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1 Future Challenges to Microbial Food Safety

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21

22 Abstract

23 Despite significant efforts by all parties involved, there is still a considerable burden of
24 foodborne illness, in which microorganisms play a prominent role. Microbes can enter the
25 food chain at different steps, are highly versatile and can adapt to the environment allowing
26 survival, growth and production of toxic compounds. This sets them apart from chemical
27 agents and thus their study from food toxicology. We summarize the discussions of a
28 conference organized by the Dutch Food and Consumer Products Safety Authority and the
29 European Food Safety Authority. The goal of the conference was to discuss new challenges to
30 food safety that are caused by microorganisms as well as strategies and methodologies to
31 counter these. Management of food safety is based on generally accepted principles of Hazard
32 Analysis Critical Control Points and of Good Manufacturing Practices. However, a more pro-
33 active, science-based approach is required, starting with the ability to predict where problems
34 might arise by applying the risk analysis framework.

35 Developments that may influence food safety in future occur on different scales (from global
36 to molecular) and in different time frames (from decades to less than a minute). This
37 necessitates development of new risk assessment approaches, taking the impact of different
38 drivers of change into account. We provide an overview of drivers that may affect food safety
39 and their potential impact on foodborne pathogens and human disease risks. We conclude that
40 many drivers may result in increased food safety risks, requiring active governmental policy
41 setting and anticipation by food industries whereas other drivers may decrease food safety
42 risks.

43 Monitoring of contamination in the food chain, combined with surveillance of human illness
44 and epidemiological investigations of outbreaks and sporadic cases continue to be important
45 sources of information. New approaches in human illness surveillance include the use of

46 molecular markers for improved outbreak detection and source attribution, sero-epidemiology
47 and disease burden estimation.

48 Current developments in molecular techniques make it possible to rapidly assemble
49 information on the genome of various isolates of microbial species of concern. Such
50 information can be used to develop new tracking and tracing methods, and to investigate the
51 behavior of microorganisms under environmentally relevant stress conditions. These novel
52 tools and insight need to be applied to objectives for food safety strategies, as well as to
53 models that predict microbial behavior. In addition, the increasing complexity of the global
54 food systems necessitates improved communication between all parties involved: scientists,
55 risk assessors and risk managers, as well as consumers.

56

57 Keywords: food safety, microbial hazards, future trends, monitoring, surveillance, risk
58 assessment, tracking and tracing, communication

59

60 1. Introduction

61 The microbiological aspects of food safety have been studied intensively for many decades. In
62 the Netherlands, the standard of food safety has increased in the last decades (Van Kreijl *et*
63 *al.*, 2006), and political attention is shifting to other food-related problems such as obesity and
64 unhealthy diets. However, even in industrialized countries, there is still a considerable burden
65 of foodborne illness. For example, in the Netherlands there are an estimated 700.000 cases of
66 illness and 80 deaths per year. The burden of foodborne disease for this country is at least
67 3800 Disability Adjusted Life Years and 65 million Euro per year (Havelaar *et al.*, 2008).
68 Also other industrialized countries report a continuing burden of foodborne illness (Flint *et*
69 *al.*, 2005, Hall *et al.*, 2005, Adak *et al.*, 2005, Anonymous 2007a, Jones *et al.*, 2007).
70 Foodborne outbreaks appear to be on the rise again in some industrialized countries, with a
71 shift from traditional problems with foods from animal origin to fresh foods such as produce
72 (Anonymous, 2008a), shellfish (Pontrelli *et al.*, 2008) and dry products and ingredients (e.g.
73 peanuts, Anonymous, 2009). Furthermore, new threats continue to be identified. The attention
74 for viruses is more recent, but no less relevant. New risks are being encountered because of
75 changing characteristics of the relevant micro-organisms, changing production
76 methodologies, changes in the environment and the ecology, and an increase of the global
77 trade of foodstuffs. In addition, demands on food safety increase steadily. Due to the nature of
78 microbes and our food chain, measures to ensure food safety have to be implemented on a
79 global scale, necessitating a global approach.

80 To discuss the challenges that microbes pose to food safety on the longer term, the Dutch
81 Food and Consumer Products Safety Authority (VWA) and the European Food Safety
82 Authority (EFSA) organized a conference on “Future Challenges to Food Safety” (Wolfheze,
83 the Netherlands, 9-12 June 2008). The goal of the conference was to discuss new challenges
84 to food safety that are caused by microbes and strategies and methodologies to counter these.

85 It was aimed at achieving conceptual breakthroughs through an imaginative combination of
86 recent developments in microbiology, epidemiology, mathematical modeling and expert
87 knowledge; using these to propose new approaches to analyze and control food safety issues
88 in the future. Such tools should enable risk assessors to pro-actively address imminent
89 problems before they cause harm. This paper provides an overview of the major themes
90 identified during the conference. The paper starts with a discussion of food safety from the
91 risk management perspective. A systems approach to identify and structure future
92 developments that may help to develop a pro-active approach to food safety is introduced,
93 followed by a more detailed discussion of relevant developments with special attention for the
94 interaction between micro-organisms and their environment, and for microbial evolution.
95 Despite the need for pro-active approaches, surveillance and monitoring are discussed as
96 important cornerstones of food safety policy and new developments in the available
97 methodology are discussed. Finally, needs related to communication between all actors in the
98 food chain are outlined.

99 **2. Risk management**

100 *Food safety demands*

101 Management of microbial food safety is a balancing act involving disparate factors. A high
102 level of safety can be achieved by rigorously heat-sterilizing the food, thereby destroying taste
103 and nutritious value. Irradiation would be another method for virtually absolute control of
104 microbial risks, but in addition to being expensive, it is not acceptable to the public at large in
105 many countries. Furthermore, some bacterial and fungal toxins are not inactivated by
106 currently used irradiation doses. The consumer demands fresh, tasty, healthy and wholesome
107 food products. Nevertheless, safety is in this framework considered an absolute requirement;
108 placing unsafe food on the market is not an option in the consumer's mind. Food laws

109 everywhere are very clear on this point. For example, the EU General Food Law
110 (Anonymous, 2002) states that: “a high level of protection of human life and health should be
111 assured in the pursuit of Community policies”. Still, placing chicken contaminated with
112 *Salmonella* or *Campylobacter* on the market is tolerated, because the consumer can
113 circumvent this risk by cooking the meat properly and taking adequate precautions against
114 cross-contamination, illustrating that responsibility for food safety is distributed over the
115 entire chain. Nevertheless, there is an increasing pressure on producers to reduce
116 contamination levels of fresh meat as far as possible and economically feasible. It has been
117 demonstrated that it is very difficult to modify consumer behavior by education campaigns
118 (Nauta *et al.*, 2008).

119 Microbial food safety differs fundamentally from chemical food safety. While chemical
120 residues and additives typically enter the food chain at more or less predictable steps,
121 microbes can enter at any step. They grow and die and interact with the food in ways that are
122 at best empirically described, but less understood in detail. The effects are also of a different
123 nature. Chemical contaminants, such as dioxins, can accumulate in the human body over the
124 years and still exert influence long after ingestion. Microbial pathogens can in some cases be
125 dormant for a certain time, but usually cause disease in a matter of days or weeks. The public
126 perception of microbial and chemical risks is also different. Residues of pesticides cause
127 public outcries if they exceed the norms, but usually will not have any noticeable detrimental
128 effect, while foodborne microbial and viral diseases are generally more accepted as facts of
129 life, as long as death or permanent harm do not occur (Hansen *et al.*, 2003)

130 One of the challenges for managers of microbial food safety risks is to put in place effective
131 controls, without unnecessarily increasing costs or reducing taste and nutritional value.
132 Microbial hazards can be introduced at any step in the production chain and the most effective
133 opportunity for controlling those hazards can very well be a different step. Microbial risk

134 management therefore requires a thorough understanding of the entire food production chain.
135 Monitoring the presence of pathogens in the end product usually is an inefficient approach to
136 hazard control, because it is impossible to test sufficient samples to obtain the necessary
137 degree of statistical power to detect contaminants at levels that may create unacceptable
138 health risks. Furthermore, by the time the potential presence of pathogens has been confirmed,
139 the optimal moment to take measures may have passed. Therefore, a pro-active approach is
140 required, starting with the producer ensuring a safe product and process design, and predicting
141 where problems might arise, rather than detecting them after they have occurred.

142 At present HACCP (Hazard Analysis Critical Control Point) programs and GMP (good
143 manufacturing practice) are mainly used to manage microbial hazards in foods. While these
144 systems have proven very effective for the control of food safety (Van Der Spiegel *et al.*,
145 2004, Arvanitoyannis and Traikou, 2005), it must be realized that they are designed on the
146 basis of known hazards, and do not necessarily take potential future developments in
147 consideration. For innovations, new validations and verifications are necessary. Furthermore,
148 it should be realized that the implications of microbial adaptability are not sufficiently taken
149 into account (McMeekin and Ross, 2002, McMeekin *et al.*, 2006). Although documentation is
150 a very important aspect of HACCP and GMP procedures, the real confidence in control
151 comes for the validity of the effectiveness of the written guidelines and the adherence to them.
152 Producers and handlers of foodstuffs are more likely to adhere to the prescribed HACCP
153 procedures if they recognize these as useful and implementable (Taylor and Taylor, 2004).

154 *Science-based risk-management*

155 Within the food safety discipline the terms “risk manager” and “risk management” are not
156 unequivocal and are used to indicate several functions and persons. As a consequence there
157 are several persons with responsibility as risk managers, each at a different step of the food
158 chain. Formally “the” risk manager is the government’s minister of public health and/or

159 his/her colleague of agriculture, as they set the standards to which food producers must
160 adhere. Furthermore, within government supervisory agencies the persons in charge of the
161 enforcement branch are often called risk managers. Often, however, the person responsible for
162 compliance to procedures within a food manufacturing company is called a “risk manager” as
163 well, as this term in fact very well describes his/her day-to-day activities. Although these
164 functions are less clearly defined in smaller operations and in primary production, the role
165 should be fulfilled in any food operation. Risk assessors, on the other hand, have a different
166 function. They provide the risk manager with science-based advice on the magnitude of risks
167 and cost-effective ways to reduce these. This advice enables the different risk managers to
168 take decisions on measures to control risks, by setting standards, by implementing in-plant
169 control measures and/or enforce existing regulations.

170 A challenge to food microbiologists in their role of risk assessors is to translate complex
171 scientific problems in such a way as to help a risk manager to make a simple yes/no decision.
172 The risk manager wants to know what standards to set, when to interfere in the production
173 process, prevent a batch from reaching the market or take another measure. Under the WTO
174 Agreements, and in particular the Agreement on the Application of Sanitary and
175 Phytosanitary Measures, considerations of food safety and animal and plant health are the
176 only legitimate reason for trade restrictions. The type of decisions in these cases is also of the
177 yes/no kind. The underlying science will have to provide the decision maker with a solid
178 rationale that will stand up in the international courts. This implies that data on the
179 microbiological status of the foods concerned must be communicated in terms of public
180 health risk with a limited margin of error, requiring a predictive power from food
181 microbiology. As zero-risk is unattainable, this approach also implies that the risk manager
182 defines a level of acceptable (tolerable) risk. In international trade, this is called the
183 Appropriate Level of Protection, equivalent to the currently realized risk level under the food

184 safety system of the importing country. Food safety managers may wish to achieve a higher
185 level of protection in future by stating additional public health targets (Anonymous 2006,
186 Anonymous 2007b).

187 *Food safety risk-management in the EU*

188 Public concern about food safety increased sharply as a result of the food scandals in the last
189 decade of the twentieth century and confidence decreased in parallel. To counter these
190 sentiments national governments and the EU established food laws and regulations that
191 strictly separate risk management from risk assessment. The idea behind this was to create
192 transparency by having the risk assessor provide advice to the risk manager completely in the
193 open. The risk assessor operates independently, based on the best available science and free
194 from influence by politics, industry or any other stakeholder. The risk assessor should give
195 objective advice, based on science while taking account of other considerations that the risk
196 manager has indicated. The risk manager can then incorporate other factors such as public
197 concern or political preferences into the decision making process.

198 The exact procedures for risk assessment differ considerably in the different member states.
199 The EU itself has mandated the European Food Safety Authority (EFSA) to carry out risk
200 assessments, either at the request of the Commission, a member state or the European
201 Parliament, or on its own initiative. The EFSA in turn has handed this task to 10 scientific
202 panels and the Scientific Committee, which it finances and supports scientifically and
203 otherwise. These panels write opinions which are passed on unchanged to the EU
204 Commission and published on the EFSA website. When strong public interest is expected a
205 press release is issued as well. The panels are comprised of scientists who operate
206 independently from risk management, and almost all come from EU-member states, though
207 this is not a formal requirement. The scientists are chosen in an EU-wide application

208 procedure on the basis of their expertise and prominence in their scientific fields, and are
209 appointed for a period of three years at a time.

210 The advice of EFSA's panels is presented as a scientific opinion to assist in the formulation of
211 risk management measures by the European Commission. Measures may be decided upon by
212 the members states in a consensus procedure, allowing political, economic and other
213 considerations to influence the decision making process.

214 *Interaction between scientists and regulators*

215 Researchers, in their role as risk assessors, need to provide the regulators, in their role as risk
216 managers, with advice that can be implemented in a practical manner. Regulators may or may
217 not have a scientific background and thus results of risk assessments have to be
218 communicated in a way that can be understood by fully informed laypersons. The process of
219 risk analysis, as defined by Codex Alimentarius, consists of risk assessment, risk management
220 and risk communication. The very first step in the process, hazard identification, is a
221 component of risk assessment. The hazard identification can come from any source. In
222 practice it is often the risk manager, who "identifies" the risk by asking for a risk assessment.
223 For a good risk assessment, the problem at stake needs to be well understood by the assessor.
224 Therefore, correct phrasing of the request is essential for a successful risk assessment
225 procedure. The regulator needs to articulate his question so that it will not be misunderstood
226 by the scientist. In short, they need to "speak each others language". This seems a trivial
227 point, but experience proves that it is not.

228 The roles of the risk assessor and the risk manager need not only to be formally separated, but
229 also with respect to substance. A risk manager has to consider more issues than science only,
230 such as stakeholder interests, public concerns and political pressure. The risk assessor needs

231 to present a science-based advice, but may anticipate the risk manager to take other than
232 scientific factors into account when selecting the risk management options.

233 **3. A systems approach to analyzing future challenges to food safety**

234 In addressing the present or future state of food safety one should investigate effects both on
235 large scales of space and time as well as on small scales (Table 1). Certain aspects slowly
236 change at a global scale, like climate change while others such as point mutations or the
237 acquisition of a plasmid by a micro-organism, occur on a molecular scale and on very short
238 time scales. In addition, certain aspects occur over longer time scales, but on a molecular
239 level, like subsequent adaptation of micro-organisms, or on a small time scale but on a larger
240 spatial scale, like the spread of a virulent micro-organism due to the large traffic of people or
241 goods. Furthermore these changes occur in micro-organisms and humans, in habitats and in
242 the environment. To accurately describe and predict processes in all these different organisms
243 and locations, on these very different spatial scales and time scales is virtually impossible, the
244 more because all these aspects interact. The risk framework of the UK Foresight project on
245 infectious diseases (Tait *et al.*, 2006) offers a useful starting point for the development of
246 scenario analysis in relation to food safety. The project has developed the following
247 definitions, which are cited literally here:

- 248 • Disease sources/emerging hazards: phenomena or biological events that: give rise to
249 potential new diseases; enable existing diseases to become more harmful; enable
250 existing diseases to infect new hosts; or enable existing diseases to spread to new
251 areas.
- 252 • Pathways: mechanisms or routes by which a disease organism can transfer from one
253 host to another, within or between species.

254 • Drivers: social, economic or physical factors that affect disease outcomes by changing
255 the behavior of disease sources or pathways.

256 • Outcomes: diseases of plants and animals at the individual, community and ecosystem
257 or farming system level, and diseases of humans at individual and societal levels.

258 A basic risk framework (Figure 1) shows the links between these different factors.

259 The PERIAPT project on emerging risks (Noteborn *et al.*, 2005) identified 8 major categories
260 of drivers, based on expert surveys. Later, we will present a tabular representation of these
261 drivers of change in the food system, and a qualitative analysis how they affect sources,
262 pathways and outcomes. To better explore these complex interrelationships among different
263 drivers, mathematical models may be helpful.

264 Mathematical models are a representation of the essential aspects of an existing system (or a
265 system to be constructed), presenting knowledge of that system in a usable form. A
266 mathematical model usually describes a system by a set of numerical variables and a set of
267 equations that establish relationships between the variables. The variables represent some
268 properties of the system, obtained by measurements or by expert opinion. The actual model is
269 the set of functions that describe the relations between the different variables. The purpose of
270 modeling is to increase our understanding of the world. The usefulness of a model rests not
271 only on its fit to empirical observations, but also on its ability to extrapolate to situations or
272 data beyond those originally described in the model (from Wikipedia, March 21, 2008).

273 Some examples of models that are currently used to analyze and to support decision making
274 on food safety:

275 • Microbial risk assessment (MRA) models (hazard identification, exposure assessment,
276 hazard characterization (including dose-response), risk characterization).

277 *Used to understand the relationships of pathogen occurrence (both prevalence and*

278 *concentration) in different steps of the food chain, to predict health risks associated*
279 *with pathogens in food, and the expected public health effects of interventions and the*
280 *setting of risk-based standards for food production.*

- 281 • Predictive microbiology (growth/death/survival).

282 *Used to understand the growth or death of micro-organisms in relation to their*
283 *implicit properties and interactions, and the intrinsic properties of the food and the*
284 *extrinsic factors of the (processing) environment. It is an important component of*
285 *MRA models, and also used for prediction of shelf-life and intrinsic safety of foods.*

- 286 • Dynamic infectious disease models.

287 *Used to understand the spread of diseases in human or animal populations, depending*
288 *on contact patterns and mode of spread of the pathogens, in relation to the*
289 *development of protective immunity.*

- 290 • Risk factor models (analytical epidemiology).

291 *Used to relate the observed occurrence of responses (e.g. illness) to the occurrence of*
292 *potential predictive factors.*

- 293 • Attribution models.

294 *Used to estimate the contribution of putative sources to the observed occurrence of*
295 *responses (e.g. illness).*

- 296 • Multi-criteria analysis models.

297 *Used to support decision makers in making evaluations of different options, based on*
298 *a combination of variables of a different nature (health, economic, societal,) with*
299 *value-based weights.*

300 All models are based on a set of (simplifying) assumptions and have specific data needs. They
301 also differ in their form (linear or non-linear, deterministic vs. stochastic, static vs. dynamic)

302 which impacts on their use for specific purposes. It is noted that all models described above
303 work at relatively low levels of aggregation, looking at specific (parts of) food chains in
304 relation to public health effects. The challenge is to develop models that are able to capture
305 the impact of different drivers on foodborne risks at higher levels of aggregation.

306 ? The overall aim of this coupling of various aggregation levels is to better understand how
307 drivers affect the evolution of foodborne illness and to determine the most important drivers.
308 This can help to react with a timely and adequate response, and support a pro-active approach,
309 targeted at future events. Generally one needs to decrease complexity in the more detailed
310 parts and move upwards to more global aspects, but also *vice-versa*, since after identifying
311 certain important aspects on a global scale one might need to change focus to the more
312 detailed level. For this, intensified linking to models in other domains is necessary, like
313 biosphere models, geospatial modeling, catastrophe modeling, climate models, remote
314 sensing, network science, statistical physics, and data mining.

315 For these models, a huge amount of data is needed such as information of food production
316 sites and global product flows (volume, origin) for high risk products (e.g. fresh meat, fresh
317 produce, shellfish), risk maps, global atlases of food consumption and production, food
318 categories with different levels of risk. Connecting them in dynamic systems can help to
319 identify rates of change. However, it is necessary to begin with low granularity, with more
320 detail based on sensitivity analysis.

321 In current risk evaluations considerable uncertainties already prevail, so, when modeling
322 future risks even larger uncertainties will exist. However, important insights can still be
323 gained using the available information, making the best informed decisions at a given point in
324 time, that later can be detailed if more and better information becomes available. Scenario
325 analysis will be particularly important to better understand the impact of different factors,
326 their interrelatedness and their uncertainties. It is a process of analyzing possible future events

327 by considering alternative possible future developments and outcomes (scenarios), and their
328 likelihood. These insights can then be used to develop a range of contingency plans to address
329 the most likely or most serious scenarios. The analysis is designed to allow improved
330 decision-making by providing more complete consideration of outcomes and their
331 implications. Typically, scenario analysis starts with the identification of possible important
332 drivers of change, and subsequently assigning a preliminary ranking of their importance.

333 **4 Trends and future developments**

334 In this section, we present an attempt to collect and structure available information on the
335 current and future aspects of microbial food safety. Table 2 gives an overview of factors
336 identified so far, according to the model presented by Tait *et al.*, (2006). We interpret the
337 sources category as referring to the pathogens; the pathways category is split into the three
338 major stages of the farm-to-fork pathway (farm, processing and consumption), and outcomes
339 are defined at the public health level. Note that there are complex interrelationships between
340 different drivers, sources, pathways and outcomes that are difficult to visualize in a two-
341 dimensional table, and hence the information must be interpreted with care. Nevertheless,
342 important insights can be gleaned from this analysis, which provides a general background
343 against which specific situations can be analyzed. Currently, it is only possible to discuss the
344 impact of drivers of change on sources and outcomes in general, qualitative terms and so an
345 attempt has been made to indicate the anticipated direction of change for specific sources and
346 overall for drivers. It is clear from Table 2 that many drivers are expected to result in an
347 increased risk to food safety, although there are also favorable exceptions, such as the lesser
348 consumption of meat due to higher food prices. Controlling such threats is a challenge to
349 governments as the only drivers assumed to result in reduced threats relate to government and
350 policies. A second important challenge is to food industries that can modulate the effects of

351 many drivers in such a way that a neutral or even positive effect on food safety can be
352 expected (see drivers under science, technology and industry).

353 Further elaboration of the crude framework sketched in this chapter requires considerable
354 inputs. It is suggested that to further develop the framework, historical examples be analyzed.
355 This will provide more detailed insight regarding relevant drivers and sources, and their
356 interaction as well as data to validate the approach. Such examples include the BSE epidemic,
357 different meatborne zoonoses (e.g. VTEC O157), shellfish poisoning and more recent
358 outbreaks in fresh produce.

359 In order to improve future responsiveness, signals about changes or breakdowns in the food
360 safety system must be received and processed in time. This implies a pro-active approach.
361 Process or production failures, including fraud and terrorist action need specific attention.
362 Risk mapping (on a global scale) can be a helpful tool. This includes observation and
363 systematically analyzing consumption patterns, processing / production changes, knowledge
364 of international production chains (trade), and data & knowledge sharing. Where necessary,
365 available data can be supplemented with expert opinions (global and multidisciplinary).

366 *Trends in food processing*

367 The trend for mildly preserved foods comes with a range of approaches being investigated,
368 mostly using minimal heating, natural preservatives and non-thermal treatment as
369 technologies and often combined preservation/hurdle technology as the principle in designing
370 the overall treatment. Such processes need to be well controlled through adequate product and
371 process design and proper implementation and monitoring through HACCP. This places a
372 responsibility on industry, including small enterprises. There are more weak links, and overall
373 the processes are less robust and more accident prone. As the scale of operation of food
374 businesses continues to increase, errors may have a bigger impact.

375 Consumers need to be aware of the criticality of the formulations and of the need to treat
376 manufactured foods either as perishable products needing proper refrigeration or requiring
377 specific conditions of preparation (for instance non-Ready-To-Eat products that need to be
378 cooked properly before consumption even though they may appear to be cooked). The
379 concern is that many consumers do not habitually read labels and are unaware of shelf-lives
380 and preparation requirements.

381 Can these new product types offer niches for concurrent, old, emerging or new microbial
382 hazards? Classical examples are refrigeration and the niche created for *Yersinia* and *Listeria*,
383 and for sporeformers by non-thermal treatments at the pasteurization level. As in many of
384 these foods spoilage organisms have been removed or suppressed, there is increased
385 opportunity for the growth of pathogens that recontaminate treated products – in the absence
386 of the “normal” spoilage signal. Noroviruses show prolonged survival during cold storage and
387 even freezing. The probability and extent of survival and of post-process contamination,
388 rather than pathogen growth opportunity, may then determine the level of consumer risk.

389 While there would be a benefit from (and indeed a need for) for irradiation technology for
390 certain applications (e.g. it is “safe”, “invisible”, no microbial issues of resistance, or of
391 recontamination when done in-pack), consumer concerns towards the technology itself and
392 about misuse to make spoiled food marketable, prohibit its wider use in practice. This implies
393 considerable communication challenges, should the technology prove to be the treatment most
394 relevant for certain applications.

395 While reducing packaging is a laudable initiative where the packaging is for “cosmetic” or
396 bulk-transport purposes, industry and consumers should be aware of those situations where
397 the packaging has a preservative function by minimizing growth and/or recontamination of
398 microorganisms.

399 *Consumer behavior*

400 Several changes in food composition related to consumer health are foreseen. These may also
401 have an impact on bacterial growth. For instance, components like salt and sugar are often
402 used to inhibit the growth of organisms, both by their water activity lowering effect, and
403 additionally solute specific effects. Their concentration cannot be safely reduced for health or
404 other non-safety reasons without adapting the product design. On the other hand, fat can be
405 seen as a vehicle for better stomach survival of pathogens, so less fat might reduce risks.
406 Lower fat may also increase the water activity of a product by having more diluted solutes in
407 the aqueous phase (Senhaji, 1977).

408 Considering the present increased level of general health of the population and better medical
409 treatments, proportionally more elderly will be present in society. These elderly often are
410 more vulnerable to foodborne diseases partly, as a result of a weakened immune system
411 increasing the risks of complications and even death. Other defence systems, such as stomach
412 acid may be impaired (achlorhydria), augmented by medication.

413 Due to changes in eating habits, certain risks might change in magnitude. For example an
414 increased consumption of fish for health benefits may result in increased microbial risks. The
415 increasing trend for fresh, pre-packaged produce or other foods that are consumed without
416 additional heating by consumers also increases consumer risk. Exotic and ethnic foods are
417 now trendy in the market, but do we understand the underlying preservation system? When
418 we change these products (adapted for new markets; altered ingredients), are we clear on how
419 this may affect safety? More and more animal species are used for food production and there
420 is little knowledge about zoonotic risks of such foods (e.g. reptile meat, Magnino *et al.*,
421 2009). New culinary techniques, such as molecular gastronomy involve more and more
422 technical creativity and exotic ingredients to improve quality and consumer acceptance, which
423 may result in unexpected risks. In the case of small restaurants, catering establishments and

424 street vendors the scale of production is small and often, knowledge and sufficient technology
425 may be lacking, resulting in avoidable errors which may lead to serious consequences for
426 consumers.

427 Improving animal welfare (e.g. by increased outdoor access) and organic food production
428 may lead to the re-introduction of pathogens with wildlife reservoirs such as *Trichinella*
429 *spiralis* and *Toxoplasma gondii* and increase the prevalence of other hazards such as
430 *Campylobacter* spp. but may reduce the prevalence of others such as *Salmonella* spp.
431 (Gebreyes et al., 2008). Reduced usage of antimicrobial agents may have a positive impact on
432 resistance development (Van der Giessen *et al.*, 2007; Hoogenboom *et al.*, 2008). Trends
433 towards continuously increasing herd size in intensive bio-husbandry may also lead to
434 increased public health risks by increased numbers of contacts between food animals,
435 including purchasing of animals from more suppliers. The potential for infections to spread
436 increases with herd size, and if such farms are concentrated in particular regions, there is also
437 an increased risk of spread between farms. On the other hand, establishment of larger, newly
438 designed farms may improve conditions for biosecurity and farm management, potentially
439 reducing zoonotic risks (Kornalijnslijper *et al.*, 2008).

440 *Price*

441 It is well known that cost is a very important consideration for the consumer when selecting
442 foods, and that profits on food products are generally quite low. Both aspects make it difficult
443 to be critical towards food safety and furthermore might occasionally result in fraud. Also,
444 costs and conservatism may lead to resistance against implementing reasonable interventions
445 or to interpret existing regulations liberally (e.g. use of approval of sick animals for
446 consumption). Such non-compliance may increase consumer risk. The Law Enforcement
447 Department of the Netherlands Food and Consumer Safety Authority experienced during the
448 2008-9 economic downturn that food producers and retailers more frequently violate

449 regulations relating to cleaning and maintenance due to cost cutting (J. van der Kooij,
450 personal communication). Increasing food prices are likely to compromise food security (in
451 terms of food availability) on a global scale. For industrialized countries, food security is less
452 at risk, but consumers may choose less costly alternatives. This may lead to less consumption
453 of animal proteins (also driven by animal welfare and environmental considerations), leading
454 to other health-related issues. Higher food prices may cause consumers to use food more
455 frequently past its shelf life, and may increase recycling of food.

456 *Global aspects*

457 Due to the increase of international travel, organisms can be spread easily and quickly over
458 the globe, and people come in contact with organisms and specific strains to which they have
459 not been exposed earlier, increasing the risk of illness. Global trade will result in a longer
460 transit distances and durations in the food chain, possibly increasing risk. Furthermore,
461 complex food chains with stakeholders in many different countries will make the management
462 of safety more difficult, especially at the initial stages of the food chain, the primary
463 production as it consists of many small farms and is increasingly global in nature. On the
464 other hand more powerful stakeholders (trade companies, supermarkets) will have the
465 intention to influence these complex chains in order to guarantee food safety. Several large
466 retailers that operate internationally have organized the GlobalG.A.P. quality control system
467 (www.globalgap.org) that aims to supervise the primary production process of all agricultural
468 products. Sourcing food from various climate areas means more variation in hazards. Border
469 controls are effective in regard to the control of only a small proportion of imported foods and
470 are less effective than hygiene controls imposed in the country of origin. Furthermore, global
471 food chains may be more vulnerable to terrorist attacks.

472 More and more harmonization will occur in international regulation of food safety by the
473 activities of e.g. the Codex Alimentarius Commission and the European Union. As a positive

474 effect, fairness in trade will increase but on the other hand the same level of contamination in
475 food may result in very different health risks in different parts of the world, due to differences
476 in e.g. demography, immune status, food preparation and consumption habits, and relevance
477 of various routes of infection.

478 *Climate change*

479 Climate change is considered to be one of the greatest current challenges to mankind,
480 affecting all sectors of society, including nutrition, food security and food safety
481 (Anonymous, 2008b). Due to climate change various risks may change, as a result of changed
482 ecological conditions on various places on the earth. Changing ecology is expected to affect
483 the distribution of plant and animal diseases. Water shortages may lead to limited quantities
484 or quality problems with irrigation water, process water or ingredient water. This may lead to
485 shifts in production areas and cultured crops, as well as an increased use of agrochemicals.
486 This trend may be increased by competition for land-use, e.g. for biofuels or for settlements.
487 Flooding may lead to increased contamination of crops in the field, or increased exposure of
488 food animals to zoonotic agents. Control of cold chains may be impeded by rising ambient
489 temperatures. Humidity may increase production of mycotoxins, whereas certain foodborne
490 pathogens may thrive better under warm conditions. The mechanisms by which climate
491 change affect food safety are highly complex and interrelated with many other societal
492 factors, The outcome of these changes strongly depends on the adequateness of societal
493 responses, both of a technical and a political nature.

494 *Science*

495 More and more public health risks, physiological and ecological traits of foodborne
496 pathogens, routes of contamination, effects of interventions, will be investigated and
497 quantified, making it possible to better balance risks, and evaluate optimal interventions to

498 control risks to an appropriate level. That is, science will have a greater role in setting criteria
499 both nationally and in international trade agreements.

500 The genomics revolution will facilitate easier and faster detection and identification methods,
501 and can in particular lead to a better mechanistic understanding of the behavior of micro-
502 organisms, both their physiology as well as their ecology. Furthermore new pathogens can be
503 uncovered, for example better detection of injured and thus less easily culturable organisms is
504 possible and more advanced methods to investigate cases and outbreaks become available.

505 *Antimicrobial resistance*

506 Usage of antimicrobial agents, both in the agricultural sector and in human health care
507 settings, contributes to the emergence of resistant microbes. While resistance in the
508 agricultural sector might be considered an economic problem with limited other
509 consequences, it is developing into a cause of growing concern for human health care (see
510 Newell et al., in an accompanying paper in this Special Issue). The overall use of
511 antimicrobial agents in food animals is high and in certain countries largely exceeds the
512 human use. The ban on usage of antimicrobials as growth promoters has, in some countries,
513 barely had an influence, as it has been replaced by increased use for therapeutic purposes
514 (Mevius and Van Pelt, 2006). Micro-organisms have an immense diversity and can easily
515 transfer genetic information, making the emergence of new hazards, and adaptation to
516 previously effective intervention methods possible.

517 At present, it is not clear what proportion of resistance encountered in human pathogens
518 originates from selection in and transfer from animal reservoirs. It is not known if measures to
519 reduce usage in the agricultural setting will lead to a rapid reduction of resistance, as this can
520 also contribute in other ways to overall fitness of the micro-organism. The benefits to human
521 health care of such measures are not quantified, as resistance may also develop due to other

522 factors. In spite of these uncertainties, the development of antimicrobial resistance in
523 agricultural settings is a cause of growing concern to public health and prudent use is
524 advocated.

525 **5. Epidemiology and surveillance**

526 Monitoring of contamination in the food chain, combined with surveillance of human illness
527 and epidemiological investigations of outbreaks and sporadic cases continue to be important
528 sources of information to evaluate the success of current food safety management systems and
529 to identify new hazards. Surveillance is defined as “the ongoing and systematic collection,
530 analysis, and interpretation of data about a disease or health condition; used in planning,
531 implementing, and evaluating public health programs” (Anonymous, 2000a). Surveillance can
532 be aimed at outbreaks or sporadic cases of foodborne disease, and continues to be a
533 cornerstone of food safety management (see the accompanying paper by Tauxe *et al.*, in this
534 issue).

535 Outbreak surveillance primarily aims to stop the outbreak by identifying incriminated
536 products and taking them from the market. Furthermore, investigations may aim to prosecute
537 those responsible, or to learn from outbreaks so as to avoid future outbreaks by identifying
538 unsafe practices that had led to the outbreak. Outbreak investigations have and will continue
539 to be an important instrument for identifying new pathogens (e.g. *Cyclospora cayatenensis*,
540 Herwaldt, 2000), new vehicles for known pathogens (e.g. *Salmonella* Tennessee in peanut
541 butter, Anonymous, 2007c), new disease syndromes associated with known pathogens (e.g.
542 febrile gastroenteritis associated with *Listeria monocytogenes*, Dalton *et al.*, 1997), and the re-
543 emergence of problems that were thought to be under control (e.g. botulinum toxins in canned
544 foods, Ginsberg *et al.*, 2007). They are important sources of data for establishing the

545 economic impact of foodborne illness on populations and may provide dose-response
546 information for microbial risk assessment (Teunis *et al.*, 2008).

547 Many countries have surveillance systems for outbreaks of foodborne illness and data are
548 reported at an aggregated level annually (Anonymous, 2007a) or over a number of years
549 (Wang *et al.*, 2007, Cretikos *et al.*, 2008). New tools are becoming available to detect
550 international outbreaks for foodborne viruses (Verhoef *et al.*, 2009). Supranational agencies
551 such as EFSA and ECDC in Europe present regular reports on foodborne outbreaks in a larger
552 region or globally (Anonymous, 2007a). Outbreak summary reports provide important
553 insights in current and emerging food safety problems but it is essential that such summaries
554 are based on systematic surveillance activities. Reports in the peer-reviewed literature may
555 suffer from publication bias and overestimate the impacts of milk/milk products,
556 miscellaneous foods (e.g. sandwiches) and desserts while underestimating those of poultry,
557 fish and shellfish, red meat/meat products and eggs/egg products (O'Brien *et al.*, 2006).

558 Molecular tools identifying causative agents in environmental and clinical samples, and
559 molecular typing techniques identifying nucleotide sequences of single genes (i.e. *fla*-typing),
560 techniques identifying sets of genetic elements (MLST, MLVA) and various restriction
561 techniques (i.e. PFGE) have proven to be very useful aids in the epidemiology of foodborne
562 illness. Developments in genotyping of pathogens and informatics have enabled the
563 recognition of diffuse or multinational outbreaks which were previously unnoted (Gerner-
564 Smidt *et al.*, 2006, Kirk *et al.*, 2004, Kroneman *et al.*, 2008).

565 Estimating the incidence of sporadic cases of foodborne illness is more complex. Most
566 existing surveillance systems are based on either notifiable disease reporting or laboratory
567 surveillance. Both systems are passive in nature, and record only a minor proportion of all
568 cases in the population. To estimate the true incidence of diseases that can be transmitted by
569 food, active surveillance is necessary and more accurate estimates are needed for under-

570 reported illness. The UK (Wheeler *et al.*, 1999, Tompkins *et al.*, 1999) and the Netherlands
571 (De Wit *et al.*, 2001a, De Wit *et al.*, 2001b, De Wit *et al.*, 2001c) have carried out population-
572 based prospective studies of infectious gastro-enteritis, combined with laboratory diagnostics
573 to assess the proportion of cases due to specific pathogens. Currently, the UK has launched
574 the second IID study (<http://www.iid2.org.uk>). Even in these large-scale projects, in a large
575 proportion of cases (60%) it was not possible to identify a causal pathogen. However, it
576 appears to be possible to reduce this diagnostic gap by the application of molecular methods
577 (Amar *et al.*, 2007). Population-based studies are expensive and time consuming, and several
578 countries have attempted to develop less costly alternatives. These include FoodNet in the
579 USA (Jones *et al.*, 2007), OzFoodnet in Australia (Kirk *et al.*, 2008), and the International
580 Collaboration on Enteric Disease Burden of Illness Studies (Flint *et al.*, 2005, Roy *et al.*,
581 2006, Thomas *et al.*, 2006). As laboratory-based surveillance only detects a fraction of all
582 illness occurring in the population, modeling approaches have been used to reconstruct the
583 surveillance pyramid (Michel *et al.*, 2000, Voetsch *et al.*, 2004, Majowicz *et al.*, 2005).
584 Serosurveillance is now being explored as a new tool to provide internationally comparable
585 estimates of the exposure of populations to foodborne pathogens (Simonsen *et al.*, 2008).
586 Although most surveillance activities are focused on gastro-intestinal illness, other symptoms
587 are also commonly associated with foodborne illness. These may be more serious or of longer
588 duration than GI illness. Furthermore, most pathogens that can be transmitted by food may
589 also be transmitted by other pathways such as water, direct human and animal contact.
590 Therefore, there is a need for source attribution to quantify the proportion of all cases that is
591 foodborne, and the food vehicles that are most frequently associated with illness (Batz *et al.*,
592 2005). Molecular typing has successfully been used for source attribution of salmonellosis
593 (Van Pelt *et al.*, 1999, Hald *et al.*, 2004) and more recently for campylobacteriosis (Wilson *et*
594 *al.*, 2008). Other methods being explored include case-control studies, outbreak studies, risk

595 assessment modeling, natural or deliberate intervention studies at population level and expert
596 elicitation. Each method is subject to specific biases, and may attribute illness to different
597 points in the food chain. Therefore, interpreting the results from attribution studies should be
598 done with care (Pires et al., 2009).

599 The World Health Organization has recently launched a new initiative to estimate the burden
600 of foodborne illness on a global scale (Stein *et al.*, 2007). This initiative is advised by experts
601 of the Foodborne Epidemiology Reference group (FERG), which assembles and appraises
602 global evidence on foodborne disease epidemiology. This action is considered necessary in
603 view of globalization, and to contribute towards meeting the Millennium Development Goals¹.
604 Results will be a basis for action at the global scale. Virtually no data on morbidity and
605 mortality exist in large areas of the world, and even more data gaps are expected for
606 attribution. Therefore, systematic reviews will be carried out and extrapolation will be
607 necessary. As an example approach, the estimates of death from diarrhea for children under 5
608 from the Childhood Epidemiology Reference group (CHERG) will be used (Boschi-Pinto *et*
609 *al.*, 2008); complemented with other methods, including expert opinion.

610 In addition to surveillance of human illness, systematic food chain surveillance is necessary to
611 inform food safety decision making. Recent EU-wide baseline studies on the prevalence of
612 zoonotic pathogens have illustrated the benefits of such standardized sampling and analytical
613 approaches. For example, in the baseline survey on the prevalence of *Salmonella* in slaughter
614 pigs, which took place between October 2006 and September 2007, it was demonstrated that
615 approximately one out of every ten slaughter pigs in the European Union was infected with
616 *Salmonella* in the lymph nodes, while one out of twelve pig carcasses was contaminated with
617 *Salmonella*. The survey also indicated large differences between Member States (Anonymous,
618 2008c). These data will be the basis for risk assessment and cost-benefit analysis of

¹ <http://www.un.org/millenniumgoals/>

619 *Salmonella* control in the slaughter pig chain to support decision making by European risk
620 managers.

621 The previous sections have described a highly complex set of interrelated factors affecting
622 future trends in food safety. Predicting the impact of these factors is highly complex and
623 surrounded by uncertainties. Hence, to be able to respond timely and appropriately, active,
624 real-time surveillance in both the human and food system and communication to professionals
625 responsible for infection control is of utmost importance.

626 **6. Methodology**

627 *Molecular Methods for complex food analysis*

628 One of the key challenges in food microbiology that has always been around and can now be
629 addressed is to assess what molecular mechanistic processes underlie the observed
630 physiological behavior of pathogens in food (see e.g. McMeekin *et al.*, 2007). Much of this
631 work relies on a proper identification of (a) the microorganisms in the food at hand and (b)
632 the food components that are relevant in determining the microbial stability of such foods.
633 The latter range from small molecules (flavor-like molecules, food preservatives and other
634 organic molecular) to the macro-ingredients i.e. proteins (peptides), sugar (polymers) and fats.
635 In many foods the microbes that are to be analyzed for are non-uniformly dispersed
636 throughout the product. This is the case for many ready-to-eat products from the chilled food
637 chain and is equally so for liquid products such as sauces and soups in which particles, as
638 putative sources of microorganisms, may be non-uniformly mixed.

639 Analysis of microorganisms in foods may be done with two objectives in mind. On the one
640 hand it may be a direct assessment related to production processes or inspection, on the other
641 hand it may be research-oriented in which physiological inferences are made from molecular
642 data. Rapid analysis techniques for use in industrial practice have to be easy to perform, low

643 cost, optimally selective and must demonstrate reproducible sensitivity and specificity. Such
644 methods need to be validated and written down in standardized protocols, preferably being
645 able to provide quantitative data of use in risk assessment and in food safety management.
646 Currently they are generally based on DNA detection systems, either specific for ribosomal
647 genes, or in the more advanced systems for specific sequences that occur along the entire
648 genome (see e.g. Wattiau *et al.*, 2008; Scaria *et al.*, 2008). Comparative genome sequencing is
649 certainly at hand nowadays. Thus, in the case of relevant, closely related bacterial isolates it is
650 increasingly easy to identify unique sequences (see e.g. the discussions in Earl *et al.*, 2008
651 and Medini *et al.*, 2008). Many of these may then be used to derive sequences amenable to
652 use in DNA chip and / or PCR based detection platforms to the benefit of the safety
653 assessment of food processing.

654 Although these methods are fast, highly specific and relatively sensitive, the application of
655 molecular-based techniques in the control of food safety seems to be limited as they suffer
656 from some serious drawbacks. The development of a horizontal method is seriously hampered
657 by the fact that food products may contain interfering components. The development of
658 horizontal methods becomes even more difficult due to a constant introduction of new
659 matrices. While they are very sensitive, low copy numbers are difficult to detect when the
660 sample size is very small. Introduction of an enrichment step preceding DNA-detection is a
661 solution, but this makes results qualitative, rather than quantitative unless cumbersome MPN
662 techniques are used. While this may not be problematic for quality assurance purposes,
663 quantitative results may be necessary for risk assessment studies. Sample preparation needs
664 close attention. Preferably, such sampling needs to be rapid and as homogeneous as possible.
665 Innovative strategies focus on the use of magnetic beads coated with cell-recognizing
666 molecules, on physical methods such as floatation, and on lysis of whole food matrices
667 (Wagner and Dahl, 2008). The latter was described originally by Hein and co-workers who

668 obtained enough bacteria from a complex set of food matrices in one-step approach taking
669 only a few hours to be able to recover DNA for further study (Rossmannith *et al.*, 2007). It has
670 yet to be established that such a procedure will also be effective for determining the
671 concentration of bacterial spores. A limitation of currently available molecular techniques is
672 also that they fail to discriminate between viable and inactivated organisms. Recent research
673 may provide future practical solutions to this as transcriptional activity around bacterial cell
674 survival / death reveals molecular markers for cell viability (Kort *et al.*, 2008).

675 Finally, assays based on detection of multiple virulence genes can still give ambiguous results
676 if there is a mixed culture to begin with. This may be for instance the case for the detection of
677 the Shiga like toxin (stx) and Intimin (eaeA) genes from *Escherichia coli* in direct molecular
678 analyses on food samples (e.g. Monday et al, 2007). The outcome will be positive with one
679 strain having both or two strains, each having one of the virulence genes.

680 The issues discussed above corroborate the notion that it is necessary to properly validate
681 such newly developed techniques. How do they compare to standard reference culture
682 techniques described in ISO-protocols, and which controls must be used? Information is
683 available on the efficacy of protocols using spiked samples, but little information is available
684 on the efficacy of developed protocols in case of naturally contaminated samples. Without
685 multi-laboratory validation, protocols for molecular techniques can be used for in-house
686 purposes, but to be used as a standard method for the detection of pathogens, molecular
687 techniques have to be validated, using a multi-laboratory approach, according to the ISO-
688 16140 protocol.

689 In analyzing the composition of foods it is also more and more possible to detail
690 comprehensively the full chemical spectrum of the compounds observed. To this end tools
691 such as liquid chromatography (LC) or gas chromatography (GC) coupled to mass
692 spectrometry (MS) are increasingly successfully used (reviewed in Hounsome *et al.*, 2008). A

693 full analysis provides valuable information on product quality as well as the environmental
694 parameters that can be most relevant to microbial survival (Beckmann et al., 2007). The
695 analysis may also be used to detect the presence of microbial spoilage (Ellis et al., 2007).
696 Pattern analysis to identify relevant compounds is the area where developments are rapid.
697 While the costs of detection at the DNA level are increasingly reducing and interpretation of
698 the data can now be automated to a large extent, this is not always as straightforward with the
699 measurements of small to medium sized (mostly) organic molecules (see e.g. review by
700 Hounsome *et al.*, 2008).

701 In the research area, molecular techniques are widely used. They can be used for the
702 identification of organisms, for behavioral studies or for studying genes involved in (the
703 regulation of) virulence and stress in response to different environmental conditions, while
704 they can also be used in evolutionary studies. This approach marks the second objective, i.e.
705 the use of genomics data to underpin physiological observations and to mechanistically
706 'explain' them. Here the analysis platform used need not be restricted to the cheaper methods,
707 focused on biomarkers only; in fact the approach should be wider in nature while costing
708 marginally more (though cost-effectiveness remains an important parameter). To pinpoint
709 which type of compound has the most effect on the microorganisms at hand it is useful to
710 analyze the genome-wide expression pattern and use the data obtained as a bioassay to
711 identify the physiologically most sensitive environmental cues. Translation of molecular data
712 into a biological meaning remains an essential subject for future studies. Application of
713 techniques from other disciplines like ecology and medicine will be very useful.

714 *Mining molecular data for new threats; metabolic capability models*

715 New methods to screen sequenced genomes with the aim of understanding the physiological
716 capability of microbes have led to the identification of major differences at the genome level
717 between common laboratory strains of e.g. *E. coli* K12, enterohemorrhagic *E. coli* and

718 uropathogenic *E. coli* (Brzuszkiewicz *et al.*, 2006; Fraser-Ligget, 2005; see also Perna *et al.*,
719 2001). Extending the analysis with state of the art rapid sequencing technique to other
720 pathogens such as bacilli and certain streptococci has led to the realization of the so-called
721 'pan' and 'core' genome concepts (see e.g. Hiller *et al.*, 2007, Ara *et al.*, 2007 and the
722 discussion in Medini *et al.*, 2008). In this classification the pan-genome is seen as being
723 composed of three elements: the core genome, a set of non-essential genes shared by several
724 isolates (strains) of the species, and a set of genes unique to an isolate. The size of each can
725 significantly differ from species to species. The core genome generally gives the basic
726 metabolic requirements of a certain species whereas the genetic plasticity of strains is
727 generated by the other sequences (Medini *et al.*, 2008 for general concepts and Earl *et al.*,
728 2008 for specifics regarding bacilli). Data on the core genome aid significantly in defining the
729 metabolic potential of an organism. Flux Balance Analysis is then often used as a modeling
730 approach to find the possible steady states that the organism can attain (Schilling, 2000). In a
731 next step such models may be detailed further to incorporate molecular signaling data at
732 various levels of complexity (see Ropers *et al.*, 2006 for a highly detailed model of carbon
733 starvation in *Escherichia coli*). Such extension should at all times be subject to scrutiny
734 though in assessing its use given the investment of effort needed versus the (food)
735 microbiological problem at hand needs to be considered.

736 **7. Interaction between micro-organisms and their environment (foods) and microbial** 737 **evolution**

738 *Understanding short-term adaptations of microbes*

739 The recent genomics revolution has facilitated the interpretation of the molecular basis of
740 microbial behavior. Examples stem from many fields and range from bacteria to filamentous
741 fungi. The response to high-end temperature stress conditions often characteristic of the

742 manufacturing process of savoury products is nowadays studied at the molecular level. This is
743 most relevant to aerobic bacterial spore formers. Various strains of bacilli produce spores
744 resistant to temperatures up to and well above those of classical sterilization at 121°C (Oomes
745 *et al.*, 2007). Keijser *et al.*, (2007) showed that spores express specific stress response genes
746 during germination, some of which are likely responsible for repair of incurred thermal
747 damage (see also Setlow 2006). In order to aim at understanding spore behavior after a
748 thermal stress, in particular mechanisms of heat damage repair, we now have the possibility of
749 utilizing the genome information for *Bacillus subtilis* 168 (Kunst *et al.*, 1997).

750 Cells subjected to acidic food conditions or to low water activity environments have been
751 studied extensively in the context of food microbiology. Specific examples of food
752 preservative stresses are those where cells have to respond to the antimicrobial action of a
753 weak-organic acid such as sorbic acid. The latter is the most widely used food preservative.
754 The common view is that the cells initially use energy driven pumps to extrude the acid from
755 the cytosol while upon full adaptation they induce the synthesis of pumps specific for
756 lipophilic weak acids (discussed for yeast extensively in Mollapour *et al.*, 2008; for recent
757 original research on sorbic acid stress response in vegetative bacteria see Ter Beek *et al.*,
758 2008).

759 Stress adaptation of microorganisms in foods or upon being exposed to food processing
760 conditions may lead to the induction of survival systems and could even induce virulence in
761 pathogens. Many phenomena i.e. resistance to preservatives, oxidizing agents and natural
762 extracts in foods are as important for successful infection as are mechanisms operative in 'in
763 host', actual infection, and survival. Erickson and Doyle (2007) have illustrated this
764 extensively for Shiga toxin-producing *Escherichia coli* and its survival on fresh produce, meat
765 and in unpasteurized juices. Successful activation of stress response systems by some but not

766 all strains may be instrumental in letting some strains adapt to the 'adverse' conditions in the
767 food chain.

768 *Presence and development of microbial virulence traits in non-human environments*

769 The following section will provide some selected examples of microbial virulence traits of
770 relevance to man of organisms present in non-human environments.

771 Foodborne pathogens may survive well in the animal production chain. Classical examples
772 include *Campylobacter jejuni*, an organism not pathogenic to avian species but highly
773 pathogenic to man (reviewed by Poly and Guerry, 2008). The organism is widely spread, as
774 was demonstrated again by, for instance, the studies of Fearnley *et al.* (2008). These authors
775 demonstrated the occurrence of hyperinvasive *Campylobacter* strains in isolates both from
776 poultry and from human sources. There is not much data yet on the molecular basis of
777 infection, be it that information on the intracellular signal transduction cascades of the
778 organism becomes more and more available (Boyd *et al.*, 2007).

779 *Salmonella* species are well-known pathogens for animals and man. Callaway *et al.* (2008)
780 have recently described their occurrence in various types of cattle. Sternberg *et al.* (2008)
781 described an outbreak of *Salmonella* infection in a Swedish dairy herd. Schmidt *et al.* (2008)
782 reported on *Salmonella enterica* infections in Swiss cattle in the summer of 2008. The various
783 serovars have meanwhile been characterized at the molecular level (Edwards *et al.*, 2002).

784 The use of such data can be in two non mutually exclusive directions. On the one hand the
785 data provide information for use in quality control settings and epidemiological surveillance.
786 On the other hand the gathered information can be used as a starting point in the formulation
787 of novel research questions such as the molecular physiological mechanisms behind the
788 observed microbial ecology. Studies aiming at answering such questions will require next to
789 kinetic data on microbial metabolism measured at the population level, also quantitative data

790 on cell - cell variation in microbial stress response in order to allow incorporation in next
791 generation predictive food microbiology models (McMeekin *et al.*, 2007). Both for non-
792 pathogenic *B. subtilis* and for pathogenic *B. cereus*, spore formation of strains attached to
793 naturally occurring biofilms is a well known phenomenon (Lindsay *et al.*, 2006). It has also
794 been documented nicely that spore-formation in a biofilm-like environment, a complex
795 colony, leads to spores with a higher thermal resistance than that observed in spores
796 originating from liquid cultures (Veening *et al.*, 2006). The (thermal) stress resistance of
797 spores is again not a direct virulence trait but it does contribute to survival in the animal chain
798 as well as transfer to the human food chain (Huck *et al.*, 2008). As such it is a crucial
799 determinant of the likelihood of intoxication of the host. Other such virulence characteristics
800 of e.g. *Bacillus cereus* include the resistance of the spores (and vegetative cells) to acid
801 facilitating the 'settlement' and toxin production of the organism in the intestine (Wijnands,
802 2008; see also Stenfors Arnesen *et al.*, 2008).

803 *Predictive modeling*

804 Crucial is the conversion of molecular physiological 'analogue' data at the population level to
805 data at the level of single cells relevant to the prediction of the behavior of low-numbers
806 exposed to stressful environments (discussed in McMeekin *et al.*, 2007; see for original
807 research amongst others Den Besten *et al.*, 2007). This provides insight into the link between
808 the genome, gene-expression, protein and metabolic functional cellular units (see for the
809 original physiology data Balaban *et al.*, 2004).). Koutsoumanis (2008) provides a clear
810 example of the variability in growth limits of individual *Salmonella* Enteritidis cells subjected
811 to NaCl stress. Another highly relevant example is the quantification of the germination and
812 outgrowth processes operative in bacterial endospores (Stringer *et al.*, 2005; Smelt *et al.*,
813 2008). Both examples do not yet include a mechanistic analysis e.g. at the level of inclusion
814 of genome-wide expression data. The initial challenge for future research is to do just that i.e.

815 study at single cell / spore level the molecular physiology in order to enable the generation of
816 mechanistic models that describe the cellular heterogeneity in genetically homogeneous
817 microbial populations. Phenotypic heterogeneity in microbial populations mediated by bi-
818 stable signaling networks is a much discussed topic in general microbiology (e.g. Veening et
819 al., 2008, Locke and Elowitz, 2009). To be of relevance to (predictive) food microbiology this
820 will require performing experiments under the relevant physiological (food) conditions and as
821 much as possible with the relevant food isolates.

822 *Taxonomy*

823 Regulators in the US use the GRAS approach (generally recognized as safe) to assess the
824 safety of microbes used in food production, while the EFSA employs the QPS (qualified
825 presumption of safety) system (Anonymous, 2007d). Basically it is assumed that a micro-
826 organism that has been used for a considerable time in food manufacturing without causing
827 problems can be considered “safe”. The difficulty in establishing these regulatory systems is
828 the breadth of the taxonomic unit for which QPS or GRAS status can be conferred. If it only
829 can be conferred at strain level, a full risk assessment will still have to be performed for any
830 other strain, even those that are closely related to the ones having GRAS or QPS status. If it is
831 applied at an overly high level, e.g. genus, it can happen that pathogenic cousins of a safe
832 strain are wrongly considered harmless. The taxonomic units concerned are defined in the
833 QPS list and the list is reviewed every year to take into account changes in the taxonomy and
834 other considerations. If the history of safe use and the body of knowledge concerns only one
835 strain, this property cannot be generalized to apply to the entire species, (an example is the
836 *Enterococcus* spp). That is, if there is a risk that closely related strains of the safe strains are
837 pathogenic, the taxonomic unit, species or genus, is not given QPS status, unless the
838 pathogenic strains can be specifically identified, for instance by the presence of virulence

839 factors. In the latter case the unit can be QPS, but with additional qualification. This is, for
840 instance, the case for some *Bacillus* species.

841 Guidelines for the selection of “safe” cultures for biopreservation exist in the area of feed, but
842 not for food (apart from the probiotics area). For general biopreservation, screening of
843 cultures for virulence factors or other genes coding for undesirable properties would be
844 relevant as well as studies of cultures possibly acquiring resistance.

845 For the approval of specific biopreservation agents (e.g. bacteriocins such as nisin)
846 governmental as well as academic and industry views on the criteria to be applied differ
847 around the world. Inconsistencies can cause problems, especially where criteria for safety
848 evaluation or for an agent’s effectiveness are too lenient or because they do not take sufficient
849 account of ill-informed use of such agents. The inverse, when a harmless strain is considered
850 pathogenic is less problematic as the only consequence is that the strain undergoes an
851 unnecessary safety assessment. Safe and robust use would need to follow general guidelines
852 on the steps to be taken, as defined in the safe design of the product or the process.

853 **8. Risk communication and education**

854 *Collaboration/communication between scientists*

855 Historically, food systems used to be fairly simple; most foods were produced and eaten
856 locally. Nowadays, a large share of our diet is produced in another country, and not
857 uncommonly, several food ingredients come from different parts of the world (Käferstein *et*
858 *al.*, 1997). Furthermore, we prefer to eat the food as fresh as possible (Doyle and Erickson,
859 2008). This trend increases the need for worldwide food safety systems and thus collaboration
860 and communication between all players in the food chain. As food chains extend or expand
861 from local chains into worldwide chains, more and different factors may affect food safety.
862 This implies that for food safety management knowledge or information from different

863 scientific disciplines needs to be combined. Furthermore, the format in which information is
864 made available needs to be standardized.

865 Food safety starts at primary production. To reduce the risk of foodborne gastroenteritis,
866 especially for foods to be eaten raw, such as fresh produce and shellfish, knowledge about
867 contamination routes and preventive measures is of great importance. In certain cases
868 interventions could be effective early in the primary production phase, including the
869 production environment. For fresh produce, grown in the open field, *Escherichia coli* (in
870 particular the verocytotoxin producing strains VTEC) is, amongst others, a food safety
871 hazard. This is underlined by a massive foodborne infection outbreak in the USA in 2006
872 (Anonymous, 2007e) caused by baby spinach eaten raw. The probable source of the VTEC in
873 this outbreak was either irrigation water, or feces from cattle or wild boar. Cattle are a known
874 source of this pathogenic bacterium (Hussein and Sakuma, 2005), yet cow manure continues
875 to be used as a main soil fertilizer in organic farming (Anonymous, 2000b). Preventive
876 measures could be a change of feeding diet in order either to reduce numbers of VTEC shed
877 by cattle (Diez-Gonzalez *et al.*, 1998; Synge, 2000) or to reduce their survival in manure-
878 amended soils (Franz *et al.*, 2005). Thus, produce safety can be increased in this case by
879 combining agricultural science and (food) microbiology.

880 In other outbreaks, preventive measures are straighter foreword. In 2008, a *C. jejuni* outbreak
881 in Alaska was linked to the consumption of raw peas contaminated on the field by Sandhill
882 crane feces. The outbreak investigation identified a lack of chlorine residual in pea-processing
883 water, which could have been easily prevented (Gardner and McLaughlin, 2008). Introducing
884 buffer zones, set-back distances and fences to restrict wildlife access to the production
885 environment of produce such as leafy greens may prevent problems with feral swine or deer
886 (Atwill, 2008). Although these solutions seem sometimes fairly simple, they could only be

887 taken due to a proper outbreak investigation that elucidated the (probable) source of the food
888 contamination.

889 In order to stop an ongoing outbreak, such outbreak investigations should be carried out
890 quickly, which relies on close collaboration between different (scientific) disciplines such as
891 microbiologists, epidemiologists, wildlife control specialists, risk communicators, etc, often
892 represented by different organisations or institutes, which may hamper the investigation.
893 Although not standing on its own, the lack of proper communication between different
894 scientific disciplines and/or institutes/departments during an outbreak investigation is shown
895 in the 2009 U.S.A. *Salmonella* Saintpaul outbreak caused by raw jalapeño and serrano pepper
896 in which more than 1400 cases were registered. This outbreak continued to spread due to
897 malfunctioning at the level of policy, the public-health system's organization and outbreak
898 response, and its communications with the media and the public as concluded by the post-
899 mortem investigation into this outbreak (Anonymous, 2008). This clearly shows that
900 collaboration of scientific disciplines is eminent to increase the safety of our food system.

901 Other examples that demonstrate the added value of combining different expertises to limit
902 the risk of foodborne illness are for instance *Vibrio* spp. in shellfish and mycotoxins in grain
903 (products). The quality of shellfish depends on the quality of the water they are grown in.
904 Pathogenic bacteria of importance in these types of products are *Vibrio* spp. The number of
905 vibrios present in the water is positively related to the water temperature (Motes *et al.*, 1998)
906 and models that predict ocean water temperatures can be used to predict the level of these
907 pathogens in shellfish, thus combining (food) microbiology and oceanography, Ford *et al.*,
908 2009). This knowledge was used by Californian lawmakers in order to ban the sale of raw
909 oysters from certain waters during the warmer months of the year (Anonymous, 2003). The
910 presence of mycotoxins on grain products is affected by weather conditions during growth
911 and harvest. As humidity increases, growth increases of the moulds that produce mycotoxins

912 on these products. Thus meteorological data are a reliable indicator of the risk of the
913 concentration of mycotoxins on grain products (Schaafsma and Hooker, 2007; Van der Fels-
914 Klerx *et al.*, 2008).

915 To determine which intervention strategy is the best or most cost effective to be taken to
916 reduce risk of foodborne illness, a detailed risk assessment needs to be conducted and
917 combining with a proper economic analysis may prove necessary. This requires a highly
918 multidisciplinary approach, involving microbiologists, epidemiologists, risk modelers,
919 economists and social scientists (Havelaar *et al.*, 2007a). An example of this approach is the
920 CARMA project, carried out in the Netherlands, to evaluate options to reduce the risk of
921 campylobacteriosis due to consumption of chicken meat (Havelaar *et al.*, 2007b).

922 For risk assessment studies, many data are needed like prevalence and numbers of foodborne
923 pathogens in food. However, these data are not always available or are not in the correct
924 format. For instance, data on the occurrence of *Salmonella* in food is mainly available as
925 “presence or absence in 25 g of product” as legislation requires testing based on this criterion
926 (Anonymous, 2005a). For risk assessment studies, however, the exact level of contamination
927 is important (Malorny *et al.*, 2008). Even when data are available in the preferred format,
928 problems may arise with nomenclature of foods or lack of other necessary details. For
929 instance, a meatball can be either made from beef or pork or a combination of both. And
930 problems increase with multiple-ingredient products, such as in lasagna. Uniformity in
931 nomenclature of foods is, therefore, of great importance and a tool such as LanguaL, a food
932 description thesaurus (www.langua.org), can be very useful.

933 In many food consumption surveys foods are categorized as, for example “beef with or
934 without sauce”, whereas the degree of cooking of the meat is of greater microbiological
935 relevance. To improve the use of data generated in food consumption surveys, closer
936 collaboration between risk assessors, food microbiologists and nutritionists is needed.

937 In the Netherlands, the Dutch Food and Consumer Product Safety Authority (VWA) works
938 closely together with the National Institute for Public Health and the Environment (RIVM) to
939 improve the quality and usefulness of the data obtained from routine monitoring programs of
940 the microbiological quality of foods. Some recent studies focused on the relative
941 microbiological risk to consumers associated with the consumption of fresh vegetables
942 (Pielaat and Wijnands, 2008) and prevalence of potentially pathogenic *Bacillus cereus* in food
943 (Wijnands *et al.*, 2006). A simple, spreadsheet-based tool is being developed to assess
944 consumer risks associated with such products using available data (Evers and Chardon, 2008).

945 These examples clearly show the benefits of inter- and intra- scientific collaboration. Close
946 personal collaboration may not always be necessary when data can be shared by other means.
947 In the scientific literature, many data are published that can be used by others. However,
948 translation of these data to a uniform data set is time consuming. In order to improve sharing
949 of data on microbial growth and inactivation, the ComBase Initiative was established, a
950 collaboration between the Food Standards Agency and the Institute of Food Research from
951 the United Kingdom, the USDA Agricultural Research Service and its Eastern Regional
952 Research Center from the United States and the Australian Food Safety Centre of Excellence
953 (Combase Consortium, 2008). ComBase is a combined database of microbial responses to
954 food environments and data can be used for predictive modelling. Recently, Combase started
955 a collaboration with the Journal of Food Protection, which request authors to submit their data
956 to the Combase database. A clearinghouse of interdisciplinary data is offered by Foodrisk.org,
957 an initiative of the Joint Institute for Food Safety and Applied Nutrition (JIFSAN), and which
958 is a collaboration between the University of Maryland (UM) and the Food and Drug
959 Administration (FDA). The clearinghouse provides data and methodology on food safety risk
960 analysis offered by the private sector, trade associations, federal and state agencies, and
961 international sources (www.foodrisk.org).

962 In conclusion, although interdisciplinary collaboration sounds very promising, it must be
963 noted that it is generally not straightforward as, for instance, the data thus made available may
964 be limited or be in the wrong format. Despite this, with some extra effort more progress may
965 be achieved than would otherwise be the case.

966 *Education*

967 New trends in food consumption patterns, e.g. the consumption of raw foods, and the
968 introduction of a wide variety of newly developed food products with each their specific way
969 of preparation (e.g. ready-to-eat; ready-to-heat), in combination with an increase in the
970 number of vulnerable people, require clear communication about food safety aspects,
971 communication between industry, consumer and government.

972 Risk managers should be aware and understand public concerns about food safety as this must
973 be the basis of a risk management strategy (Frewer, 2004). Whether such a strategy will be
974 judged as effective by the public, will depend on the expertise of food risk managers (Van
975 Kleef *et al*, 2007) and cultural variation: what is effective in one country, is not always as
976 effective in another (Van Dijk *et al*, 2008).

977 *Industry*

978 When introducing new food products or new food preparation techniques, it is crucial to
979 provide pertinent information concerning safe food handling and preparation. The food
980 industry can contribute to food safety in several ways. Labeling, providing information about
981 correct storage conditions and ways of preparation, can contribute to food safety, although the
982 addition of more information is at odds with providing clear food labels (Mills *et al*, 2004).
983 Icons can be used. The food industry can further contribute to food safety by educating
984 professionals working along the food production chain. As an example, the efforts of the

985 public-private partnership formed by the Industry Council for Development with FAO and
986 WHO may be noteworthy (Motarjemi, 2006).

987 *Consumers*

988 Presence of pathogenic bacteria on raw food materials, such as meat and fresh produce is in
989 most cases not totally avoidable, therefore intervention strategies are also needed in
990 subsequent steps of the food chain to reduce the risk of foodborne illness for the consumer. At
991 the other side of the farm-to fork continuum the consumers also play an important role in
992 maintaining food safety. Different information campaigns therefore focus on improving home
993 hygiene (Anonymous, 2008d, 2008e). However, the impact of such campaigns is often not
994 evaluated. A combined research project undertaken by social scientists, food microbiologists
995 and risk assessors showed the limited effect of such campaigns on reducing the actual level of
996 bacteria present in a meal, and on the associated risk of human illness (Nauta *et al.*, 2008).

997 Slovic (1987) developed a psychometric paradigm, which demonstrated that psychological
998 factors determine a person's response to different hazards, including those in the area of food
999 safety. Do consumers know what they should do in order to prepare a safe meal, in particular
1000 how to avoid cross-contamination and proper heating of reused food (Fischer *et al.*, 2007)?
1001 According to Nauta *et al.* (2008), consumers already possess the necessary knowledge
1002 regarding hygiene practices; this knowledge only needs to be activated. How to achieve this?
1003 What can we learn in this respect from other education campaigns, (e.g. smoking, alcohol,
1004 and fat), and from communication of medical product risks (Goldman, 2004), or from
1005 programs focusing on disease prevention and control (O'Loughlin *et al.*, 1995; Sarraf-
1006 Zadegan *et al.*, 2003).

1007 Health related behaviors are often differentially distributed across socioeconomic groups.
1008 Close collaboration with social scientists therefore seems logical. Communication with

1009 different consumer groups requires different approaches and media. Information should be
1010 targeted to specific groups at risk, like single households, pregnant women or elderly people.
1011 This is because different groups have different food preparation and cooking habits and
1012 therefore are exposed to different levels of risk. Kornelis *et al.* (2007) showed that different
1013 consumers prefer different information sources when posing questions about food safety.
1014 Two-thirds of all consumers prefer information from either institutional or social sources.
1015 *Your life*, a free magazine containing articles about fashion, lifestyle and entertainment
1016 published by the UK National Health Service, is an illustrative example of such a social
1017 source. Members of the lower socioeconomic groups are more likely to respond to
1018 information from their direct social environment (Weenig and Midden, 1997). Apparently,
1019 communication with different consumer groups requires different approaches and media. The
1020 importance of educating children through the school system cannot be emphasized enough.

1021 *Government*

1022 Food preparation and cooking practices are based on habits. This goes for consumers and
1023 often also for food professionals in small food establishments, such as food services and
1024 restaurants. Since such behavior is difficult to change, education should be a life long learning
1025 process on general aspects of food safety as hygiene and contamination routes, starting at a
1026 young age, making use of all types of media, including video-gaming. Education in food
1027 safety aspects could be combined with nutritional information. Concurrent with the
1028 development of education programs, strategies should be developed to measure the impact of
1029 such programs (Nauta *et al.*, 2008). In addition, governmental organizations should consider
1030 introducing and supporting specific education programs for consumers and professionals in
1031 small food preparation enterprises as well as for producers, especially for producers of fresh
1032 produce, as all have their responsibility with regard to food safety.

1033 Finally, while education might be expected to improve food safety in the developed world, in
1034 developing countries, economic growth rather than education might be the best way to
1035 minimalize food-related mortality and morbidity amongst children.

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1046

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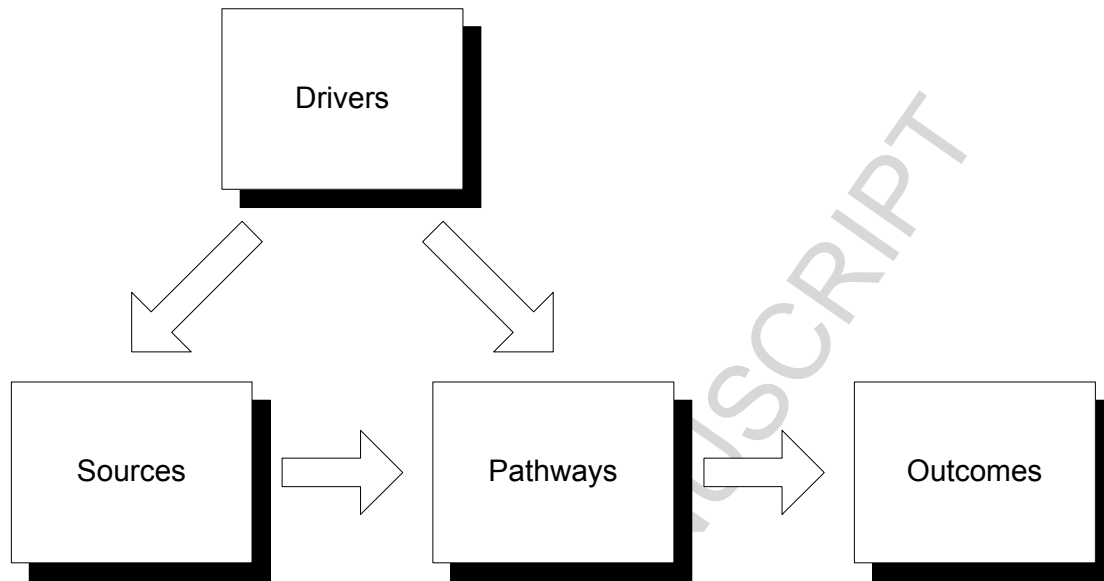
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1438 Figure 1. Basic risk framework for infectious diseases (from Tait *et al.*, 2006)



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1441 **Table 1. Different aggregation levels for evaluation of food safety.**

MICROORGANISM-RELATED FACTORS	HUMAN-RELATED FACTORS
Ecosystems	Global systems
Food chains	Regions
Food products	Countries
Food products	Consumer
Populations of micro-organisms	Human populations
Individual cells of micro-organisms	Human individuals
Cellular and molecular processes	Cellular and molecular processes

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Table 2. A systems approach to food safety.

Bold red font: Source increases risk to food safety;

Blue, normal font: Effect on risk to food safety unclear or neutral;

Green italics font: Source reduces risk on food safety.

DRIVERS	SOURCES	PATHWAYS			OUTCOMES
	<i>Pathogens</i>	<i>Farm</i>	<i>Processing/distribution</i>	<i>Preparation/Consumption</i>	<i>Public health</i>
<i>Economy</i>					
Globalization	Reduced geographical barriers to spread (of new variants)	Inadequate sanitation: higher pathogen loads Global sourcing Intensified contact structures	Long and complex supply chains Varying hygiene levels		Increased risk
Food price / income level		Less profit margins; decreased investment in food safety		Preference for cheaper alternatives (e.g. less meat and butter; discounters; home brands)	Risk not clear
<i>Science and technology and industry</i>					
Minimal processing	Adaptation		Less kill steps		Increased risk if not well controlled
Innovation		New food animal species	Step change food innovation <i>Smart packaging</i> <i>Bacteriophages</i>	<i>Smart labels</i>	Risk not clear

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DRIVERS	SOURCES	PATHWAYS			OUTCOMES
	<i>Pathogens</i>	<i>Farm</i>	<i>Processing/distribution</i>	<i>Preparation/Consumption</i>	<i>Public health</i>
Laboratory methods	Discovery of new pathogens or variants Omics approaches				Increased observed risk
<i>Culture and demography</i>					
Population growth		Polluted environments		Increased demand	Increased risk
Migration				New food habits	
Age structure				Increase in elderly More premature babies	Increased risk
<i>Nature and environment</i>					
Climate change and regional differences	Changing ecology	Droughts, floods Competition for land resources Movement of farms to new areas		Population displacement Increased difficulties to maintain cold chain	Changing spatial patterns of risk
Water, waste and energy		Irrigation water quality Waste recycling	Water/energy savings cleaning, process and ingredient water quality		Increased risk
Evolution	Emergence and transfer of virulence factors Antimicrobial resistance	New reservoirs	Increased survival	Increased infectivity	Increased risk
Population contact structures	Species jumps (spill-over from epizootics or exploitation of new	Contact zoonoses (MRSA, Q-fever)			Increased risk

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DRIVERS	SOURCES	PATHWAYS			OUTCOMES
	<i>Pathogens</i>	<i>Farm</i>	<i>Processing/distribution</i>	<i>Preparation/Consumption</i>	<i>Public health</i>
	agricultural areas)				
<i>Consumer behavior</i>					
Food choice	Psychrotrophs Re-emerging pathogens	Exotic/ethnic foods Regional products	No or mild processing, less heat treatment Increased pre-processing and -packaging	Convenience foods Year round availability Healthy foods (fish, vegetables & fruits) Less fat/salt/sugar Eating outside home	Increased risk
Food handling Technologies Attitudes/education			No acceptance of irradiation	Storage: inadequate time/temp control	Increased risk
<i>Information</i>					
Surveillance	Identification of new pathogens Detection of unexpected events		<i>Effectiveness of current controls</i>	Changes in consumption patterns: who, what, where, why?	Increase in observed risk
Education		<i>Professional education</i>		Hygiene campaigns Attitude changes to accept safe technologies	<i>Reduced risk</i>
<i>Government and policies</i>					
Regulations		<i>Standardisation</i> <i>Ban of antibiotic growth promoters</i>	<i>GHP/HACCP</i> Fraudulent behavior		Reduced risk

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DRIVERS	SOURCES	PATHWAYS			OUTCOMES
	<i>Pathogens</i>	<i>Farm</i>	<i>Processing/distribution</i>	<i>Preparation/Consumption</i>	<i>Public health</i>
Risk (-benefit) assessment		<i>Targets for pathogen reduction</i>	<i>Risk-based targets</i>		<i>Reduced risk</i>
Food defense		Agro/bioterrorism			Increased risk
<i>Agriculture</i>					
Animal friendly and organic production	<i>Reduced AMR</i>	Re-emergence (Trichinella, Toxoplasma) Higher (Campylobacter) or lower prevalence (Salmonella)			Risk not clear
Aquaculture		More farmed fish			Risk not clear
Antimicrobial use	Resistance development	Increased therapeutic use			Increased risk