cGMP IN THE FOOD INDUSTRY

Summary

Food safety is becoming an increasingly important topic on the international market. In order to guarantee the safety and quality of our food supply, statutory food safety regulations are applied on various continents and guidelines and regulations are in force for the various disciplines in this important sector (such as e.g. production, storage and transport). Is there a common denominator in that web of regulation? There is indeed one topic that takes a central role around the world and is addressed by all the relevant legislation and guidance: the obligation as a producer to make a risk analysis and accordingly equip the facility in such a way that quality and food safety is guaranteed. The GMP rules in the US have been modified to take account of this and a new chapter has been introduced in the Code of Federal Regulations (CFR Title 21 part 117), which is becoming increasingly important a year and a half after its introduction.

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WP FOOD 3/Brecon July 2018

Introduction

In the United States it is the FDA, in China the CFDA (Chinese Food and Drug Administration) and in Europe it is the EFSA (European Food Safety Authority). These are all agencies that determine food safety legislation, among other things, and in many cases take an enforcement role. In Europe enforcement is regulated at a national level, in the Netherlands this is done by the NVWA (Dutch Food and Consumer Product Safety Authority).

EUROPE
The EFSA is a European agency funded by the EU (European Union) and independent from the European legislative and executive institutions (Commission, Council, Parliament) and EU Member States. Based on scientific findings from EFSA, the European food safety policy is determined, and following this, local legislation is often developed.

In the year 2002, Regulation (EC) No 178/2002 of the European Parliament was adopted. It sets out the general principles and requirements of food law, the establishment of the EFSA and the establishment of procedures for food safety matters. The regulation is called the General Food Law (GFL) and is the basis for local food legislation in Europe for all member states.

On the basis of this GFL, many EU activities have been initiated, which have, among other things, led to the EC no. 852/2004, this regulation 'lays down general rules for food business operators on the hygiene of foodstuffs'. The chapter on General Provisions has been added to this White Paper, with the Scope of this regulation. By reading this section, it becomes clear in a few minutes what is expected of a producer in the food industry!
(See appendix1)

UNITED STATES
Since early in the 20th century, the FDA (Food and Drug Administration) has been responsible for the development and enforcement of drugs and food legislation in the U.S. This legislation for humane and veterinary food and drugs is often laid down in GMP rules (Good Manufacturing Practices), documented in the CFR (Code of Federal Regulations). The CFR is divided into 50 titles representing broad areas covered by federal regulations. Medicines and foods, both for human and veterinary use, are dealt within CFR Title 21. The GMP rules are regularly updated, and the abbreviation cGMP is intended to indicate that the legislation is 'current'.

For the pharmaceutical industry, American legislation has played an important role in the development of European regulations. In the EudraLex, the collection of rules and regulations in the EU, we also clearly recognise the GMP regulations out of the American pharmaceutical regulations.

For the European legislation within the Food sector, the EU has chosen a clearly different route, as can be seen from the above information. In the US, they have federal legislation, which can be put into effect at government level for all 51 states.
Member states within the EU can influence the way in which European legislation is implemented or translated into national legislation and regulations. The frameworks are, however, predetermined in the EU. European regulations, on the other hand, are national laws with immediate effect!

Physical hazards:

Any external object or foreign material in a food product that could lead to illness or injury following consumption falls into the category 'physical hazard'. Such foreign objects include, but are not limited to, bone or bone fragments, slivers or fragments of metal, injection needles, pieces of product packaging, fragments of stone, glassor wood, insects or other contamination, personal items and other foreign objects not normally processed during the preparation of food. Sources of such contaminants include unprocessed materials, poorly maintained facilities and equipment, incorrect production procedures and poorly disciplined employees.

Increasing food trade

The international food trade has existed for many centuries, but in the past food was primarily produced, sold and consumed locally, until fairly recently. Furthermore the world population is growing and mobility increases. As a result, today the menu offers, at home or in a restaurant, a choice of dishes on a global level, cooked with ingredients from all over the world. All over the world, people like to consume food that until a few decades ago was entirely unknown beyond the boundaries of the country of origin. As a result, the quantity of food traded internationally has grown exponentially over the course of the last century. A list can be made of the causes of the increasing range of problems related to this growth:

- Growth of the world population;
- Globalization leading to more international traffic;
- Steady increase in the length of the food supply chain;
- Less control on recall actions through complex distribution;

Importers need to be sure that the food they order will comply with their specifications, and as a consumer, of course, we want the certainty that the offered food is of good quality and free of risks to their safety. Legislation and regulations should provide this security of safe food at the global level offer. Despite this, the WHO (World Health Organisation) has expressed serious concerns about the number of cases of food poisoning around the world, and in particular the number of fatalities. A conservative estimate from 2015 suggests some 420,000 fatalities and 600 million hospital admissions resulting from food safety issues. Nevertheless, the WHO (World Health Organization) has had to determine that the number food poisoning, and above all the number of fatalities, at world level very get serious forms. (2015: cautiously estimated 420,000 fatalities and 600 million cases of ZH recordings due to food safety issues)

The WHO considers the consequences of failing food safety policy as one of the biggest treats to global health. Research has indicated that 31 "contaminants" can cause 200 various diseases, sometimes with deadly consequences. These contaminants are primarily invisible causative agents like bacteria, fungi, viruses and parasites. An analysis of the threatening dangers in the food industry gives a rough classification in 4 different categories. Some of these are visible or detectable upon consumption; in other cases, the hazards are invisible, sometimes with serious consequences for consumers. These categories are described in more detail in four information text boxes in this White Paper.

Codex Alimentarius

By the end of the 1950s, it was already apparent that the raw materials for food production were increasingly being traded on an international basis, and that this trade was exhibiting rapid growth. At the start of the 1960s, the United Nations called for rules to be defined with the objective of providing everyone, wherever they might be in the world, with access to safe, good quality food. The Codex Alimentarius was introduced for this purpose in 1963.

The Codex Alimentarius is a UN organization, under the flag of both the FAO (International Food and Agriculture Organization) and WHO (World Health Organization).

The Codex Alimentarius Commission (Codex) is an international forum in which 187 countries and 1 organization (EU) participate. This forum develops international standards for food products with the objectives of protecting international public health and promoting fairness in the trade in food products. In the Netherlands, the responsibility for participation in this international forum is shared between the Ministry of Agriculture, Nature and Food Quality and partly by the Ministry of Public Health, Welfare and Sport.

Biological and microbiological hazards:

The US **Centre for Disease Control and Prevention** (CDC) defines four levels in relation to biological hazards:

- **Level one:** bacteria and other microorganisms that can be passed from one person to another via contact or through the air and that do not result in serious illness, such as Escherichia Coli and Bacillus Subtilis (BSL 1);
- **Level two:** viruses and more serious bacteria, such as measles, influenza and salmonella. Not highly transmissible. Limited symptoms and easily treated (BSL2);
- **Level three:** strains and types of viruses that cause real harm, may lead to serious symptoms or death and spread more rapidly through the population, such as Typhus and West Nile Virus;
- **Level four:** the most serious and generally fatal viruses, highly infectious and with no medicines available, such as the Ebola virus and the Marburg virus.

More about the GMP

GMP legislation originally developed alongside the American regulations for the pharmaceutical industry. The Pure Food and Drug Act, which came into effect in the US in 1906, did not include regulations or guidance about the purity, consistency and effectiveness of drugs, resulting in errors and complications, sometimes with tragic consequences. The Congress approved the federal Food, Drug and Cosmetic Act in 1938. Businesses were now required for the first time to demonstrate that their products were safe. The FDA was empowered to monitor the compliance of the three market segments with the legislation.

During the 1960s, a need arose for an internationally oriented PRP, or 'prerequisite programme', in both the pharmaceutical and food process industries. Over the course of several years, GMP and other standards were developed and introduced by the FDA, the WHO and various European institutions. The new standards provided assurance that medicines and medical devices satisfied the strictest requirements.
The Hazard Analysis and Critical Control Points legislation for the food industry also appeared during the 1960s. NASA had a need for food with an extended storage life, because of their manned space flights. The Codex Alimentarius, mentioned above, provided recommendations relating to the broad applicability of this preventative approach to food safety and hygiene.

Meantime GMP legislation has been accepted around the world and is widely used in the food process sector as evidence that products satisfy its strict quality standards. The GMP rules should form part of a food safety or complete management system, subject to monitoring. In the US, this monitoring is carried out by the FDA, which also has an important task inspecting imported food. The monitoring and enforcement agency in the Netherlands is the NVWA, (Netherlands Food and Consumer Product Safety Authority).

General standards and guidelines for human food and animal feed are set out in CFR Title 21 Part 110, while parts 106 – 107 covers food for infants and part 111 deals with nutritional supplements. There are also GMPs for the pharmaceutical and cosmetics sectors, as well as for the animal feed industry. Anyone active in the field of human food will find time spent on the FDA.org web page well worth their while.
CFR Title 21 part 110, Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Human Food includes the following categorisation:

- **Subpart A - General Provisions**
  § 110.3 - Definitions.
  § 110.5 - Current good manufacturing practice.
  § 110.10 - Personnel.
  § 110.19 - Exclusions.
- **Subpart B - Buildings and Facilities**
  § 110.20 - Plant and grounds.
  § 110.35 - Sanitary operations.
  § 110.37 - Sanitary facilities and controls.
- **Subpart C - Equipment**
  § 110.40 - Equipment and utensils.
- **Subpart D - [Reserved]**
- **Subpart E - Production and Process Controls**
  § 110.80 - Processes and controls.
  § 110.93 - Warehousing and distribution.
- **Subpart G - Defect action levels**
  § 110.110 - Natural or unavoidable defects in foods for human use that present no health hazard.

The FSMA (Food Safety Modernization Act) has major consequences...
The Food Safety Modernization Act was signed by President Obama on 4 January 2011, with the objective of better protecting public health in the USA. All businesses producing raw materials, additives or complete (RTE) food products for the US, or exporting such goods to the US, are required to work in compliance with this Act.

The FDA's intention is to reduce the number of incidents involving food by imposing more stringent requirements for the food safety system throughout the chain of businesses active in the foodstuffs industry ('farm-to-table'). These requirements have since been translated into amendments in re-issued Good Manufacturing Practices.

The principles underlying a management process where risk assessments are the basis for the control measures to be taken, and which also provide the basis for monitoring and recording specific activities in this context (basically the HACCP), are now included separately in the GMP.

Chemical hazards:

There are two primary categories of chemical hazards:
- Prohibited substances
- Toxic or harmful substances

Obviously, no prohibited substance must occur in food or in the raw materials used in the preparation of food. Tolerance levels have been introduced for unavoidable chemical hazards. This includes products such as pesticides, herbicides, growth hormones and antibiotics, additives and processing aids, lubricants, paints, cleaning agents and decontamination agents. The quantities involved are of course extremely low and not hazardous to the health of consumers. Naturally, these very low levels must not be exceeded!

The Act also sets out how the (supervised) food safety system must be drawn up and verified by a qualified person, known as a Preventive Controls Qualified Person (PCQI), and there is clearly a greater emphasis on the training of all staff involved in the production and logistics process.

The 2011 FSMA includes new requirements set out in 4 titles, covering 89 pages of text in total.

Title I:	Improving capacity to prevent food safety problems
Title II:	Improving capacity to detect and respond to food safety problems
Title III:	Improving the safety of imported food
Title IV:	Miscellaneous provisions

The entire world market will notice that after about 70 years the American legislation has changed. You will of course be affected if you do business with the US and if you export food or food-related products, but developments in standards and regulations within the US are closely watched in other parts of the world as well, and are frequently the basis for changes to local legislation.

In Europe, we have been involved for some time already with the tracking of food safety issues, and chain liability has been set down in the GFL. Traceability of raw materials and semi-finished products has been a requirement since the start of the new century. Manufacturers are now required to demonstrate where their raw materials or semi-finished products originate from, and also to whom the end product was supplied to.

Take note: when exporting food or food packaging materials to the USA, the FDA will check the exporter's registration in the US, and their quality and food safety management system will be assessed for compliance with current legislation in the US. The mandatory appointment of a PCQI (Preventive Controls Qualified Person) must also be taken into account.

Chemical hazards / allergens:

Allergens are regarded in legal terms as chemical hazards. The labelling requirements are therefore exceptionally stringent. Where consumers with severe allergies receive incorrect information, they may become seriously ill or even die. European legislation identifies 14 substances as allergens: gluten (wheat, rye, barley, oats, spelt, khorasan wheat), shellfish, egg, fish, peanuts, soya, milk (including lactose), nuts (8 types), celery, mustard, sesame, sulphites, lupin and molluscs.

The cGMP and the FSMA

The ‘c’ in front of the letters GMP stands for ‘current’, and is intended to make it clear to the user that this edition of the GMP is the most updated edition. However, matters are simply not that straightforward right now. If you Google ‘cGMP for food’, you are likely to come across CFR Title 21 Part 110. However, there is already a completely new cGMP dealing with hazard analyses and preventative measures for human foodstuffs, entitled CFR Title 21 Part 117.

It is quite clear that this Part 117 actually reflects the requirements of the FSMA. Chapter 103 of the FSMA, in particular, describes hazard analyses and all the subsequent activities. Also employee training and supply chain program (origin registration) now stand clear in this cGMP for the food process industry.

The question arises whether everyone is aware of the changed situation in the US. Especially for those companies that export to the US, it is really important to study this cGMP.

The contents in terms of subparts and sections is set out below, in order to provide an impression of what the cGMP looks like in comparison with the 110 version. The fact that the 117 version is far more detailed and therefore requires much more of the food producer requires no explanation

Conclusion

Food safety is an increasingly important topic on the international (UN/WHO) agenda. It is more and more likely that the consequences of a food safety incident will have consequences at an international level, and the traceability of products is becoming ever more complex.

The FDA is in the final stages of implementing the FSMA programme. International partners are being authorised to conduct audits locally of businesses intending to export to the US. Regulations and guidelines based on the FSMA are being implemented at a faster rate and more comprehensively. Consider, for example, the implementation of all the diverse activities combined in the well known HACCP system (carrying out hazard analyses, subsequent implementation of control measures based on the results of those analyses, carrying out corrective actions in the event of problems and the demonstrable recording of all these activities).

Make sure that you are properly prepared, and familiarise yourself with the modified cGMP rules.

If you have implemented an HACCP certification system satisfying the requirements for a 'food safety system based on HACCP', preferably implemented in an ISO 22000 or FSCC 22000 certified management system within your organisation, only few changes will be required in order to satisfy the FDA requirements for exports to the US. Even so, in view of the many changes to international legislation in this field, it is nevertheless recommended that an assessment be carried out to verify this, before exporting to the US.

A forthcoming White Paper will be devoted entirely to the latest modifications to the ISO 22000-2018 standard published in June and the increasingly successful global introduction of FSCC 22000 certification.

ORIGIN

PP4CE (Professional Partners for Controlled Environments) is a strategic alliance between a number of specialist companies in the design, construction and maintenance of cleanrooms and laboratories in a wide range of market segments. PP4CE is also active in Medium and High Care areas within the food industry.

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Geerd is initiator of the PP4CE alliance and General Manager of Brecon International B.V., as such, strategically involved in the PP4CE alliance.
For more information, see http: www.pp4ce.com

Sources:

- FDA.Org website for a range of data on GMP;
- Various publications by the WHO, Geneva;
- Understanding GMP in the food industry (Remco Products USA);
- PUBLIC LAW 111–353—JAN. 4, 2011 Food Safety Modernization Act;
- eur-lex.europa.eu website.

ATTACHEMENT 1 - CHAPTER ONE of the EG. No. 852/2004

GENERAL PROVISIONS

Article 1 Scope

1.This Regulation lays down general rules for food business operators on the hygiene of foodstuffs, taking particular account of the following principles:

(a) primary responsibility for food safety rests with the food business operator;

(b) it is necessary to ensure food safety throughout the food chain, starting with primary production;

(c) it is important, for food that cannot be stored safely at ambient temperatures, particularly frozen food, to maintain the cold chain;

(d) general implementation of procedures based on the HACCP principles, together with the application of good hygiene practice, should reinforce food business operators' responsibility;

(e) guides to good practice are a valuable instrument to aid food business operators at all levels of the food chain with compliance with food hygiene rules and with the application of the HACCP principles;

(f) it is necessary to establish microbiological criteria and temperature control requirements based on a scientific risk assessment;

(g) it is necessary to ensure that imported foods are of at least the same hygiene standard as food produced in the Community, or are of an equivalent standard.

This Regulation shall apply to all stages of production, processing and distribution of food and to exports, and without prejudice to more specific requirements relating to food hygiene.

2. This Regulation shall not apply to:

(a) primary production for private domestic use;

(b) the domestic preparation, handling or storage of food for private domestic consumption;

(c) the direct supply, by the producer, of small quantities of primary products to the final consumer or to local retail establishments directly supplying the final consumer;

(d) collection centres and tanneries which fall within the definition of food business only because they handle raw material for the production of gelatine or collagen.

3. Member States shall establish, under national law, rules governing the activities referred to in paragraph 2(c). Such national rules shall ensure the achievement of the objectives of this Regulation.

ATTACHEMNENT 2 - CFR 21 Deel 117

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCHAPTER B--FOOD FOR HUMAN CONSUMPTION

PART 117 CURRENT GOOD MANUFACTURING PRACTICE, HAZARD ANALYSIS, AND RISK-BASED PREVENTIVE CONTROLS

FOR HUMAN FOOD

Subpart A--General Provisions

§ 117.1 - Applicability and status.
§ 117.3 - Definitions.
§ 117.4 - Qualifications of individuals who manufacture, process, pack, or hold food.
§ 117.5 - Exemptions.
§ 117.7 - Applicability of subparts C, D, and G of this part to a facility solely engaged in the storage of unexposed packaged food.
§ 117.8 - Applicability of subpart B of this part to the off-farm packing and holding of raw agricultural commodities.
§ 117.9 - Records required for this subpart.

Subpart B--Current Good Manufacturing Practice

§ 117.10 - Personnel.
§ 117.20 - Plant and grounds.
§ 117.35 - Sanitary operations.
§ 117.37 - Sanitary facilities and controls.
§ 117.40 - Equipment and utensils.
§ 117.80 - Processes and controls.
§ 117.93 - Warehousing and distribution.
§ 117.95 - Holding and distribution of human food by-products for use as animal food.
§ 117.110 - Defect action levels.

Subpart C--Hazard Analysis and Risk-Based Preventive Controls

§ 117.126 - Food safety plan.
§ 117.130 - Hazard analysis.
§ 117.135 - Preventive controls.
§ 117.136 - Circumstances in which the owner, operator, or agent in charge of a manufacturing/processing facility is not required to implement a preventive control.
§ 117.137 - Provision of assurances required under 117.136(a)(2), (3), and (4).
§ 117.139 - Recall plan.
§ 117.140 - Preventive control management components.
§ 117.145 - Monitoring.
§ 117.150 - Corrective actions and corrections.
§ 117.155 - Verification.
§ 117.160 - Validation.
§ 117.165 - Verification of implementation and effectiveness.
§ 117.170 - Reanalysis.
§ 117.180 - Requirements applicable to a preventive controls qualified individual and a qualified auditor.
§ 117.190 - Implementation records required for this subpart.

Subpart D--Modified Requirements

§ 117.201 - Modified requirements that apply to a qualified facility.
§ 117.206 - Modified requirements that apply to a facility solely engaged in the storage of unexposed packaged food.

Subpart E--Withdrawal of a Qualified Facility Exemption

§ 117.251 - Circumstances that may lead FDA to withdraw a qualified facility exemption.
§ 117.254 - Issuance of an order to withdraw a qualified facility exemption.
§ 117.257 - Contents of an order to withdraw a qualified facility exemption.
§ 117.260 - Compliance with, or appeal of, an order to withdraw a qualified facility exemption.
§ 117.264 - Procedure for submitting an appeal.
§ 117.267 - Procedure for requesting an informal hearing.
§ 117.270 - Requirements applicable to an informal hearing.
§ 117.274 - Presiding officer for an appeal and for an informal hearing.
§ 117.277 - Timeframe for issuing a decision on an appeal.
§ 117.280 - Revocation of an order to withdraw a qualified facility exemption.
§ 117.284 - Final agency action.
§ 117.287 - Reinstatement of a qualified facility exemption that was withdrawn.

Subpart F--Requirements Applying to Records That Must Be Established and Maintained

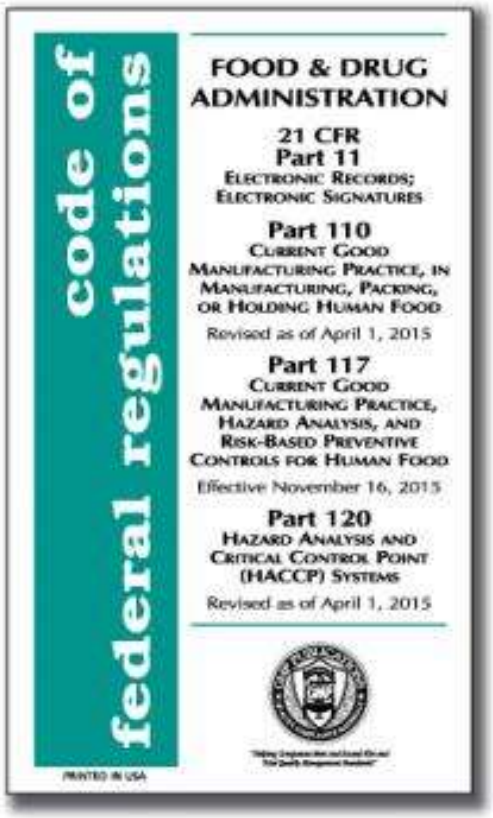
§ 117.301 - Records subject to the requirements of this subpart.
§ 117.305 - General requirements applying to records.
§ 117.310 - Additional requirements applying to the food safety plan.
§ 117.315 - Requirements for record retention.
§ 117.320 - Requirements for official review.
§ 117.325 - Public disclosure.
§ 117.330 - Use of existing records.
§ 117.335 - Special requirements applicable to a written assurance.

Subpart G--Supply-Chain Program

§ 117.405 - Requirement to establish and implement a supply-chain program.
§ 117.410 - General requirements applicable to a supply-chain program.
§ 117.415 - Responsibilities of the receiving facility.
§ 117.420 - Using approved suppliers.
§ 117.425 - Determining appropriate supplier verification activities (including determining the frequency of conducting the activity).
§ 117.430 - Conducting supplier verification activities for raw materials and other ingredients.
§ 117.435 - Onsite audit.
§ 117.475 - Records documenting the supply-chain program.

ATTACHEMENT 3 - GMP Publication 978-1-935131-26-7:

FDA announced replacement of 21 CFR Part 110 Food GMPs with the new regulation 21 CFR Part 117 Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food. This Part will replace some requirements under 21 CFR Part 110 on November 16th, 2015. Full replacement of 21 CFR Part 110 by 2016.

US FDA Title 21 CFR Parts

Part 11	Electronic Records/Electronic Signatures (ERES)
Part 110	Current Good Manufacturing Practice in Manufacturing, Packaging or Holding Human Food
Part 117	Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food
Part 120	Hazard Analysis and Critical Control Point (HACCP) Systems