

What exactly is a food additive?

**A comparative analysis between the European Union
and the United States on the scope and function of
food additives**

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List of Abbreviations

ADI	Acceptable Daily Intake
ANS	Panel on Additives and Nutrient Sources Added to Food
BSE	Bovine Spongiform Encephalopathy
CAC	Codex Alimentarius Commission
CAFAB	Competent Authority Food Assessment Body
CAS	Chemical Abstracts Service
CEF	Panel on Food Materials, Enzymes, Flavourings and Processing Aids
CFR	Code of Federal Regulations
DG Sanco	Directorate General for Health and Consumers
DNA	Deoxyribonucleic Acid
EA	Environmental Assessment
EAFUS	Everything Added to Food in the US
EDI	Estimated Daily Intake
EEC	European Economic Community
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EU	European Union
FAO	Food and Agriculture Organization
FCN	Food Contact Notification
FCS	Food Categorization System
FDA	Food and Drug Administration
FDCA	Food, Drug and Cosmetic Act
FEMA	Flavor and Extract Manufacturer's Association
FIAP	Food Improvement Agent Package
FSIS	Food Safety and Inspection Service
FTC	Federal Trade Commission
GAO	General Accounting Office
GATT	General Agreement on Tariffs and Trade
GFL	General Food Law or Regulation 178/2002
GM	Genetically Modified
GMO	Genetically Modified Organism
GRAS	Generally Recognized as Safe
JECFA	Joint FAO/WHO Expert Committee on Food Additives
NEPA	National Environmental Policy Act
NFR	Novel Foods Regulation or Regulation 257/97
OTC	Over the Counter
PCB	Polychlorinated Biphenyl
PFDA	Pure Food and Drug Act
ROQ	Register of Questions
SCF	Scientific Committee on Food
SCFCAH	Standing Committee on Food Chain and Animal Health
SPS	Sanitary and Phytosanitary
TDI	Tolerable Daily Intake
TEU	Treaty on European Union
TFEU	Treaty on the Functioning of the European Union
TTB	Alcohol and Tobacco Tax and Trade Bureau
UN	United Nations
US	United States
USDA	United States Department of Agriculture
WHO	World Health Organization
WTO	World Trade Organization

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1 Introduction

In both the European Union (EU) and United States (US), food additives must be approved before being placed on the market, through a formal application procedure that demonstrates safety of the ingredient, among other things. It can sometimes be difficult enough to gather the vast documentation to gain approval, but furthermore, the situation is actually far more complex than it initially seems. What exactly is a food additive? This question is so vital because how a substance is classified – if it fits into this definition of a food additive or not – affects how it is regulated: if and how it needs to be approved, if and how it needs to be labeled, etc. A substance that may appear to be a food additive at first glance may turn out to fit the definition of a different category of foods or food ingredients. This can naturally cause difficulties for the business wishing to market the substance, for example, either because a different (new) procedure may have to be followed, and in the extreme case, if a product on the market contains a substance that was not properly approved, it may be considered unsafe or adulterated and have to be withdrawn and/or recalled from the market.

The European Union and the United States are two regions with major food industries. Many companies market products in both places. However, their food laws are not so harmonized that a substance classified as a food additive in Europe is necessarily a food additive in the United States, and vice versa. Also, approval in one region does not imply market access in the other region. Not only are the two systems different, but each has its unclarities and complexities. This may pose confusion to companies wishing to place ingredients and food products containing such ingredients on the two markets. The aim of this paper is to conduct an in-depth analysis into what exactly a food additive is under both jurisdictions, and the consequences that these classifications may have. A comparative analysis will highlight the similarities and differences between the two systems.

One important point to note is that this is a comparison of the European Union and the (federal) United States. While the EU is a union of many countries (“Member States”) and the US is a country of many states, they are assumed to be at equivalent levels. Regulation of food additives at the Member State level in the EU¹ and at the state level in the US is not considered. Once an additive is authorized at EU level, it can be used in foods placed on the market in all Member States, plus Norway and Iceland (Food Safety Authority of Ireland 2010). Additives approved in the US can be used in all fifty states.

The sections on additives in the European Union and the United States are to clarify what exactly are additives and how are they regulated. The following comparison section focuses on the differences between food additives in the two systems. In the end, a discussion looks into why these differences may exist. While the initial focus of this paper was on food additives, it is impossible to draw a clear picture of the situation without discussing the definitions and premarket approvals of other substances. This is largely because there is some overlap between what is included as a food additive in the EU and the US (for example,

¹ A few examples of food additive regulation issues in EU Member States can be found in the following cases: Case C-95/1989, *Commission v Italy* (added nitrate) [1992] ECR I-4545; Case 153/1980, *Officer van Justitie v Koninklijke Kaasfabriek Eyssen BV* [1981] ECT 409. For further discussion see S Weatherill, *EU Consumer Law and Policy* (Cheltenham, Edward Elgar, 2005), p 43; Case C-42/1990, *Criminal proceedings against Jean-Claude Bellon* [1990] ECR I-4863, paras 16 and 17; Case 88/1979, *Criminal proceedings against Siegfried Gunnert* [1980] ECR 1827 (list taken from Caoimhin Macmaolain. *EU Food Law: Protecting consumers and health in a common market*. Volume 13 in the series *Modern Studies in European Law*. Hart Publishing, 2007)

colors, but not flavors, are considered food additives in the EU, whereas flavors, but not colors, are considered food additives in the US). It is therefore important to include these other substances that may not be considered food additives in one region, but in the other, in order to better understand the situation. The comparison between the US and EU leads to a mix of British and American spellings. Although American style is used throughout this text, quotations of EU texts and legislation titles are written using British spellings.

1.1 Problem statement

It is unclear what exactly is included in the concept of a food additive in both the EU and US. An understanding of the definitions and how they have been interpreted by regulatory agencies is essential. In addition, the function of the concepts needs to be analyzed, with a focus on a comparison between the two regions. As there is some overlap in the definitions of food additives (i.e. that some types of substances are included in one definition but not the other), it is essential to include these categories as well for a complete analysis.

1.2 Research questions

The following questions are addressed in this paper:

1. What is the concept of a food additive in both European and American legislation? What exactly is included or excluded, and what are the differences between the two?
2. What are the functions of the definitions in the two jurisdictions, i.e. how do the definitions affect the regulatory situation?
3. How do the premarket approval requirements and procedures for food additives work in the EU and US? In particular, what are the requirements in the evaluations and what are the differences between the two?
4. What are the concepts of and premarket approval requirements for GRAS products in the US, novel foods in the EU and any other substances that may be considered a food additive in either the US or the EU? What is their relation to food additives?
5. How do the definitions and systems compare with international food standards, such as those of the Codex Alimentarius Commission?
6. What are some possible explanations for the different approaches to regulation of food additives and other substances?

2 Background information

2.1 Premarket approvals

Put quite simply, conventional foods—those that have a tradition of use—are considered safe and can be placed on the market without prior approval. New or innovative products, however, typically have to undergo a premarket approval process before they can be marketed. German scholars have summarized these two categories with the ‘principle of abuse’ and the ‘prohibition principle with reservation of permission’². The ‘principle of abuse’ states that businesses are free to market products as they wish, but will be held responsible if they do not comply with general food safety rules. The ‘prohibition principle with reservation of permission’ states that businesses are forbidden to place food on the market unless permission has been obtained by authorities. In the first case, foods are essentially considered safe unless proven otherwise; in the second, foods are unsafe unless proven otherwise. Foods in the latter case are considered *a priori* hazardous. The first situation applies unless explicitly stated otherwise³.

As stated above, conventional foods are considered safe unless proven otherwise. If the authorities wish to deem a product unsafe and remove it from the market, it is their responsibility to gather the evidence that it is, in fact, unsafe. However, to place substances deemed *a priori* hazardous on the market through premarket approvals, the business wishing to obtain approval bears the burden of proof of safety. The business is responsible to provide scientific data and gather various pieces of information to prove that the substance can be marketed (Van der Meulen 2009, Van der Meulen and van der Velde 2008). Two possible reasons for the reversal of the burden of proof in premarket approval cases are that the scientific evidence might be difficult to obtain by an outsider, and also that the business with economic interest in placing the product on the market (versus society) should have to cover the costs of gathering scientific data.

Positive list systems apply to products that undergo premarket approval procedures. They are lists which state what is allowed (i.e. those foods which have been approved), thus making everything not on the lists forbidden. This is in contrast to conventional foods, which are free to be placed on the market unless explicitly banned. In the EU approval requirements exist for food additives (divided into sweeteners, colors and other additives)⁴, novel foods⁵, flavorings⁶, genetically modified foods⁷, food supplements⁸, infant formulae⁹ and foods for

² Translation by Margret Will and Doris Guenther, Food Quality and Safety Standards, as Required by EU Law and the private industry with special reference to the MEDA countries’ exports of fresh and processed fruits & vegetables, herbs and spices. A practitioners’ reference book. 2007, at p. 16, available at <http://www2.gtz.de/dokumente/bib/07-0800.pdf>; taken from Van der Meulen et al. 2012

³ These are the basic rules for food products in the US and EU. As is discussed in this paper, the situation, particularly in the US, is far more complicated than to be summarized by these generalizations. However, it provides for a fundamental understanding of the system of premarket approvals.

⁴ The list is present in Annexes II and III of Regulation 1333/2008

⁵ All applications and notifications for novel food approval are documented in http://ec.europa.eu/food/food/biotechnology/novelfood/app_list_en.pdf and http://ec.europa.eu/food/food/biotechnology/novelfood/notif_list_en.pdf#page=71, respectively. Both procedures are discussed further in Section 3.7.

⁶ The list is present in Annex I of Regulation 1334/2008

particular nutritional uses¹⁰, among others. In the US positive lists exist for food additives¹¹, color additives and dietary supplements.

There are two types of authorizations: generic and exclusive. Once products are approved under a generic authorization, anyone can place them on the market. The approval is for the food product. When products are approved under an exclusive authorization, only the authorization holder may market the product. If other businesses wish to market the same product, they are required to also undergo a premarket approval process. The approval is for the applicant only to market the food product, and can also serve as a sort of reward for businesses for investing in the procedure, at least until others gain approval as well (Van der Meulen, 2009).

2.2 Briefest of introductions to the American government setup

In order to better understand the American legal system and legislation, a brief introduction is given. The United States was founded in 1796 and is made up of 50 individual states. This paper focuses only on regulation at the federal level. The American government consists of three branches: the legislative branch, the judicial branch and the executive branch (Curtis and Dunlap 2005).

The legislative branch is made up of two houses; the Senate and the House of Representatives, which together form the US Congress. The Senate consists of 100 members (two representatives from each state) and the House of Representatives of 435 members (proportionate to each state's population), all elected by the people. The legislative branch is primarily responsible for passing laws.

The judicial branch includes all federal courts, with the Supreme Court at the highest level. It is responsible for interpreting laws, making decisions in court cases and setting precedents for future cases.

The executive branch consists of the president, the cabinet, the cabinet departments and the independent agencies. The most important departments for food regulation are the Department of Agriculture (USDA) and the Department of Health and Human Services – which includes the Food and Drug Administration (FDA).

There are actually five agencies which are primarily responsible for food regulation (Fortin 2009). The FDA regulates all food (except for meat and poultry), wild game (exotic meat), shelled eggs, bottled water, dietary supplements, drugs (over-the-counter and prescription), cosmetics and medical devices. The USDA is responsible for meat and poultry regulation, liquid eggs, egg processing, grading raw fruit and vegetable grading. The Environmental

⁷ The register of approved GMOs in the EU is provided at

http://ec.europa.eu/food/dyna/gm_register/index_en.cfm

⁸ Results of all food supplement requests for approval can be found at

<http://ec.europa.eu/food/food/labellingnutrition/supplements/food_supplements.pdf>

⁹ In the annexes of Directive 91/321 < <http://eur->

[lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1991:175:0035:0049:EN:PDF](http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1991:175:0035:0049:EN:PDF)>

¹⁰ Annex of < <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:052:0019:0025:EN:PDF>> and

¹¹ As stated in footnote 3, the situation is again far too complicated to address here. The definition of a food additive is broader than that in the EU (i.e. it includes substances such as flavorings and some GMOs). A pseudo-positive list system exists for GRAS substances. See Section 3.4.

Protection Agency (EPA) regulates tap water and pesticide residues. The Federal Trade Commission (FTC) is responsible for advertising and the Alcohol and Tobacco Tax and Trade Bureau (TTB) regulates alcohol.

Within the FDA, the Office of Food Additive Safety (OFAS) in the Center for Food Safety and Applied Nutrition (CFSAN) are responsible for regulation of food additives, GRAS substances, color additives and prior-sanctioned substances. In the case of premarket approvals for food ingredients, including food additives, the FDA is primarily responsible for receiving applications and making decisions. However, it is important to note that when a substance is intended for use in meat or poultry, the Food Safety and Inspection Service (FSIS) of the USDA also must review the application¹².

There are four types of federal laws in the US. The first is the Constitution, which is the framework of the legal system and contains the supreme law. It describes the powers of the government, lays out the rights of citizens, and lays out principles under which the government must operate¹³. The next is statutes, which are acts created by Congress and the state and local governments. Since statutes are typically quite broad, specialized administrative agencies such as the FDA and USDA create the third type of federal laws—regulations—which interpret the acts and enact operating standards. Lastly, judicial decisions in court cases establish precedents which serve as law.

2.3 Food additive legislation in the US

Regulation of food additives under the agencies and forms of law discussed above has evolved over the past few decades. Federal oversight of food additives began in the late 1800s, but some of the first official pieces of legislation governing food safety in the US were the Pure Food and Drug Act and the Meat Inspection Act, which were signed into law in 1906. While a start, criticisms of the law included not enough authority for the FDA, inadequate safety and product quality standards and regulation regarding therapeutic claims. It was not until 1938¹⁴ that the new Food Drug and Cosmetic Act (FDCA) was enacted, which required premarket approval for drugs. In 1958 the Food Additive Amendment to the FDCA was created, followed by the Color Additives Amendment in 1960. Both required premarket approvals by businesses for these products. The FDA Modernization Act of 1997 replaced the premarket approval requirement for food contact substances (included under the food additive category) with a notification procedure.

Legislation in the US is primarily contained in the US Code and in the Code of Federal Regulations (CFR). The US Code consists of the general and permanent laws of the United States and is the official compilation of federal laws¹⁵. It is divided into 50 subjects, and Title 21, Section 201 contains the FDCA, which includes laws on food additives and other

¹² See section 3.3 on approvals for more details regarding the approval procedure

¹³ Popular sovereignty, separation of powers, checks and balances, federalism, supremacy of national laws, civilian control of government

¹⁴ In 1937 an antibiotic called sulfanilamide was being used to treat bacterial diseases such as strep throat. The drug was mixed with the sweet diethylene glycol to improve the flavor; however, the resulting “Elixir of sulfanilamide” was poisonous and caused over 100 deaths, many of whom were children who took the drug to treat strep throat. Despite the existence of the Pure Food and Drug Act of 1906, there were no regulations at the time that required premarket safety approval of drugs. Congress enacted the FDCA in 1938, largely in response to the crisis.

¹⁵ For a full and more detailed description, see Chapter 1 in Curtis and Dunlap (2005)

substances. The CFR contains general and permanent laws issued by executive branch agencies and departments of the federal government. It is also divided into 50 subjects, and Title 21 includes rules on food additives and other substances.

2.4 Briefest of introductions to the European Union government setup

A short introduction to the European Union and its functions is given to provide a basic understanding of the system. After World War II, in 1958, the European Economic Community (EEC) was created between six countries: Belgium, Germany, France, Italy, Luxembourg and the Netherlands. The goal was to increase economic cooperation, and by doing so, limit the chance that new conflict could arise between the nations. The EEC grew and its functions expanded, which was shown in the name transition to the European Union (EU). In addition to promoting economic cooperation, the EU is also a political union, and covers a range of issues from food to the environment to development aid. Currently 28 nations are a part of the European Union. Only regulation at the EU level is addressed in this paper.

The foundation of the EU is laid down in the Treaty on European Union (TEU) and the Treaty on the Functioning of the European Union (TFEU). These treaties established five major institutions which are responsible for the operations of the EU: the European Parliament, the Council of the European Union, the European Commission, the Court of Justice and the Court of Auditors (Europa 2013). The first three are involved in law-making.

The Parliament represents the people—EU citizens directly elect the members every 5 years, and there are a total of 754. It is responsible for passing laws, with the Council; supervising other EU institutions; and debating and supervising the budget, with the Council.

The Council represents the governments of the Member States. It passes laws, with the Parliament; debates and supervises the budget; and is particularly involved with foreign matters such as agreements and defense policies.

The Commission (corresponding to the US cabinet) represents the interests of the EU as a whole and consists of one representative from each Member State. It initiates new proposals for laws and ensures that they are implemented, and is also responsible for day-to-day functions of the EU. Departments under the Commission are called Directorates General (DGs, corresponding to the US cabinet departments), which cover specific areas. The most relevant to food law is DG Sanco – for health and consumer policy.

The Court of Justice supports EU law in practice and settles legal disputes in a way so that EU law is applied in a uniform way in all the Member States.

The Court of Auditors' purpose is to check all people and organizations that manage EU funds and prepare annual financial reports for the Parliament and Council.

EU law is supreme law, meaning that when there are national laws which are contrary to EU law, the EU law must be followed and the national law is deemed non-existent. The EU has three forms of legally binding legislation, which are the regulation, directive and decision. The first two consist of rules which are binding and apply broadly to the people and situations described in the legislation (Van der Meulen and van der Velde 2008). A regulation is defined as legislation that “shall have general application. It shall be binding in its entirety

and directly applicable in all Member States.”¹⁶ A directive is defined as legislation that “shall be binding, as to the result to be achieved, upon each member state to which it is addressed, but shall leave to the national authorities the choice of form and methods.”¹⁷ The difference between the two is that the regulation specifies the rules so that the law is exactly the same in every Member State, and the directive states the objectives of the legislation and the deadline by when they must be reached, but allows the Member States to decide how they will fulfil the points set out in the directive. Lastly, a decision is EU law relating to a specific case. It is not a rule in itself, but an application of a rule in a specific situation with a particular person.

It is important to also discuss the European Food Safety Authority (EFSA). It is an independent agency responsible for “scientific advice and scientific and technical support for the Community’s legislation and policies in all fields which have a direct or indirect impact on food and feed safety.”¹⁸ It operates independently to ensure that there is a separation of risk management decisions (taken by the Commission, Parliament and Council) from risk assessment (EFSA). Within EFSA, there exist Scientific Panels which are responsible for providing scientific opinions of the agency on a specific topic. The Panel on Food Additives and Nutrient Sources Added to Food (ANS) and the Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) are the most relevant expert groups in this situation.

Various government agencies are involved in the approval of food additives in the EU. The specific legislation used to regulate the approval processes are discussed below.

2.5 Food additive legislation in the EU

Regulation of food additives in the EU dates back as far as 1962 with the Council Directive 62/2645/EEC on food colorings¹⁹ (although the EU was called the EEC at the time). Since then, various other pieces of legislation regarding food ingredients have been passed and amended many times. This thesis focuses on the current legislation applicable to food additives. In 2008, the Food Improvement Agent Package (FIAP) was passed, which consists of four new regulations to govern substances used in foods. The legislation includes Regulation 1331/2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings²⁰, Regulation 1332/2008 on food enzymes²¹, Regulation 1333/2008 on food additives²² and Regulation 1334/2008 on flavourings²³.

¹⁶ Article 249 Treaty Establishing the European Community

¹⁷ Article 249 Treaty Establishing the European Community

¹⁸ Article 22(2) GFL

¹⁹ Council Directive 62/2645/EEC of 23 October 1962 on the approximation of the rules of the Member States concerning the colouring matters authorized for use in foodstuffs intended for human consumption. OJ 2645/62, 11.11.62.

²⁰ Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings. OJ L 354/1, 31.12.2008. < <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:354:0001:0006:EN:PDF> >

²¹ Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on food enzymes and amending Council Directive 83/417/EEC, Council Regulation (EC) No 1493/1999, Directive 2000/13/EC, Council Directive 2001/112/EC and Regulation (EC) No 258/97. OJ L 354/7, 31.12.2008. < <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:354:0007:0015:en:PDF> >

²² Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354/16, 31.12.2008. < <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:354:0016:0033:en:PDF>>

Regulation 1331/2008 provides a common authorization procedure for food additives, food enzymes and food flavorings to test for the safety of the substances before they can be placed on the market for human consumption. The establishment of a harmonized authorization procedure which is effective, time-limited and transparent aims to facilitate their free movement within the European Community market, and thus has a beneficial effect on the health, well-being, social interests and economic interests of European citizens. The common procedure for assessment and authorization is discussed in Section 4.5.

²³ Regulation (EC) No 1334/2008 of the European Parliament and of the Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Council Regulation (EEC) No 1601/91, Regulations (EC) No 2232/96 and (EC) No 110/2008 and Directive 2000/13/EC. OJ L 354/34, 31.12.2008. < <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:354:0034:0050:en:PDF> >

3 Approach in the United States

3.1 Definition of a food

Although the concept of a food additive has not yet been discussed, it is clear by the name that they are some form of substances used in foods. It is therefore important to look at how a food is defined, in order to better understand the ways in which food additives may be used.

In the US, Congress defined ‘food’ as²⁴:

- 1) Articles used for food or drink for man or other animals,
- 2) Chewing gum, and
- 3) Articles used for components of any such article

The FDA clarified this by defining ‘food’²⁵ as human food, pet food, animal feed and substances migrating to food from food contact articles.

3.2 Definition of a food additive

Based on the above definition, food additives are considered to be foods. A “food additive” in American legislation is specifically defined as:

any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use, if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case as a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; except that such term does not include—

- (1) a pesticide chemical residue in or on a raw agricultural commodity or processed food; or*
- (2) a pesticide chemical; or*
- (3) a color additive; or*
- (4) any substance used in accordance with a sanction or approval granted prior to September 6, 1958, pursuant to this chapter, the Poultry Products Inspection Act (21 U.S.C. § 451 et seq.) or the Meat Inspection Act of March 4, 1907, as amended and extended (21 U.S.C. § 601 et seq.)*
- (5) a new animal drug; or*
- (6) an ingredient described in paragraph (ff) in, or intended for use in, a dietary supplement²⁶*

²⁴ FDCA 321(f)

²⁵ 21 CFR 170.3 (m)

²⁶ FDCA 201 (s)

To clarify the definition of an additive, “affecting the characteristics of food” does not include physical effects, such as “protecting contents of packages, preserving shape, and preventing moisture loss.” Packaging substances are only considered food additives if they migrate from the package to the food, and thus become a component of food²⁷.

This definition of a food additive places a broad range of substances under its scope. It is essentially any substance which can be expected to become a component of or affect a food. However, the definition is both broader and narrower than it may initially seem; a discussion of both aspects are presented.

3.2.1 Broader than it may seem

The definition of a food additive is broader than it may seem as it includes common ingredients that we do not normally think of²⁸ as food additives, since it is any substance that may become a component of or affect the characteristics of any food. This could include ingredients like the flour and cheese added to a pasta dish (Neltner et al., 2011).

The definition is also broader than it may seem because it includes substances that may become a component of food, such as indirect food additives (those used in food packaging and on processing equipment) (Monsanto Co. vs Kennedy 1979).

Lastly, as mentioned in the above definition of a food additive, sources of irradiation are considered food additives because they affect the characteristics of food²⁹. The first time the FDA approved irradiation³⁰ for food use was in 1963, for the treatment of wheat and wheat flour. It is currently authorized for use in red meat, poultry, fresh fruits and vegetables, dry spices and more. It is important to note that it is the “source of radiation” used to treat food that is considered a food additive. Radiation itself is not an additive, but the source of radiation/process of being irradiated is (Fortin 2009). Sources of radiation include “machines such as x-ray tubes or radioactive elements that produce radiation used for inspecting food, controlling food processing, irradiating food, heating food (including microwaves), and treating food packaging” (Neltner et al. 2011).

Sources of radiation are explicitly included in the definition of a food additive. If these are considered food additives, then why would sources of heat or pressure, to name a few, also not fall under the definition? It is stated that a food additive is any substance which affects the characteristics of a food. It is quite obvious how sources of heat, and the heating process, can affect a food. However, can a source of heat be a “substance”? A look to 21 CFR

²⁷ 21 CFR 170.3 (e)(1)

²⁸ Definition of a food additive from Dictionary.com: “Any of various natural or synthetic substances, such as salt, monosodium glutamate, or citric acid, used in the commercial processing of food as preservatives, antioxidants, emulsifiers, etc, in order to preserve or add flavour, colour or texture to processed food.”
<http://dictionary.reference.com/browse/food+additive>

²⁹ In the EU, radiation is not considered an additive. It is regulated under separate legislation: Directive 1999/2/EC and Directive 1999/3/EC

³⁰ Irradiation is the process of breaking chemical bonds through high-frequency energy, the source of which is either electricity or radioactive cobalt-60. It is effective because it damages the DNA of bacteria such as *Salmonella* and *E. coli*, plus that of insects, parasites and other spoilage microorganisms. Damaged DNA prevents reproduction of these (micro)organisms, and thus the levels at which they are present in the food. These lower levels of pathogenic micro(organisms) result in a food product which is less likely to cause food poisoning.

170.3(g) provides a response: “The word substance in the definition of the term “food additive” includes a food or food component consisting of one or more ingredients.” This definition is not comprehensive, however, because it only states “includes.” A substance can be other things not stated in the definition. Additionally, if sources of radiation are considered food additives, then there is not a clear reason why sources of heat may not be as well. However, it is possible that sources of heat are actually considered to be generally recognized as safe (GRAS) instead (see section 3.8 for more information). Although sources of heat do not appear on the GRAS list, the list is not complete since it does not include obviously safe substances (21 CFR 570.30).

3.2.2 Narrower than it may seem

Subsequent amendments excluded several categories of substances from the definition, including color additives, pesticide chemicals or their residues, new animal drugs and ingredients in dietary supplements. Each of these categories is covered by separate legislation.

While the definition still includes most substances added to food, there are further two notable categories of substances that are not subject to regulation as food additives. The first is those substances that are generally recognized as safe (GRAS), such as sodium chloride, by qualified experts (see section 3.8). The other is prior sanctioned substances, a category of substances approved before the Food Additive Amendment on 6 September 1958 (e.g. sodium nitrate and potassium nitrate used to preserve lunch meats) (see section 3.7).

The definition states that an additive is a substance that is not generally recognized as safe (GRAS), suggesting that GRAS substances are considered outside the category of additives. After doing further research, it became apparent that this definition is not always applied according to the text in the practice of the FDA. In some cases it is stated that the GRAS exemption is from the definition of a food additive, and in others it is stated that the exemption is from regulation as a food additive (i.e. that a GRAS substance is classified as a food additive but has a different regulatory process). For example, a document on food additives from the FDA website states that “A second category of substances excluded from the food additive regulation process are generally recognized as safe or GRAS substances.” (FDA and International Food Information Council, 1992). This implies that GRAS substances still fall under the title of food additives, but they are regulated differently. However, after reading the official definition, it can be concluded that GRAS substances are, in fact, a separate category than food additives. This distinction is important to clarify because, as will be shown in this document, the regulatory approval processes of food additives and GRAS substances are quite different.

3.2.3 Other food additive information

While there are many subcategories of food additives in the US, they can be divided into two general groups: direct additives and indirect additives. Direct additives are those which are added to food to serve a specific purpose. For example, aspartame is intentionally added to various foods and beverages to serve as a low-calorie replacement for sugar. Indirect additives are those which are not added directly to food but which become a part of the food during processing or due to migration from packaging materials³¹, for example.

³¹ As Fortin (2009) explains clearly: “One issue from the 1960s that FDA wrestled with was the widespread contamination of food packaging paper with PCBs. FDA took the position that food packaging materials were food additives and thus could be regulated as such. Others disputed FDA position and argued that food

Neltner et al. (2011) provide a clear understanding of the difference between preservatives and antimicrobials (regulated by FDA—as food additives or GRAS substances) and pesticide chemicals and residues (regulated by EPA). The line between the two is unclear and complicated.

For direct use on food, if applied to unprocessed food, the substance is regulated by EPA. If used on processed food, the substance is regulated by FDA. A food is still considered unprocessed if it is only being washed, colored, waxed, hydro-cooled, refrigerated, shelled (if a nut), handled to removed leaves, stems, and husks, fumigated, or packed. A food is considered processed when it is canned, frozen, cooked, pasteurized, irradiated, milled, peeled, ground, chopped, sliced, or cut. For use on food contact surfaces, EPA regulates a substance controlling pests (including microbes) only if used on the surface of equipment such as a conveyor, grinder, or countertop, and the use provides an ongoing sanitizing effect on the surface. FDA regulates it if used on food packaging, does not have an ongoing antimicrobial effect, or penetrates beyond the surface (FDA 1999).

3.2.4 Food contact substances³²

Substances that come into contact with food through manufacturing, packing, packaging, transporting or storage may be classified as “food contact substances.” These substances are not subject to the food additive premarket approval process if they do not have a technical effect in the food, are not carcinogens, do not present any health or safety concerns and do not have an adverse effect on the environment. Therefore the difference between indirect food additives (and food additives in general) and food contact substances is that food contact substances can explicitly not have a technical effect in the food. The food contact substance category actually did not exist until the FDA Modernization Act of 1997 was enacted (International Food Information Council and FDA 2010). Before this Act, food contact substances were included in the scope of indirect food additives and had to go through the formal approval process for food additives. FDA created a special notification procedure for food contact substances (see section 3.4) to maximize resources and save the time it takes to issue a new regulation for a substance. Food contact substances can be exempt from the premarket approval process for food additives since they have no technical effect in the food to which they migrate and they are present at low levels. An advantage for the businesses is they get a quicker response: within 120 days. From 2000-2010, FDA received over 1000 food contact notifications (and issued no-objection letters for 778 of them) (Neltner et al.

packaging materials—before the materials were actually used to package food—were outside the jurisdiction of the Food Additive Amendments and the FD&C Act. In *Natick Paperboard Corp v. Casper Weinberger and FDA*, the FDA seized a quantity of paper food packaging materials that contained polychlorinated biphenyls (PCBs). The toxicity of PCBs was not challenged. However, the paper manufacturers challenged the seizure because the FDA seized the paper as being “adulterated food.” The Court held that “food additive” includes any substances that may reasonably be expected to indirectly become a component of food. “Unsafe food additives”, whether intentional or incidental, are “adulterated food” under FD&C Act section 342(a)(2)(C), and therefore may be seized.”

³² In the EU food contact substances are similarly defined (any substance that comes into contact with food through packaging or processing), yet the interpretation and regulation are different. First of all, food contact substances in the EU are not regulated as food additives; they are instead regulated separately, under Regulation 1935/2004 on food contact substances. They must go through a formal premarket approval process before they can be placed on the market (versus the notification procedure in the US).

2011). The food contact substance category has essentially replaced that of indirect food additives when considering the new premarket approval applications that are received.

The exact wording in the CFR (170.3(2)) is that food contact substances are exempt from regulation as food additives. They are still technically under the category of food additives, however, as they are included in this section of the legislation. However, for the purposes of not only this paper but also for an understanding of the function of the substances, food contact substances have a different definition and a different regulation procedure than that of food additives, and are therefore essentially a separate category of substances.

3.3 Requirements food additives must meet

In order to determine which action, approval or denial, to take on the petition, the FDA must determine that it meets two requirements: safe and not deceptive to the consumer³³. “Safe” is defined as “a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.”³⁴ Although “harm” is not separately defined, “Congress evidently understood the term to mean a capacity to injure or otherwise cause disease.” The biological properties, methods used, probable consumption, cumulative effect and safety factors from animal experimentation data must also be taken into account³⁵. For an overview of the levels of safety required, refer to section 5.2.3. The safety requirement includes the Delaney Clause, which is that if an additive is found to induce cancer in man or animal, it is considered unsafe³⁶. Additionally, an environmental assessment must also be performed to confirm that the substance does not have a negative effect on the environment.

The definition of a food contact substance, as described in section 3.2.4, states that it can escape regulation as a food additive if it does not have a technical effect in the food in which it is used, is not a carcinogen, does not present a health or safety concern and does not have an adverse effect on the environment. The only difference between a food contact substance and a food additive based on this definition is that a food contact substance does not have a technical effect: this implies that an additive has a technical effect.

3.3.1 Delaney clause

The so-called Delaney clause, named after Congressman James Delaney of New York, prohibits adding a substance to food if it has been shown to cause cancer in humans or animals. It appears three times in the FDCA, in the Food Additive Amendment (1958), Color Additive Amendment (1960) and Animal Drug Amendment (1968). It does not apply to GRAS substances or prior sanctioned ingredients.

No additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for

³³ The requirements for additives in the EU are safe, not misleading and meet a technological need

³⁴ 21 CFR 170.3

³⁵ 170.20(a); 170.100(c)(5)

³⁶ 21 CFR (c)(3)

the evaluation of the safety of food additives, to induce cancer³⁷ in man or animal³⁸

The general safety requirement states that FDA should consider a variety of factors to determine safety, including probable exposure, cumulative effects and detection difficulties³⁹. However, for carcinogens the issue is simply that if a substance is found to induce cancer, it cannot be placed on the market.

However, the Delaney clause has become controversial as some additives have been approved despite studies that showed they induced cancer, including saccharin, acesulfame K, selenium, methylene chloride, butylated hydroxyanisole (BHA) Orange No. 17 and Red No. 19. When the clause first appeared in 1958, tests for toxic compounds were not nearly as sensitive as they are today. There were also only 4 known human carcinogens. The clause became controversial as tests became more sensitive and thus chemicals could be more easily detected in foods (Fortin 2009). Additionally, as of 2012, there are 200 human carcinogens (American Cancer Society, 2013) and many more known to induce cancer in animals. This list includes substances such as vitamin C and calcium, which are viewed as not only harmless, but also essential, components of a normal diet.

In a notable court case, *Public Citizen v. Young* (1987) challenged the decision of the FDA to list two color additives, Orange No. 17 and Red No. 19, based on quantitative risk assessments indicating that the cancer risks presented by these dyes were trivial. The FDA approved Orange No. 17 and Red No. 19 for use in cosmetics in 1986 even though they were found to induce cancer. The FDA stated that because the risk was so low, the colors could be approved under the *de minimis non curat lex* (“*de minimis*”) doctrine, which means “the law does not concern itself with trifles.” In other words, if the risk is so low—lower than one in a million in this case to meet the exception requirement—the risks are considered negligible. For example, the Cosmetic, Toiletry and Fragrance Association (CTFA) of the US notes that there is a one in a million lifetime risk of liver cancer if a person consumes one peanut containing the FDA-permitted level of aflatoxins only once every 250 days. Another example of an activity that poses a one in a million lifetime risk is spending 1,000 minutes (less than 17 hours) in the high-elevated city Denver, Colorado⁴⁰⁴¹. These can hardly be considered dangerous actions. The riskier dye poses 1/9 as much risk as these hypothetical situations, and the less risky one poses 1/19000 as much. The purpose of the *de minimis* doctrine is to not take the written words so literally that they lead to ridiculous results⁴². It is possible to get

³⁷ The meaning of “induce cancer” has also been subject to interpretation. In a notice published by the FDA, they stated that even if a substance causes cancer in animals, the FDA may find that it does not “include cancer in man or animal.” Looking to projections/extrapolations from test animals in risk assessment.

³⁸ The Delaney clause is not applicable in cases where color additives as a whole do not induce cancer, even if their components do. For example, D&C Green No. 6, a carcinogen, is present in D&C Green No. 5. However, D&C Green No. 5 is approved because it does not cause cancer as a whole (*Scott vs. FDA*). This is the “matrix effect” concept.

³⁹ FDCA 376(b)(5)(A)

⁴⁰ See J.A. 529, citing FDA Bureau of Foods, *Assessment of Estimated Risk Resulting From Aflatoxins in Consumer Peanut Products and Other Food Commodities* (1978)

⁴¹ Some other examples are eating 40 spoonfuls of peanut butter (liver cancer from aflatoxin), drinking 0.5 liters of wine (cirrhosis of the liver), spending two days in New York (air pollution), eating 100 charcoal-broiled steaks (cancer from benzopyrene), traveling 16 km by bicycle (accident) (<http://stanford-online.stanford.edu/sdrmda61w/session10b/slides/sld031.htm>)

⁴² See *Alabama Power*, 636 F.2d at 360 n. 89 *United States v. American Trucking Associations*

cancer with just about too much of anything. A completely risk-free world is unachievable and it is instead important to balance the costs and benefits of the additive use. Additionally, interpreting the Delaney clause too literally can even have dangerous consequences. The clause only addresses substances that induce cancer. If a certain additive is not allowed because it poses a miniscule risk of causing cancer, then a manufacturer may substitute it with a more toxic, but non-cancer-causing, substance. As the primary goal is safety, this literal interpretation of the clause would serve no benefit to the consumer (Fortin 2009).

3.4 Authorization process

The US applies a pseudo positive list system for food additives. A substance that falls under the food additive definition is presumed to be unsafe unless its safety can be demonstrated. All additives marketed in the US must undergo an evaluation procedure by the FDA⁴³ and a regulation must be issued before they are allowed on the market⁴⁴. However, the system is described as “pseudo” because substances regarded as GRAS are not subject to premarket approval and may be placed on the market with or without notifying the FDA (see section 3.8 for more details). The food additive approval process is described in both the CFR⁴⁵ and the FDCA⁴⁶. The CFR contains general information on this process, and the FDCA goes into detail on each of the steps.

Any person may petition for approval of a food additive and its conditions of use. The application must contain the following information⁴⁷.

- (1) The name and all pertinent information concerning such food additive, including, where available, its chemical identity and composition;
- (2) A statement of the conditions of the proposed use of such additive, including all directions, recommendations, and suggestions proposed for the use of such additive, and including specimens of its proposed labeling;
- (3) All relevant data bearing on the physical or other technical effect such additive is intended to produce, and the quantity of such additive required to produce such effect;
- (4) A description of practicable methods for determining the quantity of such additive in or on food, and any substance formed in or on food, because of its use; and
- (5) Full reports of investigations made with respect to the safety for use of such additive, including full information as to the methods and controls used in conducting such investigations.
- (6) Also, upon request of the Secretary, the petitioner or manufacturer of the additive shall furnish a full description of the methods used in, and the facilities and controls used for, the production of such additive.

⁴³ Although FDA is primarily responsible for food additive safety, if the proposed additive is intended to be used in meat or poultry, the FSIS in the USDA must also evaluate the substance. An example of a case when FSIS applied stricter standards was in the review of sorbic acid in meat salads. Although sorbic acid was already approved as a food additive, it was not allowed to be used in meat because it could mask spoilage caused by pathogenic spoilage bacteria (Fortin 2009).

⁴⁴ FDCA 409(a) / 21 USC 248

⁴⁵ Sections 170 to 171

⁴⁶ Section 409

⁴⁷ 21 CFR 171.1(b)(2)

- (7) Upon request of the Secretary, the petitioner shall furnish samples of the food additive involved, or articles used as components thereof, and of the food in or on which the additive is proposed to be used.

Upon receipt of the application, the following steps are supposed to be taken within the following deadlines:

Table 1. Overview of food additive approval process steps in the US (21 CFR 171.1)

Deadline	Total time elapsed	Action
15 days (after receipt of application)	15 days	FDA notifies the petitioner of acceptance or nonacceptance of the petition.
30 days (after notification)	45 days	FDA publishes a notice of the filing of the petition in the Federal Register. In the case that the proposed uses of the additive include meat or poultry, the FDA must also forward a copy of the petition to the Food Safety and Inspection Service (FSIS) of the USDA in order to determine if it meets an additional set of approval requirements.
90 days (after filing)	135 days	Action on the petition: 1) The FDA publishes a regulation in the Federal Register, including any conditions under which the additive may be safely used (in which foods, maximum quantity, any other requirements), OR 2) The FDA denies the petition (and notifies the petitioner either way)
Additional 90 days	225 days	Extension of the deadline to take action on the petition to 180 days total if additional time is needed for evaluation

Limits on the conditions of use of the additive may be set. If the additive is determined to be safe, but a tolerance limit is necessary, it must be set by the FDA no higher than necessary to achieve their intended physical or technical effect. Some other additives may be used under the principle of quantum satis, which means that only the amount reasonably required to achieve its desired effect, and no more than that (21 CFR 172.5(a)) may be used.

All food additives intended to be used in meat and/or poultry must be approved by both the FDA and the USDA (Fortin 2009). It is a two-step process. First, additives are evaluated by the FDA to ensure safety. If they pass this first step, they must then also undergo an authorization by the Food Safety and Inspection Service (FSIS) of the USDA, who evaluates the safety as well. The purpose of this second evaluation is so that additives can be evaluated, taking into considering unique characteristics of meat, poultry and eggs. The FSIS may even apply stricter standards: for example, an application was submitted for the use of sorbic acid in meat salads. Although the FDA had already approved sorbic acid as a food additive, the FSIS denied approval because the use of sorbic acid in meat salads could hide spoilage caused by pathogenic microorganisms (Fortin 2009).

3.4.1 Environmental assessment

In accordance with the National Environmental Policy Act (NEPA) of 1969, an environmental assessment (EA) must be prepared along with a food additive petition, color additive petition, request that a food contact substance is not regulated as a food additive⁴⁸ and affirmation of a food substance as GRAS or a prior-sanctioned ingredient⁴⁹. There are various exceptions to the EA requirement for the above substances as described in 21 CFR 25.32, such as to issue an interim food additive regulation (see section 3.6) and affirmation of a substance as GRAS if it is already marketed in the US. The EA must include information such as fate, exposure and effects data to demonstrate that the additive does not have a significant impact on the environment⁵⁰.

3.5 Food contact substance notification

In order to receive exemption from regulation as a food additive, a premarket notification⁵¹ for a food contact substance, called a food contact notification (FCN) must be submitted to the FDA. The notification must include the reasoning of the manufacturer or supplier as to why the food contact substance is safe, including a discussion of all information submitted and any data that are inconsistent with the determination of safety. Upon receipt of a complete notification, the FDA has 120 days to review the contents to consider the probable consumption and the potential toxicity, among other things. Upon making a decision, the FDA sends an acceptance or objection letter to the applicant. If there is no objection within this time period, the FCN becomes effective. Unlike GRAS substances, food contact substances may not be on the market until acceptance of the notification.

It is important to note that food contact substance authorization is specific and not general. An FCN is only effective for a specific manufacturer or supplier, and if another manufacturer or supplier wishes to market the same food contact substance for the same use, then they must also submit an FCN. Once a food contact substance is approved, all non-confidential or trade secret information can be disclosed, thus it is possible for other businesses to gain access to the information inside the application (FDA 2005).

3.6 Interim food additives

A subcategory of food additives are those whose status is in limbo. When information about an already approved food additive brings its safety or functionality into question, the substance may be placed into the transitional category of “interim food additives”. This category was created and first used in 1972 when FDA began to review the safety of some particular food additives. While in the interim status, additional studies and review to re-evaluate the safety of the additive must be undertaken. During this period the food additive may continue to be used under its conditions of use, which is why despite information bringing its safety into question, there must still be a reasonable certainty that the substance is not harmful and can continue to be used while further research is ongoing⁵².

⁴⁸ 21 CFR 25.20(i)

⁴⁹ 21 CFR 25.20(k)

⁵⁰ For details, see

<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditives/GRASPackaging/ucm081169.htm>

⁵¹ 21 CFR 170.100–170.106

⁵² 21 CFR 180.1(a)

Interim food additives are not intended to remain in this category. The regulations are either supposed to be reconfirmed as safe for use, or revoked, thus banning the additive from the market. The regulation may state any limitations on the use of the substance. Within 60 days after the regulation, an interested person or the FDA must agree to conduct the relevant studies to resolve the questions raised about the additive. If no person does so, the interim food additive regulation will be revoked and the additive will be removed from the market. Progress reports on the study must be filed every six months, and as soon as there is reasonable certainty that the substance is hazardous, the food additive regulation will be revoked.⁵³ Upon completion of the investigation and review of all information, the Commissioner will either issue a food additive regulation or eliminate the substance from the market. Interim food additives may thus remain on the market for an unlimited period of time if there is no information showing that the substance is either hazardous or safe.

Since the category has existed, nitrites, acrylonitrile copolymers, mannitol, brominated vegetable oil⁵⁴ and saccharin, among others, have been regulated as interim food additives⁵⁵. In all cases, additional toxicological studies were requested. The mannitol regulation was revised to authorize an additional manufacturing method. With the exception of nitrites in curing premixes, no interim food additives have thus far been permanently restricted or banned (IOM 1999).

3.7 Prior-sanctioned substances

The definition of a food additive excludes “any substance used in accordance with a sanction or approval granted prior to the enactment of this paragraph pursuant to this Act, the Poultry Products Inspection Act...or the Meat Inspection Act.” These are called prior-sanctioned substances.

They are ingredients used in food or food packaging which were sanctioned or approved by the FDA or USDA prior to the Food Additives Amendment on 6 September 1958; they are essentially food additives that were approved before the Food Additives Amendment was enacted. When Congress created a formal legal definition of a food additive and formal procedures to regulate additives, substances that were approved for the function before were placed into a separate classification. Prior-sanctioned substances are only exempt from regulation as a food additive, but they still must meet certain provisions of the FDCA. If they are adulterated or misleading, FDA can revoke their prior-sanctioned status. In addition, a prior sanctioned substance is only exempted from regulation as a food additive for a specific food use.

The only apparent difference between prior-sanctioned substances and food additives in today’s food system is that approval of prior sanctioned substances is technically irrevocable,

⁵³ 21 CFR 180.1(c)

⁵⁴ A recent news story is related to consumer concerns of brominated vegetable oil (BVO). A US citizen started an online petition against the use of BVO, an emulsifier, in the Gatorade beverage (owned by PepsiCo). BVO was placed on the interim food additive status list in the 1970s. However, the safety testing was never completed, so the ingredient has remained legal, despite being banned in the EU and other countries. Concerns over BVO are related to reproductive and behavioral issues, among others.

http://articles.chicagotribune.com/2013-01-26/news/ct-nw-gatorade-bvo-20130126_1_bvo-gatorade-sarah-kavanagh

⁵⁵ Two other interim food additive regulations were proposed but not finalized. *See* 45 Fed. Reg. 69,817 (1980) (caffeine); 42 Fed. Reg. 27,603 (1977) (BHT).

whereas food additives can be re-evaluated and have the conditions of use adjusted at any time.

There are currently around 120 ingredients approved as prior-sanctioned substances, including nitrates and nitrites, antimicrobials, antioxidants and many more (21 CFR 181).

3.8 Generally recognized as safe (GRAS) substances

A food additive is a substance which “is not generally recognized... to be safe under the conditions of its intended use.” Therefore, even if such a substance becomes a component of food, it is not considered a food additive, and thus not subject to regulation as a food additive, if it is generally recognized as safe (GRAS). To write it clearly, substances that are GRAS under their conditions of intended use are not food additives and do not require premarket approval by the FDA.

There are two ways in which substances can be classified as GRAS, based on: 1) scientific procedures or 2) common use in food before 1 January 1958. “Scientific procedures” includes “human, animal, analytical, and other scientific studies, whether published or unpublished, appropriate to establish the safety of a substance”⁵⁶. “Common use in food” is defined as “a substantial history of consumption of a substance for food use by a significant number of consumers.” General recognition of safety “requires common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food”⁵⁷.

General recognition of safety through scientific procedures requires the same quantity and quality of evidence as is necessary for approval of food additives⁵⁸. However, the definition is still quite vague and subject to interpretation. What determines common use? By a significant number of consumers? Absence of a health hazard is not enough to be considered as generally recognized as safe.

General recognition of safety through prior common use does not require such high levels of quantity or quality of scientific evidence, and instead must be based only on prior use and commonly available information⁵⁹. Although common use in food originally applied only to the United States, this decision was later modified (in the 1980s) to include use outside of the United States⁶⁰. Common use of a substance outside the US requires similar information to meet the American concept of safety: sources that confirm the history and circumstances of use, must have been widely available, etc⁶¹.

⁵⁶ 21 CFR 170.3 (f)(h)

⁵⁷ 21 CFR 170.30(a)

⁵⁸ 21 CFR 170.30(b); It is assumed that this refers to the requirements stated in section **Error! Reference source not found.** However, food additive approval applications must include all the scientific studies and proof that the substance is safe, whereas GRAS notifications only need a summary of the evidence. Additionally, the Delaney clause formally applies to food additives but not GRAS substances.

⁵⁹ 21 CFR 170.30(c)(1)

⁶⁰ This is an important difference between the US and the EU. In the EU foods and ingredients are considered novel if they have a history of common use in the EU, but common usage in other places around the world is not considered a sufficient basis for safety.

⁶¹ 21 CFR 170.30(c)(2)

Neltner et al. (2011) organize GRAS substances into six categories, which are found to be very helpful in explaining the complexity of the GRAS system. The first three, common food ingredients that were used before 1958, manufacturer self-determined GRAS substances and expert panel-determined GRAS substances, have existed since the early 1960s, soon after the 1958 Food Additives Amendment was passed. The other three categories are a result of changes that the FDA has made to the GRAS approval process over the years, and includes FDA-listed GRAS substances (from 1958-1973), FDA-affirmed GRAS substances (from 1973-1997) and FDA-reviewed GRAS notifications (1997-present).

3.8.1 Common food ingredients that were used before 1958

This list consists of ingredients such as salt, sugar, MSG and other common substances that have been added to food for decades or centuries. Often times the ingredients are not even included in the GRAS list since they are -to put it simply- quite obviously well-known to be safe for consumption. The FDA has stated that it never intended for the GRAS list to be complete primarily because of these substances; it would be a waste of resources to approve such common ingredients.

3.8.2 Manufacturer self-determined GRAS substances

Manufacturers can determine themselves if a product meets the requirements of GRAS, and can place it on the market based on their judgment. The decision must be based on acceptable scientific sources. The manufacturer runs a risk that the FDA might not agree with their decision and could take enforcement action against them, so it is common practice to first notify the FDA.

3.8.3 Expert panel-determined GRAS substances

Reports by certain expert organizations that confirm the safety of substances can be relied upon by companies when they make GRAS self-determinations. If the expert panels determine a substance to be safe, the FDA recognizes the status of their reports and considers them sufficient to serve as “general recognition” of safety, even if the substance has never been used in food before. The Flavor and Extract Manufacturer’s Association (FEMA) and the Joint Expert Committee on Food Additives (JECFA) are two independent expert agencies whose opinions have status in the FDA⁶². FEMA is an organization within the US that evaluates various flavoring substances. JECFA is an international committee established in 1956 by the United Nations Food and Agriculture Organization (FAO) and the World Health Organization (WHO) and that is now associated with the Codex Alimentarius Commission (CAC).

3.8.4 FDA-listed GRAS substances

When the Food Additives Amendment of 1958 was passed, the FDA collected a list of substances that were considered to be generally recognized as safe at the time.

3.8.5 FDA-affirmed GRAS substances

During the late 1960s, questions were raised about the safety of a group of GRAS substances: cyclamate salts. The FDA was directed to re-evaluate the safety of all current GRAS substances based on current safety standards and information (as those added to the list before were not thoroughly evaluated). If the re-evaluation confirmed a substance to

⁶² In contrast to the EU, which does not allow other opinions than that of the recognised risk assessment body (often EFSA) to be a basis for authorization decisions.

be GRAS under its intended conditions of use, FDA would affirm that by publishing a new GRAS regulation. In addition, FDA allowed individuals to file petitions themselves to request that FDA review the GRAS status of other substances.

The GRAS affirmation petition procedure is listed in the CFR. Application information must include a description of the substance, when the substance began to be used, methods for detecting the substance, and information that establishes the safety and functionality of the substance in foods. Again, similar to the approval of additives, if the proposed use includes meat and fish, the substance is subject to additional regulation by the USDA if it is first approved by the FDA. Within 30 days after the filing of the petition, the FDA sends the petition to the Federal Register. Within 60 days, any interested person may send comments which will be reviewed by the FDA in addition to the application information. The affirmation may then be confirmed or denied by the FDA. If denied, the FDA may publish a notice in the Federal Register that the substance is subject to food additive regulation. In the event that the FDA wishes to affirm GRAS status itself, the procedure starts with the filing of the petition. No time limit is set for the review period, but businesses can market substances while waiting for an affirmative decision from the FDA⁶³.

Although the CFR describes the petition procedure for GRAS affirmation, it has actually been operating under an official notification system for the past couple of decades, discussed below.

3.8.6 FDA-reviewed GRAS notifications

In 1997 the FDA announced that it no longer had sufficient resources to affirm GRAS substances, and it proposed a notification procedure by which businesses could self-determine the GRAS status of a substance. The notification procedure maximizes the resources of the FDA, so that it does not waste time and money on evaluating common ingredients. Businesses can notify the FDA of their determination, but it is not mandatory (FDA 2009c). Thus FDA may be unaware of all products that are on the market.

It can be risky, however, to market products without FDA's knowledge and consent. If the FDA discovers the use of the product and disagrees with the manufacturer's determination that it is GRAS, it may take enforcement action including fines, suspensions, withdrawals and recalls.

The 1997 notification procedure is only a proposal. FDA announced that it would operate under an interim policy under which it would accept GRAS notifications even before the final rule was published. However, the final rule still does not exist and the FDA is still operating under the interim procedure. Since the first notification was received in 1998, FDA has received and responded to approximately 200 GRAS substances, yet has not made the procedure official.

⁶³ The process can and does in fact often take years. For example, high fructose corn syrup (HFCS) was first on the market in the mid-1960s (without FDA approval). A GRAS affirmation petition was filed in 1974, but was not approved and finalized by the FDA until 1983.

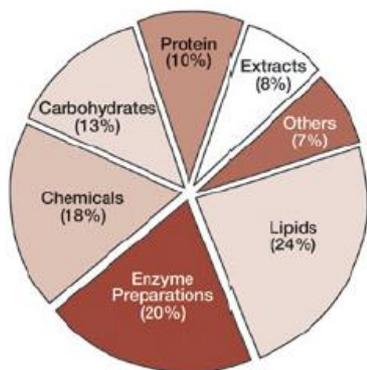


Figure 2. Types of substances for which GRAS notices have been submitted.

Figure 1. From FDA. How U.S. FDA's GRAS Notification Program Works

An FDA guidance document covers the procedure on submitting a GRAS notice (FDA 2011b).

The data required in the notification must include the following. For details on the level of scientific evidence required, refer to section 5.2.3.

1. A signed and dated GRAS exemption claim stating that the particular use of a substance is exempt from the premarket approval requirements of food additives. It must include:
 - a. The name and address of the notifier
 - b. The common or usual name of the substance
 - c. The applicable conditions of use of the substance: foods in which it is to be used, levels of use, purposes of use, and if necessary, a description of the expected consumer group
 - d. The basis for the GRAS determination, i.e. through scientific procedures or common use in food
 - e. A statement that the data used as the basis for the notification will be made available to the FDA upon request
2. Detailed information about the identity of the substance, including:
 - a. Chemical name
 - b. Chemical Abstracts Service (CAS) Registry Number
 - c. Enzyme Commission number
 - d. Empirical formula
 - e. Structural formula
 - f. Quantitative composition
 - g. Method of manufacture
 - h. Characteristic properties
 - i. Potential human toxicants
 - j. Specifications for food-grade material
3. Information on any self-limiting levels of use

4. A summary of the basis for the notification determination, i.e. that a particular use of the substance is exempt from the premarket approval requirements for food additives
 - a. For a GRAS determination through scientific procedures
 - i. Discussion of generally available and accepted scientific data, information, methods or principles that the notifier used to establish safety of the substance
 - ii. Probable consumption of the substance and cumulative effect in the diet
 - iii. Discussion of any studies or information that are contrary to the GRAS determination
 - iv. The basis for concluding that there is “consensus among experts qualified by scientific training and experience to evaluate the safety of substances added to food that there is reasonable certainty that the substance is not harmful under the intended conditions of use.”
 - b. For a GRAS determination through common use in food
 - i. Discussion of generally available data or information that the notifier used to establish safety of the substance
 - ii. Evidence of a substantial history of consumption by a significant number of consumers
 - iii. Discussion of any studies or information that are contrary to the GRAS determination
 - iv. The basis for concluding that there is “consensus among experts qualified by scientific training and experience to evaluate the safety of substances added to food that there is reasonable certainty that the substance is not harmful under the intended conditions of use.”

After the notification is received, FDA has 30 days to write to the notifier that the notification was received. Within 90 days after the notification is received, FDA must write to the notifier about the outcome of the notification with one of three responses. The first is that the FDA has no questions regarding the notifier’s basis for GRAS determination. This letter may include any points regarding labelling issues or the use of the substance in particular foods. The second type of response the FDA may give is that the notice presents an insufficient basis for a GRAS determination, such as that the scientific data and information provided do not show that the substance is generally recognized as safe by qualified experts. Lastly, the third type of letter is issued when the FDA has ended the GRAS notification evaluation at the notifier’s request⁶⁴.

This system for placing GRAS substances on the market is thus unique in that it is not required to obtain premarket approval for substances, and manufacturers can make the safety judgment themselves.

3.8.7 GRAS: who is liable?

As discussed above, under the GRAS notification procedure that the FDA has been operating under since 1997, businesses are allowed to “self-affirm” that their product is GRAS. If they submit a notification, they can place the product on the market while waiting for a confirmation. In fact, they are not even required to notify the FDA if they market a product.

Although not required, there are obviously regulatory risks involved, in case the FDA disagrees with a business's claim that a product is GRAS and removes it from the market.

If businesses themselves are allowed to classify a product as GRAS and place it on the market, then who is responsible if problems arise? What if the business notified the FDA about the product, but placed it on the market before receiving a confirmation back from the FDA, and it turned out to be unsafe? What if they didn't notify the FDA, and the FDA only became aware when consumers complained about damage that occurred to them after consumption of the product?

The business places a certain responsibility on itself by making a self-determination that a product is GRAS; it should determine that it satisfies the requirements of GRAS either through common use or scientific procedures. Yet the FDA is also responsible for ensuring that the food supply is safe. The FDA has tried to shift the burden on the businesses over time by claiming that the businesses put an unsafe food additive on the market. However, who exactly is liable in different possible situations is unclear, as the situation has not yet arisen. From what can be seen so far, there have not been serious cases (such as that a business puts an unsafe product on the market that causes many deaths). Cases in which the FDA has claimed that a product on the market is not GRAS have been milder—and businesses have generally been compliant with the FDA. It is unclear what would happen—and who would be held liable—if the situation became more serious and the issue were taken to court. The law states that foods must not be adulterated, but whether it is defined by the damages or the product's status is unknown.

3.8.8 Additional information on GRAS substances

GRAS substances are not free to be used under any conditions. Some have specific limitations on the foods in or levels at which they may be used. Even for those which do not, if the conditions of use are significantly different than for which they were allowed, such use may not be GRAS and will require a separate approval. GRAS substances are approved generically. It is important to note that the GRAS exemption only exists for food additives, and not for color additives.

The list of classified GRAS substances can be found in sections 182, 184 and 186 of the CFR. However, it is not complete, according to FDA: "Because of the large number of substances the intended use of which results or may reasonably be expected to result, directly or indirectly, in their becoming a component or otherwise affecting the characteristics of food, it is impracticable to list all such substances that are GRAS."

Included in the 1997 notification proposal was the intention of the FDA to maintain an inventory of all the GRAS notices it receives, as well as its response to them. This inventory can be found at on the FDA website⁶⁵.

3.9 Differences between food additive and GRAS

Both food additives and GRAS substances are approved⁶⁶ generically and possibly for only specific conditions of use. The main difference between GRAS determinations and premarket

⁶⁵ <http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=graslisting>

⁶⁶ The word "approved" is used loosely as GRAS substances may not be formally approved before being placed on the market.

approvals is related to who reviews the scientific data and information, and the form in which they are presented. Although substances can be approved as GRAS by the FDA, there is also the option that manufacturers can self-determine the GRAS status of their products and essentially approve that they can be placed on the market. Food additives can only be approved by the FDA⁶⁷. In addition, the application for premarket approval of food additives must include detailed scientific data and information to prove the safety of the substance. However, GRAS notifications only require a summary of the scientific data and information which was used to make the GRAS determination. FDA may request to see the original studies if they so desire, but only the summary is initially required in the application.

For a substance to be classified as GRAS through scientific procedures, the scientific data and information provided in the information must meet the requirements of that for food additive approvals. However, the main difference between GRAS substances and food additives is that for GRAS substances, there must be a consensus among qualified experts that the substance is safe under its intended conditions of use. Absence of a hazard is not enough of an argument.

GRAS substances can be marketed while waiting for (or simply without) approval from the FDA, which can serve as a huge advantage over the often lengthy food additive approval process.

Information in GRAS notifications is not kept confidential. On the other hand, much of the information in food additive petitions is (except for some things like safety data). This could be one benefit of the food additive process over the GRAS one.

Lastly, substances are either food additives or GRAS based on their intended use, that is, for specific uses in specific foods. Therefore, a substance may actually fall under multiple categories: it can be a food additive for one particular use, and a GRAS substance for another. A few notable examples: carbon dioxide is classified as a pesticide chemical when it is used for insect control and a GRAS substance when it is used as a leavening agent, processing aid or propellant; diatomaceous earth (derived from algae) is classified as a pesticide chemical when it is used for insect control, a food additive when it is used as a carrier or an anti-caking agent (in animal feed) and a GRAS substance when it is used as part of a filtration media (for human food). Approval for one use does not automatically affect other uses as GRAS as is shown in the *Coco Rico* case⁶⁸. A company marketed a beverage concentrate containing potassium nitrate to help maintain color and flavor. The FDA seized the beverages and declared that they were adulterated since potassium nitrate is an unapproved food additive. The company argued that nitrates and nitrites are not food additives since they are prior sanctioned. However, they are prior sanctioned for meat use, but not for beverages. *Coco Rico* defended themselves by arguing that there is no conclusive evidence that the use of potassium nitrates in beverages is unsafe, and that nitrates have been approved for use in meat, and they know of no difference in health effects between potassium nitrate used in meat and in beverages. However, the courts argued that the argument was invalid: approval of a prior-sanctioned substance (or GRAS substance or food additive) in one food does not make it approved in another food for another use.

⁶⁷ And the USDA, in the case that the additive is intended to be used in meat or poultry (same with GRAS)

⁶⁸ *United States v. An Article of Food, Coco Rico, Inc.* 752 F.2d 11 (1985)

3.10 Labeling requirements

Food additives and color additives do need to be included on food label ingredient lists. Spices, flavors and colors from natural sources may be listed generically (e.g. “spices”); the specific source is not necessary⁶⁹. However, artificial flavors and colors must bear the title “artificial.” In addition, certified (synthetic) colors do need to be identified with their specific name⁷⁰.

In some situations, a food additive is a risk only for a particular group of consumers. In some of these cases, the FDA requires a warning statement to be included on the label of the product, so that those that need to avoid the ingredient are more easily able to do so. Some examples of substances that must be accompanied by a warning statement are aspartame⁷¹, sorbitol, saccharin⁷², sulfites and FD&C Yellow No. 5 (tartrazine).

3.11 Color additives

Color additives in the United States are regulated separately from food additives.

A color additive is defined as⁷³:

[A] dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source and that, when added or applied to a food, drug, or cosmetic or to the human body or any part thereof, is capable (alone or through reaction with another substance) of imparting a color thereto.

It is important to note that color additives are not only used in foods!

Exceptions⁷⁴:

- Substances that impart a color to food containers are not considered color additives unless it is likely that it may be transferred to the contents of the package
- Substances that impart their own natural color when combined with other foods, such as cherries, green or red peppers, chocolate and orange juice, are not considered color additives. However, when substances, such as beet juice, are deliberately used as a color, they do classify as color additives
- If a substance is used solely for a purposes other than coloring, the imparted color must be clearly unimportant as the appearance, value, marketability or consumer acceptability is concerned
- Pesticide chemicals, soil or plant nutrients and other agricultural chemicals are exempt if the coloring is a result of affecting the natural physiological processes. However, if the chemical acts as a color or contains a color ingredient, it is a color additive

⁶⁹ 21 CFR 101.22(a)(2)

⁷⁰ 21 CFR 101.22(c)

⁷¹ The mandatory warning statement is: “Contains a source of phenylalanine”. This statement is targeted towards individuals with phenylketonuria, a genetic disease, to which aspartame is toxic.

⁷² The mandatory warning statement is: “Use of this product may be hazardous to your health. This product contains saccharin, which has been determined to cause cancer in laboratory animals.”

⁷³ 21 CFR 70.3(f)

⁷⁴ 21 CFR 70.3 (f)-(h)

Color additives must undergo a premarket approval process before gaining market access. As most of the petition information is the same as that for food additives (see section 3.3), only the differences will be discussed here. A (fully) positive list system applies to color additives. They are considered unsafe unless there is a regulation for the additive—meaning not only that they must be approved before being placed on the market, but also that there are no GRAS or prior-sanctioned substance exemption possibilities. In fact, they are considered unsafe unless they are certified or specifically exempt from the certification requirement⁷⁵. However, a substances can be listed as both GRAS and a color additive, e.g. ferrous lactate (GRAS listing at 21 CFR 184.1311 and color additive listing at 21 CFR 73.165). The reason why this substance can be listed as GRAS as well is because the uses are different: it is considered GRAS when it is used as a nutrient supplement or as a color fixative for ripe olives.

Color additives are classified into two groups: certified or exempt from certification. Certification is the default option—those who wish to be exempt from certification must make a petition which includes the reasons why certification should not be necessary for the protection of public health⁷⁶. Certified colors are synthetic and typically synthesized from substances such as petroleum or tar (traditionally coal). Color additives exempt from certification are those derived from natural sources such as plants, minerals or animals (e.g. paprika powder). The Commissioner must consider i.a. the additive composition, its manufacturing process, possible impurities and toxic potential⁷⁷. If a color additive is not exempt from certification, each batch must be tested⁷⁸. Certification involves testing new manufactured batches to ensure that the color additives meet their identity and specification requirements by performing analyses for purity, moisture and residual salts, among others.

Another difference between food additives and color additives is that submission of color additive petitions (to be used in foods) requires a fee of US \$3,000.00 (2240€ as of 12 February 2013) (no cost for food additive applications)⁷⁹.

3.12 GMOs⁸⁰

To put it simply, almost all new food ingredients are regulated in the US as food additives or GRAS substances. Foods are not regulated as whole foods (as they are in the EU), but rather the ingredients of the foods must go under premarket approvals. As food additives and GRAS substances are approved for particular uses in foods, in a way a food ingredient is approved for use in a whole food product.

⁷⁵ FDCA Section 721 (a)

⁷⁶ 21 CFR 71.18

⁷⁷ 21 CFR 71.20(b)

⁷⁸ 21 CFR 71.25

⁷⁹ 21 CFR 70.19

⁸⁰ Definitions from FDA's Statement of policy on Foods Derived from New Plant Varieties:

-“Genetic modification” means the alteration of the genotype of a plant using any technique, new or traditional.

-“Modification” is used in a broad context to mean the alteration in the composition of food that results from adding, deleting, or changing hereditary traits, irrespective of the method.

-Plant breeding is the science of combining desirable genetic traits into a variety that can be used in agriculture.

The desired traits can be broadly divided into two classes: Those that affect agronomic characteristics of the plant, and those that affect quality characteristics of the food. Agronomic characteristics include those affecting yield; resistance to diseases, insects and herbicides; and ability to thrive under various adverse environmental conditions. Quality characteristics include those affecting processing, preservation, nutrition, and flavor.

In the US, genetically modified (GM) foods are treated in the same way as conventional foods, in that ingredients are classified generally as food additives or GRAS substances. There is no separate official procedure for GM foods as there is in the EU (under Regulation 1829/2003). FDA has determined that GM foods are considered to be GRAS unless proven otherwise (FDA 1992). Its reasoning is that the only substances added to GM foods are nucleic acid proteins, which exist in the cells of every living organism and thus are considered normal components of food. In its Statement of Policy (FDA 1992), the FDA states that “In most cases, the substances expected to become components of food as a result of genetic modification of a plant will be the same as or substantially similar to substances commonly found in food, such as proteins, fats and oils, and carbohydrates.”

The FDA does note that some GM organisms might require the premarket approval process for food additives, however. In cases in which “the intended expression product in a food could be a protein, carbohydrate, fat or oil, or other substance that differs significantly in structure, function or composition from substances currently found in food....Such substances may not be GRAS and may require regulation as a food additive.” To further clarify how it is possible that a GMO may be considered GRAS, FDA further stated that “It is the intended or expected introduction of a substance into food that makes the substance potentially subject to food additive regulation. Thus, in the case of foods derived from new plant varieties, it is the transferred genetic material and the intended expression product or products that could be subject to food additive regulation, if such material or expression products are not GRAS.”

As can probably be expected, there is some disagreement over the fact that FDA considered nucleic acid proteins (the “product” in this case) to be GRAS. There is certainly not general agreement among experts that nucleic acid proteins used in GM foods are generally recognized as safe. On top of that, manufacturers can make the decision whether their product is GRAS or not. In some situations it is obvious if the new ingredient or new process to produce the food is GRAS or not, such as if it has a long established history of safe use or not. However, it is not quite so simple to determine in other cases—the criteria to meet the GRAS exemption are somewhat vague. Foods and food ingredients meet the criteria if they are comparably safe to similar conventional foods⁸¹. However, what makes a food similar enough to a conventional food can be difficult to determine. A conventional food modified in a slight way may or may not be considered conventional—and thus possibly GRAS.

In 1986 the Coordinated Framework for Regulation of Biotechnology stated FDA’s view that products from biotechnology are not fundamentally different from conventional products. It was not necessary to develop new legislation to cover GM foods and GMOs, and the existing laws under sections 402(a)(1) and 409 of the FDCA are sufficient to regulate new substances resulting from genetic modification. In fact, most non-pesticidal GMOs do not have to undergo the food additive premarket approval process because they are considered GRAS⁸².

⁸¹ The reason for the “comparably safe” standard is that it is impossible to prove 100% safety. Therefore, the FDA considers foods as safe as conventional foods to meet the required safety standard

⁸² Pesticidal GMOs are not under the jurisdiction of the FDA because they are not considered food additives or GRAS; they are instead regulated by the Environmental Protection Agency (EPA).

3.13 Where to find statuses of applications and lists of approved substances.

Lists of approved substances can be found both in the CFR and often times on the FDA website. This section provides ease of access to this information.

Food additives

The approved food additives are listed in 21 CFR in parts 170-180. The Food Additives Status List⁸³ organizes what is found in the CFR into an alphabetized list. This list also includes brief information on any limitations of use for each additive. To find the full details of an additive's approval, the regulations for each substance can be found in the Federal Register. It is important to note that this list is called the food additives *status* list: it is not a positive list of only approved additives, it also includes information on additives which have not been approved or are no longer allowed.

Food contact substances

Food contact substances in the US can be found in a list in 21 CFR parts 174-190. Additionally, a link on the FDA websites contains a list⁸⁴ of over 3000 substances which are considered to be food contact substances. However, as FDA notes:

no inference should be made about the legality of using any one of these specific substances as an "indirect" food additive. Their presence on this list only indicates that the names of these substances are found (or, in the case of some of the polymers, are implied) in 21CFR parts 175 – 178. 3237 substances

Therefore, this list includes all substances which are reasonably expected to come into contact with food, include asbestos, acrylamide, asphalt and ammonia, whether or not they have been approved.

GRAS substances

Approved GRAS substances can be found in the CFR in sections 182, 184 and 186. However, this list is not complete, as it does not include obviously safe substances that are added to food. According to FDA, "Because of the large number of substances the intended use of which results or may reasonably be expected to result, directly or indirectly, in their becoming a component or otherwise affecting the characteristics of food, it is impracticable to list all such substances that are GRAS." Since the FDA began accepting notifications for GRAS substances in 1997 it has kept a GRAS Notice Inventory⁸⁵ which documents all notifications received from companies (as of 7-2-2013 there were 451) and the FDA's response.

Prior-sanctioned substances

Prior-sanctioned substances can be found in 21 CFR part 181⁸⁶.

Color additives

Approved color additives can be found in 21 CFR Parts 70, 71, 73, 74, 80 and 82. The status of all applications (approved or not) can be found in the Color Additives Status List⁸⁷ and the

⁸³<http://www.fda.gov/food/foodingredientpackaging/foodadditives/foodadditivelistings/ucm091048.htm>

⁸⁴<http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=fcsListing>

⁸⁵<http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=grasListing&displayAll=true>

⁸⁶<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=181>

additives approved for different uses can be found in the Summary of Color Additives for Use in the United States in Foods, Drugs, Cosmetics, and Medical Devices⁸⁸.

Other

The FDA also keeps an Everything Added to Food in the US (EAFUS) list⁸⁹, which, despite its name, is still not complete. It contains less than half of all substances allowed by the FDA. It has evidently not been updated in recent years, as it contains only less than 10% of the substances approved by the FDA from 2001-2011 (Neltner et al. 2011). Additionally, as stated above, many substances (those obviously known to be safe) are not included in the list.

3.14 Conclusion

To summarize the section on the US, there are various categories under which a food substance may be classified. Food additives appear at first to be any substance added to food, but the actual concept is actually far more complex, as has been described above, since the scope is both broader and narrower than it may initially seem. Food additives are substances that become a component of food or affect the characteristics of food. Food additives are different than GRAS substances because they are not generally known to be safe through either scientific evidence or common use, and they are different than food contact substances because they have a technical effect in the final product. These have been determined to be the primary characteristics of food additives in the US. The last section in particular demonstrates the complexity of the US regulatory system of food additives, and how it is possible for new substances to fall outside the scope of a food additive and escape formal safety assessment.

⁸⁷ <http://www.fda.gov/ForIndustry/ColorAdditives/ColorAdditiveInventories/ucm106626.htm>

⁸⁸ <http://www.fda.gov/forindustry/coloradditives/coloradditiveinventories/ucm115641.htm>

⁸⁹ <http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?rpt=eafusListing&displayAll=true>

4 Approach in the European Union

4.1 Definition of a food

In order to better understand the legal context of food additives, i.e. the role that food additives play in the food industry, and in what foods they can be used, it is important to understand what exactly a food is. Regulation 178/2002⁹⁰—the General Food Law (GFL)—defines ‘food’⁹¹ as

[A]ny substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans.

‘Food’ includes drink, chewing gum and any substance, including water, intentionally incorporated into the food during its manufacture, preparation or treatment [...]

‘Food’ shall not include:

- (a) feed;*
- (b) live animals unless they are prepared for placing on the market for human consumption⁹²;*
- (c) plants prior to harvesting*
- (d) medicinal products [...]*
- (e) cosmetics [...]*
- (f) tobacco and tobacco products [...]*
- (g) narcotic or psychotropic substances [...]*
- (h) residues and contaminants⁹³*

4.2 Definition of a food additive

On 16 December 2008 the EU replaced several Directives and Decisions⁹⁴ covering food additives with the revised and consolidated Regulation (EC) No 1333/2008 on food additives⁹⁵. Article 3(2)(a) defines a food additive as follows:

Any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food, whether or not it has nutritive value, the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage

⁹⁰ Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the Food Safety Authority and laying down procedures in matters of food safety. OJ L 31/1, 1.2.2002. (General Food Law or GFL) < <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2002:031:0001:0024:EN:PDF> >

⁹¹ Article 2 GFL

⁹² In Europe, this mainly refers to oysters (Van der Meulen and van der Velde 2008)

⁹³ The only apparent difference between the definition of a food in the EU and that in the US is that the American definition includes animal feed and pet food. These products are classified separately in European legislation.

⁹⁴ See Recital 28 of Regulation 1333/2008 for the list of the 11 acts

⁹⁵ Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354/16, 31.12.2008

of such food results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods.

The following are not considered to be food additives:

- i. Monosaccharides, disaccharides or oligosaccharides and foods containing these substances used for their sweetening properties
- ii. Foods, whether dried or in concentrated form, including flavourings incorporated during the manufacturing of compound foods, because of their aromatic, sapid or nutritive properties together with a secondary colouring effect
- iii. Substances used in covering or coating materials, which do not form part of foods and are not intended to be consumed together with those foods
- iv. Products containing pectin and derived from dried apple pomace or peel of citrus fruits or quinces, or from a mixture of them, by the action of dilute acid followed by partial neutralisation with sodium or potassium salts (liquid pectin)
- v. Chewing gum bases
- vi. White or yellow dextrin, roasted or dextrinated starch, starch modified by acid or alkali treatment, bleached starch, physically modified starch and starch treated by amylolytic enzymes
- vii. Ammonium chloride
- viii. Blood plasma, edible gelatin, protein hydrolysates and their salts, milk protein and gluten
- ix. Amino acids and their salts other than glutamic acid, glycine, cysteine and cystine and their salts having no technological function;
- x. Caseinates and casein
- xi. Inulin

In a few words, a food additive as defined by EU legislation is a substance not normally consumed as a food which is intentionally added to food to serve a technological purpose. The actual concept is however more complex, as discussed below in section 4.4.

4.3 Requirements food additives must meet

The EU applies the positive list system to food additive approval; therefore, only those additives which have demonstrated to comply with Regulation 1333/2008 may be placed on the market⁹⁶.

Food additives on the EU market must meet three primary conditions⁹⁷ in order to be approved:

- 1) No safety concern for consumer health at the proposed level of use
- 2) Not misleading to the consumer
- 3) Technological need that cannot be reasonably achieved through other means

Details on the three requirements are elaborated below.

⁹⁶ Regulation 1333/2008 Article 5

⁹⁷ As stated in Article 6(1) Regulation 1333/2008

4.3.1 Requirement 1: Safe

Food additives approved in EU must not be unsafe for consumers. Although safety is not defined in Regulation 1333/2008, a look to Article 14 in the GFL can provide a definition of unsafety:

2. *Food shall be deemed to be unsafe if it is considered to be:*
 - (a) *injurious to health;*
 - (b) *unfit for human consumption.*
1. *In determining whether any food is unsafe, regard shall be had:*
 - (a) *to the normal conditions of use of the food by the consumer and at each stage of production, processing and distribution, and*
 - (b) *to the information provided to the consumer, including information on the label, or other information generally available to the consumer concerning the avoidance of specific adverse health effects from a particular food or category of foods.*
2. *In determining whether any food is injurious to health, regard shall be had:*
 - (a) *not only to the probable immediate and/or short-term and/or longterm effects of that food on the health of a person consuming it, but also on subsequent generations;*
 - (b) *to the probable cumulative toxic effects;*
 - (c) *to the particular health sensitivities of a specific category of consumers where the food is intended for that category of consumers.*
3. *In determining whether any food is unfit for human consumption, regard shall be had to whether the food is unacceptable for human consumption according to its intended use, for reasons of contamination, whether by extraneous matter or otherwise, or through putrefaction, deterioration or decay.*

Safety is assessed based on the evidence provided in the application. EFSA (2012) published a guidance document on the submission of food additive evaluations, which replaced the previous one by the Scientific Committee on Food (SCF, EFSA's predecessor) in 2001 that was provisionally endorsed by EFSA. EFSA's guidance document reflects "current thinking in risk assessment." The document extensively details the data requirements as well as the risk assessment procedure used to evaluate the additive authorizations.

The guidance on the data requirements covers four main sections: chemistry and specifications, existing authorizations and evaluation, proposed uses and exposure assessment and toxicological studies. For the toxicological studies a three-tiered approach is described, which sets different data requirements for different levels of risk and other considerations (e.g. use, animal welfare). Tier 1 requires a minimum dataset for all compounds. For those which are absorbed, demonstrate toxicity or genotoxicity, Tier 2 tests are required to gather more information. If Tier 2 results raise concerns for any specific endpoints, Tier 3 testing is required. These tests are intended to give information on any possible negative short-term or long-term effects of the additives, such as if they have the potential to cause cancer, affect reproduction, etc (see section 5.2.3 for more information on the level of scientific evidence). In addition, proposed use levels of the food additive should take into account the intake of the substance from other sources as well as if certain groups of consumers will be exposed⁹⁸.

⁹⁸ Recital 7 Regulation 1333/2008

4.3.2 Requirement 2: Not misleading

“Misleading the consumer” is elaborated as concerning issues relating to the nature, freshness, ingredient quality, naturalness of a product or production process and nutritional quality (including fruit and vegetable content)⁹⁹.

An example of a substance that was not approved as a food additive in the EU for this purpose is carbon monoxide (CO). Meat treated with CO helps to preserve its red color, making it visually appealing for consumers to purchase in supermarkets. However, its presence may mask visual evidence of spoilage, because CO can maintain the red color for more than 20 days. Masking spoilage is thus misleading to the consumer. Additionally, meat turns brown from exposure to oxygen long before it spoils, so color is a poor indicator of freshness. CO is approved in the US for this purpose, although there is some controversy, because additives in the US are also not allowed to be deceptive to the consumer (Schmit 2007).

4.3.3 Requirement 3: Technological function with a benefit to the consumer

All food additives must serve a technological function, which cannot be achieved by other means, which has an advantage or benefit for the consumer. Although a technological function is not explicitly defined (see section 4.4) the advantage or benefit for the consumer must fall into one of the following categories, as stated in Article 6(2) of Regulation 1333/2008:

- a) *Preserving the nutritional quality of the food*
- b) *Providing necessary ingredients or constituents for foods manufactured for groups of consumers with special dietary needs*
- c) *Enhancing the keeping quality or stability of a food or improving its organoleptic properties, provided that the nature, substance or quality of the food is not changed in such a way as to mislead the consumer*
- d) *Aiding in the manufacture, processing, preparation, treatment, packing, transport or storage of food, including food additives, food enzymes and food flavourings, provided that the food additive is not used to disguise the effects of the use of faulty raw materials or of any undesirable practices or techniques, including unhygienic practices or techniques, during the course of any such activities.*

4.3.4 Additional requirements

Sweeteners and colors must meet additional conditions to be included in the list of approval food additives. In addition to the three requirements discussed above, sweeteners must serve one or more of the following purposes:

- a) *replacing sugars for the production of energy-reduced food, non-cariogenic food or food with no added sugar; or*
- b) *replacing sugars where this permits an increase in the shelf-life of the food; or*
- c) *producing food intended for particular nutritional uses as defined as Article 1(2)(a) of Directive 89/398/EEC.*

Colors must serve one of the following additional purposes:

⁹⁹ Recital 7 Regulation 1333/2008

- a) *restoring the original appearance of food of which the colour has been affected by processing, storage, packing and distribution, whereby visual acceptability may have been impaired;*
- b) *making food more visually appealing;*
- c) *giving colour to food otherwise colourless.*

There are also additional restrictions for the use of food additives in foods for infants and young children¹⁰⁰.

4.4 Interpretation

As described above, the main characteristics of a food additive are: not normally consumed as a food, become a component of food, safe, not misleading and have a technological effect. The decisive criterion of what makes a food additive different from the many other substances regulated under the EU is the technological effect. There exist many other substances not normally consumed as food which also have to undergo premarket approvals: GMOs, novel foods, dietary supplements and feed additives, to name a few. Therefore this is not the criterion that defines food additives. Additionally, all foods placed on the EU market must be safe and not misleading, as it stated in the GFL (see section 4.3.1). Article 3(2)(b) of Regulation 1333/2008 also explicitly defines a processing aid as a substance which does not have a technological effect in the final product, making this a distinct difference from a food additive. If all food additives must serve a technological function, the question becomes: what exactly is a technological function?

Food additives are placed into certain functional classes based on the technological function a food additive exerts in the foodstuff (Article 3(2)(c)). The list of functional classes¹⁰¹ is shown below. The functional classes organize what is stated above into different categories of substances which serve a technological function.

1. sweeteners
2. colors
3. preservatives
4. antioxidants
5. carriers
6. acids
7. acidity regulators
8. anti-caking agents
9. anti-foaming agents
10. bulking agents
11. emulsifiers
12. emulsifying salts
13. firming agents
14. flavor enhancers
15. foaming agents
16. gelling agents
17. glazing agents
18. humectants

¹⁰⁰ As stated in Article 16 Regulation 1333/2008; see Directive 89/398/EEC for details

¹⁰¹ For descriptions of each class, refer to Annex I in Regulation 1333/2008

19. modified starches
20. packaging gases
21. propellants
22. raising agents
23. sequestrants
24. stabilisers
25. thickeners
26. flour treatment agents

Additionally, the Regulation provides a set of substances in Article 2 to which the Regulation does not apply, unless they are used as food additives (i.e. to become a component of food and to serve a technological purpose). These substances are:

- Processing aids
- Plant and plant product protection substances
- Substances added to foods as nutrients
- Substances used for the treatment of water for human consumption
- Flavorings

Processing aids normally do not become a component of foods. However, in some cases residues may persist in the final product, but as long as they do not have a technological effect, they can still be classified as processing aids.

Recital 5 of Regulation 1333/2008 explains this article further by specifying some exceptions. It states:

[S]ubstances should not be considered as food additives when they are used for the purpose of imparting flavour and/or taste or for nutritional purposes, such as salt replacers, vitamins and minerals. Moreover, substances considered as foods which may be used for a technological function, such as sodium chloride or saffron for colouring and food enzymes should also not fall within the scope of this Regulation.

Based on the above three resources, imparting flavor or taste is thus not considered a technological function by the EU, whereas the 26 categories of functional classes are indeed technological functions.

Accordingly, Recital 5 above states that salt replacers are not considered to be food additives. However, potassium chloride (E 508), the most common salt substitute, is approved as an additive in the EU. Is imparting (salty) flavor, then, considered a technological function or not? In order to investigate potassium chloride's functions, the Codex classifications of food additives¹⁰² were used. It was found that potassium chloride has other functions; it serves as a gelling agent, flavor enhancer, stabilizer and thickener—these must be the functions for which potassium chloride is approved as an additive; not its use as a salt replacer. It is important to note that substances can thus be additives for one use but not for others; the approval applies to the use and not to the substance itself. Based on this mini-investigation, it is correct that potassium chloride, a known salt replacer, is not approved for its function as a

¹⁰² Available at http://www.codexalimentarius.net/gsaonline/docs/CXS_192e.pdf; The EU stated that it bases its classification of food additives on the Codex document.

salt replacer (for taste, which is not a technological function), and instead to serve other (technological) purposes. Therefore, food additives are defined by the criterion of having a technological function.

It was stated above in Article 6(2) that additives must have a technological function which serves a benefit to the consumer, one of which is “improving its organoleptic properties”, but it has been demonstrated that flavorings are not considered to have a technological function under the scope of the definition and are therefore additives. However, organoleptic includes other properties beyond flavor and taste, such as texture. Substances that serve this purpose are indeed classified as food additives, as can be seen with the functional classes of thickeners, firming agents, etc.

An alternative interpretation of if flavor is a technological function or not can be extracted from Article 2 of Regulation 1333/2008. This article, written above, states that the Regulation does not apply to certain substances unless they are used as food additives. Flavorings are included in this list of certain substances. It can thus be read in a way that flavorings are food additives but are instead simply regulated under a different piece of legislation. However, based on the interpretation discussed above, it is considered that flavorings are not considered to be additives.

4.5 Authorization procedure

Food additives must be approved before they can be placed on the European market. The business wishing to market the additive must send an application to the Commission. EFSA performs a risk assessment¹⁰³ and forms an opinion about the safety of the additive, then the Commission and the SCoFCAH make the final decision regarding its approval.

A positive list system thus applies to food additives. It consists of two parts: Annex II of Regulation 1333/2008 is for food additives that may be placed on the market and used in foods, and Annex III which is for food additives that may be used in food additives, food enzymes and food flavorings. Additives in the latter category are typically carriers¹⁰⁴ and additives used in nutrients. In 2001, Annex II was replaced by Regulation 1129/2011¹⁰⁵ and Annex III was replaced by Regulation 1130/2011¹⁰⁶.

4.5.1 Analysis of process and requirements

At the same time that Regulation 1333/2008 on food additives was established, Regulation 1331/2008¹⁰⁷ was passed, which established a common authorization procedure for food

¹⁰³ EFSA was created in 2002 by the GFL. Before EFSA existed, its predecessor, the Scientific Committee on Food (SCF), conducted the risk assessments.

¹⁰⁴ Carriers are substances used to dissolve, dilute, disperse or otherwise physically modify a food additive or a flavoring, food enzyme, nutrient and/or other substance added for nutritional or physiological purposes to a food without altering its function (and without exerting any technological effect themselves) in order to facilitate its handling, application or use (defined in Annex I of Regulation 1333/2008)

¹⁰⁵ Commission Regulation (EU) No 1129/2011 of 11 November 2011 amending Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council by establishing a Union list of food additives

¹⁰⁶ Commission Regulation (EU) No 1130/2011 of 11 November 2011 amending Annex III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives by establishing a Union list of food additives approved for use in food additives, food enzymes, food flavourings and nutrients

¹⁰⁷ Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings

additives, food enzymes and food flavorings. The Regulation addresses the three components of “updating the Community list”:

- 1) adding a substance
- 2) removing a substance
- 3) adding, removing or changing conditions, specifications or restrictions regarding a substance already on the list

The procedure to update the Community list consists of several defined steps. First, an application made by a business or Member State is sent to the Commission. Alternatively, the Commission can also take the initiative to update the list.

Upon receipt of the application, the Commission initially must take three actions:

- 1) It must write to the applicant within 14 working days to acknowledge receipt of the application.
- 2) It must notify EFSA of the application and request its opinion, if necessary. If an additive is to be removed from the list or if there are modifications in the conditions, specifications or restrictions, then it may not be necessary if the updates are not likely to have an effect on human health.
- 3) In addition, the Commission must make the application available to the Member States.

If the Commission starts the procedure on its own initiative, it must only take the last two steps.

The evaluation and re-evaluation of food additives by EFSA is performed by the Panel on Food Additives and Nutrient Sources Added to Food (ANS). Its three primary tasks are evaluating the safety of new food additives, re-evaluating food additives that were authorised before 20 January 2009 and reviewing certain additives in response to specific requests from the European Commission based on emerging scientific information (European Food Safety Authority 2010).

When EFSA is requested to give its opinion, it shall do so within nine months of the receipt of the completed application, and forward it to the Commission, Member States and applicant. All applications received by EFSA are assigned an application number and EFSA Question number. The status of EFSA opinions can be viewed in the Register of Questions (ROQ)¹⁰⁸. However, in certain cases in which EFSA requests additional information concerning risk assessment from the applicant, the nine-month limit period can be extended. EFSA can set a new time period and inform the Commission, and if the Commission does not object within eight working days, the period is extended. If EFSA does not receive the additional information within the extended period, EFSA must base its opinion on the information already provided.

The opinion of EFSA on the safety of the food additive must include:¹⁰⁹

- a) Identity and characterization

¹⁰⁸ Available at <http://registerofquestions.efsa.europa.eu/roqFrontend/questionsList.jsf> On 11 February 2013 there were 13053 applications in the database.

¹⁰⁹ Commission Regulation (EC) No 234/2011 of 10 March 2011 implementing Regulation (EC) No 1331/2008 of the European Parliament and of the Council establishing a common authorisation procedure for food additives, food enzymes and food flavourings. OJ L 64/15, 11.3.2011.

- b) Assessment of the biological and toxicological data
- c) Dietary exposure assessment for the European population taking into account other sources
- d) Overall risk assessment, with a health-based guidance value (e.g. ADI) if possible
- e) If the exposure exceeds the guidance value, a detailed dietary exposure assessment
- f) Conclusions
- g) Other, based on the request of the Commission

No longer than nine months after receiving the opinion from EFSA (or if an opinion is not necessary, within nine months after receipt of the valid application), the Commission must submit to the Standing Committee on Food Chain and Animal Health (SCoFCAH) a draft regulation to update the Community list and present it for voting at the SCoFCAH. In the case that the Commission requests additional information from the applicant, the nine-month period may be extended. If the information is not provided within this set time period, the Commission must make its decision on the information already provided. This draft must take into account EFSA’s opinion, “any relevant provisions of Community law and any other legitimate factors relevant to the matter under consideration” and explain how it came to reach such a decision. An explanation is particularly required if the Commission’s regulation is not in line with EFSA’s opinion. If SCoFCAH supports the proposal it will be presented to the Council and the European Parliament. They can still reject it in case they consider that the authorization does not comply with the conditions of use set out in the EU legislation.

Also, the time periods may be extended by the Commission on its own initiative, or at the request of EFSA, if the extension is justified. The applicant and Member States will then be informed of the extension and its reason.

Table 2. Overview of the food additive approval process in the EU

Deadline	Total time elapsed	Action
14 days	14 days	Commission must acknowledge receipt of application; notify EFSA of the application and request its opinion, if necessary; forward the application to the Member States
9 months	9 months, 14 days	EFSA must give its opinion (with the possibility to extend this time period if additional information is requested)
9 months	18 months, 14 days	Commission must submit a draft regulation to SCoFCAH (with the possibility to extend this time period if additional information is requested)

A few years after the approval of Regulation (EC) 1331/2008, a follow-up Commission Regulation (EU) 234/2011¹¹⁰ was passed that implements Regulation 1331/2008 with details on the common authorization procedure.

¹¹⁰ Commission Regulation (EU) No 234/2011 of 10 March 2011 implementing Regulation (EC) No 1331/2008 of the European Parliament and of the Council establishing a common authorisation procedure for food additives, food enzymes and food flavourings

The Regulation established that applications for food additive approval must consist of three parts: a letter, a technical dossier and a summary of the dossier.

4. Letter

5. Technical dossier

— Administrative data includes basic information such as contact details, identity information of the additive (chemical name, CAS number, etc) and parts of the dossier to remain confidential. These data allow EFSA to properly process the application and contact the applicant¹¹¹.

— Data required for risk assessment¹¹²

- Raw data of published and unpublished studies (available on request from EFSA)
- Existing authorisations and risk assessments (including applications sent to other places)
- Proposed normal and maximum use levels
- Dietary exposure assessment
- Biological and toxicological data (toxicokinetics, subchronic toxicity, genotoxicity, chronic toxicity/carcinogenicity, reproductive and developmental toxicity)

— Data required for risk management¹¹³

- Must include information to verify that the additive meets the second two requirements for approval; namely, that there is a reasonable technological need that serves a benefit to the consumer and that it does not mislead the consumer
- (f) proposed normal and maximum use levels in the food categories mentioned in the Union list, or in a newly proposed food category, or in a more specific foodstuff belonging to one of these categories;
- (g) the exposure assessment, based on normal and maximum intended use for each of the categories or products concerned; must take into account all potential dietary sources including natural occurrence in food, non-additive use in food supplements, use as a nutrient, use as flavouring, use as food contact material, use in pharmaceuticals or cosmetic products
- (h) the amount of the food additive present in the final food as consumed by the consumer;

6. Summary of the dossier

- Must contain a statement that the product complies with the conditions laid down in Articles 6, 7, and 8 of Regulation 1333/2008
- Follow the same order as the technical dossier
- Overall conclusion on the safety of the substance for the proposed uses

By way of derogation, in the event that there is an application for a modification of the conditions of use of an already authorized food additive, the data required for risk assessment and risk management may not be required¹¹⁴. Also, if there is an application for a

¹¹¹ EFSA. Scientific opinion. Data requirements for the evaluation of food additive applications. Scientific statement of the Panel on Food Additives and Nutrient Sources added to Food. Question No EFSA-Q-2007-188. Adopted on 9 July 2009. The EFSA Journal (2009) 1188, 1-7.

¹¹² Articles 5 and 6 Regulation 234/2011

¹¹³ Article 7(1) Regulation 234/2011

¹¹⁴ Article 2(4) Regulation 234/2011

modification of the specifications of an already authorized food additive, no data beyond a justification of the request may be required. In both cases, the applicant must include a justification as to why the proposed changes do not affect the existing risk assessment¹¹⁵.

Additionally, if there is a significant change in the production method, starting materials used or particle size (e.g. through nanotechnology) in an already approved food additive, the food additive must be considered a new food additive and undergo the premarket approval process before it can be placed on the market¹¹⁶. “Significantly different” is defined in Recital 13 as, inter alia, “a change of the production method from extract from a plant to production by fermentation using a microorganism or a genetic modification of the original microorganism, a change in starting materials, or a change in particle size.”

Regulation 234/2011 is the most recently published Regulation, but applicants are required to consult the DG Sanco website for an updated practical guidance on the submission of applications¹¹⁷. The third and latest version, updated on 10 May 2012 (European Commission Health and Consumers 2012) was found on the DG Sanco website. There are a few clarifications regarding Regulation 234/2011, and some additional details are given on the logistics of submission.

Regulation 234/2011 lists three required components of the application: a letter, a technical dossier and a summary of the dossier. DG Sanco’s most recent practical guidance expands this list to also include a public summary of the dossier, a separate copy of administrative data of applicant(s) from the technical dossier, a checklist, and 2x CD/DVD containing copies of all documents mentioned above in electronic format. The three components of the technical dossier (administrative data, risk assessment data and risk management data) remain the same.

The public summary of the dossier must be prepared and written in a way for the non-professional public to understand (i.e. by avoiding scientific terms). The summary should include the benefits of the additive for consumers. It should be less extensive than the summary of the dossier.

A specific mailing address for application submission and a specific email address for questions are provided.

4.5.2 Information which must be included in the Community list

Once approved, a food additive is placed in the positive list, which is located in the Annexes of Regulation 1333/2008.

Food additives listed in these Annexes must include the following¹¹⁸:

¹¹⁵ Article 5 Regulation 234/2011

¹¹⁶ Article 12 Regulation 1333/2008

¹¹⁷ Article 3(1) Regulation 234/2011: “The applicant shall take into account the practical guidance on the submission of applications made available by the Commission (Directorate General for Health and Consumers’ website)”

¹¹⁸ Article 10(2) Regulation 1333/2008

a) *The name of the additive and its E number*

E numbers are assigned to all approved food additives, which are used for identification purposes.

b) *The foods to which it may be added*

Food additives are listed in groups of food categories in which they may be used¹¹⁹. This food categorization system (FCS) consists of 18 food categories¹²⁰, which are further divided into 153 subcategories. The number of additives which may be used in a food product varies widely. Zero food additives are allowed in unprocessed foodstuffs¹²¹, honey, butter, pasteurized and sterilized milk, natural mineral and spring water, coffee (excluding flavored instant coffee), unflavored leaf tea, sugars, dry pasta (excluding gluten-free and others for special diets) and plain unflavored buttermilk. Color additives are also not allowed in various other food products. On the other hand, more food additives are authorized for use in more processed foods, such as confectionary, savory snacks and flavored beverages. As an example, more than 250 additives are allowed to be used in the food category of edible ices (Food Safety Authority of Ireland 2010).

Additionally, legislation¹²² has allowed Member States to prohibit the use of certain food additives in foods that were considered to be traditional. For a prohibition to be allowed to continue, it had to exist before 1 January 1992. Member States had to have their traditional foods approved under the European Parliament and Council Directive 94/34/EC. The foods which are prohibited to have certain or all food additives are beer (Germany), feta cheese (Greece), 'traditional French bread' (France), preserved truffles (France), preserved snails (France), goose (France), duck (France), turkey preserves (France), 'Bergkäse' (Austria) and Mammi (Finland) (O'Rourke 2005).

c) *The conditions under which it may be used*

The conditions refer to the allowed level of use. The level should be set at the lowest level necessary to achieve the desired effect, taking into account any acceptable daily

¹¹⁹ The EU based its food category system on the Codex Alimentarius General Standard for Food Additives (cite) (Recital 4 Regulation 1129/2011)

¹²⁰ These categories are dairy products and analogues; fats and oils and fat and oil emulsions; edible ices; fruit and vegetables; confectionary; cereals and cereal products; bakery wares; meat; fish and fisheries products; eggs and egg products; sugars, syrups, honey and table-top sweeteners; salts, spices, soups, sauces, salads and protein products; foods intended for particular nutritional uses as defined by Directive 2009/39/EC; beverages; ready-to-eat savouries and snacks; desserts excluding products covered in earlier categories; food supplements; processed foods not covered in earlier categories, excluding foods for infants and young children. The count does not include category '0' which is for additives that can be used in all foods.

¹²¹ Defined in Article 3 of Regulation 1333/2008 as "a food which has not undergone any treatment resulting in a substantial change in the original state of the food, for which purpose the following in particular are not regarded as resulting in substantial change: dividing, parting, severing, boning, mincing, skinning, paring, peeling, grinding, cutting, cleaning, trimming, deep-freezing, freezing, chilling, milling, husking, packing or unpacking"

¹²² Food additives were previously regulated under Council Directive 89/107/EEC on the approximation of the laws of the Member States concerning food additives authorised for used in foodstuffs intended for human consumption. This Directive was amended by European Parliament and Council Directive 94/34/EC (OJ 1994 L 234/1).

intake (ADI) or equivalent assessment and the estimated daily intake (EDI)¹²³, including situations in which the food additive is to be used in foods expected to be eaten by certain groups of consumers.

In some situations, no maximum level of use is set for a food additive (quantum satis)¹²⁴. Quantum satis literally means ‘the amount that satisfies’ and essentially means the amount that is necessary to achieve the desired result, but not any more than that.

Additives approved to be used under quantum satis conditions are those of low concern, such as calcium carbonate (E 170), lactic acid (E 270), citric acid (E 330), pectins (E 440), fatty acids (E 570) and nitrogen (E 941). However, some additives are allowed only under restricted conditions, for example, natamycin (E 235), erythorbic acid (E 315) and sodium ferrocyanids (E 535). Natamycin is approved only as a preservative for the surface treatment of cheese and dried sausages, erythorbic acid is approved only as an antioxidant in some meat and fish food products and sodium ferrocyanids are approved only as anti-caking agents in salts and salt substitutes¹²⁵.

As an example of how these maximum levels appear in the Regulation, see Figure 2 below.

E-number	Name	Maximum level (mg/l or mg/kg as appropriate)
Bakery wares		
Bread and rolls		
Group I	Additives	
E 150a-d	Caramels	<i>quantum satis</i>
E 200-203	Sorbic acid — sorbates	2 000
E 280-283	Propionic acid — propionates	3 000

Figure 2. Example of maximum level limits in Annex II of Regulation 1333/2008

Additionally, food additives are allowed under one of the following situations which are covered by the carry-over principle¹²⁶

- a) in a compound food other than as referred to in Annex II, where the food additive is permitted in one of the ingredients of the compound food

¹²³ The ADI and EDI are established, when possible, by EFSA during the safety evaluation. The ADI is the amount of a substance that people can consume daily for a lifetime, usually expressed in mg/kg bw/day (bw=body weight). <<http://www.efsa.europa.eu/en/topics/topic/additives.htm>>

¹²⁴ Article 11 Regulation 1333/2008

¹²⁵ DG Sanco Questions and Answers on Food Additives

<http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/11/783&format=HTML&aged=0&language=EN&guiLanguage=en>

¹²⁶ Article 18 Regulation 1333/2008

- b) in a food to which a food additive, food enzyme or food flavouring has been added, where the additive:
 - i. is permitted in the food additive, food enzyme or food flavouring in accordance with Regulation 1333/2008
 - ii. has been carried over to the food via the food additive, food enzyme or food flavouring; and
 - iii. has no technological function in the final food
- c) in a food which is to be used solely in the preparation of a compound food and provided that the compound food complies with this Regulation

The carry-over principle does not apply to infant formulae, follow-on formulae, processed cereal-based foods, baby foods and dietary foods for special medical purposes intended for infants and young children as referred to the specific legislation covering these products.

- d) if there are any restrictions on the sale to the final consumer

Additionally, when approved for inclusion in the Community list under Annex II or III, a food additive may be assigned to a functional class in Annex I of Regulation 1333/2008 based on its main technological function. However, this is not a restriction for the use of the additive¹²⁷.

This extensive approval process ensures that food additives on the market are safe, serve a technological purpose and are not misleading. Since scientific information on safety in particular may constantly be changing, some additives must be re-evaluated after a certain period of time.

4.6 Re-evaluation program

Regulation 1333/2008 states that food additives should be kept under continuous observation due to changes in conditions of use and new scientific information¹²⁸. It also established that EFSA must re-evaluate the safety of all food additives that were already permitted in the EU before 20 January 2009. This is because most of the permitted additives were authorised as far back as the 1980s and 1990s, and even some in the 1970s and scientific studies and information have been updated in some cases. Based on the re-evaluations, some of the additives may need to be removed from the Community list, or their conditions of use may need to be modified. In addition, EFSA was required to develop and adopt an evaluation program by 20 January 2010¹²⁹.

The resulting Commission Regulation (EU) No 257/2010¹³⁰ set up a program for the re-evaluation of previously approved food additives. Priorities were established to evaluate the additives within a certain order and to meet certain deadlines, as follows:

¹²⁷ Article 9(1) Regulation 1333/2008

¹²⁸ Recital 14

¹²⁹ Article 32(1) Regulation 1333/2008

¹³⁰ Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives

- The re-evaluation of previously approved food colors (under Directive 94/36/EC¹³¹) must be completed by 31 December 2015
- The re-evaluation of all additives other than colors and sweeteners (under Directive 95/2/EC¹³²) must be completed by 31 December 2018
- The re-evaluation of previously approved sweeteners (under Directive 94/35/EC¹³³) must be completed by 31 December 2010

When the EFSA ANS panel developed its own criteria for setting re-evaluation deadlines for the various types of additives, it took additional information beyond the priorities in Regulation 257/2010 into account as follows:

- New scientific or technical information since the original evaluation or last assessment
- The length of time since the last evaluation
- Cases for which no ADI or a temporary ADI was established, or if the basis for the previously established ADI was unclear

The revised deadlines, largely based on functional class, are as follows:

- Most food colors - by 31 December 2011
- Aspartame - by September 2012 - this re-evaluation was advanced due to recently published new scientific data
- Remaining colors – by 31 December 2015
- Preservatives, antioxidants, glutamates, silicon dioxide - by 2015 -2016;
- Other sweeteners - by 31 December 2020;
- All other additives - by 31 December 2018

Of course EFSA may at any moment push forward the priority of an additive and begin its re-evaluation if scientific evidence emerges that the additive may pose a human health risk or may affect the safety assessment of that additive¹³⁴.

EFSA must examine various documents when re-evaluating food additives, including the original opinion and working documents of the SCF or EFSA, the original dossier, the data submitted by business operator(s) or other parties, any data from the Commission and Member States, and any relevant literature published since the last evaluation. The re-evaluation should be done according to risk assessment (European Food Safety Authority 2010c).

In order to receive the data from business operator(s) or other parties, EFSA must establish calls for data of the food additives. Relevant data include study reports from the original dossier, information on the safety of the additive not previously reviewed by the SCF or JECFA, information on the specifications, information on the manufacturing process,

¹³¹ European Parliament and Council Directive 94/36/EC of 30 June 1994 on colours for use in foodstuffs. OJ L 237/13, 10.9.94, <<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1994:237:0013:0029:EN:PDF>>

¹³² European Parliament and Council Directive 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners. OJ L 61/1, 18.3.95. <<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1995:061:0001:0040:EN:PDF>>

¹³³ European Parliament and Council Directive 94/35/EC of 30 June 1994 on sweeteners for use in foodstuffs. OJ 237, 10.9.1994. <<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1994L0035:20060815:EN:PDF>>

¹³⁴ Article 3(3) Regulation 257/2010

information on the analytical methods, information on the human exposure and the reaction and fate in food¹³⁵.

Since the re-evaluation programme has been in place, the conditions of use of three food colours have been adjusted. EFSA lowered the ADI and thus the maximum levels allowed in foods of E 104 Quinoline yellow, E 110 Sunset Yellow and E 124 Ponceau 4R.

Additionally, EFSA evaluated 11 smoke flavorings, substances which are used in foods such as meat, fish and cheese to give them a smoke flavor (versus treating them with traditional smoking procedures). It was found that two of the flavorings are considered safe, eight posed safety concerns and one could not be evaluated due to inadequate data. The review of these smoke flavorings was actually the first of its kind in the European Union—these substances had never been evaluated before. The work will result in a positive list for smoke flavorings (European Food Safety Authority 2010b).

4.7 Labeling requirements

Labeling of food additives must be in accordance with Regulation 1169/2011 (which applies from 13 December 2014) on the provision of food information to consumers¹³⁶. This Regulation states that food additives must be included in ingredient lists on food packaging, indicated by their functional class (antioxidant, preservative, color, etc) along with their specific name or E number.

In addition, table-top sweeteners containing polyols must be labelled with the warning “excessive consumption may induce laxative effects” and those containing aspartame and/or aspartame-acesulfame salt with “contains a source of phenylalanine.”¹³⁷

There are, however, a few exceptions to the mandatory labeling rule. A food additive does not have to be included in the list of ingredients if it is present in food due to the carry-over principle. Additionally, if a table-top sweetener includes “xxx-based table-top sweetener” in the title on its label, with xxx indicated the name of the sweetener(s) present in the product, the E number does not have to be included on the label (Food Safety Authority of Ireland 2010).

4.8 Flavoring definition and approval process

In order to provide a more complete picture of premarket approvals in the EU and to better compare the system with the US, the definitions and requirements of some other products are discussed.

Flavorings are covered under a separate Regulation, No 1334/2008¹³⁸. A ‘flavoring’ is defined as a product which is added to foods in order to impart or modify odour and/or taste.

¹³⁵ Article 5(2) Regulation 257/2010

¹³⁶ Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004

¹³⁷ Article 23 Regulation 1333/2008

It consists of various categories, such as flavoring substances, flavoring preparations, thermal process flavorings, smoke flavorings and flavor precursors.

Flavorings under the meaning of this Regulation include flavorings used in foods, food ingredients with flavoring properties, and source materials for and foods containing the former two substances (Article 2). The Regulation does not apply to substances which have exclusively a sweet, sour or salty taste; raw foods, and non-compound foods and mixtures such as spices, herbs and teas (Article 2). It also does not apply to smoke flavorings (which are covered by Regulation (EC) No. 2065/2003).

In order to be approved for use, flavorings and food ingredients with flavoring properties must meet two requirements: not unsafe and not misleading to the consumer (Article 4). These two requirements are also mandatory for food additives to be placed on the market. However, additives must meet an additional criterion, which is that they serve a technological purpose which has a benefit for the consumer. It was demonstrated above that flavors are not considered to have a technical function that is included in the scope of the additive definition. The approval procedure is the same for that of food additives as it is also covered in Regulation 1331/2008.

4.9 Enzyme definition and approval process

Food enzymes not used in the production of food additives are covered under Regulation 1332/2008 on food enzymes¹³⁹. Food enzymes are defined as a product obtained from plants, animals or microorganisms which contains enzymes capable of catalyzing a specific biochemical reaction and which is added to food for a technological purpose during manufacturing, processing, preparation, treatment, packaging, transport or storage of foods. They are different from food additives because they have specific biochemical actions which serve technological purposes, but they do not typically become components of food and instead are used as processing aids.

The Regulation does not apply to enzymes that are used for a function that is not technological, such as those added for nutritional or digestive reasons. Additionally, microbial cultures which may produce enzymes, such as those used in the production of cheese and wine, are not included.

Food enzymes must meet three conditions to be placed on the market: not pose a safety concern, meet technological need and not mislead the consumer. All enzymes must undergo premarket approval before they can be used in foods, again, under the same approval process stated in Regulation 1331/2008.

¹³⁸ Regulation (EC) No 1334/2008 of the European Parliament and of the Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Council Regulation (EEC) No 1601/91, Regulations (EC) No 2232/96 and (EC) No 110/2008 and Directive 2000/13/EC

¹³⁹ Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on food enzymes and amending Council Directive 83/417/EEC, Council Regulation (EC) No 1493/1999, Directive 2000/13/EC, Council Directive 2001/112/EC and Regulation (EC) No 258/97

4.10 Novel food definition and approval process

The concept of a food additive is much broader in the US than it is in the EU. In order to better compare and contrast the two systems and better understand premarket approvals of foods and food ingredients, novel foods in the EU are discussed. Regulation 258/97¹⁴⁰, the so-called Novel Foods Regulation, addresses placing novel foods or novel food ingredients on the market. To be considered novel in the EU, food has to meet two criteria: it must not have been used to a significant degree within the Community before the passage of the Regulation, and it must fall into one of the following categories¹⁴¹:

- Foods and food ingredients with a new or intentionally modified structure
- Foods and food ingredients consisting of or isolated from microorganisms, fungi or algae
- Foods and food ingredients consisting of or isolated from plants and food ingredients isolated from animals, except for foods and food ingredients obtained by traditional propagating or breeding practices and having a history of safe food use
- Foods and food ingredients to which has been applied a production process not currently used, where that process gives rise to significant changes in the composition or structure of the foods or food ingredients which affect their nutritional value, metabolism or level of undesirable substances.

It is important to note that the Regulation does not apply to food additives, flavorings and enzymes¹⁴². Thus, even if a food additive is novel, it is regulated as a food additive.

Novel foods and food ingredients must meet three primary requirements to be approved; they must not: present a danger, mislead the consumer, and differ from those foods or ingredients which they are intended to replace to such an extent that their normal consumption would be nutritionally disadvantageous for the consumer¹⁴³.

Novel foods are initially assessed by the Member State where they will be first marketed. The national competent authority receives the application and performs the risk assessment, and the Commission makes the decision. If it or if any of the other Member States object to or have questions about the initial assessment, an additional assessment is performed by EFSA, after which the Commission and SCoFCAH make the decision. Applications under the NFR and their decisions can be found at http://ec.europa.eu/food/food/biotechnology/novelfood/app_list_en.pdf

However, products that fall into the second or third categories of novel foods above may have the option to bypass the formal application procedure if the novel products are substantially equivalent to existing products. Instead, the applicant must notify the Commission when the product is placed on the market¹⁴⁴. Since novel foods are authorized exclusively (only the

¹⁴⁰ Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients

¹⁴¹ Regulation 258/97 Article 1(2)(c)-(f)

¹⁴² Article 2(1) Regulation 258/97

¹⁴³ Article 3(1) Regulation 258/97

¹⁴⁴ Article 3(4), Article 5

applicant may market the product), this notification procedure can be used when a business markets a product that is already on the market from another company.

Foods are considered novel if they were not used in the EU before 15 May 1997. Therefore, so-called exotic foods that were consumed significantly, even for hundreds of years, outside of the EU but did not enter the market by this date are still considered novel and have to undergo the approval procedure. A proposal was issued to replace the current NFR with an updated one (Commission of the European Communities 2008). Currently, foods from other countries are considered novel in the EU and regulated accordingly. The proposed version would allow the product to be placed on the market with only a notification for these products if there are no safety objections by the Member States or EFSA. However, the proposal failed because an agreement could not be reached concerning cloned animals (Council of the European Union 2011).

4.11 GMOs

Genetically modified foods in the EU have been covered under Regulations 1829/2003 and 1830/2003 concerning genetically modified foods since 2003¹⁴⁵. The Regulation covers genetically modified organisms (GMOs) for food use, food containing or consisting of GMOs and food produced from or containing ingredients produced from GMOs¹⁴⁶.

Genetically modified food additives must meet the requirements of both Regulation 1333/2008 and Regulation 1829/2003. According to Recital 12 of the GMO Regulation, a food additive which falls within the scope of the Regulation must be first authorized as a GMO before being authorized under the additive legislation (Food Safety Authority of Ireland 2010).

Requirements for GMO products, according to Article 4(1), are that they must not have adverse effects on human or animal health or the environment, mislead the consumer, or differ from the food which it is intended to replace to the extent that it would be nutritionally disadvantageous for the consumer. An overview of the approval process is given below, which is described on the Commission website¹⁴⁷.

An application for authorizing food or feed consisting of or made from a GMO must be submitted to the national authorities. The application (Regulation 1829/2003) must include:

- Purpose and scope;
- All relevant data, studies and analysis of the results;
- Monitoring plan;
- Labeling proposal;
- Detection method;
- Indication of confidential information;

The national authority acknowledges receipt of the application within 14 days. It then sends the application to EFSA for a risk assessment. This is normally performed within 6 months of

¹⁴⁵ Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. OJ L 268/1, 18.10.2003 <

http://ec.europa.eu/food/food/animalnutrition/labelling/Reg_1829_2003_en.pdf >

¹⁴⁶ Article 3(1) Regulation 1829/2003

¹⁴⁷ http://ec.europa.eu/food/plant/gmo/authorisation/final_decision_en.htm

receiving the application. EFSA then makes the application summary available to the public, who may comment, and publishes a scientific opinion in the EFSA Journal. EFSA submits its opinion to the European Commission and to EU countries.

If the application covers cultivation, EFSA delegates the environmental risk assessment to an EU country which sends EFSA its risk assessment report. The procedure is slightly different under Directive 2001/08/EC. Companies must apply to the competent authority of the EU country where the GMO is going to be marketed for the first time. That country prepares an assessment report within 90 days. It sends the application to EFSA if at least one other EU country reasonably objects to the assessment report.

Within 3 months of receiving EFSA's opinion, the Commission grants or refuses the authorization in a proposal. If it differs from EFSA's opinion, it must explain why. Authorizations are valid for 10 years (renewable).

Regulation of GMOs in the US and in the EU is thus very different. The EU takes the approach that the *process* of biotechnology triggers regulation. On the other hand, the US believes that the *product*, rather than the process, must be regulated. The product itself is also evaluated in the EU, but it is the process of biotechnology which leads to a certain approval process, whereas in the US a GM product is evaluated as any conventional food. The comparable safety standard is applied: if a GM product is not different than a conventional product, then it can be regulated as one and escape the premarket approval process (Anker and Grossman 2005).

5 Comparative Analysis and Discussion

5.1 Scope of the definitions

The concept of a food additive in both the US and EU includes and excludes certain categories of substances (see table 3). Certain fundamental categories of food ingredients are classified as food additives in both the EU and US, the EU but not the US and the US but not the EU. Table 3 offers a clear representation of what types of substances are considered food additives in the two places. In cases where a category of substances is not regulated as a food additive, it is regulated as something else; otherwise it may be perceived from the table that the EU does not regulate many types of substances, which is certainly not the case. The classifications of these different categories result in different scopes of the food additive concepts.

The US has a broader interpretation, primarily because it includes substances that can become a component of food *or* that affect the characteristics of food (e.g. irradiation, enzymes). The EU definition only includes substances which become a component of food. However, some other substances which would normally be classified as food additives are outside the scope in the US if they are generally recognized as safe. Despite these different classifications of other substances, the “core” definition of a food additive in the EU and US is essentially the same, which is that the additive must have a technological effect in the food. This interpretation makes the concepts closer than they initially appeared to be. In the EU definition of a food additive, the technological effect is explicitly stated as a requirement. In the US definition, it is more hidden. The additive definition does not state anything about having a technological effect, but rather the information on food contact substances provides a clue. Legislation on food contact substances states that they can be exempt from regulation as food additives if they do not have a technical effect. This therefore implies that food additives have a technical effect in foods. However, what exactly is included in the concept of technological appears to differ. The US (and Codex Alimentarius) consider imparting flavor and taste to be a technological function. However, the EU appears to exclude this from the concept of a technological function: it states that flavorings and other substances which impart taste are not additives.

The three criteria that food additives in the EU must meet are 1) safe, 2) not misleading and 3) technological functional which serves a benefit to the consumer. The two criteria that food additives in the US must meet are 1) safe and 2) not misleading¹⁴⁸. As discussed above, although the US does not specifically state that additives must serve a technological function, the scope appears to be similar.

The other two requirements of safe and not misleading are not necessarily the same. While the definitions of safety have relatively the same meaning (not injurious to health or unfit for human consumption in the EU and not harmful under the intended conditions of use in the US), they are still quite vague and open to interpretation. The situation is the same with being misleading or deceptive to the consumer. The questions become: how safe is safe?, and how misleading is misleading? It is up to the authorities and the courts in both jurisdictions to decide. In the author’s opinion, the US tends to be more lenient in these aspects, for example,

¹⁴⁸ The actual wording is not deceptive to the consumer.

by having the GRAS exemption, giving exotic products from other countries market access, approving carbon monoxide for use in meat and having more lenient standards for GMO approval. This is further discussed in section 5.4.

Additionally, it is also important to remember that while the EU states that its additives must meet the three main requirements listed above, the “approval of food additives should also take into account other factors relevant to the matter under consideration including societal, economic, traditional, ethical and environmental factors, the precautionary principle and the feasibility of controls”¹⁴⁹. All of these factors can also play a role in determining if a substance should be approved or not. An example of this in approvals (in general) in the EU is with hormones. Although the EU’s scientific studies showed no evidence that hormones are unsafe, they were restricted based largely on public opinion. An example of the role that the traditional factor plays in food additive approval is in the traditional foods from Member States which are exempt from the typical approval of food additives.

The two systems are fairly similar in their approval characteristics: all additives and other ingredients approved can be approved only under certain conditions, such as in which foods they may be used and if there are any maximum limits. Maximum limits are typically based on the ADI. For additives which do not need such restrictions, they are generally to be used according to quantum satis, meaning at a level no higher than is needed to achieved the desired effects and according to good manufacturing practices (GMPs).

The US and EU do have different regulatory approaches to approving new food additives and other substances (Anker and Grossman 2005). The US has a focus on the product: it looks at each food or food ingredient and determines if the final product is safe and can be approved. The EU has a focus on the process: a certain method of producing a product can trigger premarket approval. Substances may be classified into different groups based on the way in which they were produced (as is the case with GMOs and novel food categories), rather than the final product itself. However, this is not always the case: additives and other substances are often times approved with a focus on the product itself.

In addition, a substance in the US may actually fall under multiple categories: it can be a food additive for one particular use, and a GRAS substance for another. A few notable examples: carbon dioxide is classified as a pesticide chemical when it is used for insect control and a GRAS substance when it is used as a leavening agent, processing aid or propellant; diatomaceous earth (derived from algae) is classified as a pesticide chemical when it is used for insect control, a food additive when it is used as a carrier or an anti-caking agent (in animal feed) and a GRAS substance when it is used as part of a filtration media (for human food). Lastly, there is the United States v. Coco Rico (1985) case, in which potassium nitrate classified as a prior-sanctioned substance for use in meats was considered unauthorized when used in beverages. A company marketed a beverage concentrate containing potassium nitrate to help maintain color and flavor. The FDA seized the beverages and declared that they were adulterated since potassium chloride is an unapproved food additive. The company argued that nitrates and nitrites are not food additives since they are prior sanctioned. However, they are prior sanctioned for use in meat, but not in beverages. Coco Rico defended themselves by arguing that there is no conclusive evidence that the use of potassium nitrates in beverages is unsafe, and that nitrates have been approved for use in meat, and they know of no difference

¹⁴⁹ Recital 7 Regulation 1333/2008

in health effects between potassium nitrate used in meat and in beverages. However, the courts declared that the argument was invalid: approval of a prior-sanctioned substance (or GRAS substance or food additive) in one food does not make it approved in another food for another use.

While substances in the EU can also be classified as different products for different uses, it is not nearly as common as in the US. An example in the EU is that of vitamin C/ascorbic acid. When ascorbic acid is used for its functional properties (e.g. antioxidant), it is considered an additive and must be labelled as such (e.g. with an E number). However, when vitamin C is added to foods for nutritional purposes, it is classified as that and not as an additive.

5.1.1 What is included as an additive

Table 3. Substances which are classified and regulated as food additives

Substance	US	EU	Explanation
With a technological function	✓	✓	Defining criterion in both concepts of a food additive.
Feed additives	✓		The reason why feed additives are classified as food additives in the US is because feed itself is included in the definition of food. Feed is however not considered food in the EU ¹⁵⁰ , and feed additives are instead regulated under Regulation 1831/2003 ¹⁵¹
GMOs	✓		GMOs in the US are regulated as either additives or GRAS substances. In the EU, the process, not the products, of genetic modification is regulated; GMOs are covered under Regulations 1829/2003 ¹⁵² and 1830/2003 ¹⁵³ , among others.
Flavorings	✓		Flavorings may be regulated in the US as food additives or GRAS substances depending on the level of scientific evidence. In the EU imparting flavor is not considered a technological effect; flavourings are instead covered under Regulation 1334/2008 ¹⁵⁴
Enzymes	✓		Enzymes may be regulated in the US as food additives or GRAS substances depending on the level of scientific evidence. They are not additives in the EU because they do not become a component of foods, and are covered under Regulation 1332/2008 ¹⁵⁵
Irradiation	✓		Has a technological function, but is not a substance which can become a component of food (instead it affects the characteristics). Covered under EU Directive 1999/2 ¹⁵⁶ and Directive 1999/3 ¹⁵⁷ .
Migrants from packaging	✓	✓	May be additives or food contact substances (US) and additives or processing aids (EU) depending on effect in product. In the US also may be covered under the food contact substance notification and in the EU under Regulation 1935/2005 ¹⁵⁸
Food contact substances	(?)		No technological function. In the US it was discussed that while they are listed in the food additive section of the legislation, they have a different definition and a different regulatory process. Covered under the food contact substance notification (US) and various legislation summarized on the Commission website ¹⁵⁹ (EU)
Colors		✓	Specific exclusion in the US, perhaps due to the broad scope of color additives (use in other products besides food) or stricter approval requirements. Covered under 21 CFR parts 73, 74, 81, 82 ¹⁶⁰
Novel foods	(✓)		Whole foods in the US are not regulated; instead the components are. The components may be regulated as food additives or GRAS substances depending on the level of scientific evidence. In the EU, novel foods are regulated as a separate category because they are not substances which can have a technological effect in a food, and are covered under Regulation 258/97.

¹⁵⁰ “Feed” is defined in Article 3.4 of the GFL as “any substance or product, including additives, whether processed, partially processed or unprocessed, intended to be used for oral feeding to animals”. The definition of “food” also specifically exempts feed.

¹⁵¹ <http://eur-lex.europa.eu/Notice.do?val=522346:cs&lang=en&list=522346:cs.&pos=1&page=1&nbl=1&pgs=10&hwords=>

¹⁵² <http://eur-lex.europa.eu/Notice.do?val=472875:cs&lang=en&list=472875:cs.&pos=1&page=1&nbl=1&pgs=10&hwords=>

¹⁵³ <http://eur-lex.europa.eu/Notice.do?val=490336:cs&lang=en&list=490336:cs.&pos=1&page=1&nbl=1&pgs=10&hwords=>

¹⁵⁴ <http://eur-lex.europa.eu/Notice.do?val=725061:cs&lang=en&list=725061:cs.&pos=1&page=1&nbl=1&pgs=10&hwords=>

¹⁵⁵ <http://eur-lex.europa.eu/Notice.do?val=694112:cs&lang=en&list=694112:cs.&pos=1&page=1&nbl=1&pgs=10&hwords=>

¹⁵⁶ <http://eur-lex.europa.eu/Notice.do?val=488147:cs&lang=en&list=488147:cs.&pos=1&page=1&nbl=1&pgs=10&hwords=>

¹⁵⁷ <http://eur-lex.europa.eu/Notice.do?val=330208:cs&lang=en&list=330208:cs,414784:cs.&pos=1&page=1&nbl=2&pgs=10&hwords=ec~>

¹⁵⁸ <http://eur-lex.europa.eu/Notice.do?val=330208:cs&lang=en&list=330208:cs,414784:cs.&pos=1&page=1&nbl=2&pgs=10&hwords=ec~>

¹⁵⁹ http://ec.europa.eu/food/food/chemicalsafety/foodcontact/legisl_list_en.htm

¹⁶⁰ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm>

5.2 Premarket approval process comparison

5.2.1 Generic vs. exclusive

Approval of food additives in both the US and the EU is generic, meaning that once approved, any business can market them. In fact, approvals of all the types of substances discussed in this paper are generic, except for that of novel foods in the EU and food contact substances in the US, which are exclusive¹⁶¹.

5.2.2 Positive list

Approved food additives in the EU are placed on a positive list—only those on the list are allowed to be used in food products on the market. Additive applications must undergo a safety evaluation by EFSA and be approved by the Commission and the SCoFCAH in order to secure a spot in the list. The positive list—or Community list as it is called in the EU—can be found in Annexes II and III to Regulation 1333/2008.

The US, on the other hand, applies a pseudo positive list system for food additives. A substance that falls under the food additive definition is presumed to be unsafe unless its safety can be demonstrated in a premarket approval. All additives marketed in the US must undergo an evaluation procedure by the FDA and a regulation must be issued before they are allowed on the market. However, the system is described as “mixed” because substances regarded as GRAS are not subject to premarket approval and may be placed on the market with or without notifying the FDA. This somewhat resembles a negative list, in which any additive can be used as long as it is not explicitly forbidden. Approved additives and “approved” GRAS substances can be found in FDA databases and in the CFR.

¹⁶¹ In the EU, food contact substances are approved generically

5.2.3 Levels of scientific evidence that meet the standards for approval

Table 4. Information required in the safety/risk assessments

Data and information submitted	EU food additives, flavorings and enzymes	US food additives	US GRAS substances¹⁶²
Proposed uses	Proposed normal and maximum use levels, exposure assessment	Directions, recommendations, suggestions for proposed use; proposed labeling; exposure assessment	Foods in which it is to be used; purposes of use; levels of use; if necessary, a description of the expected consumer group
Categories of scientific data	<p>Toxicokinetics, subchronic toxicity, genotoxicity, chronic toxicity/carcinogenicity, reproductive and developmental toxicity</p> <p>3-tiered approach which balances data requirements against the risk: Tier 1 requires a minimum dataset for all compounds. For those which are absorbed, demonstrate toxicity or genotoxicity, Tier 2 tests are required to gather more information. If Tier 2 results raise concerns for any specific endpoints, Tier 3 testing is required. These tests are intended to give information on any possible negative short-term or long-term effects of the additives, such as if they have the potential to cause cancer, affect reproduction, etc.</p>	Genetic toxicity, acute oral toxicity, short-term toxicity, subchronic toxicity, carcinogenicity, chronic toxicity/carcinogenicity, reproduction and developmental toxicity	Same as US food additives
Level of evidence required	The application dossier should include all the available data relevant for the purpose of the risk assessment (i.e. full published papers of all references cited, full copies of	Submit full reports of all available unpublished toxicity studies on the petitioned substance as well as published toxicity studies pivotal to the safety assessment. Submit the results of a	A discussion of generally available and accepted scientific evidence regarding animal and human safety. The data should be sufficient to show that the

¹⁶² For the purposes of this table the standards required under the GRAS notification procedure are used, as this is what the FDA is currently operating under. Additionally, although there are two types of GRAS categories (by scientific evidence or common use in food), only substances classified as GRAS from scientific evidence are discussed as those from common use require information on consumption of the substance, etc. instead.

	<p>the original report of unpublished studies and corresponding individual raw data). The documentation on the gathering of the data used in the dossier should also be provided. This documentation should specify the data gathering conducted and especially the literature search strategies (assumptions made, key words used, databases used, limitation criteria, etc.). In compiling the data in the submission, applicants should also seek to interpret the data and draw conclusions. The significant findings of each study (both commissioned and published) should be highlighted, including animal data.</p> <p>See the EFSA guidance for food additive submissions (2012)¹⁶³ for more details on the data required.</p>	<p>toxicological literature search on the additive and major impurities along with the search parameters that were used. Include data that will allow the reviewer to independently evaluate and verify the results claimed. For example:</p> <ul style="list-style-type: none"> • the raw data on the concentration and stability of the test substance as administered, • the individual animal data for all endpoints, and • the pathologist's narrative and summary tables of non-neoplastic and neoplastic lesions. <p>See the FDA Redbook (2000)¹⁶⁴ for details on the toxicity studies.</p>	<p>substance is generally recognized to be safe. Only a summary of the information used to make this decision is required. Original studies and data are only submitted if requested by the FDA.</p>
Testing	<p>Toxicological studies should be carried out with the additive meeting the proposed specifications and manufactured as described in the application. Provide evidence that the requirements of the OECD principles are followed, or a justification of why another method was used.</p>	<p>A description of practicable methods for determining the quantity in or on food; any substance formed in or on food because of its use. Full reports of investigations made with respect to the safety for use of such additive, including full information as to the methods and controls used in conducting such investigations.</p>	<p>Only a discussion/summary of the scientific information, including testing, is required.</p>

The level and scope of scientific information for food additives in the EU and in the US are essentially equal.

¹⁶³ <http://www.efsa.europa.eu/en/efsajournal/doc/2760.pdf>

¹⁶⁴ <http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditivesGRASPackaging/ucm2006826.htm>

5.2.4 Who makes the decision?

In premarket approval situations, businesses typically have to file an application with the authorities for approval, and cannot market the product until the approval is obtained. This is the case in the EU for food additives (and many other substances) and in the US for food additives as well. However, the GRAS notification procedure in the US gives businesses the option to “self-approve”. They can determine the safety of their own foods and food ingredients, and based on their judgments, place the product(s) on the market—without the approval or even knowledge of the FDA. The FDA thus allows non-FDA scientists to evaluate products in place of doing it themselves.

Neltner et al. launched an investigation into FDA’s control over food ingredients in its jurisdiction. The authors looked at 10,000 chemicals, and estimated that over 3,000 never went through an FDA review and the FDA did not receive a notification for at least 1,000 of them. Many of the others are flavors and were determined by an expert panel (FEMA) to be safe. Thus the FDA has no information on 10% of the substances added to food in the US. The authors also stated the possibility of this interesting scenario: A business can submit a GRAS notification to the FDA with a summary of its evaluation findings. If the FDA, as it often does, returns questions to the applicant, and it appears as though the business may receive a letter stating that the substance cannot be approved as GRAS, it may voluntarily withdraw the notification. However, since it is not required to actually submit a notification to the FDA, the business may decide to not resubmit and market the product anyway. Although this is unlikely to happen, it is theoretically possible. In regards to who would be responsible or liable for the damage caused in this event, there is currently no clear answer. The law states that foods must not be adulterated, but whether it is defined by the damages or the product’s status it unknown. So far the FDA has tried to shift responsibility of damages to businesses, however, but no situation has yet reached this level.

5.3 Comparison with Codex Alimentarius and JECFA

The Codex Alimentarius Commission (CAC) was established by the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) in 1963. Since then it has served as an organization that develops international food standards, guidelines and codes of practice to improve the safety and quality of food that is imported and exported around the world. Codex standards and other documents are based on advanced science from independent international risk assessment organizations or other groups from FAO or WHO.

For food additives and other substances that may be present in food, the CAC performs the following tasks:

- Elaborates principles for evaluating their safety and for quantifying their risks
- Conducts toxicological evaluations and establishes Acceptable Daily Intakes (ADIs) or tolerable intakes for chronic exposure and other guidance values for acute exposure
- Assesses the performance, quality and applicability of analytical methods
- Prepares specifications of purity for food additives
- Assesses exposure of populations to chemical substances in food

Codex standards are voluntary and not binding; they can be used to develop a common language, and countries have the choice to adopt them or not. They can, and often do, serve

as a basis for national legislation. However, they do gain some legal status in the World Trade Organization (WTO) arena. The WTO agreement on Sanitary and Phytosanitary measures (SPS Agreement) gives reference to Codex food standards. It states that WTO members that follow Codex standards are not required to justify their sanitary and phytosanitary measures. On the other hand, they must prove the scientific basis for any measures not based on Codex standards (Van der Meulen and van der Velde 2008). As 99% of countries around the world are members of the Commission, Codex clearly has an impact on international food trade.

Codex defined a food additive as (Codex Alimentarius 2012b):

any substance not normally consumed as a food by itself and not normally used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition of which to food for a technological (including organoleptic¹⁶⁵) purpose in the manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food results, or may be reasonably expected to result (directly or indirectly), in it or its byproducts becoming a component of or otherwise affecting the characteristics of such foods. The term does not include contaminants or substances added to food for maintaining or improving nutritional qualities.

This is strikingly similar to the definition of a food additive in the EU. However, the EU excludes organoleptic purposes from its definition. In order to find out which came first and which was based on the other, a look was taken to the history of the legislation. The definition first appears in the Codex Alimentarius in the 3rd edition of the Codex Alimentarius Commission Procedural Manual¹⁶⁶, which is from 1973. A definition of a food additive in EU legislation appears in Directive 89/107, so it is clear that the EU based its definition on the Codex one. The American definition is different from both the EU and Codex definitions (it came first). Since the EU definition came after the Codex definition, it is evident that the EU based its on the Codex one, and therefore explicitly decided to not include organoleptic purposes as a technological function.

Additionally, Codex states that the use of food additives is justified “only when such use has an advantage, does not present an appreciable health risk to consumers, does not mislead the consumer, and serves one or more of the technological functions” as listed below:

- a. To preserve the nutritional quality of the food
- b. To provide necessary ingredients or constituents for foods manufactured for groups of consumers having special dietary needs;
- c. To enhance the keeping quality or stability of a food or to improve its organoleptic properties
- d. To provide aids in the manufacture, processing, preparation, treatment, packing, transport or storage of food

¹⁶⁵ Organoleptic is not included specifically in the EU definition of a food additive, however. Organoleptic is defined as “being, affecting or relating to qualities (as taste, color, odor, and feel) of a substance (as a food or drug) that stimulate the sense organs”(http://www.merriam-webster.com/dictionary/organoleptic)

¹⁶⁶ http://ftp.fao.org/codex/Publications/ProcManuals/Manual_03e.pdf

The CAC can request for scientific advice from the Joint FAO/WHO Expert Committee on Food Additives (JECFA), which can develop international food standards and guidelines as part of the Joint FAO/WHO Food Standards programme. JECFA serves as an independent scientific expert committee that conducts risk assessments and provides advice also to the FAO, WHO and member countries of the organizations (Codex Alimentarius 2013). It evaluates the safety of food additives, processing aids, flavoring agents, animal drug residues and contaminants, among others. To date, JECFA has evaluated over 2600 food additives alone (WHO 2013). In addition to performing risk assessments, JECFA also develops principles for safety assessments. The Committee has been meeting since 1956, with meetings normally twice a year (FAO 2012).

5.4 Possible sources of the differences

It has been discussed that the EU is more cautious than the US regarding new food products. Perhaps this difference arises from the way that the legislation and the government agencies were created and structured, or to meet consumer demands.

First a theoretical approach is taken. Two types of legal systems are civil law and common law. Civil law is a system in which the laws are written down in legal documents in a logical and organized way. Problems are foreseen and rules are created in anticipation to prevent and solve these issues. It is a “top-down” system. On the other hand, common law is created by taking decisions in reaction to problems that arise. The law is thus not created in anticipation but rather develops as necessary. Judicial decisions taken to deal with these problems make up the laws. It is a “bottom-up” system. Although both the US and EU have some elements of each legal system, in general, the EU takes a civil approach, whereas the US a common law one. Civil law systems are more cautious because the rules are laid out before rather than created in reaction to problems (Van der Meulen and van der Velde 2008)¹⁶⁷.

A look at the legislation shows how these different approaches are represented in both the EU and US. In the EU, the legislation on additives and other novel substances is most often clearly laid out in directives and regulations. When the information has to be updated, the document is amended, but when there are many changes to the legislation, a new directive or regulation is created. Although this is sometimes the case in the US, often times alternative legislation is created in response to new developments, although there is never really a major overhaul. An excellent example of this is with GRAS regulation. Although officially GRAS substances have to be approved through an affirmation process, FDA has been operating under the unofficial notification procedure since 1997—and 16 years is quite a long time to follow an unofficial procedure. The General Accounting Office (GAO) of the US also expressed this opinion by stating that “The federal regulatory system for food safety did not emerge from a comprehensive design but rather evolved piecemeal, typically in response to particular health threats or economic crises” (Robinson 2001).

It was mentioned above that civil law systems are more cautious. The following sections are largely based on the excellent comparative analysis provided by Weiner and Rogers (2002) on

¹⁶⁷ Additionally, there is one major difference between the FDA and EFSA. The FDA is responsible for both conducting risk assessment and taking risk management decisions. On the other hand, EFSA only performs risk assessments (while the Commission, Parliament, Council and Member States are responsible for risk management).

the precaution in the EU and US. Governments have two means of dealing with risks: *ex ante* precautions and *ex post* remedies (or both). *Ex ante* precautions include regulations and laws administered by agencies; regulations are forms of precautionary measures in that they exist to avoid future uncertain risks. In fact, regulations and all premarket approvals can be considered precautionary in a way. Products requiring premarket approvals are considered *a priori* hazardous and must be proven safe before they can be placed on the market.

Both strategies have their advantages and disadvantages. *Ex ante* legal systems can reduce the risk of low probability but high impact events and the problem of long latency. They may also lead to false positives, however, which occur when something considered to be harmful turns out to be not of concern. False positives may lead to financial losses, restricted freedoms and foregone health and environmental benefits of limiting technology and innovations. *Ex post* legal systems are beneficial in that they save on costs and avoid restrictions on individual freedom. However, they also run the risk of false negatives, which are when something considered to be safe ends up being harmful, and may lead to health or environmental damage. False positives are “guilty until proven innocent” whereas false negatives run the thought of “innocent until proven guilty”.

The differences in precautionary approaches to regulating certain risks may be a result of weighing the benefits and costs of *ex ante* and *ex post* regulation in different cases. There may be different social, economic and cultural factors that play a role in making the decisions. Or people in the two regions may be more susceptible to some risks over others, or they may simply place a greater value on regulating certain risks. Risks which are considered to be familiar, natural and voluntary are generally more acceptable than those which are unfamiliar, unnatural or involuntary (Slovic 1987). What is considered to be familiar, or natural, may differ in the two regions. For example, Americans are more likely to be accepting of new technologies in relation to food, e.g. GMOs, whereas these are perceived more negatively in the EU.

Additionally, the choice between *ex ante* and *ex post* remedies may stem from the differences in the legal systems, as stated by Weiner and Rogers (2002).

Ex ante precaution may be greater where *ex post* remedies against private firms are weaker. The generally stronger US system of tort law may make *ex ante* precaution a less urgent social device in the US than in Europe, where *ex post* remedies tend to be weaker. Thus US reluctance to agree to stringent versions of precaution may reflect confidence in the US legal system taken as a whole – not opposition to protecting health and the environment. And European advocacy of stringent versions of precaution may reflect an implicit assumption that, in the absence of strong *ex post* tort liability, *ex ante* regulation is the only real bulwark between risks and the public – not advocacy of draconian overregulation.

A twist on this tort-regulation interaction is that *ex ante* precaution may be greater where *ex post* remedies against the regulator are stronger. Although the US may have a more vigorous tort liability system overall, the US has a special doctrine immunizing government policymaking from tort liability, which some European governments and the EU institutions do not. Thus European regulators may seek to employ stringent *ex ante* regulation in order to shield themselves from lawsuits that could be filed against them if they left small risks unregulated.

This analysis thus provides an explanation for why the US may not be as cautious about granting market access to new products¹⁶⁸.

Another possible understanding of the differences between the systems is by taking a look at how well people accept and perceive risks, and if this has any effect on how the governments may choose to regulate the food supply for their consumers.

People are more accepting of some risks than others. According to Slovic (1987), risks that are considered to be familiar, natural and controllable are more likely to be acceptable than those that are unfamiliar, unnatural, involuntary, potentially catastrophic and presenting risks to future generations (Slovic 1999). Additionally, there are differences in the way that experts and average consumers evaluate risks.

Handler (1979) described two ways in which risk assessments are performed: science-based and value-based. The science-based method counts and calculates cases, severity of illness, hospitalizations, deaths, costs of the risk, benefits of the risk, costs of reducing the risk and balance of risk to benefits. The value-based method assesses whether risk is voluntary or imposed, visible or hidden, understood or uncertain, familiar or foreign, natural or technological, controllable or uncontrollable, mild or severe and fairly or unfairly distributed. The first balances risk against benefit and cost, and the second balances risk against dread and outrage. In general the experts assess risk with the science-based method and the consumers assess risk with the value-based method. However, there are certainly many overlaps between the two and neither experts nor consumers assess risk 100% with either method.

Nevertheless this can cause problems. As David Kessler stated, “Weighing risks against benefits sounds great, but the truth is there is no magic formula, especially when the risks are taken by one group and the benefits by another.”

Consumers in both the US and the EU have indeed objected to the way that authorities have assessed new foods and food ingredients (and drugs, pesticides, etc.). They also do express concern over possible adverse effects from consumption of certain substances. A Eurobarometer survey found that 66% of European consumers were worried about the presence of food additives such as colors, preservatives and flavorings.

Studies have shown that people are more likely to accept risks from foods if they can serve benefits, however. Frewer (2003) studied how people can tolerate higher levels of risk if they perceive a direct benefit to themselves (versus groups in society or the food industry). Cardello (2003) found that involuntary risks that come from novel food processing technologies in foods cause high levels of consumer concern. The author also showed that certain groups of consumers are “predisposed to accept or reject technological change.” As Putten (2009) demonstrated, “what is perceived to be a benefit associated with a novel food differs between countries and culture, and between different individuals at different times and within different contexts.”

¹⁶⁸ In fact, the Food Additives Amendment in 1958 was not even motivated exclusively by safety concerns. Congress stated that it wished to promote innovation in food technology by giving FDA the power to authorize poisonous substances at low levels (IOM 1999).

In general American consumers are more likely to accept these new technologies (and thus their possible associated risks and benefits¹⁶⁹) than European consumers. Americans tend to have a greater desire for innovation and a willingness to take a risk and try something new, whereas Europeans generally prefer tradition; they are more closely attached to getting their food from small local farms, and resist technologies seen as unnatural. They are more likely to be sceptical of innovations, whereas Americans tend to prefer new technologies.

As stated before both the US and EU have “safety” as a requirement to approve food additives, and the definitions are quite similar. As Marion Nestle states in her book *Safe Food*, safety is relative—and it is defined as a level which does not exceed an acceptable level of risk. This acceptable level can vary for consumers, and has been demonstrated, there is a difference in this acceptable level for consumers in the EU and in the US.

In general, the US is more lenient in its approvals, as shown throughout this paper. Examples are with GMOs, exotic foods (e.g. stevia) and more. In a few cases the EU has approved substances which are banned in the US, such as cyclamate (21 CFR 189.135).

5.5 Impact on innovation

This paper has shown the differences in the regulation of food additives and some other products in the EU and the US. While much of the discussion so far has focused on the reasons why these differences may exist, it is also interesting to take a look at the effects—and in particular, the impact on innovation. This section goes beyond the concepts to look at the premarket approvals of other substances—namely novel foods in the EU (ingredients of which are regulated as food additives or GRAS substances in the US).

First it is important to say that premarket approval processes in both places are lengthy and expensive, and can take up to several years.

Additionally, it is not always clear which premarket approval processes to follow. In the US, foods and food ingredients are either classified as a food additive or GRAS. Manufacturers can make the decision whether their product is GRAS or not. In some situations it is obvious if an ingredient GRAS or not, such as if it has a long established history of safe use or not. However, it is not quite so simple to determine in other cases—the criteria to meet the GRAS exemption are somewhat vague. Foods and food ingredients meet the criteria if they are comparably safe to similar conventional foods¹⁷⁰. However, what makes a food similar enough to a conventional food can be difficult to determine. A conventional food modified in a slight way may or may not be considered conventional—and thus possibly GRAS. A similar situation occurs in the EU when determining if a food is conventional or novel. Novel foods and food ingredients are those which were not consumed significantly in the EU before 1997. However, what exactly is “significant use”? Examples cited have been “general availability in supermarkets” and “two hectares of agricultural produce.”¹⁷¹ An example of a

¹⁶⁹ Despite the fact that consumers may weigh risks and benefits, neither the American nor European authorities allow weighing and balancing these factors in approval of substances—meaning that a potential benefit cannot be used to justify a risk in a premarket approval.

¹⁷⁰ The reason for the “comparably safe” standard is that it is impossible to prove 100% safety. Therefore, the FDA considers foods as safe as conventional foods to meet the required safety standard

¹⁷¹ These examples were cited by Member States in the Novel Foods Working Group CAFAB (Competent Authority Food Assessment Body), which is a part of the SCFCAH. Foods are considered traditional in the EU even if they were used in one Member State, as long as the use was common before 1997 (this applies even if a

novel food stated in the NFR is foods and food ingredients isolated from microorganisms and plants which have not been used for human consumption to a significant degree, but to what extent is a significant degree? Does application of a certain production process or preparation technique automatically render the food novel? To add to the complication of selecting which premarket approval process to follow, if a business chooses the wrong procedure, it is not possible to simply switch to the correct one, but instead a new procedure has to be started from the beginning¹⁷². The authorities do often assist in selecting which premarket approval procedure to choose, but there is still confusion.

Foods in the EU are considered novel if they were not in the EU market before 1997. This means that “exotic foods”—those that have been used traditionally in other nations around the world, even for hundreds or thousands of years—are unconsidered *a priori* hazardous and still have to go through the rigorous premarket approval process to be placed on the EU market¹⁷³. Knudsen et al. (2008) found that there are around 7,000 plants used in the human diet around the world, and approximately 300 of these are considered traditional in the EU. Therefore, the thousands of others may well be novel. Since 1997, when the NFR became effective, only 5 or 6 exotic plants have been approved for use on the EU market. The potential to use around 6,300 other substances could greatly diversify the food supply, but it is clear why it is not frequently taken advantage of considering the costs of time and money.

Unlike food additive approvals (both in the US and EU) and GRAS approvals, which are generic, novel food approvals are exclusive—meaning that only the applicant is authorized to place the product on the market. This exclusive authorization can serve as a sort of monopoly—a business can dominate the market competition at least until another business gains access to the market by submitting another novel foods application. The premarket approval process makes it difficult for smaller businesses, especially those from outside the EU, to place such products on the market, since approval process is long and expensive.

In practice it is illogical to require an application to demonstrate the safety of a product when it has already been proven earlier—either once or many times. For example, noni juice comes from a tropical fruit indigenous to Southeast Asia, the Caribbean and Australia. Several companies have placed and wished to place the product on the market, yet every time, a novel food application has to be completed (although a simplified notification procedure is an option in certain situations). Regulation of products can thus have a great impact on innovation and on the products which are available to consumers.

5.6 Advantages and disadvantages of each system

In order to discuss the advantages and disadvantages of ingredient regulation in each system, it is important to look from the perspective of both the business and the consumer. For a business, it is easy to see why the approach in the US is advantageous: the GRAS exemption from the food additive definition makes it easier to place innovative products on the market, in particular if they are traditional foods from other countries (regulated under the NFR in the EU) or genetically modified foods that are similar to conventional foods (regulated under

Member State joined the EU later). In the group Member States can discuss if foods are considered novel or not based on use in their home country and try to reach a common position on novel status.

¹⁷² Stevia example: novel food application was rejected in 2000, was not approved as a food additive until 2011

¹⁷³ In the US, on the other hand, it does not matter whether a food was consumed significantly in the US or outside of the country. Such “exotic foods” are considered conventional in the US and do not have to undergo premarket approval processes.

Regulation 1829/2003 and 1830/2003 in the EU). Although it would certainly be unwise to place these products on the market without conducting safety tests, the data required in the GRAS notification (if done at all) is far less burdensome than that required for regular premarket approvals. Additionally, businesses in the US have the huge advantage that they can market GRAS products right away without having to wait lengthy periods to obtain approval from the authorities, as in the EU. However, it is important to state that the food additive approval procedure itself in the US has no clear advantages over that in the EU; it also requires detailed information for approval and is expensive and time-consuming.

On the other hand, it is possible that EU businesses have an advantage in that they have a “license to produce”, and a sort of legal confirmation that their products are (more) guaranteed to be safe. This is unlikely to make a difference in trade within the EU itself, or within the US itself (if all businesses in each place are on a level playing field), but it may have value in international trade in the case that other countries wishing to import products have strict standards as well for premarket approvals of foods and food ingredients.

From the perspective of the consumer there is no clear answer. Consumers in the EU have a food supply that is less risky (not to say that the food in the US is “risky” per se but that new foods and food ingredients are treated in the EU are treated with more precaution, as shown in various examples). However, it can be argued that each system is suited to the consumers in each place; American consumers in general are more likely to accept innovative foods (particularly those with new benefits) whereas European consumers generally are not as accepting of foods that are not traditional.

6 Conclusion

The objective of this study was to delineate and compare the concepts and functions of food additives in the European Union and United States. The main findings of the research are grouped around the six research questions formulated at the beginning of the study.

1. *What is the concept of a food additive in both European and American legislation? What exactly is included or excluded, and what are the differences between the two?*

The concept of a food additive in the US is a substance which may become a component of food or affect the characteristics of a food, if it is not generally recognized as safe. The concept of a food additive in the EU is a substance that is normally not consumed as a food which is added to a food (and becomes a part of it) for a technological purpose. The definitions are more complex than they initially seem. The US has a broader interpretation than the EU does, primarily because it includes substances that can become a component of food *or* that affect the characteristics of food (e.g. irradiation, enzymes). The EU definition only includes substances which become a component of food. However, some other substances which would normally be classified as food additives are outside the scope in the US if they are generally recognized as safe. Despite these different classifications of other substances, the “core” definition of a food additive in the EU and US is essentially the same, which is that the additive must have a technological effect in the food. This interpretation makes the concepts closer than they initially appeared to be. In the EU definition of a food additive, the technological effect is explicitly stated as a requirement. In the US definition, it is more hidden. The additive definition does not state anything about having a technological effect, but rather the information on food contact substances provides a clue. Legislation on food contact substances states that they can be exempt from regulation as food additives if they do not have a technical effect. This therefore implies that food additives have a technical effect in foods. However, what exactly is included in the concept of technological appears to differ. The US (and Codex Alimentarius) consider imparting flavor and taste to be a technological function. However, the EU appears to exclude this from the concept of a technological function: it states that flavorings and other substances which impart taste are not additives. For an overview of the different types of substances included or excluded under the definitions, and the definitions between the two, see table 3 in section 5.1.1.

2. *What are the functions of the definitions in the two jurisdictions, i.e. how do the definitions affect the regulatory situation?*

Which definition a substance is classified under is so important because it affects how it is regulated: if and how it must be approved before being placed on the market, for example. In both the US and in the EU, substances are approved *for a particular use*. Therefore, a substance may be classified as an additive for one use and in another category for another use (e.g. if it has a technological effect in the final product or not, if it is generally recognized as safe or not). How a substance is defined thus affects

which approval procedure, if any, it must undergo before being placed on the market. It is for this reason that a clear understanding of the definitions is essential.

3. *How do the premarket approval requirements and procedures for food additives work in the EU and US? In particular, what are the requirements in the evaluations and what are the differences between the two?*

Food additives in both the EU and the US have to be approved by authorities before being placed on the market. The approval procedures are discussed in sections 3.4 (for the US) and 4.5 (for the EU). Both procedures involve an assessment of safety and other factors. The main requirements for approval are that the additives must be safe, not misleading/deceptive and serve a technological function (this is not explicitly stated, but rather implied, in American legislation). The specific requirements for the levels of scientific evidence were analyzed. In general, the two regions require similar types of toxicity studies, copies of all relevant studies and data, etc. (see section 1.2.3). Additives which are approved are placed on a positive list in both places. The two systems are fairly similar in their approval characteristics: all additives and other ingredients approved can be approved only under certain conditions, such as in which foods they may be used and if there are any maximum limits.

4. *What are the concepts of and premarket approval requirements for GRAS products in the US, novel foods in the EU and any other substances that may be considered a food additive in either the US or the EU? What is their relation to food additives?*

Some categories of substances or products are included in the scope of a food additive in one place but not the other. GRAS products are outside the scope of food additives since they are generally known to be safe (absence of a hazard is not enough). They are exempt from the food additive approval process and are regulated in a different way (and in fact do not even have to undergo an approval process), as discussed in sections 3.8 and 3.9. Novel foods are those products which were not significantly consumed in the EU before 1997, and they undergo another approval process, as discussed in section 4.10. Discussion of other substances is found throughout the text.

5. *How do the definitions and systems compare with international food standards, such as those of the Codex Alimentarius Commission?*

The definition of a food additive by the Codex Alimentarius Commission is quite similar to that of the EU. The American definition came first, followed by Codex, and then the EU. Therefore, it is clear that the EU based its definition on the Codex one. While the definitions are nearly the same, a major difference is that the Codex definition states that food additives are substances which are added for a technological (including organoleptic) function. It was discussed above, in section 4.4, that the EU does not consider flavoring to be a technical function and therefore excludes flavorings from the definition of food additives.

6. *What are some possible explanations for the different approaches to regulation of food additives and other substances?*

As discussed in section 5.4, the EU is generally more cautious with its approach to placing novel substances on the market. This is perhaps due to differences in how the legislation was structured, with a precautionary approach (in the EU) to a reactionary approach (in the US). The legislation on additives and other substances in the EU is more organized and laid out, where it is not so much in the US. Additionally, the differences may stem from the two means of dealing with risks: *ex ante* precautions and *ex post* remedies. Choosing between one or the other, or leaning more to one side, may be a result of social, economic or cultural factors; risk acceptance of consumer (e.g. if American consumers are more likely to accept and want innovative products whereas European consumers prefer to have food as safe as possible), or how liability is dealt with.

This study explored the definitions, functions and approval requirements of substances so that they are more understandable and can be of benefit to the food industry, academia and anyone else with an interest in food additives.

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8 Appendix

Food additive functions in the EU¹⁷⁴

1. **Sweeteners** are substances used to impart a sweet taste to foods or in table-top sweeteners;
2. **Colours** are substances which add or restore colour in a food, and include natural constituents of foods and natural sources which are normally not consumed as foods as such and not normally used as characteristic ingredients of food. Preparations obtained from foods and other edible natural source materials obtained by physical and/or chemical extraction resulting in a selective extraction of the pigments relative to the nutritive or aromatic constituents are colours within the meaning of this Regulation;
3. **Preservatives** are substances which prolong the shelf-life of foods by protecting them against deterioration caused by micro-organisms and/or which protect against growth of pathogenic micro-organisms;
4. **Antioxidants** are substances which prolong the shelf-life of foods by protecting them against deterioration caused by oxidation, such as fat rancidity and colour changes;
5. **Carriers** are substances used to dissolve, dilute, disperse or otherwise physically modify a food additive or a flavouring, food enzyme, nutrient and/or other substance added for nutritional or physiological purposes to a food without altering its function (and without exerting any technological effect themselves) in order to facilitate its handling, application or use;
6. **Acids** are substances which increase the acidity of a foodstuff and/or impart a sour taste to it;
7. **Acidity regulators** are substances which alter or control the acidity or alkalinity of a foodstuff;
8. **Anti-caking agents** are substances which reduce the tendency of individual particles of a foodstuff to adhere to one another;
9. **Anti-foaming agents** are substances which prevent or reduce foaming;
10. **Bulking agents** are substances which contribute to the volume of a foodstuff without contributing significantly to its available energy value;
11. **Emulsifiers** are substances which make it possible to form or maintain a homogenous mixture of two or more immiscible phases such as oil and water in a foodstuff;
12. **Emulsifying salts** are substances which convert proteins contained in cheese into a dispersed form and thereby bring about homogenous distribution of fat and other components;
13. **Firming agents** are substances which make or keep tissues of fruit or vegetables firm or crisp, or interact with gelling agents to produce or strengthen a gel;
14. **Flavour enhancers** are substances which enhance the existing taste and/or odour of a foodstuff;
15. **Foaming agents** are substances which make it possible to form a homogenous dispersion of a gaseous phase in a liquid or solid foodstuff;

¹⁷⁴ Annex I, Regulation 1333/2008

16. **Gelling agents** are substances which give a foodstuff texture through formation of a gel;
17. **Glazing agents** (including lubricants) are substances which, when applied to the external surface of a foodstuff, impart a shiny appearance or provide a protective coating;
18. **Humectants** are substances which prevent foods from drying out by counteracting the effect of an atmosphere having a low degree of humidity, or promote the dissolution of a powder in an aqueous medium;
19. **Modified starches** are substances obtained by one or more chemical treatments of edible starches, which may have undergone a physical or enzymatic treatment, and may be acid or alkali thinned or bleached;
20. **Packaging gases** are gases other than air, introduced into a container before, during or after the placing of a foodstuff in that container;
21. **Propellants** are gases other than air which expel a foodstuff from a container;
22. **Raising agents** are substances or combinations of substances which liberate gas and thereby increase the volume of a dough or a batter;
23. **Sequestrants** are substances which form chemical complexes with metallic ions;
24. **Stabilisers** are substances which make it possible to maintain the physico-chemical state of a foodstuff; stabilisers include substances which enable the maintenance of a homogenous dispersion of two or more immiscible substances in a foodstuff, substances which stabilise, retain or intensify an existing colour of a foodstuff and substances which increase the binding capacity of the food, including the formation of cross-links between proteins enabling the binding of food pieces into re-constituted food;
25. **Thickeners** are substances which increase the viscosity of a foodstuff;
26. **Flour treatment agents** are substances, other than emulsifiers, which are added to flour or dough to improve its baking quality.

Functions of direct food ingredients in the US¹⁷⁵

1. **Anticaking agents and free-flow agents:** Substances added to finely powdered or crystalline food products to prevent caking, lumping, or agglomeration.
2. **Antimicrobial agents:** Substances used to preserve food by preventing growth of microorganisms and subsequent spoilage, including fungistats, mold and rope inhibitors, and the effects listed by the National Academy of Sciences/National Research Council under “preservatives.”
3. **Antioxidants:** Substances used to preserve food by retarding deterioration, rancidity, or discoloration due to oxidation.
4. **Colors and coloring adjuncts:** Substances used to impart, preserve, or enhance the color or shading of a food, including color stabilizers, color fixatives, color-retention agents, etc.

¹⁷⁵ Adopted from the National Academy of Sciences/National Research Council national survey of food industries, reported to the FDA under the contract title “A Comprehensive Survey of Industry on the Use of Food Chemicals Generally Recognized as Safe” (September 1972) (21 CFR 170.3(o)).

5. **Curing and pickling agents:** Substances imparting a unique flavor and/ or color to a food, usually producing an increase in shelf life stability.
6. **Dough strengtheners:** Substances used to modify starch and gluten, thereby producing a more stable dough, including the applicable effects listed by the National Academy of Sciences National Research Council under “dough conditioner.”
7. **Drying agents:** Substances with moisture-absorbing ability, used to maintain an environment of low moisture.
8. **Emulsifiers and emulsifier salts:** Substances which modify surface tension in the component phase of an emulsion to establish a uniform dispersion or emulsion.
9. **Enzymes:** Enzymes used to improve food processing and the quality of the finished food.
10. **Firming agents:** Substances added to precipitate residual pectin, thus strengthening the supporting tissue and preventing its collapse during processing.
11. **Flavor enhancers:** Substances added to supplement, enhance, or modify the original taste and/or aroma of a food, without imparting a characteristic taste or aroma of its own.
12. **Flavoring agents and adjuvants:** Substances added to impart or help impart a taste or aroma in food.
13. **Flour treating agents:** Substances added to milled flour, at the mill, to improve its color and/or baking qualities, including bleaching and maturing agents.
14. **Formulation aids:** Substances used to promote or produce a desired physical state or texture in food, including carriers, binders, fillers, plasticizers, film-formers, and tableting aids, etc.
15. **Fumigants:** Volatile substances used for controlling insects or pests.
16. **Humectants:** Hygroscopic substances incorporated in food to promote retention of moisture, including moisture-retention agents and antidusting agents.
17. **Leavening agents:** Substances used to produce or stimulate production of carbon dioxide in baked goods to impart a light texture, including yeast, yeast foods, and calcium salts listed by the National Academy of Sciences/National Research Council under “dough conditioners.”
18. **Lubricants and release agents:** Substances added to food contact surfaces to prevent ingredients and finished products from sticking to them.
19. **Non-nutritive sweeteners:** Substances having less than 2 percent of the caloric value of sucrose per equivalent unit of sweetening capacity.
20. **Nutrient supplements:** Substances which are necessary for the body’s nutritional and metabolic processes.

21. **Nutritive sweeteners:** Substances having greater than 2 percent of the caloric value of sucrose per equivalent unit of sweetening capacity.
22. **Oxidizing and reducing agents:** Substances which chemically oxidize or reduce another food ingredient, thereby producing a more stable product, including the applicable effect listed by the National Academy of Sciences/National Research Council under “‘dough conditioners.’”
23. **pH control agents:** Substances added to change or maintain active acidity or basicity, including buffers, acids, alkalies, and neutralizing agents.
24. **Processing aids:** Substances used as manufacturing aids to enhance the appeal or utility of a food or food component, including clarifying agents, clouding agents, catalysts, flocculents, filter aids, and crystallization inhibitors, etc.
25. **Propellants, aerating agents, and gases:** Gases used to supply force to expel a product or used to reduce the amount of oxygen in contact with the food in packaging.
26. **Sequestrants:** Substances which combine with polyvalent metal ions to form a soluble metal complex, to improve the quality and stability of products.
27. **Solvents and vehicles:** Substances used to extract or dissolve another substance.
28. **Stabilizers and thickeners:** Substances used to produce viscous solutions or dispersions, to impart body, improve consistency, or stabilize emulsions, including suspending and bodying agents, setting agents, jellying agents, and bulking agents, etc.
29. **Surface-active agents:** Substances used to modify surface properties of
 - a. liquid food components for a variety of effects, other than emulsifiers, but including
 - b. solubilizing agents, dispersants, detergents, wetting agents, rehydration enhancers, whipping agents, foaming agents, and defoaming agents, etc.
30. **Surface-finishing agents:** Substances used to increase palatability, preserve gloss, and inhibit discoloration of foods, including glazes, polishes, waxes, and protective coatings.
31. **Synergists:** Substances used to act or react with another food ingredient to produce a total effect different or greater than the sum of the effects produced by the individual ingredients.
32. **Texturizers:** Substances which affect the appearance or feel of the food