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Risk Assessment Approaches to setting Thermal Processes in Food Manufacture

Report

ILSI Europe
International Life Sciences Institute

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RISK ASSESSMENT APPROACHES TO SETTING THERMAL PROCESSES IN FOOD MANUFACTURE

By David Bean, François Bourdichon, David Bresnahan, Andy Davies, Annemie Geeraerd, Tim Jackson, Jeanne-Marie Membré, Bizhan Pourkomailian, Philip Richardson, Mike Stringer, Mieke Uyttendaele and Marcel Zwietering

REPORT

COMMISSIONED BY THE ILSI EUROPE RISK ANALYSIS IN FOOD MICROBIOLOGY TASK FORCE

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1. INTRODUCTION AND BENEFITS

Thermal process technologies have been widely adopted commercially in food manufacturing throughout the world, and non-commercially in the domestic and catering sectors. The primary objective of such processes is to render foods safe from microorganisms likely to impair food safety or to cause spoilage, while retaining the good eating and nutritional qualities of the product.

Canning was one of the earliest forms of commercial food preservation to adopt the use of thermal processing and for many years the term "thermal processing" was synonymous in the food industry with canning. The key objective of canning, the heating of foods in hermetically-sealed containers, is to achieve commercial sterility – "the condition achieved by application of heat which renders food free from viable microorganisms, including those of known public health significance, capable of growing in the food at the temperatures at which the food is likely to be held during distribution and storage" (UK Department of Health, 2004).

Today, thermal processes are applied for a wide range of objectives working in concert with processes focussing on other product parameters, such as refrigeration, acidity, water activity and preservatives, to achieve product safety and stability. Such processes are applied to an extensive range of products in a wide range of packaging formats, e.g., metal cans, glass jars, pouches, plastic trays and cartons, and to products or their ingredients prior to packaging.

In many foods the sensory quality will be influenced by the metabolic activities of spoilage organisms, limiting the food's shelf-life. As a consequence, a thermal process may be applied for the destruction of not only microorganisms of public health concern, but also of those capable of growth and spoilage, and sometimes also to inactivate enzymes present in food.

The establishment of a thermal process is often a complex exercise, which must consider food composition, number and types of microorganisms present and anticipated storage conditions (CCFRA, 2008a). Process establishment should be conducted using worst-case conditions; thus, the issues associated with product, process and package must all be considered. For a comprehensive review of the factors considered in the development of thermal processes the reader is directed to Richardson (2001, 2004 & 2008). Details of the models used to calculate a thermal process are in the footnote[1].

In practice, the majority of thermal processes applied by industry include significant safety margins even beyond the safe margins developed by regulatory authorities ("safe harbour process"). These safety margins have been established to account for variability of a product, process or raw material, to address worst-case estimates developed where the information available – to assess initial microbial populations and (in the case of commercial sterility) to address both spoilage and pathogenic organisms – was limited. This precautionary approach has served the industry well; however, such processes often have a detrimental effect on product sensory quality.

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1. *The calculation of a thermal process from heat penetration data requires the use of three mathematical models. Each model may introduce an element of error in the calculated process value. The models are 1) the decimal reduction time (D value) – the time required at a constant heating temperature to reduce the number of organisms or spores by a factor of ten; 2) the kinetic value (or z value) which is a measure of the relative "killing power" of the heating temperature, and is the temperature difference required to effect a ten-fold change in the D value; 3) the integrated lethal rate, usually referred to as the F_0 value (or P-value) which is calculated by integrating the area between the curve obtained when lethal rates are plotted against time. Further details are provided in Appendix I.*

In recent years a number of research, food industry and regulatory investigators have examined the possibility of establishing thermal processes based on a more informed understanding of risk. The drivers of such an approach reflect the needs of both the consumer and the processor. For example:

- A less severe process may enable the production of a better quality product with enhanced texture, flavour and colour attributes.
- A milder process may be better for the retention of vitamins and other micronutrients or other active components in a food.
- Lower heat treatments may lead to increased throughput and possibly lower energy usage.
- Milder heat treatments may allow products not currently subjected to a thermal process to be treated by this technology.

The potential to challenge established processes has been increased by a more comprehensive understanding of the measurement and assessment of risks from food safety and spoilage organisms. This has benefited from a greater understanding of raw material and ingredient quality, growth and survival characteristics of microorganisms and the subsequent implications for manufacture, distribution and consumer use of foods. The use of a wide range of modelling techniques has provided powerful tools to aid this understanding.

Microbiological Risk Assessment (MRA) is a relatively new tool to assist in the production of safe food. It is comprised of four key elements: hazard identification, hazard characterisation, exposure assessment and risk characterisation. The overall aim is to ensure that the assessment of risk is based on a sound and objective use of scientific information. The use of MRA in food safety management was evaluated in an expert workshop hosted by ILSI (Lammerding,2007); in particular, the ways in which both government and industry can utilise the tools were evaluated using both qualitative and quantitative techniques.

The concept of Food Safety Objectives (FSOs) has been introduced to facilitate the application of meaningful food safety management practice to the interpretation of public health goals – often described as an Appropriate Level Of Protection (ALOP). ICMSF (2002) defined the FSO as "the maximum frequency and/or concentration of a microbiological hazard in a food at the time of consumption that provides the appropriate level of health protection". The output of an ILSI-Europe Workshop to explore the impact of food safety objectives on microbiological food safety management has been published (Stringer, 2005).

The current report reviews the application of risk-based concepts and risk management techniques to the establishment of process criteria for thermal processes in food manufacture and for the determination of processing parameters to meet these criteria. Such tools may be used to develop and assess alternatives to established criteria or to develop criteria where no established criteria exist.

A historical background for "safe harbour processes" is provided and a conceptual framework, which enables the consideration of multiple factors in the food chain in the development of process criteria, is presented. Approaches to microbiological modelling are discussed that can provide greater precision in the estimation of microbial lethality, potentially enabling a reconsideration of process parameters. Finally, strategies are presented to evaluate effectively, and to reduce the reliance on, safety factors and conservative calculations in the establishment of thermal processes.

2. A HISTORICAL REVIEW OF SOME SAFE HARBOUR PROCESSES

Safe harbours are generally recognised processes and process criteria that have been established over time by consensus or by regulation. The primary advantage of safe harbours is that they can be readily used by anyone to design a heat treatment process without the need for extensive information about a food's characteristics or prior knowledge of the initial microbial level. If the heat treatment process complies with these safe harbours, the processed food products are generally recognised as safe. Examples of currently accepted safe harbours are provided in Table 2.1. This chapter explores the development of a number of these processes.

Table 2.1: An overview of acknowledged safe harbours for pathogens in defined food products

Target-organism / commodity and/or process	Process Parameters / Process Criteria	Reference
Salmonella		
Comminuted fish Stuffed fish or stuffing containing fish Other raw fish	68°C (155°F) for 15 s 74°C (165°F) for 15 s 63°C (145°F) for 15 s	NACMCF (2007)
Ready to Eat (RTE) cooked beef products RTE cooked poultry products	6.5-log reduction (internal temperature of 62.8°C) 7-log reduction	IOM NRC (2003) ICMSF (2002)
Liquid whole eggs	60°C (140°F) for 3.5 min (8.75-log reduction)	NACMCF (2006)
In shell pasteurisation of eggs	5-log reduction	NACMCF (2006)
Salmonella and *E. coli* O157:H7		
Fruit juice pasteurisation	5-log reduction	NACMCF (2006)
Clostridium botulinum		
Low acid canned food	12-log reduction or probability of a viable spore being present < 10^{-9} per can (a can = 1kg) (if No = 1 g^{-1})	ICMSF (2002) IOM NRC (2003)
Non-proteolytic *C. botulinum*		
Cooked chilled foods	6-log reduction 10 min. at 90°C or equivalent lethality (e.g., 80°C for 129 min. or 85°C for 36 min.) combined with storage at chill temperature	Peck *et al.* (2006) ICMSF (2002)
L. monocytogenes		
RTE cooked fish and seafoods	6-log reduction 2 min at 70°C	NACMCF (2007) ICMSF(2002)
Milk pasteurisation	6-log reduction	Farber *et al.* (1988)
Coxiella burnetti		
Milk pasteurisation	5-log reduction 30 min at 63°C or 15 sec at 72°C	IOM NRC (2003)

2.1 The 12-log botulinum cook

Bacillus botulinus (the original name of *Clostridium botulinum*) was first recognised and isolated in 1897 by Emile van Ergmengem (van Ergmengem, 1897). Spores of mesophilic strains of *C. botulinum* were identified to be the most heat-resistant form of pathogenic organisms in low-acid, ambient-stable canned products.

CCFRA 2008b, have reviewed the history of the miminum botulinum cook for low-acid canned foods and report that the origin of the F_0 3 process relates to thermal death kinetic work carried out by a number of researchers between approximately 1921 and 1950.

The concept of a sterilising value (F_0-value) was developed by Ball (1927) and is usually expressed in minutes at 121.1°C (250°F) necessary to destroy a target microorganism. Starting from the original work by Esty and Meyer (1922) and Bigelow (1921) through subsequent analysis by Townsend *et al*. (1938) and finally by Stumbo, after 1965, the F_0 3 (minutes) minimum "*botulinum* cook" was established and is used widely today for low-acid canned foods. Stumbo calculated the time to achieve a 12-log reduction for *C. botulinum* spores from the decimal reduction time at 121.1°C ($D_{121.1}$ value) of 0.21 minutes as equivalent to 2.52 minutes or an F_0-value of 2.52.

In the calculation of an F-value, the population of *C. botulinum* is considered to be contained in an undefined unit volume or mass, which may be 1 ml, 1 g or the volume of a container. The establishment of a 12-log cook implies that a probability of survival of not more than 1 in 10^{12} containers (or another unit) is regarded as acceptable.

Considering an initial load of 100 (i.e., 10^2) spores per container and $D_{121.1}$ of 0.21 minutes for the most resistant spores of *C. botulinum*, the F value required to achieve a 10^{-12} final number of surviving spores is 0.21 (2+12) = 2.94 minutes. Based on these requirements, the F_0 of 2.94 is rounded up to 3 minutes, hence the F_0 3 minutes process. This approach is described by the U.K. Department of Health (Department of Health, 2004). Interestingly, it actually equates to a total 14-log reduction in *C. botulinum* spores.

Many sterilisation treatments are designed to achieve a considerably higher process than F_0 of 3 minutes in order to inactivate spoilage organisms, some of which have higher heat resistances than *C. botulinum* spores (Table 2.2). For example, very heat-resistant spores of strains of thermophilic *Geobacillus stearothermophilus* will be inactivated by less than a factor 10 (<1-*D*) at F_0 3. As a result, F_0-values much higher than F_0 3 are often used commercially, often in the 6-10 minute range to account not only for heat-resistant spoilage organisms but also for process variability.

Table 2.2: D-value ranges of assorted spore-forming bacteria (CCFRA, 2007)

Microorganism	D-value (minutes at 121.1°C)
Geobacillus stearothermophilus	4.0 - 5.0
Clostridium thermosaccharolyticum	3.0 - 4.0
Desulfotomaculum nigrificans	2.0 - 3.0
Clostridium botulinum (proteolytic)	0.1 - 0.23
Clostridium sporogenes	0.1 - 1.5
Bacillus coagulans	0.01 - 0.07

In ambient-stable, high-acid (pH ≤ 4.5 or 4.6; depending on region) food, lower F_0-values can be applied because the product pH is below the minimum pH for germination and outgrowth of proteolytic *C. botulinum* (pH 4.5-4.6). The acidic pH, coupled in some cases with additional activity from the acidulant (organic acids mostly), also provides a hurdle against many of the spore-forming spoilage organisms. Thus the applied F_0-value might be considerably lower than 3 for these high-acid food products.

2.2 Heat processing in the dairy industry

Initially developed by Louis Pasteur in the middle of the 19th century for the preservation of wine, pasteurisation has been applied to milk and other foods and beverages to inactivate relevant pathogens and reduce overall microbial levels to prolong shelf-life.

At the beginning of the 20th century, tuberculosis and brucellosis were diseases of major concern transmitted by milk. Initially, *Mycobacterium tuberculosis* was considered to be the most heat-resistant pathogen associated with milk (Hammer, 1948); however, by 1956, *Coxiella burnettii* was shown to be more heat-resistant than *M. tuberculosis* and minimum pasteurisation time and temperature combinations were established by regulators in the US to ensure destruction of *C. burnetti* in milk. The highest level of *C. burnetti* that had been detected in milk of infected cows was determined to be 10,000 infective guinea pig doses. The goal for minimal pasteurisation conditions was to provide an additional 10-fold "margin of safety" and seek a destruction of 100,000 infective guinea pig doses (equivalent to a 6-log reduction) (Enright *et al.*, 1957).

Since the recognition of *Listeria monocytogenes* as a foodborne pathogen in the late 1980s, it has been a primary focus in the dairy industry. Raw whole milk inoculated with 10^5 cfu/ml of *L. monocytogenes* thermally processed at 60-72°C for a minimum holding time of 16.2 s showed survival of this pathogen at temperatures up to 67.5°C. But an overall recognised pasteurisation treatment of raw milk for 15 s at 75°C would result in elimination (6-*D* reduction) of *L. monocytogenes* (Farber *et al.* 1988). Extensive investigations have been conducted on the heat resistance of the organism in many other foods. In homogenates of chicken, beef steak and carrot, *D*-values at 70 °C ranged from 0.14 to 0.27 min (Gaze *et al.*, 1989.). *L. monocytogenes* is now considered to be the most heat-resistant vegetative pathogenic bacterium in high water activity foods excluding milk and, as such, is regarded as the target organism in setting performance objectives in thermal processing. The current consensus is that the *D*-value of *L. monocytogenes* at 72°C does not exceed 15 s in foods. This means that the pasteurisation of cooked chilled foods, for a minimum of 2 min at 72°C would result in at least an 8-log reduction of the organism (Mossel & Struijk, 1991). To address variability in microbial populations as well as in the application of thermal processes, some processors apply time and temperature combinations that are above the minimum requirements.

2.3 Heat processing in the meat and poultry industries

Salmonella spp. was identified by a US Food Safety and Inspection Service risk assessment as the pathogen of concern for their Lethality Performance Standards for meat and poultry products (USFSIS, 1998). The standards define an objective of a 7-log reduction of *Salmonella* in Ready-to-Eat (RTE) poultry products and a 6.5-log reduction of *Salmonella* in RTE beef products. The rationale for these performance standards was based upon i) the establishment of a worst-case population of *Salmonella* spp. by animal species, considering baseline survey levels and probability distributions, and ii) the probability of survival of *Salmonella* spp. in 100 g of finished product after the specific lethality processes were calculated. For poultry products a worst-case level of 37,500 *Salmonella* g^{-1} was calculated based on data from baseline surveys in the poultry industry.

In a serving size of 143g of raw product (assuming a serving size of 100g of the cooked product) there would be approximately 5,362,500 (6.7-$\log_{10}$) *Salmonella* spp. A 7-log reduction of *Salmonella* is therefore considered sufficient to obtain the acceptable level of protection with some safety margin. Likewise 6.2 $\log_{10}$ was determined to be the worst-case level for beef products, and 6.5-log lethality was determined to provide an acceptable level of protection.

The assumptions behind these standards are now being debated in light of many regulatory changes at the start of the 21st century concerning the management of the safety of the whole food chain, (e.g., the introduction of a General Food Law[2] in the EU, re-organisation of several national food agencies, etc.), which have shifted the focus from end-product control to a preventive approach including a greater effort on improvements in hygiene and application of HACCP principles by the meat and poultry processing industries.

2. *The General Food Law is EU requirement and refers to EC Regulation 178/2002 = Regulation (EC) n° 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety.*

3. BEYOND SAFE HARBOUR PROCESSES

As outlined in the previous chapter many safe harbour processes have a long history and were determined based on the expertise available at the time they were established. They were derived from expert opinions based upon the best understanding of the physiology and ecology of the target organisms at the time, and often with limited information available on initial populations. Because they were intended to address microbiological hazards in all situations, safe harbours neglected the food matrix and tended to be conservative.

Some safe harbour processes were based on the outcome of deterministic models using the mean values of parameters linked to target organisms' growth and survival characteristics and incorporating simplified thermal inactivation kinetics. The models assume thermal processing to be the sole intervention for assuring product safety and often do not take into account the effect of control measures in the food chain before and after thermal processing, or additional hurdles intrinsic to the product. Moreover, a safety factor of sufficient magnitude was built in to ensure that any current or future process variation would be of no public health significance. As such they often provide a "fail-safe" approach.

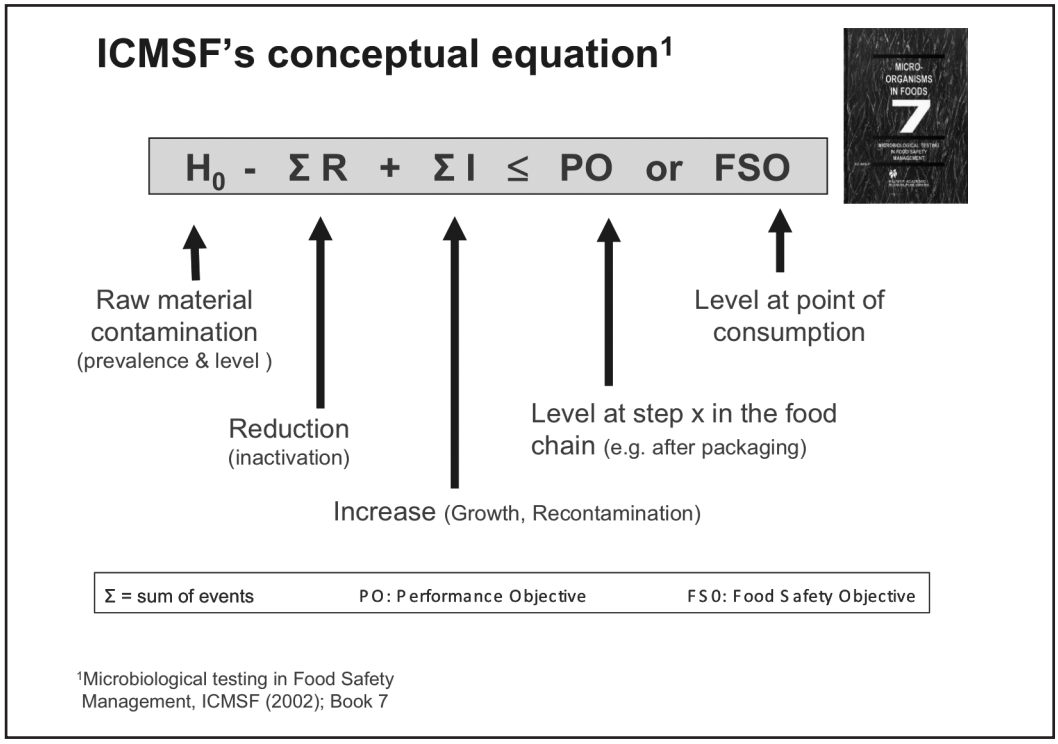
3.1 Revisiting safe harbour processes in the new safety management context

Examples of safe harbour processes with significant safety margins are those designed to achieve a 12-log reduction of proteolytic *C. botulinum* in low-acid canned food, or a 5-log reduction of *E. coli* in orange juice. However, where the initial population of the target organism is much lower than assumed, or the variability of the process can be minimised, the impact of safe harbour processes may be significantly greater than that necessary to address safety or stability objectives. This means that, in order to reduce safe harbour processes, it is necessary to have very accurate information about many factors, such as initial populations.

In practice, the application of a thermal process is only one of a variety of factors that must be controlled during a process to produce a product of the required safety and stability. Products that have received an adequate thermal process can still become a safety or stability risk if pathogenic or spoilage organisms are introduced into the product after processing. It is through an understanding and control of all factors contributing to food safety that safe harbours can be challenged and more precise thermal processes applied.

This concept can be illustrated with full chain Quantitative Microbiological Risk Assessments (QMRA), in which all factors affecting the safety objective, including the effect of thermal processing, are described. Although useful, full quantitative risk assessments are very labour and data intensive and would only be carried out to address complex or significant issues. Therefore, the International Commission on Microbiological Specifications in Foods (ICMSF) has proposed a more streamlined approach that can easily be applied to a specific process or product (Figure 3.1; ICMSF, 2002; Zwietering, 2005).

Figure 3.1: Schematic representation of new food safety management metrics proposed by ICMSF and adopted by Codex Alimentarius.



In the ICMSF equation, the initial contamination (H_0, $\log_{10}$ of concentration) minus the sum of all the inactivation (ΣR, in log reductions) plus the sum of all the occurrences of growth and/or recontamination (ΣI, in log increase) should be lower than a set Performance Objective (PO) or Food Safety Objective (FSO).

The FSO is related to a certain Appropriate Level of Protection (ALOP) and is usually established by regulators. It applies to the maximum level of the hazard considered acceptable at the point of consumption. Food processors may use this equation in order to achieve a stated FSO or, where no FSO exists, to achieve a PO identified in the HACCP study. Recently, Anderson *et al.* (2011) have built on the ICMSF risk management framework to explain how *C. botulinum* growth and toxin production may be controlled in commercially sterile foods. In such a case, by definition, growth of *C. botulinum* is unacceptable and then the term ΣI corresponds only to growth inhibition (i.e. ΣI is either null or there can even be inactivation).

This approach can be also subdivided over different parts of a food chain, where for every stage a PO is set.

$$H_0 - \Sigma R + \Sigma I < PO1$$

$$PO1 - \Sigma R + \Sigma I < PO2$$

$$PO2 - \Sigma R + \Sigma I < FSO$$

For every stage of the food chain, the initial microbial level, inactivation, growth and recontamination are managed to achieve an identified PO. In this manner the inactivation required by the thermal process developed is put into the context of other factors contributing to the PO. By understanding and adapting relevant factors in the equation, the processor has flexibility in management options to achieve the same objective (see Table 3.1).

Table 3.1: Equivalent processes with various target reductions

H_0	ΣR	ΣI	FSO/PO
2	6	2	-2
2	4	0	-2
0	2	0	-2
-2	0	0	-2

It can be seen that an equivalent level of safety can be reached by applying a severe heat treatment (reduction) in combination with a relatively high initial level or increase (growth or recontamination; or a combination of the two) (Table 3.1, line 1), or a less severe heat treatment where growth can be prevented (Table 3.1, line 2) or low initial levels can be assured (Table 3.1, lines 3 and 4). The severity of the heat treatment can thus be balanced against the level of control in the other parts of the process, or even the level of control in preceding or subsequent steps in the food processing chain.

Determination of initial levels, reductions to be achieved, potential growth that can occur, etc. must be based on solid information. Such data can be obtained from literature, databases, predictive models, surveys and experiments. The strongest determinations combine information from several of these sources. Microbiological analysis of raw materials, at different process steps or finished product may be used to verify that the process is operating as needed to achieve the PO.

3.2 Additional considerations while moving beyond current safe harbours

Alternatives to safe harbours can only be considered when it can be demonstrated that less severe processes provide an acceptable level of public health protection. Laboratory and field studies can be used where knowledge gaps exist, and QMRA techniques can be used to evaluate the safety impact of alternative processes.

Efforts to compare the public health protection of "minimal" thermal processing to that of safe harbours often focus solely on the thermal processing step itself. In contrast to the deterministic calculations used to establish many of the current safe harbours, QMRA may show the level of protection obtained using probabilistic modelling including any currently available expanded datasets representing the thermal inactivation kinetics of the target organism, advanced modelling procedures, heat transfer properties of the particular food, etc. It is clear that in a probabilistic approach the outcome of a QMRA is also a probability distribution and for that reason a zero risk is not achievable. Similarly, QMRA is not able to allocate a zero risk outcome for current safe harbours which are acknowledged to deliver safe foods.

In many cases the actual level of protection provided by a safe harbour is unclear. This makes it difficult to set the target for an alternative thermal process based upon equivalence. Apart from the 12-log *botulinum* cook, 5-log or 6-log reductions are often accepted as a "reference value" in food safety management (Gould, 1999). In contrast, the benchmark of ~ 10^{-4} is often used as the target for acceptable levels of enteric pathogens in drinking water, i.e., one infection or less per 10,000 people per year as defined by the US Environmental Protection Agency (Stine *et al.*, 2005; Hamilton *et al.*, 2006).

As illustrated in Table 3.1, the application of a less severe thermal process may be possible while achieving the same performance objective. Some points to consider in this approach are described below:

- Control and monitoring of initial contamination level (H_o) may be achieved through supplier selection and management, selection of raw materials and ingredients capable of meeting established criteria, or the use of raw materials that have been previously subjected to a bacteriocidal or bacteriostatic process.
- Growth of the target organism (ΣI) may be reduced through product formulation by including barriers/hurdles such as high salt, organic acids, modified atmosphere packaging and temperature control during the storage and distribution of perishable foods.
- Recontamination by the target organism after processing (ΣI) may be prevented through effective design and management of the post process environment, and of filling and packaging operations.
- The safety margins built into the existing thermal process necessary to achieve ΣR may be challenged through a more precise estimate of microbial lethality through greater control of process parameters or through accounting for a greater proportion of the lethality in a process.
- The heat treatment injury effect on spores could be taken into account in estimating the reduction of the microbial infective load: in addition to the lethal effect of the heat treatment (included in ΣR calculation), some viable spores remaining after the heat treatment may be injured. Due to this injury, the time for spores to recover and germinate is prolonged and the length of the lag time is increased (Peck *et al.*, 1995; Peck, 1997). As for growth kinetics, the prolongation of lag time can be determined by the stress conditions provided by the food (pH, water activity, storage temperature). By incorporating this growth inhibition (ΣI = 0) in the ICMSF equation along with the inactivation effect (ΣR > 0), it may be possible to identify a milder heat treatment leading to the same Performance Objective. For instance in the application developed by Membré *et al*. (2009) with non-proteolytic *C. botulinum* in Refrigerated Processed Foods of Extended Durability (REPFED), it was shown that a thermal process of 88°C for 10 min in a product at pH 6.3 is equivalent to a thermal process of 85°C for 10 min in a product at pH 6.0

3.3 Examples of safe harbours set using risk-based metrics

Below are three examples of studies in which safe harbour values were challenged or set using the risk-based metrics proposed by the ICMSF.

Example 1: 4.4-log reduction of E. coli O157 in frozen raw ground beef patties (ICMSF, 2002).

The United Kingdom Advisory Committee on the Microbial Safety of Food (ACMSF, 2007) recommended a "safe harbour" process criterion of 70°C for 2-min to achieve a 6-*D* reduction of *E. coli* O157:H7, *Salmonella* spp. and *L. monocytogenes* in meat products.

The ICMSF experts deduced the required log reduction from calculations split into three steps: hazard identification, exposure assessment and hazard characterisation, providing information for H_0, ΣI and PO, respectively.

Hazard identification: *E. coli* O157:H7 was identified as the hazard as it was linked to foodborne illness outbreaks and sporadic cases of foodborne illness due to the consumption of undercooked minced beef.

Exposure assessment: From a literature review, the authors concluded that a very small proportion of all the lots of ground beef contain *E. coli* O157:H7 (prevalence 5%). The authors also assumed that contaminated lots have a range in concentration (e.g., 1-1000 cfu g^{-1}). From this analysis and since *E. coli* O157:H7 was present on only a few carcasses, the authors concluded that the concentration of *E. coli* O157:H7 in trimmings would not likely exceed 100 cfu g^{-1} and this was taken as a "worst case" estimate for the initial level in minced beef burgers (H_0=2).

E. coli O157:H7 is unable to grow at temperatures below 7°C. Once carcasses are chilled, levels of the organism will not increase during fabrication, storage or distribution provided the product is maintained under refrigeration; therefore, provided these conditions are effectively controlled, $\Sigma I = 0$. A serving size was assumed to be two burgers weighing 125 g each, a common weight for commercially manufactured ground beef patties.

Hazard characterisation: Epidemiological data from outbreaks and risk estimates indicate that illness can result from the consumption of less than 100 cells, and as low as a dozen cells, particularly in more susceptible consumers. The determination of a PO from these data needed to be sufficiently conservative to reflect the degree of uncertainty, the relatively low infective dose and the severity of illness. Consequently the PO was chosen as less than one cell in a serving size (PO = -2.4).

Once the PO, H_0 and ΣI were determined, ΣR could be calculated: as

$$2+0-\Sigma R = -2.4, \text{ then: } 2 + 0 + 2.4 = \Sigma R = 4.4.$$

Therefore a minimum $\log_{10}$ reduction of 4.4 is needed during cooking of the ground beef patties in order to achieve the PO. In this example, uncertainty was accounted for by using worst-case data.

Example 2: 5-log reduction of L. monocytogenes in shrimp (Walls, 2005)

A 6-log reduction is a generally accepted safe harbour in the production of RTE (cooked) fish and seafoods (NACMCF, 2008; see also Section 2). The objective is to achieve absence per 25 g, or per extendion, absence per 100 g in the RTE products.

To determine an alternative to this safe harbour, the required information was provided by hazard identification, an exposure assessment and a hazard characterisation:

Hazard identification: *L. monocytogenes* is a pathogen, which is widespread throughout the environment and is likely to be present in raw shrimp.

Exposure assessment: From survey data analysis, the authors concluded that the concentration of *L. monocytogenes* in raw shrimp was less than 100 cfu g^{-1}, and chose an H_0 value of 2.

Considering that the shrimp was frozen, they also assumed that there was no increase in the level of the organism during cooling, packaging, distribution and retail. Moreover, if the consumer buys frozen shrimp, thaws them properly and eats them promptly there should be no net increase during consumer handling; therefore, it was concluded that $\Sigma I = 0$. Note that if shrimp were displayed at retail under refrigeration or if there was a potential for temperature abuse during consumer handling, ΣI would need to be set at a higher value. The average serving size of shrimp was assumed to be 100 g, corresponding to 5 to 10 shrimps.

Hazard characterisation: In this study, *L. monocytogenes* was considered as a sufficiently severe hazard to define a PO as 'less than 1 cfu in a serving size', i.e.,

$$PO = -2.$$

Note that in the EU and other countries, if it can be demonstrated that the RTE product does not support growth of *L. monocytogenes* throughout the shelf-life, levels up to 100 cfu g^{-1} (and thus PO = 2) may be tolerated at the final day of its stated shelf-life or time of consumption (EC Regulation 2073/2005 = European Commission Regulation (EC) No. 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs).

The required log reduction, ΣR, was calculated as $2 + 0 + 2 = 4$. Assuming uncertainty and variability in the calculations, for instance due to seasonal variations or differences in heat resistance of the bacteria, the authors added a 1-log safety margin and the final log reduction was chosen as $\Sigma R = 5$.

Example 3: Salmonella in pasteurised frozen foods (Membré et al., 2007)

The UK ACMSF defines a safe harbour of 70°C for 2 min to achieve 6-*D* reductions of *E. coli* O157:H7, *Salmonella* spp. and *L. monocytogenes* in meat products.

This study also used a risk assessment approach to determine the reduction necessary to achieve the equivalent level of protection to this safe harbour taking into account other aspects of the product and process (Figure 3.1). The necessary reduction was determined with the following process:

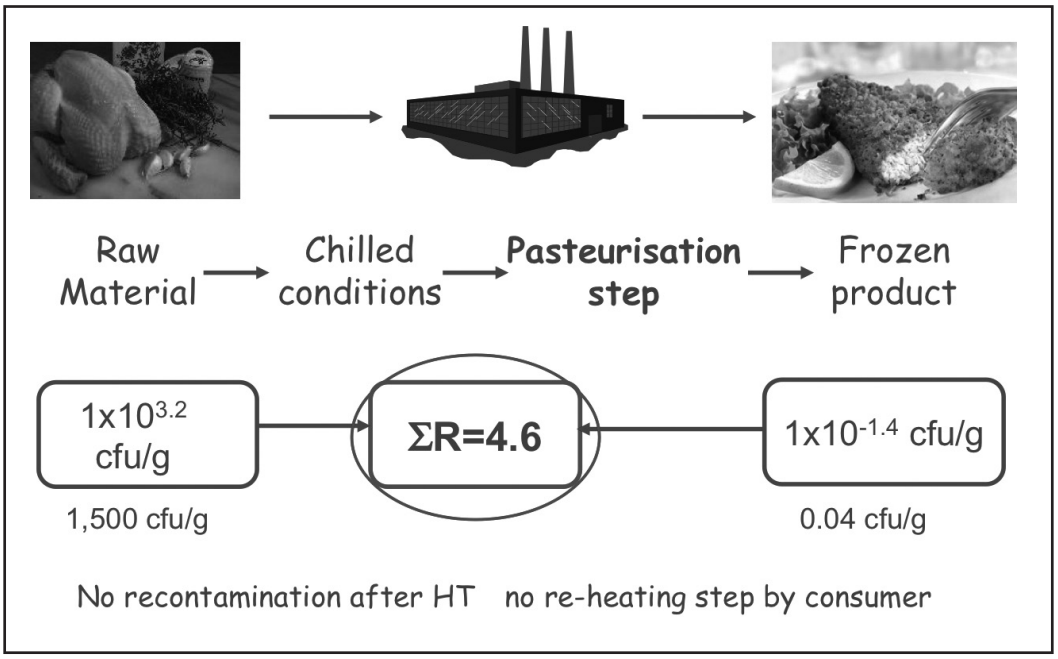
Hazard identification: *Salmonella* was identified as the foodborne hazard of concern.

Exposure assessment: H_0 was determined from a literature review. Two possibilities for H_o were explored i) a worst-case level of 1500 cfu g^{-1}, and ii) a distribution of values reported in literature: 1 cfu g^{-1} as a minimum, 10 as the most likely value, 1500 as the maximum. In addition, two prevalence rates were explored: 100% (worst-case) or 5.7%, based on a survey reported by the Food Standards Agency (2001).

During manufacturing, the cooked chicken is rapidly frozen and remains frozen during the subsequent process, storage and distribution up to the point of consumer use. If effective separation of cooked and raw processes and effective employee- practices are in place at the manufacturer, no recontamination will occur. As a result, $\Sigma I = 0$.

Hazard characterisation: the UK's Public Health Laboratory Service (PHLS) guidelines state that an RTE food is deemed unacceptable and potentially hazardous if any *Salmonella* spp. are detected in 25g of food: PO was chosen as -1.4.

Figure 3.2: Schematic representation of the inputs included in setting ΣR.



The safe harbour was deduced from these three inputs by addition and subtraction of the figures (Figure 3.2). Using the worst-case scenario and thus raw chicken contamination H_0 = 3.18 based on the log (1500 cfu g^{-1}) (100% prevalence), the performance criterion is defined as 3.18 + 0 + 1.4 = 4.58.

For the second analysis, calculation of heat treatment knowing the required performance criterion (log-reduction), several approaches were described, some simple and some more complex ones (due to probabilistic distributions), but all of them in the same order of magnitude: at 70 °C, the required heat treatment time was estimated around 0.3-0.4 min. However, the authors reported that the heat treatment time estimated by this 'ICMSF method' would not achieve the FSO with 100% probability. For example, they determined that with 5.7% of raw chicken initially contaminated, a heat treatment of 70 °C for 0.3 min leads to a probability to meet the FSO "1 in 25g" of 99.9%.

To assess whether 99.9%, or another value, is acceptable, the authors suggested that, when an FSO is provided by the food authorities, it should be associated with the probability of compliance (e.g., "FSO of 1 in 25 g obtained with a probability of 99.9%").

3.4 Validation of risk based assessment

Validation has been defined as "obtaining evidence that a control measure or combination of control measures, if properly implemented, is capable of controlling the hazard to a specified outcome" (CAC/RCP-1, 1969). It is essential that any new or alternative approach to setting a thermal process can be validated. Effective validation is an important component of HACCP, to ensure that appropriate food safety outcomes are defined and that control measures and related limits, monitoring and verification activities are sufficient to achieve these outcomes (Kirby, 1999). Likewise, as thermal processes are established or safe harbours challenged, sufficient evidence is needed to gain acceptance of the process by regulatory authorities as equivalent to the safe harbour and able to provide safe product.

The Codex Alimentarius Commission has provided guidance on the steps in the validation of food safety control measures and approaches to obtaining the data needed in this evaluation (CAC/GL 69-2008, 2008). The ICMSF conceptual framework and risk assessment approaches presented in this ILSI report can support these approaches by providing or contributing to the evidence necessary to validate the objectives and limits of thermal processes.

Where predictive modelling approaches and other assumptions are used in process determination, evidence may be needed to validate the methods by confirming that the outcomes are reflective of the process or food system in practice.

4. THERMAL PROCESSING AND FOOD SUPPLY CHAIN

The previous section introduced the use of the ICMSF conceptual equation (Figure 3.1) to determine the ΣR required during a process. In practice the reduction that is possible at a particular step in the process may be limited due to operational or sensory considerations. In such cases, control at other steps in the food chain may be necessary in order to manage H_0 or ΣI and to ensure that the PO or FSO can be met. Controls at the processor or at the raw material supplier often have direct influence on these parameters; however, in many cases, management of conditions in the supply chain are critical for their control.

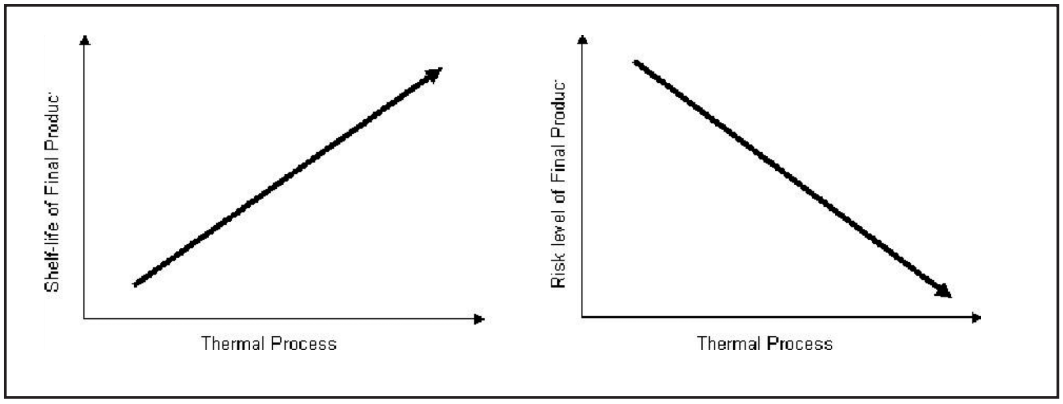
The food supply chain incorporates activities at each step where the food is stored or prepared or handled, as well as the transfer from one location to the next. In this report the supply chain refers to the entire pathway taken by the raw material from the field on the farm to the consumer via retail or catering (farm to fork). Some of the supply chain stages are:

- Growth and harvest
- Storage at primary production
- Transport to processing site
- Storage at processing site
- Transport to retail or catering
- Processing at catering
- Storage at retail or catering
- Consumer purchase transport and storage,

ΣI may be controlled throughout the supply chain both by maintaining hygienic conditions to prevent increases due to cross-contamination, and by maintaining time and temperature conditions during processing, storage and distribution to prevent or limit increases in microbial populations. Time and temperature conditions in the supply chain are critical to the shelf-life of perishable products or materials; their importance may be affected by product composition as well as by reductions achieved during thermal processes applied at earlier or later stages of the process.

The management of time and temperature in the supply chain is in effect managing risk. Thermal processing that targets pathogen reduction reduces the risk associated with the product. Within the supply chain, it must be assured that this risk does not increase to a level potentially reducing the effectiveness of control measures or to a level that could have a direct impact on consumer safety. When assessing the interaction between the thermal process, risk and shelf-life, it must be noted that for an increased shelf-life a more severe thermal process is necessary (shifting from pasteurisation to sterilisation) and to decrease risks also a more severe treatment is required (Figure 4.1).

Figure 4.1: Simplified relationship between shelf-life and risk level of product relative to the thermal process it receives.



These risk management processes can be better illustrated through the following example, where several scenarios are discussed to demonstrate various aspects of risk assessment and risk management in the supply-chain.

Raw food products may often naturally contain a variety of pathogenic microorganisms and as a result are considered to be high risk without further processing. Thermal processes may be applied as a control measure to reduce this risk level, consistent with the heat sensitivity of the micro-organisms of concern and their levels prior to processing. Such processing may be applied to inactivate all such microorganisms present or to reduce them to an acceptable level. In the latter case, if pathogens are present and able to grow in the product matrix, management of storage and handling conditions after thermal processing (i.e., maintenance under chilled or frozen conditions) may be necessary to prevent an increase in the risk level. Consider raw minced beef. This product has been reported to contain up to 10^3 g^{-1} *E. coli* O157:H7 (Todd *et al.*, 1988) and in certain cases up to $2x10^3$ g^{-1} *L. monocytogenes* (Comi *et al.*, 1992). Consumption of this product in its raw state would almost certainly lead to many cases of disease from both pathogens.

As such, this is a high-risk product to all consumers. Thermal processing to reduce *E. coli* O157:H7 by 6-logs would significantly reduce the risk from the presence of the organism, but due to a greater heat resistance, would only reduce *L. monocytogenes* by 2-log. At the higher initial levels reported by Comi *et al.* (1992) 1.3-log g^{-1} of viable *L. monocytogenes* may still be present in the cooked minced beef. As a result, the risk to all consumers from *E. coli* O157:H7 has been addressed, while there remains some risk for the young and elderly due to the presence of *L. monocytogenes*, particularly if storage conditions enable *L. monocytogenes* levels to increase. For the cooked minced beef to be a low risk for both pathogens, the thermal process would need to be sufficient to inactivate expected levels of *L. monocytogenes*. Under the following scenarios, the supply chain may need to be managed differently in order to effectively to manage risk to acceptable levels. There are two options open; one is to maintain the risk level and the other to allow it to increase, but not beyond an unacceptable level. For a hypothetical scenario the acceptable risks may be set as 1 g^{-1} *E. coli* O157:H7 and 100 g^{-1} *L. monocytogenes* (i.e. PO = 0 or 2 respectively).

Unprocessed (e.g.) raw meat:

- Handling at ambient temperature (15-35°C) – the pathogens will grow rapidly and the risk to the consumer increases, as a higher dose would be received on consumption if consumed raw; more stringent cooking would be needed to inactivate the high levels present sufficiently.

- Handling chilled (1-4°C) – *E. coli* O157:H7 would not grow, but *L. monocytogenes* would, albeit at a slow rate, and the risk to some consumers will increase as a higher dose would be received on consumption.
- Handling deep frozen (below -18°C) – Both pathogens stop growing and hence the risk remains at the same level.

Processed to reduce *E. coli* O157:H7 by 6-logs:

- Handling at ambient temperature (15-35°C) – the potentially surviving pathogens will grow rapidly from a lower concentration than unprocessed. The product is low risk for *E. coli* O157:H7 as viable organisms are unlikely to be present. If high levels of *L. monocytogenes* were present prior to heat treatment, a proportion of the population may survive, which could grow during storage to an unacceptable level. Therefore, the supply chain has to be managed to minimise the time at this temperature range.
- Handling chilled (1-4°C) – *E. coli* O157:H7, if present, would not grow but *L. monocytogenes* will continue, albeit at a slow rate. In a similar means to the previous example, in time *L. monocytogenes* may increase and reach an unacceptable level. Therefore, the supply chain has to be managed to ensure that the time the product is exposed to this temperature does not allow *L. monocytogenes* to increase to unsafe levels.
- Handling deep frozen (below 18°C) – Both remaining pathogens stop growing and hence the risk remains at the same level.

Commercially sterilised:

- After such a treatment one can assume the packaged product to be free from pathogens. Therefore, the time and temperature requirements for handling do not exist with regards to food safety, only quality.

Practical considerations often influence the options available for supply chain controls. For example, costs or sensory considerations associated with storage temperatures (ambient, chilled, frozen) and transport time.

5. QUANTIFICATION OF MICROBIAL INACTIVATION

Previous sections have discussed approaches to challenging safe harbour process criteria through assessment of required ΣR based on other factors in the process and supply chain. Where safe harbour processes have been prescribed to achieve a required ΣR, they are often conservative due to limitations in the data available on the behaviour of a target pathogen or due to the use of overly simplistic estimates of microbial destruction during the process. Mathematical modelling of microbial inactivation may help to provide a more accurate picture of what is happening during the process, enabling the establishment of more accurate and possibly less conservative thermal process parameters that more precisely meet the required ΣR.

For illustrative purposes, assessment of modelling approaches in this section will be based on the following (simplified) assumptions: all experimental data come from a carefully designed and carefully sampled challenge test, where one specific microbial species is added to a chosen food (model) system under study and subsequently subjected to a chosen relevant time-temperature profile (see Appendix I for details on these assumptions).

To determine the inactivation achieved during such challenge tests, one needs to evaluate changes in numbers of microbial pathogens or spoilage microorganisms as a function of time, using so-called primary models. Additionally, one needs to evaluate the effects of various food product and environmental variables (such as temperature, water activity (a_w), pH, fat content, etc.) that can influence the inactivation rate. The effects of these variables on the inactivation rate can be described by so-called secondary models. In combination with a (possibly time-varying) temperature profile, these primary and secondary models can be used to predict inactivation based upon the experimental dataset. To be practical for every application, realistic values are necessary for each of the model parameters. The current section presents modelling approaches appropriate for practical applications, and more complex approaches currently more suited for experimental studies.

5.1 Primary models describing the time-dependent course of microbial inactivation

The basic model used to describe bacterial inactivation is the first order model (Rahn, 1945; cited in Pflug and Holcomb, 1977), in which it is assumed that the rate of change (or derivative) of microbial numbers with respect to time (with d*N* the change in bacterial numbers N in an infinitesimal small change in time d*t*) relates linearly with the actual level of microbial numbers:

$$\frac{\mathrm{d}N}{\mathrm{d}t} = -\mathrm{k}N \qquad (1)$$

Here, the derivative will be negative because the microbial numbers decrease with time. This model contains only one parameter, *k*, the specific inactivation rate (with units time^{-1}, and "specific" indicating that it is the inactivation rate we obtain by dividing d*N*/d*t* by *N*, so the inactivation rate per unit of microbial number).

At constant (temperature) conditions, *k* does not change over time and this differential equation can be solved as:

$$N = N_0 \exp(-kt)$$

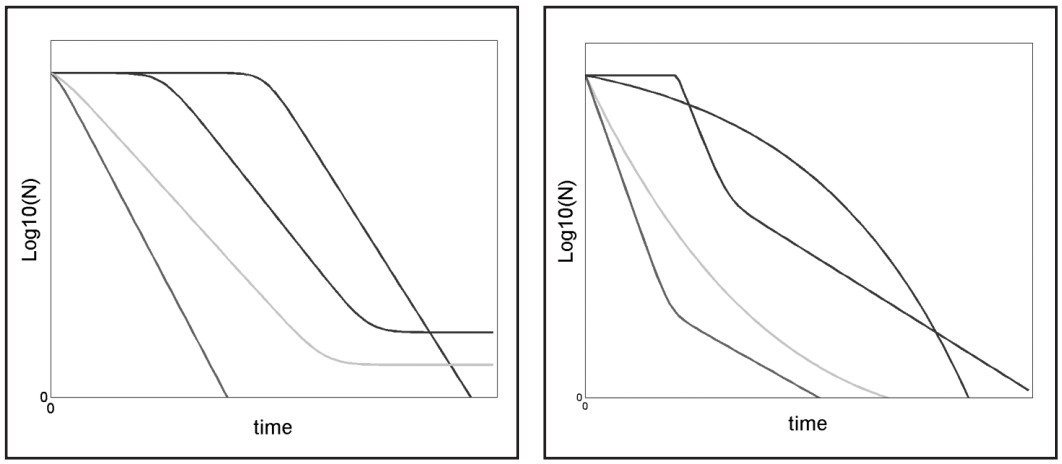
with numbers decreasing exponentially and with the N_o the initial number of organisms (at time zero), which must be known: equation (1) gives only information on the derivative (or slope); for the translation into an explicit (time-dependent) equation, one must provide information on where to start the equation.

This model describes the same behaviour as the well-known destruction rate concept for microbial loss as coined by Stumbo (1948),

$$\log \frac{N}{N_o} = -\frac{t}{D} \qquad (2)$$

with *D* the decimal reduction time (time needed to reduce the microbial population by 90%) and log denoting the decimal logarithm. The corresponding shape is presented in Figure 5.1, (left graphic), by the curve furthest left.

Figure 5.1: Possible shapes of microbial inactivation curves.



Left graph: from left to right, log-linear inactivation; log-linear with tailing; log-linear with a preceding shoulder and tailing; log-linear with a preceding shoulder.
Right graph: from left to right, biphasic inactivation; concave inactivation; biphasic with a preceding shoulder; convex inactivation.

Evidently, these equations can be related to each other, resulting in:

$$D = \frac{\ln(10)}{k} \quad or \quad k = \frac{\ln(10)}{D} \qquad (3)$$

All these equations indicate that the logarithm of the microbial numbers divided by the initial number of micro-organisms has a linear relationship with time. However, in certain cases the inactivation clearly deviates from the linear description, as shown by the variety of survival curves shapes observed from experimental data (Figure 5.1). For the interested reader, more advanced modelling approaches are succinctly presented in Appendices II and III. For end-users in the food industry not familiar with developing software code for modelling purposes, Geeraerd *et al.* (2005) proposed GInaFiT, a freeware Add-in for Microsoft Excel®. The tool is useful for the quantification of microbial inactivation in user-specified experimental data, by testing the basic inactivation model, as presented in equation (2), as well as the more advanced models presented in Appendices II and III.

5.2 Secondary models for the influence of temperature and the properties of the food product and heating menstruum on the decimal reduction time

The main parameter to describe in secondary models is the decimal reduction time *D* (or the equivalent inactivation rate, *k*). The main variable for inactivation is the temperature. The original Bigelow (1921) approach focussed on the effect of temperature on the TDT (Thermal Death Time) curves relating the logarithm of the time to reach thermal death to temperature; thermal death is defined as the time needed for the thermal treatment such that afterwards no growth occurred in the food product under reasonable circumstances. This has been taken up later on in a similar manner for the effect of temperature on the decimal reduction time *D* as follows:

$$D = D_{ref} \cdot 10^{\frac{T_{ref} - T}{z}} \tag{4}$$

with D_{ref} the decimal reduction time at a specified reference temperature T_{ref} (°C) and *z* the temperature increase (°C) needed to reduce the *D*-value by a factor of 10 (i.e., a 90% reduction, as in the definition of the *D*-value itself). Table 5.1 illustrates typical orders of magnitude of *D* and *z*. Here, log (D_{ref}) denotes the logarithm of the *D*-value at T_{ref}. Generally speaking, the *z* value is fairly constant for a given organism, regardless of variables such as the intrinsic properties of the food product. This offers useful perspectives for model calculations (as will be illustrated below).

Table 5.1: Some examples of D and z values of spore forming organisms and vegetative cells.

Microorganism	T_{ref} [°C]	*z* [°C] mean (range)	Log(D_{ref}) range	D_{ref} [min] range	Reference
Sporeformer (in general)	121.1	10 (7 to 12)	-2 to 0.69	0.01 to 5	Holdsworth (2004)
Vegetative cells (in general)	70	5 (4 to 7)	-1.52 to 1.04	0.03 to 11	Mossel *et al.* (1995)
C. botulinum proteolytic types (ABF)	120	10.2	-0.78 (-1.24 to 0.32)	0.17 (0.058 to 0.48)	van Asselt and Zwietering (2006)
L. monocytogenes	70	7.0	-1.06 (-1.84 to 0.28)	0.087 (0.014 to 0.52)	van Asselt and Zwietering (2006)

Considering the combined influence of different environmental conditions like pH and salt concentration on the decimal reduction time *D* or, alternatively, k, existing models can be catalogued as:

- Linear Arrhenius models, for example $\ln(k) = C_0 + C_1/T + C_2 pH + C_3 pH^2$, with C_0 - C_3 parameters to be identified on experimental data (Davey, 1993).
- Models making use of the decimal reduction time *D*, as coined by Stumbo (1948), and derived by extending equation (4) in a systematic way.
- Polynomial or response surface models, for example
  Log $k = a + bT + (c \times pH) + (eT^2 \times pH) + (f \times pH^2)$ with parameters *a* – *f* to be identified on experimental data (Fernández *et al.*, 1996).

Features and some key references are summarised in Table 5.2.

Table 5.2: Model features and key references of commonly used secondary inactivation modelling approaches (adapted from Geeraerd et al., 2004).

Model features for modelling k or D	Model Type		
	I. Linear Arrhenius	II. Stumbo-type	III. Polynomial (response surface)
Practical interpretability of parameters	No	Yes	No
Number of parameters as function of d factors			
d =1 (e.g., T)	Davey (1993)	Bigelow (1921)	Not used
d =2 (e.g., T and pH)	Davey (1993)	Mafart and Leguérinel (1998)	Fernández *et al*. (1996); Gaillard *et al*. (1998a)
d = 3 (e.g., T, pH and a_w)	Cerf *et al*. (1996)	Gaillard *et al*. (1998b)	Blackburn *et al*. (1997)
d = 4 (e.g., T, pH, % sodium chloride and % sodium pyrophosphate)	unknown	unknown	Juneja and Eblen (1999)
Factors are considered	Additive on a log scale, so multiplicative on a linear scale	Additive on a log scale, so multiplicative on a linear scale	Multiplicative on a log scale
Extendibility towards additional factors	Possible, limited to additive effects	Possible, limited to additive effects	Possible

All these model types have an acceptable quality of fit and have been applied to a range of microorganisms. The most widely used model type is the Bigelow model containing a practical and easily interpreted parameter, the *z*-value: the temperature (or other factor) increase needed to lower the *D*-value by a ten-fold factor (90% reduction). As such, the relationship between *log(D)* and temperature is log-linear with slope *-1/z*. This characteristic simplifies the calculation of the effect of a thermal treatment even under time-varying temperature conditions, as only two parameters, namely *z* and D_{ref}, are needed. An example is the model of Gaillard *et al*. (1998b) where the basic Bigelow model is extended modularly to include the effect of pH and water activity on microbial inactivation:

$$D = D_{ref} \cdot 10^{-\left(\frac{T-T_{ref}}{z_T}\right)} \cdot 10^{-\left(\frac{pH-pH_{ref}}{z_{pH}}\right)^2} \cdot 10^{-\left(\frac{aw-1}{z_{aw}}\right)} \qquad (5)$$

where pH_{ref} is the pH of maximum heat resistance (generally pH 7 for spores), z_T is the commonly used thermal *z*-value, z_{pH} is the distance of *pH* from pH_{ref} that leads to a ten-fold reduction of the decimal reduction time, z_{aw} is the distance of water activity a_w from 1 that leads to a ten-fold increase of the decimal reduction time, and D_{ref} is the *D*-value at T_{ref} and pH_{ref} and water activity equal to 1.

The determination of parameters such as z_T, z_{pH}, z_{aw} and D_{ref} is classically performed based on survival studies in laboratory media. Hence, one must be cautious when extrapolating the obtained secondary models to practical applications in real food products. Food properties such as fat and carbohydrate content also play an important role (van Asselt and Zwietering, 2006). For example, heat resistance data for various pathogens (ICMSF, 1996) indicate the strong influence of the type of substrate on microbial resistance. In addition, the physiological state of the cells (induced heat resistance or sub-lethal injury, see Appendix I) can also markedly influence decimal reduction times.

5.3 Guidelines for application of mathematical models for prediction purposes

In this context, we assume that the (possibly time-varying) temperature profile for a specific processing step is available, either via representative monitoring devices, or via the output of dedicated heat transfer models. Furthermore, we assume that this temperature profile is approximated via (possibly very small) time intervals with constant temperature (static temperature). This second assumption is not essential, as we could use dynamic models, but we add this assumption for the ease of illustration.

Often the more simple models can be quite easily applied for prediction purposes, since generally applicable estimates can be used, such as a *z*-value of 10°C for spores. For many organisms D_{ref} and *z* values can be estimated (van Asselt and Zwietering, 2006), meaning that one can easily estimate inactivation at various temperatures as a function of time by combining equations (2) and (4). If additional parameters such as z_{pH} and z_{aw} are known, these effects can also be included. For more complex primary and secondary models generally accepted parameters are often not readily available, making it difficult to use such models in predictions. In such cases where specific models are required, but there are insufficient data for their creation, new datasets must be generated in order to enable the prediction of inactivation over a wide range of conditions. In time, databases may be developed, such as those that currently exist for *D* and *z* values (ICMSF, 1996; van Asselt and Zwietering, 2006). Much work is still needed to make more complex models described herein more practical for general application. Examples of approaches to predictions with various levels of complexity follow.

5.3.1 First level of complexity: a safe harbour approach

The simplest approach is to combine equations (2) and (4), making use of globally accepted parameter values such as a D_{ref}-value of 0.21 min at 121.1°C and *z*-value of 10°C for *C. botulinum* (proteolytic A&B). This procedure will deliver a suitable description for most applications, thereby constituting a safe harbour approach. Another example is the first record in Table 5.3, referring to the current consensus safe harbour for *L. monocytogenes* in RTE-food products (*D*-value not exceeding 15 seconds at 72°C).

By following this approach, we are focussing on the most important variables influencing microbial inactivation, i.e., vegetative cells or spores and temperature. Other influences such as pH and water activity of the food product, species and strain variability and process variability are not taken into account. It has been shown that these effects are *generally* negligible in comparison with the variability of published *D*-values (van Asselt and Zwietering, 2006).

5.3.2 Second level of complexity: an approach based on database exploitation

When a large database of *D*-values is available for a microorganism in a given product or product group, a more precise estimate of parameter values is possible. Table 5.3, record 2a, summarises the information on *L. monocytogenes* in various food products where an upper limit of the 95% prediction interval (PI) for the *D*-value of 0.274 min at 72°C is indicated. (This value is based upon 940 values of *D* extracted from 14 literature references for various food products) – please refer to van Asselt and Zwietering (2006). This confirms the validity of the safe harbour as mentioned above for the first level of complexity. If the data specific for dairy products (280 data-points extracted from literature) are used, a smaller *D*-value of 0.104 min is obtained, and specifically for milk (226 data-points extracted from literature) a *D*-value of 0.091 min (also upper 95%-PI). These values were obtained by analysing data reported in Figure 3. Such more-specific information gives better-targeted values, and for a specific product group a better estimate, leading in this case to a clearly smaller *D*-value than that used to determine the safe harbour. The ability to calculate such specific targeted values requires ample data, such as those available for the inactivation of *L. monocytogenes*

in milk, fish, meat or vegetables. This approach may not be possible for some product groups, such as butter or potato slices, for which only a few published *D*-values are available (van Asselt and Zwietering, 2006). Hence, in such cases, the overall D_{72}-value of 0.274 min (Table 5.3, record 2a) should be relied upon.

This level of complexity allows the use of published specific parameter values in combination with equations (2) and (4). The above example illustrates that to be most effective, database approaches should focus on information specific to the food product under study as opposed to the, sometimes very wide, range of observed *D*-values for a microorganism. In this respect, ComBase (www.combase.cc; Baranyi and Tamplin, 2004) is a very useful database as inactivation data, reported either as raw data or as a lumped *D*-value, can conveniently be searched for by a specific food product-pathogen combination. If sufficient information at different temperatures is present, a *z* value may also be extractable, but this is not always possible.

Alternatively, somewhat more advanced models may be used. For example, assume that for *L. monocytogenes* the Weibull model (presented in Appendix III) with its parameters *b* and δ, is valid. We can use the *D*-value as δ; however, a value for *b* is also needed relevant to the food product under evaluation. Perhaps in the future databases of consensus *b*-values will be established for various conditions. Until then experimental data are needed to determine the *b*-value for each product, limiting the current practicality of the model (Table 5.3, record 2b).

5.3.3 Third level of complexity: an approach based on user-generated experimental data

In some cases experimental data may be generated to evaluate heat inactivation in a specific matrix or process. Tools such as the freeware GInaFit (Geeraerd *et al.*, 2005) allow the user to identify suitable primary models for user-specific experimental data and this may be augmented, where appropriate, with information from databases. Under mild thermal (and actually also non-thermal) treatment conditions, microbial inactivation frequently does not proceed in a log-linear manner (see, for example, Sergelidis and Abrahim, 2009). Hence, a primary model more complex than equation (2) is needed to describe the microbial survival kinetics accurately. If the Weibull model is used, for example, the experimental data can be used to estimate Weibull parameters *b* and δ (shape and scale parameters) (Table 3.1, record 3). As *b* is typically a temperature independent parameter for a specific strain or food product (van Boekel, 2002), there is generally no need to develop a secondary model. If data are available for the parameter δ for several values of temperature, pH and water activity models like equation (5) can also be used (replacing *D* by the δ parameter of the Weibull model, see Appendix III).

The developed models give rise to the following possibility going beyond safe harbour approaches. Imagine the assessment of an existing thermal treatment process with a pre-specified duration and associated temperature profile. The developed models use the case-specific experimental data and lead to an accurate quantification of the number of log reductions attained during the existing thermal treatment process. As the safe harbours constitute a fail-safe approach, it is expected that the number of log reductions, quantified by the accurate and dedicated models, is higher than the number of log reductions needed (required ΣR within the ICMSF concept). Hence, process optimisation comes within reach as model calculations enable us to pinpoint how much the process duration can be shortened or the treatment temperature lowered, while still guaranteeing the required ΣR.

Table 5.3: Three different levels of complexity to be distinguished when quantifying the microbial inactivation through modelling approaches – illustration on L. monocytogenes

Level of complexity – key word	D_{ref} [min] [a]	T_{ref} [°C]	z [°C]	b [-]
1 – Safe harbour	0.25	72	7	Not needed
2a – Extended database for D and z[a]	0.274 (all products) 0.104 (dairy) 0.091 (milk)	72	7 6.4 6.2	Not needed
2b – Extended database for D, z and b	0.091 (milk)	72	6.2	Needed, but databases for b not available yet
3 – Case-specific	All model parameters needed are extracted from specifically designed and conducted experiments			

[a] Data derived from database as described in van Asselt and Zwietering (2006), specifically for dairy and milk. Value is upper 95%-prediction interval.

6. PROCESS CONTROL IN COMMERCIAL PROCESSING

Previous sections have demonstrated how a risk assessment approach can be utilised better to define the required ΣR for a thermal process or to determine the processing conditions necessary to achieve the ΣR more precisely through a better estimation of microbial lethality.

Once the ΣR is established, the processor has no choice but to design the process to deliver the minimum required conditions consistently to the entire product. The process design engineer and operator are then faced with another risk assessment; that is, how close to the minimum required conditions can they operate the process. In an attempt to improve the sensory quality, the process can run close to the required minimums, running the risk of crossing the established process bounds and having to reject under-processed product. When the food safety process limits are met and the spoilage process is not, then a risk assessment is needed in order to determine the risk of having spoiled product in the market and the resulting economic impact. That risk is usually very difficult to determine and therefore not meeting the spoilage process targets often has the same consequences as not meeting the food safety process requirements if the product needs to be reprocessed, reworked or destroyed.

This is the balancing act that often must be considered when designing a microbial count-reduction process; the process must always deliver the minimum requirements and that running closer to the required minimums increases the risks of not meeting them and therefore resulting in unsafe or potentially spoiled, under-processed product.

On the other hand, designing a process that is robust in delivering the target thermal process can lead to excessive heat treatments that, whilst assuring product safety, reduce the sensory quality of the final product. This occurs because the manufacturer generally combines a series of worst-case conditions that are used to establish the boundary conditions under which the process will operate. For a canning operation, for example, these may include the container dimensions, the cook temperature, process time and product factors that will influence the heating and cooling rates of products, such as fill weight, headspace, initial temperature, viscosity and solid/liquid ratio. Alternatively, for a continuous flow process such as a UHT (Ultra Heat Treated) or pasteurisation, these may include product flow rate, viscosity and solids content.

The challenge to the processor is to validate the process using conditions that are sufficiently outside those experienced in normal production to reduce the chances of ever operating outside those boundary conditions.

Operating outside the boundary conditions is known as a process deviation. Process deviations can lead to the production of under-processed, unsafe foods and almost invariably lead to process inefficiencies and product yield losses. Under-processed foods must be evaluated for their safety and either destroyed or reprocessed if the safety is not assured. Inefficiencies result both from having to analyse the deviation and bringing the process back to a state where it can produce safe product again. Yield losses result from having to dispose of unsafe product and from having to stop and restart the process.

In the future, probabilistic modelling approaches may well be used to understand the interaction of these worst-case conditions better and thus to define a more realistic (less conservative) thermal process. In addition to using these risk assessment approaches, the canning industry has for many

years looked at ways to reduce the limits of the various line tolerances that are encompassed in the worst case analysis such that they can be run closer to the conditions that satisfy the minimum heat treatment objective. This includes using much more accurate sensors and more sophisticated and robust control systems. As an example, in continuous flow systems such as pasteurisers and UHT systems, the lethality is frequently calculated from a constant temperature holding tube after the final heater. Often the end of the hold tube temperature is run several degrees above the required minimum. This is done to account for any fluctuations in the control that may result in a loss-in-sterility event due to low temperatures. A process temperature closer to the required minimum temperature allowed could be used if the calibrations are accurate and the control is robust.

For continuous flow systems using a hold tube, often the divert points for the flow and temperature are determined assuming the other parameter is at its divert point. So a flow divert setting is calculated assuming the temperature is at its divert point while the temperature divert is calculated assuming the flow is at its divert point. Calculation schemes to take into account the actual lethality could be used, whereby if the flow or temperature divert limit is not met; then the actual value of the other parameter at that time could be examined to see if the minimum lethality is met. In this way it may be possible to run closer to the divert conditions without increasing the number of times a divert condition is encountered. Careful consideration of these schemes needs to be given since the instantaneous lethality calculation does not always ensure that all the fluid particles have achieved that level of sterilisation.

Often continuous flow systems run with a single temperature set-point, but with varying flow set-points. The flow will vary according to the demands of the downstream operations. Some processes can be controlled in such a way as to match the heating profile to the throughput rate to maintain the required lethality while also maintaining product quality (see example below).

One way to reduce over processing is to include aspects of the heat treatment that may not currently be accounted for in the calculation of the accumulated lethality, e.g., contributions from heating or cooling phases. These segments of the cycle can only be considered if they are demonstrably validated in terms of time and temperature distribution, and there is an understanding of the behaviour of product heating and cooling rate during these phases. Therefore, in order to take account of more of the thermal processing, additional validation, perhaps equipment modifications and, most likely, more sophisticated controls are required. This may lead to more critical control points that would perhaps increase the potential for deviations.

Some model-based scheduled processes (e.g., Ball, 1923; Ball, 1928; Ball & Olson, 1957; Gillespie, 1951) allow for partial contribution to the total process lethality from the "come-up" and cooling phases of the steriliser or pasteuriser cycle. Advanced heat transfer modelling techniques could provide process time and temperature cycles according to the actual conditions in the retort (Weng, J. Z., 2005).

In this way the total process time would be dependent on the actual retort conditions and the excess time and temperature of the retort cycle can be reduced. In continuous flow processes such as pasteurisers and UHT systems, product is generally pumped through a heat exchange system where it is heated to the required process temperature. Product then enters a holding tube where it is held at processing temperature for the required time to achieve the desired lethality, after which it is cooled as quickly as possible to minimise further thermal degradation. The lethal treatment in these processes is usually only derived from the holding tube and not the heating and cooling sections of the process. The thermal treatment as the product is being heated and cooled could be considered to be part of the lethality process provided reasonable residence time assumptions are made and the temperature distribution within the steriliser or pasteuriser is properly understood within the operating bounds of the model. More validation work is required to ensure the necessary

understanding of heat transfer in each of the process phases before it is possible to apply model-based control. Validation, monitoring and control will be essential.

Example – Aseptic System Profile Control

With many continuous flow systems, it is desirable to be able to adjust the flow rate through the system in order to match the output to the downstream systems (e.g., filler, packaging equipment). The holding tube where the lethality credit taken is designed for the fastest flow rate. As the flow slows down, if the temperatures were kept the same throughout the heating and cooling equipment, the amount of heat abuse would go up, potentially to undesirable levels.

One measure of the product abuse is called the cook value (C_0).

$$C_0 = \int_0^t 10^{(T-100)/22} dt$$

C_0 is very similar to the F_0-value except that the reference temperature is 100 °C and the *z*-value is one intended to match quality attribute reactions. The *z*-values for these reactions are generally much higher than for microbial destruction. In this example a *z*-value of 22 °C was used. Testing showed that if the cook value remains below 100 minutes, then the product is of acceptable quality.

The heating system is designed in a way that allows an adjustment of the temperature profile. An empirical heat transfer model is used to adjust the temperature profile, including the holding tube temperature, as the flow rate varies in response to the level in a downstream aseptic surge tank. The divert conditions were also adjusted in such a manner as always to ensure a minimum differential between the actual flow and the maximum allowed and the actual temperature and the actual allowed was maintained.

Figure 5 (a-c) show different temperature profiles and the resulting accumulated cook value (C_0) and lethality (F_0). This demonstrates the need to consider the dynamics of a system in order to achieve the safety limit while maintaining quality.

Figure 5a: The normal heating profile during production near the maximum flow rate.

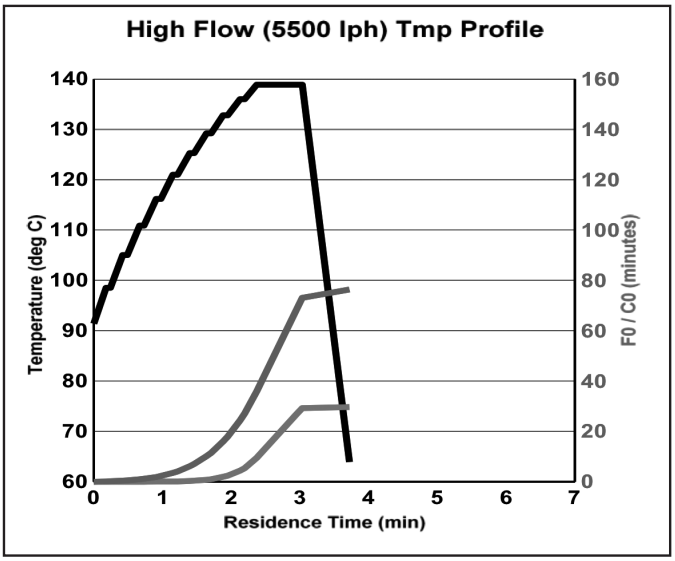


Figure 5b: The temperature profile with a flow rate near the minimum flow without an adjustment of the temperature profile. It can be seen that the F_0 and C_0 values are almost double those in Figure 5a and the C_0 value is in an unacceptable range.

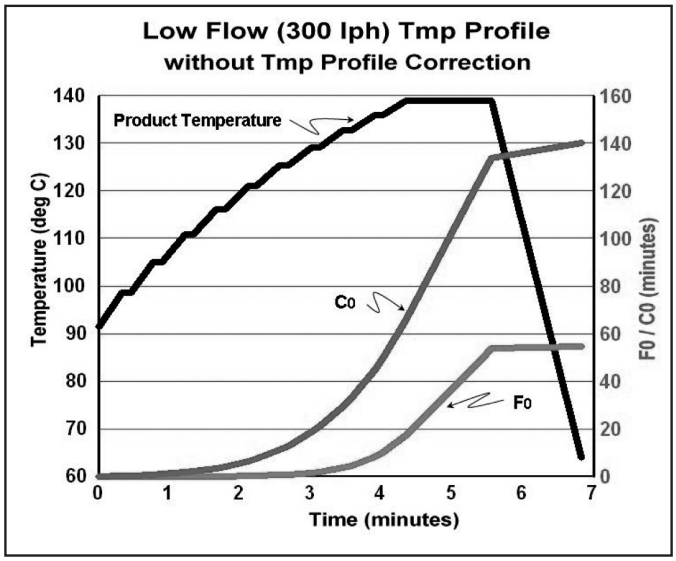
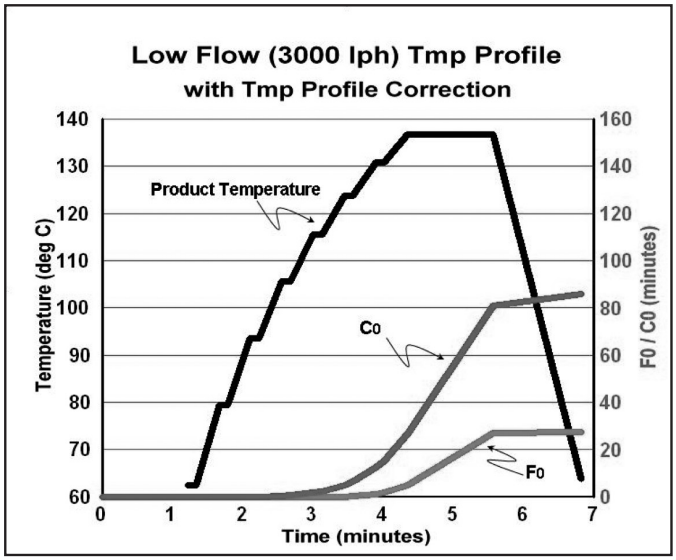


Figure 5c: The temperature profile at the lower flow with the temperature profile adjusted to match the flow. Here it can be seen that the F_0 and C_0 values are nearly identical to those at the higher flow rate.



7. CONCLUSIONS

For certain microbial hazards and food systems, thermal process parameters and performance objectives have been established by regulatory authorities or by consensus of industry and academia based on past experience. Such "safe harbour" processes can readily be used by anyone to design a thermal process without the need for extensive information about a food's characteristics or on initial microbial populations. Historically, many safe harbours were developed with limited knowledge of microbial levels and distributions in products, limited understanding or simplistic models of microbial growth or inactivation. By design, safe harbours are conservative processes, developed to account for the variability of a product, process or raw material or to account for worst-case estimates. In practice, thermal processes applied by industry often include additional safety margins beyond established safe harbours to account for process variability and or spoilage concerns.

Sensory, nutritional and economic considerations often drive efforts to challenge established processes. Additionally, safe harbours do not exist for all thermal-processing scenarios, and food processors must establish process criteria sufficient to achieve microbiological safety and stability. Such efforts are aided by a greater understanding of microbial ecology of foodstuffs, advances in modelling of microbial growth and lethality and the development of Quantitative Microbiological Risk Assessment tools.

The ICMSF conceptual equation provides a framework, which can be used to evaluate the role of the thermal process in the context of other parameters necessary to achieve a desired Performance Objective. Information on the initial populations, increase in population due to growth or recontamination during manufacture, storage or distribution and other factors that may contribute to microbial reductions can be used to gain more precise estimates of the reductions that are necessary during a thermal process. As such, the approach can be used to establish a new thermal process or to demonstrate the equivalence of a food system to a regulatory or consensus safe harbour by demonstrating that control of all factors, including the thermal process, can achieve the same performance objective.

The use of more complex models of microbial inactivation may help to provide a more accurate picture of what is happening during the process, enabling the establishment of less conservative thermal process parameters that more precisely meet process criteria by:

1. Predicting with greater accuracy the performance of a specified thermal process.
2. Calculating with greater accuracy the time needed at a specified treatment temperature, or the temperature needed for a specified treatment duration to attain a stated performance level.

Where limited experimental data are available for a specific product application, extended databases of published *D*- and *z*-values can be used to develop more precise estimates of lethality. The determination of lethality requirements for a thermal process must evaluate risks associated with raw materials, product formulation and packaging, distribution conditions and desired shelf-life, but must also account for variability inherent in the processing system. Opportunities exist to reduce the thermal processing parameters established to achieve lethality requirements through more precise measurements of processing conditions and through a greater accounting of lethality achieved during the process. However, for economic reasons (capital expenditure), process efficiency, product yield and potentially increased number of validations, there often remains in practice a wide margin between the nominal (scheduled process) and critical operating conditions.

8. GLOSSARY OF TERMS

Appropriate Level Of Protection (ALOP) – Level of protection deemed appropriate by the member (country) establishing a sanitary or phytosanitary measure to protect human, animal or plant life or health within its territory.

Colony forming unit (cfu) – a measure of viable bacterial or fungal numbers.

Cook value (C_0) – a measure of the product abuse in thermal processing.

Decimal reduction time (*D*-value) – the time required at a constant heating temperature to reduce the number of organisms or spores by a factor of ten.

Food Safety Objective (FSO) – "the maximum frequency and/or concentration of a microbiological hazard in a food at the time of consumption that provides the appropriate level of health protection".

Integrated lethal rate (F_0 value) – calculated by integrating the area between the curve obtained when lethal rates are plotted against time.

HACCP – Hazard Analysis and Critical Control Points.

Kinetic value (*z*-value) – a measure of the relative "killing power" of the heating temperature; it is the temperature (or other factor) difference needed to lower the *D* value by a ten-fold factor (90% reduction).

Lethality Performance Standards – standards defined by US Food Safety and Inspection Service based on reduction of contamination by *Salmonella* spp.

Microbiological risk assessment (MRA) – a tool to assist in the production of safe food; it comprises four key elements: hazard identification, hazard characterisation, exposure assessment and risk characterisation.

Miminum *botulinum* cook – time to achieve a 12-log reduction for *C. botulinum* spores.

Performance Objective (PO) – the maximum frequency and/or concentration of a microbiological hazard in a food at a given point (e.g., packaging) during its production.

Quantitative Microbiological Risk Assessment (QMRA) - quantitative characterisation and estimation of potential adverse health effects associated with exposure of individuals or populations to hazards.

Ready-to-eat (RTE) – processed food, which does not require further processing by the consumer.

Safe harbour process – Generally recognised processes and process criteria that have been established over time by consensus or by regulation.

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10. APPENDICES

Appendix I: Lethality Target Calculation

Establishing the lethality target for a thermal process requires a risk assessment of all aspects of the raw materials, processing methods and the anticipated onward distribution. Key issues include initial microbiological load, target organism, presence of other preservation hurdles, desired shelf-life and product and process variability. Distributions around the thermal processing target are not considered. Rather the thermal processing target becomes the minimum process that is to be delivered.

The thermal processing target is often expressed as the log reduction of a specific organism. This is then frequently given as an F-value, which is the time required at a reference temperature to achieve the desired log reduction. Knowing the *D*-value at a reference temperature allows for calculating the F-value as follows:

$$F_{Tref} = D_{Tref} \times \log reduction$$

For example if the *D*-value at 110°C of the target organism is 0.25 minutes and it is desired to reduce the population by 4 logs, then the target F-value is as follows:

$$F_{110} = D_{110} \times 4 = 0.25 \times 4 = 1 \min$$

Incorporating the *z*-value allows for calculating the equivalent processes at other temperatures. The time (t) required for achieving the F_{110} of one minute at 118°C if the *z*-value for the specific organism is 8°C is as follows:

$$t = \frac{F_{Tref/z}}{10^{(T-Tref)/z}} = \frac{F_{110/8}}{10^{(118-110)/8}} = \frac{1}{10^{1}} = 0.1 \min$$

Applying the relationship above should be done within the bounds of the thermal-death-time tests that were used to calculate the *z*-value for the organism.

If conditions are changing over time, lethality can be accumulated over the thermal cycle by employing the following relationship (keeping in mind the appropriate range of applicable temperatures):

$$F_{Tref/z} = \int_0^t 10^{(T-Tref)/z} dt$$

For processes that are concerned with the reduction of *C. botulinum*, the reference temperature and *z*-value for the F-value are 121°C and 10°C respectively. This particular F-value is known as the F_0.

Appendix II: Reflections on the simplified assumptions

The basic assumptions that all experimental data come from a carefully designed and sampled challenge test, where one specific microbial species is added to a chosen food (model) system under study, deserve the following considerations.

1. Microorganisms typically occur heterogeneously distributed in raw materials used for food production. This implies that, when a heat treatment is conducted as uniformly as technically possible, the resulting microbial levels in the food product remain heterogeneously distributed. Generally, initial levels, as reflected in the H_0 term of the ICMSF-equation (Figure 3.1), can be controlled by avoiding ingredients with a history of contamination, and by using dedicated sampling plans for microbiological testing (ICMSF, 2002). More information on the impact of microbial distributions on food safety management can be found in the ILSI Europe report "Impact of Microbial Distributions on Food Safety" (Bassett, 2010).

2. Microorganisms also display variability in thermal resistance, even within one species. van Asselt and Zwietering (2006) give some examples related to the known difference between the heat resistance of proteolytic and non-proteolytic *C. botulinum* and various *B. cereus* strains. In addition, one particular strain can also display differences in heat resistance due to its recent history, for example, an inverse relation between induced thermo-tolerance and heating rate was reported in case studies of *L. monocytogenes* (Hassani *et al.*, 2005) and *Salmonella* Typhimurium (Juneja and Marks, 2003). Conversely, some sub-lethally injured microorganisms may have a lower heat resistance.

Appendix III: Advanced modelling approaches

Occasionally experimental data deviate from typical linear inactivation kinetics. This Appendix considers the dynamics of alternative survival curves and models.

Convex and concave behaviour

This behaviour can be described by the Weibull model (two parameters). Especially useful is the re-parameterisation from Mafart *et al*. (2002):

$$\log\left(\frac{N}{N_o}\right) = -\left(\frac{t}{\delta}\right)^b$$

since the parameter δ of this equation is interpretable, being the first decimal reduction time (i.e., the time needed to reduce N_0 to $N_0/10$). This equation can either describe a log-linear inactivation identical to Equation (2) ($b = 1$), a convex curve ($b > 1$, the inactivation rate increases in time, far right curve in Figure 5.1, right graphic) or a concave curve ($b < 1$, the inactivation rate decreases in time, second left curve in Figure 5.1, right graphic).

Biphasic behaviour

Biphasic behaviour can be explained by the presence of two populations, each with a different inactivation rate (Cerf, 1977):

$$\log\left(\frac{N}{N_0}\right) = \log\left((1-f)\cdot\exp\left(-k_{sens}t\right) + f\cdot\exp\left(-k_{res}t\right)\right)$$
$$= \log\left((1-f)\cdot 10^{-t/D_{sens}} + f\cdot 10^{-t/D_{res}}\right)$$

where $(1 - f)$ and f are the initial proportion of the sensitive fraction and the resistant fraction, respectively, f typically being several magnitudes smaller than $(1\text{-}f)$. The values k_{sens} and k_{res} are the specific inactivation rates of the sensitive and resistant fractions, respectively, and D_{sens} and D_{res} their corresponding decimal reduction times. This model contains three parameters and is illustrated in Figure 5.1, (right graphic), by the curve on the left.

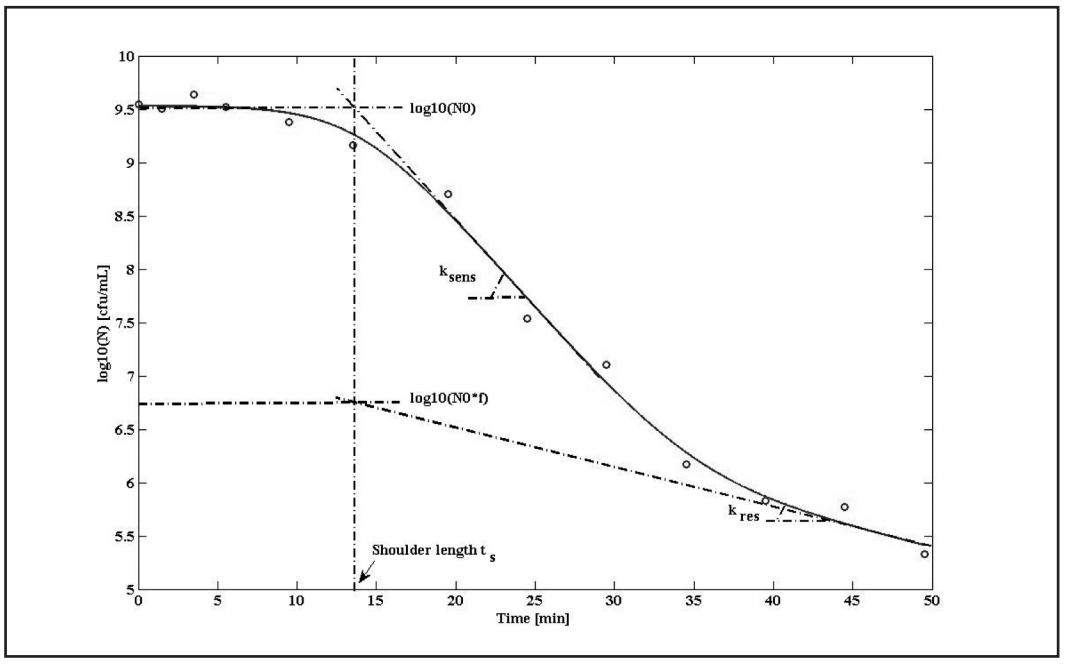
Flexible models

The model of Geeraerd *et al*. (2005) is a flexible model that encompasses many different behaviours and with interpretable parameters.

$$\log\left(\frac{N}{N_0}\right) = \log\left\{\begin{array}{l}(1-f)\cdot\exp\left(-k_{sens}\cdot t\right)\cdot\dfrac{\exp\left(k_{sens}\cdot t_s\right)}{1+\left[\exp\left(k_{sens}\cdot t_s\right)-1\right]\cdot\exp\left(-k_{sens}\cdot t\right)} \\ +f\cdot\exp\left(-k_{res}\cdot t\right)\cdot\left(\dfrac{\exp\left(k_{sens}\cdot t_s\right)}{1+\left[\exp\left(k_{sens}\cdot t_s\right)-1\right]\cdot\exp\left(-k_{sens}\cdot t\right)}\right)^{\frac{k_{res}}{k_{sens}}}\end{array}\right\}$$

In addition to having a two phase inactivation, this model contains also a shoulder phase (with a time length indicated by t_s), and in total has four parameters, which can all be interpreted: specific inactivation rate of the sensitive fraction of the microbial population k_{sens}, specific inactivation rate of the resistant fraction of the microbial population k_{res} and f the initial proportion of the resistant fraction. The corresponding shape is presented in Figure 5.1, (right graphic), by the third from left curve and Figure A.1. All four parameters and the initial population level $\log_{10}(N_0)$ are graphically interpretable, as illustrated in Figure A.1, below, on experimental data of *E. coli* K12 at 55°C in BHI-medium (Valdramidis *et al.*, 2006). The interpretation of the model parameters is indicated, with the following values resulting from the model parameter estimation procedure: $\log_{10}(N_0)$= 9.53, $k_{sens} = \ln(10)/D_{sens}$ = 0.40 min^{-1}, $k_{res} = \ln(10)/D_{res}$ =0.085/min, t_s = 14 min and f = 0.00155.

Figure A.1: Example of the Geeraerd et al. (2005) inactivation model



The advantage of these interpretable parameters is that this model can easily be reduced in complexity, if the data do not have specific characteristics; for example, if the data do not display a shoulder behaviour, the shoulder length t_s will be identified as (approximately) being equal to zero, and the equation reduces automatically to the equation for biphasic behaviour. In addition, the third from left curve in Figure 5.1 (right graphic), can reduce in complexity to all four curves in Figure 5.1 (left graphic). This reduction in the number of parameters is very important, since every parameter in the primary model can be dependent again on the conditions, meaning that, for every parameter, secondary models need to be developed, which can result in increasing complexity and potentially even less accurate overall models in certain cases. Another advantage of interpretable parameters is that it is easier to estimate initial parameter values and that it is easier to interpret, criticise and compare results.

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