Microbial Risk Assessment: Where Did This Come From and Why Do I Need to Pay Attention?

Robert L. Buchanan

Introduction

In recent years, risk assessment techniques have been increasingly used by national governments and international bodies to provide a framework for discussing the scientific facts and issues related to food safety issues. Risk assessment provides a structured approach for organizing and evaluating data that is both "transparent" and provides a means for measuring the uncertainty associated with the findings. In the past, food safety risk assessments have been primarily limited to the determination of the levels of specific chemicals that can be introduced into the food supply without having an adverse impact on public health. Microbiological food safety concerns had been historically considered too complex to be amenable to anything more rigorous than highly qualitative safety evaluations. However, advances in predictive food safety microbiology over the preceding 10 years laid the foundation for the development of microbial risk assessment methods. Thus, the past 5 years has seen an increasing number of reports in the scientific literature establishing microbial food safety risk assessment as a developing science.

Examples of Quantitative Microbial Risk Assessments

Early attempts to assess the risk associated with infectious biological agents focused on drinking water (Macler and Regli, 1993). The impetus for this initiative was the need to assess the relative risks associated with bacterial, viral, and protozoan contamination against those associated with use of the disinfectant chemicals (e.g., chlorine) used to eliminate them. The general approach was to establish a target tolerable risk (e.g., less than one *Giardia* infection per 10,000 people per year), and then conduct a risk assessment to evaluate the ability of current water treatment approaches to meet that goal. A series of risk assessments were done for enteric viruses, bacteria, and protozoa (Gerba and Haas, 1988; Rose and Gerba, 1991; Rose et al., 1991). While an important step in establishing the efficacy of quantitative risk assessment, these initial quantitative assessments focused largely on establishing dose-response relations, and were relatively simplistic in regard to exposure assessments (Gale, P. 1996). They did not consider factors affecting exposure such as pathogen distributions in the raw water or the changes in pathogen levels likely to occur as a result of water treatment and distribution.

An extension of this approach was used to conduct a quantitative assessment of the risk of acquiring a viral infection from the consumption of contaminated raw shellfish (Rose and Sobsey, 1993.). A non-threshold model for infection was employed for the dose-response assessment which included a consideration of the probability of infection, morbidity, and mortality. Subsequently, Todd and Harwig (1996) conducted a series of semi-quantitative risk assessments to characterize the risk associated with the consumption of four food classes.

One of the first attempts to assess the microbiological risks associated with a food process was a quantitative hazard assessment for *L. monocytogenes* in milk processing that was conducted to evaluate the efficacy of current milk production and pasteurization practices (Peeler and Bunning, 1994). Six key production or processing factors were identified. Using this hazard assessment, the investigators concluded that there was less than a 2% probability that one *L. monocytogenes* would occur in 5.9×10^{10} gallons of pasteurized milk. Cassin et al. (1996) commented that this value was likely an overestimation of the risk due to the methods used to calculate overall risk. They recommended the use of Monte Carlo simulation techniques to achieve a more accurate estimate.

Buchanan and Whiting (1996) proposed that dynamic risk assessment models could be developed to link exposure and dose-response models. Using a hypothetical example, they demonstrated that initial raw product pathogen distribution data could be coupled to predictive microbiology models to provide a dynamic exposure model. The results from the exposure model then served as the input for dose-response models. They further demonstrated that this approach could be used to characterize complex, multiple step processes using Monte Carlo techniques. While different terms have been coined by various investigators (e.g., process risk model (Cassin et al., 1998), dynamic fault tree model (Marks et al., 1998)), "product/pathogen pathway analyses" have been the basis for many of the quantitative microbial risk assessments reported recently. They have in common the use of a series of probabilistic and stochastic predictive microbiology models to de-

Robert L. Buchanan, U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
200 C-Street SW, Washington, DC, USA 20204
Telephone: 1-202-205-5053. Fax: 1-202-401-5053
E-mail: rbuchana@bangate.fda.gov
Reciprocal Meat Conference Proceedings, Volume 52, 1999.

scribe factors affecting exposure, and then using the result of the exposure assessment as the input for dose-response models as a means of linking exposure to human health impact.

Three areas that have received a great deal of attention in relation to being the subject of microbial risk assessment research have been *S. enteritidis* in eggs and egg products, *L. monocytogenes* in ready-to-eat foods, and enterohemorrhagic *E. coli* in ground beef.

Salmonella Enteritidis

The simultaneous emergence of egg-associated *S. enteritidis* outbreaks in Europe and North America stimulated several attempts to identify and quantify the risk factors that contribute to the incidence of human health problems. The sporadic nature of contamination in combination with the complexity of how eggs are produced, processed, distributed, prepared, and consumed has led to a need for methods to compare control strategies to determine which are likely to be effective both in terms of public health assurance and economics. Using production, survey, and epidemiological data, Todd (1996) used a traditional risk assessment approach to evaluate the increased risk associated with the use of cracked eggs in Canada. This included an assessment of potential risk management options. As a means of demonstrating the use of predictive microbiology to achieve dynamic microbial risk assessment models, Whiting and Buchanan (1997) performed a product/pathogen pathway analysis to quantify the risk of acquiring a *S. enteritidis* infection from homemade mayonnaise made from pasteurized liquid whole eggs. This eleven-step model incorporated factors from farm (e.g., % of infected flocks) to consumer (e.g, serving size, duration and temperature of home storage). The model allowed the effects of changes in a variety of environmental, formulation, and raw material variables on the infection probability profile to be readily calculated. More recently, a multi-disciplinary team from the U.S. Department of Agriculture completed an assessment of the risk of acquiring salmonellosis from shell eggs and egg products (Baker et al., 1998). This assessment expands previous efforts by considering a range of products and practices, and by the inclusion of cost-benefit estimates for different control strategies.

Listeria monocytogenes

The establishment of "non-zero" microbiological criteria for *L. monocytogenes* in ready-to-eat foods has been a subject of debate. The lack of a clearly defined threshold value for *L. monocytogenes* infections among susceptible populations has been the area of concern. It is unlikely that human dose-response data can ever be acquired (Buchanan et al., 1997), so alternative approaches to determining dose-response relations have been investigated (Buchanan et al., 1997; Farber et al., 1996) to estimate the risks associated with different levels of contamination. Several qualitative and semi-quantitative assessments of survey and epidemiological data have suggested that the risks associated with the low levels of *L. monocytogenes* often found in ready-to-eat foods are minimal and that they are inconsequential in relation to public health strategies (Buchanan et al., 1997; Farber et al., 1996; Hitchens, 1996.). Based on a risk evaluation of these data and assessments, ICMSF (1996) proposed a microbiological criterion of 100 cfu/g be established for *L. monocytogenes*. Miller et al. (1997) demonstrated how a combination of microbial risk assessment models, predictive microbiology models, and simulation modeling techniques could be used in HACCP programs to establish critical limits and other process criteria that would assure that the microbiological criterion proposed by ICMSF would be consistently met.

Enterohemorrhagic *Escherichia coli*

The association of highly infectious enterohemorrhagic *E. coli* with ground beef has also stimulated the use of risk assessment and predictive microbiology techniques to identify important risk factors and to evaluate potential control strategies. Marks et al. (1998) developed a dynamic quantitative risk model for factors contributing the overall risks associated with the production and consumption of ground beef. Cassin et al. (1998a) developed a dynamic model for ground beef production and consumption; however, they expanded their model to include factors that contribute to the contamination of beef during slaughter operations. Zwitering and Hasting (1997a, b) modeled the steps in ground beef manufacturing operations. They used process engineering simulation modeling in combination with predictive microbiology models to quantify the contributions that individual steps have on the overall risks associated with the process. They concluded that this approach would be applicable to both the development of quantitative microbial risk assessments, and the establishment of critical control points and their critical limits for HACCP programs.

In addition to the three pathogens above, a limited number of quantitative microbial risk assessments have been attempted with other microorganisms, including Bacillus cereus (Zwitering et al., 1996), Salmonella on pork carcasses (Berends et al., 1996a, 1996b, 1997), and *Salmonella* on broilers (Oscar, 1997), and the presence of *Taenia saginata* on New Zealand beef (van der Logt et al., 1997)

The cited studies should not be considered all inclusive. New research articles are published monthly that describe advances in the techniques for microbial risk assessments. In addition, several large microbial risk assessment are currently underway by different Federal agencies. The FDA is currently conducting two formal risk assessment on microbiological issues. The first is a risk ranking exercise being in done in collaboration with the USDA FSIS to identify the foods that pose the greatest risk to consumers in relation to foodborne *L. monocytogenes*. The assessment will focus on the total dietary exposure to the pathogen and whether the risk of listeriosis is effectively limited to products with elevated levels of the organism. It will also examine the effect of specific food characteristics such as ability to support the growth of *L. monocytogenes* and the duration of refrigerated storage. The second risk assessment is product/pathogen path-

way analysis examining the transmission of *Vibrio parahaemolyticus* via raw molluscan shellfish conducted in collaboration with the National Marine Fisheries Service. The assessment is being undertaken to analyze the effectiveness of current microbiological standards for reopening contaminated shellfish beds. The project also includes an evaluation of the public health significance of the emergence of new, potentially more virulent pathogenic isolates of *V. parahaemolyticus*.

Chemical Versus Microbial Food Safety Risk Assessments

The overall goal of conducting quantitative risk assessments related to microbiological and chemical concerns of foods is the same; that is estimating the risks associated with hazards in the food supply. However, unique characteristics associated with foodborne microbiological hazards make microbial risk assessments simultaneously easier and more difficult than assessments conducted for food chemical hazards. Understanding these differences leads to understanding the strengths and limitations of microbial risk assessment. Some of the characteristics that make microbiological assessments different from chemical assessments are:

(1) Microbial risks are generally the result of single exposures. Each exposure to a pathogen or its toxin represents an independent, non-cumulative event. This is in comparison to chemical risk assessments where one of the primary focuses is the cumulative effects of carcinogens and other long-term chemical toxicities. Even chronic sequelae associated with pathogens is generally the result of a single exposure. Multiple exposures over time lead to the development of immunity and thus lessen overall risks.

(2) The response of humans to infectious pathogens is highly variable. This variability reflects the variability in the immune status of humans. Individuals within the population can range from highly resistant to extremely susceptible depending on their genetics, age, physiological status, and a variety of other biological and socioeconomic factors that influence the complex systems that enable the body to protect itself against infection. A classic example is the use of vaccines. While the general population might be highly susceptible to a disease agent such as measles, the risk of adverse effects becomes diminishingly small for any segment of the population that has been protected by prior vaccination.

Since the disease process for infectious agents involves their multiplication in the host, there is often little correlation between the levels of the pathogen ingested and the severity of the disease response, particularly when considering exposures to low doses of the biological agent (Haas, 1983; Crockett et al., 1996). Secondary infections resulting from the person-to-person spread also have be considered when estimating the risks associated with highly infectious biological agents (e.g., enterohemorrhagic *E. coli*, *Shigella*, *Salmonella typhi*).

(3) The levels of many toxic compounds in foods are relatively stable or decline over time as a result of degradation or dilution. The same is true for certain classes of microorganisms. Pathogenic bacteria can increase a billion-fold in less than a day if a meat product was temperature abused. Conversely, pathogen numbers can decrease a billion-fold in minutes as a result of a simple cooking step. This potential for changes in pathogen levels, and the accompanying need to consider the incidence of abuse and related factors greatly complicates exposure assessments, that is, the number of pathogen cells or amount of microbial toxin actually ingested by consumers.

(4) Microorganisms are dynamic and adaptable. Two isolates of the same species can have highly disparate disease capabilities. For example, most *E. coli* are non-pathogenic, but specific isolates such as *E. coli* O157:H7 are associated with life threatening diseases. The virulence of isolates can be also affected by the food matrix in which they are present. Thus, microbial risk assessments must deal with the biovariability of the pathogen, the host, and the food.

(5) Microbiological risk assessments differ from chemical risk assessments in relation to the emphasis placed on the hazard identification phase of the assessment. Most food chemical risk assessments are associated with the "pre-market approval" of compounds that that will either be purposefully added to foods or that inadvertently get there as a result of environmental contamination. Conversely, most microbiological risk assessments are associated with post-market considerations.

(6) Disease reporting systems for several well known foodborne pathogens provide a potential means for validating risk assessment models that is generally not available for most food chemicals.

Methods for Microbiological Risk Assessments

There are a variety of potential methods that could be employed for conducting microbial risk assessments, but in general these are likely to fall into two broad categories: risk ranking or product/pathogen pathways.

Risk Ranking

As the name implies, risk ranking is a process for ranking hazards in relation to the impact they have on public health. This is most often used as a means of setting priorities when multiple public health concerns are competing for limited resources. It is also used to identify those segments or attributes of a highly complex problem that warrant first consideration. Risk ranking exercises can be either qualitative or quantitative. While quantitative assessments are preferable, lack of knowledge, time, or resources may require the assessment to be limited to qualitative considerations.

Product/Pathogen Pathway Analysis:

The purpose of product/pathogen pathway analyses is to identify the likely sources of a pathogen and elucidate the impact that various activities associated with the production, processing, marketing, and consumption of a food product have on consumer risks. The basic approach in a product/pathogen pathway analysis is to examine the pathway leading to the consumption of the product, starting with the raw ingredients and including all production, processing, marketing, and consumption factors that have a substantial impact on the final risk faced by the consumer. Like risk ranking, product/pathogen pathway analyses can be qualitative or quantitative. Fully quantitative analyses are generally performed through the development of a dynamic model. Such models are particularly useful for assessing the likely impact of different risk management control options.

The ability to perform realistic product/pathogen pathway analyses has become a reality due to developments in three areas: the availability of software for personal computers that provide investigators with powerful simulation modeling tools such as Monte Carlo analysis (Vose, 1998; Cassin et al., 1998b), the availability of predictive microbiology models that allow microbiological behavior in foods and food processes to be described mathematically (Buchanan and Whiting, 1996, 1998; Whiting and Buchanan, 1992; 1994; 1997), and the development of models and data that can be used to describe dose-response relations (Haas, 1983; Crockett et al., 1996; Buchanan et al., 1997; Coleman and Marks, 1998). Product/pathogen pathway analyses are increasingly being coupled with cost benefit analyses to provide more detailed "risk management option assessments" to policy developers (Morales and McDowell, 1998).

Frameworks for Microbial Risk Assessments

The rapid advances in quantitative microbial food safety risk assessment during the last five years have been the direct result of the acute need for these techniques at the national and international levels. Even before techniques for conducting microbial risk assessments had been published, various advisory bodies had begun considering how such information could and should be acquired and used. The Council for Agricultural Science and Technology strongly endorsed the use of risk assessment techniques by government agencies to focus microbial food safety initiatives (CAST, 1994, 1998). The International Life Science Institute provided a general framework for assessing risks associated with human exposures to disease-causing agents (ILSI, 1996). The U.S. National Advisory Committee on Microbiological Criteria for Foods developed a framework document for the use of risk assessment techniques for illnesses caused by biological agents in foods (NACMCF, 1998). The International Commission on Microbiological Specifications for Foods provided extensive guidance on how risk assessment techniques could be applied to microbiological issues for food in international trade (ICMSF, 1998). The Codex Committee for Food Hygiene has also recently adopted a framework for the conduct of microbial food safety risk assessment (CCFH, 1998), and that framework document is currently before the Codex Alimentarius Commission for adoption.

While using somewhat different terminologies, these framework documents recommend a risk assessment framework consistent with what has evolved for food chemicals (NRC, 1983). This includes four steps which consist of (1) a phase for the identification and initial characterization of the hazard, (2) determination of the population's exposure to the hazard, (3) elucidation of the relationship between exposure to the hazard and the frequency and severity of adverse effects in the population, and (4) an integrated characterization of the risks associated with the hazard. These steps are not necessarily sequential; steps 2 and 3 often considered simultaneously and then integrated in step 4.

Concluding Remarks

Quantitative microbial food safety risk assessment is emerging as a powerful new tool for evaluating complex issues associated with food safety, food hygiene, domestic and international trade, and food standards. The importance of this in relation to efforts to ensure that Federal regulation are "science-based" and "risk-based" is reflected in this area being specifically highlighted in the President's Food Safety Initiative, and the establishment of risk assessment groups in all Federal agencies associated with the assessment or management of food safety risks. However, like most new concepts, the use of microbial risk assessment must be carefully managed to insure that less than rigorous use of the techniques does not discredit this approach before it has a chance to become more widely accepted. This is particularly true for applications to issues related to international commerce. The disparate capabilities among countries to conduct quantitative microbial risk assessments is a potential barrier to acceptance of these techniques. Microbial risk assessments cannot be viewed is a "high-tech" tool that is used by developed countries as a means for forcing their positions on developing countries. The establishment of an independent expert panel as a means for avoiding this potential problem is currently being considered by WHO and FAO.

References

Baker, A., E. Ebel, A. Hogue, R. McDowell, R. Morales, W. Schlosser, and R. Whiting. 1998. *Salmonella* Enteritidis risk assessment: Shell eggs and egg products. USDA Food Safety and Inspection Service. Washington, DC.

Berends, B. R., F. Van Knapen, and J. M. A. Snijders. 1996a. Suggestions for the construction, analysis and use of descriptive epidemiological models for the modernization of meat inspection. International Journal of Food Microbiology 30:27-29.

Berends, B. R., H. A. P. Urlings, J. M. A. Snijders, and F. Van Knapen. 1996b. Identification and quantification of risk factors in animal management and transport regarding *Salmonella* spp. in pigs. International Journal of Food Microbiology 30:37-53.

Berends, B. R., F. Van Knapen, J. M. A. Snijders, and D. A. A. Mossel. 1997. Identification and quantification of risk factors regarding *Salmonella* spp. in pork carcasses. International Journal of Food Microbiology 36:199-206.

Buchanan, R. L., and R. C. Whiting. 1996. Risk assessment and predictive microbiology. Journal of Food Protection 59:1996 Suppl. 31-36.

Buchanan, R. L., and R. C. Whiting. 1998. Risk assessment: A means for linking HACCP and public health. Journal of Food Protection 61:1531-1534

Buchanan, R. L., W. G. Damert, R. C. Whiting, and M. van Schothorst. 1997. Use of epidemiologic and microbial food survey data to develop a "worst-case" estimate of the dose-response relationship between *Listeria monocytogenes* levels and the incidence of foodborne listeriosis. Journal of Food Protection 60:918-922.

Cassin, M. H., G. M. Paoli, R. S. McColl, and A. M. Lammerding. 1996. A comment on "Hazard assessment of *Listeria monocytogenes* in the processing of bovine milk," *Journal of Food* Protection 57, 689-697 (1994). Journal of Food *Protection* 59:341-343.

Cassin, M. H., A. M. Lammerding, E. C. D. Todd, W. Ross, and R. S. McColl. 1998A. Quantitative risk assessment for *Escherichia coli* O157:H7 in ground beef hamburgers. International Journal of Food Microbiology 41:21-44.

Cassin, M. H., G. M. Paoli, and A. M. Lammerding. 1998b. Simulation modeling for microbial risk assessment. Journal of Food Protection 61:1560-1566.

CAST (Council for Agricultural Sciences and Technology). 1994. Foodborne pathogens: Risks and consequences. Task Force Report 122, Washington, DC.

CAST (Council for Agricultural Sciences and Technology). 1994. Foodborne pathogens: Risks and consequences. Updated Recommendations. Washington, DC.

CCFH (Codex Alimentarius Committee on Food Hygiene). 1998. Principles and guidelines for application of microbiological risk assessment. (CCFH 99/13)

Coleman, M. and H. Marks. 1998. Topics in dose-response modeling. Journal of Food Protection 61:1550-1559.

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

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

Gale, P. 1996. Developments in microbiological risk assessment models for drinking water - A short review. Journal of Applied Bacteriology 81:403-410.

Gerba, C. P., and C. N. Haas. 1988. Assessment of risks associated with enteric viruses in contaminated drinking water, p. 489-494. *In* J. J. Lichtenber, J. A. Winter, C. I. Weber, and L. Fradkin (ed.), Chemical and biological characterization of sludges, sediments, dredge spoils, and drilling muds. ASTM STP 976. American Society for Testing and Materials, Philadelphia, PA.

Haas, C. N. 1983. Estimation of risk due to low doses of microorganisms: A comparison of alternative methodologies. American Journal of Epidemiology 118:573-582.

Hitchens, A. D. 1996. Assessment of alimentary exposure to *Listeria monocytogenes*. International Journal of Food Microbiology 30:71-85.

ICMSF (International Commission on Microbiological Specifications for Foods). 1996. Report to Food Hygiene Committee of Codex Alimentarius - Principles for the establishment and application of microbiological criteria for foods. Washington, DC.

ICMSF (International Commission on Microbiological Specifications for Foods). 1998. Potential application of risk assessment techniques to microbiological issues related to international trade in food and food products. Journal of Food Protection 61:1075-1086.

ILSI (International Life Sciences Institute). 1996. A conceptual framework to assess the risks of human disease following exposure to pathogens. Risk Analysis 16:841-848.

Macler, B. A. and S. Regli. 1993. Use of microbial risk assessment in setting US drinking water standards. International Journal of Food Microbiology 18:245-256.

Marks, H. M., M. E. Coleman, C. -T. J. Lin, and T. Roberts. 1998. Topics in microbial risk assessment: Dynamic flow tree process. Risk Analysis 18:309-328.

Morales, R. A. and R. M. McDowell. 1998. Risk assessment and economic analysis for managing risks to human health from pathogenic microorganisms in the food supply.

Miller, A. J., R. C. Whiting, and J. L. Smith. 1997. Use of risk assessment to reduce listeriosis incidence. Food Technology 51(4):100-103.

NACMCF (National Advisory Committee on Microbiological Criteria for Foods). 1998. Principles of risk assessment for illnesses caused by foodborne biological agents. Journal of Food Protection 61:1071-1074.

Oscar, T. P. 1997. Use of computer simulation modeling to predict the microbiological safety of chicken. Proc. 32nd National Meeting Poultry Health Processing. Georgetown, DE.

Peeler, J. T., and V. K. Bunning. 1994. Hazard assessment of *Listeria monocytogenes* in the processing of bovine milk. Journal of Food Protection 57:689-697.

Rose, J. B., and C. P. Gerba. 1991. Use of risk assessment for development of microbial standards. Water Science and Technology 24(2):29-34.

Rose, J. B., and M. D. Sobsey. 1993. Quantitative risk assessment for viral contamination of shellfish and coastal waters. Journal of Food Protection 56:1043-1050.

Rose, J. B., C. N. Haas, and S. Regli. 1991. Risk assessment and control of waterborne giardiasis. American Journal of Public Health 81, 709-713.

Todd, E. C. D. 1996. Risk assessment of use of cracked eggs in Canada. International Journal of Food Microbiology 30:125-143.

Todd, E. C. D., and J. Harwig. 1996. Microbial risk analysis of food in Canada. Journal of Food Protection 59:1996 Suppl.10-18.

van der Logt, P. B., S. C. Hathaway, and D. J. Vose. 1997. Risk assessment model for human infection with the cestode *Taenia saginata*. Journal of Food Protection 60:1110-1119.

Vose, D. J. 1998. The application of quantitative risk assessment to microbial food safety. Journal of Food Protection 61:640-648.

Whiting, R. C. and R. L. Buchanan. 1992. Use of Predictive Modeling in a HACCP Program. Proceedings of the 2nd ASPET International Conference on Predictive Microbiology HACCP. p. 125-141.

Whiting, R. C., and R. L. Buchanan. 1994. IFT scientific status summary: Microbial modeling. Food Technology 44(6):113-120.

Whiting, R. C. and R. L. Buchanan. 1997. Development of a quantitative model for *Salmonella enteritidis* in pasteurized liquid egg. International Journal of Food Microbiology 36:111-125.

Zwitering, M. H., J. C. de Wit, and S. Notermans. 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.

Zwitering, M. H., and A. P. M. Hasting. 1997a. Modelling the hygienic processing of foods - A global process overview. Trans. Indus. Chem. Engin. 75:159-167.

Zwitering, M. H., and A. P. M. Hasting. 1997b. Modelling the hygienic processing of foods - Influence of individual process stages. Trans. Indus. Chem. Engin. 75:168-173.