10. FOOD SUPPLEMENTS QUALITY AND SAFETY REQUIREMENTS

10.1. Introduction in Food safety. Legislation in force

Safety of food means safety of raw materials, of methods of processing, transport, distribution and retail. Safety of food include food hygiene that is consisting in five key principles according to World Health Organization (WHO): preventing contaminating food with pathogens and cross-contamination by separation raw and processed foods and using the appropriate technological and storing parameteres.

ISO 22000 is a standard developed by the International Organization for Standardization dealing with food safety, which specifies the requirements for a food safety management system that involves interactive communication, system management, prerequisite programs and HACCP principles. In 2003, the WHO and FAO published the *Codex Alimentarius* which serves as a guideline to food safety through Codex standards.

EU Food safety legislation. EU Hygiene rules are established for all kind of food even are conventional, organic, traditional or even novel with some specific requirements for each of them especially for the way of producing and labelling.

The General Principles of Food Law (Articles 5 to 10) entered into force on 21 February 2002. Existing food law principles and procedures must be adapted by 1 January 2007 in order to comply with the general framework established by Regulation EC/178/2002**.**

General Objectives. The food law aims at ensuring a high level of protection of human life and health, taking into accounts the protection of animal health and welfare, plant health and the environment. This integrated "farm to fork" approach is now considered a general principle for EU food safety policy. Food law, both at national and EU level, establishes the rights of consumers to safe food and to accurate and honest information. The EU food law aims to harmonize existing national requirements in order to ensure the free movement of food and feed in the EU.

The food law recognizes the EU's commitment to its international obligations and will be developed and adapted taking international standards into consideration, except where this might undermine the high level of consumer protection pursued by the EU.

Risk Analysis. The Regulation establishes the principles of risk analysis in relation to food and establishes the structures and mechanisms for the scientific and technical evaluations which are undertaken by the European Food Safety Authority (EFSA).

Depending on the nature of the measure, food law, and in particular measures relating to food safety must be underpinned by strong science. The EU has been at the forefront of the development of the risk analysis principles and their subsequent international acceptance. Regulation EC 178/2002 establishes in EU law that the three inter-related components of risk analysis (risk assessment, risk management and risk communication) provide the basis for food law as appropriate to the measure under consideration. Clearly not all food law has a scientific basis, e.g. food law relating to consumer information or the prevention of misleading practices does not need a scientific foundation.

Scientific assessment of risk must be undertaken in an independent, objective and transparent manner based on the best available science.

Risk management is the process of weighing policy alternatives in the light of results of a risk assessment and, if required, selecting the appropriate actions necessary to prevent, reduce or eliminate the risk to ensure the high level of health protection determined as appropriate in the EU.

In the risk management phase, the decision makers need to consider a range of information in addition to the scientific risk assessment. These include, for example, the feasibility of controlling a risk, the most effective risk reduction actions depending on the part of the food supply chain where the problem occurs, the practical arrangements needed, the socio-economic effects and the environmental impact. Regulation EC/178/2002 establishes the principle that risk management actions are not just based on a scientific assessment of risk but also take into consideration a wide range of other factors legitimate to the matter under consideration.

Transparency. Food safety and the protection of consumer interests are of increasing concern to the general public, non-governmental organizations, professional associations, international trading partners and trade organizations. Therefore, the Regulation establishes a framework for the greater involvement of stakeholders at all stages in the development of food law and establishes the mechanisms necessary to increase consumer confidence in food law.

This consumer confidence is an essential outcome of a successful food policy and is therefore a primary goal of EU action related to food. Transparency of legislation and effective public consultation are essential elements of building this greater confidence. Better communication about

food safety and the evaluation and explanation of potential risks, including full transparency of scientific opinions, are of key importance.

Regulation EC 1333/2008 sets the rules on food additives: definitions, conditions of use, labelling and procedures.

It contains:

- Technological functions of food additives: Annex I
- Union list of food additives approved for use in food additives and conditions of use: Annex II
- Union list of food additives approved for use in food additives, food enzymes and food flavourings, and their conditions of use.: Annex III
- Traditional foods for which certain Member States may continue to prohibit the use of certain categories of food additives: Annex IV
- Additives labelling information for certain food colours: Annex V

Food labelling. Legislation is applicable until 12 December 2013 and covers:

- General rules on food labelling
- Rules for specific foods e.g. beef or chocolate.

Directive 2000/13/EC on labelling, presentation and advertising of foods is the main EU legislation on the subject.

EU rules after 13 December 2013: The new EU Regulation 1169/2011 on the provision of food information to consumers considerably changes existing legislation on food labelling including:

- Nutrition information on processed foods;
- Origin labelling of fresh meat from pigs, sheep, goats and poultry;
- Highlighting allergens e.g. peanuts or milk in the list of ingredients;
- Better legibility i.e. minimum size of text;
- Requirements on information on allergens also cover non pre-packed foods including those sold in restaurants and cafés.

Health & Nutrition Claims. In December 2006, the Regulation (EC) N° 1924/2006 on nutrition and health claims made on foods was adopted by the Council and Parliament. For the first time, this Regulation lays down harmonised rules across the European Union for the use of nutrition claims such as “low fat”, “high fibre” or health claims such as “reducing blood cholesterol”.

This Regulation foresees implementing measures to ensure that any claim made on foods' labelling, presentation or marketing in the European Union is clear, accurate and based on evidence accepted

by the whole scientific community. Consequently foods bearing claims that could mislead consumers will be eliminated from the market. In addition, in order to bear claims, foods will have to have appropriate nutrient profiles which will be set. This will enhance the consumers' ability to make informed and meaningful choices.

Further, this Regulation respects fair competition and protects innovation in the area of foods. It also facilitates the free circulation of foods bearing claims as any food company will be able to use the same claims on its products everywhere in Europe.

Many traditional foods have resisted on the market because of a high nutritive value or for providing wellbeing evidence in people. Some European projects in bioactive compounds were developed to find the benefits of some local/regional Traditional Foods (ex. bioactive compounds in food from Black Sea area, subject included in FP6).

Nutrition Labelling is governed by Council Directive 90/496/EEC, as amended by Commission Directives 2003/120/EC and 2008/100/EC.

In January 2008 the Commission adopted a proposal for a Regulation of the European Parliament and of the Council on the provision of food information to consumers to update and revise the Community legislation on general food labelling and nutrition labelling. The proposals for the amendment of the nutrition labelling aspects of the Community rules took into account consultations in 2003 and 2006, and impact assessments prepared in 2004 and 2007.

Food Contaminants. The basic principles of EU legislation on contaminants in food are in Council Regulation 315/93/EEC of 8 February 1993:

- food containing a contaminant to an amount unacceptable from the public health viewpoint and in particular at a toxicological level, shall not be placed on the market;
- contaminant levels shall be kept as low as can reasonably be achieved following recommended good working practices;
- maximum levels must be set for certain contaminants in order to protect public health.

Maximum levels for certain contaminants in food are set in Commission Regulation (EC) No 1881/2006. This Regulation entered into force on 1 March 2007. Maximum levels in certain foods are set for the following contaminants: nitrate, mycotoxins (aflatoxins, ochratoxin A, patulin, deoxynivalenol, zearalenone, fumonisins), metals (lead, cadmium, mercury, and inorganic tin), 3-MCPD, dioxins and dioxin-like PCBs and polycyclic aromatic hydrocarbons (benzo(a)pyrene).

Pesticide Residues. Directive 91/414/EEC laid down the evaluation, authorisation, and approval of active substances at EU-level and national authorisations of products – shows in its Annex 1 the list of Approved substances.

Food contact materials are materials and articles intended to come into contact with foods such as: packaging materials; cutlery and dishes; processing machines; containers; materials and articles in contact with water for human consumption.

The term does not cover fixed public or private water supply equipment.

New legislation:

– Regulation EU 1183/2012 for plastic materials and articles intended for contact with food amending Regulation (EU) No 10/2011;

– Corrigendum to Regulation EU 1183/2012 for plastic materials and articles intended for contact with food amending Regulation (EU) No 10/2011;

– Regulation EU 1282/2011 for plastic materials and articles intended for contact with food amending Regulation (EU) No 10/2011;

– Regulation EU 321/2011 for restricting Bisphenol A use in plastic infant feeding bottles;

– Regulation EU 284/2011 for import procedures for polyamide and melamine plastic kitchenware from China and Hong Kong.

Food Hygiene. In the White Paper on Food Safety the Commission outlined a radical revision of the Community's food safety hygiene rules, under which food operator's right through the food chain will bear primary responsibility for food safety. The new regulations merge, harmonise and simplify detailed and complex hygiene requirements previously contained in a number of Council Directives covering the hygiene of foodstuffs and the production and placing on the market of products of animal origin. They innovate in making a single, transparent hygiene policy applicable to all food and all food operators right through the food chain "from the farm to the fork", together with effective instruments to manage food safety and any future food crises throughout the food chain.

Community legislation covers all stages of the production, processing, distribution and placing on the market of food intended for human consumption. 'Placing on the market' means the holding of food for the purpose of sale, including offering for sale, or any other form of transfer, whether free of charge or not, and the sale, distribution and other forms of transfer themselves.

The new hygiene rules were adopted in April 2004 by the European Parliament and the Council. They became applicable on 1 January 2006. They are provided for in the following key acts:

– Regulation (EC) 852/2004 on the hygiene of foodstuffs, 29 April 2004;
– Regulation (EC) 853/2004 laying down specific hygiene rules for food of animal origin, 29 April 2004;
– Regulation (EC) 854/2004 laying down specific rules for the organisation of official controls on products of animal origin intended for human consumption, 29 April 2004;
– Directive 2004/41/EC repealing certain Directives concerning food hygiene and health conditions for the production and placing on the market of certain products of animal origin intended for human consumption and amending Council Directives 89/662/EEC and 92/118/EEC and Council Decision 95/408/EC, 21 April 2004.

10.2. The main hazards in food supplements

The main hazards for Food Supplements are the same for other foods and are coming from outside processing area or from processing technological steps. Hazards that are coming from outside processing area usually are coming though raw materials and ingredients, water and food contact materials. During the technological processing can occur other hazards by using unapropriate technological parameters (time, temperature and pressure) or by different unexpected causes (as different accidental contamination with copper or other metal chips from the equipments, lubricants, cleaning and sanitizing agents).

Table 1. RASFF reports within the herbs and spices product category between 01/01/2004 and 01/01/2014. Source J.L. Banach, I. Stratakou, H.J. van der Fels-Klerx, H.M.W. den Besten, M.H. Zwietering, European alerting and monitoring data as inputs for the risk assessment of microbiological and chemical hazards in spices and herbs.

Category	**Number of reports**	**Frequency (Percentage)**
Total	1831	100
Notification type		
Alert	448	24.5
Border rejection	534	29
Information	710	39
Information for attention	112	6
Information for follow-up	27	1.5
Hazard categories		

Adulteration/Fraud	13	<1
Allergens	8	<1
Biotoxins (other)	2	<1
Chemical contamination (other)	1	<1
Composition	416	23
Food additives and flavorings	93	5
Foreign bodies	31	2
GMO/novel food	6	<1
Heavy metals	9	<1
Industrial contaminants	4	<1
Labelling absent/incomplete/incorrect	4	<1
Mycotoxins	501	27
Non-pathogenic microorganisms	61	3
Organoleptic aspects	21	1
Packaging aspects	1	<1
Pathogenic microorganisms	425	23
Pesticide residues	198	11
Radiation	28	2

10.2.1. Hazards coming from outside Food supplements processing area (raw materials, ingredients, others)

The hazards coming from outside processing area are both chemical or microbiological hazards and are influenced by how much herbs or other ingredient producers are informed and trained in food safety and the quality of supplier services.

These hazards have chemical or microbiological origin and it very much depends on the type of raw material, ingredients and food contact materials.

By ISO 22000 standard implementation and HACCP quality system most of these hazards are minimizing or even removed. Some high incidence hazards are summarized bellow.

10. 2.1.1 Hazards coming from raw materials and ingredients

Therapies involving herbal medicinal products and supplements have shown promising potential with the efficacy of a good number of herbal products but some products remain untested and their

use are either poorly monitored or not even monitored at all. The consequence of this is an inadequate knowledge of their mode of action, potential adverse reactions, contraindications, and interactions with existing orthodox pharmaceuticals and functional foods to promote both safe and rational use of these agents.

The general perception that herbal remedies or drugs are very safe and devoid of adverse effects is not only untrue, but also misleading. Herbs have been shown to be capable of producing a wide range of undesirable or adverse reactions some of which are capable of causing serious injuries, life-threatening conditions, and even death. Numerous and irrefutable cases of poisoning have been reported in the literature (Vanherweghem and Degaute, 1998; Cosyns et al., 1999; Ernst, 2002). A number of Chinese herbal medicines and other herbal medicines from different parts of the world have also been implicated in cases of poisoning. Many of them have been shown to contain toxic compounds which are capable of reacting with cellular macromolecules including DNA, causing cellular toxicity, and/or genotoxicity (Rietjens et al., 2005). For the purpose of demonstration and argumentation of all over-said, side effects of only a few commonly used herbal medicines are described below by Martins Ekor (2014), who expressed in the review „Frontiers in Pharmacology" certain issues related to adverse reactions and challanges in monitoring safety of herbal medicines, as follow:

„Aristolochic acids and *Aristolochia* species. Following the discovery of the nephrotoxic and carcinogenic potentials of aristolochic acids (Vanherweghem et al., 1993), several studies confirmed their genotoxic activity (Kohara et al., 2002; Fang et al., 2011; Hwang et al., 2012). Schmeiser et al. (1996) demonstrated the presence of aristolochic acids-related DNA adducts in renal tissues of patients. These mutagenic adducts when formed are usually poorly repaired (Sidorenko et al., 2012) and are capable of persisting for years in DNA (Nortier et al., 2000). Aristolochic acids I and II have been identified in different Asian medicinal plants and also reported to be present in slimming products. This has led to the banning of medicinal products containing these acids in Belgium, UK, Canada, Australia, and Germany (Hashimoto et al., 1999; Lee et al., 2002; Zhou et al., 2013).

Misidentification of medicinal plants and mislabeling herbal medicinal products are sometimes responsible for some of the observed adverse events or interaction and that is the reason it is important to assess herbal medicines for possible presence of adulterants."

„Ephedra sinica. *Ephedra* is a very popular herb with long history of traditional use in respiratory conditions (Zhang et al., 1999; Bensky et al., 2004). This herb, whose efficacy has been demonstrated in a number of randomized double-blind clinical trials (Boozer et al., 2002; Haller et al., 2005; Kim et al., 2008), is currently included in the Chinese Pharmacopoeia for therapeutic use and classified as non-toxic. It is an ingredient in commonly used formulary preparations such as Xiaoqinglong Heji for common cold and Zhisou Dingchuan Koufuye for asthma (Chinese Pharmacopoeia Commission, 2010). *Ephedra* has been marketed in the US as a weight-loss dietary supplement and its use associated with a number of serious cardiovascular and central nervous systems (CNSs) adverse effects (Verduin and Labbate, 2002; Hackman et al., 2006; Hallas et al., 2008; Chen et al., 2010). Several case reports have also linked the use of *Ephedra sinica* and *Ephedra*-containing dietary supplements to adverse events such as hepatotoxicity (Skoulidis et al., 2005; Schoepfer et al., 2007), neurotoxicity (Varlibas et al., 2009), and transient blindness (Moawad et al., 2006).”

„Aconitum **species.** *Aconitum carmichaeli* and *Aconitum kusnezoffii* are used traditionally for pain relief (Chinese Pharmacopoeia Commission, 2010). The toxicity of the medicinal plants derives primarily from the presence of diester diterpene alkaloids such as aconitine, mesaconitine, and hypaconitine in them (Xu et al., 2005). Severe cases of cardiac toxicity from consumption of aconitine-containing herbal preparation manifesting as ventricular tachycardia and fibrillation and eventually leading to death have been reported (Tai et al., 1992; Fujita et al., 2007; Dhesi et al., 2010; Lin et al., 2011). In other studies bradycardia and hypotension were observed (Chan, 2009). Clinical cases of aconitine poisoning from *A. kusnezoffii* consumption have also been reported (Chan and Critchley, 1994; Chan, 2002).”

„Tussilago farfara. Traditionally, *Tussilago farfara* has been used effectively for thousands of years for the treatment of acute and chronic cough and it is generally regarded as non-toxic (Chinese Pharmacopoeia Commission, 2010). Total alkaloids and senkirkine isolated from this plant, on the other hand, have been demonstrated to be hepatotoxic (Zhang et al., 2008). Recently, the potential health effects of the pyrrolizidine alkaloids found in *T. farfara* was reviewed and hepatic veno-occlusive disease and cirrhosis were suggested as the major potential disease outcome in human (Edgar et al., 2011).”

„Ginkgo biloba **and Ginseng.** *Ginkgo biloba* has found widespread use in a variety of conditions and several products such as elixirs, extracts, tea, as well as capsules and tablets that may differ in terms of content, have been made from the dried root (Sparreboom et al., 2004). The whole root

which contains ginsenosides is usually used because these compounds possess specific pharmacologic effects that may oppose each other (Chong and Oberholzer, 1988). Over 30 ginsenosides have been identified and these compounds are being investigated for their ability to inhibit cell proliferation, tumor cell invasion, and/or metastasis (He et al., 2011; Kim et al., 2012). Recently, the ability of ginsenosides to modulate signaling pathways involving cell cycle, inflammatory, or growth factor pathways, was demonstrated (Nag et al., 2012; Dunnick and Nyska, 2013). The plant extracts appear to be relatively safe, although headache, dizziness, restlessness, nausea, vomiting, diarrhea, and dermal sensitivity are the most common side effects that have been observed. *Ginkgo* has been demonstrated to be capable of inhibiting platelet-activating factor and altering bleeding times. Therefore, cautious use had been advised in individuals or patients on anticoagulants therapy (Boullata and Nace, 2000). The ability of ginkgo to induce liver cancer in experimental model was reported recently and genotoxic mechanisms were suggested to play some role in the carcinogenic process (National Toxicology Program, 2012; Dunnick and Nyska, 2013). In addition to the carcinogenic effects in the liver and thyroid, ginkgo has also been shown to be capable of inducing tumorigenesis in the nasal cavity. Some other authors, however, have attributed the nasal lesions to gastric reflux/post gavage reflux through the nasopharyngeal duct (Damsch et al., 2011a,b).

Ginseng used as herbal remedies has different botanical sources generally obtained from several *Panax* species including *Panax quinquefolius, Panax Ginseng*, and *Panax pseudoginseng*. In large or excessive doses, *Ginseng* has been reported to cause agitation, insomnia, and elevation of blood pressure (Baldwin et al., 1986; Dunnick and Nyska, 2013). Other adverse effects that have reported include transient nervousness, excitation, insomnia, inability to concentrate, headache, epistaxis, and allergies. A case of severe but non-fatal Stevens–Johnson syndrome was reported following a 3-day *Ginseng* administration (Dega et al., 1996). Also, spontaneous bleeding from the iris into the anterior chamber of the eye was linked to the use of *G. biloba* extract (Rosenblatt and Mindel, 1997).Separate case reports had also linked the use of *G. biloba* to the development of bilateral subdural hematomas and subarachnoid hemorrhage (Rowin and Lewis, 1996; Vale, 1998).”

„Kava (*Piper methysticum*). Kava is known for its CNS depressant activity and it is commonly used as an anxiolytic agent. Commonly reported side effects of this medicinal plant include headache, dizziness, gastrointestinal discomfort, and localized numbness after oral ingestion. Large dosages has been shown to be capable of giving rise to dry, scaly skin, and yellowish discoloration of the skin and nails, photosensitivity and redness of the eye. Excessive consumption of kava may

also lead to photophobia and diplopia (Boullata and Nace, 2000). The muscle relaxant and anticonvulsant effects of this plant have been attributed to its active pyrones constituent. In 2002, the US Food and Drug Administration received several reports of liver-related injuries alongside that of a previously healthy young female who eventually required liver transplantation following consumption of kava-containing products. This prompted the FDA to alert consumers on the potential risk of severe liver injury associated with the use of kava-containing dietary supplements. This liver-related risks also prompted regulatory agencies in other countries including Germany, Switzerland, France, Canada, and the UK to warn consumers about the potential risks of kava use and also went on to consider the withdrawal of kava-containing products from the market (U.S. Food and Drug Administration, 2002). In over 25 reports of adverse events outside the US, kava-containing products were associated with liver-related injuries like hepatitis, cirrhosis, and liver failure with some of the affected patients eventually requiring liver transplants (U.S. Food and Drug Administration, 2002)."

„St. John's Wort. *Hypericum perforatum,* popularly known as St. John's wort, contains active compounds, such as hypericin, hyperforin, and melatonin. It was once used against viral infections but has gained increased use for mild depressive symptoms (Bennett et al., 1998; Rey and Walter, 1998). Adverse effects reportedly associated with its use include allergic reactions, headache, dizziness, restlessness, fatigue, dry mouth, nausea, vomiting, constipation, and photosensitivity. Hyperesthesia and a syndrome of dyspnea and hyperventilation with flushing headache, mydriasis, nausea, palpitations, and tremor, have been reported (Rey and Walter, 1998).,,

10.2.1.2. Chemical hazards

Mycotoxins are mostly found in herbs and other ingredients if there is an unappropriate parameters for their storage (ex. humidity). Mycotoxins are secondary metabolites produced by moulds either in crops during unfortunate weather conditions or during storage of raw materials/ingredients/foods under humid conditions. There were found about 400 mycotoxins but only several are very toxic for human body.

Some of these are:

Fumonisis are mycotoxins produced by genera *Fusarium*. Fumonisin B1 is the most prevalent and toxic

of the fumonisins. Food products can be contaminated during growth, storage, and processing and fumonisins are heat stable, light stable, water soluble, poorly absorbed, poorly metabolized, and rapidly excreted by animals.

Another mycotoxins are the four major **aflatoxins** called B_1, B_2, G_1, and G_2 based on their fluorescence under UV light (blue or green) and relative chromatographic mobility during thin-layer chromatography. Aflatoxin B_1 is the most potent natural carcinogen known and is usually the major aflatoxin produced by toxigenic strains. Aflatoxins are difuranocoumarin derivatives produced by many strains of *Aspergillus flavus,* a common contaminant in agriculture, and *Aspergillus parasiticus*; Natural contamination of cereals, oilseeds, nuts, dried fruits, spices etc. is a common occurrence. Sometimes crops become contaminated with aflatoxin in the field before harvest, where it is usually associated with drought stress or during storage under specific conditions that favor mold growth. Dairy products can indirect be contamined by aflatoxin M_1, less carcinogenic hydroxylated form of B1, which is metabolically biotransformed in cow's body. The International Agency for Research on Cancer has classified aflatoxin B_1 as a group I carcinogen[1].

Ochratoxin A is a metabolite of *Aspergillus ochraceus*. It has been found in barley, oats, rye, wheat, etc. There is also concern that ochratoxin may be present in certain wines, especially those from grapes contaminated with *Aspergillus carbonarius*. The International Agency for Research on Cancer has rated ochratoxin as a possible human carcinogen (category 2B) [6]. Ochratoxin can be transmitted to meat through improper quality of fodder.

The trichothecenes, a family of more than sixty sesquiterpenoid metabolites produced by a number of fungal genera, including *Fusarium, Trichoderma*, *Trichothecium*, and others, are commonly found as food and feed contaminants. Diacetoxyscirpenol, deoxynivalenol, and T-2 are the best studied of the trichothecenes produced by *Fusarium* species. Deoxynivalenol is one of the most common mycotoxins found in grains: barley, corn, rye, safflower seeds, wheat, and mixed feeds.

Zearalenone, ZEN, (6-[10-hydroxy-6-oxo-*trans*-1-undecenyl]-B-resorcyclic acid lactone) is a secondary metabolite from *Fusarium graminearum*. The zearalenones are also biosynthesized by *Fusarium culmorum*, *Fusarium equiseti*, and *Fusarium crookwellense*. All these species are regular contaminants of cereal crops worldwide. The recommended safe human intake of ZEN is estimated

[1] International Agency for Research on Cancer. 1982. The evaluation of the carcinogenic risk of chemicals to humans. IARC Monograph Supplement 4. International Agency for Research on Cancer, Lyon, France.

to be 0.05 µg/kg of body weight per day but in foodstuffs the level of ZEN are not yet regulated anywhere.

Table 2. Specific hazards as reported in the hazard category mycotoxins in RASFF between 01/01/2004 and 01/01/2014. Source J.L. Banach, I. Stratakou, H.J. van der Fels-Klerx, H.M.W. den Besten, M.H. Zwietering, European alerting and monitoring data as inputs for the risk assessment of microbiological and chemical hazards in spices and herbs.

Category	**Number of reports**	**Frequency (Percentage)**
Total	1024	100
Specific Hazards		
Aflatoxin B1	497	49
Aflatoxins (non-specified)	419	41
Ochratoxin A	101	10

The most reported products for aflatoxin B1 and for non-specified aflatoxins were chilies (45%), nutmeg (18%), and paprika (10%). Ochratoxin A was mainly reported in paprika and chilies at 53% and 17%, respectively, and in pepper (7%) and nutmeg (7%).

Several notifications of aflatoxin B1, 59% of the total aflatoxin B1 notifications, and 60% of the total aflatoxin (non-specified) notifications, were reported to come from India.

The current ML for aflatoxin B1 is 5.0 mg/kg and for the sum of aflatoxins (B1, B2, G1, and G2) is 10.0 mg/kg (European Commission, 2006, 2010b) for the following species of spices:

- *Capsicum* spp.: dried fruits thereof, whole or ground, including chilies, chili powder, cayenne and paprika;
- Piper spp.: fruits thereof, including white and black pepper;
- *Myristica fragrans:* nutmeg;
- *Zingiber officinale:* ginger;
- *Curcuma longa:* turmeric,

and mixtures of spices containing one or more of the abovementioned spices (European Commission, 2006, 2010b).

More recently, Commission Regulation (EU) 2015/1137 also amended Regulation 1881/2006 with respect to MLs for ochratoxin A at 20 mg/kg (European Commission, 2015a) in particular for *Capsicum* spp.: dried fruits thereof, whole or ground, including chilies, chili powder, cayenne and paprika) and for licorice root (used as an ingredient for herbal infusions). For spices, including dried

spices, Piper spp. (fruits thereof, including white and black pepper), *Myristica fragrans* (nutmeg), *Zingiber officinale* (ginger), *Curcuma longa* (turmeric), as well as the mixtures of spices containing one of the abovementioned spices, the ML is 15 mg/kg (European Commission, 2006, 2010a, 2015a).

Dioxines are mainly found in fatty tissues of animals. Dioxines, a group of chemically-related compounds, are found throughout the world in the environment, being persistent environmental pollutants. Over 90% of human exposure to dioxins is through food, mainly through animal origin food.

The name "dioxins" is often used for the family of structurally and chemically related polychlorinated dibenzo para dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). Certain dioxin-like polychlorinated biphenyls (PCBs) with similar toxic properties are also included under the term "dioxins". 419 types of dioxin-related compounds have been identified but only about 30 of these are considered to have significant toxicity, with TCDD (*2,3,7,8-tetrachlorodibenzo para dioxin)* being the most toxic.

Dioxins are coming from different industrial processes (e.g. paper or pesticides manufactures so on) through water or soil contaminated but can also result from natural processes (e.g. forest fires) or by burning dried herbs or leaves when in country side people clean the yards (or backyard burning of trash). In this way the soil is contaminated and plants/herb can cumulate dioxins. Exposure of humans to high levels of dioxins may result in skin lesions, altered liver function, impairment of the immune system, or even several types of cancer.

Agrochemicals as insecticides, herbicides, fungicides, fertilizers, rodenticides, nitrates can also be chemical hazards and contaminate the herbs which will be further used for producing food supplements. If they are not used according with the best agricultural practices it is possible to be found residues of these chemicals in agro foodstuff.

Heavy metals are sometimes polluting soil and air, very much depending of the industrial level of the area. The main hazard from heavy metals are associated with lead, cadmium, mercury and arsenic contamination. Food is the most important source of cadmium, mercury, lead and arsenic exposure.

Packaging materials can come with several chemical hazards as the following substances: antimony, tin, lead, perfluorooctanoic acid (PFOA), semicarbazida, benzophenone, isopropyl thioxanthone (ITX), bisfenol A**.**

10.2.1.3. Microbiological hazards

Many pathogenic microorganism notifications included hazards such as coliforms, Enterobacteriaceae, sulfite reducing anaerobes, and fungi. Pathogenic microorganisms, particularly *Salmonella* spp (i.e. basil, mint, peppermint and). and pathogenic *Bacillus* spp. (chili and curry), were identified as a potential concern in dried herbs.

Examples about food poisoning were given by related articles for frozen ginger contaminated by *Bacillus pumilus* (Norway,2008), fresh basil (*Ocimum basilicum*) contaminated by *Shigella sonnei* (Israel, 2011), ground cumin contaminated by *B. cereus*, *Clostridium perfringens* and *Salmonella caracas* (United Kingdom, 2011) and contaminated herbal extracts of *Althea officinalis* (Bulgaria, 2013).

Table 3. Microorganisms as reported in the hazard category pathogenic microorganisms in RASFF between 01/01/2004 and 01/01/2014. Source J.L. Banach, I. Stratakou, H.J. van der Fels-Klerx, H.M.W. den Besten, M.H. Zwietering, European alerting and monitoring data as inputs for the risk assessment of microbiological and chemical hazards in spices and herbs.

Category	Levels (CFU/g)	Number of reports	Frequency (Percentage)
Total		500	100
Specific Hazards			
Aerobic Plate Counts [a]	$2.5x10^5$	1	<1
Aspergillus spp.[b]	$5x10^2$	3	1
Bacillus spp.	$1x10^3$-$3x10^8$	41	8
Campylobacter spp.	Presence in 25 g	1	<1
Clostridium spp.	$2x10^2$-10^3	7	1
Coliforms	70-$3x10^5$	2	<1
Enterobacteriaceae[a]	$4x10^3$-$4x10^4$	6	1
Escherichia coli	10^3-10^5	61	12
Fungi[a]	$3x10^3$-$6x10^4$	6	1
Salmonella spp.	Presence in 25 g	369	74
Shigella spp.	N/A[c]	1	<1
Staphylococcus aureus	$3x10^4$	1	<1
Sulfite reducing anaerobes[a]	$2x10^3$	1	<1

a Overlaps with the RASFF hazard category non-pathogenic microorganisms.
b Only one notification had this level reported.
c N/A: not applicable.

10. 2. 2. Hazards coming from environment and processing

Benzene is ubiquitous in the atmosphere. It has been identified in air samples of both rural and urban environments and in indoor air. Although a large volume of benzene is released to the environment, environmental levels are low because of efficient removal and degradation processes.

The U.S. Food and Drug Administration funded for 5 years period a study to determine the amount of volatile organics in food from 1996 to 2000. Benzene was found in over 40 type of foods. Foods with the highest level of benzene were ground beef (maximum 190 ppb), raw bananas (maximum 132 ppb), carbonated cola (maximum 138 ppb), and coleslaw with dressing (maximum 102 ppb)[2]. During food processing or because of the equipment food can be accidentally contaminated by **copper or other metal chips, lubricants, cleaning, and sanitizing agents**.

Microbiological hazards in processing are the same as for raw materials. More, into the processing area, biofilms occur when bacteria form a slime layer upon a surface and provide an environment for pathogens to proliferate. The adhesion of pathogenic bacteria to a biofilm is a food safety hazard because the biofilm can detach and become a significant source of food contamination.

10.3. How to keep food/food suplements safety?

Good agricultural practices ensure herbal material homogeneity based on phenotypic characteristics. The main variables are climatic, soil-related (edaphic), and genetic influences on phenotypes. With GCP, the variables include, in addition, subspecific heterogeneity and lack of bulk authenticity. These variables influence the phytochemistry of the herbs and, consequently, that of their raw extracts.

Table 4. Good agricultural practice (GAP)—guidelines formedicinal herb authenticity, homogeneity, and purity. Source: Suresh Govindaraghavan, Nikolaus J. Sucher, Quality assessment of medicinal herbs and their extracts: Criteria and prerequisites for consistent safety and efficacy of herbal medicines

Emphasis	**Criteria**
Site selection	Ecological and social impact
	Climatic and edaphic data
Germplasm	Botanical authenticity to species and subspecific taxon (variety/cultivar)
	Retention of voucher specimens (herbarium)
	Seed/propagule homogeneity and purity and propagation data
Cultivation management	Irrigation data
	Fertilizer application
	Pesticide/fungicide/weedicide treatments
Harvesting, processing, and storage	Optimal time of harvest (based on biomass/constituent assay)
	Physical processing (sorting, drying, milling) methods
	Packaging and storage methods
Raw material quality control	Identification of sorted and processed material (pharmacopeial and other methods)

[2] Greenberg, A, Weisel, CP, Benzene, POTENTIAL FOR HUMAN EXPOSURE, 2006, USDA, U.S. Department of Agriculture.

	Analysis for moisture, foreign matter, ash content
	Impurity profiling of heavy metals, pesticides, mycotoxins
Documentation	Raw herb processing — batch documentation from site selection to quality control
	Retention of batch documentation for vendor audits (until expiry)

Good authentication and identification practice (GPAIP) for medicinal herbs require:

- A validated guidance document for 'good plant authentication practice' for medicinal herbs in consultation with plant taxonomy experts (GIM — general identification method for a given taxon);
- Preparation and retention of herbarium vouchers (standard operating procedures; SOPs);
- Certificate of botanical authenticity by a specialist taxonomist;
- Herbarium reference number;
- Information on subspecific taxon (variety/cultivar);
- DNA barcoding (genomic profiling) — GAM (general analytical method);
- Document to link to the bulk (harvested/collected) medicinal herb batch;
- GMP documentation on the medicinal herb batch;
- SOPs and GTM (general technical methods) for the batch process — drying, sorting, and cutting of whole plant and plant part to specified size for further processing;
- A validated guidance document for 'good identification practice' for sorted/powdered plant materials;
- Macroscopic and microscopic identification methods (general analytical methods) for a given plant part of a specific taxon — pharmacopeial identification methods are a good starting point;
- Chemoprofiling as an identification tool for the plant part of a specific plant taxon — utility of pattern recognition (GTM — HPTLC/HPLC/GC/CE);
- Batch documentation for organized cultivation/GAP/wildcrafted herbs.

Source: Suresh Govindaraghavan, Nikolaus J. Sucher, Quality assessment of medicinal herbs and their extracts: Criteria and prerequisites for consistent safety and efficacy of herbal medicines

The Good Manufacturing Practices have the highest importance in food processing with the aim to prevent any contamination of food through technological steps, from the raw materials, ingredients and food contact materials reception till the consumers.

Good Manufacturing Practices is a guide which is ellaborated by each company for its specific conditions including the type of foods that are processed. It should comprise all technological specifications and general and operational procedures necessary to prevent food against contamination.

Some of general procedures are reffering to reception of raw materials, ingredients and food contact materials and cross-contamination, supplier selection, records so on.

For avoiding both microbiological and chemical contamination the reception of raw materials, ingredients and food contact materials has to be made by follow a special procedure which includes the criteria of supplier selection and the quality requirements for all the materials (i.e laboratory tests).

For avoiding cross-contamination (concerning allergenic or/and microbiological aspects) on production lines there is necessary to have some specific procedures concerning separation of the flows within processing area. The main flows are for materials and ingredients (with allergenic substances or not), food contact materials, additives, final products, personnel, etc.

For **microbiological safety hazards** include pathogenic bacteria, viruses, and parasites. For better prevention against microbiological hazard periodically training programs and effective hygienic practices for employees are necessary to have. The hygienic practices has to include both the hygiene of employee and labour working environment hygiene (cleaning and sanitation). Hygienic design is very important especially to prevent contamination into the sites where may be impossible to reach and clean with normal cleaning and sanitizing procedures. Examples include hollow rollers on conveyors, cracked tubular support rods, the space between close-fitting metal-to-metal or metal-to-plastic parts, worn or cracked rubber seals around doors, and on-off valves and switches. Good hygienic design of equipment requests that the materials used for food processing equipments to be easily cleanable for better sanitation but also to be built by appropriate, non-corrosive materials to avoid metal chips contamination. More, there is necessary a routine and preventive maintenance program for keeping a good hygiene in the processing area and sorroundings.

Microbiological contamination can occur also because of insects or rodents; in this sense a procedure for keeping the processing area free of these sources of contamination is necessary.

Chemical safety hazards during the food processing include intentionally added chemicals (e.g., allergens), unintentionally added chemicals (e.g., cleaners and solvents), and natural toxins (e.g., mycotoxins). Chemicals can also contaminate food through corrosion of metal processing equipment/utensils and residues of cleaning chemicals left on processing equipment. Further,

adding too much of an approved ingredient, such as a vitamin in vitamin-fortified products, or additives may compromise the safety of foods.

Another chemical hazard can be the substances used against pests. The way of using facilities for controlling pests is needed to be procedured.

Another kind of contamination is **physical contamination** with materials that do not belong in food, like glass, wood, rocks or metal and which cause physical safety hazards.

Production line staff can be a major source of contamination. Jewelry can fall off or break, fingernails can break, and pens can fall into food. Jewelry removal is required under GMPs. If pens are metallic, a metal detector can detect them. Production workers' fingernails should be cut short and gloves should be worn under certain processing conditions.

References

1. Banach, J.L., Stratakou, I., van der Fels-Klerx, H.J., den Besten, H.M.W., Zwietering, M.H. -*European alerting and monitoring data as inputs for the risk assessment of microbiological and chemical hazards in spices and herbs*, Food Control 69 (2016) 237e249;
2. Basgel, S., Erdemoglu, S.B. - *Determination of mineral and trace elements in some medicinal herbs and their infusions consumed in Turkey*, Science of the Total Environment 359 (2006) 82– 89;
3. Beardall, J. M., and J. D. Miller, 1994, *Disease in humans with mycotoxins as possible causes*, p. 487-539. *In*J. D. Miller and H. L. Trenholm (ed.), Mycotoxins in grains. Compounds other than aflatoxin. Eagan Press, St. Paul, Minn;
4. Cosyns, J.P., Jadoul, M., Squifflet, J.P., Wese, F.X, van Yepersele de Strihou, C. – *Urothelial lesions in Chinese herb nephropathy*. Am.J.Kidney Dis. 33, 1011-1017, (1999), doi: 10.1016/50272-6386(99)70136-8;
5. Ekor, M.- *The growing use of herbal medicines: issues relating to adverse reactions and challanges in monitoring safety*, Frontiers in pharmacology, (2014), vol.4, art. 177, pp. 1-10, doi: 10.3389/fphar.2013.00177
6. Elviss, N.C., Little, C.L., Hucklesby, L., Sagoo, S., Surman-Lee, S., de Pinna, E., Threlfall, E.J. on behalf of the Food, Water and Environmental Surveillance Network - *Microbiological study of fresh herbs from retail premises uncovers an international outbreak of salmonellosis*, International Journal of Food Microbiology 134 (2009) 83–88.

7. Ernst, E. - *Toxic heavy metalsand undeclared drugs in Asian herbal medicines*, Trends Pharmacol. Sci., (2002), 23, 136-139, doi: 10.1016/S0165-6147(00)01972-6

8. Food and Agriculture Organization of the United Nations. World Health Organization. *Summary report of the sixty-fourth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)*. Retrieved July 24, 2008, from: http://www.who.int/entity/ipcs/food/jecfa/summaries/summary_report_64_final.pdf;

9. Govindaraghavan, S., Sucher, N, J.- *Quality assessment of medicinal herbs and their extracts: Criteria and prerequisites for consistent safety and efficacy of herbal medicines*, Epilepsy & Behavior 52 (2015) 363–371;

10. Kroes, B. H. *The legal framework governing the quality of (traditional) herbal medicinal products in the European Union*, Journal of Ethnopharmacology 158 (2014) 449–453;

11. Mottram DS, Wedzicha BL, Dodson AT. *Acrylamide is formed in the Maillard reaction*. Nature 2002; 419(6906): 448–449;

12. Rietjens, I.M., Martena, M.J., Boersma, M.G., Spiegelenberg, W., Alink, G.M.- *Molecular mechanisms of toxicity of important food-borne phytotoxins*. Mol. Nutr. Food Res. (2005), 49, 139-158, doi:10.1002/mnfr.200400078.

13. Sagoo, S.K, Little, C.L., Greenwood, M., Mithani, V., Grant, K.A., McLauchlin, J., de Pinna, E., Threlfall, E.J. - *Assessment of the microbiological safety of dried spices and herbs from production and retail premises in the United Kingdom*, Food Microbiology 26 (2009) 39–43;

14. Stadler RH, Blank I, Varga N, et al. *Acrylamide from Maillard reaction products*. Nature 2002, 419(6906):449–450;

15. Tripathy, V., Basak, B.B., Varghese, T.S, Saha, A.- *Residues and contaminants in medicinal herbs—A review* Phytochemistry Letters 14 (2015) 67–78;

16. Trucksess, M. W., and Y. Tang, - *Solid phase extraction method for patulin in apple juice and unfiltered apple juice*, (2001), p. 205-213. *In*M. W. Trucksess and A. F. Pohland (ed.), Mycotoxin protocols. Humana Press, Totowa, N.J. [PubMed];

17. Vanherweghem, J.L., Degaute, J.P.- *The policy of admission to the education in medicine and dentistry in French speaking community of Belgium*, Acta Clin. Belg. (1998), 53, pp 2-3;

18. Wang, Z., Huang, L. - *Panax quinquefolius: An overview of the contaminants*, Phytochemistry Letters 11 (2015) 89–94;

19. Zweifel, C., Stephan, R.- *Spices and herbs as source of Salmonella-related foodborne diseases*, Food Research International 45 (2012) 765–769.

European Commission, 2006,

European Commission, 2010 b

European Commission, 2015a