Characterization Calculation Summary

The risk characterization element of the QMRA integrates the exposure and dose-response assessments with the consequence analysis in order to calculate the human health risk. The end result of the consumption phase (i.e., step C3) is the input for the dose-response assessment, and based on the probability of illness given the ingested dose, the number of exposed people, and the population specific probability of an adverse health outcome, any number of risks can be estimated. A summary of the risk characterization calculations is given in Table 3.20.

Table 3.20: Risk Characterization Calculations

Step	Description	Distribution/Model	Calculation	Unit
D1	Dose-Response (P(Illness|Dose)	Analyst-selected Model and Data Sets	*f*(C3)	probability
D2	Number of Illnesses Given Dose	Analyst-defined number exposed	D1*(# exposed)	people
D3	Number of Hospitalizations Given Illness	Beta D3*i*[a] (*i* = 1–3)	D2*D3*i*	people
D4	Number of HUS/TTP Cases Given Hospitalization	Beta D4*i* (*i* = 1–3)	D3*D4*i*	people
D5	Number of Deaths Given HUS/TTP	Beta D5*i* (*i* = 1–3)	D4*D5*i*	people
D6	Number of HUS/TTP Cases Given Illness	Beta D6*i* (*i* = 1–3)	D2*D6*i*	people
D7	Number of Death Given Illness	Beta D7*i* (*i* = 1–3)	D2*D7*i*	people

[a]Beta distribution for specific risk characterization step, based on population type(i.e., normal, susceptible, or mixed)

4. ENGINEERING-BASED PROBABILISTIC RISK ASSESSMENT APPLICATION RESULTS

4.1 Results Overview

The model described in the exposure assessment is integrated with the dose-response assessment in order to estimate a number of different risks for a particular outbreak. The exposure assessment estimates not only the level of *E. coli* O157:H7 contamination along the various steps of the cheese manufacturing and distribution processes, but also provides an estimate of the dose. The dose-response model is then used to describe the probability of illness given the estimated dose. Finally, the adverse health consequences resulting from illness can be characterized. The result is an estimate of the overall likelihood and magnitude of the adverse health outcomes from the exposure to the ingested dose of *E. coli* O157:H7, with the associated uncertainty.

One of the key advancements of this research is the development of a model that can assess any number of scenarios for the cheese manufacturing and distribution process and provide various risk estimates for these scenarios. The Dynamic Master Logic (DML) decomposition of the process into basic elements with various options allows this model to represent the cheese-making process for a wide variety of cheese types and also account for mistreatment of the cheese during production and distribution. While previous research focused on a process risk model (PRM) in order to assess one particular scenario, the DML concept results in the ability to construct and analyze multiple scenarios. Furthermore, by changing the selections

within a scenario, various sensitivity analyses can be performed and possible mitigation strategies assessed.

The results discussed in this chapter are based on a particular scenario developed with the model, with the purpose of demonstrating how the model can be used as both a risk assessment and risk management tool. A case study is performed in order to demonstrate how the model can be used as a risk assessment tool by estimating the *E. coli* O157:H7 contamination at various points along the exposure path and then characterizing the adverse health consequences. In addition, critical points in the cheese exposure path that most significantly influence risk are identified in the case study and used to identify possible risk mitigations. These various mitigation strategies are then imposed on the case study; by comparing the results from the control strategies to the baseline case study, the model demonstrates its value as a risk management and decision making tool as well. Finally, a worst-case analysis is performed on the case study in order to determine the sensitivity of the model to a variety of factors.

4.2 Methodology

The results of this risk assessment consider both aleatory and epistemic uncertainty. As discussed in Chapter 1, an important part of a probabilistic quantitative microbial risk assessment (QMRA) is the inclusion of both types of uncertainty. Again, aleatory uncertainty, or variability, refers to the real and identifiable differences in nature and represents the diversity in a well-characterized population or parameter. In contrast, epistemic uncertainty arises from a lack of

knowledge, and may be related to the model used to characterize the risk, the parameters used to provide values for the model, or both (Thompson, 2002). Thus, recognizing and characterizing both the aleatory and epistemic uncertainty in a risk assessment is important, as these have different implications in the risk assessment results, and therefore, the risk management decisions (Thompson, 2002). If aleatory and epistemic uncertainties are not separated within a risk assessment, the simulation on such a model randomly selects from all the distributions (i.e., aleatory uncertainty distributions and epistemic uncertainty distributions). The resultant output distribution is a composite distribution of both uncertainty components. The output distribution becomes difficult to interpret in this case, as the vertical scale represents neither aleatory nor epistemic uncertainty. To this end, information is lost regarding what part of the resultant distribution is due to the inherent variability and what part is due to a lack of knowledge. In other words, mixing the aleatory and epistemic uncertainty eliminates the ability to determine how much of the total uncertainty comes from variability and from epistemic uncertainty (Vose, 2000). For this reason, it is crucial that aleatory and epistemic uncertainty be separated within the risk assessment.

Separating the aleatory and epistemic uncertainty within a risk assessment results in the ability to identify which part of the total uncertainty is due to epistemic uncertainty and/or aleatory uncertainty. This is important when making risk management decisions because if the total uncertainty is due mostly to aleatory uncertainty then additional data collection is not warranted; the only way to reduce the total uncertainty is to change the physical system. In contrast, if the total

uncertainty is due mostly to epistemic uncertainty then collecting additional information reduces the uncertainty and improves future estimates. Thus, the separation of aleatory and epistemic uncertainty underscores the steps that can be taken to reduce the total uncertainty of the model, and measures the value of more information versus potential changes to the system (Vose, 2000).

Clearly, it is important to develop a second-order model (i.e., a model that separates uncertainty and variability), and there are several Monte Carlo simulation approaches that can be used to accomplish this task. A two-dimensional Monte Carlo simulation methodology is used in this model to properly disaggregate and evaluate the consequences of aleatory and epistemic uncertainty. This methodology employs a two-loop approach in which the aleatory and epistemic uncertainties are simulated separately. The resultant outputs illustrate the aleatory uncertainty about the x-axis and the epistemic uncertainty about the y-axis.

4.3 Case Study

4.3.1 Baseline Case Study Assumptions

The results generated for the baseline case study are based on one particular scenario entered into the model. The following tables list the sub-system elements, basic elements, and options for the basic elements, as well as the selections made for the baseline case study for each of the system elements (i.e., production, distribution, consumption, and risk characterization). Table 4.1 documents the selections made for the production phase, with these selections emulating cheddar cheese production. An initial distribution of 10±10 CFU/ml is entered as the concentration of *E. coli*

O157:H7 in the raw milk. The milk is held in storage for 2 days at a temperature between 5-8ºC, and receives no heat treatment. Consistent with cheddar cheese production, a mesophilic starter culture is then added to the milk. The curd is cut and then cooked at a temperature of 36-40ºC, also consistent with cheddar cheese. The whey is removed, a dry salt is applied to the cheddar cheese curds, and the salted curds are then placed in hoops and pressed. Typically, cheddar cheese is ripened for at least 60 days; in addition, the PMO Revision 2001 states that raw milk cheese must be ripened for at least 60 days. Thus, a ripening time of 75 days is selected.

Table 4.1: Production Phase Case Study Selections

Step	Sub-System Element Description	Basic Elements	Options	Case Study Selection
A0	Initial *E. coli* O157:H7 Contamination (CFU/ml)	---	Analyst-defined	10 ± 10 CFU/ml
A1	Contamination after Milk Storage	Time	1 day 2 days 3 days 4 days 5 days	2 days
		Temperature	Temp ≤5˚C 5˚C < Temp < 8˚C Temp = 8˚C Temp > 8˚C	5˚C < Temp < 8˚C
A2	Contamination after Milk Heat Treatment	Milk Treatment	Pasteurized Milk Unpasteurized Milk Heat Treated Milk	Unpasteurized Milk
A3	Contamination after Addition of Coagulant	Type of Starter Culture	Mesophilic Thermophilic	Mesophilic
		Milk Treatment	Determined by A2 selection	---
A4	Contamination after Cutting of Curd	Milk Treatment	Determined by A2 selection	---
A5	Contamination after Cooking of Curd	Temperature	30˚C ≤ Temp < 32˚C 33˚C ≤ Temp ≤ 35˚C 36˚C ≤ Temp ≤ 40˚C Temp > 40˚C	36˚C ≤ Temp ≤ 40˚C
		Milk Treatment	Determined by A2 selection	---
A6	Contamination after Separation of Curd and Whey	Milk Treatment	Determined by A2 selection	---
A7	Contamination after Salting	Type of Salt	Dry Brine	Dry
		Milk Treatment	Determined by A2 selection	---
A8	Contamination after Hooping and Pressing	Milk Treatment	Determined by A2 selection	---
A9	Contamination after Packaging and Ripening	Time	14 days 27 days 45 days 75 days 90 days 104 days 150 days	75 days
		Milk Treatment	Determined by A2 selection	---

Table 4.2 documents the selections made for the distribution phase. The pH of cheddar cheese is 6.0, and this selection is held constant through the various steps in the distribution phase. Next, minimum and maximum times are entered for each step. Finally, the temperature is selected for each step. The temperatures selected for the baseline case study are meant to reflect moderate temperature abuse.

Table 4.2: Distribution Phase Case Study Selections

Step	Sub-System Element Description	Basic Elements	Options	Case Study Selection
B1	Contamination after Storage, before Transportation	pH[1]	4.5 5 5.5 6 6.5 7 7.5 8 8.5	6.0
		Time	Analyst-defined	1 - 24 hours
		Temperature	5˚C 8˚C 10˚C 12˚C 19˚C 28˚C 37˚C 42˚C	5˚C
B2	Contamination after Transportation to Retail	Time	Analyst-defined	1 - 12 hours
		Temperature	5˚C 8˚C 10˚C 12˚C 19˚C 28˚C 37˚C 42˚C	10˚C
B3	Contamination after Retail Storage	Time	Analyst-defined	1 - 120 hours
		Temperature	5˚C 8˚C 10˚C 12˚C 19˚C 28˚C 37˚C 42˚C	5˚C
B4	Contamination after Transportation to Consumer	Time	Analyst-defined	1- 2 hours
		Temperature	5˚C 8˚C 10˚C 12˚C 19˚C 28˚C 37˚C 42˚C	12˚C
B5	Contamination after Consumer Storage	Time	Analyst-defined	1 - 336 hours
		Temperature	5˚C 8˚C 10˚C 12˚C 19˚C 28˚C 37˚C 42˚C	5˚C

[1]pH held constant for remaining distribution steps

Table 4.3 documents the selections made for the consumption phase. The only input for the consumption phase is the number of servings of cheese consumed. The serving size is entered as a minimum and maximum. For the baseline case study,

it is assumed that the average person consumes between 1-3 servings of contaminated cheese.

Table 4.3: Consumption Phase Case Study Selections

Step	Sub-System Element Description	Basic Elements	Options	Case Study Selection
C1	Contamination in One Serving	---	---	---
C2	Number of Servings Consumed	Serving Size	Analyst-defined	1 – 3 servings
C3	Ingested Dose	---	---	---

Finally, Table 4.4 documents the selections made for the risk characterization portion of the model. For the risk characterization element, several selections are made for the dose-response model and the data set for parameter estimation basic elements. By generating results for various dose-response models, the model uncertainty can be assessed; furthermore, by generating results for a particular dose-response model using various data sets for the parameter estimation, the parameter uncertainty of the dose-response model can be evaluated. Thus, for the baseline case study, both the beta-Poisson and Weibull-Gamma dose-response models are selected for comparison purposes. The data sets selected for parameter estimation of the dose-response models are: all human *E. coli*, *E. coli* O157:H7 rabbit, and *S. dysenteriae*. It should be noted that the data sets selected for the parameter estimates of the beta-Poisson and Weibull-Gamma models are those that resulted in significant fits. Lastly, the AHP weighted-average models for the beta-Poisson and Weibull-Gamma relationships are also examined, as the AHP weighted-average models provide an alternative way to assess the data uncertainty associated with the dose-response models.

The adverse health outcomes characterized in this model are based on a particular outbreak scenario in which a group of individuals consume cheese from the same production and distribution scenarios. A population of 1,500 people is exposed to the *E. coli* O157:H7 contaminated cheese. The number of illnesses given the ingested dose is estimated for the population. In addition, for both the normal and susceptible populations, the number of hospitalizations given illness, the number of HUS/TTP cases given hospitalization, the number of deaths given HUS/TTP, the number of HUS/TTP cases given illness, and the number of deaths given illness are estimated in the risk characterization element of the model.

Table 4.4: Risk Characterization Case Study Selections

Step	Sub-System Element Description	Basic Elements	Options	Case Study Selection
D1	Dose-Response (P(Illness|Dose))	Dose-Response Model	Exponential Beta-Poisson Weibull-Gamma AHP beta-Poisson AHP Weibull-Gamma	Beta-Poisson Weibull-Gamma AHP beta-Poisson AHP Weibull-Gamma
		Data Set for Parameter Estimation	All Data All Human Data All *E. coli* Data All Human *E. coli* Data EPEC Infant Diarrheal *E. coli* *E. coli* O157:H7 Rabbit Data *Shigella* spp. *S. dysenteriae* *S. flexneri*	All Human *E. coli* Data *E. coli* O157:H7 Rabbit Data *S. dysenteriae*
D2	Number of Illnesses Given Dose	Number of People Exposed	Analyst-defined	1,500 people
		P(Illness|Dose)	Determined by D1 selection	---
D3	Number of Hospitalizations Given Illness	Number of People Exposed	Determined by D2 selection	---
		P(Illness|Dose)	Determined by D1 selection	---
		P(Hospitalization|Illness)	Normal Susceptible Mixed	Normal Susceptible
D4	Number of HUS/TTP Cases Given Hospitalization	Number of People Exposed	Determined by D2 selection	---
		P(Illness|Dose)	Determined by D1 selection	---
		P(Hospitalization|Illness)	Normal Susceptible Mixed	Normal Susceptible
		P(HUS|Hospitalization)	Normal Susceptible Mixed	Normal Susceptible
D5	Number of Deaths Given HUS/TTP	Number of People Exposed	Determined by D2 selection	---
		P(Illness|Dose)	Determined by D1 selection	---
		P(Hospitalization|Illness)	Normal Susceptible Mixed	Normal Susceptible
		P(HUS|Hospitalization)	Normal Susceptible Mixed	Normal Susceptible
		P(Death|HUS)	Normal Susceptible Mixed	Normal Susceptible
D6	Number of HUS/TTP Cases Given Illness	Number of People Exposed	Determined by D2 selection	---
		P(Illness|Dose)	Determined by D1 selection	---
		P(HUS|Illness)	Normal Susceptible Mixed	Normal Susceptible
D7	Number of Death Given Illness	Number of People Exposed	Determined by D2 selection	---
		P(Illness|Dose)	Determined by D1 selection	---
		P(Death|Illness)	Normal Susceptible Mixed	Normal Susceptible

Based on these selections, results are generated for the scenario entered in the model. The end result is an estimate of the distribution of *E. coli* O157:H7 contamination at various points along the exposure path, and the adverse health consequences resulting from illness. The results are presented in the form of complementary cumulative distributions and show both the uncertainty and the variability; the graphs depict the 90% confidence level, the 25th, 50th, and 75th percentiles, and the mean for the probability of exceedance.

4.3.2 Baseline Case Study Results

4.3.2.1 Contamination after Production

Based on the initial contamination level and the selections made in the production phase of the model, the number of *E. coli* O157:H7 in 1 kg of cheese after production is estimated. Figure 4.1 shows both the variability and uncertainty of the predicted distribution of *E. coli* O157:H7 after production and depicts the probability of exceeding a given amount of contamination in 1 kg of cheese.

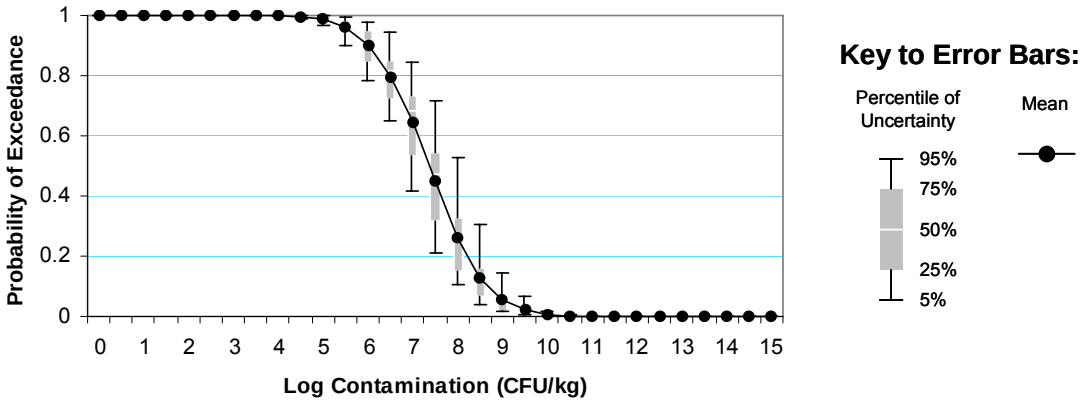
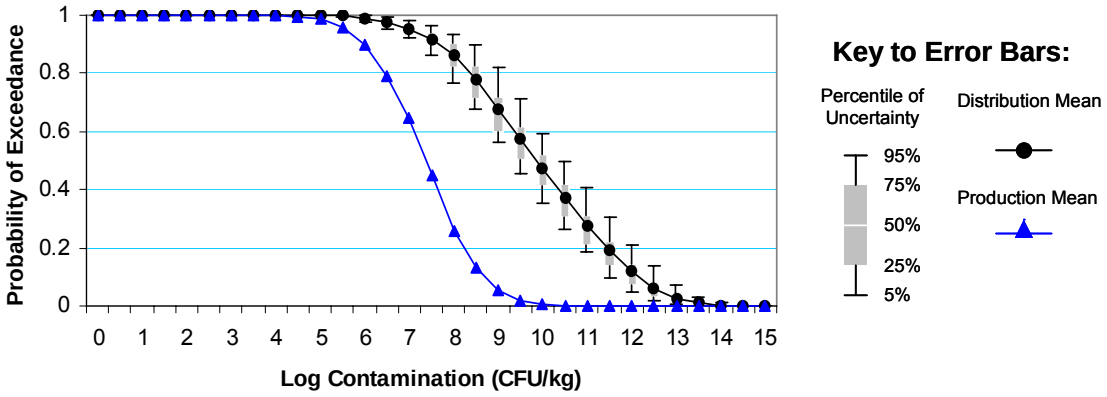


Figure 4.1: Variability and uncertainty for probability of exceeding contamination level per 1 kg cheese after production

Figure 4.1 shows a 0.79 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg, with the 90% confidence interval for the probability of exceeding this contamination level ranging from 0.65-0.94. There is approximately a 0.26 probability of exceeding a contamination level of 8.0 CFU/kg, with a 90% confidence interval of 0.11-0.53. These results demonstrate that a moderate level of initial contamination in combination with moderate abuse during the production phase can lead to high levels of *E. coli* O157:H7 contamination in the final cheese product.

4.3.2.2 Contamination after Distribution

Based on the contamination level at the end of the production phase and the selections made in the distribution phase of the model, the number of *E. coli* O157:H7 in 1 kg of cheese after distribution is estimated. Figure 4.2 shows the predicted distribution of *E. coli* O157:H7 after the distribution phase. In addition, the mean contamination after production is superimposed for the purpose of comparing of the contamination levels between the two phases. A numerical comparison of the contamination levels after production and distribution for the 5^{th} percentile, mean, and 95^{th} percentile of the 0.50 probability of exceedance is also shown.



	Production	Distribution
5th percentile	6.67	9.25
Mean	7.25	9.75
95th percentile	8.05	10.50

Figure 4.2: Variability and uncertainty for probability of exceeding contamination level per 1 kg cheese after distribution, superimposed with contamination after production results

There is a 0.97 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg after distribution, with a 90% confidence interval of 0.95-1.0. For a contamination level of 8.0 CFU/kg, there is a 0.86 probability of exceedance, with a 90% confidence interval of 0.77-0.94. Figure 4.2 also illustrates the increase in the level of contamination after distribution as compared to the contamination after production. Thus, given the contamination level after production, the mild temperature abuse in the distribution phase results in an increase in contamination. It should be noted that the increase is significant, as the uncertainty ranges for the contamination after production and contamination after distribution do not overlap.

4.3.2.3 Contamination per Gram

Based on the contamination level at the end of the distribution phase, the number of *E. coli* O157:H7 per gram of cheese is estimated. Figure 4.3 shows the predicted distribution of *E. coli* O157:H7 per gram of cheese.

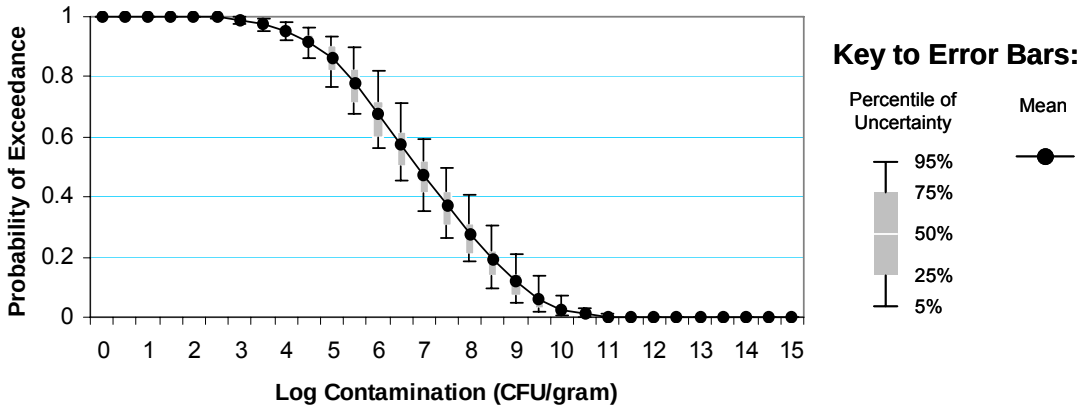


Figure 4.3: Variability and uncertainty for probability of exceeding contamination level per gram of cheese

Figure 4.3 shows that there is a 0.57 probability of exceeding a contamination level of 6.5 CFU/g, with a 90% confidence interval for the probability of exceedance ranging from 0.46-0.71. In addition, there is a 0.27 probability of exceeding 8.0 CFU/g, with a 90% uncertainty range from 0.19-0.41.

4.3.2.4 Contamination per Serving

The *E. coli* O157:H7 contamination in 1 kg of cheese after the distribution phase is also used to estimate the contamination per serving, with a serving being one ounce, or 28 grams, of cheese. Figure 4.4 shows both the variability and uncertainty of the predicted distribution of *E. coli* O157:H7 per one ounce serving of cheese.

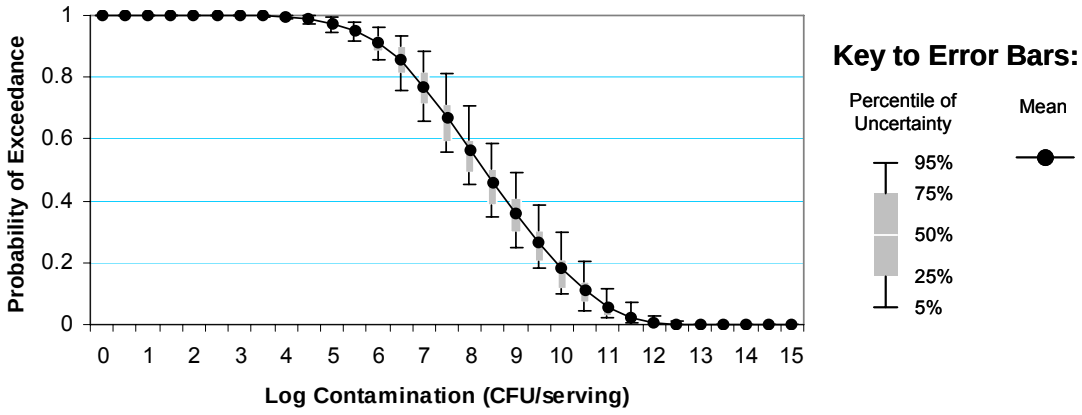


Figure 4.4: Variability and uncertainty for probability of exceeding contamination level per one ounce serving of cheese

Figure 4.4 shows approximately a 0.85 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/serving, with a 90% confidence interval of 0.76-0.93. For a contamination level of 8.0 CFU/serving there is a 0.56 probability of exceedance, with a 90% confidence interval of 0.45-0.71.

4.3.2.5 Contamination per Dose

The ingested dose varies depending on the number of servings consumed. For the baseline case study, it is assumed that the average person consumes between 1-3 servings of contaminated cheese. Using the *E. coli* O157:H7 contamination per serving and the number of servings consumed the dose is estimated. Figure 4.5 shows the predicted distribution of the dose of *E. coli* O157:H7.

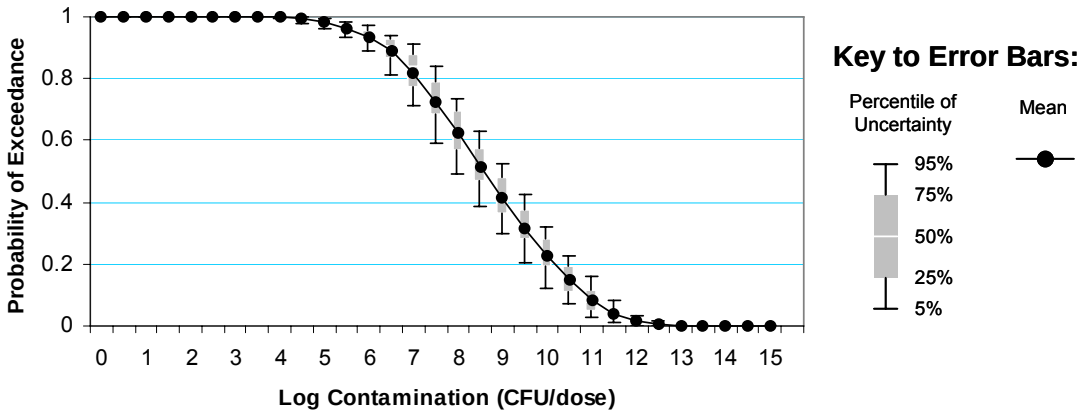


Figure 4.5: Variability and uncertainty for probability of exceeding contamination level per dose

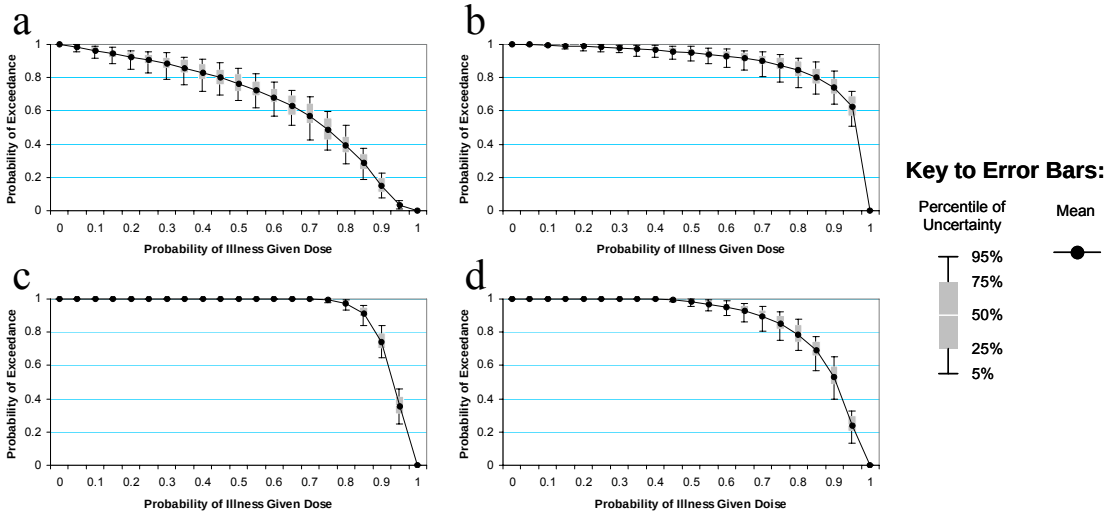
There is a 0.89 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/dose, with the 90% confidence interval for the probability of exceedance at this contamination level ranging from 0.81-0.94. For a contamination level of 8.0 CFU/dose, there is a 0.62 probability of exceedance with a 90% confidence interval of 0.49-0.73.

4.3.2.6 Probability of Illness

4.3.2.6.1 Beta-Poisson Dose-Response Model

The dose-response assessment uses the ingested dose as an input in the dose-response model in order to estimate the probability of illness. For the baseline case study, both the beta-Poisson and Weibull-Gamma models are examined, using three different data sets for the parameter estimates. The data sets for parameter estimation are: all human *E. coli*, *E. coli* O157:H7 rabbit, and *S. dysenteriae*. In addition, the AHP weighted-average models for the beta-Poisson and Weibull-Gamma relationships are also examined. Figure 4.6 compares the estimates of the probability of illness for the beta-Poisson model for the three data sets investigated and for the

AHP weighted-average model as well. A numerical comparison of the probability of illness for the various beta-Poisson dose-response models for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance is also shown.



	All human *E. coli*	*E. coli* O157:H7 rabbit	*S. dysenteriae*	AHP
5th percentile	0.64	0.95	0.92	0.87
Mean	0.74	1.00	0.93	0.90
95th percentile	0.80	1.00	0.94	0.93

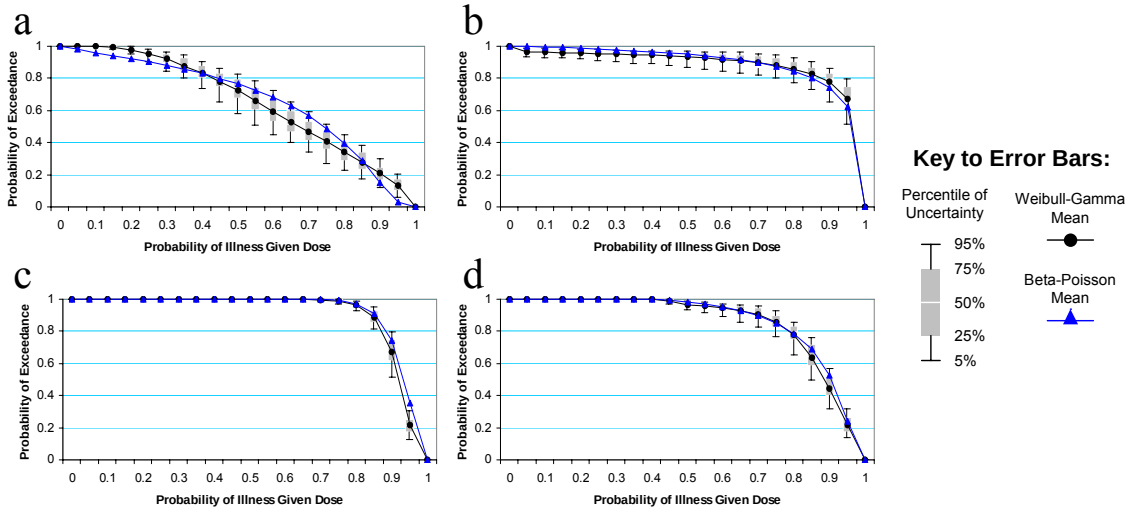
Figure 4.6: Variability and uncertainty for probability of illness given ingested dose using beta-Poisson model for (a) all human *E. coli*, (b) *E. coli* O157:H7 rabbit, (c) *S. dysenteriae*, and (d) AHP weighted-average

By generating results for a particular dose-response model using various data sets for the parameter estimation, the parameter uncertainty of the dose-response model can be evaluated. Figure 4.6a shows the results for the beta-Poisson model using parameters estimated from the all human *E. coli* data. There is a 0.90 probability of exceeding a probability of illness of 0.25, with a 90% confidence interval for the probability of exceedance of 0.83-0.96; in contrast, there is a 0.49 probability of exceeding a probability of illness of 0.75, with a 90% confidence range

from 0.36-0.60. Figure 4.6b shows the results for the beta-Poisson model using parameters estimated from the *E. coli* O157:H7 rabbit data. This results in a 0.98 probability of exceeding a probability of illness of 0.25, with a 90% confidence interval of 0.96-1.00; there is a 0.87 probability of exceeding a probability of illness of 0.75, with a 90% confidence range from 0.78-0.94. Figure 4.6c shows the results for the beta-Poisson model using parameters estimated from the *S. dysenteriae* data. There is approximately a 1.00 probability of exceeding a probability of illness of 0.25; there is a 0.99 probability of exceeding a probability of illness of 0.75, with a 90% confidence interval of 0.98-1.00. Obviously, there is wide dispersion among the results of the beta-Poisson model using these three data sets for the parameter estimates, indicating much parameter uncertainty. The *S. dysenteriae* data set provides the most conservative estimate of the probability of illness, followed by the *E. coli* O157:H7 rabbit and all human *E. coli* data sets. The AHP weighted-average model is derived from these three data sets and provides an alternative method to account for the data and parameter uncertainty associated with the dose-response relationship for *E. coli* O157:H7. Figure 4.6d shows the results for the AHP weighted-average beta-Poisson model. This model results in a 1.00 probability of exceeding a probability of illness of 0.25; there is a 0.85 probability of exceeding a probability of illness of 0.75, with a 90% confidence interval of 0.75-0.92.

4.3.2.6.2 Weibull-Gamma Dose-Response Model

In order to examine the model uncertainty, the probability of illness given the ingested dose is also estimated with the Weibull-Gamma model. For the baseline case study, the same data sets are used for the parameter estimates of the Weibull-Gamma model and the AHP weighted-average Weibull-Gamma model is investigated as well. Figure 4.7 compares the estimates of the probability of illness for the Weibull-Gamma model for the three data sets and the AHP weighted-average model; the mean beta-Poisson probability of illness is superimposed for the purpose of model comparison. A numerical comparison of the probability of illness for the various Weibull-Gamma dose-response models is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	All human *E. coli*	*E. coli* O157:H7 rabbit	*S. dysenteriae*	AHP
5th percentile	0.55	0.95	0.90	0.85
Mean	0.66	1.00	0.92	0.88
95th percentile	0.75	1.00	0.93	0.91

Figure 4.7: Variability and uncertainty for probability of illness given ingested dose using Weibull-Gamma model for (a) all human *E. coli*, (b) *E. coli* O157:H7 rabbit, (c) *S. dysenteriae*, and (d) AHP weighted-average, superimposed with mean beta-Poisson results

Figure 4.7 illustrates the parameter uncertainty for the Weibull-Gamma model. Similar to the beta-Poisson model, comparison of the three data sets for the Weibull-Gamma model shows a wide dispersion among the results. Again, the *S. dysenteriae* data set provides the most conservative estimate of the probability of illness followed by the *E. coli* O157:H7 rabbit and all human *E. coli* data sets. In addition, Figure 4.7 also illustrates the model uncertainty through comparison of the results for the beta-Poisson and Weibull-Gamma models.

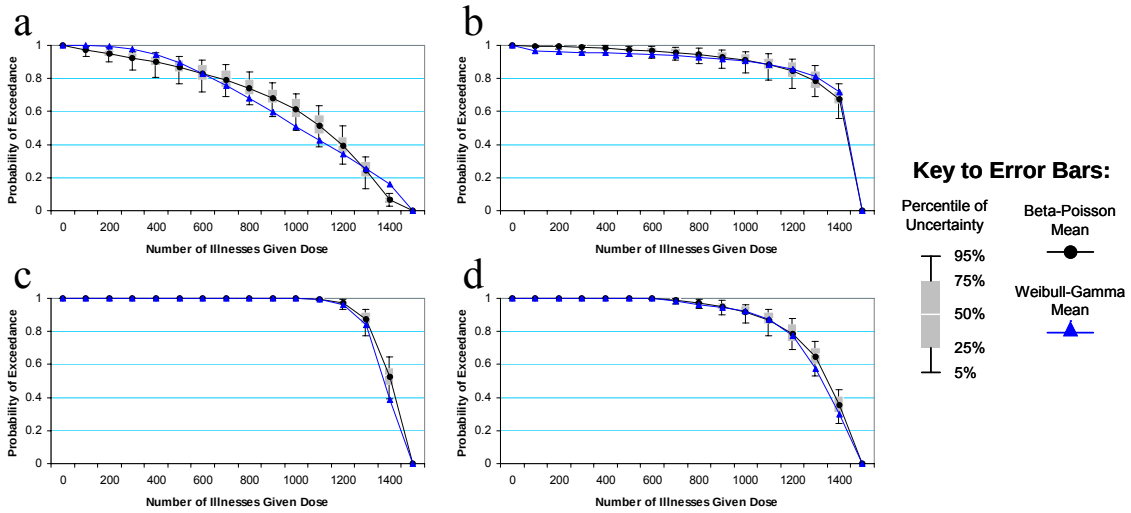
Figure 4.7a shows the results for the Weibull-Gamma model using parameters estimated from the all human *E. coli* data. There is a 0.95 probability of exceeding a probability of illness of 0.25, with a 90% confidence interval of 0.91-0.98; in contrast, there is a 0.41 probability of exceeding a probability of illness of 0.75, with a 90% uncertainty range for the probability of exceedance of 0.27-0.51. Comparison with the beta-Poisson model shows a slight difference in the shape of the curve, with the results of the beta-Poisson model generally being less severe for lower probabilities of illness and more severe for higher probabilities of illness. The results for the Weibull-Gamma model using parameters estimated from the *E. coli* O157:H7 rabbit data are shown in Figure 4.7b, with a 0.95 probability of exceeding a probability of illness of 0.25, with a 90% uncertainty range of 0.91-0.98. There is a 0.88 probability of exceeding a probability of illness of 0.75, with a 90% confidence range from 0.80-0.95; however, when compared to the beta-Poisson model, the results of the Weibull-Gamma model using *E. coli* O157:H7 parameter estimates are slightly less severe. Figure 4.7c gives the results for the Weibull-Gamma model using parameters estimated from the *S. dysenteriae* data. There is approximately a 1.00 probability of

exceeding a probability of illness of 0.25; there is a 0.99 probability of exceeding a probability of illness of 0.75, with a 90% confidence interval of 0.97-1.00. For the *S. dysenteriae* data set, the results of the Weibull-Gamma model are slightly less severe. Lastly, Figure 4.7d shows the results for the AHP weighted-average Weibull-Gamma model. This model results in a 1.00 probability of exceeding a probability of illness of 0.25; there is a 0.85 probability of exceeding a probability of illness of 0.75, with a 90% confidence interval of 0.77-0.93. The results of the AHP weighted average models for the beta-Poisson and Weibull-Gamma relationships are very similar, with the Weibull-Gamma model resulting in slightly lower probabilities of exceedance. It should be noted that the differences between the beta-Poisson and Weibull-Gamma models for the *S. dysenteriae* data set and the AHP weighted-average are not significant, as the uncertainty ranges for these models overlap.

4.3.2.7 Number of Illnesses Given Dose

The baseline case study investigates an *E. coli* O157:H7 cheese-related outbreak affecting 1,500 people. Since the normal and susceptible populations are assumed to have the same vulnerability to illness, the number of illnesses in the outbreak is the same for the normal and susceptible populations. The probability of illness estimated from the dose-response model is used to estimate the number of people in the outbreak that become ill given the ingested dose. Thus, the estimate of the number of illnesses given the ingested dose is dependent on both the dose-response model selected and the data sets selected for the parameter estimates of the model, as well as the number of people affected in the outbreak. Figure 4.8 represents the number of illnesses given the dose based on the beta-Poisson dose-

response model for the all human *E. coli*, *E. coli* O157:H7 rabbit, and *S. dysenteriae* data sets, as well as the AHP weighted average model; the mean Weibull-Gamma number of illnesses given the ingested dose is superimposed for the purpose of model comparison. A numerical comparison of the number of illnesses for the various beta-Poisson dose-response models is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	All human *E. coli*	*E. coli* O157:H7 rabbit	*S. dysenteriae*	AHP
5th percentile	1000	1400	1325	1300
Mean	1100	1500	1400	1350
95th percentile	1200	1500	1500	1400

Figure 4.8: Variability and uncertainty for number of illnesses given ingested dose using beta-Poisson model for (a) all human *E. coli*, (b) *E. coli* O157:H7 rabbit, (c) *S. dysenteriae*, and (d) AHP weighted-average, superimposed with mean Weibull-Gamma results

Figure 4.8a shows the number of illnesses given the ingested dose for an exposed population of 1,500 people based on the beta-Poisson model using parameters estimated from the all human *E. coli* data. There is a 0.95 probability of exceeding 200 illnesses, and the 90% confidence interval for the probability of exceedance for 200 illnesses ranges from 0.90-0.99; however, there is a 0.74

probability of exceeding 800 illnesses, with a 90% confidence interval of 0.64-0.84. Figure 4.8b shows the results for the number of illnesses given the ingested dose using the beta-Poisson model with parameters estimated from the *E. coli* O157:H7 rabbit data. This results in a 0.99 probability of exceeding 200 illnesses, with a 90% confidence interval of 0.98-1.00; there is a 0.94 probability of exceeding 800 illnesses, with a 90% confidence range for the probability of exceedance from 0.89-0.98. The results in Figure 4.8c are based on the beta-Poisson model using parameters estimated from the *S. dysenteriae* data. There is a 1.00 probability of exceeding both 200 and 800 illnesses; in fact, there is a 0.52 probability of exceeding 1400 illnesses, with a 90% confidence interval for the probability of exceedance ranging from 30.9-0.65. Figure 4.8d shows the number of illnesses for the AHP weighted-average beta-Poisson model. This model results in a 1.00 probability of exceeding 200 illnesses; the probability of exceeding 800 illnesses is 0.97, with a 90% confidence interval of 0.94-1.00.

As stated before, the estimate of the number of illnesses given the ingested dose is dependent on the dose-response model and the data sets selected for the parameter estimates of the model. Therefore, the most conservative estimate of the number of illnesses is given by the dose-response model using the *S. dysenteriae* data set. As expected, the variability and uncertainty among the results of the beta-Poisson models in Figure 4.6 carries over to the estimates for the number of illnesses given the ingested dose in Figure 4.8. Although only the mean is plotted for the Weibull-Gamma model, the variability is the same as seen in Figure 4.7, and it is assumed the uncertainty would carry over as well.

4.3.2.8 Population Specific Risk Consequences

As previously stated, the normal and susceptible populations are assumed to have a similar vulnerability to illness following the ingestion of *E. coli* O157:H7, but the susceptible population has an increased propensity for severe health outcomes progressing from illness. The population-specific adverse health outcomes that can be estimated from the model include: number of hospitalizations given illness, number of HUS cases given hospitalization, number of deaths given HUS, number of HUS cases given illness, and number of deaths given illness. To illustrate the differences in health consequences between the normal and healthy populations, the number of hospitalizations given illness, number of HUS cases given illness, and number of deaths given illness are investigated for the two population types.

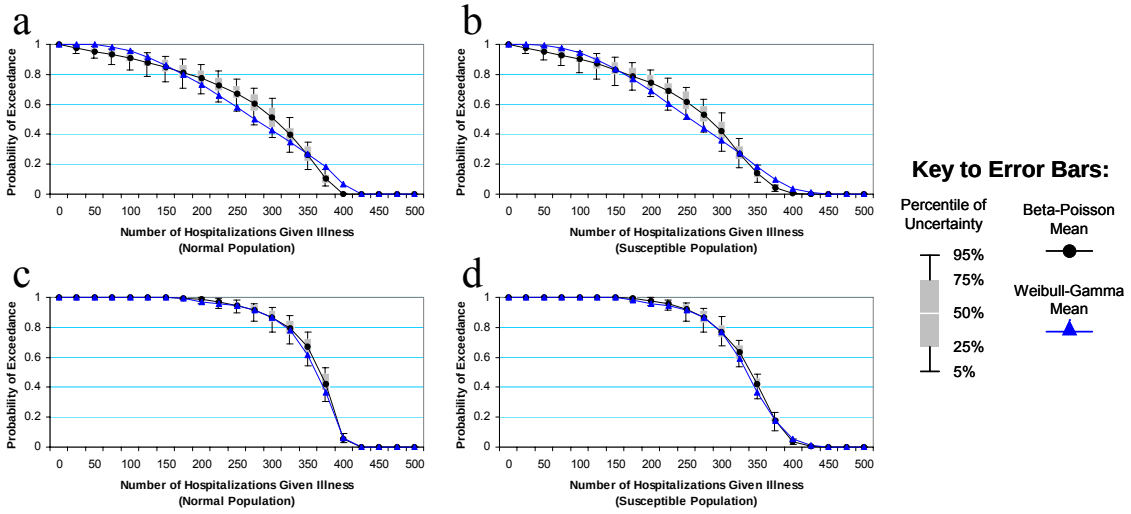
For the baseline case study, these consequences are examined in detail for the beta-Poisson all human *E. coli* data set and the beta-Poisson AHP weighted-average model, with the mean Weibull-Gamma model results superimposed. As with the estimate of the number of illnesses, the results generated for these adverse health outcomes are also dependent on both the dose-response model and data set used for the parameter estimates of the model. The parameter and model uncertainty illustrated in Figures 4.6 and 4.7 is carried through to the estimates of the adverse health consequences.

The all human *E. coli* data set and AHP weighted-average models are selected because of the diversity in the results obtained. As seen in the estimates for the probability of illness, the dose-response model using the all human *E. coli* data set provides the least conservative prediction of illness; thus, the dose-response model

using the all human *E. coli* data set can be considered the "best case" result. In contrast, the AHP weighted-average model provides a much more conservative estimate (similar to the dose-response models using the *E. coli* O157:H7 rabbit and *S. dysenteriae* data sets), but has the added benefit of addressing the data uncertainty associated with the dose-response model parameters.

4.3.2.8.1 Number of Hospitalizations Given Illness

Based on the probability of illness given the ingested dose resulting from the dose-response model, the population specific probability of hospitalization given illness, and the number of people exposed in the outbreak, the number of hospitalizations given illness is estimated for the population type. Figure 4.9 represents the number of hospitalizations given illness based on the beta-Poisson all human *E. coli* data set and the beta-Poisson AHP weighted-average model for the normal and susceptible populations, with the mean Weibull-Gamma results superimposed. A numerical comparison of the number of hospitalizations for the beta-Poisson all human *E. coli* data set and beta-Poisson AHP weighted-average model for the normal and susceptible populations is also shown for the 5^{th} percentile, mean, and 95^{th} percentile of the 0.50 probability of exceedance.



	All human *E. coli*		AHP	
	Normal	**Susceptible**	**Normal**	**Susceptible**
5th percentile	260	250	345	330
Mean	300	270	365	335
95th percentile	325	205	375	350

Figure 4.9: Variability and uncertainty for number of hospitalizations given illness using all human *E. coli* beta-Poisson model for (a) normal population and (b) susceptible population, and AHP weighted-average beta-Poisson model for (c) normal population and (d) susceptible population, superimposed with mean Weibull-Gamma results

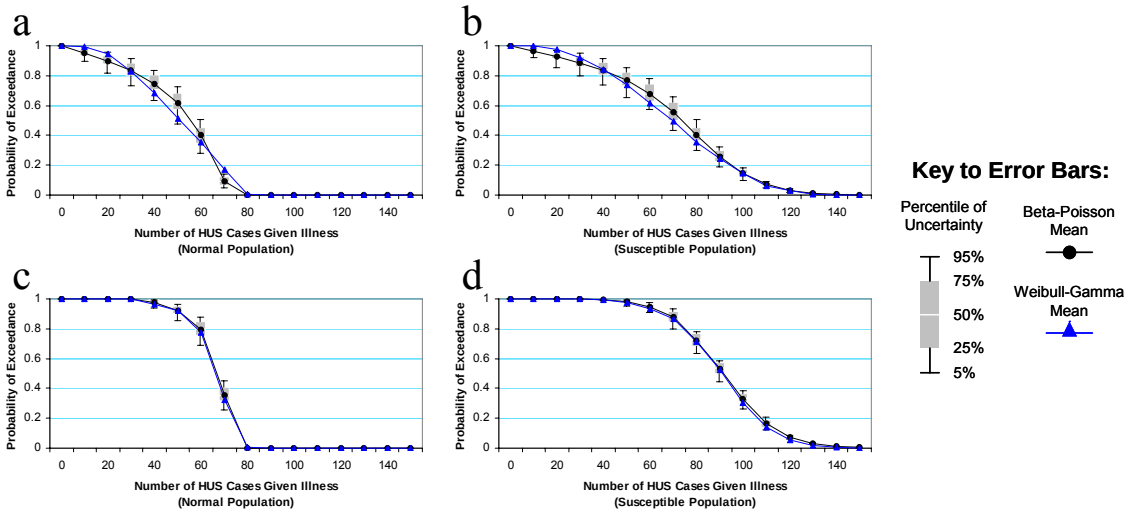
Figure 4.9a shows the number of hospitalizations given illness for the normal population, based on the beta-Poisson model with the all human *E. coli* data set. The probability of exceeding 250 hospitalizations is 0.67, with a 90% uncertainty range of 0.55-0.77. Figure 4.9b shows the results for the susceptible population, with a 0.62 probability of exceeding 250 hospitalizations and a 90% confidence range of 0.50-0.72. Figure 4.9c depicts the number of hospitalizations given illness for the normal population, based on the AHP weighted-average beta-Poisson model. The probability of exceeding 250 hospitalizations is 0.95, with a 90% uncertainty range of 0.90-0.98. Figure 4.9d gives these same results for the susceptible population; there is a 0.92 probability of exceeding 250 hospitalizations with a 90% confidence interval for the

probability of exceedance ranging from 0.84-0.96. It is worth noting that the differences between the beta-Poisson and Weibull-Gamma models are not significant.

Figure 4.9 shows that there is not a significant difference in the number of hospitalizations given illness for the normal and susceptible populations for any of the models investigated. This is due to inconsistency in the consequence data for this particular adverse health outcome. The data collected for the susceptible population appears to under-estimate the number of hospitalizations given illness as compared to the normal population. Additional consequence data for the susceptible population may help to alleviate this discrepancy.

4.3.2.8.2 Number of HUS Cases Given Illness

Based on the probability of illness given the ingested dose resulting from the dose-response model, the population specific probability of HUS given illness, and the number of people exposed, the number of HUS cases given illness is estimated. Figure 4.10 represents uncertainty and variability for the number of HUS cases given illness based on the beta-Poisson all human *E. coli* data set and the beta-Poisson AHP weighted-average model for the normal and susceptible populations, with the mean Weibull-Gamma results superimposed. A numerical comparison of the number of HUS cases for the beta-Poisson all human *E. coli* data set and beta-Poisson AHP weighted-average model for the normal and susceptible populations is shown for the 5^{th} percentile, mean, and 95^{th} percentile of the 0.50 probability of exceedance.



	All human *E. coli*		AHP	
	Normal	**Susceptible**	**Normal**	**Susceptible**
5th percentile	49	65	64	88
Mean	55	72	67	90
95th percentile	60	80	70	93

Figure 4.10: Variability and uncertainty for number of HUS cases given illness using all human *E. coli* beta-Poisson model for (a) normal population and (b) susceptible population and AHP weighted-average beta-Poisson model for (c) normal population and (d) susceptible population, superimposed with mean Weibull-Gamma results

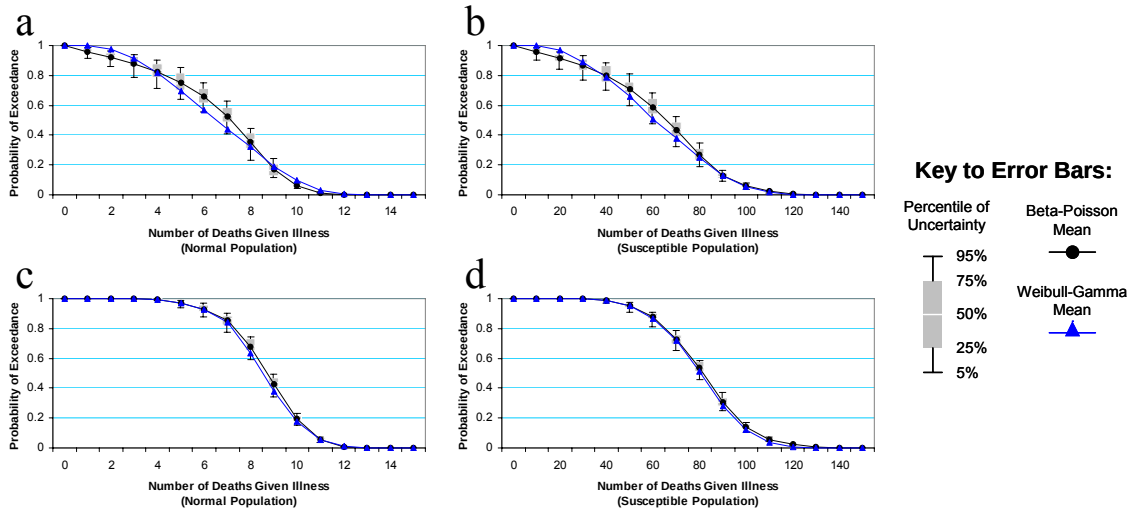
Figure 4.10a depicts the number of HUS cases given illness for the normal population based on the beta-Poisson model with the all human *E. coli* data set. The probability of exceeding 50 HUS cases is 0.62 with a 90% uncertainty range of 0.47-0.72. Figure 4.10b shows the probability of exceeding 50 HUS cases is 0.77 for the susceptible population, with a 90% confidence interval of 0.65-0.85. In addition, there is a 0.15 probability of exceeding 100 HUS cases, with a 90% confidence interval of 0.10-0.18. Figures 4.10c-d depicts the number of HUS cases given illness based on the AHP weighted-average beta-Poisson model for the normal and susceptible populations, respectively. The probability of exceeding 50 HUS cases is 0.92 with a 90% confidence interval of 0.85-0.97 for the normal population. In

contrast, the probability of exceeding 50 HUS cases is 0.98 for the susceptible populations, with a 90% uncertainty range of 0.95-1.00. Additionally, there is a 0.33 probability of exceeding 100 HUS cases, with a 90% confidence interval of 0.26-0.39.

For both models investigated, there is a significant difference in the number of HUS cases for the normal and susceptible populations. As expected, both models show that the susceptible population has a greater propensity for developing HUS as compared to the normal population. Again, only small differences are noted between the estimates based on the beta-Poisson and Weibull-Gamma models. The mean results of the Weibull-Gamma models are, in general, well within the uncertainty ranges for the beta-Poisson models, suggesting that the difference between the models is not significant.

4.3.2.8.3 Number of Deaths Given Illness

Finally, based on the probability of illness given the ingested dose resulting from the dose-response model, the population specific probability of death given illness, and the number of people exposed, the number of deaths given illness is estimated. Figure 4.11 depicts the number of deaths given illness based on the beta-Poisson all human *E. coli* data set and the beta-Poisson AHP weighted-average model for the normal and susceptible populations, with the mean Weibull-Gamma results superimposed. A numerical comparison of the number of deaths for the beta-Poisson all human *E. coli* data set and beta-Poisson AHP weighted-average model for the normal and susceptible populations is shown for the 5^{th} percentile, mean, and 95^{th} percentile of the 0.50 probability of exceedance.



	All human *E. coli*		AHP	
	Normal	**Susceptible**	**Normal**	**Susceptible**
5th percentile	6.7	59	8.3	78
Mean	7.0	65	8.7	80
95th percentile	7.5	70	9.0	83

Figure 4.11: Variability and uncertainty for number of deaths given illness using all human *E. coli* beta-Poisson model for (a) normal population and (b) susceptible population and AHP weighted-average beta-Poisson model for (c) normal population and (d) susceptible population, superimposed with mean Weibull-Gamma results

Figure 4.11a depicts the number of deaths given illness for the normal population based on the beta-Poisson model with the all human *E. coli* data set. The probability of exceeding 5 deaths is 0.75 with a 90% uncertainty range of 0.64-0.85. Figure 4.11b shows the probability of exceeding 50 deaths is 0.71 for the susceptible population, with a 90% confidence interval of 0.60-0.81. Figures 4.11c-d depict the number of deaths given illness based on the AHP weighted-average beta-Poisson model for the normal and susceptible populations, respectively. The probability of exceeding 5 deaths is 0.97 with a 90% confidence interval of 0.94-0.99 for the normal population, while the probability of exceeding 50 deaths is 0.95 for the susceptible populations, with a 90% uncertainty range of 0.91-0.98.

For both models investigated, there is a factor of ten difference in the number of deaths for the normal and susceptible populations. As seen with the estimates for the number of illnesses, hospitalizations, and HUS cases, the mean results of the Weibull-Gamma models are well within the uncertainty ranges for the beta-Poisson models, suggesting that the difference between the models is not significant.

4.3.3 Mitigation Strategies

Obviously, the baseline case study demonstrates how a moderate level of initial contamination in combination with moderate abuse during the production and distribution phases can result in potentially high levels of *E. coli* O157:H7 contamination in cheese. If ingested, these high levels of contamination result in a large number of illnesses, hospitalizations, HUS cases, and even deaths. Several factors are identified in the baseline case study as critical points in the exposure path that influence not only the *E. coli* O157:H7 contamination level, but also the associated human health risk. By changing the model selections at these critical points, risk management options can be compared.

The factors identified as critical points in the exposure path correspond with the steps in either the production or distribution phases. However, it should be noted that only certain steps in the production phase can be changed to improve the contamination level. For example, since the baseline case study emulates cheddar cheese production, changing the cooking temperature or type of salting is not an option. The factors identified as possible mitigation strategies for the production phase include: milk storage time and temperature (step A1), milk heat treatment (step A2), and ripening time (step A9). The factors identified as possible mitigation

strategies for the distribution phase are the temperature conditions during the various storage and transportation steps (steps B1-B5). The influence of these various steps on the *E. coli* O157:H7 contamination are investigated separately as single step mitigations and in combination as multiple step mitigations.

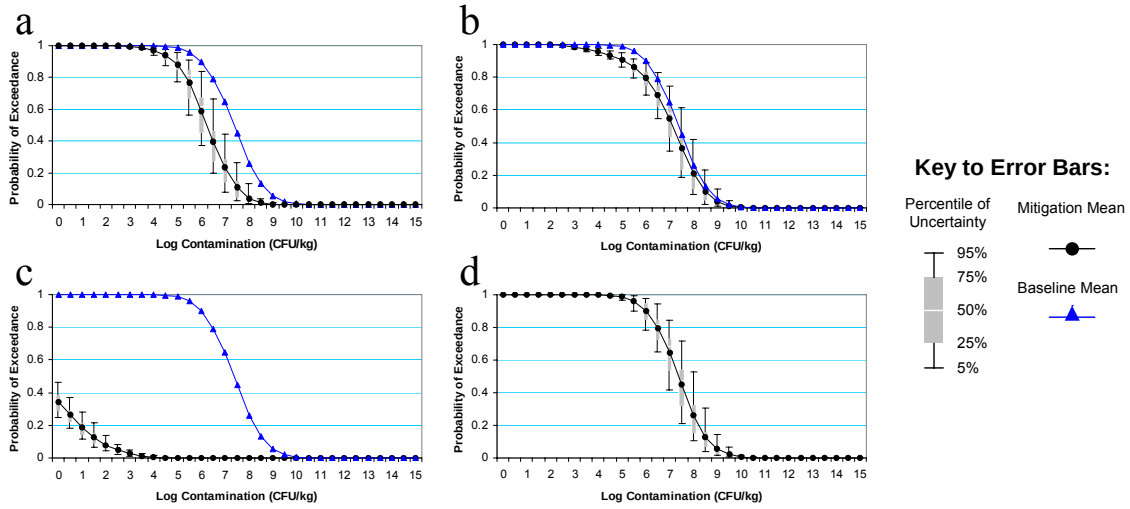
4.3.3.1 Single Step Mitigation Strategies

Several single step mitigation strategies are explored for the baseline case study. The conditions at a particular step are changed and the effects of the mitigation strategy are then compared to the baseline results. Comparisons are made for the contamination level after production, the contamination level after distribution, the contamination level per dose, and the number of illnesses given the ingested dose for the all human *E. coli* beta-Poisson model and AHP weighted-average dose-response model. The first mitigation explored involves reducing the milk storage time and temperature, from 2 days to 1 day and from 5-8°C to less than 5°C. Second, the effect of lengthening the ripening time, from 75 days to 150 days, on *E. coli* O157:H7 contamination level is investigated. The third mitigation explores the effect of pasteurization on contamination levels. Finally, the temperatures during the distribution phase are reduced to 5°C for all steps; although several steps are involved in this mitigation, it is treated as a single step mitigation as the same option (i.e., temperature) is changed at the various steps.

4.3.3.1.1 Contamination after Production

The number of *E. coli* O157:H7 in 1 kg of cheese after production is estimated for each of the four single step mitigation strategies imposed. Figure 4.12 shows the predicted distribution of *E. coli* O157:H7 after production for the various mitigation

strategies along with the baseline mean. A numerical comparison of the contamination level after production for the various single step mitigations is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	Storage Time & Temp	Ripening Time	Pasteurization	Distribution Temp
5th percentile	5.40	6.60	-1.50	6.67
Mean	6.25	7.10	-1.00	7.25
95th percentile	6.80	7.75	-0.10	8.05

Figure 4.12: Variability and uncertainty for probability of exceeding contamination level per 1 kg cheese after production for various mitigation strategies: (a) reduction in storage time and temperature, (b) increase in ripening time, (c) pasteurization, and (d) reduction in distribution temperatures, superimposed with mean baseline results

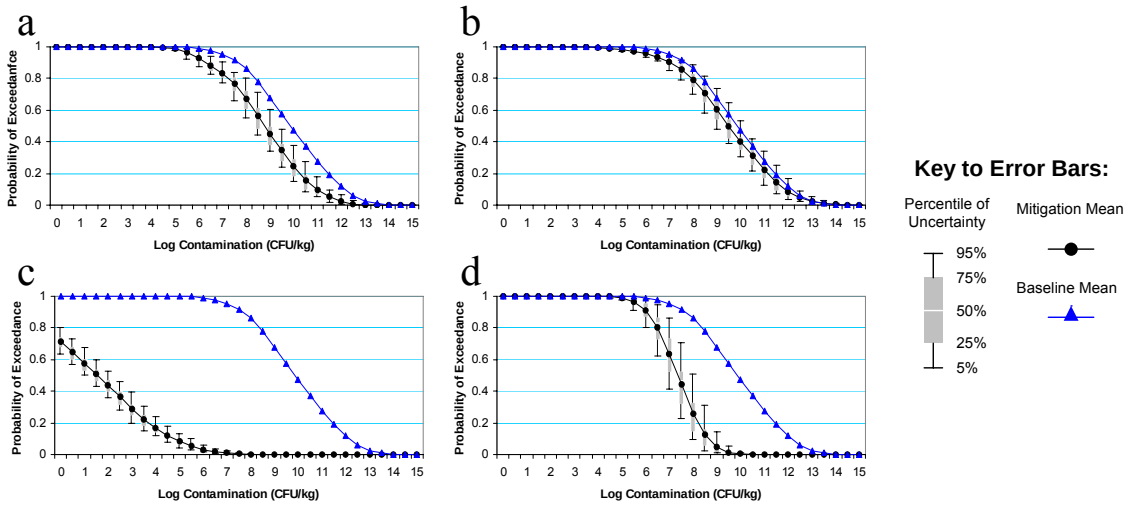
Figure 4.12a shows the probability of exceeding the contamination level per 1 kg cheese after production for the reduced storage time and temperature mitigation strategy. There is a 0.40 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg, with a 90% uncertainty range from 0.20-0.66. Figure 4.12b shows the results for the increased ripening time mitigation strategy. The probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg is 0.69, with a 90% confidence interval of 0.55-0.83. Figure 4.12c shows the result of pasteurization

on the estimated contamination levels after production. These results show a 0.00 probability of exceeding a contamination level of 6.5 CFU/kg. In fact, there is only a 0.19 probability of exceeding a contamination level of 1 CFU/kg, with a 90% confidence interval from 0.11-0.28. Finally, Figure 4.12d shows the same contamination level after production since the changes to the distribution temperature do not impact the production phase.

When compared with the mean baseline result, which has a 0.79 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg, with a 90% confidence interval from 0.65-0.94, it is apparent that the reduced milk storage time and temperature provides a significant reduction in the *E. coli* O157:H7 contamination levels after production. The increased ripening time also decreases contamination; however, the mean for this mitigation strategy is still within the uncertainty range for the baseline results, suggesting the difference is not significant. However, as expected, the pasteurization mitigation provides the most dramatic and significant decrease in contamination.

4.3.3.1.2 Contamination after Distribution

The number of *E. coli* O157:H7 in 1 kg of cheese after distribution is estimated for each of the four single step mitigation strategies imposed. Figure 4.13 shows the predicted distribution of *E. coli* O157:H7 after distribution for the various mitigation strategies along with the baseline mean. A numerical comparison of the contamination level after distribution for the various single step mitigations is shown for the 5^{th} percentile, mean, and 95^{th} percentile of the 0.50 probability of exceedance.



	Storage Time & Temp	Ripening Time	Pasteurization	Distribution Temp
5th percentile	8.25	8.90	1.00	6.75
Mean	8.75	9.50	1.50	7.30
95th percentile	9.40	10.10	2.10	8.00

Figure 4.13: Variability and uncertainty for probability of exceeding contamination level per 1 kg cheese after distribution for various mitigation strategies: (a) reduction in storage time and temperature, (b) increase in ripening time, (c) pasteurization, and (d) reduction in distribution temperatures, superimposed with mean baseline results

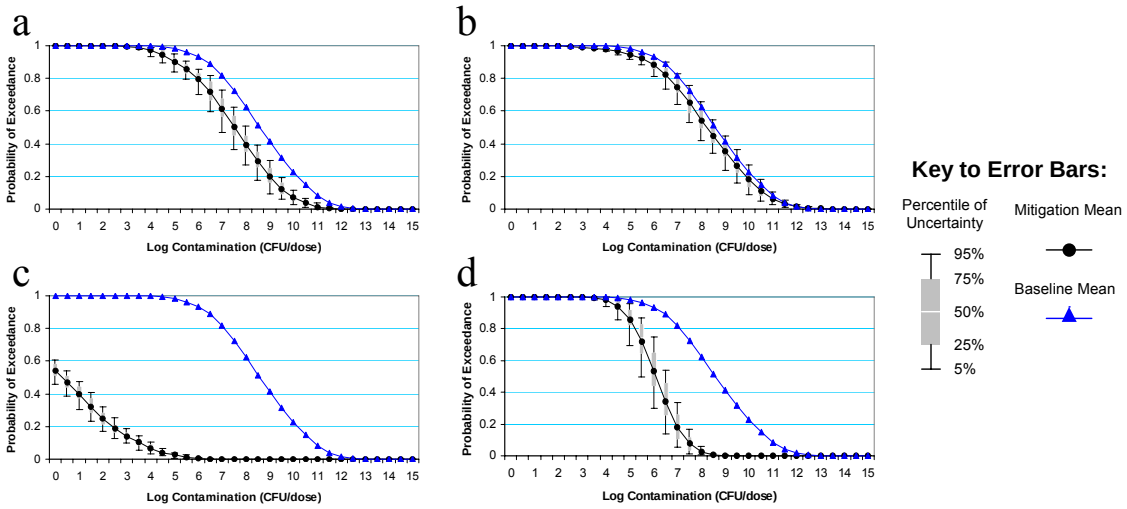
Figure 4.13a shows the probability of exceeding the contamination level per 1 kg cheese after distribution for the reduced storage time and temperature mitigation strategy. There is a 0.88 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg, with a 90% uncertainty range from 0.83-0.94. Figure 4.13b shows the results for the increased ripening time mitigation strategy. The probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg is 0.94, with a 90% confidence interval of 0.91-0.97. Figure 4.13c shows the result of pasteurization on the estimated contamination levels after distribution. These results show a 0.20 probability of exceeding a contamination level of 6.5 CFU/kg, with a 90% confidence interval from 0.00-0.03. Finally, Figure 4.13d shows the contamination level after

distribution for the reduced distribution temperatures. The probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg is 0.80, with a 90% uncertainty range of 0.62-0.95.

When compared with the mean baseline result, which has a 0.97 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg, with a 90% confidence interval from 0.95-1.00, it is apparent that the reduced milk storage time and temperature and the increased ripening time mitigations provide only a small decrease in the *E. coli* O157:H7 contamination levels after distribution. The decreased distribution temperatures result in a significant decrease in the contamination level after distribution; however, the pasteurization mitigation provides the most dramatic decrease in contamination.

4.3.3.1.3 Contamination per Dose

Next, the effect of the various single step mitigation strategies on the contamination of *E. coli* O157:H7 per dose is explored. Again, the ingested dose varies depending on the number of servings consumed, and it is assumed that the average person consumes between 1-3 servings of contaminated cheese. Based on the *E. coli* O157:H7 contamination per serving and the number of servings consumed, the dose is estimated for each mitigation strategy. Figure 4.14 shows the predicted distribution of *E. coli* O157:H7 contamination per dose for the various mitigation strategies along with the baseline mean. A numerical comparison of the contamination per dose for the various single step mitigations is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	Storage Time & Temp	Ripening Time	Pasteurization	Distribution Temp
5th percentile	6.90	7.40	-0.50	5.50
Mean	7.50	8.25	0.25	6.10
95th percentile	8.00	8.75	0.75	6.60

Figure 4.14: Variability and uncertainty for probability of exceeding contamination level per dose for various mitigation strategies: (a) reduction in storage temp and time, (b) increase in ripening time, (c) pasteurization, and (d) reduction in distribution temperatures, superimposed with mean baseline results

Figure 4.14a shows the probability of exceeding the contamination level per dose for the reduced storage time and temperature mitigation strategy. This mitigation strategy results in a 0.72 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/dose, with a 90% uncertainty range from 0.59-0.82. Figure 4.14b shows the results for the increased ripening time mitigation strategy. The probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/dose is 0.82, with a 90% confidence interval of 0.73-0.90. Figure 4.14c depicts the results of pasteurization on the estimated contamination level per dose. The results show a 0.00 probability of exceeding a contamination level of 6.5 CFU/dose. Effectively, there is only a 0.40 probability of exceeding a contamination level of 1 CFU/dose, with a 90% confidence interval from 0.30-0.48. Finally, Figure 4.14d

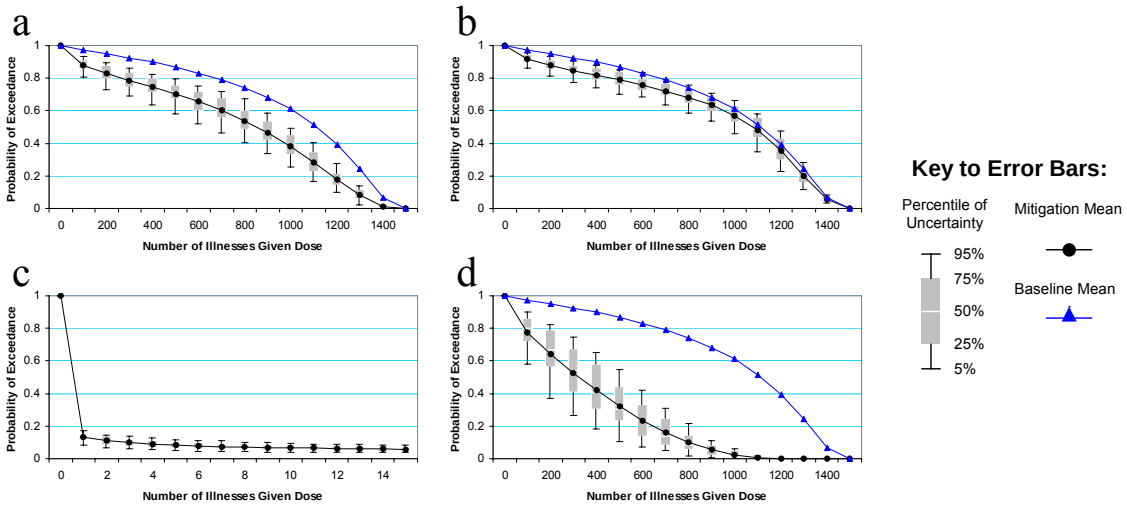
shows the results the decrease in distribution temperatures on the *E. coli* O157:H7 per dose. There is a 0.34 probability of exceeding a contamination level of 6.5 CFU/dose, with a 90% uncertainty range of 0.14-0.54.

The baseline case study resulted in a 0.89 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/dose, with a 90% uncertainty range of 0.81-0.94. The reduced milk storage time and temperature, pasteurization, and decreased distribution temperatures all provide significant reductions in the *E. coli* O157:H7 contamination per dose, as there is no overlap between the uncertainty ranges for these mitigations and the baseline uncertainty range. However, the pasteurization mitigation provides the most dramatic decreases in contamination, followed by the decrease in distribution temperatures. The increased ripening time alone decreases contamination as well; however, the mean for this mitigation strategy is still within the uncertainty range for the baseline results, suggesting the difference is not as significant as the other options.

4.3.3.1.4 Number of Illnesses Given Dose

Finally, the effect of the various single step mitigation strategies on the number of illnesses given the ingested dose is examined for a population of 1,500 people. Again, the estimate of the number of illnesses given the ingested dose is dependent on both the dose-response model selected and the data sets selected for the parameter estimates of the model, as well as the number of people affected in the outbreak. The number of illnesses is estimated for each of the mitigation strategies using the all human *E. coli* and AHP weighted-average beta-Poisson dose-response models. The all human *E. coli* dose-response model is considered to provide the least

conservative estimate, while the AHP weighted-average provides a more conservative estimate. Figure 4.15 shows the predicted distribution of the number of illnesses given the ingested dose for the various single step mitigation strategies along with the baseline mean based on the beta-Poisson dose-response model for the all human *E. coli* data set. A numerical comparison of the number of illnesses for the all human *E. coli* beta-Poisson dose-response model for the various single step mitigation strategies is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	Storage Time & Temp	Ripening Time	Pasteurization	Distribution Temp
5th percentile	600	950	0	130
Mean	800	1100	0	300
95th percentile	1000	1200	0	530

Figure 4.15: Variability and uncertainty for number of illnesses given ingested dose using all human *E. coli* beta-Poisson model for various mitigation strategies: (a) reduction in storage temp and time, (b) increase in ripening time, (c) pasteurization, and (d) reduction in distribution temperatures, superimposed with mean baseline results

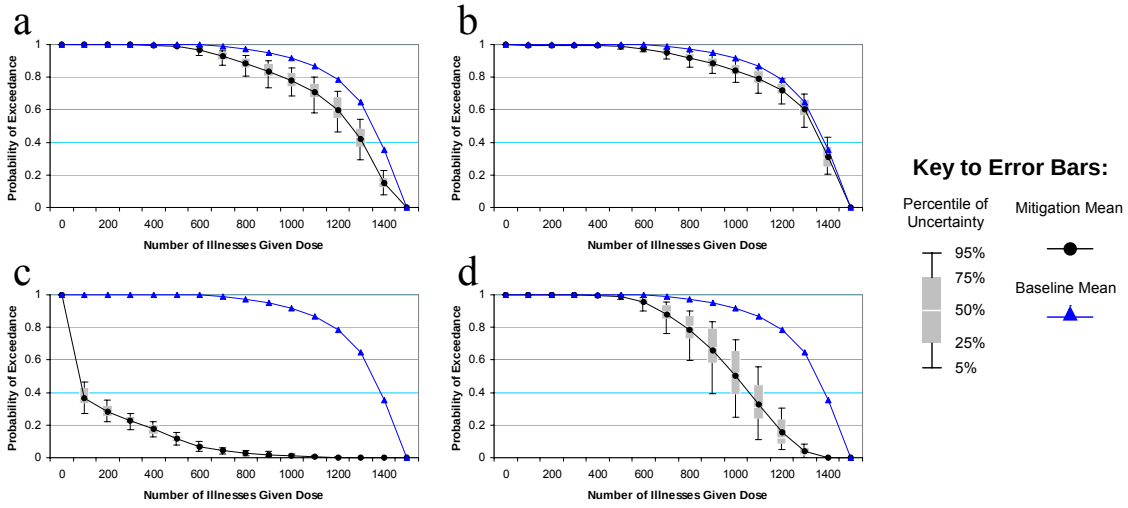
Figure 4.15a shows the probability of exceeding the number of illnesses given the ingested dose for an exposed population of 1,500 people for the reduced storage

time and temperature mitigation strategy. This mitigation strategy results in a 0.83 probability of exceeding 200 illnesses, with a 90% uncertainty range from 0.73-0.90. Figure 4.15b depicts the results for the increased ripening time mitigation strategy. The probability of exceeding 200 illnesses is 0.88, with a 90% confidence interval of 0.81-0.92. Figure 4.15c shows the results of pasteurization on the estimated number of illnesses. The results show a 0.13 probability of exceeding 1 illness, with a 90% uncertainty range of 0.08-0.17; it should be noted that the baseline mean is not plotted on Figure 4.15c due to the different x-axis scales. Finally, Figure 4.15d depicts the results of decreased distribution temperatures on the estimated number of illnesses. There is a 0.64 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.37-0.82.

Comparison of the mitigation strategies to the baseline mean for the number of illnesses given the ingested dose based on the all human *E. coli* beta-Poisson model demonstrate a noticeable reduction in the number of illnesses. The baseline case study resulted in a 0.95 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.90-0.99. Again, the reduced milk storage time and temperature, pasteurization, and decreased distribution temperatures all provide significant reductions in the number of illnesses, as there is no overlap between the uncertainty ranges for these mitigations and the baseline uncertainty range. The pasteurization mitigation provides the most dramatic decreases in the number of illnesses, as this mitigation essentially eliminates the possibility of illness. The increased ripening time decreases the number of illnesses as well; however, the mean

for this mitigation strategy is still within the uncertainty range for the baseline results, suggesting the difference is not as significant as the other options.

The number of illnesses given the ingested dose is also estimated using the AHP weighted-average beta-Poisson model, as this model provides a more conservative estimate. Figure 4.16 shows both the variability and uncertainty of the predicted distribution of the number of illnesses given the ingested dose for the various mitigation strategies along with the baseline mean based on the AHP weighted-average beta-Poisson dose-response model. A numerical comparison of the number of illnesses for the AHP weighted-average beta-Poisson dose-response model for the various single step mitigation strategies is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	Storage Time & Temp	Ripening Time	Pasteurization	Distribution Temp
5th percentile	1150	1300	25	850
Mean	1250	1330	40	1000
95th percentile	1300	1350	90	1125

Figure 4.16: Variability and uncertainty for number of illnesses given ingested dose using AHP weighted-average beta-Poisson model for various mitigation strategies: (a) reduction in storage temp and time, (b) increase in ripening time, (c) pasteurization, and (d) reduction in distribution temperatures, superimposed with mean baseline results

Figure 4.16a shows the probability of exceeding the number of illnesses given the ingested dose based on the AHP weighted-average beta-Poisson dose-response model for an exposed population of 1,500 people for the reduced storage time and temperature mitigation strategy. There is a 1.00 probability of exceeding 200 illnesses; there is a 0.88 probability of exceeding 800 illnesses, with a 90% confidence interval for the probability of exceedance of 0.81-0.93. Figure 4.16b shows the results for the increased ripening time mitigation strategy. The probability of exceeding 200 illnesses is 1.00; there is a 0.92 probability of exceeding 800 illnesses, with a 90% uncertainty range of 0.86-0.96. Figure 4.16c depicts the results of pasteurization on the estimated number of illnesses; the baseline mean is not plotted due to the different x-axis scales. Figure 4.16c has a 0.28 probability of exceeding 200 illnesses, with a 90% confidence interval for the exceedance probability of 0.22-0.35. There is a 0.03 probability of exceeding 800 illnesses, with a 90% uncertainty range of 0.01-0.04. Finally, Figure 4.16d depicts the results of the decreased distribution temperature on the number of illnesses given the ingested dose, with a 1.00 probability of exceeding 200 illnesses. There is a 0.78 probability of exceeding 800 illnesses, with a 90% uncertainty range of 0.60-0.90.

Comparison of the mitigation strategies to the baseline mean for the number of illnesses given the ingested dose based on the AHP weighted-average beta-Poisson model demonstrate a reduction in the number of illnesses given the ingested dose as well. The baseline case study resulted in a 1.00 probability of exceeding 200 illnesses; there is a 0.97 probability of exceeding 800 illnesses, with a 90% uncertainty range of 0.94-1.00. The reduced milk storage time and temperature,

pasteurization, and decreased distribution temperatures all provide significant reductions in the number of illnesses, as there is no overlap between the uncertainty ranges for these mitigations and the baseline uncertainty range. The pasteurization mitigation provides the most dramatic decreases in the number of illnesses, as this mitigation reduces the number of illnesses by more than factor of ten. The increased ripening time decreases the number of illnesses as well; however, the mean for this mitigation strategy is still within the uncertainty range for the baseline results, suggesting the difference is not as significant as the other options.

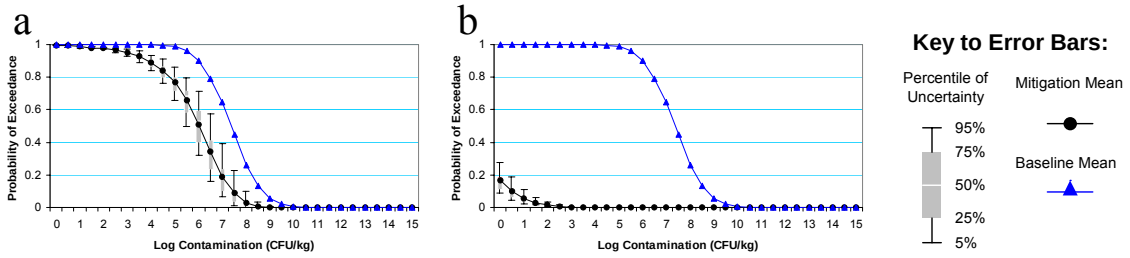
4.3.3.2 Multiple Step Mitigation Strategies

The single step mitigation strategies previously explored are combined in order to examine the effect of changes in multiple steps on the *E. coli* O157:H7 contamination at various steps throughout the model. From the single step mitigations examined, it is obvious that pasteurization provides the most significant impact on the contamination level and, therefore, the adverse health consequences; however, raw milk cheeses are still very popular. The purpose of the multiple step mitigations is to determine if a series of improvements in the production and distribution phases can eliminate enough contamination to make a "safe" cheese. In addition, pasteurization is added to these multiple step mitigations in order to show the best possible outcomes for the given initial contamination level. The combinations explored in the multiple step mitigations are: (a) reduced milk storage time and temperature and increased ripening time, (b) reduced milk storage time and temperature, increased ripening time, and reduced distribution temperatures, (c) reduced milk storage time and temperature, increased ripening time, and

pasteurization, and (d) reduced milk storage time and temperature, increased ripening time, reduced distribution temperatures, and pasteurization. It should be noted that the reduced milk storage time and temperature, increased ripening time, reduced distribution temperatures, and pasteurization mitigation represents ideal handling and conditions throughout the production and distribution phases.

4.3.3.2.1 Contamination after Production

The number of *E. coli* O157:H7 in 1 kg of cheese after production is estimated for each of the four multiple step mitigation strategies imposed. Figure 4.17 shows the predicted distribution of *E. coli* O157:H7 after production for the multiple step mitigation strategies affecting the production phase along with the baseline mean. A numerical comparison of the contamination level after production for the multiple step mitigations for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance is also shown.



	Storage Time & Temp, Ripening Time	Storage Time & Temp, Ripening Time, Pasteurization
5th percentile	5.50	-2.50
Mean	6.00	-2.00
95th percentile	6.30	-1.50

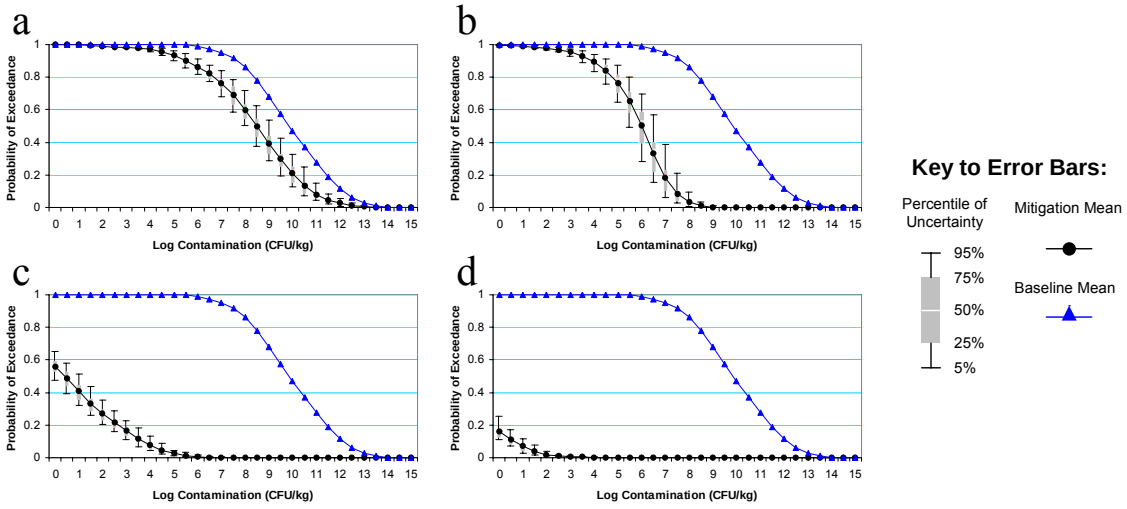
Figure 4.17: Variability and uncertainty for probability of exceeding contamination level per 1 kg cheese after production for multiple step mitigation strategies: (a) reduction in storage time and temperature and increase in ripening time, (b) reduction in storage time and temperature, increase in ripening time, and pasteurization, superimposed with mean baseline results

It should be noted that Figure 4.17 only shows the results for the multiple step mitigations that affect the production phase. The affect of changes made to the distribution phase will not affect the contamination after production. Figure 4.17a shows the probability of exceeding the contamination level per 1 kg cheese after production for the combined effects of reduced storage time and temperature and increased ripening time. There is a 0.99 probability of exceeding an *E. coli* O157:H7 contamination level of 1.0 CFU/kg, with a 90% uncertainty range from 0.98-1.00. The probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg is 0.34, with a 90% uncertainty range of 0.16-0.58. Figure 4.17b shows the results for the combination of reduced storage time and temperature, increase ripening time, and pasteurization. The probability of exceeding an *E. coli* O157:H7 contamination level of 1.0 CFU/kg is 0.05, with a 90% confidence interval of 0.02-0.11. The probability of exceeding a contamination level of 6.5 CFU/kg is 0.00.

The baseline result has a 0.79 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg, with a 90% confidence interval from 0.65-0.94. The reduced storage time and temperature and increased ripening time mitigation provides a significant reduction in the contamination level, as there is no overlap of the uncertainty range with the baseline; however, the contamination level after production is still very high. The addition of pasteurization to the reduced storage time and temperature and increased ripening time is noteworthy, as the contamination is effectively eliminated.

4.3.3.2.2 Contamination after Distribution

The number of *E. coli* O157:H7 in 1 kg of cheese after distribution is estimated for the multiple step mitigation strategies. Figure 4.18 shows the predicted distribution of *E. coli* O157:H7 after distribution along with the baseline mean. A numerical comparison of the contamination level after distribution for the various multiple step mitigations is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	Storage Time & Temp, Ripening Time	Storage Time & Temp, Ripening Time, Distribution Temp	Storage Time & Temp, Ripening Time, Pasteurization	Storage Time & Temp, Ripening Time, Distribution Temp, Pasteurization
5th percentile	8.00	5.50	-0.10	-2.75
Mean	8.50	6.00	0.50	-2.00
95th percentile	9.10	6.30	1.00	-1.50

Figure 4.18: Variability and uncertainty for probability of exceeding contamination level per 1 kg cheese after production for multiple step mitigation strategies: (a) reduction in storage time and temperature and increase in ripening time, (b) reduction in storage time and temperature, increase in ripening time, and reduction in distribution temperatures, (c) reduction in storage time and temperature, increase in ripening time, and pasteurization, and (d) reduction in storage time and temperature, increase in ripening time, reduction in distribution temperatures, and pasteurization, superimposed with mean baseline results

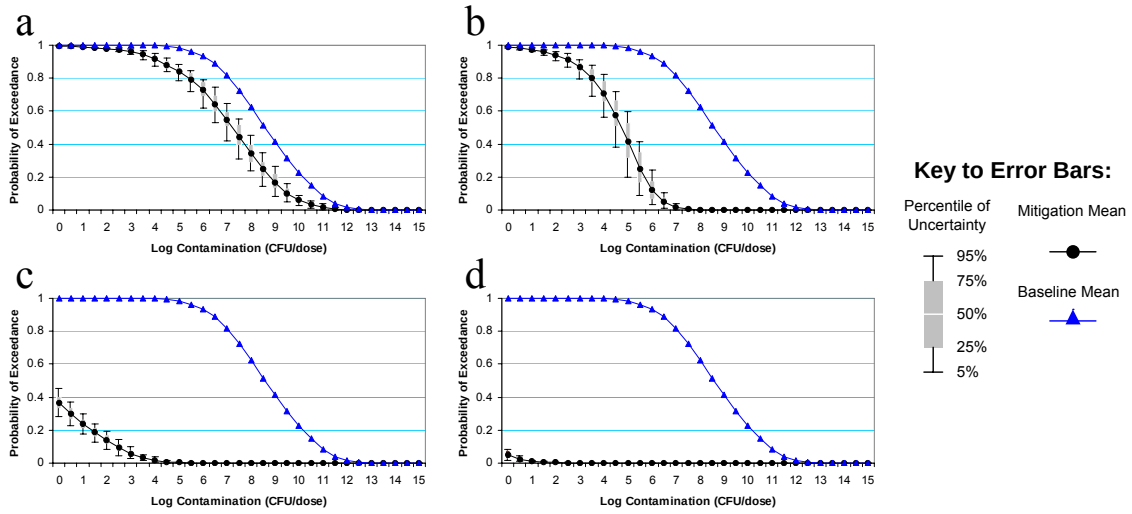
Figure 4.18a shows the results for the combined mitigation of reduced storage time and temperature and increased ripening time; there is a 0.82 probability of exceeding a contamination level of 6.5 CFU/kg, with a 90% uncertainty range of 0.77-0.87. For this combined mitigation, there is a 1.00 probability of exceeding a contamination level of 1.0 CFU/kg. Figure 4.18b examines the effects of reduced storage time and temperature, increased ripening time, and reduced distribution temperatures. This results in a 0.33 probability of exceeding 6.5 CFU/kg, with a 90% confidence interval for the probability of exceedance of 0.16-0.41. There is a 0.99 probability of exceeding 1.0 CFU/kg, with a 90% confidence interval of 0.98-1.00. Figure 4.18c shows the results for the combined effects of reduced storage time and temperature, increased ripening time, and pasteurization. This multiple step mitigation results in a 0.00 probability of exceeding 6.5 CFU/kg. The probability of exceeding a 1.0 CFU/kg contamination level is 0.41, with a 90% uncertainty range of 0.32-0.51. Finally, 4.18d explores the effects of reduced storage time and temperature, increased ripening time, reduced distribution temperatures, and pasteurization. There is a 0.00 probability of exceeding a contamination level of 6.5 CFU/kg. In addition, there is a 0.07 probability of exceeding 1.0 CFU/kg, with a 90% confidence interval of 0.03-0.12.

The baseline mean has a 0.97 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg, with a 90% confidence interval from 0.95-1.00. When compared with the mean baseline result, the reduced storage time and temperature and increased ripening time mitigation provides the smallest reduction in contamination; the addition of reduced distribution temperatures to this mitigation

strategy results in a marked improvement. However, pasteurization is still key in eliminating *E. coli* O157:H7 contamination. It should be noted that the combination of reduced storage time and temperature, increased ripening time, decreased distribution temperatures, and pasteurization mitigation strategy represents proper handling of the cheese in the production and distribution phases. The model shows that even with a moderate level of initial contamination, a relatively "safe" cheese can still be produced with pasteurization and proper handling.

4.3.3.2.3 Contamination per Dose

The effect of the multiple step mitigation strategies on the contamination of *E. coli* O157:H7 per dose is also explored. Based on the *E. coli* O157:H7 contamination per serving and the number of servings consumed, the dose is estimated for the various multiple step mitigation strategies. Figure 4.19 shows the predicted distribution of *E. coli* O157:H7 contamination per dose for the multiple step mitigations along with the baseline mean. A numerical comparison of the contamination level per dose for the various multiple step mitigations for the 5^{th} percentile, mean, and 95^{th} percentile of the 0.50 probability of exceedance is shown.



	Storage Time & Temp, Ripening Time	Storage Time & Temp, Ripening Time, Distribution Temp	Storage Time & Temp, Ripening Time, Pasteurization	Storage Time & Temp, Ripening Time, Distribution Temp, Pasteurization
5th percentile	6.60	4.20	-1.50	-4.00
Mean	7.25	4.75	-1.00	-3.50
95th percentile	7.50	5.25	-0.25	-2.75

Figure 4.19: Variability and uncertainty for probability of exceeding contamination level per dose for multiple step mitigation strategies: (a) reduction in storage time and temperature and increase in ripening time, (b) reduction in storage time and temperature, increase in ripening time, and reduction in distribution temperatures, (c) reduction in storage time and temperature, increase in ripening time, and pasteurization, and (d) reduction in storage time and temperature, increase in ripening time, reduction in distribution temperatures, and pasteurization, superimposed with mean baseline results

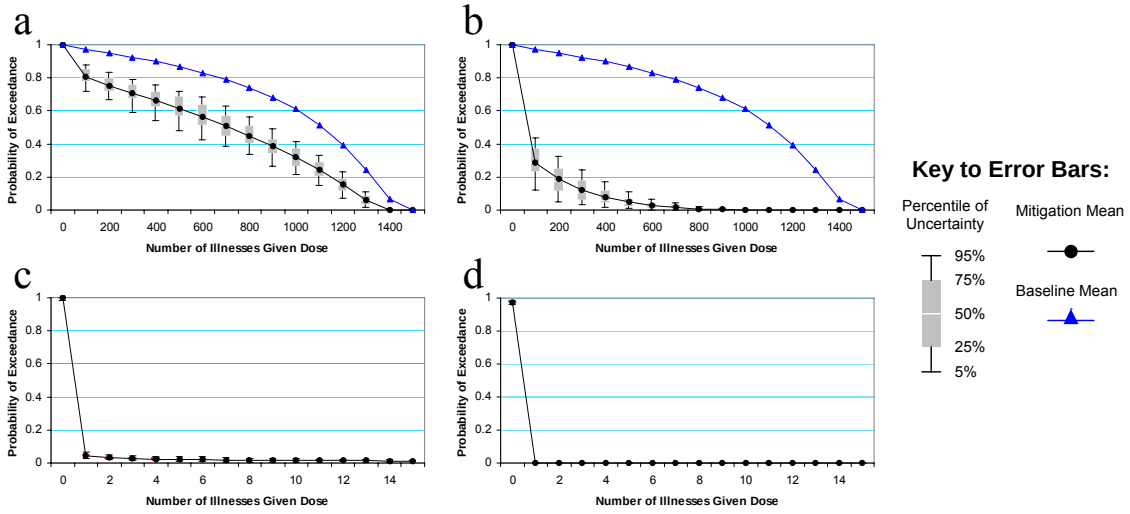
Figure 4.19a shows the results for the combined mitigation of reduced storage time and temperature and increased ripening time; there is a 0.64 probability of exceeding a contamination level of 6.5 CFU/kg, with a 90% uncertainty range of 0.53-0.75. For this combined mitigation, there is a 0.99 probability of exceeding a contamination level of 1.0 CFU/kg, with a 90% uncertainty range of 0.98-1.00. Figure 4.19b examines the effects of reduced storage time and temperature, increased ripening time, and reduced distribution temperatures. This results in a 0.05 probability of exceeding 6.5 CFU/kg, with a 90% confidence interval for the

probability of exceedance of 0.00-0.11. There is a 0.97 probability of exceeding 1.0 CFU/kg, with a 90% confidence interval of 0.96-0.98. Figure 4.19c shows the results for the combined effects of reduced storage time and temperature, increased ripening time, and pasteurization. This multiple step mitigation results in a 0.00 probability of exceeding 6.5 CFU/kg. The probability of exceeding a 1.0 CFU/kg contamination level is 0.24, with a 90% uncertainty range of 0.18-0.27. Finally, 4.19d explores the effects of reduced storage time and temperature, increased ripening time, reduced distribution temperatures, and pasteurization. There is a 0.00 probability of exceeding a contamination level of 6.5 CFU/kg. In addition, there is only a 0.01 probability of exceeding 1.0 CFU/kg, with a 90% confidence interval of 0.00-0.01.

The baseline mean has a 0.89 probability of exceeding an *E. coli* O157:H7 contamination level of 6.5 CFU/kg, with a 90% confidence interval from 0.81-0.94. Again, when compared to the baseline mean, the most significant reductions in contamination are seen with the mitigation strategies involving pasteurization. The mitigation strategy representing proper handling eliminates almost all contamination. The reduced storage time and temperature, increased ripening time, and pasteurization strategy also significantly reduces contamination. However, comparison of these two mitigation strategies also demonstrates the significant impact temperature abuse during the distribution phase has on the contamination levels.

4.3.3.2.4 Number of Illnesses Given Dose

Finally, the effect of the multiple step mitigation strategies on the number of illnesses given the ingested dose is examined for a population of 1,500 people. The number of illnesses is estimated for each of the mitigation strategies using the all human *E. coli* and AHP weighted-average beta-Poisson dose-response models. Figure 4.18 shows the predicted distribution of the number of illnesses given the ingested dose for the mitigation strategies along with the baseline mean for the all human *E. coli* beta-Poisson dose-response model. A numerical comparison of the number of illnesses for the all human *E. coli* beta-Poisson dose-response model for the various multiple step mitigation strategies is shown for the 5^{th} percentile, mean, and 95^{th} percentile of the 0.50 probability of exceedance.



	Storage Time & Temp, Ripening Time	Storage Time & Temp, Ripening Time, Distribution Temp	Storage Time & Temp, Ripening Time, Pasteurization	Storage Time & Temp, Ripening Time, Distribution Temp, Pasteurization
5th percentile	500	25	0	0
Mean	700	50	0	0
95th percentile	900	80	0	0

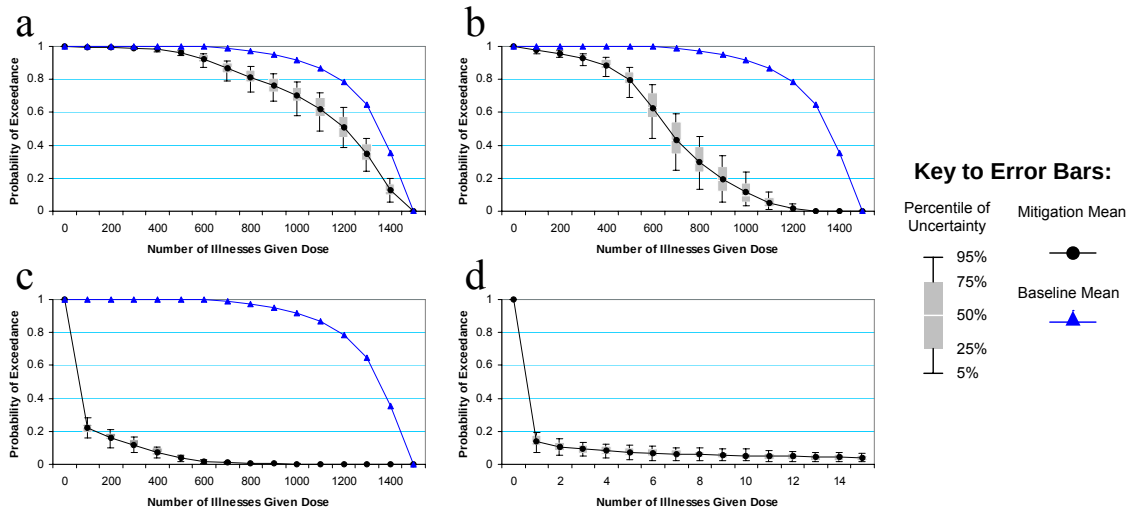
Figure 4.20: Variability and uncertainty for number of illnesses given ingested dose using all human *E. coli* beta-Poisson model for multiple step mitigation strategies: (a) reduction in storage time and temperature and increase in ripening time, (b) reduction in storage time and temperature, increase in ripening time, and reduction in distribution temperatures, (c) reduction in storage time and temperature, increase in ripening time, and pasteurization, and (d) reduction in storage time and temperature, increase in ripening time, reduction in distribution temperatures, and pasteurization, superimposed with mean baseline results

Figure 4.20a shows the probability of exceeding the number of illnesses given the ingested dose based on the all human *E. coli* beta-Poisson dose-response model for an exposed population of 1,500 for the reduced storage time and temperature and increased ripening time mitigation strategy. There is a 0.75 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.67-0.83; in contrast, there is a 0.45 probability of exceeding 800 illnesses, with a 90% confidence interval for the probability of exceedance of 0.34-0.57. Figure 4.20b examines the effects of reduced storage time and temperature, increased ripening time, and reduced distribution

temperatures for the all human *E. coli* beta-Poisson dose-response model. There is a 0.19 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.05-0.33. Figures 4.20c and d show these same mitigations with the addition of pasteurization, but are shown a different scale. For the reduced storage time and temperature, increased ripening time, and pasteurization mitigation strategy there is a 0.04 probability of exceeding 1 illness, with a 90% uncertainty range from 0.02-0.07. For the reduced storage time and temperature, increased ripening time, reduced distribution temperatures, and pasteurization mitigation strategy essentially eliminates the possibility of illness, as there is a 0.00 probability of exceeding 1 illness.

For the all human *E. coli* beta-Poisson model, the baseline case study results in a 0.95 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.90-0.99; the probability of exceeding 800 illnesses is 0.74, with a 90% confidence interval of 0.64-0.84. Comparison of the reduced storage time and temperature and increased ripening time multiple step mitigation strategy to the baseline mean for the number of illnesses given the ingested dose demonstrates only a small reduction in the number of illnesses given the ingested dose. The combined effects of reduced storage time and temperature, increased ripening time, and reduced distribution temperatures have more significant results as compared to the baseline. However, the most dramatic decrease in illness is seen with the addition of pasteurization to the mitigation strategies; both multiple step mitigation strategies involving pasteurization effectively eliminate illness from occurring.

Figure 4.21 shows the results of the number of illnesses given the ingested dose for the multiple step mitigation strategies along with the baseline mean for the AHP weighted-average dose-response model. A numerical comparison of the number of illnesses for the AHP weighted-average beta-Poisson dose-response model for the various multiple step mitigation strategies is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	Storage Time & Temp, Ripening Time	Storage Time & Temp, Ripening Time, Distribution Temp	Storage Time & Temp, Ripening Time, Pasteurization	Storage Time & Temp, Ripening Time, Distribution Temp, Pasteurization
5th percentile	1100	580	5	0
Mean	1200	675	8	0
95th percentile	1275	775	10	0

Figure 4.21: Variability and uncertainty for Number of Illnesses given Ingested Dose using AHP weighted-average beta-Poisson model for multiple step mitigation strategies: (a) reduction in storage time and temperature and increase in ripening time, (b) reduction in storage time and temperature, increase in ripening time, and reduction in distribution temperatures, (c) reduction in storage time and temperature, increase in ripening time, and pasteurization, and (d) reduction in storage time and temperature, increase in ripening time, reduction in distribution temperatures, and pasteurization, superimposed with mean baseline results

Figure 4.21a shows the probability of exceeding the number of illnesses given the ingested dose based on the AHP weighted-average beta-Poisson dose-response model for an exposed population of 1,500 for the reduced storage time and temperature and increased ripening time mitigation strategy. There is a 0.99 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.99-1.00; there is a 0.81 probability of exceeding 800 illnesses, with a 90% confidence interval for the probability of exceedance of 0.73-0.88. Figure 4.21b examines the effects of reduced storage time and temperature, increased ripening time, and reduced distribution temperatures for the AHP weighted-average beta-Poisson dose-response model. There is a 0.96 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.93-0.98. In addition, there is a 0.30 probability of exceeding 800 illnesses, with a 90% uncertainty range of 0.13-0.45. Figures 4.21c and d show these same mitigations with the addition of pasteurization. Figure 4.21c shows there is a 0.16 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.10-0.21. There is a 0.00 probability of exceeding 800 illnesses. Figure 4.21d shows a 0.14 probability of exceeding 1 illnesses, with a 90% uncertainty range of 0.07-0.19.

For the AHP weighted-average beta-Poisson model, the baseline case study results in a 1.00 probability of exceeding 200 illnesses; the probability of exceeding 800 illnesses is 0.97, with a 90% confidence interval of 0.94-1.00. Comparison of the reduced storage time and temperature and increased ripening time multiple step mitigation strategy to the baseline mean for the number of illnesses given the ingested dose demonstrates only a small reduction in the number of illnesses given the ingested dose. The combined effects of reduced storage time and temperature,

increased ripening time, and reduced distribution temperatures have more significant results as compared to the baseline. However, the most dramatic decrease in illness is seen with the addition of pasteurization to the mitigation strategies. Reduced storage time and temperature, increased ripening time, and pasteurization leads to a factor of ten reduction in the number of illnesses, while the addition of decreased distribution temperatures to this mitigation strategy results in a factor of 100 reduction in the number of illnesses.

4.3.4 Worst-Case Sensitivity Analyses

In addition to being a risk assessment and risk management tool, the model can also be used for sensitivity analysis. The baseline case study represents a moderate level of initial contamination and moderately abusive production and distribution phases; the results show that under these conditions, potentially high levels of *E. coli* O157:H7 can develop in the cheese and resulting in serious adverse health consequences. The results of the mitigation strategies demonstrate that pasteurization is a key step in the reduction of *E. coli* O157:H7 contamination in cheese. The purpose of the worst-case analysis is to examine the effects of pasteurization under high levels of initial contamination and severe abuse during the production and distribution phases.

Two worst-case analyses are investigated in order to determine the sensitivity of the model to pasteurization, severe abuse, and initial contamination. Table 4.5 provides a comparison between the baseline selections and the worst-case selections for the production and distribution phases. The results of these worst-case analyses are compared to the baseline results for the contamination level after production, the

contamination level after distribution, the contamination level per dose, and the number of illnesses given the ingested dose for the all human *E. coli* beta-Poisson model and AHP weighted-average dose-response model.

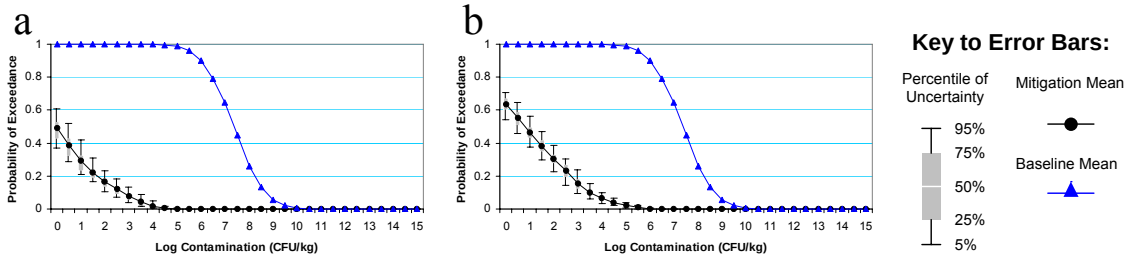
Table 4.5: Production and Distribution Selections for Baseline and Worst-Case Simulations

Step	Sub-System Element Description	Baseline Case Study	Worst-Case Production and Distribution	Worst-Case Initial Contamination and Production
A0	Initial *E. coli* O157:H7 Contamination (CFU/ml)	10 ± 10 CFU/ml	10 ± 10 CFU/ml	100 ± 100 CFU/ml
A1	Contamination after Milk Storage	2 days; 5˚C<T< 8˚C	5 days; T> 8˚C	5 days; T> 8˚C
A2	Contamination after Milk Heat Treatment	Unpasteurized Milk	Pasteurized Milk	Pasteurized Milk
A3	Contamination after Addition of Coagulant	Mesophilic	Mesophilic	Mesophilic
A4	Contamination after Cutting of Curd	---	---	---
A5	Contamination after Cooking of Curd	36˚C ≤ Temp ≤ 40˚C	36˚C ≤ Temp ≤ 40˚C	36˚C ≤ Temp ≤ 40˚C
A6	Contamination after Separation of Curd and Whey	---	---	---
A7	Contamination after Salting	Dry	Dry	Dry
A8	Contamination after Hooping and Pressing	---	---	---
A9	Contamination after Packaging and Ripening	75 days	45 days	45 days
B1	Contamination after Storage, before Transportation	pH 6.0; 1-24 hours; 5˚C	pH 6.0; 1-24 hours; 10˚C	pH 6.0; 1-24 hours; 5˚C
B2	Contamination after Transportation to Retail	1-12 hours; 10˚C	1-12 hours; 10˚C	1-12 hours; 5˚C
B3	Contamination after Retail Storage	1-120 hours; 5˚C	1-120 hours; 10˚C	1-120 hours; 5˚C
B4	Contamination after Transportation to Consumer	1-2 hours; 12˚C	1-2 hours; 10˚C	1-2 hours; 5˚C
B5	Contamination after Consumer Storage	1-336 hours; 5˚C	1-336 hours; 10˚C	1-336 hours; 5˚C

4.3.4.1 Contamination after Production

The number of *E. coli* O157:H7 in 1 kg of cheese after production is estimated for both of the worst-case analyses. Figure 4.22 shows the predicted distribution of *E. coli* O157:H7 after production for the worst-case analyses along with the baseline mean. A numerical comparison of the contamination level after production for the

worst-case analyses for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance is also shown.



	Worst-Case Production & Distribution	Worst-Case Initial Contamination & Production
5th percentile	-0.50	0.25
Mean	-0.10	0.75
95th percentile	0.60	1.30

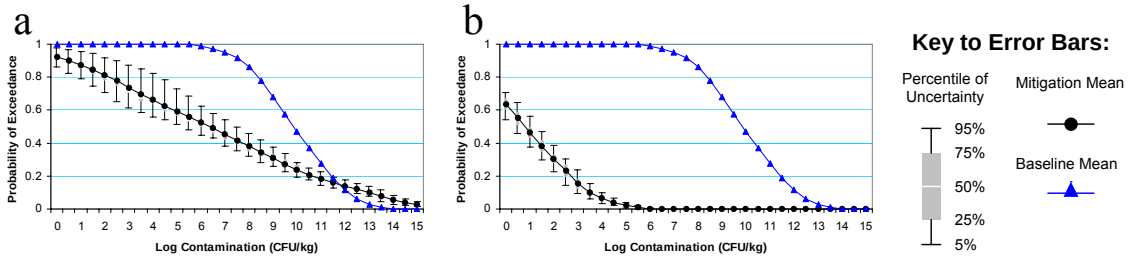
Figure 4.22: Variability and uncertainty for probability of exceeding contamination level per 1 kg cheese after production for worst case analyses (a) worst-case production and distribution selections, (b) worst-case initial contamination and production selections, superimposed with mean baseline results

Figure 4.22a shows the probability of exceeding the contamination level per 1 kg cheese after production for the worst-case production and distribution selections. There is a 0.29 probability of exceeding an *E. coli* O157:H7 contamination level of 1.0 CFU/kg, with a 90% uncertainty range from 0.21-0.42. Figure 4.22b shows the results for the worst-case initial contamination and production selections. The probability of exceeding an *E. coli* O157:H7 contamination level of 1.0 CFU/kg is 0.47, with a 90% confidence interval of 0.38-0.56. In comparison, the baseline result has a 1.00 probability of exceeding a contamination level of 1.0 CFU/kg. Both worst-case analyses demonstrate that despite severe abuse conditions, pasteurization still makes a significant impact on the level of contamination. Comparison of the worst-

case analyses shows that the higher initial contamination level results in a significantly higher contamination after production.

4.3.4.2 Contamination after Distribution

The number of *E. coli* O157:H7 in 1 kg of cheese after distribution is estimated for both of the worst-case analyses imposed. Figure 4.23 shows the predicted distribution of *E. coli* O157:H7 after distribution for the worst cases analyses along with the baseline mean. A numerical comparison of the contamination level after distribution for the worst-case analyses is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	Worst-Case Production & Distribution	Worst-Case Initial Contamination & Production
5th percentile	5.00	0.25
Mean	6.50	0.75
95th percentile	7.50	1.30

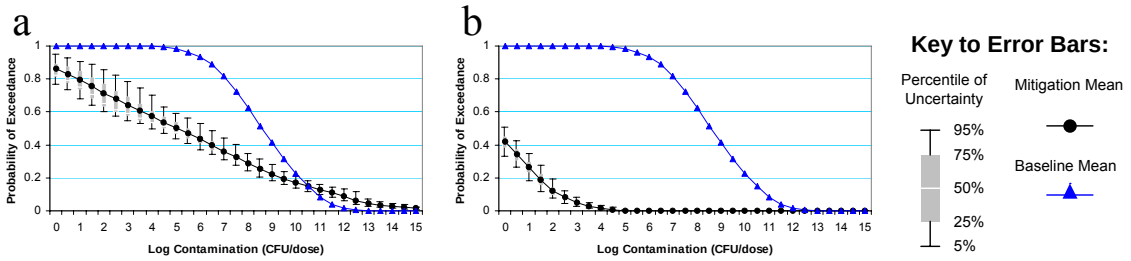
Figure 4.23: Variability and uncertainty for probability of exceeding contamination level per 1 kg cheese after distribution for worst case analyses (a) worst-case production and distribution selections, (b) worst-case initial contamination and production selections, superimposed with mean baseline results

Figure 4.23a shows the probability of exceeding the contamination level per 1 kg cheese after distribution for the worst-case production and distribution selections. There is a 0.87 probability of exceeding an *E. coli* O157:H7 contamination level of 1.0 CFU/kg, with a 90% uncertainty range from 0.79-0.96. Figure 4.23b shows the results for the worst-case initial contamination and production selections. The

probability of exceeding an *E. coli* O157:H7 contamination level of 1.0 CFU/kg is 0.47, with a 90% confidence interval of 0.38-0.56. In comparison, the baseline result has a 1.00 probability of exceeding a contamination level of 1.0 CFU/kg. It is apparent that pasteurization makes a significant impact on the level of contamination after distribution as compared to the baseline. However, the worst-case selections for distribution temperatures significantly increase the *E. coli* O157:H7 contamination level. In fact, the worst-case distribution temperatures have more of an impact on the contamination level after distribution than high levels of initial contamination. In addition, when the worst-case initial contamination and production analysis is compared to the contamination after production in Figure 4.22b, it is also apparent that when distribution temperatures are kept at 5ºC, no increase in contamination occurs.

4.3.4.3 Contamination per Dose

The effect of the worst-case analyses on the contamination of *E. coli* O157:H7 per dose is also explored. Based on the *E. coli* O157:H7 contamination per serving and the number of servings consumed, the dose is estimated for the worst-case analyses. Figure 4.24 shows the predicted distribution of *E. coli* O157:H7 contamination per dose along with the baseline mean. A numerical comparison of the contamination per dose for the worst-case analyses for the 5^{th} percentile, mean, and 95^{th} percentile of the 0.50 probability of exceedance is also shown.



	Worst-Case Production & Distribution	Worst-Case Initial Contamination & Production
5th percentile	4.00	-1.00
Mean	5.00	-0.50
95th percentile	6.50	0.05

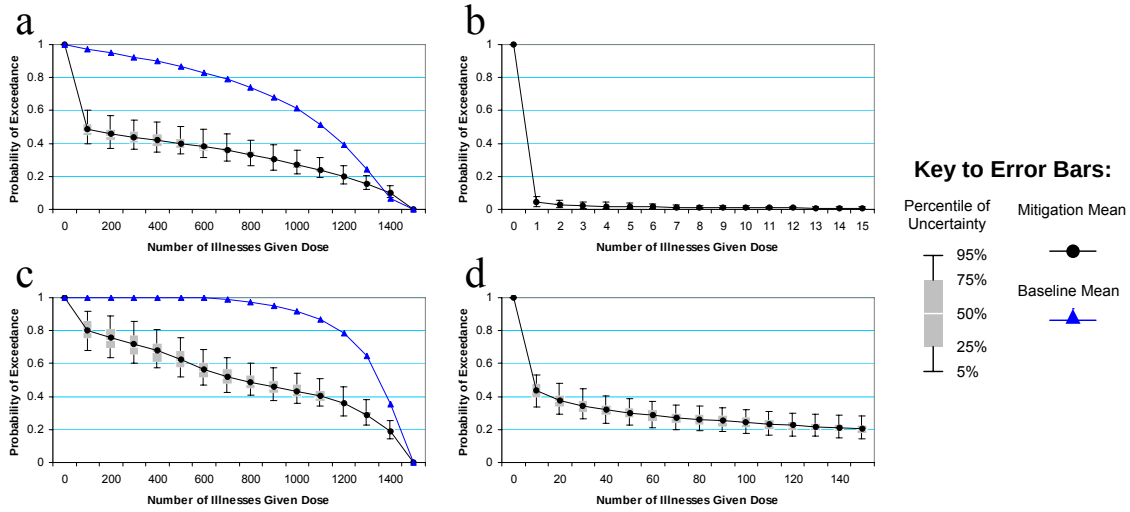
Figure 4.24: Variability and uncertainty for probability of exceeding contamination level per dose for worst case analyses (a) worst-case production and distribution selections, (b) worst-case initial contamination and production selections, superimposed with mean baseline results

Figure 4.24a shows the probability of exceeding the contamination level per 1 dose for the worst-case production and distribution selections. There is a 0.80 probability of exceeding an *E. coli* O157:H7 contamination level of 1.0 CFU/kg, with a 90% uncertainty range from 0.68-0.90. Figure 4.23b shows the results for the worst-case initial contamination and production selections. The probability of exceeding an *E. coli* O157:H7 contamination level of 1.0 CFU/kg is 0.27, with a 90% confidence interval of 0.18-0.35. In comparison, the baseline result has a 1.00 probability of exceeding a contamination level of 1.0 CFU/kg. Again, the temperature abuse during the distribution phase has a significant impact on the contamination level per dose.

4.3.4.4 Number of Illnesses Given Dose

The effect of both worst-case analyses on the number of illnesses given the ingested dose is examined for a population of 1,500 people. The number of illnesses is estimated for each of the worst-case analyses using the all human *E. coli* and AHP

weighted-average beta-Poisson dose-response models. Figure 4.25 shows the predicted distribution of the number of illnesses given the ingested dose for the worst-case analyses along with the baseline. A numerical comparison of the number of illnesses for the all human *E. coli* beta-Poisson and AHP weighted-average beta-Poisson dose-response models for the worst-case analyses is shown for the 5th percentile, mean, and 95th percentile of the 0.50 probability of exceedance.



	All human *E. coli*		AHP	
	Worst-Case Production & Distribution	**Worst-Case Initial Cont. & Production**	**Worst-Case Production & Distribution**	**Worst-Case Initial Cont. & Production**
5th percentile	75	0	550	5
Mean	100	0	750	8
95th percentile	500	0	1100	10

Figure 4.25: Variability and uncertainty for number of illnesses given ingested dose for worst case analyses using all human *E. coli* beta-Poisson dose-response model for (a) worst-case production and distribution selections, (b) worst-case initial contamination and production selections, and using AHP weighted-average beta-Poisson dose-response model for (c) worst-case production and distribution selections, (d) worst-case initial contamination and production selections, superimposed with mean baseline results

Figure 4.25a shows the probability of exceeding the number of illnesses given the ingested dose based on the all human *E. coli* beta-Poisson dose-response model

for an exposed population of 1,500 for the worst case production and distribution selections. There is a 0.46 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.37-0.57. Figure 4.25b examines the effects of the worst case initial contamination and production selections for the all human *E. coli* beta-Poisson dose-response model. There is a 0.05 probability of exceeding 1 illness, with a 90% confidence range from 0.02-0.08. Figure 4.25c shows the probability of exceeding the number of illnesses given the ingested dose based on the AHP weighted-average beta-Poisson dose-response model for an exposed population of 1,500 for the worst-case production and distribution selections. There is a 0.76 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.64-0.89. Figure 4.25d examines the effects of the worst-case initial contamination and production selections for the all human *E. coli* beta-Poisson dose-response model. There is a 0.37 probability of exceeding 20 illnesses, with a 90% uncertainty range of 0.29-0.48.

For the all human *E. coli* beta-Poisson model, the baseline case study resulted in a 0.95 probability of exceeding 200 illnesses, with a 90% uncertainty range of 0.90-0.99. Again, these worst-case analyses indicate that pasteurization is extremely effective in reducing the consequences of *E. coli* O157:H7 contamination. It is also interesting to note that temperature abuse during the distribution phase is worse, in terms of number of resulting illnesses, than a high level of initial contamination. For the AHP weighted-average beta-Poisson model, the baseline case study resulted in a 100% probability of exceeding 200 illnesses. Even with the more conservative estimates of the AHP weighted-average model, the impact of pasteurization is obvious. Again, the results for the AHP weighted-average beta-Poisson model

emphasize the fact that initial contamination levels are less important than controlling temperature abuse during the distribution phase.

4.4 Discussion of Results

Several conclusions can be made from the successful application of the engineering-based decomposition methodology to the problem of *E. coli* O157:H7 contamination in cheese. First, in terms of model uncertainty, the results show there is not a significant difference between the beta-Poisson and Weibull-Gamma models for the data sets investigated; this holds true for the AHP weighted-average models as well. Although there are slight differences in the shapes of the curves, in general, the areas of uncertainty of the two models overlap indicating that the difference is not significant.

In terms of the parameter uncertainty of the dose-response models, there is wide dispersion among the results. The differences in the probability of illness estimated with the three data sets emphasize the difficulty of developing the dose-response parameters for *E. coli* O157:H7. Due to ethical considerations, surrogate pathogen and *E. coli* O157:H7 animal data must be used for parameter estimation. The three data sets (i.e., all human *E. coli*, *E. coli* O157:H7 rabbit, and *S. dysenteriae*) used for parameter estimation of the beta-Poisson and Weibull-Gamma models are those data sets that resulted in significant fits (i.e., the minimum deviance did not exceed the 5^{th} percentile of the χ^2 distribution); however, the results generated using these data sets are significantly different. The results show that the all human *E. coli*

data set provides the least conservative estimate of the probability of illness, followed by the *E. coli* O157:H7 rabbit and *S. dysenteriae* data sets.

While the parameter uncertainty can be assessed through comparison of the results, the AHP weighted-average method provides an alternative way to address the data uncertainty by considering all of the relevant available data and ranking the importance of this data. The results show that the weighted-average models developed with the AHP method provide reasonable probabilities of illness. As expected, the AHP weighted-average dose-response model provides a compromise between the least conservative probability of illness estimated with the all human *E. coli* data set and most conservative probability of illness estimated with the *S. dysenteriae* data set. In addition, the AHP weighted-average models are validated with both clinical trial data and outbreak data. The results show that the AHP weighted-average models provide reasonable fits to the outbreak data and the best fit (as compared to the all human *E. coli*, *E. coli* O157:H7 rabbit, and *S. dysenteriae* dose-response models) to the clinical trial data. These positive results from the validation lend confidence to the results generated with the AHP weighted-average models.

In terms of sensitivity analysis, the results show that milk heat treatment is the most important factor in controlling *E. coli* O157:H7 contamination in cheese. In fact, pasteurization alone is effective in controlling contamination in a moderately abusive production and distribution scenario, as well as in worst-case scenarios. The results also show that distribution temperatures have a significant impact on *E. coli* O157:H7 contamination. The worst-case sensitivity analyses show that worst-case

distribution temperatures have more of an impact on the contamination level than high levels of initial contamination. Obviously, pasteurization is effective in eliminating the majority of initial contamination, but temperature abuse during the distribution phase allows any remaining contamination to grow significantly. The results of this model are also somewhat sensitive to milk storage time and temperature; however, ripening time had very little impact on *E. coli* O157:H7 contamination levels.

The mitigation strategies investigated also emphasize the importance of pasteurization. Whether used as a single mitigation or in combination with other mitigations, pasteurization is the key element in eliminating *E. coli* O157:H7 contamination in cheese. In fact, even in a moderately abusive scenario, the multiple step mitigations that do not involve pasteurization are not enough to control contamination levels.

The results shown in this chapter demonstrate the successful application of the engineering decomposition methodology to a food safety problem. The reduction of the problem to its basic elements through the use of the DML methodology allows this model to represent a wide variety of cheese types, assess possible mistreatment of the cheese during production and distribution, evaluate potential mitigation strategies, and perform sensitivity analyses. Thus, the engineering-based approach to QMRA results in a more flexible risk model which can be used as both a risk assessment and risk management tool.

5. DISCUSSION

5.1 Discussion Overview

The probabilistic risk assessment model to study *E. coli* O157:H7 contamination in cheese accomplishes all of the goals of a traditional quantitative microbial risk assessment (QMRA). This model quantitatively accounts for the uncertainty of *E. coli* O157:H7 contamination in cheese, estimates the likelihood and magnitude of *E. coli* O157:H7 contamination at various points along the exposure path, predicts the various human health risks associated with ingestion of *E. coli* O157:H7 contaminated cheese, and identifies the risk-significant contributors and possible mitigation strategies. However, this risk model offers advancements over the traditional approach as well. First, by integrating microbial data and probabilistic-based engineering models and methods within the traditional QMRA framework, this model addresses some of the deficiencies of the traditional approach. The use of these non-traditional methods allows the model to account for data, parameter, and model uncertainty, as well as variability throughout the cheese manufacturing and distribution processes. Second, the recognition and characterization of both aleatory and epistemic uncertainty throughout the model allows for the separation of these elements, and this disaggregation of total uncertainty results in a more powerful risk management tool. Third, validation of the dose-response model lends credence to the results of the risk model; therefore, the results of the risk model can be used both as an absolute assessment of the risk and as a relative measurement of mitigation and control strategies. Finally, the adaptation of the reductionist approach results in a

more systematic approach to food safety problems which captures the interdependencies and interrelationships of the basic elements. While this research provides many improvements over previous risk assessments, it is also acknowledged that there are areas for improvement. Both the advancements of this research as well as the areas needing improvement are discussed relative to the exposure assessment, dose-response assessment, and risk characterization.

5.2 Advancements and Areas for Improvement

5.2.1 Exposure Assessment

The use of the Dynamic Master Logic (DML) methodology in the structuring of the exposure assessment results in a more powerful process risk model. Previous process risk models (PRM) have investigated only one specific scenario. The DML methodology decomposes the system into system elements, sub-system elements, basic elements, and options, thus identifying the variability throughout the cheese manufacturing and distribution processes. By basing both the underlying mathematical model and the Probabilistic Risk Assessment of *E. coli* O157:H7 in Cheese (PRAEC) interface on this hierarchical framework, any number of different scenarios can be analyzed. Thus, scenarios can represent different cheese types and different processes among manufacturers, as well as assess the impact of abuse during production and distribution. In addition, the DML concept models the relationships between the basic elements, thereby capturing the interdependencies. This systematic approach to food safety risk assessment ensures that all relevant activities, events, processes, etc. are captured in the risk model, and that the associations between these

elements are also captured. While the DML structure provides an excellent foundation for the model, this structure could be expanded at the top-level to provide an even more accurate representation of the cheese manufacturing process. The scope of the exposure assessment is restricted to cheese production, distribution, and consumption, with the user selecting the distribution of initial contamination. The model could be expanded to include the on-farm processes associated with milk production, and DML decomposition could be used to identify the system elements, sub-system elements, basic elements, and options of this process.

Another advancement of this research is the recognition, characterization, and separation of aleatory and epistemic uncertainty throughout the model. The use of a hierarchical structure is vital in recognizing and separating these uncertainties, with the DML structure identifying the variability throughout the process. The separation of the aleatory and epistemic uncertainty results in the ability to identify which part of the total uncertainty is due to lack of knowledge and/or variability. This disaggregation of total uncertainty results in a more powerful risk management tool, as it is possible to determine the steps that can be taken to reduce the total uncertainty of the model. Additional information will reduce the epistemic uncertainty and improve future risk estimates, while potential changes to the physical system will reduce the aleatory uncertainty. In addition, data and parameter uncertainties are accounted for throughout the model in a variety of ways. These advancements in the characterization of uncertainty, as well as areas for improvement, are discussed relative to the production, distribution, and consumption phases.

5.2.1.1 Production

Modeling the growth and survival of *E. coli* O157:H7 in cheese during manufacturing and ripening is a multifaceted problem due to the complexity of cheese and the disparity within the experimental data. The multiplicative factors (MF) method models the increase or decrease in *E. coli* O157:H7 contamination and provides a technique for addressing inconsistency, deficiency, and uncertainty associated with the experimental data used to describe contamination in the production phase; the Bayesian updating process accounts for the parameter uncertainty associated with the MF distributions.

First, the cheese-making process is extremely complex because cheese itself is biologically and biochemically dynamic, and understanding cheese manufacturing and ripening involves a wide range of scientific disciplines including biology, microbiology, chemistry, enzymology, molecular genetics, rheology, etc. (Fox, 1993). Therefore, understanding the growth and survival of pathogens in cheese is also complex, as there are a number of factors (i.e., time, temperature, pH, salt content, moisture content, fat content, starter cultures, secondary cultures, etc.) that influence microbial growth. The wide variety of cheeses and the variability in the cheese-making process only further complicates the analysis of this process.

Second, this risk assessment is based solely on experimental data and information available in the open literature. Although many experiments have examined *E. coli* O157:H7 contamination levels during cheese manufacturing and ripening, there is much disparity among the data. Typically, these experiments add a given amount of *E. coli* O157:H7 to milk (either pasteurized or unpasteurized) and

monitor the contamination level at various points during the cheese production process. The amount of initial contamination and the points during production at which the contamination is measured varies among the experiments. In addition, the contamination level during production is dependent on a number of influencing factors, and these experiments differ in the influencing factors monitored. Finally, these experiments examine a wide variety of cheese types, leading to much variability in the cheese production process used.

The MF method offers not only a simplified approach to microbial modeling, but also a method for dealing with multiple data sources and data limitations. The MF approach deals with the data inconsistency by developing a multiplier to move from step to step along the production path. Thus, the MF is concerned not with absolute level of contamination, but rather with the relative increase or decrease in contamination level. So, despite the experimental inconsistencies in the initial contamination level, the MF method can be applied. In addition, the MF method is flexible in that a MF can be calculated for whichever points in the cheese production process are monitored in the experimental data. Finally, the MF method ignores the influencing factors for which there are not enough data to develop a multiplier. This results in some influencing factors not being singled out in the decomposition process, but rather rolled into the MF.

While the MF clearly simplifies a very complex problem and allows for maximum use of the experimental data, it is acknowledged that this modeling concept may oversimplify the problem of microbial growth in cheese. While this method has the advantage of being applicable to areas which lack data, perhaps the use of

predictive microbial models to areas in which sufficient data exists should be explored. Another possibility is to further decompose the steps with sufficient data in order to consider more than two influencing factors. Results using these more complex MFs could then be compared to results generated with traditional microbial predictive models in order to determine the worthiness of the MF method. Regardless of the model used to estimate the growth and survival of *E. coli* O157:H7 during manufacturing, the production phase may benefit from additional steps and further gradation of those steps. For example, steps could be added in the production phase to allow for the possibility of re-contamination after the milk heat treatment step.

5.2.1.2 Distribution

Similar to the production phase, the distribution phase uses the Bayesian updating procedure to account for the parameter uncertainty associated with the Gompertz parameters. Furthermore, the distribution phase could also benefit from additional steps and further gradation. Steps could be added to the distribution phase to account for both the death/inactivation of the bacteria and the growth limitations caused by insufficient nutrients, metabolic wastes, and competition from other bacteria. The starter and secondary cultures added in the cheese-making process continue to allow the cheese to ripen and may inhibit the growth of microbial pathogens, such as *E. coli* O157:H7. The effects of ripening need to be accounted for during the distribution phase. This might be accomplished either through the addition of a dampening factor to the Gompertz equation or by using an additional model that considers microbial community dynamics. One such model is the Lotka-Volterra competition model which provides a basic model for the population growth of two

interacting species (Powell et al., 2004). Further gradation of the options at each step would increase the accuracy of the model as well. For example, the distribution steps modeling growth of *E. coli* O157:H7 might be expanded to include the effects of sodium chloride concentration on *E. coli* O157:H7 growth, although data is needed to include this option. Finally, the DML structure could be expanded to account for additional model uncertainty. Specifically, there are a number of equations which model bacterial growth (i.e., Gompertz, Baranyi, three-phase linear, etc.). The risk model could be improved by allowing for selection among various growth, inactivation, and competition models in the distribution phase.

5.2.1.3 Consumption

The consumption phase could be improved through the addition of a step that considers the likelihood of consumption. Currently, the model assumes that all people exposed in an outbreak consume the *E. coli* O157:H7-contaminated cheese; in other words, it is assumed that all people in an outbreak are equally likely to consume contaminated cheese. This may not be realistic, particularly for cheese with high levels of contamination, and may lead to over-estimation of the number of illnesses and adverse health consequences. A likelihood function for consumption would relate the likelihood of consuming *E. coli* O157:H7-contaminated cheese to the level of contamination. This function would consider both mitigations to behavior and prohibitions to consumption in order to more accurately describe the probability of consuming contaminated cheese.

5.2.2 Dose-Response Assessment

The dose-response assessment clearly benefits from the adaptation of engineering models and methods. First, the DML methodology allows for selection among various traditional and newly proposed dose-response models, thereby accounting for model uncertainty. Second, the uncertainty associated with the dose-response model is addressed in two ways. The parameters for the dose-response models are estimated from a number of different data sets and the resultant probability of illness, calculated from the various data sets, is compared in order to assess the uncertainty. Additionally, the Analytical Hierarchy Process (AHP) method provides an alternative way to address the data uncertainty associated with dose-response data. Previous research shows that various *Shigella* spp. and *E. coli* strains have some biological similarities to *E. coli* O157:H7 in terms of pathogenicity. In addition, animal studies involving *E. coli* O157:H7 may also provide insight on human responses to *E. coli* O157:H7. While none of these alternatives provide an exact relationship for an *E. coli* O157:H7 dose-response model, alternatives that are biologically similar to *E. coli* O157:H7 should be considered when developing a dose-response model for *E. coli* O157:H7. The AHP method accomplishes this objective by developing weighted-average beta-Poisson and Weibull-Gamma dose-response models that consider all of the available data and rank the importance of this data.

Another advancement of this research is the validation of the dose-response model. QMRAs have been performed to determine the risk of *E. coli* O157:H7 infection from various foods, but the dose-response models used in these risk

assessments have yet to be fully validated. Comparison of actual observations in outbreak data to the predicted observation lends credence to the developed dose-response models. Furthermore, the results of a validated risk model can be used both as an absolute assessment of the risk and as a relative measurement of mitigation and control strategies. It is desirable to validate dose-response models with human epidemiological information; this is especially important in the case of *E. coli* O157:H7 since the underlying data are based on animal studies and surrogate pathogens. Validation of the dose-response model ensures accuracy and assesses uncertainty.

This research validates the dose-response models developed using the clinical trial data and the AHP weighted-average dose-response relationships by comparing the model estimates with actual human outbreak information. The AHP weighted-average models provide reasonable fits to the outbreak data. In addition, it the AHP weighted-average models provide the best fit to all of the available clinical trial data. However, there are some problems with this validation. First, the outbreak data available typically occurred at lower doses, whereas the clinical trial data that these models are based on typically utilize higher doses, making validation at lower doses difficult. Despite this, the AHP weighted-average models provide a reasonable fit to the outbreak data. Second, the outbreak data available for validation is very limited and additional outbreak data are required for further validation of all of the dose-response models investigated in this research. Third, the vehicles of transmission in the outbreak data varied widely and only one of the outbreaks is caused by contaminated cheese.

Although the dose-response models are successfully validated, there is a larger concern with the underlying assumption that the normal and susceptible populations have similar vulnerabilities to illness. This assumption stems from the fact that the feeding studies used to develop the dose-response model involving health adults, indicating that the dose-response relationship is likely to be inaccurate for the susceptible population. However, there is no data available to develop a dose-response model specifically for the susceptible population. Thus, the differences between the susceptible and normal populations are captured in the severe health outcomes progressing from illness.

5.2.3 Risk Characterization

The risk characterization also benefits from the use of the DML methodology, as any number of different risks can be estimated. In addition, the uncertainty associated with the severe health outcomes progressing from illness is also addressed through Bayesian inference for both the normal and susceptible populations. However, additional data for the susceptible population is needed; contrary to expert opinion, the data collected for the susceptible population indicates the same propensity for hospitalization given illness as the normal population.

Another advantage of the DML framework is that it lends itself to risk mitigation and control strategy assessment as well as sensitivity analysis. The PRAEC interface allows options in a scenario to be easily changed, making it simple to assess the impact of the change on the contamination level or human health risk; in this way, the risk model provides a means to analyze the relationship between the risk and the factors that might be used to mitigate the risk.

5.3 Engineering-Based Probabilistic Risk Assessment Limitations

This research introduces a new methodology for QMRA using adapted engineering tools and techniques. The application of this engineering-based approach to the problem of *E. coli* O157:H7 contamination in cheese lends confidence that this methodology can be applied to other food safety problems. However, while the advancements and contributions of this new methodology have been previously discussed, it should also be acknowledged that there are limitations to the engineering-based approach. The engineering-based methodology can be more intensive in terms of the time and labor required to establish the model and acquire the data needed to quantify this more detailed model; thus, the engineering-based approach could be most costly to implement.

This engineering-based methodology can be labor intensive due to the reductionist approach. As the system is further decomposed into more refined basic elements, the engineering-based approach requires more data. The more detailed the model, the more data is required, as there are more combinations of the various options of the basic elements. Each of these combinations has an underlying model that requires data in order to be quantified. Thus, it takes time not only to establish all of the basic elements of the model, but also to find data to quantify these basic elements. Another limitation of the engineer-based approach is that it can be limited or driven by the available data. The risk model for a particular problem can be decomposed only to the level permitted by the data. Therefore, for foods and pathogens which have a substantial amount of associated experiment data, the risk model can be far more detailed than for food-pathogen combinations which lack

experimental data. However, the engineering-based approach is still valuable in cases where data is limited. The risk model can be derived to the level possible, and the results of this model can be used to evaluate the relative risk and assess possible mitigation or control strategies. In addition, the systematic approach of the engineering-based methodology can be useful in identifying areas where additional research and data is needed.

5.4 Conclusion

Despite the areas needing improvement, this research has successfully adapted probabilistic-based engineering methods and techniques to a food safety problem. The adaptation of these engineering methods results in numerous advancements, while still accomplishing the main goals of a QMRA. The risk model developed in this research provides a more systematic approach to food safety problems, and also captures the relationships and dependencies between basic elements. In addition, the engineering-based risk assessment methodology adapts methods for characterizing and propagating both aleatory and epistemic uncertainty about the mathematical models and the model parameters. The disaggregation of the aleatory and epistemic uncertainties throughout the risk model results in a more powerful risk management tool. The validation of the dose-response relationship lends confidence and credibility to the results of the model, while also ensuring accuracy and assessing uncertainty; consequently, the model can be used both as an absolute assessment of the risk and as a relative measurement of the effectives of mitigation and control strategies. The successful application of the engineering-based risk assessment

methodology to *E. coli* O157:H7 contamination in cheese suggests that these adapted methodologies and techniques can be applied to food safety problems.

Appendix I: User-Interface

Again, the Dynamic Master Logic (DML) modeling concept is a knowledge management methodology, relying on the fact that complex systems can generally be decomposed into hierarchies. This hierarchy model is primarily used to explain and simulate system behavior, by modeling system elements and the relationships between those elements. The system elements are further decomposed into sub-system elements, basic element, and various options for each basic element in order to account for the variability within the cheese-making process. Thus, the DML methodology is used not only to structure the overall cheese model, but also to develop the Probabilistic Risk Assessment of *E. coli* O157:H7 in Cheese (PRAEC) software interface.

For each of the system elements (i.e., production, distribution, consumption, and risk characterization) a user-interface module is developed. The sub-system elements, basic elements, and options for the basic elements, as identified in the DML decomposition, are given in each of the user-interface modules. The user then selects among the various options in order to develop the scenario to be analyzed. The PRAEC interface is developed within Microsoft Excel using the @RISK add-in, and linked to the database with Visual Basic for Applications (VBA). Developing the risk model in this way lends itself to Monte Carlo simulation, in which the simulation represents not only the variability throughout cheese process, but also the uncertainty in the mathematical model of the process. Figures AI.1-AI.3 show the PRAEC interface modules for the various system elements. It should be noted that the consumption and risk characterization modules are combined.

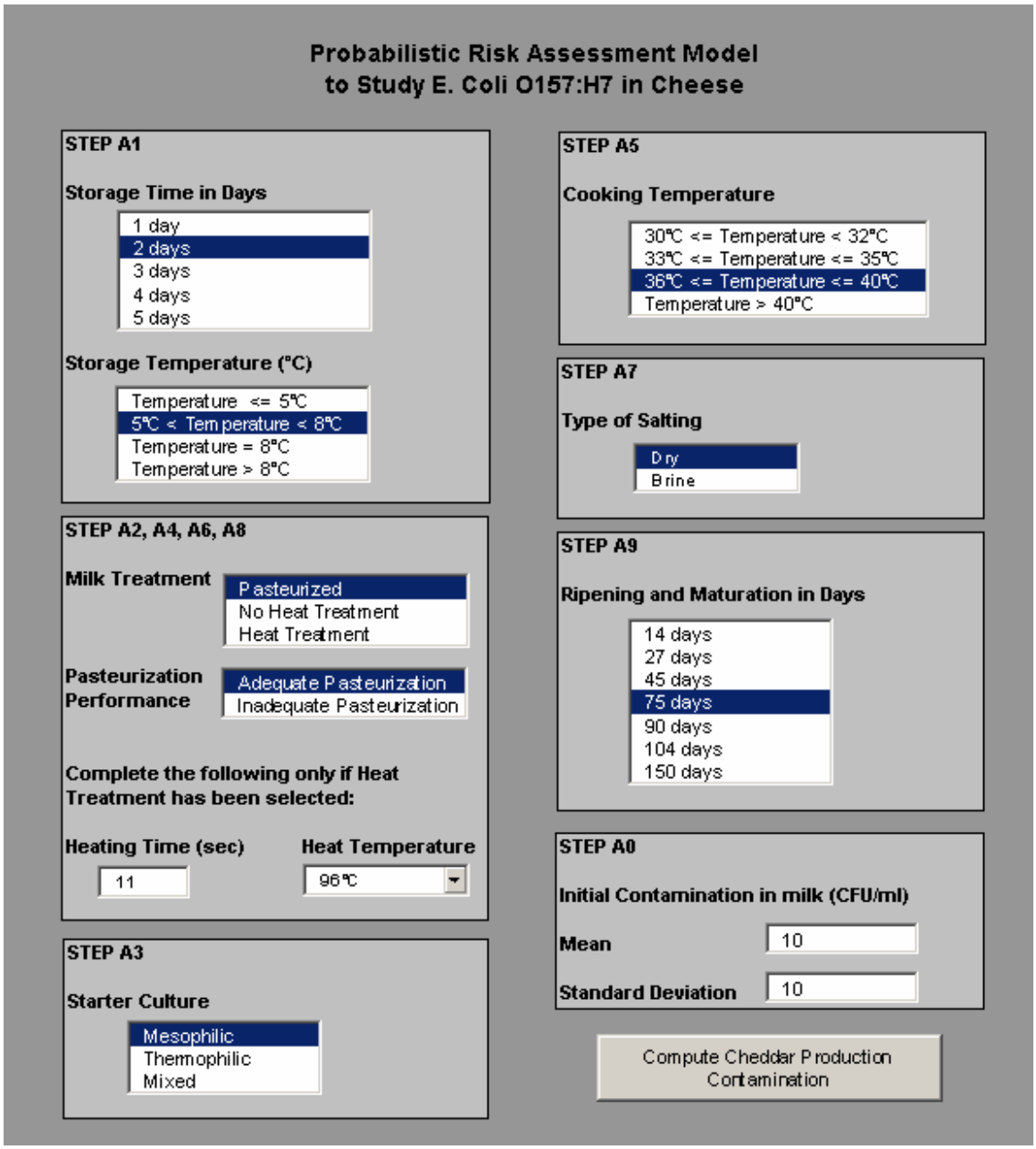


Figure AI.1: Production Phase User-Interface Module based on DML Decomposition

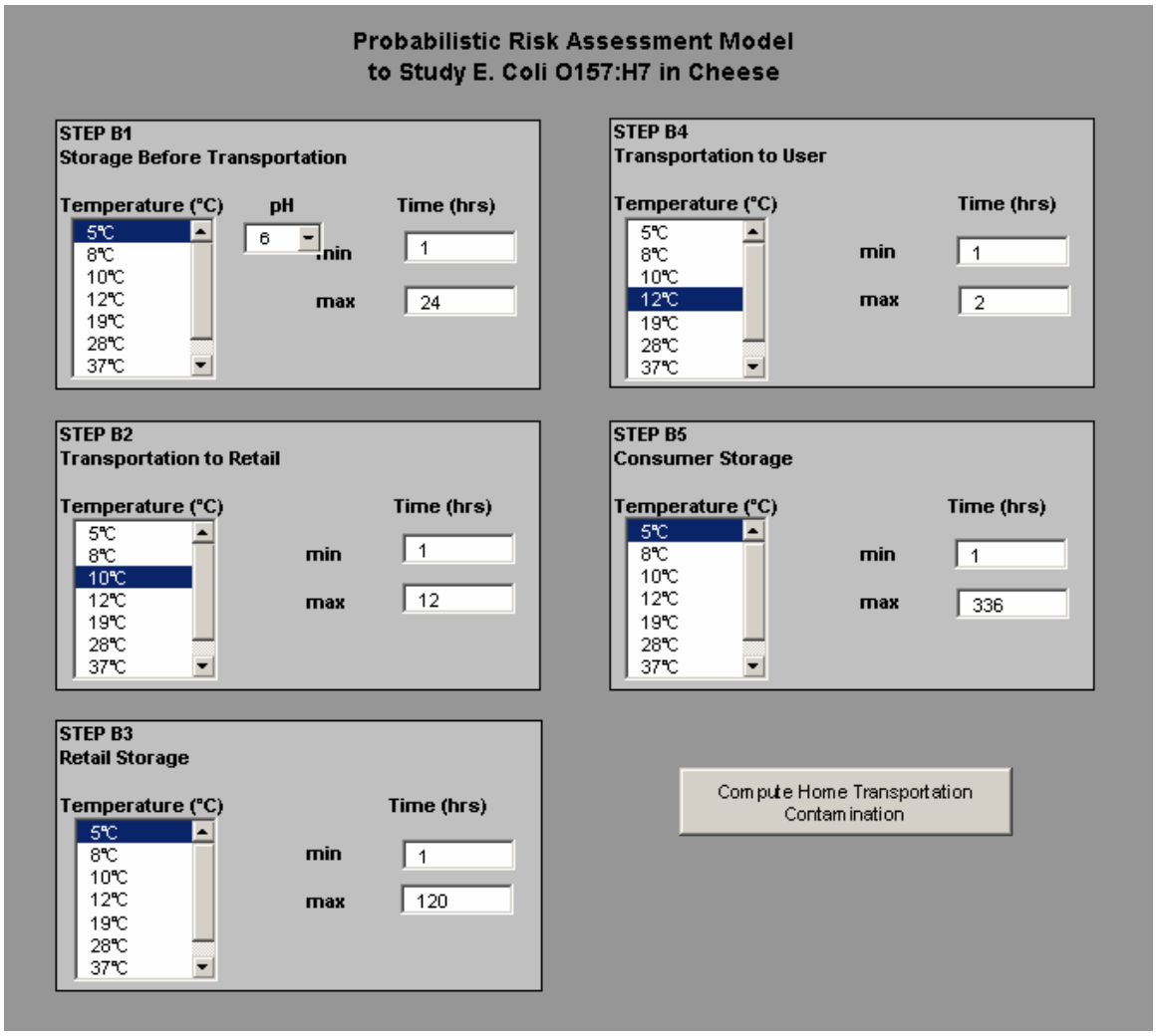


Figure AI.2: Distribution Phase User-Interface Module based on DML Decomposition

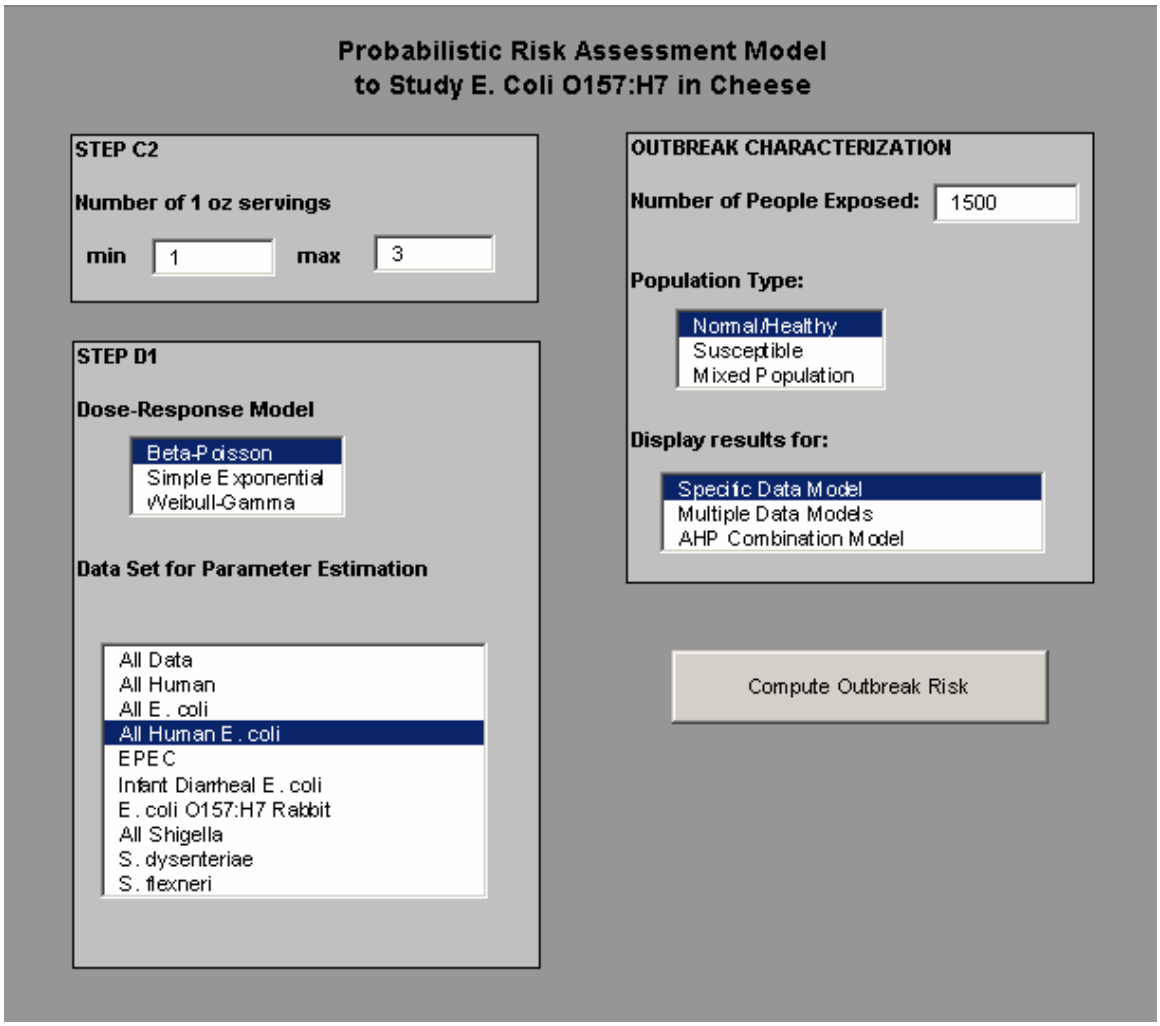


Figure AI.3: Consumption Phase/Risk Characterization User-Interface Module based on DML Decomposition

Appendix II: Multiplicative Factor Parameter Development

The multiplicative factor (MF) is the mathematical predictive model used to propagate the contamination through the production phase. The MF is essentially a "multiplier" that allows the contamination to be propagated through the model. If a selection increases the contamination, the multiplier will be greater than 1; if a selection decreases the contamination, the multiplier will be between 0 and 1. These multipliers are calculated by obtaining the contamination level at the input and output of the step from the experimental data in the literature.

In order to consider the uncertainty associated with the multiplicative factors (MF), the MFs are in the form of a distribution. Although the MFs are assumed to follow a lognormal distribution, no prior knowledge of the parameters of the distribution is assumed. For each MF distribution, non-informative uniform prior distributions are assumed for both the mean and standard deviation. Using data from the literature, multipliers are calculated for each option from the level of contamination at the input and output of a step. These multipliers are the "observed" data and used as evidence for developing the likelihood function in the Bayesian updating process. The Bayesian updating results in posterior distributions for the mean and standard deviation of the MF distribution.

Tables AII.1-AII.9 contain the @RISK functions used in the risk model for the various options at each step of the production phase. These tables include the posterior parameter distributions determined from the Bayesian updating procedure, as well as the MF distributions that are created from the parameter distributions. In addition, the sources from which the likelihood data is obtained are referenced.

Tables AII.10-AII.24 provide the data from which these parameter distributions are created for the various options at each step of the production phase.

Table AII.1: Milk Storage Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A1_i} [a]	σ_{A1_i}	
A1	$A1_1$	1 day; t > 8°C	=RiskLognorm(μ_{A1_1} , σ_{A1_1})	=RiskLognormAlt(5%, 1.744, 50%, 12.24, 95%, 28.06)[b]	=RiskLognormAlt(5%, 3.222, 50%, 56.00, 95%, 258.9)	Altieri et al., 1997; Heuvelink et al., 1998; Mamani et al., 2003; Massa et al., 1999; Palumbo et al., 1997; Wang et al., 1997; Weeratna and Doyle, 1997
	$A1_2$	1 day; t = 8°C	=RiskLognorm(μ_{A1_2} , σ_{A1_2})	=RiskLognormAlt(5%, 1.011, 50%, 2.300, 95%, 13.23)	=RiskLognormAlt(5%, 0.9709, 50%, 4.563, 95%, 16.2134)	
	$A1_3$	1 day; 5°C < t < 8°C	=RiskLognorm(μ_{A1_3} , σ_{A1_3} , RiskTruncate(1,10))[c]	=RiskLognormAlt(5%, 1.110, 50%, 2.791, 95%, 8.745)	=RiskLognormAlt(5%, 1.82, 50%, 31.17, 95%, 241.0)	
	$A1_4$	1 day; t < 5°C	=RiskLognorm(μ_{A1_4} , σ_{A1_4})	=RiskLognormAlt(5%, 0.04448, 50%, 0.4544, 95%, 0.9380)	=RiskLognormAlt(5%, 0.8888, 50%, 19.36, 95%, 236.2)	
	$A1_5$	2 day; t > 8°C	=RiskLognorm(μ_{A1_5} , σ_{A1_5} , RiskTruncate(1,50))	=RiskLognormAlt(5%, 2.176, 50%, 16.35, 95%, 37.29)	=RiskLognormAlt(5%, 4.207, 50%, 62.17, 95%, 258.0)	
	$A1_6$	2 day; t = 8°C	=RiskLognorm(μ_{A1_6} , σ_{A1_6} , RiskTruncate(1,20))	=RiskLognormAlt(5%, 1.86, 50%, 12.07, 95%, 27.91)	=RiskLognormAlt(5%, 3.531, 50%, 58.22, 95%, 256.4)	
	$A1_7$	2 day; 5°C < t < 8°C	=RiskLognorm(μ_{A1_7} , σ_{A1_7} , RiskTruncte(1,10))	=RiskLognormAlt(5%, 1.067, 50%, 1.691, 95%, 7.733)	=RiskLognormAlt(5%, 0.07307, 50%, 1.480, 95%, 28.48)	
	$A1_8$	2 day; t < 5°C	=RiskLognorm(μ_{A1_8} , σ_{A1_8})	=RiskLognormAlt(5%, 0.04314, 50%, 0.4651, 95%, 0.9426)	=RiskLognormAlt(5%, 1.298, 50%, 22.360, 95%, 226.90)	
	$A1_9$	3 day; t > 8°C	=RiskLognorm(μ_{A1_9} , σ_{A1_9} , RiskTruncate(1,100))	=RiskLognormAlt(5%, 2.002, 50%, 12.930, 95%, 28.110)	=RiskLognormAlt(5%, 4.742, 50%, 56.580, 95%, 255.2)	
	$A1_{10}$	3 day; t = 8°C	=RiskLognorm($\mu_{A1_{10}}$, $\sigma_{A1_{10}}$, RiskTruncate(1,50))	=RiskLognormAlt(5%, 1.976, 50%, 12.39, 95%, 27.940)	=RiskLognormAlt(5%, 3.873, 50%, 54.320, 95%, 254.2)	

$A1_{11}$	3 day; 5°C < t < 8°C	=RiskLognorm($\mu_{A1_{11}}$, $\sigma_{A1_{11}}$, RiskTruncate(1,20))	=RiskLognormAlt(5%, 1.370, 50%, 4.958, 95%, 9.374)	=RiskLognormAlt(5%, 1.790, 50%, 28.58, 95%, 242.6)
$A1_{12}$	3 day; t < 5°C	=RiskLognorm($\mu_{A1_{12}}$, $\sigma_{A1_{12}}$)	=RiskLognormAlt(5%, 0.04201, 50%, 0.4791, 95%, 0.9404)	=RiskLognormAlt(5%, 1.402, 50%, 24.130, 95%, 231.4)
$A1_{13}$	4 day; t > 8°C	=RiskLognorm($\mu_{A1_{13}}$, $\sigma_{A1_{13}}$, RiskTruncate(1,))	=RiskLognormAlt(5%, 3.120, 50%, 42.730, 95%, 118.40)	=RiskLognormAlt(5%, 7.149, 50%, 101.50, 95%, 273.7)
$A1_{14}$	4 day; t = 8°C	=RiskLognorm($\mu_{A1_{14}}$, $\sigma_{A1_{14}}$, RiskTruncate(1,150))	=RiskLognormAlt(5%, 3.337, 50%, 42.610, 95%, 117.00)	=RiskLognormAlt(5%, 7.747, 50%, 106.20, 95%, 272.1)
$A1_{15}$	4 day; 5°C < t < 8°C	=RiskLognorm($\mu_{A1_{15}}$, $\sigma_{A1_{15}}$)	=RiskLognormAlt(5%, 1.749, 50%, 12.120, 95%, 28.01)	=RiskLognormAlt(5%, 2.872, 50%, 49.630, 95%, 251.7)
$A1_{16}$	4 day; t < 5°C	=RiskLognorm($\mu_{A1_{16}}$, $\sigma_{A1_{16}}$)	=RiskLognormAlt(5%, 0.04405, 50%, 0.4711, 95%, 0.9412)	=RiskLognormAlt(5%, 1.684, 50%, 24.330, 95%, 251.7)
$A1_{17}$	5 day; t > 8°C	=RiskLognorm($\mu_{A1_{17}}$, $\sigma_{A1_{7}}$, RiskTruncate(1,200))	=RiskLognormAlt(5%, 4.553, 50%, 78.620, 95%, 373.4)	=RiskLognormAlt(5%, 12.000, 50%, 147.80, 95%, 286.0)
$A1_{18}$	5 day; t = 8°C	=RiskLognorm($\mu_{A1_{18}}$, $\sigma_{A1_{18}}$, RiskTruncate(1,200))	=RiskLognormAlt(5%, 3.913, 50%, 57.120, 95%, 202.2)	=RiskLognormAlt(5%, 9.693, 50%, 125.20, 95%, 278.2)
$A1_{19}$	5 day; 5°C < t < 8°C	=RiskLognorm($\mu_{A1_{19}}$, $\sigma_{A1_{19}}$, RiskTruncate(1,))	=RiskLognormAlt(5%, 1.426, 50%, 3.178, 95%, 20.870)	=RiskLognormAlt(5%, 0.9731, 50%, 3.318, 95%, 74.34)
$A1_{20}$	5 day; t < 5°C	=RiskLognorm($\mu_{A1_{20}}$, $\sigma_{A1_{20}}$)	=RiskLognormAlt(5%, 0.04786, 50%, 0.4725, 95%, 0.9444)	=RiskLognormAlt(5%, 2.262, 50%, 32.600, 95%, 241.2)

[a]where *i* represents a specific multiplicative factor based on the options selected; for A1, *i*=20

[b]RiskLognormAlt is an @RISK function which specifies a lognormal distribution, based on the 5th, 50th, and 95th percentiles

[c]RiskTruncate is an @RISK function that truncates the input distribution; truncating a distribution restricts samples drawn from the distribution to values within the entered minimum-maximum range

Table AII.2: Milk Heat Treatment Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A2_i}	σ_{A2_i}	
A2	$A2_1$	Pasteurized	=RiskLognorm(μ_{A2_1} , σ_{A2_1} , RiskTruncate(0,0.0001))	=RiskLognormAlt(5%, 5.08E-5, 50%, 4.96E-4, 95%, 9.50E-4)	=RiskLognormAlt(5%, 11.55, 50%, 18.51, 95%, 35.74)	FSIS, 2004; Goff, 1995; Gunasekera et al., 2002; Rosenau, 2006; Stabel, 2003; USDA, 2004
	$A2_2$	Unpasteurized	=RiskLognorm(μ_{A2_2} , σ_{A2_2})	=RiskLognorm(1.000, 0.1)[a]	=RiskLognorm(0.1, 0.1)	
	$A2_3$	Heat Treatment, 50°C, TBD seconds	=RiskLognorm(μ_{A2_3} , σ_{A2_3})	N/A[b]	N/A	
	$A2_4$	Heat Treatment, 56°C, TBD seconds	=RiskLognorm(μ_{A2_4} , σ_{A2_4})	N/A	N/A	
	$A2_5$	Heat Treatment, 60°C, TBD seconds	=RiskLognorm(μ_{A2_5} , σ_{A2_5})	N/A	N/A	
	$A2_6$	Heat Treatment, 63°C, TBD seconds	=RiskLognorm(μ_{A2_6} , σ_{A2_6})	N/A	N/A	
	$A2_7$	Heat Treatment, 65°C, TBD seconds	=RiskLognorm(μ_{A2_7} , σ_{A2_7})	N/A	N/A	
	$A2_8$	Heat Treatment, 68°C, TBD seconds	=RiskLognorm(μ_{A2_8} , σ_{A2_8})	N/A	N/A	
	$A2_9$	Heat Treatment, 72°C, TBD seconds	=RiskLognorm(μ_{A2_9} , σ_{A2_9})	N/A	N/A	
	$A2_{10}$	Heat Treatment, 76°C, TBD seconds	=RiskLognorm($\mu_{A2_{10}}$, $\sigma_{A2_{10}}$)	N/A	N/A	
	$A2_{11}$	Heat Treatment, 80°C, TBD seconds	=RiskLognorm($\mu_{A2_{11}}$, $\sigma_{A2_{11}}$)	N/A	N/A	
	$A2_{12}$	Heat Treatment, 89°C, TBD seconds	=RiskLognorm($\mu_{A2_{12}}$, $\sigma_{A2_{12}}$)	N/A	N/A	
	$A2_{13}$	Heat Treatment, 90°C, TBD seconds	=RiskLognorm($\mu_{A2_{13}}$, $\sigma_{A2_{13}}$)	N/A	N/A	
	$A2_{14}$	Heat Treatment, 94°C, TBD seconds	=RiskLognorm($\mu_{A2_{14}}$, $\sigma_{A2_{14}}$)	N/A	N/A	
	$A2_{15}$	Heat Treatment, 96°C, TBD seconds	=RiskLognorm($\mu_{A2_{15}}$, $\sigma_{A2_{15}}$)	N/A	N/A	

	$A2_{16}$	Heat Treatment, 100°C, TBD seconds	=RiskLognorm($\mu_{A2_{16}}$, $\sigma_{A2_{16}}$)	N/A	N/A	

[a]Results in a MF of 1, allowing all of the contamination from step A1 to proceed to step A3
[b]Not Available; parameter distributions determined from temperature and user-defined seconds

Table AII.3: Addition of Coagulant Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A3_i}	σ_{A3_i}	
A3	$A3_1$	Pasteurized, Mesophilic	=RiskLognorm(μ_{A3_1} , σ_{A3_1} , RiskTruncate(1,20))	=RiskLognormAlt(5%, 1.009, 50%, 1.019, 95%, 1.275)	=RiskLognormAlt(5%, 0.5401, 50%, 0.6073, 95%, 1.163)	Barbosa et al., 1993a; Barbosa et al., 1993b; Govaris et al., 2002; Hudson et al., 1997; Kornacki and Marth, 1982; Leuschner and Boughflower, 2002; Maher et al., 2001; Park et al., 1973; Ramsaran et al., 1998; Reitsma and Henning, 1996; Spano et al., 2003; Teo et al., 2000
	$A3_2$	Unpasteurized, Mesophilic	=RiskLognorm(μ_{A3_2} , σ_{A3_2} , RiskTruncate(1,20))	=RiskLognormAlt(5%, 1.018, 50%, 1.234, 95%, 2.376)	=RiskLognormAlt(5%, 0.5573, 50%, 1.141, 95%, 3.250)	
	$A3_2$	Pasteurized, Thermophilic	=RiskLognorm(μ_{A3_3} , σ_{A3_3} , RiskTruncate(1,20))	=RiskLognormAlt(5%, 1.010, 50%, 1.141, 95%, 1.616)	=RiskLognormAlt(5%, 1.028, 50%, 1.485, 95%, 2.387)	
	$A3_2$	Unpasteurized, Thermophilic	=RiskLognorm(μ_{A3_4} , σ_{A3_4} , RiskTruncate(1,20))	=RiskLognormAlt(5%, 1.008, 50%, 1.102, 95%, 1.529)	=RiskLognormAlt(5%, 0.7331, 50%, 1.125, 95%, 2.015)	

Table AII.4: Cutting of Curd Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A4i}	σ_{A4i}	
A4	$A4_1$	Pasteurized	=RiskLognorm(μ_{A41} , σ_{A41} , RiskTruncate(1,50))	=RiskLognormAlt(5%, 1.009, 50%, 1.108, 95%, 1.317)	=RiskLognormAlt(5%, 0.8835, 50%, 1.057, 95%, 1.290)	Bachman and Spahr, 1995; Barbosa et al., 1993a; Fox et al., 2000; Frank et al., 1977; Frank et al., 1978; Govaris et al., 2002; Hudson et al., 1997; Kornacki and Marth, 1982; Leuschner and Boughflower, 2002; Maher et al., 2001; Park et al., 1973; Reitsma and Henning, 1996; Spano et al., 2003
	$A4_2$	Unpasteurized	=RiskLognorm(μ_{A42} , σ_{A42} , RiskTruncate(1,50))	=RiskLognormAlt(5%, 1.029, 50%, 1.398, 95%, 2.711)	=RiskLognormAlt(5%, 2.647, 50%, 3.702, 95%, 5.693)	

Table AII.5: Cooking of Curd Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A5i}	σ_{A5i}	
A5	$A5_1$	Pasteurized, 30°C≤t≤32°C	=RiskLognorm(μ_{A51} , σ_{A51} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.418, 50%, 1.828, 95%, 2.400)	=RiskLognormAlt(5%, 0.8261, 50%, 1.072, 95%, 1.469)	Barbosa et al., 1993b; Fox et al., 2000; Frank et al., 1978; Hudson et al., 1997; Kornacki and Marth, 1982; Maher et al., 2001; Reitsma and Henning, 1996; Spano et al., 2003
	$A5_2$	Unpasteurized, 30°C ≤t≤32°C	=RiskLognorm(μ_{A52} , σ_{A52} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.418, 50%, 1.828, 95%, 2.400)	=RiskLognormAlt(5%, 0.8261, 50%, 1.072, 95%, 1.469)	
	$A5_3$	Pasteurized, 33°C ≤t≤35°C	=RiskLognorm(μ_{A53} , σ_{A53} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.166, 50%, 2.474, 95%, 10.800)	=RiskLognormAlt(5%, 1.137, 50%, 2.932, 95%, 20.53)	
	$A5_4$	Unpasteurized, 33°C ≤t≤35°C	=RiskLognorm(μ_{A54} , σ_{A54} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.166, 50%, 2.474, 95%, 10.800)	=RiskLognormAlt(5%, 1.137, 50%, 2.932, 95%, 20.53)	
	$A5_5$	Pasteurized, 36°C ≤t≤40°C	=RiskLognorm(μ_{A55} , σ_{A55} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.050, 50%, 1.675, 95%, 4.952)	=RiskLognormAlt(5%, 2.691, 50%, 4.802, 95%, 11.39)	
	$A5_6$	Unpasteurized, 36°C ≤t≤40°C	=RiskLognorm(μ_{A56} , σ_{A56} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.050, 50%, 1.675, 95%, 4.952)	=RiskLognormAlt(5%, 2.691, 50%, 4.802, 95%, 11.39)	
	$A5_7$	Pasteurized, t>40°C	=RiskLognorm(μ_{A57} , σ_{A57} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.050, 50%, 1.675, 95%, 4.952)	=RiskLognormAlt(5%, 2.691, 50%, 4.802, 95%, 11.39)	
	$A5_8$	Unpasteurized, t>40°C	=RiskLognorm(μ_{A58} , σ_{A58} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.050, 50%, 1.675, 95%, 4.952)	=RiskLognormAlt(5%, 2.691, 50%, 4.802, 95%, 11.39)	

Table AII.6: Separation of Curd and Whey Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A6_i}	σ_{A6_i}	
A6	$A6_1$	Pasteurized	=RiskLognorm(μ_{A6_1} , σ_{A6_1} ; RiskTruncate(1, 30))	=RiskLognormAlt(5%, 1.852, 50%, 12.680, 95%, 28.200)	=RiskLognormAlt(5%, 3.433, 50%, 54.560, 95%, 255.500)	Barbosa et al., 1993a; Frank et al., 1977; Frank et al., 1978; Leuschner and Boughflower, 2002; Park et al., 1973; Ramsaran et al., 1998; Rash and Kosikowski, 1982a; Rash and Kosikowski, 1982b; Teo et al., 2000
	$A6_2$	Unpasteurized	=RiskLognorm(μ_{A6_2} , σ_{A6_2} ; RiskTruncate(1, 30))	=RiskLognormAlt(5%, 1.834, 50%, 12.220, 95%, 27.970)	=RiskLognormAlt(5%, 3.016, 50%, 47.040, 95%, 254.500)	

Table AII.7: Salting Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A7_i}	σ_{A7_i}	
A7	$A7_1$	Pasteurized, Dry	=RiskLognorm(μ_{A7_1} , σ_{A7_1} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.003, 50%, 1.044, 95%, 1.186)	=RiskLognormAlt(5%, 1.567, 50%, 1.818, 95%, 2.153)	Frank et al., 1978; Fox et al., 2000; Govaris et al., 2002; Hudson et al., 1997; Kornacki and Marth, 1982; Maher et al., 2001; Park et al., 1973; Ramsaran et al., 1998; Rash and Kosikowski, 1982a; Reitsma and Henning, 1996; Spano et al., 2003
	$A7_2$	Unpasteurized, Dry	=RiskLognorm(μ_{A7_2} , σ_{A7_2} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.009, 50%, 1.097, 95%, 1.402)	=RiskLognormAlt(5%, 0.6356, 50%, 0.8950, 95%, 1.373)	
	$A7_3$	Pasteurized, Brine	=RiskLognorm(μ_{A7_3} , σ_{A7_3} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 2.218, 50%, 2.990, 95%, 3.940)	=RiskLognormAlt(5%, 0.0125, 50%, 0.1046, 95%, 2.530)	
	$A7_4$	Unpasteurized, Brine	=RiskLognorm(μ_{A7_4} , σ_{A7_4} , RiskTruncate(1,30))	=RiskLognormAlt(5%, 1.047, 50%, 1.637, 95%, 3.940)	=RiskLognormAlt(5%, 3.255, 50%, 4.993, 95%, 9.245)	

Table AII.8: Hooping and Pressing Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A8_i}	σ_{A8_i}	
A8	$A8_1$	Pasteurized	=RiskLognorm(μ_{A8_1} , σ_{A8_1} , RiskTruncate(1,50))	=RiskLognormAlt(5%, 1.022, 50%, 1.264, 95%, 1.887)	=RiskLognormAlt(5%, 2.139, 50%, 2.671, 95%, 3.449)	Frank et al., 1978; Fox et al., 2000; Govaris et al., 2002; Hudson et al., 1997; Kornacki and Marth, 1982; Manolopoulou et al, 2003; Reitsma and Henning, 1996; Teo et al., 2000
	$A8_2$	Unpasteurized	=RiskLognorm(μ_{A8_2} , σ_{A8_2} , RiskTruncate(1,50))	=RiskLognormAlt(5%, 1.070, 50%, 1.976, 95%, 7.960)	=RiskLognormAlt(5%, 1.750, 50%, 3.949, 95%, 15.720)	

Table AII.9: Packaging and Ripening Multiplicative Factor Distributions

Step	MF	Options Selected	MF Distribution (@RISK Function)	Parameter Distribution (@RISK Function)		References
				μ_{A9_i}	σ_{A9_i}	
A9	$A9_1$	Pasteurized, 14 days	=RiskLognorm(μ_{A9_1} , σ_{A9_1} , RiskTruncate(0,))	=RiskLognormAlt(5%, 0.01722, 50%, 0.2457, 95%, 0.8333)	=RiskLognormAlt(5%, 0.7383, 50%, 1.495, 95%, 4.060)	Bachman and Spahr, 1995; Barbosa et al., 1993a; Barbosa et al., 1993b; Fox et al., 2000; Frank et al., 1977; Frank et al., 1978; Govaris et al., 2002; Hudson et al., 1997; Kornacki and Marth, 1982; Leuschner and Boughflower, 2002; Maher et al., 2001; Manolopoulou et al, 2003;
	$A9_2$	Unpasteurized, 14 days	=RiskLognorm(μ_{A9_2} , σ_{A9_2} , RiskTruncate(0,))	=RiskLognormAlt(5%, 0.01722, 50%, 0.2457, 95%, 0.8333)	=RiskLognormAlt(5%, 0.7383, 50%, 1.495, 95%, 4.060)	
	$A9_3$	Pasteurized, 27 days	=RiskLognorm(μ_{A9_3} , σ_{A9_3} , RiskTruncate(0,))	=RiskLognormAlt(5%, 0.202, 50%, 0.2675, 95%, 0.8513)	=RiskLognormAlt(5%, 2.088, 50%, 3.061, 95%, 5.030)	
	$A9_4$	Unpasteurized, 27 days	=RiskLognorm(μ_{A9_4} , σ_{A9_4} , RiskTruncate(0,))	=RiskLognormAlt(5%, 0.202, 50%, 0.2675, 95%, 0.8513)	=RiskLognormAlt(5%, 2.088, 50%, 3.061, 95%, 5.030)	

$A9_5$	Pasteurized, 45 days	=RiskLognorm(μ_{A9_5} , σ_{A9_5} , RiskTruncate(0,))	=RiskLognormAlt(5%, 0.01707, 50%, 0.2218, 95%, 0.7652)	=RiskLognormAlt(5%, 1.134, 50%, 1.710, 95%, 3.099)	Park et al., 1973; Ramsaran et al., 1998; Rash and Kosikowski, 1982a; Rash and Kosikowski, 1982b; Reitsma and Henning, 1996; Teo et al., 2000
$A9_6$	Unpasteurized, 45 days	=RiskLognorm(μ_{A9_6} , σ_{A9_6} , RiskTruncate(0,))	=RiskLognormAlt(5%, 0.01707, 50%, 0.2218, 95%, 0.7652)	=RiskLognormAlt(5%, 1.134, 50%, 1.710, 95%, 3.099)	
$A9_7$	Pasteurized, 75 days	=RiskLognorm(μ_{A9_7} , σ_{A9_7} , RiskTruncate(0,))	=RiskLognormAlt(5%, 0.01008, 50%, 0.1379, 95%, 0.6121)	=RiskLognormAlt(5%, 1.351, 50%, 1.863, 95%, 2.783)	
$A9_8$	Unpasteurized, 75 days	=RiskLognorm(μ_{A9_8} , σ_{A9_8} , RiskTruncate(0,))	=RiskLognormAlt(5%, 0.01807, 50%, 0.2248, 95%, 0.7875)	=RiskLognormAlt(5%, 0.9317, 50%, 1.534, 95%, 3.244)	
$A9_9$	Pasteurized, 90 days	=RiskLognorm(μ_{A9_9} , σ_{A9_9} , RiskTruncate(0,1))	=RiskLognormAlt(5%, 0.0515, 50%, 0.4422, 95%, 0.9296)	=RiskLognormAlt(5%, 0.4376, 50%, 1.505, 95%, 14.570)	
$A9_{10}$	Unpasteurized, 90 days	=RiskLognorm($\mu_{A9_{10}}$, $\sigma_{A9_{10}}$, RiskTruncate(0,1))	=RiskLognormAlt(5%, 0.04048, 50%, 0.4464, 95%, 0.9420)	=RiskLognormAlt(5%, 1.839, 50%, 3.861, 95%, 13.520)	
$A9_{11}$	Pasteurized, 104 days	=RiskLognorm($\mu_{A9_{11}}$, $\sigma_{A9_{11}}$, RiskTruncate(0,1))	=RiskLognormAlt(5%, 0.01277, 50%, 0.1672, 95%, 0.6682)	=RiskLognormAlt(5%, 1.523, 50%, 2.210, 95%, 3.498)	
$A9_{12}$	Unpasteurized, 104 days	=RiskLognorm($\mu_{A9_{12}}$, $\sigma_{A9_{12}}$, RiskTruncate(0,1))	=RiskLognormAlt(5%, 0.03423, 50%, 0.3823, 95%, 0.9298)	=RiskLognormAlt(5%, 0.8569, 50%, 2.866, 95%, 36.670)	
$A9_{13}$	Pasteurized, 150 days	=RiskLognorm($\mu_{A9_{13}}$; $\sigma_{A9_{13}}$, RiskTruncate(0,1))	=RiskLognormAlt(5%, 0.01684, 50%, 0.2176, 95%, 0.7649)	=RiskLognormAlt(5%, 1.339, 50%, 1.950, 95%, 3.146)	
$A9_{14}$	Unpasteurized, 150 days	=RiskLognorm($\mu_{A9_{14}}$; $\sigma_{A9_{14}}$, RiskTruncate(0,1))	=RiskLognormAlt(5%, 0.0216, 50%, 0.3094, 95%, 0.8954)	=RiskLognormAlt(5%, 0.4823, 50%, 1.771, 95%, 17.890)	

Table AII.10: Milk Storage Multiplicative Factor Data (Step A1)

Type of Milk	Holding Temperature	Reference	Multiplicative Factor, Step A1				
			24 hours	48 hours	72 hours	96 hours	120 hours
Pasteurized	5°C	Wang et al., 1997	0.759	0.575	0.427	0.331	0.251
Pasteurized	5°C	Altieri et al., 1997	N/A[a]	19.498	N/A	194.985	N/A
Pasteurized	5°C	Altieri et al., 1997	N/A	3.981	N/A	100.000	N/A
Pasteurized	8°C	Weeratna and Doyle, 1997	N/A	N/A	10.000	N/A	N/A
Pasteurized	8°C	Wang et al., 1997	1.995	3.981	7.943	15.849	31.623
Pasteurized	8°C	Palumbo et al., 1997	1.000	1.000	1.259	1.995	3.162
Pasteurized	8°C	Palumbo et al., 1997	1.585	3.162	3.981	5.012	6.310
Pasteurized	8°C	Palumbo et al., 1997	1.995	1.995	2.239	2.239	630.957
Pasteurized	8°C	Palumbo et al., 1997	1.000	0.794	1.000	1.259	1.585
Pasteurized	8°C	Palumbo et al., 1997	1.585	7.943	79.433	79.432	79.432
Pasteurized	8°C	Palumbo et al., 1997	0.631	0.398	0.316	0.251	0.316
Pasteurized	8°C	Palumbo et al., 1997	2.511	6.310	25.119	31.623	39.811
Pasteurized	8°C	Palumbo et al., 1997	1.000	0.794	0.794	0.631	0.501
Pasteurized	8°C	Palumbo et al., 1997	1.995	6.310	19.953	25.119	31.623
Pasteurized	8°C	Palumbo et al., 1997	1.000	0.794	0.631	0.631	0.501
Pasteurized	8°C	Palumbo et al., 1997	7.943	15.849	63.100	79.432	100.000
Pasteurized	8°C	Palumbo et al., 1997	1.000	1.259	1.000	1.000	1.585
Pasteurized	12°C	Palumbo et al., 1997	3.162	10.000	100.00	398.107	10000.000
Pasteurized	12°C	Palumbo et al., 1997	31.623	100.000	794.328	3162.278	6309.573
Pasteurized	12°C	Palumbo et al., 1997	10.000	39.811	316.228	1258.925	316.228
Pasteurized	12°C	Palumbo et al., 1997	15.849	63.096	251.189	501.187	1258.925
Pasteurized	12°C	Palumbo et al., 1997	1.259	6.310	15.849	100.000	316.228
Pasteurized	12°C	Palumbo et al., 1997	1.000	1.000	1.000	79.433	1584.893
Pasteurized	12°C	Palumbo et al., 1997	2.511	15.849	100.00	158.489	251.189
Pasteurized	12°C	Palumbo et al., 1997	3.162	10.000	31.622	100.00	398.107
Pasteurized	12°C	Palumbo et al., 1997	2.511	19.953	100.000	125.893	199.526
Pasteurized	12°C	Palumbo et al., 1997	1.995	10.000	39.811	125.893	398.107
Pasteurized	12°C	Palumbo et al., 1997	10.000	63.096	316.228	398.107	630.957
Pasteurized	12°C	Palumbo et al., 1997	6.309	100.00	501.187	1584.893	3162.278
Pasteurized	15°C	Wang et al., 1997	12.023	144.544	1737.801	20892.960	251188.600
Pasteurized	15°C	Palumbo et al., 1997	79.433	10000.000	63095.730	1995262.000	630957.300
Pasteurized	15°C	Palumbo et al., 1997	316.228	25118.860	251188.600	50118.72	25118.860

Pasteurized	15°C	Palumbo et al., 1997	100.000	10000.000	100000.000	1000000.000	125892.500
Pasteurized	15°C	Palumbo et al., 1997	158.489	1258.925	100000.000	15848.930	15848.930
Pasteurized	22°C	Wang et al., 1997	10.964	120.226	1318.257	14454.400	158489.300
Pasteurized	25°C	Weeratna and Doyle, 1997	350000.000	400000.000	400000.000	500000.000	N/A
Pasteurized	25°C	Altieri et al., 1997	N/A	331.131	N/A	131.826	N/A
Pasteurized	25°C	Altieri et al., 1997	N/A	1000.000	N/A	3981.072	N/A
UHT[b]	4°C	Mamani et al., 2003	2.188	1.072	0.851	0.269	0.214
UHT	4°C	Mamani et al., 2003	0.631	0.158	0.100	0.040	0.025
UHT	4°C	Mamani et al., 2003	0.200	0.200	0.158	0.126	0.100
UHT	5°C	Palumbo et al., 1997	1.000	1.000	1.000	1.000	1.000
UHT	5°C	Palumbo et al., 1997	1.000	1.000	1.000	1.000	1.000
UHT	5°C	Palumbo et al., 1997	1.000	1.000	1.000	1.000	1.000
UHT	5°C	Palumbo et al., 1997	1.000	1.000	1.000	1.000	1.000
UHT	7°C	Heuvelink et al., 1998	0.562	0.316	0.316	0.355	0.316
UHT	8°C	Palumbo et al., 1997	1.000	0.794	1.000	0.794	0.631
UHT	8°C	Palumbo et al., 1997	1.000	1.259	3.162	3.981	5.011
UHT	8°C	Palumbo et al., 1997	1.259	1.585	3.981	19.953	39.810
UHT	8°C	Palumbo et al., 1997	0.794	0.158	0.251	2.512	0.316
UHT	12°C	Palumbo et al., 1997	3.162	31.623	316.228	6309.573	100000.000
UHT	12°C	Palumbo et al., 1997	6.310	19.953	316.228	3162.278	21622.780
UHT	12°C	Palumbo et al., 1997	7.943	158.489	3162.278	25118.860	251188.600
UHT	12°C	Palumbo et al., 1997	1.585	15.849	79.432	794.328	1995.262
UHT	15°C	Heuvelink et al., 1998	15.849	1000.000	1258.925	2511.886	3162.278
UHT	15°C	Palumbo et al., 1997	63.096	10000.000	630957.300	630957.300	630957.300
UHT	15°C	Palumbo et al., 1997	31.623	3162.278	158489.300	1000000.000	1000000.000
UHT	15°C	Palumbo et al., 1997	1000.000	158489.300	1000000.000	1000000.000	1995262.000
UHT	15°C	Palumbo et al., 1997	39.811	6309.573	630957.300	630957.300	630957.300
UHT	20°C	Mamani et al., 2003	1000.000	16218.100	12022.640	8912.509	6606.934
UHT	20°C	Mamani et al., 2003	14791.080	1288250.000	741310.200	524807.500	371535.200
UHT	20°C	Mamani et al., 2003	58884.370	6025596.000	4365158.000	3162278.000	2290868.000
Unpasteurized	5°C	Wang et al., 1997	0.759	0.575	0.437	0.331	0.251
Unpasteurized	7°C	Heuvelink et al., 1998	1.259	3.162	5.012	10.000	15.849
Unpasteurized	8°C	Massa et al., 1999	0.944	0.899	0.889	0.693	0.589
Unpasteurized	8°C	Massa et al., 1999	0.938	0.879	0.844	0.687	0.591
Unpasteurized	8°C	Massa et al., 1999	1.000	0.825	0.615	0.585	0.465

Unpasteurized	8°C	Massa et al., 1999	1.000	2.169	2.071	8.309	11.378
Unpasteurized	8°C	Massa et al., 1999	1.000	20.054	26.667	95.477	133.188
Unpasteurized	8°C	Massa et al., 1999	1.154	18.685	11.538	127.774	182.319
Unpasteurized	8°C	Massa et al., 1999	1.167	1.831	0.758	8.379	11.652
Unpasteurized	8°C	Wang et al., 1997	1.259	1.585	1.995	2.511	3.162
Unpasteurized	8°C	Palumbo et al., 1997	1.000	1.000	1.000	1.000	1.000
Unpasteurized	12°C	Palumbo et al., 1997	1.000	1.000	1.000	1.000	1.000
Unpasteurized	15°C	Wang et al., 1997	3.802	54.954	54.954	208.930	794.328
Unpasteurized	15°C	Heuvelink et al., 1998	50.119	39.811	39.811	63.096	100.00
Unpasteurized	22°C	Wang et al., 1997	3.981	2.511	2.511	1.000	0.794

[a]Not Available
[b]Ultra Heat-Treated

Table AII.11: Milk Heat Treatment Multiplicative Factor Data (Step A2)

Type of Milk	Reference	Multiplicative Factor, Step A2
Unpasteurized	Goff, 1995	0.000000000001
Unpasteurized	Stabel, 2003	0.00001
Unpasteurized	Rosenau, 2006	0.00001
Unpasteurized	Gunasekera et al., 2002	0.0001
Unpasteurized	USDA, 2004	0.00001
Unpasteurized	FSIS, 2004	0.0001

Table AII.12: Addition of Coagulant Multiplicative Factor Data (Step A3)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A3
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	1.000
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	1.000
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.411
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	1.333
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.400
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.550
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.420
Romano	Pasteurized	Thermophilic	Brine	46°C	Hudson et al., 1997	1.260
Feta	Pasteurized	Mesophilic	Brine	30°C	Hudson et al., 1997	2.510
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.160
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.160
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	2.510
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	2.510
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.980
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.980
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.980
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.980
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.160
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.160
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	6.310
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	6.310
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.000
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.000
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.790
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.890
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.120
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.260
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.000
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	6.310
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	3.980
Feta	Pasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	19.950
Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	2.000

Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	2.000
Camembert	Pasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	2.000
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	0.910
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.260
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.260
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.260
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.260
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Feta	Pasteurized	Thermophilic	Brine	30°C	Govaris et al., 2002	2.000
Feta	Pasteurized	Mesophilic	Brine	30°C	Govaris et al., 2002	1.410
Telemes	Pasteurized	Thermophilic	Brine	31-35°C	Govaris et al., 2002	2.510
Telemes	Pasteurized	Thermophilic	Brine	31-35°C	Govaris et al., 2002	2.510
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	1.000
Soft-Cheese	Pasteurized	Mesophilic	Dry	45°C	Leuschner and Boughflower, 2002	3.160
Soft-Cheese	Pasteurized	Mesophilic	Dry	45°C	Leuschner and Boughflower, 2002	3.160
Prato	Pasteurized	Mesophilic	Brine	42°C	Barbosa et al., 1993a	2.000

Table AII.13: Cutting of Curd Multiplicative Factor Data (Step A4)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A4
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	2.667
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Fox et al., 2000	6.400
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.893
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	1.125
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	1.262
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	1.125
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	1.262
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.356
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.796
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	10.000
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	5.623
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	10.000
Swiss	Unpasteurized	Thermophilic	Brine	53°C	Bachman and Spahr, 1995	0.0001
Semi-Hard	Unpasteurized	Thermophilic	Brine	42°C	Bachman and Spahr, 1995	50.119
Colby	Pasteurized	Mesophilic	Dry	39°C	Hudson et al., 1997	1.585
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	2.239
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	1.778
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	2.239
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.162
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.162
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.162
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.162
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	25.119
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	25.119
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	14.125
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	14.125
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.981
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.981
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	7.943
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.981
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.000
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.000

Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.790
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.890
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.120
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.260
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.000
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	2.512
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.256
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.000
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.256
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	1.256
Feta	Pasteurized	Thermophilic	Brine	30°C	Govaris et al., 2002	5.623
Feta	Pasteurized	Mesophilic	Brine	30°C	Govaris et al., 2002	3.548
Telemes	Pasteurized	Thermophilic	Brine	31-35°C	Govaris et al., 2002	10.000
Telemes	Pasteurized	Thermophilic	Brine	31-35°C	Govaris et al., 2002	6.310
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	1.122
Soft-Cheese	Pasteurized	Mesophilic	Dry	45°C	Leuschner and Boughflower, 2002	1.096
Soft-Cheese	Pasteurized	Mesophilic	Dry	45°C	Leuschner and Boughflower, 2002	0.794

Table AII.14: Cooking of Curd Multiplicative Factor Data (Step A5)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A5
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	2.500
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.842
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Fox et al., 2000	2.500
Colby	Pasteurized	Mesophilic	Dry	39°C	Hudson et al., 1997	3.162
Romano	Pasteurized	Thermophilic	Brine	46°C	Hudson et al., 1997	25.119
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	1.412
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	3.162
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	1.412
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	19.953
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	19.953
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	25.119
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	25.119
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	6.310
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	6.310
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	11.220
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	11.220
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	7.943
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	7.943
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	12.589
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	12.589
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	1.585
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	0.050
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	0.040
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	0.079
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	0.063
Prato	Pasteurized	Mesophilic	Brine	42°C	Barbosa et al., 1993a	1.000

Table AII.15: Separation of Curd & Whey Multiplicative Factor Data (Step A6)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A6
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	44.375
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	40.625
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	6.475
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	14.125
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	17.783
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	15.849
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	17.783
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	50.119
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	31.623
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	44.668
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	10.000
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	17.783
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	10.000
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	2.818
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	2.818
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	2.818
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	5.012
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	10.000
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	6.310
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	6.310
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.995
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	3.981
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.256
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	1.995
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	1.585
Feta	Pasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	1.259
Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	2.512
Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	3.162
Camembert	Pasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	3.162
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	0.910
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	120.226
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	162.181

Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	13.490
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	27.542
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	45.709
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	61.660
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	269.153
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	891.251
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	30902.950
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	85113.800
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	100000.000
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	45.709
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	6.607
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	1380.384
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	208.923
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	0.001
Soft-Cheese	Pasteurized	Mesophilic	Dry	45°C	Leuschner and Boughflower, 2002	1.445
Soft-Cheese	Pasteurized	Mesophilic	Dry	45°C	Leuschner and Boughflower, 2002	0.794

Table AII.16: Salting Multiplicative Factor Data (Step A7)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A7
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.550
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.550
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	3.750
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	3.750
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Fox et al., 2000	0.510
Colby	Pasteurized	Mesophilic	Dry	39°C	Hudson et al., 1997	2.239
Romano	Pasteurized	Thermophilic	Brine	46°C	Hudson et al., 1997	1.000
Romano	Pasteurized	Thermophilic	Brine	46°C	Hudson et al., 1997	1.000
Feta	Pasteurized	Mesophilic	Brine	30°C	Hudson et al., 1997	10.000
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	2.818
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	2.818
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	2.818
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.995
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.995
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.995
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.995
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	2.512
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	2.512
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259

Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	10.000
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.100
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	19.953
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.501
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	15.849
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.398
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	15.849
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.501
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	3.981
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.005
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	8.913
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.224
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	6.310
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	251188.600
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	10.000
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	10.000
Feta	Pasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	5.012
Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	19.953
Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	19.953
Camembert	Pasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	25.119
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	2.138
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	0.013
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	0.010
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	0.016
Mozzarella	Unpasteurized	Thermophilic	Brine	35°C	Spano et al., 2003	0.063
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	1.122
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	0.955
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	1.259
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	0.447
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	0.631
Feta	Pasteurized	Thermophilic	Brine	30°C	Govaris et al., 2002	1.413
Feta	Pasteurized	Mesophilic	Brine	30°C	Govaris et al., 2002	1.259

Telemes	Pasteurized	Thermophilic	Brine	31-35°C	Govaris et al., 2002	1.413
Telemes	Pasteurized	Thermophilic	Brine	31-35°C	Govaris et al., 2002	1.259

Table AII.17: Hooping & Pressing Multiplicative Factor Data (Step A8)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A8
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	2.455
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.083
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	1.502
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	1.062
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.069
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Fox et al., 2000	2.549
Romano	Pasteurized	Thermophilic	Brine	46°C	Hudson et al., 1997	0.0001
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	112.202
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.891
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	35.481
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	1.000
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	8.913
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	1.122
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.162
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	3.162
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.585
Feta	Pasteurized	Mesophilic	Brine	30°C	Manolopoulou et al, 2003	4.169
Feta	Pasteurized	Mesophilic	Brine	30°C	Manolopoulou et al, 2003	67.608
Feta	Pasteurized	Mesophilic	Brine	30°C	Manolopoulou et al, 2003	131.825
Prato	Pasteurized	Mesophilic	Brine	42°C	Barbosa et al., 1993a	1.995

Table AII.18: Ripening (14 days) Multiplicative Factor Data (Step A9)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A9
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.070
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.111
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.103
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.103
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.130
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	2.600
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.594
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	1.297
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.756
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Fox et al., 2000	0.115
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.141
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	1.259
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.562
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.200
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.050
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.447
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.708
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.316
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.708
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.050
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.316
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.794
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.794
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.032
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.562
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.631
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.891
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259

Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.200
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.259
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.398
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.000
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	5.623
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	7.943
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.501
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	1.412
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.631
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	0.200
Feta	Pasteurized	Mesophilic	Brine	30°C	Manolopoulou et al, 2003	0.004
Feta	Pasteurized	Mesophilic	Brine	30°C	Manolopoulou et al, 2003	0.089
Feta	Pasteurized	Mesophilic	Brine	30°C	Manolopoulou et al, 2003	1.202
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	2.691
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	1.175
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	0.871
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	1.413
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	1.047
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	4.169
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	1.905
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	1.514
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.692
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.741
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.246
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	1.047
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	1.096
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	2.455
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	2.188
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	0.398
Prato	Pasteurized	Mesophilic	Brine	42°C	Barbosa et al., 1993a	0.501

Table AII.19: Ripening (27 days) Multiplicative Factor Data (Step A9)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A9
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.368
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.067
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.089
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.093
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.090
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.077
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	1.105
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.277
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.500
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Fox et al., 2000	0.120
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.891
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.891
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	1.000
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.501
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.631
Camembert	Pasteurized	Mesophilic	Dry	32°C	Frank et al., 1977	0.794
Semi-Hard	Unpasteurized	Thermophilic	Brine	42°C	Bachman and Spahr, 1995	0.002
Colby	Pasteurized	Mesophilic	Dry	39°C	Hudson et al., 1997	0.100
Romano	Pasteurized	Thermophilic	Brine	46°C	Hudson et al., 1997	1.000
Feta	Pasteurized	Mesophilic	Brine	30°C	Hudson et al., 1997	0.001
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.708
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.794
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.708
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.100
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.158
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.316
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.501
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.316

Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.526
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.526
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.526
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.316
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.316
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.100
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.251
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.398
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.562
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.316
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.631
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	0.398
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	0.079
Feta	Pasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	1.259
Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	5.011
Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	0.079
Camembert	Pasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	1.122
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	0.398
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	0.214
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	0.589
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	1.288
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	0.302
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982a	0.692
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.275
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.871
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	1.349
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.955
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.447
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.347
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.269
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	0.794
Prato	Pasteurized	Mesophilic	Brine	42°C	Barbosa et al., 1993a	1.000

Table AII.20: Ripening (45 days) Multiplicative Factor Data (Step A9)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A9
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.400
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.010
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.424
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.323
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	1.327
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.100
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.187
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	2.000
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Fox et al., 2000	0.556
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.501
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.794
Brick	Pasteurized	Mesophilic	Brine	37°C	Frank et al., 1978	0.794
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.000
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.200
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	1.000
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.100
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.794
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.708
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.891
Colby	Pasteurized	Mesophilic	Dry	40°C	Kornacki and Marth, 1982	0.501
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.316
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.501
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.224
Camembert	Pasteurized	Mesophilic	Dry	33°C	Park et al., 1973	0.158
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	1.413
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	1.995
Feta	Pasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	0.398

Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	0.316
Camembert	Unpasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	3.162
Camembert	Pasteurized	Mesophilic	Dry	33°C	Ramsaran et al., 1998	2.239
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	0.158
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.741
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.562
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.468
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	2.239
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	1.202
Camembert	Pasteurized	Mesophilic	Dry	33°C	Rash and Kosikowski, 1982b	0.490
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	1.259
Prato	Pasteurized	Mesophilic	Brine	42°C	Barbosa et al., 1993a	0.398

Table AII.21: Ripening (75 days) Multiplicative Factor Data (Step A9)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A9
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	2.839
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.167
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	3.128
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	4.731
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.142
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.167
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	4.000
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.324
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Fox et al., 2000	1.273
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	0.355
Feta	Unpasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	0.631
Feta	Pasteurized	Mesophilic	Brine	30°C	Ramsaran et al., 1998	3.981
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	0.891
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	0.251
Prato	Pasteurized	Mesophilic	Brine	42°C	Barbosa et al., 1993a	0.063

Table AII.22: Ripening (90 days) Multiplicative Factor Data (Step A9)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A9
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	10.857
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.033
Smear-Ripened	Unpasteurized	Mesophilic	Brine	37°C	Maher et al., 2001	0.708
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	1.585
Prato	Pasteurized	Mesophilic	Brine	42°C	Barbosa et al., 1993a	2.511

Table AII.23: Ripening (104 days) Multiplicative Factor Data (Step A9)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A9
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	2.307
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.500
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.202
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.008
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	1.234
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	10.600
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	1.632
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.290
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	0.631

Table AII.24: Ripening (150 days) Multiplicative Factor Data (Step A9)

Type of Cheese	Type of Milk	Starter Culture	Type of Salt	Cooking Temperature	Reference	Multiplicative Factor, Step A9
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	3.636
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	1.000
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.500
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	20.000
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.241
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Pasteurized	Mesophilic	Dry	38°C	Reitsma and Henning, 1996	0.200
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.800
Cheddar	Unpasteurized	Mesophilic	Dry	38°C	Teo et al., 2000	0.561
Parmesan	Pasteurized	Thermophilic	Brine	52°C	Barbosa et al., 1993b	0.158

Appendix III: Gompertz Equation Parameter Development

The Gompertz equation is used to describe the effect of temperature and pH on the growth of *E. coli* O157:H7 during the distribution phase. Based on the data obtained from the literature, distributions for the Gompertz equation parameters B, M, and C are estimated using a Bayesian approach similar to the one described for the multiplicative factors. Again, a lognormal distribution is assumed for each of the Gompertz parameters (i.e., B, M, and C), as these parameters describe bacterial survival. However, no prior knowledge of the parameters (i.e., mean and standard deviation) of the lognormal distribution describing the Gompertz parameters is assumed; therefore, non-informative uniform prior distributions are assumed for both the mean and the standard deviation. Data for B, M, and C are obtained from the literature, and this data serves as the likelihood in the Bayesian updating process. The Bayesian updating results in posterior distributions of the mean and standard deviation of the Gompertz parameters.

Tables AIII.1-AIII.3 contain the @RISK functions used in the risk model for the various combinations of pH and temperature for B, M, and C of the Gompertz equation; these combinations for B, M, and C apply to all of the steps in the distribution phase. The tables include the posterior distributions for the mean and standard deviation, determined from the Bayesian updating procedure, as well as the distributions for B, M, and C that are created from the parameter distributions. In addition, the sources from which the likelihood data is obtained are referenced. Table AIII.4 provides the data from which each these parameter distributions are created.

Table AIII.1: Step B1-B5 Gompertz Equation Distributions, Parameter B

Gompertz Parameter B	Options Selected	Gompertz Parameter B Distribution (@RISK Function)	Parameter B Distribution (@RISK Function)		References
			μ_{Bi} [a]	σ_{Bi}	
B_1	5ºC, pH 4.5	=RiskLognorm(μ_{B1}; σ_{B1}, RiskTruncate(0,1))[b, c]	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	Buchanan and Bagi, 1997; Buchanan et al., 1993; Buchanan et al., 1997; Buchanan and Klawitter, 1992; Coleman et al., 2003; Hao and Brackett, 1993; Rajkowski and Marmer, 1995; Sutherland et al., 1995; Sutherland et al., 1997
B_2	8ºC, pH 4.5	=RiskLognorm(μ_{B2}; σ_{B2}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
B_3	10ºC, pH 4.5	=RiskLognorm(μ_{B3}; σ_{B3}, RiskTruncate(0,1))	=RiskLognorm (0.003642, 0.01820)	=RiskLognorm(0.006307, 0.03154)	
B_4	12ºC, pH 4.5	=RiskLognorm(μ_{B4}; σ_{B4}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
B_5	19ºC, pH 4.5	=RiskLognorm(μ_{B5}; σ_{B5}, RiskTruncate(0,1))	=RiskLognorm (0.2638, 0.1319)	=RiskLognorm(0.03194, 0.1597)	
B_6	28ºC, pH 4.5	=RiskLognorm(μ_{B6}; σ_{B6}, RiskTruncate(0,1))	=RiskLognorm (0.1281, 0.6406)	=RiskLognorm(0.09474, 0.4737)	
B_7	37ºC, pH 4.5	=RiskLognorm(μ_{B7}; σ_{B7}, RiskTruncate(0,1))	=RiskLognorm (0.1022, 0.5108)	=RiskLognorm(0.1318, 0.6591)	
B_8	42ºC, pH 4.5	=RiskLognorm(μ_{B8}; σ_{B8}, RiskTruncate(0,1))	=RiskLognorm (0.2270, 1.1351)	=RiskLognorm(0.05449, 0.2724)	
B_9	5ºC, pH 5.0	=RiskLognorm(μ_{B9}; σ_{B9}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
B_{10}	8ºC, pH 5.0	=RiskLognorm(μ_{B10}; σ_{B10}, RiskTruncate(0,1))	=RiskLognorm (0.0007, 0.0035)	=RiskLognorm(0.0014, 0.007)	
B_{11}	10ºC, pH 5.0	=RiskLognorm(μ_{B11}; σ_{B11}, RiskTruncate(0,1))	=RiskLognorm (0.00595, 0.02975)	=RiskLognorm(0.007372, 0.03686)	
B_{12}	12ºC, pH 5.0	=RiskLognorm(μ_{B12}; σ_{B12}, RiskTruncate(0,1))	=RiskLognorm (0.03775, 0.1888)	=RiskLognorm(0.06056, 0.3028)	
B_{13}	19ºC, pH 5.0	=RiskLognorm(μ_{B13}; σ_{B13}, RiskTruncate(0,1))	=RiskLognorm (0.06819, 0.3409)	=RiskLognorm(0.02370, 0.1185)	
B_{14}	28ºC, pH 5.0	=RiskLognorm(μ_{B14}; σ_{B14}, RiskTruncate(0,1))	=RiskLognorm (0.3025, 1.5125)	=RiskLognorm(0.1481, 0.7404)	

B_{15}	37ºC, pH 5.0	=RiskLognorm(μ_{B15}; σ_{B15}, RiskTruncate(0,1))	=RiskLognorm (0.1022, 0..5108)	=RiskLognorm(0.1318, 0.6591)
B_{16}	42ºC, pH 5.0	=RiskLognorm(μ_{B16}; σ_{B16}, RiskTruncate(0,1))	=RiskLognorm (0.2270, 1.1351)	=RiskLognorm(0.05449, 0.2724
B_{17}	5ºC, pH 5.5	=RiskLognorm(μ_{B17}; σ_{B17}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{18}	8ºC, pH 5.5	=RiskLognorm(μ_{B18}; σ_{B18}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{19}	10ºC, pH 5.5	=RiskLognorm(μ_{B19}; σ_{B19}, RiskTruncate(0,1))	=RiskLognorm (0.01292, 0.06457)	=RiskLognorm(0.008972, 0.04486)
B_{20}	12ºC, pH 5.5	=RiskLognorm(μ_{B20}; σ_{B20}, RiskTruncate(0,1))	=RiskLognorm (0.02149, 0.1070)	=RiskLognorm(0.01505, 0.07527)
B_{21}	19ºC, pH 5.5	=RiskLognorm(μ_{B21}; σ_{B21}, RiskTruncate(0,1))	=RiskLognorm (0.06804, 0.3402)	=RiskLognorm(0.03156, 0.1578)
B_{22}	28ºC, pH 5.5	=RiskLognorm(μ_{B22}; σ_{B22}, RiskTruncate(0,1))	=RiskLognorm (0.1954, 0.9770)	=RiskLognorm(0.1121, 0.5603)
B_{23}	37ºC, pH 5.5	=RiskLognorm(μ_{B23}; σ_{B23}, RiskTruncate(0,1))	=RiskLognorm (0.2044, 1.0219)	=RiskLognorm(0.08603, 0.4301)
B_{24}	42ºC, pH 5.5	=RiskLognorm(μ_{B24}; σ_{B24}, RiskTruncate(0,1))	=RiskLognorm (0.2270, 1.1351)	=RiskLognorm(0.05449, 0.2724)
B_{25}	5ºC, pH 6.0	=RiskLognorm(μ_{B25}; σ_{B25}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{26}	8ºC, pH 6.0	=RiskLognorm(μ_{B26}; σ_{B26}, RiskTruncate(0,1))	=RiskLognorm (0.002, 0.01)	=RiskLognorm(0.0031, 0.01552)
B_{27}	10ºC, pH 6.0	=RiskLognorm(μ_{B27}; σ_{B27}, RiskTruncate(0,1))	=RiskLognorm (0.0131, 0.0655)	=RiskLognorm(0.006189, 0.03094)
B_{28}	12ºC, pH 6.0	=RiskLognorm(μ_{B28}; σ_{B28}, RiskTruncate(0,1))	=RiskLognorm (0.03080, 0.1540)	=RiskLognorm(0.02991, 0.1145)
B_{29}	19ºC, pH 6.0	=RiskLognorm(μ_{B29}; σ_{B29}, RiskTruncate(0,1))	=RiskLognorm (0.1146, 0.5731)	=RiskLognorm(0.03950, 0.1975)
B_{30}	28ºC, pH 6.0	=RiskLognorm(μ_{B30}; σ_{B30}, RiskTruncate(0,1))	=RiskLognorm (0.1632, 0.8160)	=RiskLognorm(0.09276, 0.4638)

B_{31}	37ºC, pH 6.0	=RiskLognorm(μ_{B31}; σ_{B31}, RiskTruncate(0,1))	=RiskLognorm (0.2044, 1.0219)	=RiskLognorm(0.08603, 0.4301)
B_{32}	42ºC, pH 6.0	=RiskLognorm(μ_{B32}; σ_{B32}, RiskTruncate(0,1))	=RiskLognorm (0.4240, 2.1202)	=RiskLognorm(0.2111, 1.0555)
B_{33}	5ºC, pH 6.5	=RiskLognorm(μ_{B33}; σ_{B33}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{34}	8ºC, pH 6.5	=RiskLognorm(μ_{B34}; σ_{B34}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{35}	10ºC, pH 6.5	=RiskLognorm(μ_{B35}; σ_{B35}, RiskTruncate(0,1))	=RiskLognorm (0.01791, 0.08956)	=RiskLognorm(0.001523, 0.007614)
B_{36}	12ºC, pH 6.5	=RiskLognorm(μ_{B36}; σ_{B36}, RiskTruncate(0,1))	=RiskLognorm (0.03692, 0.1846)	=RiskLognorm(0.06641, 0.3320)
B_{37}	19ºC, pH 6.5	=RiskLognorm(μ_{B37}; σ_{B37}, RiskTruncate(0,1))	=RiskLognorm (0.06908, 0.3454)	=RiskLognorm(0.03950, 0.1980)
B_{38}	28ºC, pH 6.5	=RiskLognorm(μ_{B38}; σ_{B38}, RiskTruncate(0,1))	=RiskLognorm (0.1858, 0.9288)	=RiskLognorm(0.06428, 0.3214)
B_{39}	37ºC, pH 6.5	=RiskLognorm(μ_{B39}; σ_{B39}, RiskTruncate(0,1))	=RiskLognorm (0.3054, 1.5270)	=RiskLognorm(0.1459, 0.7294)
B_{40}	42ºC, pH 6.5	=RiskLognorm(μ_{B40}; σ_{B40}, RiskTruncate(0,1))	=RiskLognorm (0.4240, 2.1202)	=RiskLognorm(0.2111, 1.0555)
B_{41}	5ºC, pH 7.0	=RiskLognorm(μ_{B41}; σ_{B41}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{42}	8ºC, pH 7.0	=RiskLognorm(μ_{B42}; σ_{B42}, RiskTruncate(0,1))	=RiskLognorm (0.001667, 0.008333)	=RiskLognorm(0.004083, 0.02041)
B_{43}	10ºC, pH 7.0	=RiskLognorm(μ_{B43}; σ_{B43}, RiskTruncate(0,1))	=RiskLognorm (0.00626, 0.0313)	=RiskLognorm(0.007654, 0.3827)
B_{44}	12ºC, pH 7.0	=RiskLognorm(μ_{B44}; σ_{B44}, RiskTruncate(0,1))	=RiskLognorm (0.02542, 0.1271)	=RiskLognorm (0.01166, 0.5832)
B_{45}	19ºC, pH 7.0	=RiskLognorm(μ_{B45}; σ_{B45}, RiskTruncate(0,1))	=RiskLognorm (0.05792, 0.2896)	=RiskLognorm(0.03414, 0.1707)
B_{46}	28ºC, pH 7.0	=RiskLognorm(μ_{B46}; σ_{B46}, RiskTruncate(0,1))	=RiskLognorm (0.2259, 1.1295)	=RiskLognorm(0.05186, 0.2593)

B_{47}	37ºC, pH 7.0	=RiskLognorm(μ_{B47}; σ_{B47}, RiskTruncate(0,1))	=RiskLognorm (0.3054, 1.5270)	=RiskLognorm(0.1459, 0.7294)
B_{48}	42ºC, pH 7.0	=RiskLognorm(μ_{B48}; σ_{B48}, RiskTruncate(0,1))	=RiskLognorm (0.4240, 2.1202)	=RiskLognorm(0.2111, 1.0555)
B_{49}	5ºC, pH 7.5	=RiskLognorm(μ_{B49}; σ_{B49}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{50}	8ºC, pH 7.5	=RiskLognorm(μ_{B50}; σ_{B50}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{51}	10ºC, pH 7.5	=RiskLognorm(μ_{B51}; σ_{B51}, RiskTruncate(0,1))	=RiskLognorm (0.00626, 0.0313)	=RiskLognorm(0.007654, 0.3827)
B_{52}	12ºC, pH 7.5	=RiskLognorm(μ_{B52}; σ_{B52}, RiskTruncate(0,1))	=RiskLognorm (0.02248, 0.1124)	=RiskLognorm(0.03089, 0.1545)
B_{53}	19ºC, pH 7.5	=RiskLognorm(μ_{B53}; σ_{B53}, RiskTruncate(0,1))	=RiskLognorm (0.08139, 0.4070)	=RiskLognorm(0.05086, 0.2543)
B_{54}	28ºC, pH 7.5	=RiskLognorm(μ_{B54}; σ_{B54}, RiskTruncate(0,1))	=RiskLognorm (0.2028, 1.0138)	=RiskLognorm(0.7392, 0.3696)
B_{55}	37ºC, pH 7.5	=RiskLognorm(μ_{B55}; σ_{B55}, RiskTruncate(0,1))	=RiskLognorm (0.2779, 1.3898)	=RiskLognorm(0.1389, 0.6946)
B_{56}	42ºC, pH 7.5	=RiskLognorm(μ_{B56}; σ_{B56}, RiskTruncate(0,1))	=RiskLognorm (0.4240, 2.1202)	=RiskLognorm(0.2111, 1.0555)
B_{57}	5ºC, pH 8.0	=RiskLognorm(μ_{B57}; σ_{B57}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{58}	8ºC, pH 8.0	=RiskLognorm(μ_{B58}; σ_{B58}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{59}	10ºC, pH 8.0	=RiskLognorm(μ_{B59}; σ_{B59}, RiskTruncate(0,1))	=RiskLognorm (0.00626, 0.0313)	=RiskLognorm(0.007654, 0.3827)
B_{60}	12ºC, pH 8.0	=RiskLognorm(μ_{B60}; σ_{B60}, RiskTruncate(0,1))	=RiskLognorm (0.02529, 0.1265)	=RiskLognorm(0.01630, 0.08151)
B_{61}	19ºC, pH 8.0	=RiskLognorm(μ_{B61}; σ_{B61}, RiskTruncate(0,1))	=RiskLognorm (0.03602, 0.1801)	=RiskLognorm(0.007951, 0.3975)
B_{62}	28ºC, pH 8.0	=RiskLognorm(μ_{B62}; σ_{B62}, RiskTruncate(0,1))	=RiskLognorm (0.1626, 0.8129)	=RiskLognorm(0.01692, 0.08462)

B_{63}	37ºC, pH 8.0	=RiskLognorm(μ_{B63}; σ_{B63}, RiskTruncate(0,1))	=RiskLognorm (0.2779, 1.3898)	=RiskLognorm(0.1389, 0.6946)
B_{64}	42ºC, pH 8.0	=RiskLognorm(μ_{B64}; σ_{B64}, RiskTruncate(0,1))	=RiskLognorm (0.3063, 1.5314)	=RiskLognorm(0.2093, 1.0464)
B_{65}	5ºC, pH 8.5	=RiskLognorm(μ_{B65}; σ_{B65}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{66}	8ºC, pH 8.5	=RiskLognorm(μ_{B66}; σ_{B66}, RiskTruncate(0,1))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
B_{67}	10ºC, pH 8.5	=RiskLognorm(μ_{B67}; σ_{B67}, RiskTruncate(0,1))	=RiskLognorm (0.00626, 0.0313)	=RiskLognorm(0.007654, 0.3827)
B_{68}	12ºC, pH 8.5	=RiskLognorm(μ_{B68}; σ_{B68}, RiskTruncate(0,1))	=RiskLognorm (0.01173, 0.05866)	=RiskLognorm(0.01066, 0.05331)
B_{69}	19ºC, pH 8.5	=RiskLognorm(μ_{B69}; σ_{B69}, RiskTruncate(0,1))	=RiskLognorm (0.03602, 0.1801)	=RiskLognorm(0.007951, 0.3975)
B_{70}	28ºC, pH 8.5	=RiskLognorm(μ_{B70}; σ_{B70}, RiskTruncate(0,1))	=RiskLognorm (0.1418, 0.7092)	=RiskLognorm(0.03468, 0.1734)
B_{71}	37ºC, pH 8.5	=RiskLognorm(μ_{B71}; σ_{B71}, RiskTruncate(0,1))	=RiskLognorm (0.2553, 1.2764)	=RiskLognorm(0.7873, 0.3937)
B_{72}	42ºC, pH 8.5	=RiskLognorm(μ_{B72}; σ_{B72}, RiskTruncate(0,1))	=RiskLognorm (0.3063, 1.5314)	=RiskLognorm(0.2093, 1.0464)

[a]where *i* represents a specific parameter B based on the pH and temperature options selected; *i*=72

[b]RiskLognorm is an @RISK function which specifies a lognormal distribution based on the mean and standard deviation

[c]RiskTruncate is an @RISK function that truncates the input distribution; truncating a distribution restricts samples drawn from the distribution to values within the entered minimum-maximum range

Table AIII.2: Step B1-B5 Gompertz Equation Distributions, Parameter M

Gompertz Parameter M	Options Selected	Gompertz Parameter M Distribution (@RISK Function)	Parameter M Distribution (@RISK Function)		References
			μ_{Mi}	σ_{Mi}	
M_1	5ºC, pH 4.5	=RiskLognorm(μ_{M1}; σ_{M1}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	Buchanan and Bagi, 1997; Buchanan et al., 1993; Buchanan et al., 1997; Buchanan and Klawitter, 1992; Coleman et al., 2003; Hao and Brackett, 1993; Rajkowski and Marmer, 1995; Sutherland et al., 1995; Sutherland et al., 1997
M_2	8ºC, pH 4.5	=RiskLognorm(μ_{M2}; σ_{M2}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
M_3	10ºC, pH 4.5	=RiskLognorm(μ_{M3}; σ_{M3}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 2.502, 50%, 39.47, 95%, 204.1)[a]	=RiskLognorm(73.83, 29.78)	
M_4	12ºC, pH 4.5	=RiskLognorm(μ_{M4}; σ_{M4}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
M_5	19ºC, pH 4.5	=RiskLognorm(μ_{M5}; σ_{M5}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.003443, 50%, 3.021, 95%, 201.9)	=RiskLognorm(61.95, 28.34)	
M_6	28ºC, pH 4.5	=RiskLognorm(μ_{M6}; σ_{M6}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 4.874, 50%, 25.78, 95%, 132.3)	=RiskLognorm(29.45, 35.45)	
M_7	37ºC, pH 4.5	=RiskLognorm(μ_{M7}; σ_{M7}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.00175, 50%, 13.61, 95%, 233.6)	=RiskLognorm(66.39, 73.24)	
M_8	42ºC, pH 4.5	=RiskLognorm(μ_{M8}; σ_{M8}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8277, 50%, 7.794, 95%, 66.05)	=RiskLognorm(4.509, 25.43)	
M_9	5ºC, pH 5.0	=RiskLognorm(μ_{M9}; σ_{M9}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
M_{10}	8ºC, pH 5.0	=RiskLognorm(μ_{M10}; σ_{M10}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 6.229, 50%, 88.11, 95%, 340.2)	=RiskLognorm(187.2, 65.34)	
M_{11}	10ºC, pH 5.0	=RiskLognorm(μ_{M11}; σ_{M11}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 49.18, 50%, 147.4, 95%, 353.0)	=RiskLognorm(126.2, 88.15)	
M_{12}	12ºC, pH 5.0	=RiskLognorm(μ_{M12}; σ_{M12}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0, 50%, 62.12, 95%, 173.3)	=RiskLognorm(41.93, 21.35)	
M_{13}	19ºC, pH 5.0	=RiskLognorm(μ_{M13}; σ_{M13}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 9.554, 50%, 24.08, 95%, 61.07)	=RiskLognorm(9.34, 26.56)	

M_{14}	28ºC, pH 5.0	=RiskLognorm(μ_{M14}; σ_{M14}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 1.936, 50%, 9.749, 95%, 45.38)	=RiskLognorm(12.43, 18.45)
M_{15}	37ºC, pH 5.0	=RiskLognorm(μ_{M15}; σ_{M15}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.00175, 50%, 13.61, 95%, 233.6)	=RiskLognorm(66.39, 73.24)
M_{16}	42ºC, pH 5.0	=RiskLognorm(μ_{M16}; σ_{M16}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8277, 50%, 7.794, 95%, 66.05)	=RiskLognorm(4.509, 25.43)
M_{17}	5ºC, pH 5.5	=RiskLognorm(μ_{M17}; σ_{M17}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{18}	8ºC, pH 5.5	=RiskLognorm(μ_{M18}; σ_{M18}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{19}	10ºC, pH 5.5	=RiskLognorm(μ_{M19}; σ_{M19}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 1.265, 50%, 37.73, 95%, 298.9)	=RiskLognorm(55.91, 93.13_
M_{20}	12ºC, pH 5.5	=RiskLognorm(μ_{M20}; σ_{M20}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.5364, 50%, 25.94, 95%, 254.1)	=RiskLognorm(36.12, 61.20)
M_{21}	19ºC, pH 5.5	=RiskLognorm(μ_{M21}; σ_{M21}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 9.874, 50%, 27.74, 95%, 77.45)	=RiskLognorm(24.31, 47.34)
M_{22}	28ºC, pH 5.5	=RiskLognorm(μ_{M22}; σ_{M22}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.4148, 50%, 12.38, 95%, 132.3)	=RiskLognorm(25.83, 40.69)
M_{23}	37ºC, pH 5.5	=RiskLognorm(μ_{M23}; σ_{M23}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 1.510, 50%, 8.486, 95%, 49.8)	=RiskLognorm(12.88, 11.93)
M_{24}	42ºC, pH 5.5	=RiskLognorm(μ_{M24}; σ_{M24}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8277, 50%, 7.794, 95%, 66.05)	=RiskLognorm(4.509, 25.43)
M_{25}	5ºC, pH 6.0	=RiskLognorm(μ_{M25}; σ_{M25}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{26}	8ºC, pH 6.0	=RiskLognorm(μ_{M26}; σ_{M26}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 49.18, 50%, 103.4, 95%, 321.0)	=RiskLognorm(164.5, 72.5)
M_{27}	10ºC, pH 6.0	=RiskLognorm(μ_{M27}; σ_{M27}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 45.26, 50%, 149.5, 95%, 317.6)	=RiskLognorm(64.73, 80.52)
M_{28}	12ºC, pH 6.0	=RiskLognorm(μ_{M28}; σ_{M28}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 45.13, 50%, 76.42, 95%, 126.4)	=RiskLognorm(20.31, 40.23)

M_{29}	19ºC, pH 6.0	=RiskLognorm(μ_{M29}; σ_{M29}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 5.881, 50%, 16.63, 95%, 47.11)	=RiskLognorm(8.498, 24.60)
M_{30}	28ºC, pH 6.0	=RiskLognorm(μ_{M30}; σ_{M30}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 1.191, 50%, 12.428, 95%, 92.83)	=RiskLognorm(14.36, 12.36)
M_{31}	37ºC, pH 6.0	=RiskLognorm(μ_{M31}; σ_{M31}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 1.510, 50%, 8.486, 95%, 49.8)	=RiskLognorm(12.88, 11.93)
M_{32}	42ºC, pH 6.0	=RiskLognorm(μ_{M32}; σ_{M32}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8277, 50%, 7.794, 95%, 66.05)	=RiskLognorm(4.509, 25.43)
M_{33}	5ºC, pH 6.5	=RiskLognorm(μ_{M33}; σ_{M33}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{34}	8ºC, pH 6.5	=RiskLognorm(μ_{M34}; σ_{M34}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{35}	10ºC, pH 6.5	=RiskLognorm(μ_{M35}; σ_{M35}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 58.19, 50%, 102.4, 95%, 148.8)	=RiskLognorm(6.123, 36.94)
M_{36}	12ºC, pH 6.5	=RiskLognorm(μ_{M36}; σ_{M36}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 5.474, 50%, 83.81, 95%, 302.9)	=RiskLognorm(73.04, 89.01)
M_{37}	19ºC, pH 6.5	=RiskLognorm(μ_{M37}; σ_{M37}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 10.17, 50%, 29.45, 95%, 86.04)	=RiskLognorm(18.34, 65.37)
M_{38}	28ºC, pH 6.5	=RiskLognorm(μ_{M38}; σ_{M38}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 3.907, 50%, 11.20, 95%, 34.58)	=RiskLognorm(7.49, 5.32)
M_{39}	37ºC, pH 6.5	=RiskLognorm(μ_{M39}; σ_{M39}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.9664, 50%, 7.121, 95%, 47.82)	=RiskLognorm(4.988, 6.453)
M_{40}	42ºC, pH 6.5	=RiskLognorm(μ_{M40}; σ_{M40}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8277, 50%, 7.794, 95%, 66.05)	=RiskLognorm(4.509, 25.43)
M_{41}	5ºC, pH 7.0	=RiskLognorm(μ_{M41}; σ_{M41}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{42}	8ºC, pH 7.0	=RiskLognorm(μ_{M42}; σ_{M42}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 5.113, 50%, 67.34, 95%, 265.1)	=RiskLognorm(190.2, 65.34)
M_{43}	10ºC, pH 7.0	=RiskLognorm(μ_{M43}; σ_{M43}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 5.929, 50%, 86.66, 95%, 313.1)	=RiskLognorm(96.90, 71.35)
M_{44}	12ºC, pH 7.0	=RiskLognorm(μ_{M44}; σ_{M44}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 21.46, 50%, 62.25, 95%, 165.7)	=RiskLognorm(25.64, 40.34)

M_{45}	19ºC, pH 7.0	=RiskLognorm(μ_{M45}; σ_{M45}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 8.40, 50%, 35.34, 95%, 156.4)	=RiskLognorm(38.49, 75.34)
M_{46}	28ºC, pH 7.0	=RiskLognorm(μ_{M46}; σ_{M46}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 4.665, 50%, 9.03, 95%, 18.03)	=RiskLognorm(3.245, 2.366)
M_{47}	37ºC, pH 7.0	=RiskLognorm(μ_{M47}; σ_{M47}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.9664, 50%, 7.121, 95%, 47.82)	=RiskLognorm(4.988, 6.453)
M_{48}	42ºC, pH 7.0	=RiskLognorm(μ_{M48}; σ_{M48}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8576, 50%, 5.910, 95%, 41.90)	=RiskLognorm(4.362, 3.246)
M_{49}	5ºC, pH 7.5	=RiskLognorm(μ_{M49}; σ_{M49}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{50}	8ºC, pH 7.5	=RiskLognorm(μ_{M50}; σ_{M50}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{51}	10ºC, pH 7.5	=RiskLognorm(μ_{M51}; σ_{M51}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 5.929, 50%, 86.66, 95%, 313.1)	=RiskLognorm(96.90, 71.35)
M_{52}	12ºC, pH 7.5	=RiskLognorm(μ_{M52}; σ_{M52}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 5.113, 50%, 69.34, 95%, 275.1)	=RiskLognorm(54.67, 20.81)
M_{53}	19ºC, pH 7.5	=RiskLognorm(μ_{M53}; σ_{M53}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 2.502, 50%, 29.47, 95%, 204.1)	=RiskLognorm(62.83, 29.78)
M_{54}	28ºC, pH 7.5	=RiskLognorm(μ_{M54}; σ_{M54}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 2.371, 50%, 10.23, 95%, 44.97)	=RiskLognorm(9.34, 27.34)
M_{55}	37ºC, pH 7.5	=RiskLognorm(μ_{M55}; σ_{M55}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.7003, 50%, 8.540, 95%, 76.86)	=RiskLognorm(6.435, 9.347)
M_{56}	42ºC, pH 7.5	=RiskLognorm(μ_{M56}; σ_{M56}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8576, 50%, 5.910, 95%, 41.90)	=RiskLognorm(4.362, 3.246)
M_{57}	5ºC, pH 8.0	=RiskLognorm(μ_{M57}; σ_{M57}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{58}	8ºC, pH 8.0	=RiskLognorm(μ_{M58}; σ_{M58}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{59}	10ºC, pH 8.0	=RiskLognorm(μ_{M59}; σ_{M59}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 5.929, 50%, 86.66, 95%, 313.1)	=RiskLognorm(96.90, 71.35)
M_{60}	12ºC, pH 8.0	=RiskLognorm(μ_{M60}; σ_{M60}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 42.01, 50%, 117.0, 95%, 220.8)	=RiskLognorm(17.32, 30.66)

M_{61}	19ºC, pH 8.0	=RiskLognorm(μ_{M61}; σ_{M61}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 18.26, 50%, 45.91, 95%, 99.65)	=RiskLognorm(6.943, 18.24)
M_{62}	28ºC, pH 8.0	=RiskLognorm(μ_{M62}; σ_{M62}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.7937, 50%, 2.238, 95%, 31.83)	=RiskLognorm(2.356, 40.94)
M_{63}	37ºC, pH 8.0	=RiskLognorm(μ_{M63}; σ_{M63}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.7003, 50%, 8.540, 95%, 76.86)	=RiskLognorm(6.435, 9.347)
M_{64}	42ºC, pH 8.0	=RiskLognorm(μ_{M64}; σ_{M64}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8576, 50%, 5.910, 95%, 41.90)	=RiskLognorm(4.362, 3.246)
M_{65}	5ºC, pH 8.5	=RiskLognorm(μ_{M65}; σ_{M65}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{66}	8ºC, pH 8.5	=RiskLognorm(μ_{M66}; σ_{M66}, RiskTruncate(0,500))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
M_{67}	10ºC, pH 8.5	=RiskLognorm(μ_{M67}; σ_{M67}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 5.929, 50%, 86.66, 95%, 313.1)	=RiskLognorm(96.90, 71.35)
M_{68}	12ºC, pH 8.5	=RiskLognorm(μ_{M68}; σ_{M68}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 59.30, 50%, 110.7, 95%, 185.0)	=RiskLognorm(58.34, 24.95)
M_{69}	19ºC, pH 8.5	=RiskLognorm(μ_{M69}; σ_{M69}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 18.26, 50%, 45.91, 95%, 99.65)	=RiskLognorm(6.943, 18.24)
M_{70}	28ºC, pH 8.5	=RiskLognorm(μ_{M70}; σ_{M70}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 1.750, 50%, 13.47, 95%, 89.73)	=RiskLognorm(8.945, 7.355)
M_{71}	37ºC, pH 8.5	=RiskLognorm(μ_{M71}; σ_{M71}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.7003, 50%, 8.540, 95%, 76.86)	=RiskLognorm(6.435, 9.347)
M_{72}	42ºC, pH 8.5	=RiskLognorm(μ_{M72}; σ_{M72}, RiskTruncate(0,500))	=RiskLognormAlt(5%, 0.8576, 50%, 5.910, 95%, 41.90)	=RiskLognorm(4.362, 3.246)

[a]RiskLognormAlt is an @RISK function which specifies a lognormal distribution, based on the 5th, 50th, and 95th percentiles

Table AIII.3: Step B1-B5 Gompertz Equation Distributions, Parameter C

Gompertz Parameter C	Options Selected	Gompertz Parameter C Distribution (@RISK Function)	Parameter C Distribution (@RISK Function)		References
			μ_{Ci}	σ_{Ci}	
C_1	5ºC, pH 4.5	=RiskLognorm(μ_{C1}; σ_{C1}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	Buchanan and Bagi, 1997; Buchanan et al., 1993; Buchanan et al., 1997; Buchanan and Klawitter, 1992; Coleman et al., 2003; Hao and Brackett, 1993; Rajkowski and Marmer, 1995; Sutherland et al., 1995; Sutherland et al., 1997
C_2	8ºC, pH 4.5	=RiskLognorm(μ_{C2}; σ_{C2}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
C_3	10ºC, pH 4.5	=RiskLognorm(μ_{C3}; σ_{C3}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.1621, 50%, 0.3781, 95%, 0.9256)	=RiskLognorm(0.7059, 0.05673)	
C_4	12ºC, pH 4.5	=RiskLognorm(μ_{C4}; σ_{C4}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
C_5	19ºC, pH 4.5	=RiskLognorm(μ_{C5}; σ_{C5}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.4503, 50%, 4.836, 95%, 9.495)	=RiskLognorm(3.595, 2.455)	
C_6	28ºC, pH 4.5	=RiskLognorm(μ_{C6}; σ_{C6}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 3.502, 50%, 5.544, 95%, 9.328)	=RiskLognorm(1.730, 0.08838)	
C_7	37ºC, pH 4.5	=RiskLognorm(μ_{C7}; σ_{C7}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 1.203, 50%, 5.170, 95%, 9.644)	=RiskLognorm(1.685, 0.4249)	
C_8	42ºC, pH 4.5	=RiskLognorm(μ_{C8}; σ_{C8}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.312, 50%, 6.608, 95%, 8.083)	=RiskLognorm(0.1477, 0.8607)	
C_9	5ºC, pH 5.0	=RiskLognorm(μ_{C9}; σ_{C9}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)	
C_{10}	8ºC, pH 5.0	=RiskLognorm(μ_{C10}; σ_{C10}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.1621, 50%, 0.4281, 95%, 0.9756)	=RiskLognorm(1.004, 0.04408)	
C_{11}	10ºC, pH 5.0	=RiskLognorm(μ_{C11}; σ_{C11}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.004819, 50%, 0.8608, 95%, 7.533)	=RiskLognorm(3.070, 1.717)	
C_{12}	12ºC, pH 5.0	=RiskLognorm(μ_{C12}; σ_{C12}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.01153, 50%, 6.440, 95%, 12.98)	=RiskLognorm(2.430, 11.26)	
C_{13}	19ºC, pH 5.0	=RiskLognorm(μ_{C13}; σ_{C13}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.111, 50%, 6.653, 95%, 8.368)	=RiskLognorm(1.898, 0.06373)	

C_{14}	28ºC, pH 5.0	=RiskLognorm(μ_{C14}; σ_{C14}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 4.521, 50%, 5.369, 95%, 6.357)	=RiskLognorm(0.5668, 0.05693)
C_{15}	37ºC, pH 5.0	=RiskLognorm(μ_{C15}; σ_{C15}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 1.203, 50%, 5.170, 95%, 9.644)	=RiskLognorm(1.685, 0.4249)
C_{16}	42ºC, pH 5.0	=RiskLognorm(μ_{C16}; σ_{C16}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.312, 50%, 6.608, 95%, 8.083)	=RiskLognorm(0.1477, 0.8607)
C_{17}	5ºC, pH 5.5	=RiskLognorm(μ_{C17}; σ_{C17}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{18}	8ºC, pH 5.5	=RiskLognorm(μ_{C18}; σ_{C18}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{19}	10ºC, pH 5.5	=RiskLognorm(μ_{C19}; σ_{C19}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.5580, 50%, 3.530, 95%, 8.875)	=RiskLognorm(3.623, 1.980)
C_{20}	12ºC, pH 5.5	=RiskLognorm(μ_{C20}; σ_{C20}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 3.863, 50%, 6.724, 95%, 10.34)	=RiskLognorm(1.926, 0.1253)
C_{21}	19ºC, pH 5.5	=RiskLognorm(μ_{C21}; σ_{C21}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 4.803, 50%, 7.206, 95%, 10.98)	=RiskLognorm(2.006, 0.08349)
C_{22}	28ºC, pH 5.5	=RiskLognorm(μ_{C22}; σ_{C22}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 2.906, 50%, 6.032, 95%, 9.659)	=RiskLognorm(1.827, 0.1788)
C_{23}	37ºC, pH 5.5	=RiskLognorm(μ_{C23}; σ_{C23}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 4.946, 50%, 7.154, 95%, 9.611)	=RiskLognorm(1.378, 0.0725)
C_{24}	42ºC, pH 5.5	=RiskLognorm(μ_{C24}; σ_{C24}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.312, 50%, 6.608, 95%, 8.083)	=RiskLognorm(0.1477, 0.8607)
C_{25}	5ºC, pH 6.0	=RiskLognorm(μ_{C25}; σ_{C25}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{26}	8ºC, pH 6.0	=RiskLognorm(μ_{C26}; σ_{C26}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 1.872, 50%, 2.007, 95%, 2.238)	=RiskLognorm(3.158, 1.239)
C_{27}	10ºC, pH 6.0	=RiskLognorm(μ_{C27}; σ_{C27}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 2.458, 50%, 5.326, 95%, 8.663)	=RiskLognorm(1.689, 0.2036)
C_{28}	12ºC, pH 6.0	=RiskLognorm(μ_{C28}; σ_{C28}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 6.005, 50%, 6.934, 95%, 7.986)	=RiskLognorm(1.938, 0.02839)
C_{29}	19ºC, pH 6.0	=RiskLognorm(μ_{C29}; σ_{C29}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.589, 50%, 6.700, 95%, 8.011)	=RiskLognorm(1.004, 0.04408)

C_{30}	28ºC, pH 6.0	=RiskLognorm(μ_{C30}; σ_{C30}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.5139, 50%, 4.824, 95%, 9.470)	=RiskLognorm(1.820, 0.0909)
C_{31}	37ºC, pH 6.0	=RiskLognorm(μ_{C31}; σ_{C31}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 4.946, 50%, 7.154, 95%, 9.611)	=RiskLognorm(1.378, 0.0725)
C_{32}	42ºC, pH 6.0	=RiskLognorm(μ_{C32}; σ_{C32}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.312, 50%, 6.608, 95%, 8.083)	=RiskLognorm(0.1477, 0.8607)
C_{33}	5ºC, pH 6.5	=RiskLognorm(μ_{C33}; σ_{C33}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{34}	8ºC, pH 6.5	=RiskLognorm(μ_{C34}; σ_{C34}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{35}	10ºC, pH 6.5	=RiskLognorm(μ_{C35}; σ_{C35}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 3.586, 50%, 7.154, 95%, 10.89)	=RiskLognorm(0.6322, 0.4835)
C_{36}	12ºC, pH 6.5	=RiskLognorm(μ_{C36}; σ_{C36}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.4654, 50%, 4.731, 95%, 9.460)	=RiskLognorm(3.112, 1.239)
C_{37}	19ºC, pH 6.5	=RiskLognorm(μ_{C37}; σ_{C37}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 4.844, 50%, 6.966, 95%, 9.251)	=RiskLognorm(1.949, 0.06707)
C_{38}	28ºC, pH 6.5	=RiskLognorm(μ_{C38}; σ_{C38}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 4.781, 50%, 6.839, 95%, 9.105)	=RiskLognorm(1.930, 0.07057)
C_{39}	37ºC, pH 6.5	=RiskLognorm(μ_{C39}; σ_{C39}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.827, 50%, 6.896, 95%, 8.068)	=RiskLognorm(0.5668, 0.05693)
C_{40}	42ºC, pH 6.5	=RiskLognorm(μ_{C40}; σ_{C40}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.312, 50%, 6.608, 95%, 8.083)	=RiskLognorm(0.1477, 0.8607)
C_{41}	5ºC, pH 7.0	=RiskLognorm(μ_{C41}; σ_{C41}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{42}	8ºC, pH 7.0	=RiskLognorm(μ_{C42}; σ_{C42}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.0774, 50%, 0.7228, 95%, 1.553)	=RiskLognorm(2.040, 0.08349)
C_{43}	10ºC, pH 7.0	=RiskLognorm(μ_{C43}; σ_{C43}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 2.132, 50%, 5.420, 95%, 9.115)	=RiskLognorm(1.753, 0.2254)
C_{44}	12ºC, pH 7.0	=RiskLognorm(μ_{C44}; σ_{C44}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.720, 50%, 6.990, 95%, 8.358)	=RiskLognorm(0.5479, 0.2477)
C_{45}	19ºC, pH 7.0	=RiskLognorm(μ_{C45}; σ_{C45}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 3.036, 50%, 5.817, 95%, 9.167)	=RiskLognorm(1.806, 0.1276)

C_{46}	28ºC, pH 7.0	=RiskLognorm(μ_{C46}; σ_{C46}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.166, 50%, 6.634, 95%, 8.400)	=RiskLognorm(0.7359, 0.05673)
C_{47}	37ºC, pH 7.0	=RiskLognorm(μ_{C47}; σ_{C47}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.827, 50%, 6.896, 95%, 8.068)	=RiskLognorm(0.5668, 0.05693)
C_{48}	42ºC, pH 7.0	=RiskLognorm(μ_{C48}; σ_{C48}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.4879, 50%, 4.806, 95%, 9.442)	=RiskLognorm(3.212, 1.239)
C_{49}	5ºC, pH 7.5	=RiskLognorm(μ_{C49}; σ_{C49}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{50}	8ºC, pH 7.5	=RiskLognorm(μ_{C50}; σ_{C50}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{51}	10ºC, pH 7.5	=RiskLognorm(μ_{C51}; σ_{C51}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 2.132, 50%, 5.420, 95%, 9.115)	=RiskLognorm(1.753, 0.2254)
C_{52}	12ºC, pH 7.5	=RiskLognorm(μ_{C52}; σ_{C52}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.4838, 50%, 4.867, 95%, 9.412)	=RiskLognorm(1.930, 0.1354)
C_{53}	19ºC, pH 7.5	=RiskLognorm(μ_{C53}; σ_{C53}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 3.762, 50%, 6.208, 95%, 8.926)	=RiskLognorm(1.845, 0.1101)
C_{54}	28ºC, pH 7.5	=RiskLognorm(μ_{C54}; σ_{C54}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 3.763, 50%, 6.419, 95%, 9.156)	=RiskLognorm(1.278, 0.1169)
C_{55}	37ºC, pH 7.5	=RiskLognorm(μ_{C55}; σ_{C55}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.581, 50%, 7.140, 95%, 8.814)	=RiskLognorm(0.4568, 0.05693)
C_{56}	42ºC, pH 7.5	=RiskLognorm(μ_{C56}; σ_{C56}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.4879, 50%, 4.806, 95%, 9.442)	=RiskLognorm(3.212, 1.239)
C_{57}	5ºC, pH 8.0	=RiskLognorm(μ_{C57}; σ_{C57}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{58}	8ºC, pH 8.0	=RiskLognorm(μ_{C58}; σ_{C58}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{59}	10ºC, pH 8.0	=RiskLognorm(μ_{C59}; σ_{C59}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 2.132, 50%, 5.420, 95%, 9.115)	=RiskLognorm(1.753, 0.2254)
C_{60}	12ºC, pH 8.0	=RiskLognorm(μ_{C60}; σ_{C60}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 6.027, 50%, 7.586, 95%, 9.980)	=RiskLognorm(0.1087, 0.09556)
C_{61}	19ºC, pH 8.0	=RiskLognorm(μ_{C61}; σ_{C61}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 1.442, 50%, 8.189, 95%, 15.124)	=RiskLognorm(2.073, 0.4672)

C_{62}	28ºC, pH 8.0	=RiskLognorm(μ_{C62}; σ_{C62}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 7.168, 50%, 7.499, 95%, 7.853)	=RiskLognorm(0.1355, 0.8288)
C_{63}	37ºC, pH 8.0	=RiskLognorm(μ_{C63}; σ_{C63}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 5.581, 50%, 7.140, 95%, 8.814)	=RiskLognorm(0.4568, 0.05693)
C_{64}	42ºC, pH 8.0	=RiskLognorm(μ_{C64}; σ_{C64}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.4879, 50%, 4.806, 95%, 9.442)	=RiskLognorm(3.212, 1.239)
C_{65}	5ºC, pH 8.5	=RiskLognorm(μ_{C65}; σ_{C65}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{66}	8ºC, pH 8.5	=RiskLognorm(μ_{C66}; σ_{C66}, RiskTruncate(0,9))	=RiskLognorm (1E-10, 5E-10)	=RiskLognorm(1E-7, 5E-7)
C_{67}	10ºC, pH 8.5	=RiskLognorm(μ_{C67}; σ_{C67}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 2.132, 50%, 5.420, 95%, 9.115)	=RiskLognorm(1.753, 0.2254)
C_{68}	12ºC, pH 8.5	=RiskLognorm(μ_{C68}; σ_{C68}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 6.027, 50%, 7.586, 95%, 9.980)	=RiskLognorm(0.1087, 0.09556)
C_{69}	19ºC, pH 8.5	=RiskLognorm(μ_{C69}; σ_{C69}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 1.442, 50%, 8.189, 95%, 15.12)	=RiskLognorm(2.073, 0.4672)
C_{70}	28ºC, pH 8.5	=RiskLognorm(μ_{C70}; σ_{C70}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 7.168, 50%, 7.499, 95%, 7.853)	=RiskLognorm(0.1355, 0.8288)
C_{71}	37ºC, pH 8.5	=RiskLognorm(μ_{C71}; σ_{C71}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 6.768, 50%, 6.989, 95%, 7.353)	=RiskLognorm(0.1710, 0.7099)
C_{72}	42ºC, pH 8.5	=RiskLognorm(μ_{C72}; σ_{C72}, RiskTruncate(0,9))	=RiskLognormAlt(5%, 0.4879, 50%, 4.806, 95%, 9.442)	=RiskLognorm(3.212, 1.239)

Table AIII.4: Gompertz B, M, and C Parameter Data

Temperature	pH	Reference	Gompertz Parameter		
			B (log (CFU/ml)/h)	M (h)	C (log CFU/ml)
5ºC	4.5	Buchanan et al., 1993	0	0	0
5ºC	4.5	Buchanan et al., 1993	0	0	0
5ºC	5.5	Buchanan and Klawitter, 1992	0	0	0
5ºC	5.5	Buchanan and Klawitter, 1992	0	0	0
5ºC	5.5	Buchanan et al., 1993	0	0	0
5ºC	6.5	Buchanan and Klawitter, 1992	0	0	0
5ºC	6.5	Buchanan and Klawitter, 1992	0	0	0
5ºC	6.5	Buchanan et al., 1993	0	0	0
5ºC	7.5	Buchanan and Klawitter, 1992	0	0	0
5ºC	7.5	Buchanan and Klawitter, 1992	0	0	0
5ºC	7.5	Buchanan et al., 1993	0	0	0
5ºC	8.5	Buchanan et al., 1993	0	0	0
8ºC	5.0	Rajkowski and Marmer, 1995	0.0028	451.90	2.02
8ºC	5.0	Rajkowski and Marmer, 1995	0	0	0
8ºC	5.0	Rajkowski and Marmer, 1995	0	0	0
8ºC	5.0	Rajkowski and Marmer, 1995	0	0	0
8ºC	5.5	Buchanan and Klawitter, 1992	0	0	0
8ºC	5.5	Buchanan and Klawitter, 1992	0	0	0
8ºC	6.0	Buchanan and Klawitter, 1992	0	0	0
8ºC	6.0	Buchanan and Klawitter, 1992	0	0	0
8ºC	6.0	Rajkowski and Marmer, 1995	0.0063	291.90	6.68
8ºC	6.0	Rajkowski and Marmer, 1995	0.0057	341.20	6.75
8ºC	6.0	Rajkowski and Marmer, 1995	0	0	0
8ºC	6.0	Rajkowski and Marmer, 1995	0	0	0
8ºC	6.5	Buchanan and Klawitter, 1992	0	0	0
8ºC	6.5	Buchanan and Klawitter, 1992	0	0	0
8ºC	7.0	Buchanan and Klawitter, 1992	0	0	0
8ºC	7.0	Buchanan and Klawitter, 1992	0	0	0
8ºC	7.0	Rajkowski and Marmer, 1995	0.01	566.50	5.01
8ºC	7.0	Rajkowski and Marmer, 1995	0	0	0
8ºC	7.0	Rajkowski and Marmer, 1995	0	0	0
8ºC	7.0	Rajkowski and Marmer, 1995	0	0	0

8ºC	7.5	Buchanan and Klawitter, 1992	0	0	0
8ºC	7.5	Buchanan and Klawitter, 1992	0	0	0
8ºC	8.5	Buchanan and Klawitter, 1992	0	0	0
8ºC	8.5	Buchanan and Klawitter, 1992	0	0	0
10ºC	4.5	Buchanan and Klawitter, 1992	0	0	0
10ºC	4.5	Buchanan and Klawitter, 1992	0	0	0
10ºC	4.5	Buchanan et al., 1997	0.011	153.43	3.99
10ºC	5.0	Rajkowski and Marmer, 1995	0.006	247.50	6.04
10ºC	5.0	Rajkowski and Marmer, 1995	0.0041	306.7	6.35
10ºC	5.0	Rajkowski and Marmer, 1995	0	0	0
10ºC	5.0	Rajkowski and Marmer, 1995	0	0	0
10ºC	5.0	Sutherland et al., 1997	0.0056	179.77	3.80
10ºC	5.5	Buchanan and Klawitter, 1992	0.022	82.99	8.00
10ºC	5.5	Buchanan and Klawitter, 1992	0	0	0
10ºC	5.5	Coleman et al., 2003	0.014	154.88	9.00
10ºC	5.5	Coleman et al., 2003	0.023	98.12	9.70
10ºC	5.5	Coleman et al., 2003	0.0082	143.91	7.60
10ºC	5.5	Coleman et al., 2003	0.016	81.95	8.80
10ºC	5.5	Buchanan and Klawitter, 1992	0.011	129.69	7.60
10ºC	5.5	Buchanan and Klawitter, 1992	0	0	0
10ºC	5.5	Buchanan et al., 1997	0.23	77.31	6.70
10ºC	6.0	Sutherland et al., 1997	0.0045	170.11	5.40
10ºC	6.0	Rajkowski and Marmer, 1995	0.013	96.00	6.40
10ºC	6.0	Rajkowski and Marmer, 1995	0.013	117.60	6.31
10ºC	6.0	Rajkowski and Marmer, 1995	0.013	213.60	6.44
10ºC	6.0	Rajkowski and Marmer, 1995	0.022	251.40	3.61
10ºC	6.5	Buchanan and Klawitter, 1992	0.017	102.76	7.80
10ºC	6.5	Buchanan and Klawitter, 1992	0.017	107.56	7.20
10ºC	6.5	Buchanan et al., 1997	0.20	98.74	6.82
10ºC	7.0	Rajkowski and Marmer, 1995	0.016	136.79	6.35
10ºC	7.0	Rajkowski and Marmer, 1995	0.013	130.41	6.23
10ºC	7.0	Rajkowski and Marmer, 1995	0	0	0
10ºC	7.0	Rajkowski and Marmer, 1995	0	0	0
12ºC	5.0	Rajkowski and Marmer, 1995	0.13	74.00	6.57
12ºC	5.0	Rajkowski and Marmer, 1995	0.024	82.30	6.58

12ºC	5.0	Rajkowski and Marmer, 1995	0	0	0
12ºC	5.0	Rajkowski and Marmer, 1995	0	0	0
12ºC	5.5	Buchanan and Klawitter, 1992	0.20	75.21	8.10
12ºC	5.5	Buchanan and Klawitter, 1992	0.018	104.91	7.40
12ºC	5.5	Buchanan and Klawitter, 1992	0.026	64.34	7.00
12ºC	5.5	Buchanan and Klawitter, 1992	0.020	89.35	6.80
12ºC	5.5	Buchanan et al., 1993	0	0	0
12ºC	5.5	Buchanan et al., 1997	0.016	75.71	8.28
12ºC	6.0	Buchanan and Klawitter, 1992	0.021	69.72	7.80
12ºC	6.0	Buchanan and Klawitter, 1992	0.020	80.37	7.50
12ºC	6.0	Buchanan and Klawitter, 1992	0.025	62.93	7.20
12ºC	6.0	Buchanan and Klawitter, 1992	0.031	76.29	6.80
12ºC	6.0	Buchanan et al., 1997	0.022	63.26	7.01
12ºC	6.0	Rajkowski and Marmer, 1995	0.043	56.90	6.77
12ºC	6.0	Rajkowski and Marmer, 1995	0.018	76.10	6.33
12ºC	6.0	Rajkowski and Marmer, 1995	0.087	93.40	6.68
12ºC	6.0	Rajkowski and Marmer, 1995	0.011	125.90	6.54
12ºC	6.5	Buchanan and Klawitter, 1992	0.020	75.74	7.70
12ºC	6.5	Buchanan and Klawitter, 1992	0.0068	320.25	6.00
12ºC	6.5	Buchanan and Klawitter, 1992	0	0	0
12ºC	6.5	Buchanan and Klawitter, 1992	0.23	25.66	7.00
12ºC	6.5	Buchanan and Klawitter, 1992	0.011	386.23	4.40
12ºC	6.5	Buchanan and Klawitter, 1992	0	0	0
12ºC	6.5	Buchanan et al., 1993	0.028	51.57	6.42
12ºC	6.5	Buchanan et al., 1993	0.028	54.40	6.93
12ºC	6.5	Buchanan et al., 1997	0.019	73.53	7.30
12ºC	6.5	Buchanan et al., 1997	0	0	0
12ºC	7.0	Buchanan and Klawitter, 1992	0.020	78.09	7.90
12ºC	7.0	Buchanan and Klawitter, 1992	0.024	75.88	7.40
12ºC	7.0	Rajkowski and Marmer, 1995	0.037	52.92	6.88
12ºC	7.0	Rajkowski and Marmer, 1995	0.042	71.20	6.77
12ºC	7.0	Rajkowski and Marmer, 1995	0.018	86.63	6.59
12ºC	7.0	Rajkowski and Marmer, 1995	0.012	128.83	6.51
12ºC	7.5	Buchanan and Klawitter, 1992	0.022	117.89	7.50
12ºC	7.5	Buchanan and Klawitter, 1992	0	0	0

12ºC	7.5	Buchanan and Klawitter, 1992	0.018	90.38	7.80
12ºC	7.5	Buchanan and Klawitter, 1992	0	0	0
12ºC	7.5	Buchanan et al., 1997	0.012	130.16	7.37
12ºC	8.0	Buchanan and Klawitter, 1992	0.037	106.46	7.90
12ºC	8.0	Buchanan and Klawitter, 1992	0.014	131.45	7.90
12ºC	8.5	Buchanan and Klawitter, 1992	0.020	94.61	7.70
12ºC	8.5	Buchanan and Klawitter, 1992	0.014	119.10	7.00
12ºC	8.5	Buchanan et al., 1993	0	0	0
19ºC	4.5	Buchanan and Klawitter, 1992	0.040	42.33	8.10
19ºC	4.5	Buchanan and Klawitter, 1992	0.091	94.54	7.80
19ºC	4.5	Buchanan and Klawitter, 1992	0	0	0
19ºC	4.5	Buchanan and Klawitter, 1992	0	0	0
19ºC	4.5	Buchanan and Klawitter, 1992	0.034	47.03	5.90
19ºC	4.5	Buchanan and Klawitter, 1992	0.020	123.95	4.80
19ºC	4.5	Buchanan and Klawitter, 1992	0	0	0
19ºC	4.5	Buchanan and Klawitter, 1992	0	0	0
19ºC	4.5	Buchanan et al., 1997	0.010	183.42	6.31
19ºC	5.0	Buchanan and Klawitter, 1992	0.040	35.24	7.90
19ºC	5.0	Buchanan and Klawitter, 1992	0.048	37.20	7.10
19ºC	5.0	Rajkowski and Marmer, 1995	0.89	22.70	6.28
19ºC	5.0	Rajkowski and Marmer, 1995	0.10	14.30	6.10
19ºC	5.0	Rajkowski and Marmer, 1995	0.068	20.60	6.12
19ºC	5.0	Rajkowski and Marmer, 1995	0.062	22.10	6.73
19ºC	5.5	Buchanan and Klawitter, 1992	0.085	23.98	8.20
19ºC	5.5	Buchanan and Klawitter, 1992	0.034	66.93	7.20
19ºC	5.5	Coleman et al., 2003	0.056	23.82	8.90
19ºC	5.5	Coleman et al., 2003	0.059	20.23	10.00
19ºC	5.5	Coleman et al., 2003	0.058	21.13	8.10
19ºC	5.5	Coleman et al., 2003	0.055	23.29	7.40
19ºC	5.5	Buchanan and Klawitter, 1992	0.093	19.55	7.10
19ºC	5.5	Buchanan and Klawitter, 1992	0.039	67.69	6.80
19ºC	6.0	Buchanan and Klawitter, 1992	0.093	28.00	7.40
19ºC	6.0	Buchanan and Klawitter, 1992	0.067	26.68	7.20
19ºC	6.0	Rajkowski and Marmer, 1995	0.13	11.15	6.76
19ºC	6.0	Rajkowski and Marmer, 1995	0.18	11.03	6.23

19ºC	6.0	Rajkowski and Marmer, 1995	0.13	14.67	6.30
19ºC	6.0	Rajkowski and Marmer, 1995	0.092	15.48	6.53
19ºC	6.5	Buchanan and Klawitter, 1992	0.087	21.17	7.70
19ºC	6.5	Buchanan and Klawitter, 1992	0.073	26.59	8.30
19ºC	6.5	Buchanan and Klawitter, 1992	0.045	38.43	7.50
19ºC	6.5	Buchanan and Klawitter, 1992	0.020	70.75	7.60
19ºC	6.5	Buchanan and Klawitter, 1992	0.085	18.11	7.10
19ºC	6.5	Buchanan and Klawitter, 1992	0.088	25.54	7.40
19ºC	6.5	Buchanan and Klawitter, 1992	0.045	38.43	7.50
19ºC	6.5	Buchanan and Klawitter, 1992	0.019	68.78	6.70
19ºC	6.5	Buchanan et al., 1997	0.076	18.53	7.16
19ºC	7.0	Buchanan and Klawitter, 1992	0.095	26.33	7.70
19ºC	7.0	Buchanan and Klawitter, 1992	0.053	53.24	7.40
19ºC	7.0	Buchanan and Klawitter, 1992	0.095	27.77	7.30
19ºC	7.0	Rajkowski and Marmer, 1995	0.081	14.80	6.78
19ºC	7.0	Rajkowski and Marmer, 1995	0.090	15.50	6.69
19ºC	7.0	Rajkowski and Marmer, 1995	0.052	36.23	6.57
19ºC	7.0	Rajkowski and Marmer, 1995	0.032	67.88	6.87
19ºC	7.0	Buchanan and Klawitter, 1992	0.088	21.98	7.70
19ºC	7.0	Buchanan and Klawitter, 1992	0.098	17.26	5.54
19ºC	7.5	Buchanan and Klawitter, 1992	0.093	19.91	7.60
19ºC	7.5	Buchanan and Klawitter, 1992	0.026	143.62	6.70
19ºC	7.5	Buchanan and Klawitter, 1992	0.088	17.08	7.30
19ºC	7.5	Buchanan and Klawitter, 1992	0.011	150.21	6.30
19ºC	8.0	Buchanan and Klawitter, 1992	0.040	41.94	7.90
19ºC	8.0	Buchanan and Klawitter, 1992	0.041	45.22	7.70
19ºC	8.0	Buchanan et al., 1997	0.027	53.25	10.16
28ºC	4.5	Buchanan and Klawitter, 1992	0.17	10.92	7.30
28ºC	4.5	Buchanan and Klawitter, 1992	0.98	17.18	7.50
28ºC	4.5	Buchanan and Klawitter, 1992	0.018	60.38	4.50
28ºC	4.5	Buchanan and Klawitter, 1992	0.077	54.90	4.70
28ºC	4.5	Buchanan and Klawitter, 1992	0.14	14.25	6.10
28ºC	4.5	Buchanan and Klawitter, 1992	0.26	21.00	6.40
28ºC	4.5	Buchanan and Klawitter, 1992	0.030	45.21	5.40
28ºC	4.5	Buchanan and Klawitter, 1992	0.021	104.16	5.20

28ºC	5.0	Rajkowski and Marmer, 1995	0.23	7.50	5.60
28ºC	5.0	Rajkowski and Marmer, 1995	0.51	8.40	5.55
28ºC	5.0	Rajkowski and Marmer, 1995	0.30	8.20	5.14
28ºC	5.0	Rajkowski and Marmer, 1995	0.17	17.90	5.20
28ºC	5.5	Buchanan and Klawitter, 1992	0.20	6.87	7.90
28ºC	5.5	Buchanan and Klawitter, 1992	0.12	50.58	6.70
28ºC	5.5	Buchanan and Klawitter, 1992	0.26	6.66	7.30
28ºC	5.5	Buchanan and Klawitter, 1992	0.055	40.69	6.00
28ºC	6.0	Rajkowski and Marmer, 1995	0.25	6.33	6.03
28ºC	6.0	Rajkowski and Marmer, 1995	0.27	6.70	6.21
28ºC	6.0	Rajkowski and Marmer, 1995	0.144	10.55	5.99
28ºC	6.0	Rajkowski and Marmer, 1995	0.055	23.06	6.53
28ºC	6.5	Buchanan and Klawitter, 1992	0.19	8.17	7.70
28ºC	6.5	Buchanan and Klawitter, 1992	0.19	9.14	7.40
28ºC	6.5	Buchanan and Klawitter, 1992	0.15	14.26	7.50
28ºC	6.5	Buchanan and Klawitter, 1992	0.11	25.48	7.70
28ºC	6.5	Buchanan and Klawitter, 1992	0.20	7.61	7.00
28ºC	6.5	Buchanan and Klawitter, 1992	0.17	8.96	6.90
28ºC	6.5	Buchanan and Klawitter, 1992	0.16	12.07	7.00
28ºC	6.5	Buchanan and Klawitter, 1992	0.15	23.55	7.10
28ºC	7.0	Buchanan and Klawitter, 1992	0.15	11.49	8.00
28ºC	7.0	Buchanan and Klawitter, 1992	0.20	10.69	7.40
28ºC	7.0	Buchanan et al., 1997	0.21	9.10	6.55
28ºC	7.0	Rajkowski and Marmer, 1995	0.29	5.70	6.18
28ºC	7.0	Rajkowski and Marmer, 1995	0.27	6.47	6.14
28ºC	7.0	Rajkowski and Marmer, 1995	0.28	10.04	6.20
28ºC	7.0	Rajkowski and Marmer, 1995	0.20	11.61	6.32
28ºC	7.0	Buchanan and Klawitter, 1992	0.18	7.86	7.50
28ºC	7.5	Buchanan and Klawitter, 1992	0.20	7.87	7.40
28ºC	7.5	Buchanan and Klawitter, 1992	0.12	26.46	7.50
28ºC	7.5	Buchanan and Klawitter, 1992	0.19	7.63	7.20
28ºC	7.5	Buchanan and Klawitter, 1992	0.16	24.55	6.90
28ºC	7.5	Buchanan et al., 1997	0.21	7.26	6.36
28ºC	8.0	Buchanan and Klawitter, 1992	0.17	7.93	7.60
28ºC	8.0	Buchanan and Klawitter, 1992	0.15	9.53	7.40

28ºC	8.5	Buchanan and Klawitter, 1992	0.16	9.03	7.50
28ºC	8.5	Buchanan and Klawitter, 1992	0.091	18.62	7.40
28ºC	8.5	Buchanan and Klawitter, 1992	0.16	8.90	7.40
28ºC	8.5	Buchanan and Klawitter, 1992	0.15	25.58	7.70
37ºC	4.5	Buchanan and Klawitter, 1992	0.11	12.61	6.80
37ºC	4.5	Buchanan and Klawitter, 1992	0	0	0
37ºC	4.5	Buchanan and Klawitter, 1992	0.28	10.11	5.20
37ºC	4.5	Buchanan and Klawitter, 1992	0.011	139.34	4.80
37ºC	5.5	Buchanan and Klawitter, 1992	0.28	4.56	7.30
37ºC	5.5	Buchanan and Klawitter, 1992	0.10	37.49	6.20
37ºC	5.5	Coleman et al., 2003	0.27	6.50	9.30
37ºC	5.5	Coleman et al., 2003	0.26	6.29	9.30
37ºC	5.5	Coleman et al., 2003	0.13	5.71	6.60
37ºC	5.5	Coleman et al., 2003	0.13	5.89	6.60
37ºC	5.5	Buchanan and Klawitter, 1992	0.32	5.50	7.20
37ºC	5.5	Buchanan and Klawitter, 1992	0.14	22.99	6.30
37ºC	6.5	Buchanan and Klawitter, 1992	0.36	4.19	7.60
37ºC	6.5	Buchanan and Klawitter, 1992	0.14	17.60	7.10
37ºC	6.5	Buchanan and Klawitter, 1992	0.40	4.20	6.90
37ºC	6.5	Buchanan and Klawitter, 1992	0.10	22.64	6.70
37ºC	6.5	Buchanan et al., 1997	0.39	3.94	6.92
37ºC	6.5	Buchanan et al., 1997	0.44	4.18	6.21
37ºC	7.5	Buchanan and Klawitter, 1992	0.40	4.39	7.60
37ºC	7.5	Buchanan and Klawitter, 1992	0.17	13.08	7.30
37ºC	7.5	Buchanan and Klawitter, 1992	0.40	5.54	7.20
37ºC	7.5	Buchanan and Klawitter, 1992	0.15	18.66	6.60
37ºC	8.5	Buchanan and Klawitter, 1992	0.34	5.13	7.10
37ºC	8.5	Buchanan and Klawitter, 1992	0.19	30.86	7.10
37ºC	8.5	Buchanan and Klawitter, 1992	0.24	11.50	6.80
42ºC	4.5	Buchanan and Klawitter, 1992	0.19	10.51	6.10
42ºC	4.5	Buchanan and Klawitter, 1992	0.27	13.57	6.50
42ºC	6.5	Buchanan and Klawitter, 1992	0.38	4.14	7.50
42ºC	6.5	Buchanan and Klawitter, 1992	0.15	32.89	7.20
42ºC	6.5	Buchanan and Klawitter, 1992	0.52	3.71	6.30
42ºC	6.5	Buchanan et al., 1997	0.64	3.56	6.37

42ºC	8.5	Buchanan and Klawitter, 1992	0.42	4.17	7.00
42ºC	8.5	Buchanan and Klawitter, 1992	0	0	0
42ºC	8.5	Buchanan and Klawitter, 1992	0.35	10.59	6.30
42ºC	8.5	Buchanan et al., 1997	0.46	4.19	5.98

References

Altieri, C., Corbo, M.R., and Massa, S. (1997). A note on growth and survival of *Escherichia coli* O157:H7 in fresh pasteurized milk. Advances in Food Sciences, 19, 22-24.

Anonymous. (1994a). Two clusters of haemolytic uraemic syndrome in France. Communicable Diseases Report, 4, 29.

Anonymous. (1994b). *E.coli* O157 phage type 28 infections in Grampian. Communicable Diseases and Environmental Health, Scotland, Weekly Reports 28 (No. 94/46) 1.

Anonymous. (1997). Report of an *E. coli* O157 Outbreak Associated with the Consumption of Cheese. Environmental Health Service Unit, Wyre Borough Council, UK.

Bachmann, H.P. and Spahr, U. (1995). The Fate of Potentially Pathogenic Bacteria in Swiss Hard and Semihard Cheeses Made from Raw Milk. Journal of Dairy Science, 78, 476-483.

Baker, A.R., Ebel, E.D., Hogue, A.T., McDowell, R.M., Morales, R.A., Schlosser, W.D., and Whiting, R. (1998). *Salmonella enteritidis* Risk Assessment: Shell Eggs and Egg Products. USDA Food Safety and Inspection Service, Washington, DC.

Barbosa, C.G., Robbs, P.G., and da Costa Raimundo, S.M. (1993). Behavior of *Staphylococcus aureus* and of *Escherichia coli* and Injury Formation During Production and Storage Phases of "Prato" Cheese. Revista de Microbiologia, 24, 118-124.

Barbosa, C.G., Robbs, P.G., and Favarin, V. (1993). Behaviour of *Staphlyococcus aureus* and of *Escherichia coli* and Injury Formation During Production and Storage Phases of Parmesan Cheese. Revista de. Microbiologia., 24, 111-117.

Battistotti, B., Bottazzi, V., Piccinardi, A., and Volpato, G. (1983). Cheese: A Guide to the World of Cheese and Cheesemaking. New York: Facts on File.

Bell, B.P., Goldoft, M., Griffin, M.P., Davis, M.A., Gordon, D.C., Tarr, P.I., Bartleson, C.A., Lewis, J.H., Barrett, T.J., Wells, J.G., Baron, R., and Kobayashi, J. (1994). A multistate outbreak of *E. coli* O157:H7 associated bloody diarrhea and hemolytic uremic syndrome from hamburgers. Journal of the American Medical Association, 272, 1349-1353.

Bell, C. and Kyriakides, A. (1998). *E. coli*: A practical approach to the organisms and its control in foods. New York: Chapman & Hall.

Bemrah, N., Sanna, M., Cassin, M.H>, Griffiths, M.W., and Cerf, O. (1998). Quantitative risk assessment of human listeriosis from consumption of soft cheese made from raw milk. Preventive Veterinary Medicine, 37, 129-145.

Besser, R.E., Lett, S.M., Weber, J.T., Doyle, M.P., Barrett, T.J., and Wells, J.G. (1993). An outbreak of diarrhea and hemolytic uremic syndrome from *Escherichia coli* O157:H7 in fresh-pressed apple cider. Journal of the American Medical Association, 269, 2217-2220.

Blackburn, C. de W., Curtis, L.M., Humpheson, L., Billon, C., and McClure, P.J. (1997). Development of thermal inactivation models for *Salmonella enteritidis* and *Escherichia coli* O157:H7 with temperature, pH and NaCl as controlling factors. International Journal of Food Microbiology, 38, 31-44.

Bleem, A. (1994). Escherichia coli O157:H7 in Raw Milk: A Review. Animal Health Insight, 1-9.

Boyce, T.G., Swerdlow, D.L., and Griffin, P.M. (1995). *Escherichia coli* O157:H7 and the hemolytic uremic syndrome. New England Journal of Medicine, 333, 364-368.

Buchanan, R.L. (1997). National Advisory Committee on Microbiological Criteria for Foods "Principles of Risk Assessment for Illnesses Caused by Foodborne Biological Agents." Journal of Food Protection, 60, 1417-1419.

Buchanan, R.L. and Bagi, L.K. (1997). Effect of Water Activity and Humectant Identity on the Growth Kinetics of *Escherichia coli* O157:H7. Food Microbiology, 14, 413-423.

Buchanan, R.L. and Doyle, M.P. (1997). Foodborne Disease Significance of *Escherichia coli* O157:H7 and Other Enterohemorrhagic *E. coli*. Foodtechnology, 51, 69-76.

Buchanan, R.L. and Klawitter, L.A. (1992). The Effect of Incubation Temperature, Initial pH, and Sodium Chloride on the Growth Kinetics of Escherichia coli O157:H7. Food Microbiology, 9, 185-196.

Buchanan, R.L., Bagi, L.K., Goins, L.V., and Philips, J.G. (1993). Response Surface Models for the Growth Kinetics of Escherichia coli O157:H7. Food Microbiology, 10, 303-315.

Buchanan, R.L., Whiting, R.C., and Damert, W.C. (1997). When is Simple Good Enough: A Comparison of the Gompertz, Baranyi, and Three Phase Linear

Models for Fitting Bacterial Growth Curves. Food Microbiology, 14, 313-326.

Buzby, J.C. (2002). Economics of Foodborne Disease: *E. coli*. ERS: Economic Research Service, United States Department of Agriculture, Briefing Room. Available at: http://www.ers.usda.gov/Briefing/FoodborneDisease/ecoli/.

Buzby, J.C., Roberts, T., Lin, C.T.J., and MacDonald, J.M. (1996). Bacterial foodborne disease: Medical costs and productivity losses. Agricultural Economic Report (USDA) No. 741.

Cassin, M., Lammerding, A., Todd, E., Ross, W. and McColl, S. (1998). Quantitative Risk Assessment for *Escherichia coli* O157:H7 in Ground Beef Hamburgers. International Journal of Food Microbiology, 41, 21-44.

Centers for Disease Control. (1993). Preliminary Report: Foodborne Outbreak of *Escherichia coli* O157:H7 Infections from Hamburgers, Western United States, 1993. Morbidity and Mortality Weekly Report, 42, 258-263.

Centers for Disease Control. (1997). Outbreaks of *Escherichia coli* O157:H7 Infection and Cryptosporidiosis Associated with Drinking Unpasteurized Apple Cider, Connecticut and New York, October 1996. Morbidity and Mortality Weekly Report, 46, 4-8.

Centers for Disease Control. (1999). Outbreaks caused by Shiga toxin-producing *Escherichia coli*, Summary of 1998 Surveillance Data. Available at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/files/ecoli_98summary.pdf

Centers for Disease Control. (2000). Outbreak of *Escherichia coli* O157:H7 Infection Associated with Eating Fresh Cheese Curds—Wisconsin, June 1998. Morbidity and Mortality Weekly Report, 49, 911-913.

Centers for Disease Control. (2000). Outbreaks caused by Shiga toxin-producing *Escherichia coli*, Summary of 1999 Surveillance Data. Available at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/files/ecoli_99summary.pdf

Centers for Disease Control. (2001). Outbreaks caused by Shiga toxin-producing *Escherichia coli*, Summary of 2000 Surveillance Data. Available at: http://www.cdc.gov/foodborneoutbreaks/ecoli/2000_summaryLetter.pdf

Centers for Disease Control. (2002). Outbreaks caused by Shiga toxin-producing *Escherichia coli*, Summary of 2001 Surveillance Data. Available at: http://www.cdc.gov/foodborneoutbreaks/ecoli/CSTEletter2001.pdf

Centers for Disease Control. (2003). Outbreaks caused by Shiga toxin-producing *Escherichia coli*, Summary of 2002 Surveillance Data. Available at: http://www.cdc.gov/foodborneoutbreaks/ecoli/CSTE2002.pdf

Coleman, M.E., Tamplin, M.L., Phillips, J.G., and Marmer, B.S. (2003). Influence of agitation, inoculum density, pH, and strain on growth parameters of *Escherichia coli* O157:H7—relevance to risk assessment. International Journal of Food Microbiology, 83, 147-160.

Council for Agricultural Science and Technology. (1994). Foodborne Pathogens: Risks and Consequences. Report No. 122.

Crockett, C.S., Haas, C.N., Fazil, A., Rose, J.B., Gerba, C.P. (1996). Prevalence of shigellosis in the U.S.: Consistency with dose-response information. International Journal of Food Microbiology, 30, 87-99.

D'Aoust, J.Y., Park, C.E., Szabo, R.A., Todd, E.C.D., Emmons DB., and McKellar, R.C. (1988). Thermal Inactivation of *Campylobacter* Species, *Yersinia enterocolitica*, and Hemorrhagic *Escherichia coli* O157:H7 in Fluid Milk. Journal of Dairy Science, 71, 3230-3236.

Davies, F.L. and Law, B.A. (1984). Advances in the microbiology and biochemistry of cheese and fermented milk. New York: Elsevier Applied Science.

Davis, J.G. (1965). Cheese. New York: American Elsevier Pub. Co.

Dennis, M.J. (2000). The Hazards Posed by Verocytotoxin Producing *E. coli* (VTEC) in the Context of the Production of Unpasteurized Milk Cheese. Institute of Food Research, Colney, Norwhich. NR4 &UA.

Dennis, S.B., Buchanan, R.L., and Miller, A.J. (2001). Microbial Risk Assessment: Achievements and Future Challenges. Food Safety Magazine.

Doyle, M.P. and Schoeni, J.L. (1984). Survival and growth Characteristics of *Escherichia coli* Associated with Hemorrhagic Colitis. Applied and Environmental Microbiology, 48, 855-856.

Doyle, M.P., Zhao, T., and Meng, J. (1997). Food Microbiology: Fundamentals and Frontiers. Washington, DC: ASM Press.

Duffy, G., Garvey, P., Skandamis, P.N., McDowell, D.A., Wasteson, and Coia, J. (2001). Survival and Growth of Verocytotoxigenic *E. coli*, Technical Booklet on Survival and Growth of VTEC, Concerted Action CT98-3935. Dublin: Teagase, The National Food Centre.

Duffy, G., Whiting, R.C., and Sheridan, J.J. (1999). The effect of a competitive microflora, pH and temperature on the growth kinetics of *Escherichia coli* O157:H7. Food Microbiology, 16, 299-307.

Duffy, S., and Schaffner, D.W. (2002). Monte Carlo simulation of the risk of contamination of apples with *Escherichia coli* O157:H7. International Journal of Food Microbiology, 78, 245-255.

Duncan, S.E. and Hackney, C.R. (1994). Relevance of *Escherichia coli* O157:H7 to the Dairy Industry. Dairy, Food and Environmental Sanitation, 14, 656-660.

Dupont, H.L., Hornick, R.B., Dawkins, A.T., Synder, M.J., and Formal, S.B. (1969). The response of man to virulent *Shigella flexneri*. Journal of Infectious Disease, 119, 296-299.

Dupont, H.L., Hornick, R.B., Synder, M.J., Libonati, J.B., Formal, S.B., and Gangarosa, E.J. (1972). Immunity in shigellosis: Protection induced by oral live vaccine or primary infection. Journal of Infectious Disease, 125, 12-16.

Ebel, E., Schlosser, W., Kause, J., Orloski, K., Roberts, T., Narrod, C., Malcolm, S., Coleman, M., and Powell, M. (2004). Draft Risk Assessment of the Public Health Impact of *Escherichia coli* O157:H7 in Ground Beef. Journal of Food Protection, 67, 1991-1999.

Economic Research Service (2004). Economics of Foodborne Disease. Available at: http://www.ers.usda.gov/briefing/FoodborneDisease/features.htm

Farber, J.M., Ross, W.H., and Harwig, J. (1996). Health risk assessment of *Listeria monocytogenes* in Canada. International Journal of Food Microbiology, 30, 145-156.

Food Safety and Inspection Service. (2001). Draft Risk Assessment of the Public Health Impact of *Escherichia coli* O157:H7 in Ground Beef. Available at: http://www.fsis.usda.gov/OPPDE/ rdad/FRPubs/00-023N/00-023NReport.pdf

Food Safety and Inspection Service. (2004). National Advisory Committee on Microbiological Criteria for Foods, Requisite Scientific Parameters for Establishing the Equivalence of Alternative Methods of Pasteurization. Available at: http://www.fsis.usda.gov/ophs/nacmcf/2004/NACMCF_Pasteurization_082704.pdf

FoodNet, Centers for Disease Control. (1999). FoodNet Surveillance Report for 1999 (Final Report). Available at: http://www.cdc.gov/foodnet/annual/1999/FoodNet__1999_Annual_Report__part_1.pdf

FoodNet, Centers for Disease Control. (2000). FoodNet Surveillance Report for 2000 (Final Report). Available at: http://www.cdc.gov/foodnet/annual/2000/2000final_report.pdf

FoodNet, Centers for Disease Control. (2001). FoodNet Surveillance Report for 2001 (Final Report). Available at: http://www.cdc.gov/foodnet/annual/2001/2001annualreport_pdf.pdf

FoodNet, Centers for Disease Control. (2002). FoodNet Surveillance Report for 2002(Final Report). Available at: http://www.cdc.gov/foodnet/annual/2002/2002executive_summary.pdf

FoodNet, Centers for Disease Control. (2003). FoodNet Surveillance Report for 2003(Final Report). Available at: http://www.cdc.gov/foodnet/annual/2003/2003_report.pdf

Fox, P.F. (1993). Cheese: Chemistry, Physics and Microbiology Volume 1. New York: Chapman & Hall.

Fox, P.F., Guinee, T.P., Cogan, T.M., and McSweeney, P.L.H. (2000). Fundamentals of Cheese Science. Gaithersburg: Aspen Publishing.

Frank, J.F., Marth, E.H., and Olson, N.F. (1977). Survival of Enteropathogenic and Non-Pathogenic *Escherichia coli* During the Manufacture of Camembert Cheese. Journal of Food Protection, 40, 835-842.

Frank, J.F., Marth, E.H., and Olson, N.F. (1978). Behavior of Enteropathogenic *Escherichia coli* During Manufacture and Ripening of Brick Cheese. Journal of Food Protection, 41, 111-115.

Gerba, C.P., Rose, J.B., and Haas, C.N. (1996). Sensitive populations: who is at the greatest risk? International Journal of Food Microbiology, 30, 113-123.

Goff, D. (1995). Dairy Science and Technology Education, University of Guelph, Canada. Available at: http://www.foodsci.uoguelph.ca/dairyedu/TDT.html

Govaris, A., Papageorgiou, D.K., and Papatheodorou, K. (2002). Behavior of *Escherichia coli* O157:H7 during the Manufacture and Ripening of Feta and Telemes Cheese. Journal of Food Protection, 65, 600-615.

Griffin, P.M and Tauxe, R.V. (1991). The Epidemiology of Infections Caused by *Escherichia coli* O157:H7, Other Enterohemorrhagic *E. coli*, and the Associated Hemolytic Uremic Syndrome. Epidemiologic Reviews, 13, 60-98.

Griffin, P.M., Ostroff, S.M., Tauxe, R.V., Greene, K.D., Wells, J.G., and Lewis, J.H. (1988). Illnesses associated with *Escherichia coli* O157:H7 infections. Annals of Internal Medicine, 109, 705-712.

Gunasekera, T., Sorensen, A., Attfield, P.V., Sorensen, S.J., and Veal, D.A. (2002). Inducible Gene Expression by Nonculturable Bacteria in Milk after Pasteurization. Applied and Environmental Microbiology, 68, 1988-1993.

Haas, C.N. (1994). Dose-Response Analysis Using Spreadsheets. Risk Analysis, 14, 1097-1100.

Haas, C.N., Rose, J.B., and Gerba, C.P. (1999). Quantitative Microbial Risk Assessment. New York: John Wiley & Sons, Inc.

Haas, C.N., Thayyar-Madabusi, A., Rose, J.B., Gerba, C.P. (2000). Development of a dose-response relationship for *Escherichia coli* O157:H7. International Journal of Food Microbiology, 1748, 153-159.

Heuvelink, A.E., Bleumink, B., van den Biggelaar, F.L.A.M., Te Giffel, M.C., Beumer, R.R., and de Boer, E. (1998). Occurrence and Survival of Verocytotoxin-Producing *Escherichia coli* O157 in Raw Cow's Milk in the Netherlands. Journal of Food Protection, 61, 1597-1601.

Hao, Y.Y. and Brackett, R.E. (1993). Growth of *Escherichia coli* O157:H7 in modified atmosphere. Journal of Food Protection, 56, 330-332.

Holcomb, D.L., Smith, M.A., Ware, G.O., Hung, Y.C., Brackett, R.E., and Doyle, M.P. (1999). Comparison of Six Dose-Response Models for Use with Food-Borne Pathogens. Risk Analysis, 19, 1091-1100.

Hoornstra, E. and Notermans, S. (2001). Quantitative microbiological risk assessment. International Journal of Food Microbiology, 66, 21-29.

Hornish, L., Predy, G., Hislop, N., Chui, L., Kowalewska-Grochowska, K., Trottier, L., Kreplin, C., and Zazulak, I. (2005). An Outbreak of *E. coli* O157:H7 Hemorrhagic Colitis Associated with Unpasteurized Gouda Cheese. Canadian Journal of Public Health, 96, 182-184.

Hudson, L.M., Chen, J., Hill, A.R., and Griffiths, M.W. (1997). Bioluminescence: A Rapid Indicator of Escherichia coli O157:H7 in Selected Yogurt and Cheese Varieties. Journal of Food Protection, 60, 891-897.

Institute of Food Science and Technology. (1998). Food Safety and Cheese. Food Science & Technology Today, 12, 117-122.

Institute of Food Science and Technology. (2004). Verocytotoxin-Producing *E. coli*: Food Poisoning and Its Prevention. Available at: http://www.ifst.org/hottop1.htm

Johnson, E.A., Nelson, J.H., and Johnson, M. (1990). Microbiological Safety of Cheese Made from Heat-Treated Milk. Part III. Technology, Discussion, Recommendations, Bibliography. Journal of Food Protection, 53, 610-623.

June, R.C., Ferguson, W.W., and Worfel, M.T. (1953). Experiments in Feeding Adult Volunteers with *Escherichia coli* 55, B5, a Coliform Organism Associated with Infant Diarrhea. American Journal of Hygiene, 57, 222-236.

Keene, W.E., and Sazie, E. (1997). An outbreak of *E. coli* O157:H7 infections traced to jerky made from deer meat. Journal of the American Medical Association, 277, 1229-1232.

Keene, W.E., Hedbery, K., Herriott, D.E., Hancock, D.D., McKay, R.W., Barrett, T.J., and Fleming, D.W. (1997). A prolonged outbreak of Escherichia coli O157:H7 infections caused by commercially distributed raw milk. Journal of Infectious Diseases, 176, 815-818.

Kornacki, J.L. and Marth, E.H. (1982). Fate of Nonpathogenic and Enteropathogenic *Escherichia coli* During the Manufacture of Colby-like Cheese. Journal of Food Protection, 45, 310-316.

Kosikowski, F. (1977). Cheese and Fermented Milk Foods. Ann Arbor: Edwards Brothers.

Lammerding, A.M., and Fazil, A. (2000). Hazard identification and exposure assessment for microbial food safety risk assessment. International Journal of Food Microbiology, 58, 147-157.

Law, B.A. (1999). Technology of Cheesemaking. Boca Raton: CRC Press LLC.

LeBlanc, J.J. Implication of Virulence Factors in *Escherichia coli* O157:H7 Pathogenesis. Clinical Reviews in Microbiology, 29, 277-296.

Leuschner, R.G.K., and Boughflower, M.P. (2002). Laboratory-scale preparation of soft cheese artificially contaminated with low levels of *Escherichia coli* O157, *Listeria monocytogenes*, and *Salmonella enterica* serovars *Typhimurium*, *Enteritidis*, and *Dublin*. Journal of Food Protection, 65, 508-514.

Levine, M.M., Berquist, E.J., Nailin, D.R., Waterman, D.H., Hornick, R.B., Young, C., and Sotman, S. (1978). *Escherichia coli* strains that cause diarrhea but do not produce heat labile or heat-stable enterotoxins and are non-invasive. Lancet, 1, 1119.

Levine, M.M., Dupont, H.L. and Formal, S.B. (1973). Pathogenesis of *Shigella dysenteriae* (Shiga) dysentery. Journal of Infectious Disease, 127, 261-269.

Lindqvist, R., Sylven, S., and Vagsholm, I. (2002). Quantitative microbial risk assessment exemplified by *Staphylococcus aureus* in unripened cheese made from raw milk. International Journal of Food Microbiology, 78, 155-170.

MacDonald, K.L. (1985). A multistate outbreak of gastrointestinal illness caused by enterotoxigenic *Escherichia coli* in imported semisoft cheese. Journal of Infectious Diseases, 151, 716-720.

Maher, M.M., Jordan, K.N., Upton, M.E., and Coffey, A. (2001). Growth and survival of *E. coli* O157:H7 during the manufacture and ripening of a smear-ripened cheese produced from raw milk. Journal of Applied Microbiology, 90, 201-207.

Manolopoulou, E., Sarantinopoulous, P., Zoidou, E., Aktypis, A., Moschopoulou, E., Kandarakis, I.G., and Anifantakis, E.M. (2003). Evolution of microbial populations during traditional Feta cheese manufacture and ripening. International Journal of Food Microbiology, 82, 153-161.

Mamani,Y., Quinto, E.J., Simal-Gandara, J., and Mora, M.T. (2003). Growth and survival of *Escherichia coli* O157:H7 in different types of milk stored at 4˚C or 20˚C. Journal of Food Science, 68, 2558-2563.

Marek, P., Nair, M.K.M., Hoagland, T., and Venkitanarayanan, K. (2004). Survival and growth characteristics of *Escherichia coli* O157:H7 in pasteurized and unpasteurized Cheddar cheese whey. International Journal of Food Microbiology, 94, 1-7.

Marks, H.M., Coleman, M.E., Lin, C.T.L., and Roberts, T. (1998). Topics in Microbial Risk Assessment: Dynamic Flow Tree Process. Risk Analysis, 18, 309-328.

Martin, M.L., Shipman, L.D., Wells, J.G., and Potter, M.E. (1996). Isolation of *Escherichia coli* O157:H7 from dairy cattle associated with two cases of hemolytic uremic syndrome. Lancet, 2, 1043.

Massa, S., Goffredo, E., Altieri, C. and Natola, K. (1999). Fate of *Escherichia coli* O157:H7 in unpasteurized milk stored at 8˚C. Letters in Applied Microbiology, 28, 89-92.

Mead, P.S. and Griffin, P.M. (1998). *Escherichia coli* O157:H7. Lancet, 352, 1207-1212.

Mead, P.S., Slutsker, L., Dietz, V., McCaig, L.F., Bresee, J.S., Shapiro, C., Griffin, P.M., and Tauxe, R.V. (1999). Food-Related Illness and Death in the United States. Emerging Infectious Diseases, 5, 607-625.

Measurement Methods: The Analytical Hierarchy Process. (2005). Information and Discussion Forum on Priority Setting in Agricultural Research. Available at: http://www.isnar.cgiar.org/Fora/Priority/MeAnalit.htm

Nataro, J.P. and Kaper, J.B. (1998). Diarrheagenic *Escherichia coli*. Clinical Microbiology Reviews, 11, 142-201.

Nauta, M.J., and van der Giessen, J.W.B. (1998). Human exposure to *Mycobacterium paratuberculosis* via pasteurized milk: a modeling approach. The Veterinary Record, 143, 293-296.

Nauta, M.J., Evers, E.G., Takumi, K., and Havelaar, A.H. (2001). Risk Assessment of Shiga-toxin Producing *E. coli* O157 in Steak Tartare in the Netherlands. RIVM Rep. 257851003, PO Box 1, 3720 BA Bilthoven, The Netherlands.

Nooitgedagt, A.J. and Hartog, B.J. (1988). A survey of the microbiological quality of Brie and Camembert cheese. Netherlands Milk and Dairy Journal, 42, 57-72.

Notermans, S., Dufrenne, J., Teunis, P., Beumer, R., Giffel, M.T., and Weem, P.P. (1997). A risk assessment study of *Bacillus cereus* present in pasteurized milk. Food Microbiology, 14, 143-151.

Olsen, S.J., MacKinon, L.C., Goulding, J.S., Bean, N.H., and Slutsker, L. (2000). Surveillance for Foodborne Disease Outbreaks, United States, 1993-1997. Morbidity and Mortality Weekly Report, 51, 1-51.

Ostroff, S.M., Griffin, P.M., Tauxe, R.V., Shipman, L.D., Greene, K.D., Wells, J.G., Lewis, J.H., Blake, P.A., Kobayashi, J.M. (1990). A statewide outbreak of *Escherichia coli* O157:H7 infections in Washington state. American Journal of Epidemiology, 132, 239-247.

Pai, C.H., Kelly, J.K., and Meyers, G.L. (1986). Experimental infection of infant rabbits with verotoxin producing *E. coli*. Infection and Immunity, 51, 16-23.

Palumbo, M.S., Pickard, A., and Call, J.E. (1997). Population Changes and Verotoxin Production of Enterohemorrhagic *Escherichia coli* Strains Inoculated in Milk and Ground Beef Held at Low Temperatures. Journal of Food Protection, 60, 746-750.

Park, H.S., Marth, E.H., and Olson, N.F. (1973). Fate of Enteropathogenic Strains of *Escherichia coli* During the Manufacture and Ripening of Camembert Cheese. Journal of Milk and Food Technology, 36, 543-546.

Peeler, J.T. and Bunning, V.K. (1994). Hazard assessment of *Listeria monocytogenes* in the processing of bovine milk. Journal of Food Protection, 57, 689-697.

Potter, M.E. (1996). Risk Assessment Terms and Definitions. Journal of Food Protection, Supplement, 6-9.

Powell, M., Ebel, E., and Schlosser, W. (2001). Considering uncertainty in comparing the burden of illness due to foodborne microbial pathogens. International Journal of Food Microbiology, 69, 209-215.

Powell, M., Schlosser, W., and Ebel, E. (2004). Considering the complexity of microbial community dynamics in food safety risk assessment. International Journal of Food Microbiology, 92, 171-179.

Powell, M.R. (2000). Dose-Response Envelope for *Escherichia coli* O157:H7. Quantitative Microbiology, 2, 141-163.

Rajkowski, K.T. and Marmer, B.S. (1995). Growth of *Escherichia coli* O157:H7 at Fluctuating Incubation Temperatures. Journal of Food Protection, 58, 1307-1313.

Ramsaran, H., Chen, J., Brunke, B. et al. (1998). Survival of bioluminescent *Listeria monocytogenes* and *Escherichia coli* O157 : H7 in soft cheeses. Journal of Dairy Science, 1810-1817.

Rash, K.E., and Kosikowski, F.V. (1982). Behavior of Enteropathogenic *Escherichia coli* in Camembert Cheese Made from Ultrafiltered Milk. Journal of Food Science, 47, 728-732.

Rash, K.E., and Kosikowski, F.V. (1982). Influence of Lactic Acid Starter Bacteria on Enteropathogenic *Escherichia coli* in Ultrafiltration Prepared Camembert Cheese. Journal of Dairy Science, 65, 537-543.

Read, R.B., Schwartz, C., and Litsky, W. (1961). Studies on Thermal Destruction of *Escherichia coli* in Milk and Milk Products. Applied Microbiology, 9, 415-418.

Reitsma, C.J. and Henning, D.R. (1996). Survival of Enterohemorrhagic *Escherichia coli* O157:H7 During the Manufacture and Curing of Cheddar Cheese. Journal of Food Protection, 59, 460-464.

Riley, L.W., Remis, R.S., Helgerson, S.D., McGee, H.B., Wells, J.G., Davis, B.R., Hebert, R.J., Olcott, E.S., Johnson, L.M., Hargrett, N.T., Blake, P.A., and Cohen, M.L. (1983). Hemorrhagic Colitis Associated with a Rare *Escherichia coli* Serotype. The New England Journal of Medicine, 308, 681-685.

Rosenau, M.J. (2006). Milk pasteurization. Available at: http://en.wikipedia.org/wiki/Pasteurization

Ryan, C.A., Tauxe, R.V., Hosek, G.W., Wells, J.G., Stoesz, P.A., McFadden, H.W., Smith, P.W., Wright, G.F., and Blake, P.A. (1986). *Escherichia coli* O157:H7 diarrhea in a nursing home: clinical empidemiologic and pathological findings. Journal of Infectious Diseases, 154, 631-638.

Sanaa, M., Coroller, L., and Cerf, O. (2004). Risk Assessment of Listeriosis Linked to the Consumption of Two Soft Cheeses Made from Raw Milk: Camembert or Normandy and Brie of Meaux. Risk Analysis, 24, 389-399.

Schlundt, J. (2000). Comparison of microbiological risk assessment studies published. International Journal of Food Microbiology, 58, 197-202.

Shinagawa, K., Hu, D.Y., and Yoshida, S. (1997). Correspondence and problem for enterohemorrhagic *E. coli* O157 outbreak in Morioka city, Iwate. Bulletin, National Institute of Public Health 46, 104-112 (in Japanese).

Slutsker, L., Ries, A.A., Maloney, K., Wells, J.G., Greene, K.D., and Griffin, P.M. (1998). A nationwide case-control study of *Escherichia coli* O157:H7 infection in the United States. Journal of Infectious Diseases, 177, 962-966.

Spano, G., Goffredo, E., Beneduce, L., Tarantino, D., Dupuy, A., and Massa, A. (2003). Fate of *Escherichia coli* O157:H7 during the manufacture of Mozzarella cheese. Letters in Applied Microbiology, 36, 73-76.

Stabel, J.R. (2003). Effective Methods for Postharvest Intervention in Dairy Processing. Journal of Dairy Science, 86, 10-15.

Steahr, T.E. (1994). Food-borne illness in the United States: geographic and demographic patterns. International Journal of Environmental Health Research, 4, 183-195.

Strachan, N.J.C., Doyle, M.P., Kasuga, F., Rotariu, O., and Ogden, I.D. (2005). Dose response modeling of *Escherichia coli* O157 incorporating data from foodborne and environmental outbreaks. International Journal of Food Microbiology, 103, 35-47.

Strachan, N.J.C., Fenlon, D.R., and Ogden, I.D. (2001). Modeling the vector pathway and infection of humans in an environmental outbreak of *Escherichia coli* O157. FEMS Microbiology Letters, 203, 69-73.

Su, C. and Brandt, L.J. (1995). *Escherichia coli* O157:H7 Infection in Humans. Annals of Internal Medicine, 123, 698-707.

Sutherland, J.P., Bayliss, A.J., and Braxton, D.S. (1995). Predictive Modeling of Growth of *Escherichia coli* O157:H7: The Effects of Temperature, pH and Sodium Chloride. International Journal of Food Microbiology, 25, 29-49.

Sutherland, J.P., Bayliss, A.J., Braxton, D.S., and Beaumont, A.L. (1997). Predictive Modeling of Growth of *Escherichia coli* O157:H7: Inclusion of Carbon Dioxide as a Fourth Factor in a Pre-Existing Model. International Journal of Food Microbiology, 37, 113-120.

Teo, A., Schlesser, J.E., Madsen, K., and Gerdes, R. (2000). Survival of Naturally Occurring Coliforms, a Streptomycin-Resistant Strain Of *E. coli* K12 (ATCC 35695) or *E. coli* O157:H7 during the Aging Period of Hard Cheeses Made from Unpasteurized Milk. National Center for Food Safety and Technology.

Thompson, K.M. (2002). Variability and Uncertainty Meet Risk Management and Risk Communication. Risk Analysis, 22, 647-654.

Tilden, J., Young, W., and MacNamara, A.M. (1996). A new route of transmission for *Escherichia coli*: infection from dry fermented salami. American Journal of Public Health, 86, 1142-1145.

Tuttle, J., Gomez, T., Doyle, M.P., Wells, J.G., Zhao, T., Tauxe, R.V., and Griffin, P.M. (1999). Lessons from a large outbreak of *Escherichia coli* O157:H7 infections: insights into the infectious dose and method of widespread contamination of hamburger patties. Epidemiology of Infections, 122, 185-192.

Uchimura, M., Kishida, K., and Yoda, K. (1997). An outbreak of enterohemorrhagic *E. coli* O157:H7 in a daycare. China Perfecture. Infect. Agents Survey Rep., 18, 309-310 (in Japanese).

United States Department of Agriculture. (2001). Grade "A" Pasteurized Milk Ordinance. Available at: http://www.cfsan.fda.gov/~ear/pmo01toc.html

United States Department of Agriculture. (2003). Approximate pH of Foods and Food Products. Available at: http://www.cfsan.fda.gov/~comm/lacf-phs.html

United States Department of Agriculture. (2004). Juice and HACCP Hazards and Controls Guidance. Available at: http://www.cfsan.fda.gov/%7Edms/juicgu10.html

Upton, P. and Coia, J. (1994). Outbreak of E. coli infection associated with pasteurized milk supply. The Lancet, 344, 1015.

Varnam, A.H. and Sutherland, J.P. (1994). Milk and Milk Products: Technology, Chemistry and Microbiology. London: Chapman & Hall.

Vose, D. (1998). The applications of quantitative risk assessment to microbial risk assessment. Journal of Food Protection, 61, 640-648.

Vose, D. (2000). Risk Analysis: A Quantitative Guide. New York: John Wiley & Sons, Inc.

Wang, G., Zhao T., and Doyle, M.P. (1997). Survival and Growth of Escherichia coli O157:H7 in Unpasteurized and Pasteurized Milk. Journal of Food Protection, 60, 610-613.

Warrner, M., Kuo, K., Williams, L., and Ruden, R. (1996). Lake associated outbreak of *E. coli* O157:H7. MMWR Morbidity and Mortality Weekly Report, 45, 437-439.

Weeratna, R.D., and Doyle, M.P. (1991). Detection and production of verotoxin 1 of *Escherichia coli* O157:H7 in food. Applied and Environmental Microbiology 57, 2951-2955.

Wells, J.G., Shipman, L.D., Greene, K.D., Sowers, E.G., Green, J.H., and Cameron, D.N. (1991). Isolation of *Escherichia coli* serotype O157:H7 and other Shiga-like-toxin producing *E. coli* from dairy cattle. Journal of Clinical Microbiology, 29, 985-989.

World Health Organization. (1995). Application of risk to food standards issues: Report of the Joint FAO/WHO Expert Consultation, WHO/FNU/FOS/95.3.

Zwietering, M.H., de Wit, J.C., and Notermans, S. (1996). Application of predictive microbiology to estimate the number of *Bacillus cereus* in pasteurized milk at the point of consumption. International Journal of Food Microbiology, 30, 55-70.