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Food Safety

Some Global Trends

Edited by Yehia El-Samragy

FOOD SAFETY - SOME GLOBAL TRENDS

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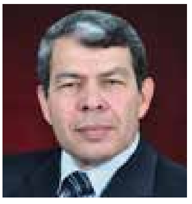
Meet the editor



For over four decades Dr. Yehia El-Samragy has had a professional career bridged between academia and industry. He is a Professor Emeritus of Food Science at Ain Sham University, Cairo, Egypt, and a visiting Research Professor at Cornell University, Ithaca, NY, and Utah State University, Logan, UT, USA. He is an international expert trainer of Food Safety and Quality Management Systems. He worked as an expert at a number of international organizations, including FAO, UNIDO, UNDP, JECFA, ISO, USAID, ACDI-VOCA and DANIDA, in different projects comprising technology transfer, food standards, food product development, waste utilization, cleaner production and implementation of integrated management systems. He is an IRCA lead auditor/tutor of QMS and Food Safety (HACCP and ISO/FSSC 22000) (IRCA Certificate #01182132) and a lead instructor, FSPCA Preventive Controls for Human Food Course (FSPCA Certificate #d16e213f). He has extensive experience in delivering training courses on QMS, HACCP and ISO/FSSC 22000 in Egypt, Libya, Sudan, Zambia, Tanzania, Ghana, Sierra Leone, Liberia, Gambia, South Africa, Saudi Arabia, Yemen, Jordan, Dubai, Sharjah, Syria, Bahrain, Lebanon, Kazakhstan, Russia, the USA and Canada.

Contents

Preface

This is not a textbook about how to establish, document, operate, maintain and continually improve a specific food safety system; rather, this is a book that handles various subjects that might help to maximise the understanding of elements that should be taken into consideration to ensure provision of a safe end product and ultimately food that is safe for human consumption.

The challenge for food producers and distributors when deciding on a method to deal with media attention focused on contaminated food is discussed using concrete examples from some food industries. The roles and/or responsibilities of scientific and regulatory agencies, food safety systems and certification bodies that are in control of food safety crises within the food chain are also addressed.

The unique challenges to food safety legislation in some developing countries in Asia (India and Nepal), West Africa (Ghana and Nigeria) and East Africa are presented through case studies of food safety situations in those countries. This book also includes a review of the major innovative approaches/strategies that could accelerate implementation of food safety legislation and bring it to function more effectively in these parts of the world.

Biofilm formation, which protects bacteria from an adverse environment, has been known to represent a health risk, in addition to interfering with therapy against pathogenic bacteria in humans. The text addresses the discovery that a combination of traditional Chinese medicine and antibiotics could improve the antibacterial activity and remove bacterial biofilm effectively, discussing the active constituent of traditional Chinese medicines and the different effects of quorum sensing and quorum-sensing inhibition on Gram-positive and Gram-negative bacterium.

The book also takes a look at the morphological and biochemical characteristics, as well as possible measures, to guard against bacterial species that cause food poisoning in the context of a potential bioterrorist attack. Some examples of using foodborne pathogens as bioterrorist weapons, as well as several important advantages that make them attractive as possible bioterrorist weapons to achieve high lethality, fear, panic and chaos in the community, are explained.

I hope that the information and concepts contained within this text can be adapted and put into practice based on the needs of the reader.

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Chapter 1

Introductory Chapter: Food Safety Concepts

Yehia El-Samragy

Additional information is available at the end of the chapter

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1. Introduction

On a global scale, there has been a notable elevation in the extent of foodborne diseases, in addition to disturbances in the international food trade resulting from recurrent disputes with regards to food safety requirements. In order for improvements to be recognized in food safety systems, most of these systems need to be reviewed and further developed. It is especially crucial at the present time, for both developed and developing countries, to create and propagate food safety systems in accordance with the principals of risk-based thinking and risk assessment. Therefore, it is important to be equipped with important knowledge on the principles and practices of food safety systems and the trend that will take food processors away from a merely reactive approach to food safety procedures, to a more proactive one.

2. Responsibility of food safety

The responsibility of the control of food safety worldwide is shared between several different agencies and ministries of the same country. The roles and responsibilities of these bodies may be quite different but most of the time can be considered as a kind of duplication of the same regulatory activity where unnecessary routine inspection visits and a lack of coordination are common. Moreover, the expertise and resources of these different agencies are varied, which can create a conflict between the responsibilities for protecting public health and obligations toward either facilitating trade or developing an industry or a sector.

3. Development of national food safety system

Provision of information for government agencies to assist in the development of national food control systems and to promote effective collaboration between all the different agencies involved in the management and control of food safety has become the utmost importance. The importance of developing effective relationships and mutual support among government agencies and institutions involved in the control of food safety and other interested parties, particularly the food industry and consumer associations, will enhance the establishment of effective food safety systems that positively impact the public health.

Since 1990s, food safety systems and code of practices have been developed substantially. These developments have been driven primarily by the implementation of the Hazard Analysis and Critical Control Point (HACCP) system for ensuring food safety worldwide, as well as compliance with International Organization for Standardization (ISO)-issued standards by different sectors of the food industry, including but not limited to the food chain. As a result, it has now become a necessity for students being prepared to start their career paths in the food industry to become educated about these safety systems, while still in their undergraduate programs.

The most important method for protecting public health is by promoting food safety that has long been recognized as a governmental responsibility in any country. It has improved through a series of statutory and regulatory requirements that responded to the fact that a significant proportion of human illnesses and deaths often have their origin in the food supply.

4. Objectives of food safety studies

Most of the food safety studies were to place emphasis on microbiological criteria used currently in the different food commodities, as the issues surrounding food safety criteria are common to all sectors of the food chain. The observation of foodborne disease and the monitoring of microbial contaminants of food, both from a public health standpoint and control measures of the effectiveness of food safety criteria must be practiced. The suggested science-based strategy for developing food safety criteria, including the standard operating procedures and instructions for their implementation, should be described for obtaining the best data to support this process.

Therefore, the scope of each study should cover these food safety criteria and should work to evaluate the scientific basis for existing microbiological criteria applicable to the selected food sectors, in addition to the extent to which these standards are suitable tools of ensuring the safety of such foods within any food safety systems based on the Hazard Analysis and Critical Control Point System (HACCP). The scope should follow the science-based process to set up food safety criteria and recommend guidelines as to what data are adequate and appropriate for use in developing new, or improving current criteria. The extent of the study should examine whether current criteria fulfill what they are required to achieve and the need to connect science-based criteria to public health objectives. Revision of the need for performance standards as control measures of food safety hazards and the way such criteria are implemented within HACCP system should take place to the extent that ensures processing of safe food. The recommended amendments for continual improvement should take into consideration the requirements of all the interested parties, i.e., consumer, industry, and food legislators.

Moreover, the availability of different food safety standards to agencies in charge of regulation should be oriented toward creating a connection between performance indicators and not only public health targets but also the economical aspects of food safety criteria, in addition to providing recommendations for continual development. This can be done via implementation and subsequent development of science-based criteria for food safety; criteria that include principals for managing the degree of risk for foodborne illnesses and becoming familiar with the elements that contribute to that risk.

The safety of our food products must always be given top priority in all that we do through selecting the best standards for an operation and then defining, implementing, maintaining, and continuously improving the food safety system. It is very important along all the steps of this process that food professionals monitor the specific sources related to the standard of choice along with staying up-to-date on current food safety-related news and incidents.

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Chapter 2

Food Safety: Food Crisis Management

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Additional information is available at the end of the chapter

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Abstract

Food safety is a complex topic, and the various market participants are involved, such as authorities, non-governmental organisations (NGOs), consumer protection bodies and the media, have a very different, often emotionally charged perspective. This poses a particular challenge to producers and distributors when deciding on a method to deal with media attention on unhealthy food, with contaminations and residuals. There are numerous examples of crises caused by impermissible residuals. This shall be illustrated using concrete examples from the egg, game and poultry industries.

Keywords: basics food law, health risks, microbiological dangers, residuals, HACCP concept, standards, crisis management, preventions

1. Introduction

Food safety is paramount in the food chains with raw materials contaminations, improper treatment or storage and incorrect declarations or expiration dates having become a daily occurrence. Almost every German food company, as well as food companies in other countries, experiences at least one so-called food crisis over the course of its activities. These are often triggered by inconspicuous events that are not indicative of a threat initially. However, experience has shown that what seems like harmless negative customer feedback or complaints can give rise to a full-blown crisis. The consequences are often initiated by media warnings, which might in turn lead to product recalls. These are subsequently published by the supervisory authorities in the European Rapid Alert System for Food and Feed—RASFF [1]. This is associated with high costs and time expenditures for those parties involved. As a result, recalls can even threaten the very existence of the distributing company responsible. Moreover, the distribution of unsafe food is usually associated with significant image loss. At the same time, the question arises when food should be considered hazardous to health following the legal intention of the general administrative regulations of the EU Rapid Alert System. The Article Food Safety and Crisis Management illustrates this using several real practical examples, which the author Caspar von der Crone has overseen as responsible manager [2] over the last years.

2. Basics of food safety

The general rule is: Food that is not safe may not be distributed. This is regulated by EU Regulation (EC) No. 178/2002 (Basic Regulation) [3]. In addition, national regulations apply as for example the German Food and Commodities Act (LFGB) [4]. In a European Law framework, food is only considered unsafe if it can be assumed that it is harmful to health. In addition, food is also considered unsafe if it can be assumed that it is not suitable for human consumption. A differentiation is in order here, as the first description is concerned with defending against health risks, while the second description only serves to secure commercial consumer interests. Put differently, consumers' commercial interests—and not their physical integrity—should be protected from bad buys and unpleasant surprises to the greatest possible extent.

The objective is a sustainable business condition along the entire process chain, as shown in **Figure 1** (overview), under the inclusion of ecological, economical and social aspects. This applies in equal measure to the entire value-added chain, under the consideration of the respective process steps, starting at the producer and ending at the consumer. The legal requirements must be included, as well as the interests and requirements of NGOs, paying particular attention to consumer's expectations, who make the decision in the end and are an important part of the process chain.

Figure 1. Food safety and dialogue between relevant groups.

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3. Control scenarios

Modern food control, in other words, is the control for 'means of live' [5]. **Figure 2** is still at a nascent stage; however, its roots date back far into the past. Controls to ensure that consumer demands for healthy food were met have been in place for ages. German Food Law's history can be traced to the Middle Ages. Here, the objectives were to fight wine adulterating or counteract the growing public health risk posed by raw materials that are hazardous for health, among others. Regulations for meat production were introduced at a very early stage, with relevant hygiene directives. Regulations concerning the restructuring of food contact materials (LMBG) were introduced in the 1970s, which allowed the state to act to protect consumers against damage to health.

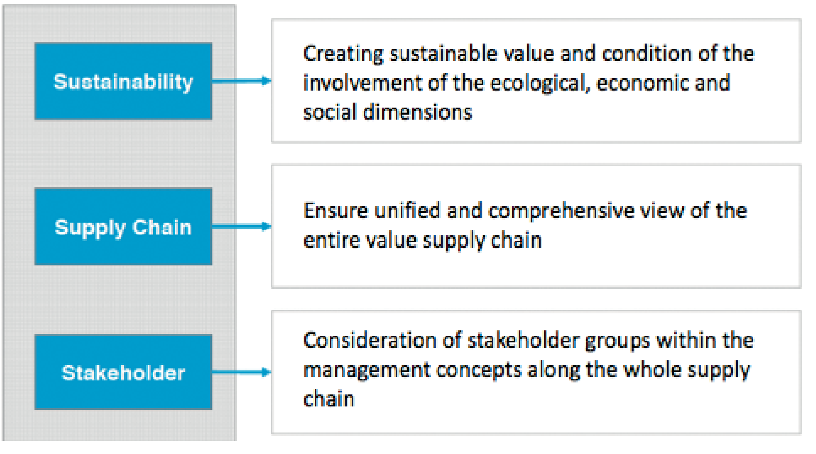

Figure 2. Transparency, sustainability and responsibility along the process chain.

The survey conducted by the European Commission in their White Paper on Food Safety from 2000 is additionally worth mentioning. In it, the Commission worked out a division of food safety responsibilities between the involved actors, with the main responsibility for food safety lying with the feed producers, the farmers and the food producing companies. In this context, the HACCP concept (Hazard Analysis and Critical Control Point) was introduced, which obligates the food company operators to danger analyses and conceptual assessments. The FAO/WHO Codex Alimentarius offers an internationally binding version, which in turn is part of the 'General Principles of Food Hygiene'. With the HACCP concept, health risks posed by food should be identified, evaluated and managed.

The HACCP consists of seven principles:

1. Conduct a hazard analysis.
2. Identify the critical control points (CCPs).
3. Establish critical limits.
4. Monitor CCPs.

5. Establish corrective action. These shall be implemented if monitoring shows that a certain CCP is no longer under control.
6. Preparing procedures to verify and confirm the successful operation of the HACCP system.
7. Recordkeeping that considers all processes and records concerning the principles and their application.

With the EU Basic Food Regulation, the European Food Safety Authority (EFSA) was established. The EFSA assumes tasks that relate to the scientific evaluation of relevant food topics at the EU level. The EFSA is also the point of contact for the scientific evaluations related to certain approval procedures, for example during the approval of food additives.

Every food producer is subject to controls along the entire process chain, starting at the farmer/producer up to the food retailer, to inspect the adherence to relevant production standards. Over the last years, many standard-setting bodies have established themselves on the market. In the area of egg production, this is the KAT System (Association for Controlled Alternative Animal Husbandry) [6]; for meat production, the QS GmbH (Quality scheme for food) [7]. Both systems cover the entire process chain with specific standards and criteria, and they are ultimately demanded by retailers for animal product distribution. The International Featured Standard (IFS) [8] is another controlling body, a standard developed by the food retailers that places very stringent process quality and traceability demands on processing companies. The IFS Standard offers additional safety guarantees. The controls take place annually, with the so-called integrity audits (unannounced inspections) offering further security. By now, producers and distributors from across the globe operate by the IFS Standard to meet globalised quality, transparency and efficiency demands. It ensures that the certified companies attain a high quality and product safety standard.

Figure 1 represents the dialogue between scientific and regulatory actors within the process chain.

Biological, chemical and physical agents, as well as insufficient allergenic property information, can all pose health hazards. Additionally, the German General Administrative Regulation for the implementation of the Rapid Alert System for Food, Food Contact Material and Feed (*AVV Schnellwarnsystem*) [9] offers a guideline for the evaluation of a food that poses a potential health hazard. However, it should be noted that the General Administrative Regulation has no legally binding qualities and solely serves to harmonise the implementation of Food Law. Put differently, the General Administrative Regulation has an internally binding effect for the Food Enforcement Authority at most.

The normal consumer usage conditions should first be considered when deciding whether a food product is safe or not. For example, this relates to improper handling, which runs counter to the principle of proper kitchen hygiene in a private residence such as improper storage of products that should be refrigerated.

The result is that hazardous food products purchased by consumers should be recalled publicly via the media, while the product that is ‘only’ unsuitable for human consumption will be recalled ‘quietly’ through the commercial buyers.

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Biological, chemical and physical agents, as well as insufficient information about allergenic properties, can pose particularly significant consumer health hazards. The normal consumer usage conditions should first be considered at all levels when deciding whether a food product is safe or not. This means that those types of usage which are not normal but at the same time imaginable should also not lead to situations that might be hazardous. However, improper handling after purchasing, insufficient adherence to hygienic principles in private residences, incorrect storage of products that should be stored under refrigerated conditions, or also the consumption of raw poultry might have negative health effects and lead to illness. Even if this lies outside the distributor's scope of responsibilities, it might be hard to interpret evidence pertaining hereto.

The high incidence of salmonella in the beginning of the 1990s is a good example of this. The illness was primarily caused by the consumption of eggs or egg products (tiramisu and other dishes containing raw eggs). Even though the root cause was improper handling and failure to adhere to refrigeration guidelines, eggs were still suspected to be highly pathogenic, which subsequently led to a significant consumption reduction. German legislators reacted with national cooling regulations from the 18th day onwards. This regulation was only lifted a few years ago, when it is known that cause and effect had been mixed up. There are still salmonellae; however, consumer education through advice on egg storage after purchase, as well as consistent salmonellae monitoring at the production level, led to a greater degree of food safety. The same problems have not occurred, even though the regulation prescribing cooling from the 18th day onwards has been lifted.

This serves to illustrate that a decision on a food product's safety should also consider that information communicated to the consumer—including label information and cooking recommendations—contributes to safety. The packaging advice 'heat before consumption' is another classic example that helps avoid health hazards; this instruction points out to the consumer that the food should be treated accordingly, that is to say, not consumed raw.

This particularly applies to raw poultry meat, for the lion's share of relevant germs is killed if these products are heated at 70°C for at least 10 min. This also includes good kitchen hygiene and know-how on handling and processing food intended for immediate consumption.

4. Hazard to human health

The exact definition of a hazard to human health as it relates to regulations is not concretised or clarified further legally. However, as it concerns a hazard that is triggered by the consumption of affected food, the basics of Food Law apply at the least. Following Article 3 (14) of the Basic Regulation, a hazard is a biological, chemical or physical agent in a foodstuff, or condition of a foodstuff, that might negatively influence health.

In principle, physical, biological and chemical hazards to human health are imaginable. However, in the production of food commodities, focus is clearly placed on 'chemical components' due to the complex structures [10].

Biological dangers that originate from the commodity itself are not plausible. If finished products, such as kitchen utensils, are passed onto the consumer, there is only limited necessity due to the common household cleaning before use.

The circumstances are different for convenience food. A possible, if still unlikely, practical scenario might be the contamination of food commodities during production, for example due to an ill employee. Today, legal requirements (instruction obligations) make the risk of transmitting certain legally relevant illnesses significantly less likely and rather negligible.

Food commodities can also pose a threat through physical contamination. Foreign bodies, as well, are not that uncommon. Material fatigue and damages might lead to foreign bodies entering a food product such as metal residues because of a malfunctioning or broken metal detector.

Another example comes from game: metal residues from pellets have led to a (in part complete) ban on wild hare meat. However, this was not due to the metal residues themselves, but rather due to the fact that the pellets contained lead. Lead residues in game can pose a risk to human health from a food inspection perspective. Pellets containing lead were the standard hunting shot until recently. The German Federal Ministry of Food and Agriculture (BMEL) [11], German Federal Institute for Risk Assessment (BfR) [12] and the European Poultry, Egg and Game Association (EPEGA) [13] have assumed responsibility and performed large-scale lead-residual monitoring in killed game. The research project 'Food Safety of Killed Game' can be accessed publicly on the BMEL website.

The results did not indicate a direct health hazard with proper hunting. However, the indicated consumption was rather negligible at 0.5 kg per inhabitant. All the same, heavy game consumers (hunters), children and pregnant women were deemed at risk. The situation has led to changes as lead-containing shot is increasingly replaced by lead-free ammunition since then. This makes game a safe product again. This example shows that small effects can lead to serious issues that cast shadows over entire industries.

5. Microbiological hazards

Food hazards are most commonly caused by microbiological organisms. Generally speaking, bacteria play a vital role in food production. Useful bacteria influence food properties positively, think of aromas. Unwanted bacteria in and on food can negatively influence product quality as spoilage agents or even pose a food safety risk as pathogenic agents.

Many food products—of animal origin in particular—present an ideal culture medium for bacteria, offering optimal living and multiplication conditions. A classic example is the salmonellae in the products containing raw egg or raw poultry mentioned before. Good hygiene is essential in impeding the multiplication and spread of microorganisms. This also includes the systematic cooling of food products of animal origin, which additionally stops the spreading of germs. This makes compliance with the cooling chain another important preventative measure, just like proper heating.

The Commission Regulation (EC) No. 2073/2005 [14] on microbiological criteria for foodstuffs offers a legal foundation. This regulation contains the so-called hygiene package from 2004, with it, the European Union renewed its food hygiene regulations. Since 2004, there has been another paradigm shift in the distribution of food product of animal origin. Another example from the commercial exploitation of game: This industry was also plagued by complaints and scandals that cast a shadow on the commercial viability of game distribution, as old traditions were followed, and the cooling chain was not immediately adhered to, or adhered to at all, after the kill. This led to microbiological values that in part far exceeded the regulated maximum values and in turn led to recalls and closures of game-processing companies. In his function as the General Manager of European Poultry, Egg and Game Association, the author of this article initiated regulations for good game hygiene, connected to a microbiological assessment. This was in the interest of the associations' member companies and served as a foundation for consumer health protection. Extensive studies of killed game under various cooling requirements and game carcase treatment after killing showed that it is well possible to adhere to the microbiological regulations. The so-called game guidelines [15], with specific provision for the handling of killed game and distribution regulations, as well as the associated consequences, have established standards that ultimately contributed to restoring consumer trust, making properly treated game considered a safe food product again.

The illustrations and explanations on food safety mentioned above merely represent a foray into Food Law. The regulations are very complex at a national and EU level and cannot be treated more comprehensively in this article. In the following discussion of food safety, further practical examples serve to illustrate the influence of crisis management and food safety.

6. Levels of responsibilities and competences

All parties involved in refining food products, at all levels, are responsible for their safety, with the primary responsibility placed on the producer. The responsibilities of producers and distributors are orientated following the principle of concrete influences within the scope of

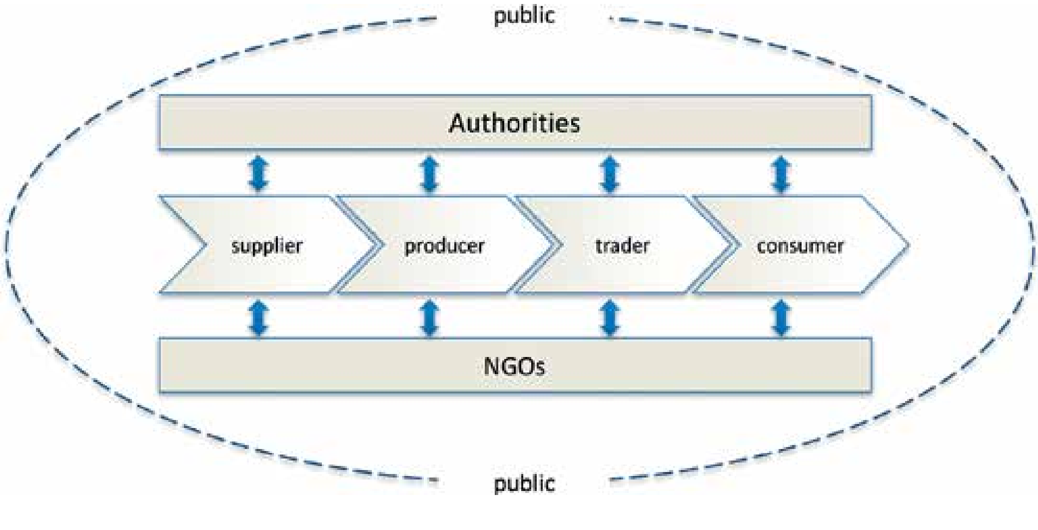

Figure 3. The process chain: Levels and participants.

activities. Additionally, the producers should, in the context of their business activities, take all measures appropriate to recognise potential hazards, befitting the properties of the products they deliver, and to take precautions against potential consumer hazards.

Figure 3 illustrates the various process levels. Here, each participant bears equal responsibility for the safety of a certain product, from production to the final customer purchase. The parties involved should assure that the condition and labelling of the product adhere to all legal requirements along the entire chain. The requirements that apply at the various process levels are provided by the government, while nongovernmental organisations significantly influence the public opinion formation process during crises. A constructive dialogue with the supply chain should take place with the relevant stakeholders.

7. Crisis management

Crisis management above all entails crisis management in collaboration with the responsible authorities. Attempts by a company to cover up or ignore an issue are particularly problematic.

The author of this article has faced numerous crises up front, providing the practical experience to manage these. In the following, practical crisis examples are used to illustrate and elucidate what measures can be used in what ways to guarantee a future-proof presentation of prevention.

Some essential perspectives on crisis management:

Customer, authority, or consumer complaints cannot be left unanswered. They are a vital source of information about the safety of a company's products. In principle, it does not matter whether a customer complains that a product expired before the indicated expiry date, or that this is documented in an officially logged complaint. In all cases, the same concrete circumstance applies, namely, that the products expired before the expiry date. This might have various causes, some of which might not be attributable to the producer (for example, an interruption of the cooling chain at the retailer).

If the food business operator fails to follow up on this complaint and fails to process this complaint in an appropriate manner, the situation might develop into an actual crisis. This rings true particularly considering the fact that authorities, after repeat comparable violations, no longer assume negligence but rather accuse the food business operator of intent.

Within a crisis management context, all procedures and work instructions relating to the handling process of complaints should be defined. An example of this is the development of forms for consumer complaints to help employees summarise complaints by phone or in writing, with an accompanying work instruction. Here, the development of a crisis plan is of the utmost importance, and this is a type of work instruction that prescribes how to act in crisis situations. This not only applies to the company itself; authorities are also obligated to develop crisis plans. This is fundamentally regulated by the Basic Regulation of the European Commission, which drafts a general crisis management strategy together with the European Food Safety Authority (EFSA) and the member states. This strategy is used if the preventive, curative, and reductive risk measures defined in the Basic Regulation do not suffice.

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Another method to improve food safety lies in informing consumers, by increasing their knowledge of food and certain potential hazards related to food. Poultry offers another example. If it is cleaned in water that is subsequently used to wash lettuce leaves, this might lead to salmonellae finding their way into the food. This is why good kitchen hygiene practices are of cardinal importance. Gaps in consumer knowledge can be filled by relevant product information or by informational campaigns. This information should be written in simple language.

This goes to show that 'risk minimisation' is a very diverse topic, some practical examples are explored in the following.

8. Residues and dioxins

The so-called dioxin crisis at the end of 2011 led to an official warning about foodstuff that was not suitable for distribution. This crisis primarily affected eggs and poultry. Noteworthy about this crisis is not the circumstance that fatty acids in milk which might contain dioxins—primarily intended for technical purposes—were potentially mixed in with compound feed for animal rearing in a feed plant. The actual cause was dioxins in this feed that stored themselves in the fatty acid, leading to egg and poultry meat contamination, among other animal product contaminations, later.

Dioxins have led to significant problems in the past. The first of these was a chemical accident in Seveso, Italy, in the middle of the 1970s, with approx. 2 kg of dioxins released into the environment, leading to serious diseases. Dioxin is considered a carcinogen with significant adverse health effects, which in turn explains the fears of consumers, as well as the potential effects of dioxin residues.

The Belgian dioxin crisis took place in 1999. The improper use of frying oils in animal feed led to dioxin findings in eggs. At the time, this had catastrophic effects on egg consumption, which was virtually reduced to zero out of fear for diseases. The emotional perception played an enormous role in this, even though only relatively minor dioxin traces were found. However, the actual problem was that the egg origins could not be traced, which led to all eggs being taken off of retailers' shelves.

As a consequence, the Association for Controlled Alternative Animal Husbandry (KAT), at the time headed by Caspar von der Crone, advocated a general ban on feed with animal protein. While this might increase production costs, it would allow the industry to regain consumer trust, capable of contributing significantly to food safety.

Another case occurred in 2002, the so-called Nitrofen scandal. Nitrofen is an herbicide that had been used in the agricultural industry. It turned out later that Nitrofen is a carcinogen that is not broken down by the body but rather stored in animal fatty tissue, which can in turn be found in the eggs of laying hens. These residuals were found in the summer of 2002. Nitrofen was one of many pesticides already forbidden in the EG but still allowed in the DDR up to 1999. This led to remaining stock with contaminated feed in a storage after the German reunification, which was in turn inspected and cleaned insufficiently before being fed to laying hens as organic feed, among others.

This gave rise to another scandal, in the area of organic production, with extensive recall actions as a result. The affected companies could be identified exactly in the beginning. The database system developed by KAT at the time, striving to safeguard traceability, as well as the newly introduced identification measures for individual eggs with origin labelling, proved to be an effective preventative measure. For the first time, it was possible to recall contaminated eggs in a targeted manner, avoiding any negative effects or harm to consumers.

The affected companies suffered significant losses, even threatening their very existence, but managed to rebuild trust through consistent action-taking. There was an awareness that product traceability is one of the most important food safety criteria in crisis situations. This led to the EC decision to adopt individual egg labelling as a binding requirement for egg distributors across the EU.

The dioxin crisis of 2011 took place under similar circumstances. Affected companies were closed, and recall actions were initiated. Media pressure was enormous, and consumers were requested to either return or destroy food, primarily eggs and poultry. Thanks to KAT and the mandatory producer code printed on each egg [16], the eggs origins could be traced. The names of the affected companies—publicly traceable through the code—were disclosed by authorities with an accompanying warning. However, the eggs already reached consumers' refrigerators, as the dioxin was discovered in November, but the authorities did not inform consumers of dioxin residue hazards until January 2012. At this point, most eggs were already consumed. Similar recall actions were initiated for poultry; however, this proved to be significantly more difficult as poultry was not distributed using the same traceability system as the KAT individual egg labelling system. This led to immense reputation damage, as well as more critical consumer attitudes, and in turn reduced egg consumption. Interestingly, the organic food industry benefited from this, as consumers expected that the organic industry adhered to stronger regulations and was subject to more stringent controls, improving safety.

At the end of 2014, the organic food industry was rattled by several events. Residues of a corrosive agent and a fungal toxin were discovered, and the products of numerous companies were stripped of the right to be sold with an organic seal as a result. The contaminated feed, still labelled as 'organic' by a Dutch distributor, had been distributed to organic farmers in Germany.

A total of 2000 tonnes of affected feed, sunflower cake, was distributed by a Dutch distributor as organic feed. Organically producing laying hen companies, as well as pig, cattle and sheep farmers, were affected.

There are no special restrictions for pesticide in place in conventional farming, quite different from organic production, which uses stricter standards. The affected companies faced grave consequences. Goods that had already been delivered were recalled by regional authorities, and goods that were being produced currently could not be distributed for a certain period. It is interesting to note that these regulations were only implemented in individual German states, while the remaining lion's share of cakes contaminated with pesticides could still be processed for organic production in other EU countries. There was no health hazard, but rather a component in the feed that is not permitted in organic production.

Regional German authorities, in the meantime, considered this circumstance consumer deception following the EU Regulation on Organic Farming [17], as this stipulates that only uncontaminated organic feed can be used.

The most recent incident took place in the Netherlands in 2017, where the banned insecticide (against mites) Fipronil was used. Again, contaminated eggs reached the market—almost exclusively eggs produced in the Netherlands—which resulted in a recall for eggs with the NL (the Netherlands) identification. Egg products were also affected, as were processed products such as cakes, noodles and other products containing egg. Here too, the individual egg identification system proved very effective, with targeted recall measures, allowing for the continued distribution of uncontaminated goods. However, processed products remained in a grey area.

9. Preventative measures

Crisis situations can occur suddenly and unexpectedly, even in a carefully managed company. Internal business process problems as well as external, unforeseen difficulties might be the cause. Therefore, a preventative strategy should consider all potential measures that might equip a company to deal with such situations.

This includes general preventative measures (quality measures, self-controlling systems following the HACCP concept principles, traceability, claims and complaints, false management, and the like). Additionally, specific measures should be considered such as the development of a crisis plan and special measures for at-risk products.

Therefore, any properly managed company requires a quality management book, in which the procedural instructions regarding quality politics, as well as the principles of quality assurance, are defined. By now, also in the light of increasing pressure of retailers, systems following the International Feature Standard (IFS) have established themselves. This includes the British Retail Consortium (BRC) [18] and Global Standard for Food Safety, with similar regulations.

A vital component of a quality management system is the aforementioned HACCP concept, which is required following Art. 5 of the Regulation 852/2002 (EC) No. 852/2004 on Food Hygiene. This regulation prescribes that food business operators must develop, implement and maintain one or more procedures based on the HACCP principles.

10. Summary

Food safety is a very complex topic. Crises have repeatedly led to product recalls in the past and significantly contributed to consumer unrest. This not only influenced consumption, which collapsed in part, but also resulted in significant damage to the reputation of the product itself. The examples mentioned from the egg, poultry and game industries illustrate this very clearly. Minor triggers have shown time, and again that a critical light was cast on many food products, also clean food products. Dioxins on forbidden ingredients can be considered criminal. Environmental residues or soil contaminations, on the other hand, are difficult to assess for producers and pose a risk that is hard to perceive. Oftentimes, these findings are caused by so-called inherited contaminations, as can be seen in the organic egg industry during the Nitrofuran crisis. Producers cannot be held accountable for this; however, they do bear the full risk and consequences associated with this. Unfortunately, it has shown repeatedly in the past that economic factors alone led to crises. The initial use of cheap additives and other ingredients, which did not appear to contain contaminations but did in the end, have contributed to this. Therefore, the food producer should be aware of the responsibilities associated to these activities. However, it can certainly be recommended to inspect purchased feed and similar products before use. Suppliers should have a certain certification. Product recalls by authorities and public disclosure, as well as rapid alert systems (EC), are further sensible measures. However, prevention is better than cure, and high-quality production, as well as adherence to stringent standards, is paramount.

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Chapter 3

Food Safety Legislation in Some Developing Countries

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Additional information is available at the end of the chapter

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Abstract

Developing countries have uniquely intriguing challenges to implementation of food safety regulations as presented at a global scale and thus would benefit from a scientific approach that best suits them. Some common characteristics of food processing industries in the developing world include: they are small scale, cottage in size, mostly start at backyard or in dingy premises, more often than not, are managed by non-food technologists and who are reluctant to engage food technologists whom they believe could be more expensive or unnecessary addition to their current needs. At the same time, they are a bit skeptical of regulating institutions, have no idea as to the acts and legal requirements regulating food business premises and hence prefer keeping their business unofficial. From the foregoing, it is critical that approaches that address these challenges are applied in implementing food safety standards. This chapter reviews these unique challenges and presents case studies from Asia, West Africa and East Africa as well as innovative approaches/*strategies* that could accelerate implementation of food safety legislations in the developing world.

Keywords: developing countries, food safety, food safety legislation

1. Introduction

Food safety systems in developing countries are weak, fragmented, and not effective to protect consumer's health or help countries competing for export markets. Improving food safety often costs much (or is associated with additional costs which could only be recouped by the items fetching more money) and many developed countries experience real challenge in making food safety legislations work. At least, this is the perception of majority of SMEs. Many years later after the unveiling of codex and ISO standards, these countries' domestic markets suffer from sustained food safety-related issues ranging from food-borne illnesses to food fraud. In spite of this, a lot of stride has been made with regard to development or adoption of international standards; however, what remains to be seen is the full implementation and hence marked decrease in food safety-related incidences [1].

Food safety concept continues to gain attention particularly in developing countries. Many countries rely purely on small scale (subsistence) and street vendors to feed their populations. Yet, these traders are not usually included in the mainstream food safety systems. In flow of substandard and poor quality goods, corruption, low income, unjust trade, and political turmoil are ills deviling developing economies, and this adds to the challenge of food safety systems' operation. Generally, few of the developed countries have formalized agriculture systems. To this extent, farm implements, fertilizers, seeds crop management practices, and manufacturing are scattered across vast geographical locations. Food insecurity, political instability, outbreaks of communicable diseases and natural disasters are challenges that compete for government attention; hence, food safety is often not prioritized. Yet, the definition of food security from the 1996 World Food Summit Plan of Action mentions access to sufficient, safe, nutritious and affordable food to all people at all times. Often, it seems that in developing countries, not enough emphasis is put on the safety aspect of food security [2].

According to published data by FAO and WHO, about 2000 food-borne-related deaths occur daily in Africa. Over 700,000 food-borne illnesses recorded annually are due to diarrheal-related illnesses and from contaminated food and water. *Salmonella*, *Shigella flexneri*, *Shigella sonnei*, *Clostridium perfringens* and other parasites are major culprits. An alarming average of 3.3–4.1 episodes of diarrheal diseases among children in Africa has also been recorded annually. Coupled with malaria, HIV, TB, these become more debilitating, creating a huge dent on the public health's integrity. Food-borne illnesses lead to reduced productivity, disability, early deaths, low incomes and hence low access to food and the problem becomes cyclic. Illegal use of food additives, (E110, E102, E104, and E124) in local and imported foodstuff including infant foods, is an alarming case. Unless an approach that understands the unique challenges of developing economies are employed, the great food safety legislations may remain in revered books of codex without having a real impact on food safety situation in the developing world [2].

2. Why food safety legislation must work in the developing economies?

First, developing countries bear the greatest global burden of food-borne illnesses and death. The strain this adds to an already stretched public health services is huge. Second, regional and international trade is becoming extremely invaluable. For this reason, more sensitivity to food safety is needed. Benefits of safe, adequate, and nutritious food abound. It is crucial to long-term economic growth, good health, and productivity. It is also associated with a happier population that would enjoy reduced conflict. Countries in Africa and the rest of the developing world have some form of legislation regarding food safety. Some of this, however, are most rudimentary, archaic and at times not based on sound science. For these legislations to benefit the rest of the countries, there must be a push to align them to World Trade Organization (WTO)'s agreement on the application of Sanitary and Phytosanitary (SPS) and Technical Barriers to Trade (TBT) agreements and the Codex standards and codes of practice. Some of the standards are not science-based as required by Codex in a bid to help facilitate regional and international trade among different countries. This then curtails international trade and sometimes creating a bad notion of standards among processors. Several factors hamper the push to realize the implementation of food safety legislations in the countries such as inadequate technical capacity, lack of awareness of economic loss arising from poor quality foods, and weak enforcement of regulations among others [1]. The unveiling of the ISO allowed for HACCP to be upgraded through the International Standard ISO22000:2005 (Food Safety Management Systems—Requirements for any organization in the food chain). The ISO technical committee on food safety created in 1947 is one of ISO's oldest and most fruitful committees, with over 830 published regulations and 125 more in the pipeline. ISO standards have played a crucial role in promoting global standards, development of harmonization and awareness creation. In many developing countries, ISO 22000:2005 is not a mandatory food safety requirement and perhaps due to its complexity, cost of compliance or technicalities, only few companies that most of the times have qualified food safety experts manage to get the certification.

2.1. Key food safety regulations at the world stage with an impact on developing economies' food safety

Africa has been reported to enjoy over 5% annual economic growth in the recent decade, and this growth rate is predicted to continue or even improve in the next couple of years. For African countries, opulence and affluence among her populace is creating a reason for demand of high quality safe and mostly longer lasting products [2]. This can also be said accurately of the rest of the developing economies especially in Asia as well as South America. The Sanitary and Phytosanitary (SPS), World Trade Organization (WTO)'s—Technical Barriers to Trade (TBT) agreements are some of the regulations that require attention of all countries involved in any trans-border trade particularly of agricultural produce. The developing economies are huge exporters of raw or semi-processed agricultural goods, and these put them directly under the requirements of these legislations. Though there exists food safety standards in almost every country in one form or the other, these standards do not adequately help to improve food safety because of two main reasons. First, imports even of poor quality foods are not curtailed sometimes due to laxity, incapacity, or corruption. Some of the regulations are far stricter even beyond the codex requirements this more often than not hinders trade especially inter-regional trade. Second, there is very low level of implementation of regulations across board. This is why the regularization of laws and their harmonization should come into play. There are few global organizations that are at the forefront and with the expertise and neutrality to help countries navigate this concept of global standards harmonization. One such initiative is the Global Harmonization Initiative (GHI). More about the structure strategies and aims of the GHI and other such bodies are discussed in a later subheading.

2.2. Models of national food safety and quality control systems

In general, it can be surmised that there are three major models adopted by countries in national food control systems: the single agency model relies on one organization or umbrella body which is mandated with all the functions of controlling food safety. This model has the advantage that food safety issues are accorded priority, and they can be highly effective. The second model implies multiple agency scenarios. In this case, the role of food safety is sector and commodity-specific. In this system, the roles could also be devolved to federal, local governments or counties and the national level. Some challenges with this model are: duplicity of functions, conflicts, and differing expertise at national and at the regional level, reduced domestic consumer confidence and confusion among stakeholders as to which laws to comply with. The third model is an integrated system: in this system, agencies are assigned jurisdiction based on aspects of food safety which cut across all the sectors such as policy development, coordination, inspection, education, and training. Irrespective of the model that best suits a country, it must be based on the principles of transparency, inclusiveness, integrity; clarity of roles, accountability, science/risk-based approach and equivalence as the benchmarks against which its success is measured [3].

3. Components of a good national food safety system and the status of each in the developing countries

3.1. National food safety policy

This gives the general direction and thrust to the food industry in a country and defines the collective vision for all the actors in the food chain in a country. The presence of a Food Safety policy (FSP) is critical to coordinated function of all the organizations charged with the responsibility to deliver food safety. It is in this document that governments must state and demonstrate food safety and its relation to economic and public health. The case studies of the developing countries here demonstrate at least governments' understanding and commitment to setting up a food safety and nutrition policy.

3.2. Food legislation

Once a food safety policy is in place and adopted, this gives room for appropriate accompanying legislation. The legislation must be updated, based on science; give spell out clearly the roles and obligations of each concerned organization, and above all be enforced. For many developing countries, the full enforcement is a missing ingredient. For food safety legislations to succeed, they must cover all components of the food supply chain. Often in Africa, and the rest of the developing countries, food safety legislations leave out the informal sector which is a major contributor to food value chain and hence any accompanying ills.

3.3. National food standards development platform

There is great variety of indigenous foods in the developing world. Many countries do not have standards that govern preparation and trade of these indigenous foods. Effort is put currently through Codex Alimentarius Commission's (CAC) Working Groups to change this. This move should be encouraged and many countries ought to bring on the table several of their native foods. However, the standards development process must be supported by scientific data on nutritional and safety aspects of food which is a gap that needs to be filled. In addition, the standards development must be responsive and internationally oriented and the body responsible be accorded a clear mandate.

3.4. Science-based risk assessment (RA)

Legislation and standards that serve the intended purposes in guaranteeing food safety and cross border trade must be science-based. WHO and FAO had earlier, in 1992, stated that risk analysis must be the basis of any food safety framework [12], but in developing countries, lack of expertise, low investment in the requisite infrastructure, and difficulty in collecting own toxicological data is a hindrance to RA. This challenge is a huge one and requires collaborative and innovative efforts from all stakeholders. Toxicological exposure data in many developing countries is very scanty, inaccurate, and usually not timely. To help developing countries to conduct risk assessment, FAO/WHO studies is a great place to start but unless these are closely related to the country's specific needs, priority may differ from those of FAO and WHO and depending on FAO/WHO's focus data may take long to finally capture the aspirations of specific countries.

3.5. Inspection

Food quality inspections demonstrate or validate the success or failure of food safety legislations. Legislations that are not enforced are not beneficial at all. This is a major setback in all the aspects of the developing countries. Many factors contribute to this; including low status often awarded to food safety officers, inadequate logistical support, and cumulative tasks required of them hence intermittent attention to the task of inspection. Inadequate geographical coverage in all areas of the country by inspectors of food legislations and neglect of rural community means that their food safety concerns often go unaddressed.

3.6. Laboratory testing services

Inspections, and other aspects of food safety monitoring, depend largely on validation, and this is partly conducted by testing of samples to ensure enforcement of legislation. Rapid laboratory testing is also critical to implementation of food-borne illness' outbreak surveillance. In many cases, laboratory facilities in developing economies whether in Asia or Africa are old, poorly equipped and with either very few personnel or with low competency.

3.7. Capacity

Capacity to implement food safety legislations is a major determiner of success or failure of a food safety management system at the country level. Inadequate capacity is a bottleneck that cuts across many areas. This may be due to lack of competent personnel, lack of funding or poor logistical support to carry out the different aspects dealing in food safety.

3.8. Training and education in food safety

Food safety legislation requires regular, planned ongoing training, and upgrading of knowledge for food control officers, law enforcers, consumers and all stakeholders. Many factors regarding food safety change from time to time. This may include status of chemicals for use as food additives, and even specifications like microbial criteria or tolerable daily intakes. Competent, updated and, a responsive team is required to harness these developments for the purposes of making food safety legislations work.

3.9. Epidemiological surveillance

One of the key hurdles to success of food safety legislations is dealing with unreported cases, of illnesses and deaths that arise from food-related illnesses. There must be a link and a close one at that between the food safety enforcing bodies, and the public health departments. Not just that countries must strive to strengthen the epidemiological data collection tools, but also the consumers ought to be well informed about the procedures and benefits of reporting every case even to including suspected cases.

3.10. Codex Alimentarius Commission (CAC) membership

Membership to CAC is voluntary as well as adoption of its standards. It focuses on ensuring consumer safety and promotion of trade. The CAC's legislation should only be a bare minimum and since they are based on science, they avail the platform that supports countries to provide safe and nutritious foods to their domestic as well as for international market. On this score over 50 African countries are members of CAC and this puts them at a platform to engage on food safety legislation [4].

4. Gaps and the hindrances to full implementation of food safety legislations in developing countries

So far, there are a number of factors that make it difficult for the food safety legislation to work "perfectly" in the developing countries. One of these reasons is minimal application of HACCP to food processing industry and particularly because its implementation is not a mandatory requirement. On the other hand, multinationals and some special food value chains, particularly the export-oriented ones, have adopted HACCP or even stricter systems as has been demanded by their customers in these markets. Of course, this varies across countries with South Africa leading other African countries in embracing third party certification of food companies. Developing countries must be made to understand and appreciate the fact that food safety management systems that work, provide more benefits to the citizenry and is better for the economy. These facts, however, may never have been so clearly stated and understood by those responsible for food safety legislation, implementation, and monitoring [2].

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4.1. The two faces of developing countries' food safety management systems

Most developing countries at least host multinational companies that are crucial and that serve a niche market. This includes the likes of Coca Cola, Unilever, Mars Incorporated, and Wrigley's among others. These are companies whose food safety management systems are extremely strict. In most cases, they are more focused on the use of their internal standards and auditing techniques than they do rely on the inspections mounted by governments. They have systems replete with a robust backup and huge capacity in terms of laboratories, personnel and necessary logistics. Unfortunately, in the developing countries, these lie and operate side by side with the uncoordinated; unregulated street food supply chain that indeed are greater sources of food especially for the urban, poor and middle class dwellers. The existence of the two tier-food safety operations in the developing economies: the multinationals and the local startups, is a phenomenon that must be harnessed as a learning point to enable food safety be addressed to all who are affected by it.

5. Case studies: status of food safety legislation in West Africa

5.1. Food safety legislation in Ghana

Ghana's food production system is dominated by informal—very intricate-small- and medium-sized enterprises (SMEs). Hazard Analysis and Critical Control Point (HACCP) systems are not applied by SMEs and occasionally by the large food processors in a reactionary manner, that is, in response to a food safety threatening incident or at the behest of consumers in foreign markets. Most of the local foods and brews are not necessarily included in the standards in Ghana, and this leaves a gap in which food safety programmes cannot be implemented yet these foods contribute massively to the quantity and nutritional intake of the population. These neglected food supply chains could easily be the source of food-borne illnesses and even death. Essentially, there is low literacy that people who are sensitive about food safety are seen to be doing so out of their affluence or to belong to a different class than everybody else. Compared to other challenges like lack of electricity, roads, and food insecurity due to inadequate supplies, food safety is not a priority to most developing countries. This may be the reason why inadequate funding is put toward this endeavor.

This lack of priority means many food supply chains for the majority of the rural areas and town dwellers are not regulated, and to compound this further, traceability mechanisms are almost nonexistent. However, for a few commodities traded formally and internationally, reasonable food safety parameters and legislations are in place. These commodities include; cereals, fruits, vegetables, oil seed, cocoa, and shea nuts. Ghana Food Safety Authority is faced with an inadequate food testing capacity quagmire. This is in reference to equipment, personnel, and the location of the main government laboratory in Accra, serving the whole country [5].

5.1.1. Main actors in ensuring food safety in Ghana

The various Ministries Departments and Agencies have been set up drawing form various legislations. There is, however, a need to have these standards revised and aligned to modern food regulations. Ghana Standards Boards' mandate is to establish and promulgate standards. It also promotes standardization in industry and commerce thus promoting industrial efficiency. Further, it promotes welfare, health and safety for consumers. In addition, it runs the certification scheme, inspection of food safety operations and metrology. Government of Ghana has several ministries involved in food safety legislation; with the ministry of Environment and Science, Trade and Industry, Ministry of Health, and Ministry of Food and Agriculture taking the leading roles. In the Ghanaian system standards setting formulation/drafting and advice is divorced from the bodies involved in control and enforcement of legislation. There is also separation of risk analysis and advice from the bodies mandated with management and operationalization of the food safety system. However, Ghana has also taken an important step in drafting the National Food Safety Action Plan (NFSAP) to restructure food safety, agriculture, and health institutions to improve efficiency and governance. Such a move allows for a coordinated effort among Ministries, Departments and Agencies, allowing for smooth operations, avoiding duplication of duties, eliminating conflicts and encouraging better enforcement of food safety legislation [5].

5.2. Food safety legislations in Nigeria

Food safety in Nigeria is undermined by inadequate application of Good Agricultural Practices (GAP), abuse of agrochemicals, use of pesticides for fishing, misuse of pesticides for stored grains, chemical contaminants like lead poisoning, and abuse of additives (butylated hydroxyl anisole, nitrates/nitrites). Other challenges include use of toxic packaging material with degradable components, public ignorance, uncoordinated approach and lack of technical expertise, including poor laboratory facilities. On top of this, there is inadequate enforcement of the available legislations. At the same time, food-threatening droughts force inclusion of contaminated food in to the value chain.

5.2.1. Components of national food safety control in Nigeria

The legal framework mirrors that of Ghana with major components being: legislation, policy, institutionalization (institutional framework), inspection, and laboratory testing services. National food safety policy was established in 1999. The establishment of the food safety policy in Nigeria set the country on a path toward well-coordinated food safety legislation. It recognizes the roles of the public sector and that of private sector in addressing challenges of food safety in a multisectoral model [6].

5.2.2. Bodies responsible for food safety legislation in Nigeria

The country boasts of numerous food-related legislations. The laws focus on consumer protection, proper coordination, development of relevant policy, and priority setting in enforcing food legislation. It advocates HACCP as the basis to all food production and processing operations. The other organizations in Nigeria, charged with food safety include the Ministry of Health, National Agency for Food and Drug Administration and Control, the Standards Organization of Nigeria, Ministry of Agriculture and Research and Development and Fisheries, Plant Quarantine Service, the Consumer Protection Council, Federal Ministry of Environment and, Federal Ministry of Trade and Industry. It also recognizes the role of university, research, and local governments in creating awareness and training of personnel for most food safety focused agencies. The key factors to successful food legislation in Nigeria are increased public awareness and customer education about the dangers of neglect of food safety. There should also be better coordination among the bodies charged with responsibilities for food safety. Lastly, capacity building by training of personnel, producers and regulators is vital toward achieving success in implementation of food safety legislation. The SMEs should be urged to form associations for ease of government support in terms of training and awareness creation [6].

5.3. Status of food safety legislation in East African Community (EAC)

Kenya has over 22 Food safety-related legislations under different Departments and Agencies. Kenya became a member of the Codex Alimentarius Commission in 1969. It has since played some crucial functions in various Codex committees and is currently chairing the CCAFRICA region. It has also adopted more than 100 Codex standards. Kenya has developed a National Food and Nutrition Security Policy. Food Safety is a key pillar of the policy document and it can be found under the subtopic of "Food Safety, Standards and Quality Control." The proposed National Food Safety Authority will be an innovative platform. Chiefly it will be mandated to conduct risk assessment, an area that has been grossly underrepresented in Kenya and the rest of the developing economies. It is also expected to promote human health and ensure better coordination among all the multiple-stakeholders in food safety. The Kenya's food safety management model is integrated with several bodies across different sectors mandated to ensure safety quality and promotion of trade for specific products in some cases [7]. Kenya is an integral member of the East African Community (EAC). The East African Community has been keen to harmonize several commodity standards with a total of 42 standards recorded as having been harmonized. The thrust has been to facilitate trade and remove barriers allowing for faster movement of goods across borders and thus reducing food losses. Most of these achievements have been through the Working Groups on various commodities. Despite the efforts directed to securing food safety in Kenya, foodborne illnesses, and outbreaks, fraud, and other ills are still reported with regularity [7].

5.4. The food safety situation in Asia contrasted to Africa

Having looked at some cases of developing countries in Africa, the focus shifts to understanding the food safety scenarios of developing countries in Asia. Two countries that are an important part of the Asian continent, Nepal and India are presented in a bit of depth. Developing countries in Asia have definitely unique food safety scenarios. Nepal, for example, became a member of WTO in the 2004, and hence food safety has acquired a reasonable interest. The most important challenges are as follows:

- Poor food safety regulation and enforcement infrastructure
- Inadequate technical and regulatory, assessment of conformity
- Inspections are difficult as the food producers, processors, traders and retailers are in large numbers and scattered across the country.

5.4.1. Major regulations governing food safety in Nepal

Nepal is a member of CAC, WTO, FAO, and South Asian Association for regional cooperation (SAARC). It is also a member of the World Organization for Animal Health (OIE) and Bay of Bengal Initiative for Multi-sectoral Technical and Economic Cooperation (BIMSTEC). The country drafted its first food legislation in 1966. This piece of legislation was called the Food Act. The Food Act spelled out the basis for control of inspection of food premises, destruction of nonconforming products and ensuring safety and quality of imported foods. This was then followed by the Plant Protection Act of 1972 and Animal Health and Livestock Services Act of 1998. The upsurge in international trade and economic liberations in Nepal in the 1990s made food safety a priority as it became critical for acceptance of products traded internationally. Initially, the focus of food safety strategies was toward end product testing. Increasingly though, the knowledge of HACCP and other important food safety systems has resulted in the focus moving to the "farm to fork" continuum. Food safety legislation is increasingly based on HACCP principles even though this is not mandatory yet. Owing to the fact that the country does not have a traceability component, effecting recalls, understanding sources of food contamination, and hence mitigation in times of food-borne outbreaks becomes very cumbersome and may take too long [8].

5.4.1.1. Food safety institutional framework in Nepal

The Food safety and quality management system in Nepal is under the Ministry of Agriculture and Cooperatives. This it done through the Department of Food Technology and Quality, which is focused on safety and quality of food in the market and ready to eat food. While the Department of Livestock and that of Agriculture are charged mostly with handling safety at primary production of food. The Nepal Council for Standards and the Nepal Bureau of Standards and Metrology are charged with standards development and implementation in Nepal. They are the standards governing body and custodians. Nepal Council for Standards (NCS) is mandated to approve all Nepalese standards while the Nepal Bureau of Standards and Metrology (NBSM) functions as the secretariat that prepares the standards. NBSM has developed and adopted more than 100 standards related to food. Through the South Asian Regional Standards Organization (SARSO), the country is also actively involved in development of regional standards. The Food Standards Board (FSB), advices government on standards and principles and also ensures that they are aligned to international standards. [8].

5.4.2. Food safety legislation in India and the institutional frame work

The food safety and quality management systems in India are under the mandate of the Food Safety and Standards Authority of India (FSSAI). There exists an increased demand for safe, high-quality food and greater choices among the Indian consumers. Food safety incidences like the 2015-withdrawal of *Maggi noodles* and the governments' surveillance of food-related illnesses contribute to create awareness on food safety among Indian consumers. Still, over the years, many food-borne illnesses are unreported and foodborne out brakes are erratically reported. In 2006, about 13.2% of households reported food-borne illness. Food Safety Standards Act (FSTA) of 2006 was designed to improve the overall safety of consumers and aid advancement in international trade. Food Safety Standards Authority of India (FSSAI) is wholly responsible for food safety matters. However, even after a decade of transitioning, there are still overlaps of legislations between the Bureau of Indian Standards and FSSAI especially with regard to milk. The same case is observed in fruits and vegetables as both the FSSAI and Agricultural Marketing Standards apply yet both are based on CAC standards. These incidences confuse consumers and make it difficult for producers to distinguish whether the regulations are mandatory or not. Finally, there also exist state-level legislations that require compliance, and this sometimes complicates the intra-state trade [9].

5.4.2.1. The focus for better operation of food safety and management system in India

There is a need to improve capacity to enable effective inspection and monitoring of food safety conditions in India. Prosecution and administration of food laws require to be devolved at the state level but currently lies at national level and therefore far flung areas are hardly reached. The country needs to improve laboratory access that currently is deficient and efforts should be made to improve on the number of specialists in the food safety related fields. The main focus in India's food safety management system is on upgrading laboratories and collaboration between the AGMARK and the FSSAI labs and the sharing of data. This way, only failed samples should be passed on to the national reference laboratory. The universities and FFSAI need to train and employ food safety experts. There is a need to increase awareness of all stakeholders especially on updated regulations. There must be increased emphasis on training of food handlers especially among the informal and small-scale food processors and producers. Currently, awareness is disproportionate among the rural consumers, and yet, these consumers like everyone else deserve good quality food. Use of mass media campaigns to target rural consumers will improve their awareness. Lastly, it is crucial to remove overlap in responsibilities of the organizations and assign clear mandates and modes of collaboration must be agreed [9].

6. The role of GHI and other professional societies in implementing food safety legislation in the developing economies

GHI was launched in 2004 by the International Division of IFT and the European Federation of Food Science and Technology (EFFoST) in collaboration with Food Safety Magazine and Elsevier Science. GHI officially achieved the status of a nonprofit, charitable association in 2007 and is registered in Vienna, Austria. GHI aims to harmonize food safety legislations and regulations based on solid science as datum for building consensus. GHI identifies issues presented with justification and evidence, then prioritizes them depending on the availability of experts as Working Groups (WGs) who then evaluate evidence provided to address the specific issue at hand [10]. Making food safety work in the developing countries requires a knowledgeable population. More often than not, the masses are easy to persuade and sometimes fall prey to misleading reports on food safety. Sometimes, politicians are culprits who twist food safety issues for political gain even when the claims are not scientifically sound. A case in point was the anti-GMO crusades conducted in Kenya in 2014–2015 leading up to the government's ban on production and trade of GMOs. GHI in its approach to promotion of harmonization of food laws is addressing serious issues that could be exploited to make food safety work in developing countries. These are discussed below.

6.1. Development of working groups on nomenclature of food safety

The organization believes that meaningful consensus building regarding food safety legislations and regulations can only be achieved if stakeholders have the same understanding of the working definitions of terms used in the area of food science and technology. This is often taken for granted, yet GHI experts prove that even among English-speaking nations like the UK and the USA, some terms used can markedly differ in their meaning. Take the definition of food additives for example, this is markedly different between Canada, US, EU and Japan. GHI has a Working Group Nomenclature on Food Safety and Quality, which had started with harmonization of Russian and English legislations particularly with regard to definitions of terms used in food safety and quality. Such a common definition will lead to a better understanding among food safety experts and enhance consensus building among the developing countries as well with the promise of better implementation of food safety legislation and regulations [11].

6.2. Training and education

The GHI Working Group on Education's aims to develop a curriculum for educating the public and all stakeholders in the food value chain is very timely. The curriculum is targeting food handlers and also everybody else in the food value chain. The WG aims to create training tools and materials written in simple understandable language and including use of pictorials targeting those who are not able to read. In addressing the knowledge gap, GHI works to ensure that certain key messages in food safety need to be presented in the local languages and in a manner that is understood to the media, political class, and consumers. GHI is of the opinion that food safety legislations and regulations are often written in a manner and a language that is difficult to understand even for trained professionals. Regulations must be "translated" into understandable language, so that people affected can appreciate them.

6.3. GHI wants regulations to be based on good science

GHI's impartiality can be harnessed to help promote consensus on standards and eradicate possible barriers and destruction of an otherwise safe food due to different countries' legislation. Evidently, it is not for lack of consensus among scientists that differences in food safety legislation occur but rather in the language and communication of the science to various stakeholders. To improve this, building of capacity in terms of personnel, data management, and risk assessment is critical. Most regulations, however, should be the same in all countries; differences may only be needed because of specific eating patterns or genetic issues, like in Japan and Finland where a large part of the population has no beta-galactosidase and therefore cannot digest lactose, which makes too high concentrations of cow's milk in food products toxic for such people. GHI wants to harmonize the regulations so that trade barriers are removed and food is not destroyed at the border just because the regulations between countries differ [10, 11].

6.4. Global incident alert network

The GHI is developing a Global Incident Alert Network for unauthorized food additives. In such a case, whenever it is found that an illegal (unauthorized) substance that can harm consumers is added to food, in any part the world, the individual who discovered that is tasked with the role of alerting a dedicated committee who will then have the means and the protocol to verify the issue within a short period of time and communicate the same to the relevant authorities who should then take the necessary actions to correct the situation. If necessary, this may be done anonymously, avoiding represailles by the employer. Such an initiative can also help developing economies and enhance transparency and adherence to food safety rules and regulations [11].

6.5. FAO, CAC and other international organizations

Codex Alimentarius Commission (CAC) is an intergovernmental body that is involved in development of food safety standards and is officially recognized by WTO as the arbitrator in conflicts involving food safety legislation between countries or companies at the international level [12]. Though CAC has done a great deal in this regard, it has faced a few challenges that derail its efforts in harmonizing food safety regulations. First, it meets annually and this means the matters agreed at such meetings do not receive speedy progress. Second, the participants to these committees are not always food technologist with grounding on food safety; furthermore, they may strive to secure the interest of the countries they represent as a priority. The African Union (AU) has formed expert committees that mirror those of Codex. These food safety experts' committees now can offer thoughts considered as Africa's position on food safety matters. This is a key development as it offers a focal point of responding and dissemination of information. The AU is also fronting the formation of the African Food Safety Authority that will set standards for monitoring Africa's food supply chain, an equivalent of the European Food Safety Authority (EFSA). There must be a good political will for food safety legislations to work in the developing economies and this initiative being spearheaded by the political arm of AU may just be the right recipe for stimulating local action [2, 11].

6.6. Innovations that could lead to a faster and better legislation of food safety in the developing world

The first strategy is the implementation of the rapid alert and response system: that was proposed by GHI in 2014. This system if operationalized can lead to information sharing across the countries. Sharing strategic information could easily save lives by stopping potential food-borne outbreaks before it happens or at least at a very early stage. Analysis of some of the major incidents involving food-borne illnesses in the world indicate that a majority of them would have been prevented had there been a proper reporting channel from those who were involved but who did not talk due to fear of reprisals and possible loss of jobs [11]. Operationalization of such an alert would enthuse consumer confidence leading to increase the economic development. Such a move would stimulate demand for high quality products that puts the whole food safety management system of the developing countries on a higher trajectory. Easier reporting channels, operationalization of help lines, including mobile apps that consumers and small-scale processors can reach to seek help and meet with experts in food safety can provide huge impact.

The second aspect that needs quick redress is regional risk assessment. Due to the nature of funding and capacity required to make this happen, countries and institutional collaborations in this area will help developing countries to not only cost-share requisite infrastructure, but also the ensuing data that may be similar in a number of cases. Such an undertaking will help countries avoid duplication of efforts, reduce unnecessary spending on infrastructure, and enhance better collaboration on matters of risk analysis data among neighboring countries.

Third, knowledge and training of populations on the food safety basics is the most important aspect in making food safety work best in developing economies. Food technologist and the food technology organizations including those adhering to the IUFoST ought to play a bigger role in pushing food safety agenda and particularly in the area of training and education. Both IUFoST and GHI have a training component (the universal food safety curriculum) that is envisaged to greatly improve consumer and other stakeholders' confidence to play their role of keeping processors and vendors in check with regard to food safety. Creation of awareness to consumers about their rights and privileges confers them confidence and empowers them to keep the food industry and government on toes to deliver on their food safety mandate. All food processors and street vendors, regardless of their remote location and "small" service, must be encouraged to register into clusters of 50–100 or even smaller groups through which expert knowledge on basic hygiene and safe food handling practices can be passed on to them.

Fourth, every single cottage industry that is set up must be made comfortable to realize that the food safety legislations are actually for their good and not meant to keep them away from business. This requires a better working relationship between law enforcing bodies and these food startups. The focus for these legislating bodies should be to midwife these businesses first to profitability through functioning food safety systems, rather than focus on levies when the factories can hardly break even.

Fifth, massive and urgent educational input is required in the area of abuse of additives, or fraud in using chemicals like calcium carbide as an artificial ripening agent in fruits and vegetables by unscrupulous traders in countries like India, and some places in Kenya [13]. Or even the use of formalin in meat preservation, or large doses of sodium metabisulphite in meat preservation to mention a few. The use of these and other cancer causing chemicals must be addressed to consumers and processors and their relation to cancer or the ensuing impact of that, on households and public health explained. It is very critical to make sure that people are made aware of the dangers of the use of such chemicals and their abuse. However, the education must be complete by making consumers understand the relationship between dose, exposure and the possibility of dangers particularly on additives. This way alarmistic remarks that cause panic resulting in loss of what would essentially be good food, will be avoided [11].

Lastly, laboratory facilities are key pillars to ensuring food safety in developing countries. However, they require huge initial investments, high running costs, and very well-trained personnel who are equally expensive to sustain. Developing countries should be encouraged to consider setting up regional centers of analysis, intra-country laboratories, shared regional analytical capacity, and even regional training. This suggestion when implemented will greatly lower the costs and improve access to laboratory analytical facilities. The collaborating countries can also realize a state-of-the-art facility thus enabling quick in-depth analysis that is very important in case of mounting surveillance or diagnostics in cases of disease outbreaks. The private sector involvement and support in availing laboratory analysis and facilities should also be considered seriously as a means to bridging the gap.

6.7. Next dimension to making food safety work in developing economies

Education is key area that must be addressed to provide capacity. Safety consciousness as a culture along the entire value chain is key.Food Biosecurity or Defense is increasingly becoming important, yet most developing countries are yet to begin to put policy mechanisms or laws that govern their food value chains and protect it from fresh threats like bio-insecurity or even bioterrorism. This also goes to developing countries' capacity in responding to biosafety concerns and accompanying legislation. It is high time developing countries begin to deal with the concepts of GMOs based on evidence and perhaps exploit this area that may lead to sufficient foods, thus eliminating the need to allow unsafe foods to enter the value chains due to food insufficiency [11]. Even though the countries have differing opinions on GMOs, the inadequate capacity to test for transgenics in developing economies makes it twice critical that some form of harmonized response based on evaluated and impartial evidence, be reached to facilitate transboundary movement of GMOs.

7. Conclusions

This chapter has focused on the unique challenges to food safety legislation in some developing economies and the innovative ways in which the stake holders should approach the subject and make it more effective. It has also presented case studies of food safety situations in some developing countries: Asia (India and Nepal), West Africa (Ghana and Nigeria) and East Africa. Finally, it proposes major innovations that could be put into play to make food safety legislation work more effectively in the developing economies.

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Conflict of interest

The authors have no conflicts of interest in addressing this topic.

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Chapter 4

Quorum Sensing Inhibition and Anti-Biofilm Activity of Traditional Chinese Medicines

Xihong Zhao, Fenghuan Zhao and Nanjing Zhong

Additional information is available at the end of the chapter

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Abstract

Bacterial biofilm, a special stage which a large amount of bacteria are adhere to surface, increase resistance to antimicrobial agents. However, all the bacteria are possibly developed into biofilm, and bacterial biofilm is more difficult to remove from environment comparing to planktonic bacteria, which can be a strike to food industry. Many researchers have showed that traditional Chinese medicines contribute to the reduction of bacterial formation, since the important factor (quorum sensing) in biofilm formation is inhibited by traditional Chinese medicines. In this review, the effect of traditional Chinese medicines and its inhibition mechanism of biofilm formation on common bacterium biofilm are summarized, which provide a new direction for the removal of bacterial biofilm.

Keywords: Chinese medicine composition, biofilm, quorum sensing

1. Introduction

Bacterial biofilms, a bacterium growth state, which can attach to living and non-living surfaces, consist of a small part of bacteria and self-produced hydrated matrix of extracellular polymeric substances. Biofilm bacteria are more resistant to antimicrobials compared with planktonic bacteria, which cause their elimination from food processing facing great challenges [1]. The emergence of bacterial resistance to conventional antimicrobials clearly shows that new biofilm control and removal strategies need to be proposed. Quorum sensing (QS), is an important mechanism of bacteria protection that enable bacteria to deliver special signal in response to changes of cell density in a certain environment, causing biofilm formation and other virulence factors [2]. When the bacterial population densities reach a certain threshold, bacteria will regulate virulence, biofilm formation, luminescence and etc. Virulence expression and biofilm formation, protecting bacteria from adverse environment, are considered to be harmful for pathogen therapy and human healthy life [3]. The normal operation of QS system requires the participation of signal molecules, such as acylhomoserine lactone [4]. In a word, the reagents that can inhibit QS regulation will interfere with biofilm formation, which means that the reagent possess ability of QS inhibition (QSI) [5]. As we know, traditional Chinese medicine has been applied for antibacterial and anti-inflammatory for many years. However, studies on traditional Chinese medicine for drug discoveries have focused mainly on its antibacterial property. A few attention has been given to its quorum sensing inhibition and anti-biofilm activity [6]. Thus, the ability to disrupt this signaling process and QS signals may be advantageous in the removal or prevention of bacterial biofilm. Different Chinese medicine composition shows different effects on QS [7]. In order to provide references for QSI to control biofilm formation, the effects of traditional Chinese medicines and its inhibition mechanism of biofilm formation—QS on common bacterium biofilm are reviewed in this article.

2. Different QS on gram positive and gram negative bacterium

Quorum sensing, a cell-to-cell communication system, plays a key role in biofilm formation. When cell-to-cell signals arrive at a certain threshold, bacteria will secrete adhesion molecule and develop into biofilm with three dimensional structures [8]. Biofilm formation is a dynamic state which consists of (i) attachment, (ii) microcolony formation, (iii) maturation and (iv) dispersion [9, 10]. Quorum sensing affects the whole process of biofilm development. It is recognized that biofilms are mainly regulated by quorum sensing [11]. With quorum sensing response to the environment, bacterium occurs to the secretion of signaling molecules, the expression of the corresponding gene, and the secretion of extracellular polysaccharide (EPS) [12]. The study showed that the content of proteins, carbohydrates, and nucleic acids matrix increased significantly in the mature biofilm, since the biofilm matrix could protect the embedded cells from harmful conditions [13]. It has been reported that signal molecules play an initial role in QS system, and different signaling molecules are secreted by different bacterium: (i) N-Acyl homoserine lactones (AHLs), which are synthesized by LuxI-type enzyme, are mainly functioned in gram-negative bacterium, such as *Aeromonas hydrophila* [14] and *Pseudomonas aeruginosa* [15]. Most of gram-negative bacteria generate and detect several autoinducers, including C4-HSL, 3OH C4 HSL, lsovalery-HSL and etc. The chain length of AHLs can vary from 4 to 18 carbons, where oxidation status of the third carbon can change from fully reduced to fully oxidized [16]. The regulation of AHLs controls a series of target functions, such as biofilm formation, motility, fluorescence synthesis, expression of virulence genes and production of virulence factors [17]. When the concentration of signals arrives at a certain threshold, AHLs automatically enter the bacterium, binding to the cognate receptor to form an autoinducer-receptor complex, which causes the expression of functional gene (**Figure 1**). AHLs defective *P. aeruginosa* produced less virulence factors and less biofilm, and are diffusible signal molecules that may cause infections in human [16]. (ii) Gram-positive

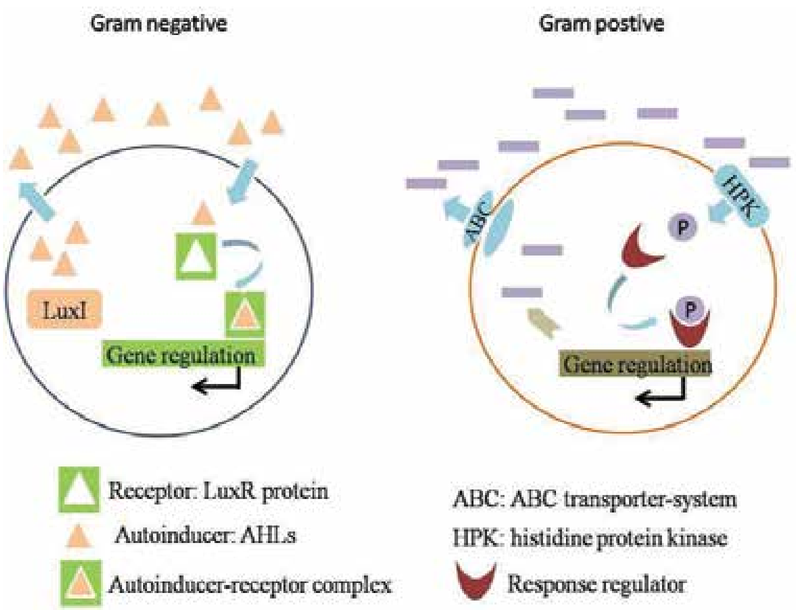

Figure 1. A graphic diagram of QS molecular signaling network.

bacterium is mainly regulated by autoinducing peptides (AIPs) [18]. Since AIPs cannot pass through the cytoderm by itself, bacterium response to the environment through two-component protein, transmit the signal to the cell. The activation of the receptor kinase takes place when reaching the threshold level. The sensor kinase protein can be activated and then phosphorylate the response regulator protein, which bind to the target promoter, and subsequently transcriptional activates the genes for the two-component regulatory system, resulting in autoinduction in a dynamic range [19]. The production of AIP is expressed by relevant genes, then releasing out of extracellular membrane (**Figure 1**). (iii) Autoinducer-2 (AI-2), a signal molecule produced by LuxS, widely existed in both gram-positive and gram-negative bacterium. AI-2, which involved in regulating the many bacterium biofilms, was thought to be a universal signal molecule [20]. It has been demonstrated that regulation of AI-2 plays a significant role in biofilm formation in many kinds of bacteria. DPD is known to undergo intra-molecular cyclization to form distinct biologically active signal molecules, which collectively called AI-2. Thus, the AI-2 signal should not be recognized as a single structure, but a family of isomers, each bacterium representing a different mode of perception [21]. (2S, 4S)-2-methyl-2, 3, 3, 4 tetrahydroxytetrahydrofuryl borate (S-THMF-borate) is the AI-2 signal of *Vibrionaceae*, while *S. Typhimurium* produces (2R, 4S)-2-methyl-2, 3, 3, 4- tetrahydroxytetrahydrofuran (R-THMF) as AI-2 signal. Quorum sensing pathways of AI-2 differs due to different bacterial species [22]. Most of the gram-positive bacteria are sensitive to penicillin, while gram-negative bacteria are not usually influenced by penicillin. Thus, the application of QS inhibitor is of great significance in biofilm inhibition and bacteria removal [23]. The process of QS can be disrupted by different mechanisms: (i) inhibiting the production of QS signal molecules (AHL, AI-2 and AIP), (ii) reducing the activity of QS signal molecules, (iii) degradation of QS signal molecules, (iv) designing the analogues of signal molecules as QSI [24]. The regulation of QS may play a dual role on bacteria. Interferon with QS process can prevent bacteria from biofilm protection and virulence expression, but it is limited that antibiotic---antimicrobial cannot disrupt QS regulation. Traditional Chinese medicine is popular as QS inhibitors to disrupt QS signals, and thereby destroy bacterial biofilm and virulence expression without killing bacterium itself [25].

3. QSI on gram positive bacteria

Staphylococcus is one of the kinds as common and representative gram positive bacterial pathogens in the research of QS and biofilm development. Quorum-sensing regulation plays a vital role in the biofilm formation of many bacterial pathogens [26]. As previous mentioned, *LuxS* emzyme participated in the synthesis of AI-2, which had an indispensable impact on biofilm development of staphylococci quorum-sensing system. Δ*luxS* mutant strain shows more biofilm formation in vitro and enhanced virulence in *Staphylococcus epidermidis* of biofilm-associated infection. The inhibitors of *luxS* expression in vitro can be a promising QS inhibitor for the prevention of biofilm and virulence [27]. Burdock leaf ethanol fraction suppressed biofilm formation of *S. aureus* and *Listeria monocytogenes*. It was found that burdock leaf ethanol fraction (1.25 mg/ml) entirely inhibited (100%) the *S. aureus* biofilm formation, which was lower than MIC of the fraction. GC–MS/MS analysis shows that eight active compounds from burdock leaf fraction interfered with quorum sensing regulation and disrupted the composition of signaling molecules, thereby affecting the function of the quorum sensing system and disturbing biofilm formation. Eight active compounds should be exactly identified for real applications [28]. Later study analyzed 34% ethanol elution fraction of burdock leaf, found that 10 active compounds exhibited anti-biofilm activity, including chlorogenic acid, caffeic acid, p-coumaric acid, quercetin, ursolic acid, rutin, luteolin, crocin, benzoic acid and tenacissoside I. According to the metabolic fingerprints of burdock leaf fractions, chlorogenic acid and quercetin were demonstrated to be a potential antibiofilm of *Salmonellaty phimurium* compounds in burdock leaf [29]. *S. aureus* strains were tested for a relation between the ability of *S. aureus* attachment in polystyrene and the agr quorum-sensing system phenotype. Less of agr-positive strains cause biofilm formation, showing a vital impact of agr on biofilm development. Inhibitor of agr is as quorum-sensing blockers for *S. aureus* prevention [30]. The emergence of methicillin resistant *S. aureus* (MRSA) caused antibiotic invalidity and required new drugs for treating infectious diseases. *Chamaecyparis obtusa* essential oil had antibacterial effect against MRSA, finding *agr*A expression was inhibited with *C. obtusa* essential oil. Thus, *C. obtusa* essential oil regulates quorum-sensing to inhibit MRSA biofilm formation [31]. Study shows a certain concentration of *baicalein* (32 μg/mL and 64 μg/mL) clearly inhibited biofilm formation in vitro, and the combined use of vancomycin and baicalein generally enhance disruption of biofilms. 32 μg/mL and 64 μg/mL *baicalein* downregulate the quorum-sensing system regulators agrA and affecting biofilm development. Therefore, *baicalein* can inhibit the quorum sensing system while enhancing the permeability of *vancomycin* and reducing the production of staphylococcal enterotoxin A and α-hemolysin as well as inhibiting *S. aureus* biofilm formation. It is predicted that *baicalein* will be a novel drug candidate for *S. aureus* infections [32]. There are differences on the combination of ethanolic extracts of eight traditional Chinese medicines and four antibiotics. The ethanolic extracts of *Isatis tinctoria*, *Scutellaria baicalensis* and *Rheum palmatum* enhance the antimicrobial activity of four antibiotics on resistance of methicillin resistant *S. aureus* [33]. In summary, traditional Chinese medicine extracts inhibit QS and biofilm formation by controlling QS molecular signals, and usually regulating the cell to cell QS---AI-2. Recently, scientists deeded crude extract of anti-QS activity and Chinese herbal medicinal ingredient should be taken in-depth study in the future.

4. QSI on gram negative bacteria

Previous studies have demonstrated that a large majority of traditional Chinese medicine show great sensitivity to gram negative bacteria QS and biofilm. It is well-known on the research of QS that *Chromobacterium violaceum CV026* and *P. aeruginosa* PA01 is regard as two biomonitor strains to detect QSI on traditional Chinese medicine [34]. Twenty kinds of traditional Chinese medicine plants generally used in South-East Asia were screened for QS inhibition using two biomonitor strains, *P. aeruginosa* and *C. violaceum* CV026 PA01—gram negative bacteria. *C. violaceum* CV026, which can produce AHL signal molecule, produce purple pigment. *P. aeruginosa* PA01 control swarming through QS regulation. Thus, the change of purple pigment and swarming can be used to reflect the regulation of QS. This study found that 8 kinds of traditional Chinese medicine extracts possess QSI ability in *C.violaceum* CV026, and 4 kinds of traditional Chinese medicine extracts possess QSI ability in PA01. *Lilium brownie* and *Panax pseudoginseng* extracts possess QSI ability both in PA01 and CV026, which are meaningful for various biofilm inhibitions. The findings revealed that there are rich sources of plants on traditional Chinese medicine that contain components are able to break QS and QS-related virulence factors. However, the specific compounds and mechanism should be applied into deeper study [35]. Four organic solvents (n-hexane, DCM, methanol and 50% v/v acetone) were used to extract *Ficus carica* and *Perilla frutescens* in another study. The tests of *C. violaceum* CV026 and *P. aeruginosa* PA01 finds the extract of *F. carica* with dichloromethane an*d of P. frutescens* with MeOH show the obvious inhibition of QS activity. Both of them display anti-QS ability. It is not sure the ingredient and inhibition concentration of crude extracts [36]. Study found that methanolic extract of *Phyllanthus amarus* interrupted the ability of *C. violaceum* CV026 to response towards exogenously supplied N-hexanoylhomoserine lactone, exhibiting the anti-quorum sensing activity. In addition, as the concentrations of the methanolic extracts of *P. amarus* increased, swarming motility, pyocyanin production and *lecA: lux* expressions in *P. aeruginosa* PA01 were reduced. Methanolic extracts of *P. amarus* may serve as promising anti-pathogenic drugs due to its anti-quorum sensing properties [37]. Ginseng aqueous extract at concentrations of 0.5–2.0% significantly inhibited *P. aeruginosa* biofilm formation. Oral administration of ginseng extracts in mice did not affect phagocytosis of a PAO1-filM mutant. According to previous study, Ginseng aqueous extract may prevent biofilm development by the regulation of QS [38]. Quorum sensing inhibitors could inhibit biofilm formation, but the exact role of quorum sensing in various stages of biofilm attachment, maturation, and dispersal is not clear. In vitro the combination of antibiotic and QS inhibitor generally lead to increase bacterial lethality, compared with treatment by an antibiotic alone. The combination of tobramycin and baicalin hydrate reduced the *burkholderia cenocepacia* infection. Among this study, baicalin hydrate targets the acylhomoserine lactone-based QS system present in *B. cepacia* complex organisms [39]. Curcumin from *Curcuma longa* (turmeric), an anti-QS agent, was demonstrated to inhibit the biofilm formation of *E. coli*, *P. aeruginosa* PAO1, *Proteus mirabilis* and *Serratia marcescens*, interfering with their QS systems. The treatment with curcumin may attenuate the QS-dependent factors, including exopolysaccharide production, alginate production, swimming and swarming motility of uropathogens. Curcumin is as a QSI for urinary tract treatment [40]. Three anthocyanidins (pelargonidin, cyanidin and delphinidin) decreased the formation of *P. aeruginosa* PAO1 biofilm at low sub-MIC (0.125 MIC). Comparing with ampicillin and streptomycin, delphinidin show the most active of anti-biofilm activity. Water-soluble delphinidin structure could be used for the design of the novel and more effective anti-biofilm agents [41]. N-acylhomoserine lactone (AHL)-based QS plays vital role in biofilm formation and virulence expression. Three Chinese herbal ingredients namely are salicylic acid, tannic acid and trans-cinnamaldehyde, are as AHL synthase inhibitors to inhibit quorum sensing. Natural products targeting AHL synthase may provide anti-QS signal synthesis for prevention of pathogenic bacteria [42]. Traditional Chinese herbs could inhibit key biofilm-associated genes in *P. aeruginosa*. *Herba patriniae* extract showed significantly reduction on the biofilm formation and change the structure of the *P. aeruginosa* biofilms. Further studies showed *H. patriniae* extract promoted its swarming motility. The possible inhibition mechanism is that *H. patriniae* may regulate QS to control bacterial biofilm and swarming [43]. Study found that 30 mg/ml of *Melia dubia* seed ethanolic extract inhibited biofilm, hemolysis and swarming motility by 92.1, 20.9, and 48.52%, suggesting that the ethanolic extract possessed potency to restrain quorum sensing of uropathogenic *E. coli* [5]. It has been demonstrated that quorum sensing quenching effect exists in traditional Chinese medicine plants, foreseeing the tremendous prospect of QSI application on traditional Chinese medicine [44]. The concrete mechanism of traditional Chinese herbs is unsure, but some chemical components have been found in traditional Chinese herbs. It is believed that most of traditional Chinese medicines are as promising QS inhibitors for bacterial infection and biofilm disruption. Traditional Chinese medicines may be a novel material for infectious diseases and food safety with antibiotic.

5. Active constituent of traditional Chinese medicines

To sum up the above arguments, most researches of QSI on gram negative bacteria have been taken into deep consideration. It has been demonstrated that *P. aeruginosa* PA01 and *C. violaceum* CV026 can detect QSI of gram negative bacteria. Furthermore, the active constituent of traditional Chinese medicines also has been shown in the research. Most of active constituents are extracts of water-alcohol, since aqueous extracts are more effective on biofilm inhibition than organic solvent. *Panax pseudoginseng* extracts on mouse test and experiment in vitro

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Type	Components of TCM	Bacterium	References
Flavonoids	Baicalein	*S. aureus*	[32]
	Baicalin	*B. cenocepacia*	[39]
	Anthocyanidin	*P. aeruginosa*	[41]
	Curcumin	*E. coli* & *P. aeruginosa*	[40]
Organic acid	Salicylic acid	*P. aeruginosa*	[42]
	Chlorogenic acid	*Salmonella*	[29]
Essential oil	*Chamaecyparis obtusa*	MRSA	[31]

Table 1. Effective components of TCM on bacterial biofilm.

found that aqueous extracts control biofilm formation by the regulation of QS [45]. In addition, methyl alcohol and ethyl alcohol, especially ethanol extract, are regarded as the common solvent to extract traditional Chinese medicines. Anthocyanidins, salicylic acid, baicalin and curcumin show inhibition of QS and QS-dependent biofilm, which can be assumed traditional Chinese medicines plants containing these components control QS regulation (**Table 1**). Now the combination of these components and antibiotic to kill bacteria are more effective that single antibiotic, so it is hopeful that the components can treat bacterial infection efficiently. Except for Staphylococcus, QSI on other gram negative bacteria is less mentioned. Ethanol extract of traditional Chinese medicines also possess strongly anti-biofilm property, but the mechanism of QS to biofilm inhibition is still unsure. Similarly, the active constituents on gram positive bacteria are flavonoid and organic acid, such as chlorogenic acid, chrysophanic acid and baicalein (**Table 1**). In summary, it is found that flavonoids extracted on TCM can be used as a hopeful QS inhibitor. Some of organic acid and essential oil not only reveal antibacterial property, but also show biofilm inhibition. Thus, it is believed that traditional Chinese medicines containing these components can hinder QS regulation and biofilm formation, and the plants with anti-QS and anti-biofilm property should be taken into consideration.

6. Conclusion

Different components of traditional Chinese medicine also exert anti-QS activities on the gram-positive bacteria and gram-negative bacteria. Gram-negative bacteria seems sensitive to QS inhibitor, since *C. violaceum* CV026 and *P. aeruginosa* PA01 are usually as biomonitor strains for detection of QSI [46]. Common pathogenic bacteria, such as *S. epidermidis* [47], *S. aureus* [48], *E. coli* [49] and *P. aeruginosa* [50], are mainly interfered with biofilm development and toxicant release by QS regulation. It has been found that the combination of traditional Chinese medicine and antibiotics could improve the antibacterial activity and remove bacterial biofilm effectively. Nowadays most of traditional Chinese medicines are screened for a pathogenic bacterium QSI. However, less reports show a broad spectrum QS activity on traditional Chinese medicines [51]. Therefore, screening traditional Chinese medicine ingredients with anti-QS function, can treat the common pathogens biofilm and remove drug-resistant bacteria, being promising drugs for antibiotics auxiliary treatment. Antibiosis activity has been shown in many Chinese medicine ingredients, but now antibiotics are still the priority drugs for clinic treatment of infectious diseases. The following problems are for the better development of traditional Chinese medicine in the future. The first step is to explore QS mechanism of traditional Chinese medicine, enable traditional Chinese medicine ingredients inhibit the specific pathogens biofilm this phenomenon reach a theoretical stage thus people can have a more profound understanding. Secondly, the researches of traditional Chinese medicine still experience in a basically experimental stage. Experimental in vivo and clinical trials on traditional Chinese medicine should be strengthened, only which can lead to a further application. The last but not least, the specific efficacy of traditional Chinese medicine should be confirmed, and try to use new methods on extracting them. Since traditional Chinese medicine work usually by complex inducers, novel methods like metabolic engineering can be applied to increase the active ingredient dramatically in the meanwhile decrease the cost. It is hoped that traditional Chinese medicine could be used for food safety in the food industry.

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Conflict of interest

All authors declare that they have no conflict of interest.

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Chapter 5

Foodborne Bacteria: Potential Bioterrorism Agents

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Additional information is available at the end of the chapter

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Abstract

Bioterrorist attacks are usually associated with airborne infections because of their easy dissemination and maximal effect on the human population. However, foodborne pathogens represent potential bioterrorist weapons, as the consumption of safe food affects every individual in the society. Most of the foodborne microorganisms can be readily isolated from natural sources and can cause severe outbreaks with a number of hospitalized persons. Biological agents, which may contaminate food products, are bacteria, viruses, yeasts, parasites, or chemical substances with microbial origin. They cause more than 200 diseases—ranging from diarrhea to cancers. Typical symptoms of food poisoning are abdominal cramps, nausea, vomiting, upset stomach, diarrhea, fever, dehydration, and others. Most isolated bacterial agents responsible for foodborne infections include bacteria from genera such as *Salmonella, Shigella, Bacillus, Clostridium, Listeria, Campylobacter, Escherichia, Staphylococcus, Vibrio, Enterobacter*, and *Yersinia*. In this chapter, we discuss the bacterial species causing food poisoning in the context of a potential bioterrorist attack. We review in a concise manner their morphological and biochemical characteristics, as well as the treatment and possible prevention measures. Popular examples of attacks with food poisoning agents and their impact on the society are also given.

Keywords: food poisoning, public health, bioterrorist agents, bacterial infections, prevention

1. Introduction

Bioterrorism refers to the use of infectious agents or other harmful biological or biochemical substances for terroristic purposes. Usually, the measures against bioterrorist attacks are focused on the aerosol infections, as airborne microorganisms can easily affect many people and lead to maximal morbidity when entering the respiratory tract. However, in some cases, the aim of a bioterrorist attack is not to achieve high lethality but also to produce fear, panic, and chaos in the community. In this context, the intentional dissemination of bacterial agents causing food poisoning is a potential bioterrorist threat.

The first attempts to use the pathogenic properties of some microorganisms in a destructive manner dated many centuries ago. In particular, bacteria causing food poisoning were extremely suitable as many of them (plague, cholera) were epidemically spread in the past and easily available for war and bioterrorist purposes. The plague is a typical example with many naturally occurred outbreaks and one well-documented intentional epidemic in human history: in 1346, during the Tatar siege of Caffa on the Crimean Peninsula, infected corpses have been catapulted in the city to cause a local outbreak which finally resulted in one of the most devastating epidemics in Europe—the Black Death [1].

In the beginning of the twentieth century, biological agents were used on a scientific basis by different national governments for war purposes. The effects of anthrax, cholera, glanders, dysentery, tetanus, typhus, salmonella, tularemia, and typhus with pox were less or more successfully studied and tested on animals and humans [1–3]. Comprehensive studies on the use of botulinum toxin were also undertaken during World War II, especially by the US government which intended to use prostitutes to assassinate Japanese officers by gelatin capsules loaded with botulinum toxin [4].

In the next decades, despite the ratification of a Convention on the prohibition of the development, production and stockpiling of bacteriological (biological) and toxin weapons and on their destruction (usually referred to as the Biological Weapons Convention) in 1972–1975, most of the countries have continued to work and design new biological agents to be used as weapons in eventual war conflicts. In such a way, fundamental knowledge was gained and it was just a question of time to be used for destructive purposes.

At the end of the twentieth century, the changed geopolitical situation resulted in less confrontation between the countries but in the appearance of different political, religious, or nationalistic extremist movements with well-qualified and motivated members, prepared to use the available knowledge and technologies. Between 1990 and 1995, at least three bioterrorist attacks with botulinum neurotoxin failed in Japan [5]. During the same decade, the international community found thousands of litters of botulinum toxin, anthrax, and aflatoxin in Iraq that were ready to be used as mass destruction weapons [6].

The biggest bioterrorist attack in the USA occurred in 1984 with a foodborne pathogen—*Salmonella typhimurium*—which was used to contaminate salad bars in restaurants in Oregon [7]. Members of the religious commune "Bhagawan Shree Rajneesh" tried to sabotage the local elections and succeeded in infecting 751 persons.

In 1996, intentionally contaminated muffins and doughnuts caused severe gastroenteritis in 12 laboratory staff members in a large laboratory in the USA [8]. The investigations revealed *Shigella dysenteriae* type 2, identical to the laboratory's stock strain, as the causative agent of the outbreak. However, the origin and the purpose of this attack remained unknown.

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The most popular bioterrorist attacks occurred in 2001 over the whole territory of the USA when spores of *Bacillus anthracis* were sent via post letters to different governmental and public institutions. As a result of these attacks, 22 persons were infected and 5 of them died.

In the twenty-first century, with the enlarged terrorist activity, the preparedness of society for bioterrorist attacks, including intentional food poisoning, should also expand to guarantee quick response and adequate action. The main foodborne pathogens with a potential to be used as a biological weapon should be known, as well as their prevention and treatment.

2. Classification of foodborne bacteria as potential bioterrorist weapons

The Centers for Disease Control and Prevention (CDC) recognizes three categories of biological agents in respect of bioterrorism [9]:

- Category A: These are high-priority agents posing a risk to national security because of their easy dissemination, high mortality rates, and high public health impact. They require special action for public health preparedness.
- Category B: These are the second highest priority agents. They have moderately easy dissemination, moderate morbidity rates, and low mortality rates. These microbes require specific enhancements of diagnostic capacity and enhanced disease surveillance.

Bacterial species	**Disease**
Category A	
Bacillus anthracis	Anthrax
Clostridium botulinum	Botulism
Yersinia pestis	Plague
Category B	
Brucella spp.	Brucellosis
Enterobacteria (*Salmonella spp*, *Shigella spp.*, *Escherichia coli O157:H7*)	Salmonellosis, dysentery, other gastrointestinal diseases
Staphylococcus aureus	Food intoxication
Clostridium perfringens	Food intoxication, gas gangrene
Vibrio spp.	Cholera and cholera-like diseases
Category C	
Not cited	

Table 1. Categories of foodborne bacteria (and their corresponding diseases) as possible bioterrorist agents (according to [9]).

- Category C: These include the third highest priority agents, which are emerging pathogens that could be easily engineered. They have potential for high morbidity and mortality rates and major health impacts.

Table 1 shows which foodborne bacterial pathogens fall into these three categories of potential biological weapons. *Bacillus anthracis* is the bacterium most likely to be used as a bioterrorist agent because its spores are widely spread in nature and it easily grows under nonspecific conditions in the laboratory. Anthrax spores can be released at any place as aerosols but also can be put in food and drink. However, airborne route of transmission is more dangerous for the society and therefore preferred for terroristic purposes. Historically no intentional cases of foodborne transmission of anthrax are cited and as the objective of this chapter is to summarize food poisoning agents as potential biological weapons, *Bacillus anthracis* should not be considered further in the text.

3. Foodborne bacteria that can be used as potential bioterrorist agents

3.1. *Clostridium botulinum*

Clostridium botulinum is a Gram-positive, anaerobic spore-forming bacterium, which is common in soils, sediments, animal excrements, and gastrointestinal tract of birds and mammals. It causes botulism. The three forms of the disease are known—foodborne, wound, and infant botulism. The foodborne botulism is the most common form and represents an intoxication which occurs after the ingestion of food contaminated with botulinum toxin. It is mainly caused by botulinum toxin type A, B, and E [10]. The wound botulism is a result of the invasion of a wound with *C. botulinum*. Finally, the infant botulism is an intestinal infection of the non-matured gastrointestinal tract of babies after the consumption of food contaminated with *C. botulinum* (usually honey or water). The symptoms start 18–24 h after the consumption of infected food or after the entry of bacteria into the traumatized tissue. The disease is usually severe—in the foodborne form, it manifests with abdominal cramps, headaches, and vomiting. In all forms of the disease, late symptoms include paralysis of eye muscles (ptosis of eyelid and damage of accommodation), difficulty in swallowing, speech, and breathing.

Diagnosis of botulism is often difficult and consists of toxin demonstration in serum, fecal, or food samples. Patients suspicious of botulism should be hospitalized immediately and the treatment should start immediately with antitoxin administration. The therapy includes intubation and ventilation, as paralysis of respiratory muscles is the primary cause of death from botulism [11]. Antibiotic treatment with penicillin, tetracycline, metronidazole, and chloramphenicol is also recommended but aminoglycosides should be avoided as they may cause additional complication.

The botulinum toxin is a neurotoxic protein of two polypeptide chains linked with a disulfide bond [12]. Nine types of the toxin exist—from A to H (C is divided into C1 and C2) [13]. The mechanism of action consists of the inhibition of the acetylcholine release in the neuromuscular synapses, which results in blocking the neural impulse transmission and muscle paralysis.

Currently, botulinum toxin is considered as the strongest toxic substance in the world—1 g may cause the death of millions of people. The symptoms of botulism, as well as the bacterial characteristics, classify *Clostridium botulinum* in category A of biological agents with the potential to be used as a terroristic tool (**Table 1**). The disease is associated with severe neuromuscular damage, urgent need of hospitalization, and intubation. In the case of massive infection, the hospital infrastructure of any country could not provide adequate care for all patients. In addition, the bacterium has a high morbidity and relatively easy cultivation and transport. The transmission via aerosols is considered to be the most dangerous in a potential bioterrorist attack, but the alimentary mechanism of infection spread is also possible, as it is historically well known although logistically limited [5, 6].

The typical clinical manifestation of descendent flaccid paralysis put botulism in a specific category but misdiagnosis is common and represents an additional issue in a hypothetical bioterrorist act. In 1985, a major outbreak of botulism in Vancouver had remained unrecognized for a long time. Twenty-eight individuals were infected with contaminated restaurant food but were hospitalized with different diagnoses before the proper epidemiological investigation [14].

3.2. *Yersinia pestis*

Yersinia pestis is a Gram-negative, rod-shaped bacterium, which causes plague. Currently, *Yersinia pestis* strains are endemic in areas in Southeast Asia, Africa, and North and South America. Natural reservoirs are wild and synanthropic rodents, which are infected by fleas bites. People are usually accidental hosts but are extremely sensitive to the infection [15].

Yersinia pestis produces both exo- and endotoxins and a variety of different enzymes to enhance its virulence. The generation time is very short and infection with one bacterial cell may result in the death of the host.

The plague is a high-priority pathogen with endemic occurrence and with a high tendency for epidemic and pandemic spread. The main clinical forms are bubonic, pneumonic, intestinal, and septicemic. The proper diagnosis is based on the symptoms of the patient and the epidemiological history. The bubonic plague manifests with swollen lymph nodes, fever, malaise, and fatigue. The septicemic and pneumonic forms are more challenging for diagnosis, as their symptoms are identical to those of other Gram-negative septicemia and respiratory diseases [16].

The treatment involves streptomycin, tetracycline, or levofloxacin administration. Antibiotic resistance is rarely observed, but the therapy should start in time.

Pneumonic plague may be a devastating weapon in biological war. In contrast to the bubonic form of the disease, it can be transmitted person to person via air droplets [17]. Epidemiology of an intentionally caused outbreak will differ significantly from the naturally occurring infections. The most possible way of transmission will be again the release of bacteria in the form of aerosols [18], but other attacks, such as food or water poisoning, are also possible. The first symptoms of such a hypothetical epidemic will be indistinguishable from other pneumonic or intestinal diseases. The size of the damage will depend on the quantity of the material used for the attack, the strain characteristics, and the environmental conditions. Symptoms will appear 1–6 days after the exposition and the lethal cases will be reported rapidly. The occurrence of morbidity in non-endemic areas, as well as the lack of dead rodents, should be the first signs to consider an intentionally caused plague epidemic [19].

3.3. *Brucella spp.*

Brucella species are Gram-negative coccobacilli or short rods. Three major human pathogens cause the zoonotic infection brucellosis—*B. melitensis, B. abortus,* and *B. suis*. The source and reservoir of the bacteria are sick animals—goats, sheep, cows, pigs, and dogs. Main transmission routes are contact, erogenic, and alimentary (foodborne). After an incubation period of 1–6 weeks, nonspecific symptoms such as fatigue, fever, sweating, and muscle pain occur. Enlarged lymph nodes and liver are frequently found. Arthritis, meningitis, encephalitis, pyelitis, and so on may develop in severe forms. Some signs and symptoms may persist for longer periods of time.

Tetracycline, ampicillin, or streptomycin are administered for therapy. Longer treatment of 2–3 weeks is often required, as brucellae localize intracellularly.

Brucellae are category B organisms used as potential agents of bioterrorism (**Table 1**). Due to effective veterinary measures to protect public health, brucellosis has become a rare disease in developed countries and no application in a bioterrorist attack has been reported so far [20].

3.4. Enterobacteria

3.4.1. Salmonella spp.

The genus *Salmonella* is part of the family *Enterobacteriaceae* and consists of rod-shaped, Gram-negative, flagellated facultative anaerobes.

Salmonellae are divided into two categories: invasive typhoidal serotypes causing typhoid fever and non-typhoidal *Salmonella* causing salmonellosis [21].

Unlike typhoidal salmonellae (*Salmonella Typhi* and *Salmonella Paratyphi)*, where humans are the only recognized reservoir, the main reservoir of non-typhoidal *Salmonella* is the intestinal tract of different domestic animals which often results in the contamination of foodstuffs [22]. Salmonella is predominantly found in eggs, poultry, dairy products, fresh fruits, and vegetables [23].

Gastrointestinal symptoms usually start 4–72 h after the ingestion of contaminated food or water and last for 4–7 days. They include fever, chills, nausea, vomiting, abdominal cramping, and diarrhea. Diarrhea is usually self-limiting and may be grossly and bloody. After the onset of the disease, salmonellae are excreted in feces for approximately 5 weeks.

Although salmonellosis is regarded as a relatively mild disease, severe illness and death can occur in some cases—particularly in infants, elderly, and immuno-compromised patients [24]. Bacteremia appears in 5–10% of infected persons and in some cases may progress to focal infection, such as meningitis, bone, and joint infection [25].

Salmonella infections generally do not require treatment. A correct rehydration is the most important, while antibiotics are prescribed only in severe cases.

The safety measures for the prevention of Salmonella infection include washing hands before food processing and especially after handling raw meats; cooking meat, and eggs thoroughly; avoiding consumption of foods containing raw eggs or milk; and avoiding direct contact between uncooked meat with food that will not be cooked.

As *Salmonella spp*. are readily available and have the potential to cause outbreaks with moderate morbidity, but with significant effects on public health, they are included in group B of possible biological agents (**Table 1**). Organizations or individuals with limited biological knowledge and laboratory access can easily use them for bioterrorist purposes, as in the case of the biggest bioterrorist attack in the USA (see the Introduction, section [7]).

3.4.2. Shigella spp.

Bacteria of the genus *Shigella* are a common cause of bacterial diarrhea worldwide, especially in developing countries. There are four different species: *Shigella dysenteriae* (serogroup A), *Shigella flexneri* (serogroup B), *Shigella boydii* (serogroup C), and *Shigella sonnei* (serogroup D) [26]. Shigellae are Gram-negative, non-motile, and facultative anaerobic pathogens [27].

Humans are the only reservoirs for these bacteria and the disease is transmitted person to person by the fecal-oral route.

Shigella is highly contagious and 10–100 bacteria can initiate infection when sanitation or personal hygiene is poor. Patients at the highest risk for disease are young children in daycare centers, refugee camps, and nurseries [28].

Shigella, unlike *Vibrio cholerae* and most *Salmonella* species, is acid resistant and survives passage through the stomach to reach the intestine. Shigellae attach to, invade, and replicate in the mucosal epithelium of the distal ileum and colon, causing inflammation and ulceration [28]. Shigella infection is generally limited to the intestinal mucosa, and bacteremia due to *Shigella* is rare.

S. dysenteriae produces a (Shiga) toxin, which can cause damage to the intestinal epithelium and glomerular endothelial cells, the latter leading to kidney failure [28].

Shigellosis is characterized by fever, abdominal pain, and watery diarrhea with traces of blood and pus. The disease is usually self-limiting but may become life threatening if patients are immuno-compromised or if adequate medical care is not available. The treatment consists of oral rehydration and antibiotics administration [29].

Shigella may be released through the deliberate contamination of food or water supplies during a hypothetical terrorist attack. Secondary transmission can result from exposure to the stool of infected individuals because the diarrheal fluids are highly infectious.

To prevent the spread of bacteria, appropriate sanitation measures should be taken: sewage disposal and water chlorination, insect control, handwashing, and proper cooking of food [28].

3.4.3. Escherichia coli O157:H7

Escherichia coli is the most common and important member of the genus *Escherichia*. This organism is a Gram-negative, rod-shaped, facultative anaerobic bacterium. Most *E. coli* strains are part of the normal intestinal flora of healthy humans and animals. However, there are some strains associated with a variety of diseases, including gastroenteritis, urinary tract infections, and meningitis. Among them, enterohemorrhagic *E. coli* (EHEC) are defined as pathogenic *E. coli* strains that produce Shiga toxins and can cause severe illness such as hemorrhagic colitis and the life-threatening sequelae hemolytic uremic syndrome, characterized by hemolytic anemia, thrombocytopenia, and renal injury. *E. coli* O157:H7 was first recognized as a pathogen in 1982 during an outbreak investigation of hemorrhagic colitis in Oregon and Michigan, the USA [30]. This *E. coli* O157:H7 outbreak was linked to under-cooked ground beef hamburgers and cheeseburgers sold from a fast-food restaurant chain. The most frequent route of transmission for *E. coli* O157:H7 is via the consumption of contaminated food and water Raw or undercooked meat, unpasteurized dairy products, and fruit juices have been frequently implicated in reported outbreaks [31]. In addition, *E. coli* can also spread directly from person to person, particularly in child day-care units. *E coli O157:H7* has a low infectious dose and resists in the environment for more than 10 months [32]. A potential airborne transmission has also been reported [33].

The essential factor of *E. coli O157:H7* pathogenesis is the production of Shiga toxins (Stx-1, Stx-2, or both), which disrupt protein synthesis of the host. Stx-1 is identical to the Shiga toxin I produced by *Shigella dysenteriae*, while Stx-2 is more toxic [32].

The diseases caused by EHEC ranges from mild, uncomplicated diarrhea to hemorrhagic colitis with severe cramping (abdominal pain) and bloody diarrhea. The incubation time is from 3 to 4 days. Occasionally vomiting occurs in approximately half of the patients. Fever is either low grade or absent. The illness lasts for 4–10 days and is usually self-limited.

All people are susceptible to hemorrhagic colitis, but young children and the elderly are affected more seriously. In a terrorist attack, *E. coli* would most likely spread via food and water contamination. Secondary transmission can result from exposure to the stool of already infected patients, as diarrheal fluids are highly infectious. The period of infectivity of stool is typically a week or less in adults but 3 weeks in one-third of children.

Patients can be protected with standard sanitation precautions and handwashing is of particular importance. For uncomplicated cases, rehydration is the only treatment needed. Fluid and electrolyte replacement is important when diarrhea is watery or there are signs of dehydration. Antibiotics are often avoided in *E. coli O157:H7* infections since some evidence suggests that antibiotic treatment may lead to complications.

Currently, no vaccine is available to prevent *E. coli O157:H7* infections.

3.5. *Staphylococcus aureus*

Staphylococcus aureus is the second leading cause of gastroenteritis in the world (after salmonellosis) [34]. Its food-poisoning property is due to the production of staphylococcal enterotoxins preformed in the food.

Staphylococci are non-spore-forming cocci, arranged in clusters. They are osmo-tolerant to high sugar (up to 20%) and salt (up to 10%) concentrations. These bacteria can propagate in a wide range of temperatures from 6°C to 45–47°C [35]. Although they cannot survive at high cooking temperatures, their toxins (A, B, C1, C2, C3, D, E, G, K, I, and J) are resistant to heat and can be cooked for hours at 100°C without destruction. In addition, staphylococcal enterotoxins do not affect the smell and the taste of the food.

Staphylococcus aureus is found on the skin, mammary glands, nose, and throat of about 25% of healthy people [36]. So, the personnel in restaurants can be a significant source of contamination, as one of the typical ways of infection spread is the contact-alimentary route.

Staphylococcal toxins are extremely fast-acting—the incubation period is from 20 to 30 min to 6–8 h after the consumption of contaminated food. Vomiting, nausea, abdominal cramps, and diarrhea are common symptoms and they usually resolve in 1–2 days. Only in rare cases, deaths have been reported, as a result of acute hypotension. Treatment is supportive with fluid and electrolyte replacement.

The prophylactics of staphylococcal food poisoning is done by using proper hygiene and sanitation measures when preparing food. The most critical are handwashing with soap or alcohol; wearing gloves; fast cooling; and fridge storage of prepared food [37].

Staphylococcal toxins could be successfully used as a biological weapon by both food contamination or aerosolization. In this context, enterotoxin B, which may cause fever, cough, difficulty in breathing, headache, vomiting, and nausea, is the most promising [36]. It is stable and water soluble, can be easily aerosolized, but however is rarely lethal [38]. Only higher exposure to the toxin could lead to septic shock and death in some people.

3.6. *Clostridium perfringens*

Clostridium perfringens is a Gram-positive spore-forming bacterium. Spores can be found in soil, while the vegetative forms are normal flora of gut and vagina. Depending on the entry portal into the host, *Clostridium perfringens* causes gas gangrene (clostridial myonecrosis) or food toxicoinfection. It is classified into five serotypes (A, B, C, D, and E) on the basis of production of four main toxins—alpha, beta, epsilon, and iota [39].

The gas gangrene is an acute, severe wound infection with a highly invasive character. Bacteria propagate in the traumatized tissue (muscles) and produce a variety of toxins. The most important is the α-toxin (lecithinase), which destroys the cell membranes, including those of the erythrocytes, and leads to hemolysis. The enzymatic activity is responsible for gas release in the infected tissues. Clinically, the infection manifests as pain, edema, cellulitis, and necrosis in the wound area. The mortality rate is relatively high. Laboratory diagnosis consists of anaerobic cultivation and biochemical tests. Penicillin G is the preferred antibiotic, but more important is the chirurgical treatment of the wound.

The incubation period of the foodborne infection is 8–16 h and the disease is characterized by watery diarrhea, cramps, and vomiting. Usually, it gets resolved in 12–24 h and the treatment is predominantly symptomatic [40].

Clostridium perfringens produces at least 12 toxins and one or more of them can be used as a biological weapon. The neurotoxin epsilon is the most promising as biological agent [9]. It is found in zoonotic *C. perfringens* type B and D [38]. The zoonosis represents as rapid toxemia usually in sheep but also in goat and cattle. The ingested spores germinate rapidly, propagate, and produce a non-active protoxin of 311 amino acids. After an intestinal proteolysis, a potent and lethal necrotizing toxin is synthetized. It enters the blood stream and causes kidney damage and pulmonary edema [41]. The toxin also has extreme neurotropism which results in serious neurological injury [42].

Knowledge about the effect of the toxin on humans is not available—all data are obtained from animal experiments. However, one can speculate that to produce a significant impact on the society, the aerosolic form of the toxin should be used [43].

3.7. Pathogenic *Vibrio species*

V. cholerae, V. parahaemolyticus, and *V. vulnificus* are the most important species responsible for food poisoning among the Gram-negative, comma-shaped bacteria from the genus *Vibrio*.

Three types of *V. cholerae* are known: type 01, type 0139, and type non-01 [44]. Type 01 is typically linked with classic cholera (biotypes Inaba, Ogawa, Hykoschima and El Tor), while type 0139 can cause cholera-like illness and atypical infections. These bacteria are found in sea and ocean coastal waters. Approximately two-thirds of *V. cholerae* food poisoning is linked to the consumption of raw or not sufficiently heat-treated sea products. The vibrios easily survive under 10°C and multiply fast under temperatures of 30–37°C with a generation time of 12–18 min in raw seafood. Vibrio species can divide in an alkaline environment and under the high concentration of NaCl (up to 10%) but cannot resist high temperatures (>70°C) and dehydration.

Vibrios of type 01 cause classic cholera, which is transmitted usually by drinking water but also with contaminated food and human contacts. The incubation period is relatively short—from 6 h to 5 days—and the most typical symptom is the watery diarrhea with profuse, "rice-water" stool. The massive water and electrolyte loss, as well as the severe intoxication, is due to the cholera toxin, produced during the intestine colonization. The diarrhea lasts for 6–7 days and in the cases of cholera gravis, which results in severe dehydration, up to 60% of patients can die.

V. parahaemolyticus usually causes milder cholera-like infections [45] and only 3% of all strains are pathogenic and responsible for acute gastroenteritis. Typical symptoms are nausea, vomiting, stomach aches, sub-febrile temperature, and watery or watery-bloody diarrhea. The incubation period is 12–96 h after the consumption of contaminated food or water and the disease lasts up to several days but in rare cases, it can extend to 10 days with septicemia and host death.

V. vulnificus is associated with wound infections after a contact with contaminated seawater or sea animal species. It causes septicemia with a lethality of approximately 50% and rarely induces gastroenteritis in individuals with liver damage.

The treatment of cholera requires urgent, adequate, and well-timed rehydration. Usually, oral rehydration with low osmolarity or cereal-based solution and, when necessary, replacement of intravenous fluids and electrolytes are sufficient to reduce the lethal cases to 1% of all infected patients [46, 47]. In addition, zinc supplementation can reduce the duration and the severity of diarrhea in children with cholera [48]. Antibiotics, although a secondary measure, also help, as they limit the duration of the disease. They are recommended in moderately and severely ill patients, but their choice should be determined by the local antibiotic sensitivity patterns. Doxycycline is recommended as a first-line treatment for adults, while azithromycin is recommended for children and pregnant women [36].

As cholera is a typical water- and foodborne infection the prophylaxis is associated with high personal hygiene and sanitation measures. Bottled, boiled, or treated water should be used for drinking and food preparing in endemic areas or during outbreaks. Any seafood should also be freshly cooked and served hot. Vaccination, although not generally recommended, is useful for travelers to areas of active cholera transmission.

Because *Vibrio cholerae* is a waterborne bacterium, the most likely bioterrorism use will be via contaminated water and/or food. In 1961, China alleged that cholera has been used as a weapon in Hong Kong by the US army. In 1969, Egypt also alleged the "imperialistic aggressors" of using cholera in Iraq in 1966 [49]. However, due to the regular chemical treatment of public water supplies (at least in the developed countries), it will be difficult to cause a high-scale damage.

4. Conclusion

Foodborne bacterial pathogens, although less attractive as possible bioterrorist weapons, are of interest as they possess several important advantages. First, they can be readily found in nature and their isolation and multiplication are relatively easy. No specific knowledge is needed. Second, their diffusion does not require expensive and complicated devices and technologies—they can be released by simple contamination of food or drinks in any catering establishment. Third, the intentionally caused outbreaks will be almost indistinguishable from the naturally occurring epidemics, especially in the beginning. Finally, food poisoning can affect a large number of people before recognizing the source of contamination and hence produce significant panic and chaos in the society.

Conflict of interest

Authors declare the absence of any conflict of interest related to this work.

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Food safety is defined as the concept that food will not cause harm to the consumer when it is prepared and/or eaten according to its intended use. Most food product recalls and food-related outbreaks are fully considered as food safety failures. Many risk-based food safety standards, e.g., HACCP, BRC, SQF, ISO/FSSC 22000, are designed to prevent such issues from occurring. Any food recall or food-related outbreak may be attributed to the likelihood of a risk assessment, which in some way failed to identify and control the risk. The essence and true nature of food safety hazards are affected by resources of the food facility, e.g., human, work environment, infrastructure, availability and accessibility of food safety information. Thus, food specialists should establish and manage the parameters of the applied food safety systems to achieve the food safety objectives that produce food in compliance with regulatory and statutory requirements. It is important to understand what exactly will make an end product unsafe and ensure that the necessary control measures are in place to prevent it from happening. Understanding the basic food safety concepts can lead to improvement of the current food safety systems and/or standards.

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