7.2: Regulation of Consumer Products and Drug Safety

Regulation of Consumer Products and Drug Safety

Consumer products are often called household products. It is important to know what a category of product is called in the area of the world of interest.

For example, in the United States, cosmetic products are defined by the FDA as those products "intended to be applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance without affecting the body's structure or functions." While cosmetics are often thought of as being make-up products such as eye-liner, lipstick, or nail polish, the FDA definition includes skin-care creams, lotions, powders, and perfumes. However, soap products are excluded from FDA's definition of cosmetics.

In comparison, in the European Union (EU), the European Commission's definition of cosmetic products includes soap, shampoo, deodorant, toothpaste, perfumes, and makeup.

It is also important to keep in mind that some products are known by different names. For example, what is known as a cloth or disposable diaper in the United States is called a nappy in several other countries.

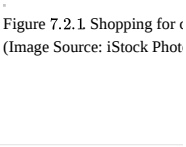

Figure 7.2.1 Shopping for c
(Image Source: iStock Phot

U.S. Consumer Product Safety Commission (CPSC)

The U.S. Consumer Product Safety Commission (CPSC) is charged with "protecting the public from unreasonable risks of injury or death associated with the use of the consumer products" under its jurisdiction such as toys, cribs, power tools, cigarette lighters, and household chemical-containing products. The CPSC considers if a product could pose a fire, electrical, chemical, or mechanical (such as choking) hazard. CPSC's work, including research, product recalls, education, and administration of regulations, laws, and standards, has resulted in a decline in the rate of deaths and injuries associated with consumer products over the past several decades.

Consumer exposure standards are developed for hazardous substances and articles by the CPSC. The authority under the Federal Hazardous Substance Act (FHSA) pertains to substances other than pesticides, drugs, foods, cosmetics, fuels, and radioactive materials. The CPSC-required warning labels on containers of household products that are toxic, corrosive, irritants, or sensitizers help consumers to safely store and use those products and to give them information about immediate first aid steps to take if an accident happens. Highly toxic substances are labeled with DANGER; less toxic substances are labeled with WARNING or CAUTION.

Figure 7.2.2 CPSC danger label for a gas-powered generator
(Image Source: CPSC)

The CPSC's basis for a determination of highly toxic has been death in laboratory rats at an oral dose of 50 mgs, or an inhaled dose in rats of 200 ppm for one hour, or a 24-hour dermal dose in rabbits of 200 mg/kg. A substance is corrosive if it causes visible destruction or irreversible damage to the skin or eye. If it causes damage that is reversible within 24 hours, it is designated an irritant. An immune response from a standard sensitization test in animals is sufficient for designating the substance a sensitizer.

CPSC is a member of the U.S. Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), a permanent committee of the National Institutes of Environmental Health Science (NIEHS) under the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). ICCVAM was created "to establish, wherever feasible, guidelines, recommendations, and regulations that promote the regulatory acceptance of new or revised scientifically valid toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing animal tests and ensuring human safety and product effectiveness."

European Commission General Product Safety Directive (GPSD)

In the EU, the European Commission's General Product Safety Directive (GPSD) requires producers and distributors to place only safe consumer products on the market and to take all necessary measures to prevent risks to consumers. The GPSD excludes certain product categories covered by specific European safety regulations. It provides an alert system (Rapid Alert System for non-food dangerous products – "RAPEX") between the Commission and EU Member States, Norway, Iceland and Liechtenstein.

U.S. Food and Drug Administration (FDA)

The FDA oversees food safety, tobacco products, dietary supplements, prescription and non-prescription drugs, vaccines, blood products, medical devices, electromagnetic radiation emitting devices, cosmetics, animal foods, and veterinary products.

Drugs

Manufacturers of new pharmaceuticals must obtain formal FDA approval before their products can be marketed. Drugs intended for use in humans must undergo animal studies and human clinical trials to determine toxic dose levels prior to filing a New Drug Application (NDA).

Did you know?

During the late 1950s the drug Thalidomide was used to control nausea and vomiting in pregnancy in Canada, Europe, Australia, and parts of Asia. After the drug came on the market, reports appeared of children born with missing limbs, with upper limbs usually more affected than lower limbs. In addition to damage to arms and legs, faces, eyes, ears, and genitalia, internal organs including the heart, kidney, and gastrointestinal tract were damaged.

Thalidomide did not reach the US market due to the efforts of an astute FDA drug reviewer, Dr. Frances Oldham Kelsey, who insisted that thalidomide be fully tested before approval. In response to the episode, the Kefauver Harris Amendment to the Federal Food, Drug, and Cosmetic Act became law in 1962. The amendment requires drug manufacturers to give proof of the effectiveness and safety of a drug before it can be approved.

Thalidomide continues to be prescribed under strict supervision as a treatment for multiple myeloma, leprosy, certain complications of human immunodeficiency virus (HIV), and autoimmune disorders. In the 2000s, children with thalidomide-related birth defects were noted in Brazil due to the use of thalidomide to treat leprosy. Pregnant women were being exposed when family members took the drug.

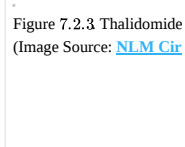

Figure 7.2.3 Thalidomide
(Image Source: NLM Cir

An NDA covers all aspects of a drug's effectiveness and safety, including:

- Pharmacokinetics and pharmacological effects.
- Metabolism and postulated mechanism of action.
- Associated risks of the drug.
- Intended uses and therapeutic efficacy.
- Risk:benefit relationship.
- Basis for package inserts supplied to physicians.

The FDA does not issue exposure standards for drugs. Instead, it approves an NDA that contains guidance for usage and warnings concerning potential side effects of a drug. The manufacturer is required to provide this information to physicians prescribing the drug as well as to others that may purchase or use the drug. Information on a drug's harmful side effects is provided in three main ways:

1. Labeling and package inserts that accompany a drug and explain approved uses, recommended dosages, and effects of overexposure.
2. Publication of information in the Physicians' Desk Reference (PDR) and other publically available databases.
3. Direct-to-consumer advertisements.

Figure 7.2.4. Drugs must ir
(Image Source: iStock Pho

The package insert labels and the PDR contain the following information:

- Description
- Clinical pharmacology
- Indications and usage
- Contraindications
- Warnings
- Precautions
- Adverse reactions
- Interactions
- Overdosage
- Available forms
- Dosage and administration

Figure 7.2.5. Sample package insert for a fictional prescription drug
(Image Source: FDA)

Food Additives

The FDA is responsible for the approval of food additives. Standards are different depending on whether they are direct food additives or indirect food additives.

Direct food additives are intentionally added to foods for functional purposes. Examples of direct food additives include:

- Processing aids
- Texturing agents
- Preservatives
- Flavoring and appearance agents
- Nutritional supplements

Approval usually designates the maximum allowable concentrations in a food product.

Figure 7.2.6. A worker in a food production plant adds a mix of dry flavoring and processing agents to meat
(Image Source: iStock Photos, ©)

Indirect food additives are not intentionally added to foods and they are not natural constituents of foods. They become a constituent of the food product from environmental contamination during production, processing, packaging, and storage. Examples of indirect food additives are:

- Antibiotics administered to cattle.
- Pesticide residues remaining after production or processing of foods.
- Chemicals that migrate from packaging materials into foods.

Exposure standards indicate the maximum allowable concentration of these substances in food.

New direct food additives must undergo stringent review by FDA scientists before they can be approved for use in foods. The manufacturer of a direct food additive must provide evidence of the safety of the food additive in accordance with specified uses. The safety evaluation is conducted by the toxicity testing and risk assessment procedures previously discussed with derivation of the ADI. In contrast to pharmaceutical testing, virtually all toxicity evaluations are conducted with experimental laboratory animals.

FDA approval of all new food additives has been requires since the Food, Drug and Cosmetic Act (FDCA) was amended in 1958. At that time, all existing food additives were Generally Recognized as Safe (GRAS) and no exposure standard was developed. Many of GRAS substances have since been reevaluated and maximum acceptable levels have been established. However, under the law, a substance may be determined to be GRAS for an intended use and introduced into the food supply as such without prior approval by FDA. FDA maintains a searchable database of GRAS substances.

Figure 7.2.7. Select Committee on GRAS Substances searchable database

The FDA reevaluation of GRAS substances requires that specific toxicity tests be conducted based on the level of the GRAS substance in a food product. For example, the lowest level of concern is for an additive used at 0.05 ppm in the food product. Only short-term tests (a few weeks) are required for those compounds. In contrast, a food additive used at levels higher than 1.0 ppm must be tested for carcinogenicity, chronic toxicity, reproductive toxicity, developmental toxicity, and mutagenicity.

The 1958 amendment to the Food, Drug and Cosmetic Act law is known as the Delaney Clause. This clause prohibited the addition of any substance to food that has been shown to induce cancer in man or animals. The implication was that any positive result in an animal test, regardless of dose level or mechanism, is sufficient to prohibit use of the substance. In this case, the allowable exposure level is zero. In 1958, chemical levels could only be measured in parts per thousand whereas analytical methods today allow some chemical levels to be measured down to parts per trillion or quintillion. Such levels might represent negligible cancer risks and Congress has repeatedly amended the Delaney Clause to create more and more exceptions. In 1996, the Delaney Clause was repealed, and the "zero–risk" standard was changed to one of "reasonable certainty."

Food Safety in the European Union (EU)

General Food Law

The basic principles for the EU's food safety policy are defined in the EU's General Food Law (Regulation (EC) No 178/2002), adopted in 2002. This regulation:

- Lays down general principles, requirements and procedures that underpin decision making in matters of food and feed safety, covering all stages of food and feed production and distribution.
- Sets up an independent agency responsible for scientific advice and support, the **European Food Safety Authority (EFSA)** - see below for more information.
- Creates the main procedures and tools for the management of emergencies and crises as well as the Rapid Alert System for Food and Feed (RASFF).

Figure 8. Flags of the European Union and various member nations
(Image Source: iStock Photos, ©

European Food Safety Authority (EFSA)

The European Food Safety Authority (EFSA) was set up in 2002 and is based in Parma, in Italy. It carries out risk assessments before certain foods are allowed to be sold in the EU. The agency was legally established by the EU under the General Food Law - Regulation 178/2002. The General Food Law created a European food safety system in which responsibility for risk assessment (science) and for risk management (policy) are kept separate. EFSA is responsible for the former area, and also has a duty to communicate its scientific findings to the public.
EFSA provides scientific advice to the European Commission and EU countries, to help them take effective decisions to protect consumers. It also plays an essential role in helping the EU respond swiftly to food safety crises. EFSA's remit covers:

- Food and feed safety
- Nutrition
- Animal health and welfare
- Plant protection
- Plant health

It also considers, through environmental risk assessments, the possible impact of the food chain on the biodiversity of plant and animal habitats (discover EFSA topics, EFSA scientific work areas, and application resources by food sector area). EFSA publishes all its scientific outputs, including its scientific opinions, in the EFSA Journal. It also issues a range of supporting publications.
Most of EFSA's work is undertaken in response to requests for scientific advice from the European Commission, the European Parliament and EU Member States. EFSA also carry out scientific work on own initiative, in particular to examine emerging issues and new hazards and to update our assessment methods and approaches. This is known as "self-tasking." EFSA's quality management system (QMS) has been awarded an ISO 9001:2015 certificate, the international standard for quality management.
EFSA's Scientific Panels of experts are responsible for the bulk of EFSA's scientific assessment work. Each of the 10 Panels is dedicated to a different area of the food and feed chain. The Scientific Committee has the task of supporting the work of the Panels on cross-cutting scientific issues. It focuses on developing harmonized risk assessment methodologies in fields where EU-wide approaches are not yet defined.
EFSA staff support the Scientific Panels and Scientific Committee in carrying out most of the Authority's scientific work. The membership of EFSA's Scientific Committee and Panels is renewed every three years (see also Working practices and EFSA Strategy 2020 - Trusted science for safe food).

The EU General Food Law deals with a wide range of issues related to food in general and food safety in particular, including food information and animal welfare. It covers all parts of the food chain from animal feed and food production to processing, storage, transport, import and export, as well as retail sales. It also establishes the principles for risk analysis. These stipulate how, when, and by whom scientific and technical assessments should be carried out in order to ensure that humans, animals, and the environment are properly protected.

EU Food Safety Policy

The EU's food safety policy covers food from farm to fork. The EU food policy comprises:

- Comprehensive legislation on food and animal feed safety and food hygiene.
- Sound scientific advice on which to base decisions.
- Enforcement and checks.

Where specific consumer protection is justified, there may be special rules on:

- Use of pesticides, food supplements, colorings, antibiotics, or hormones.
- Food additives, such as preservatives and flavorings
- Substances in contact with foodstuffs, for example, plastic packaging.
- Labeling of ingredients that may cause allergies.
- Health claims such as "low-fat" or "high-fiber."

The EU's Rapid Alert System for Food and Feed (RASFF) was launched in 1979 and allows information on food and feed to be shared quickly and efficiently between all the relevant bodies at national and EU-level. In a similar vein, the EU Notification System for Plant Health Interceptions (EUROPHYT) is the EU's notification and rapid alert system for plant products entering and being traded within the EU. It helps to prevent the introduction and spread of plant disease and plant pests.
The EU's Trade Control and Expert System (TRACES) is a system for tracking live animals and food and feed of animal origin as they enter the EU and are traded within the EU. It links veterinary authorities across and outside the EU, and enables veterinary services and businesses to react swiftly when a health threat is discovered.

Regulatory Science in the European Union

The following tables describe regulatory science in the EU, including links to the relevant agencies. The list is a work in progress.

Regulatory Science (the table below is best viewed on a computer browser)

Area	Regulatory Science (click links for more information)
Animal health and welfare	European Food Safety Authority
Animal feed	European Food Safety Authority
Biological hazards	European Food Safety Authority
Biocidal Active Substances	European Chemicals Agency
Biocidal Products	European Chemicals Agency
Botanicals	European Food Safety Authority
Consumer products	European Commission General Product Safety Directive (GPSD)
Communicable diseases	European Centre for Disease Prevention and Control
Food additives	European Food Safety Authority
Food ingredients	European Food Safety Authority
Food Colors	European Food Safety Authority
Food Contact Materials	European Food Safety Authority
Food enzymes	European Food Safety Authority
Food Supplements	European Food Safety Authority
Non-plastic food contact materials	European Food Safety Authority
Plastics and plastic recycling	European Food Safety Authority
Smoke Flavorings	European Food Safety Authority
Sweeteners	European Food Safety Authority
Food packaging	European Food Safety Authority
GMO	European Food Safety Authority
Plant Health	European Food Safety Authority
Pesticides	European Food Safety Authority
Nutrition	European Food Safety Authority
Nutrient sources	European Food Safety Authority
Vitamins and minerals	European Food Safety Authority

List above shows regulatory authorities over specific areas of science in the European Union

Regulatory Authorities (the table below is best viewed on a computer browser)

Agency (click links for more information)	Area of Authority
European Food Safety Authority (EFSA)	• Animal health and welfare • Biological hazards • Chemical contaminants • Cross-cutting science • Food ingredients and food packaging • GMO • Nutrition • Pesticides • Plant health • Chemicals • Biocides
European Chemicals Agency (ECHA)	Scientific evaluation, supervision and safety monitoring of medicines
European Medicines Agency (EMEA)	Communicable diseases
European Centre for Disease Prevention and Control (ECDC)	

List above shows regulatory authorities and their specific areas of science in the European Union

Cross-Cutting Science (the table below is best viewed on a computer browser)

Area	Regulatory Agency **(click links for more information)**
Chemical mixtures	European Food Safety Authority
Cloning	European Food Safety Authority
Emerging risks	European Food Safety Authority
Endocrine active substances	European Food Safety Authority
Margin of Exposure	European Food Safety Authority
Nanotechnology	European Food Safety Authority
Threshold of Toxicological Concern	European Food Safety Authority
Bee health	European Food Safety Authority
Machine learning	European Food Safety Authority

List above shows regulatory authorities over cross-cutting science in the European Union.

Knowledge Check

1) Consumer exposure standards are developed for hazardous substances and articles by the:

a) U.S. Food and Drug Administration (FDA)
b) U.S. Consumer Product Safety Commission (CPSC)
c) General Product Safety Directive (GPSD)

Answer

U.S. Consumer Product Safety Commission (CPSC)

2) Exposure standards for pharmaceuticals are:

a) Issued by the U.S. Food and Drug Administration (FDA)
b) Developed by the Environmental Protection Agency
c) Recommended guidance developed by the U.S. Food and Drug Administration (FDA)

Answer

Recommended guidance developed by the U.S. Food and Drug Administration (FDA)

3) The FDA develops exposure standards for both direct and indirect food additives. Which of the following is an example of an indirect food additive?

a) A preservative added to food products
b) An antibiotic administered to cattle
c) Natural and artificial flavorings
d) A nutritional supplement, such as Vitamin A

Answer

An antibiotic administered to cattle

4) Under the Delaney Clause of 1958, the FDA:

a) Required physicians to strictly adhere to exposure standards for pharmaceuticals
b) Prohibited the addition of any substance to food that has been shown to induce cancer in humans or animals
c) Authorized the addition of potentially carcinogenic substances to food as long as the concentration is at 0.05 ppm or less

Answer

Prohibited the addition of any substance to food that has been shown to induce cancer in humans or animals

5) In the European Union, what regulatory authority is responsible for chemicals and biocides?

a) European Centre for Disease Prevention and Control (ECDC)
b) European Food Safety Authority (EFSA)
c) European Chemicals Agency (ECHA)

Answer

European Food Safety Authority (EFSA)