Spoke

Solving Solubility with Science

A Glossary of Organizations and Terms Related to the Manufacturing and Toxicological Assessment of Drug/Cosmetic Products

The laws and regulations governing the development and marketing of drugs and cosmetics can be very confusing. In this White Paper, we provide functional definitions of common phrases used in the manufacturing and toxicological assessment of drug/cosmetic products as well as some useful links aimed at aiding the understanding of this sometimes-complicated landscape.

Technical Brief

Vol. 1

Issue 7

The document is divided into three groups: (i.) Chemistry Manufacturing and Controls (CMC); (ii.) Preclinical Safety Evaluation; and (iii.) Trade/ Regulatory Associations. The subjects are alphabetized within each group. Each of the three groups has an Appendix where more detail is provided. The definitions are simple, with the intent of providing practical, common-sense information. Additional details are provided in links, where applicable.

This guide should be used to obtain information regarding safety and regulatory requirements for the use of ingredients, e.g., excipients, in finished drug and cosmetic products. It is important to recognize the differences between law, regulation and regulatory guidance in understanding the rules of the road. In addition, the practical implementation of all laws, regulations and guidances can depend upon recent policy created by a regulatory agency, such as Warning Letters, or upon recent court decisions that modify, update or extend previous understanding. In general, caution should be taken with overly literal interpretations of regulation and guidance documents.

There are also overarching principles that connect and differentiate regulated industries of which one must be aware. The Doctrine of Intended Use (DOIU) is one such principle. DOIU discriminates products by *how they will be used* rather than by *what they contain*. This is important because although the category of drugs is mutually exclusive with the category of cosmetics, the same is not true for ingredients found in drugs or cosmetics. For example, ascorbic acid can be found in either a drug or a cosmetic. If the explicit function of the ascorbic acid in a finished product is to treat or prevent scurvy, that product is a drug. Whereas if the function is to beautify the skin, that product is a cosmetic.

A drug is defined in the U.S. and around the globe as a product "intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease." Since it is not possible to regulate how consumers/patients actually use a product, DOIU holds that a product is classified by what a company claims about a product (i.e. "intended for use"), especially through product labelling and marketing. If a manufacturer labels a product for drug-uses or provides instructions to use a product as a drug, it is a drug for regulatory purposes. This is why descriptions of cosmetic products (and food and dietary supplements) only use so-called "structure/function" language (e.g. supports the integrity of skin), which describes the effects based upon action on the structure or function of the human body and not it terms of something that diagnoses, cures, mitigates, treats or prevents a disease.

We hope the information in this document can be helpful in two ways. First, as a simple reference for considering terms and definitions, e.g., What are ISO standards and how are they used (enforced). Second, a portal to greater depth regarding efficacy, safety and regulation of products/ingredients.

I. CHEMISTRY MANUFACTURING AND CONTROLS (CMC) – See Appendix I

A. **Current Good Manufacturing Practice (cGMP)** is a standard set of principles designed to ensure that food, drugs and cosmetics are manufactured to standards that ensure they meet specific requirements for identity, strength, quality, and purity. Note that previously cosmetic manufactures were not strictly required to follow cGMP's but with the enactment of The Modernization of Cosmetics Regulation Act of 2022 (MoCRA), this will no longer be the case. While the mentioned industries are required to follow GMP, the specific rules and the extent of their enforcement differ significantly, reflecting the higher risks associated with pharmaceutical products compared to cosmetics for example.

B. ICH Guidelines: These are guidelines developed by the International Council on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration. The purpose is to make recommendations on ways to achieve greater harmonization in the interpretation and application of

technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines (https://www.ich.org/).

C. INCI: International Nomenclature of Cosmetic Ingredients is a standardized system of naming chemicals, especially cosmetic ingredients, which is used globally. the U.S. Food and Drug Administration (FDA) requires the use of INCI (International Nomenclature of Cosmetic Ingredients) names for the labeling of cosmetic products.

D. International Pharmaceutical Excipient Council: An international trade association devoted to safety of pharmaceutical excipients and the harmonization of regulatory standards and pharmacopoeias (https://ipecamericas.org/).

E. ISO: International Standards Organization is an independent, non-regulatory body working to establish technical standards in many areas including manufacturing and safety. Whereas ISO standards have no legal authority, regional governments may adopt them as law (https://www.iso.org/standards.html).

F. US Pharmacopoeia/National Formulary: Independent organizations establishing standards for drugs (e.g., USP) and excipients (e.g., NF). In the US, the USP process begins after FDA approval of a drug product. FDA has authorized USP as the official compendium for drug products (https://www.uspnf.com/).

G. GRAS: Generally Recognized as Safe, referring to direct or indirect food additives. There is a regulatory process for establishing GRAS status for foods. The term GRAS is applied loosely to other areas, e.g., cosmetics, excipients, without a clear meaning or regulatory course of action.

II. TOXICOLOGY – See Appendix II

A. ICH Guidelines: (https://www.ich.org/).

B. FDA Guidance Documents: (https://www.fda.gov/regulatory-information/search-fda-guidance-documents)

C. IPCS INCHEM: International Programme on Chemical Safety offers quick and easy electronic access to thousands of searchable full-text documents on chemical risks and the sound management of chemicals (https://www.inchem.org/#/)

D. ECHA: The European Chemicals Agency (https://echa.europa.eu/)

III. TRADE/REG AGENCIES: INFORMATION REGARDING SAFETY AND REGULATORY STATUS OF CHEMICALS/DRUGS – See Appendix III

A. CE: Cosmetic Europe, the European equivalent of PCPC (https://cosmeticseurope.eu/).

B. CHPA: Consumer Healthcare Products Association is dedicated to educating health professionals about the benefits of over-the-counter medicines (OTCs) and dietary supplements. The Association is an advocate of responsible self-medication as a part of the total healthcare arena (https://www.chpa.org/).

C. SCCS: The European Commission is the governing body of the EU, independent of State interests. It has the Scientific Committee for Cosmetic Safety (SCCS) as an expert panel charged with human safety of cosmetic ingredients. Opinions are issued in this regard (https://health.ec.europa.eu/scientific-

committees/scientific-committee-consumer-safety-sccs_en).

D. EMEA: European Medicines Agency's main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use in EU (https://www.ema.europa.eu/en).

E. FDA: Food and Drug Administration is the regulatory authority in the US for food, drugs, cosmetics, dietary supplements, tobacco and biologics. FDA publishes guidance, rules and regulations in the Federal Register (https://www.fda.gov/).

F. IFPMA: International Federation of Pharmaceutical & Associations is a non-profit, non-governmental organization representing industry associations from global stakeholders. Clinical trial results are published at this site (https://ifpma.org/).

G. PCPC: Personal Care Products Council is a trade group that has established an independent review of ingredients called Cosmetic Ingredient Review to establish human safety (https://www.personalcarecouncil.org/).

H. PhRMA: Pharmaceutical Research and Manufacturers of America is a trade association. It has established a clinical research site where drug trials may be published (https://phrma.org/).

I. WHO: The World Health Organization is the United Nations specialized agency for health. It was established on 7 April 1948. WHO's objective, as set out in its Constitution, is the attainment by all peoples of the highest possible level of health (https://extranet.who.int/pqweb/medicines/international-pharmacopoeia)

J. OECD: Organization for Economic Co-operation and Development testing guidelines for chemicals (https://www.oecd.org/).

K. Brexit: Brexit had a significant impact on the regulation of drugs and cosmetics in the United Kingdom, leading to notable changes in the legal and regulatory landscape.

For drugs, post-Brexit, the UK ceased to be part of the European Medicines Agency (EMA), which meant that it no longer participated in the centralized procedure for drug approval across the EU. Consequently, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) assumed full responsibility for the regulation and approval of pharmaceuticals in the UK. This shift required pharmaceutical companies to navigate a separate regulatory system for the UK market, distinct from the EU, potentially affecting the availability and approval timelines of new drugs in the UK.

In the cosmetics sector, the UK established its own regulatory framework, distinct from the EU's regulations. The UK Cosmetics Regulation, part of The Product Safety and Metrology etc. (Amendment etc.) (EU Exit) Regulations 2019, became applicable to cosmetic products sold in England, Scotland, and Wales. This UK-specific regulation diverged from the EU's approach, necessitating changes in compliance, especially regarding labeling, product safety assessments, and notification procedures. Northern Ireland, however, continued to align with EU regulations, creating a unique regulatory situation within the UK.

APPENDIX I. Chemistry Manufacturing and Controls (CMC)

In the United States, any manufacturer of finished food products is ultimately responsible for the producing safe and legal products. One critical step in doing so is to deal only with suppliers that thoroughly understand and comply with Federal requirements such as GRAS and GMPs.

For pharmaceuticals, the WHO Quality Assurance of Pharmaceuticals provides a compendium of guidelines and quality inspection: https://apps.who.int/iris/bitstream/handle/10665/43532/9789241547086_eng.pdf?sequence=1&isAllowed=y

A. Good Manufacturing Practice (GMP)

Good Manufacturing Practice or GMP (also referred to as 'cGMP' or 'current Good Manufacturing Practice') is a term that is recognized worldwide for the control and management of manufacturing and quality control testing of foods and pharmaceutical products. These regulations, which have the force of law, require that manufacturers, processors, and packagers of drugs, medical devices, some food, blood and now cosmetics when MoCRA is implemented to take proactive steps to ensure that their products are safe, pure, and effective. GMP regulations require a quality approach to manufacturing, enabling companies to minimize or eliminate instances of contamination, mix-ups, and errors. This in turn, protects the consumer from purchasing a product which is ineffective or even dangerous. Failure of firms to comply with GMP regulations can result in very serious consequences including recall, seizure, fines, and jail time.

In the US, GMP is regulated by the US Food and Drug Administration under the authority of the Federal Food, Drug, and Cosmetic Act (See Chapter IV for food, and Chapter V, Subchapters A, B, C, D, and E for drugs and devices.). Guidance documents for industry partners can be found at https://www.fda.gov/animal-veterinary/guidance-industry/chemistry-manufacturing-and-controls-cmc-guidances-industry-gfis.

In Europe, GMP is regulated under Commission Directive 2003/94/EC (http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/dir_2003_94/dir_2003_94_en.pdf),

The WHO also has issued guidelines for GMP (http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/) and the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH; see below) has issued GMP guidelines for active pharmaceutical ingredients (http://www.ich.org/LOB/media/MEDIA433.pdf).

GMP regulations address issues including recordkeeping, personnel qualifications, sanitation, cleanliness, equipment verification, process validation, and complaint handling. Most GMP requirements are very general and open-ended, allowing each manufacturer to decide individually how to best implement the necessary controls. This provides much flexibility, but also requires that the manufacturer interpret the requirements in a manner which makes sense for each individual business.

GMP is also sometimes referred to as "cGMP". The "c" stands for "current," reminding manufacturers that they must employ technologies and systems which are up to date in order to comply with the regulation. Systems and equipment used to prevent contamination, mix-ups, and errors, which may have been "top-of-the-line" or “state-of-the-art” 20 years ago, may be less than adequate by today's standards.

B. ICH Guidelines (https://www.ich.org/)

The International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.

The purpose is to make recommendations on ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines.

The objective of such harmonization is a more economical use of human, animal and material resources, and the elimination of unnecessary delay in the global development and availability of new medicines whilst maintaining safeguards on quality, safety and efficacy, and

regulatory obligations to protect public health. This Mission is embodied in the *Terms of Reference of ICH*.

ICH provides guidelines for drug substances (the active pharmaceutical ingredient) and drug products (the final marketed product). The topics covered include stability, analytical validation, impurities, pharmacopoeias, biotech products, specifications, GMP, pharmaceutical development and quality risk assessment. The guidelines are available at the ICH website (https://www.ich.org/). Information on CMC in ICH can be found under Quality guidelines https://www.ich.org/page/quality-guidelines.

C. International Organization for Standardization (ISO) (http://www.iso.org/iso/en/ISOOnline.frontpage)

ISO is a network of the national standards institutes of 157 countries, based on one member per country, with a Central Secretariat in Geneva, Switzerland, that coordinates the system. ISO (International Organization for Standardization) is the world's largest developer of standards. Although ISO's principal activity is the development of technical standards, ISO standards also have important economic and social repercussions.

ISO is a non-governmental organization: its members are not, as is the case in the United Nations system, delegations of national governments. Nevertheless, ISO occupies a special position between the public and private sectors. This is because, on the one hand, many of its member institutes are part of the governmental structure of their countries or are mandated by their government. On the other hand, other members have their roots uniquely in the private sector, having been set up by national partnerships of industry associations.

Therefore, ISO can act as a bridging organization in which a consensus can be reached on solutions that meet both the requirements of business and the broader needs of society, such as the needs of stakeholder groups like consumers and users.

ISO standards are voluntary. As a non-governmental organization, ISO has no legal authority to enforce their implementation. A certain percentage of ISO standards - mainly those concerned with health, safety or the environment - has been adopted in some countries as part of their regulatory framework or is referred to in legislation for which it serves as the technical basis. Such adoptions are sovereign decisions by the regulatory authorities or governments of the countries concerned; ISO itself does not regulate or legislate. The unwritten relationships are:

- European countries: handshake agreement with ISO
- US: arms distance
- Other geographies, i.e., India, some Asian countries: adopt ISO standards as regulatory rule.

D. International Pharmaceutical Excipients Council (IPEC)

From the IPEC website (http://www.ipec.org/) and (https://ipecamericas.org/)

IPEC is a federation of three independent regional industry associations headquartered in the United States (IPEC-Americas), Europe (IPEC Europe), and Japan (JPEC). Each association focuses its attention on the applicable law, regulations, science, and business practices of its region. The three associations work together on excipient safety and public health issues, in connection with international trade matters, and to achieve harmonization of regulatory standards and pharmacopoeial monographs. (http://www.ipecamericas.org/index.html)

Under U.S. law, a new pharmaceutical excipient, unlike an active drug, has no regulatory status unless it can be qualified through one or more of the three approval mechanisms available for components used in finished drug dosage forms, e.g.:

- GRAS determination pursuant to 21 CFR 182, 184, and 186;
- approval of a food additive petition in 21 CFR 171; and
- as contained in an NDA approval for a specific drug product and for a particular function or use in that dosage form.

All three mechanisms are time consuming, inordinately expensive, and have become increasingly complex in

recent years. None has a formal safety evaluation process or suitable approval process specifically for excipients. In addition, varying national drug registration or approval systems and differences in excipient monograph specifications among the three major pharmacopoeias, the PhEur, JP, and USP make it virtually impossible to produce a single finished drug formulation that can be marketed on a global basis. Note that the FDA has recently announced the Pilot Program for the Review of Innovation and Modernization of Excipients (PRIME). Its too early to tell how effective this will be at increasing the number of available excipients.

This situation is unlikely to change until:

· National drug approval systems are expanded to permit reasonable procedures for acceptance of new excipients and new excipient uses;

· An appropriate system exists for qualifying excipient suppliers and their products;

· Harmonization of compendia standards for more widely used pharmaceutical excipients is achieved among the major pharmacopoeias; and

· There is mutual recognition and mutual acceptance of pharmaceutical safety and effectiveness data from other national systems among the industrialized countries.

E. WHO/International Pharmacopoeia

(http://www.who.int/medicines/publications/pharmacopoeia/overview/en/index.html)

From the WHO/INP website: "The International Pharmacopoeia (IntPh) provides a collection of recommended quality specifications and methods of analysis for selected pharmaceutical products, excipients, and dosage forms. Recommended procedures are intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmacopoeial requirements. Tests described in the volume are designed to determine impurities on which attention should be focused, to fix the limits of those that are tolerable to a certain extent, and to indicate methods for ensuring the absence of those that are undesirable. In most cases, recommended tests rely on simple, classical chemical techniques suitable for use in developing countries.

The work on The International Pharmacopoeia is carried out in collaboration with members of the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations as well as specialists from industry and other institutions."

For reference purposes WHO compiles a list of national, regional and international pharmacopoeias

F. U.S. Pharmacopeia (USP)/National Formulary (NF)

The United States Pharmacopeia (USP) (http://www.usp.org/) is the official public standards-setting authority for all prescription and over-the-counter medicines, dietary supplements, and other healthcare products manufactured and sold in the United States. USP sets standards for the quality of these products and works with healthcare providers to help them reach the standards. USP's standards are also recognized and used in more than 130 countries. These standards have been helping to ensure good pharmaceutical care for people throughout the world for more than 185 years.

In 1975, the USP acquired the National Formulary. The scope of each was redefined in 1977: USP standards for drug substances and dosage forms; NF standards for excipients. The USP–NF is a book of public pharmacopeial standards that contains standards for medicines, dosage forms, drug substances, excipients, medical devices, and dietary supplements.

The U.S. Federal Food, Drug, and Cosmetics Act designates the USP–NF as the official compendia for drugs marketed in the United States. A drug product in the U.S. market must conform to the standards in USP–NF to avoid possible charges of adulteration and misbranding. The USP–NF is also widely used by manufacturers wishing to market therapeutic products worldwide. Meeting USP–NF standards is accepted globally as assurance of high quality.

In the United States, USP's role usually begins after the Food and Drug Administration (FDA) approves a drug for the market. USP works with pharmaceutical manufacturers and regulators to establish the public standards that approved drugs must continue to meet for quality, strength, and purity and to assure their safety and efficacy. Once USP standards are established and official, they are enforceable by the FDA.

G. Generally Recognized as Safe (GRAS)

"GRAS" is an acronym for the phrase **G**enerally **R**ecognized **A**s **S**afe. Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act (the Act), any substance that is intentionally added to food is a food additive, that is subject to premarket review and approval by FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use, or unless the use of the substance is otherwise excluded from the definition of a food additive (https://www.fda.gov/food/food-ingredients-packaging/generally-recognized-safe-gras)

From Burdock and Carabin (2004), GRAS is defined as ". . . a system for review and approval of ingredients for addition to food, was conceived at a time when the need for a less doctrinaire review of food ingredients was critical. The GRAS approval process for a food ingredient relies on the judgment of "...experts qualified by scientific training and experience to evaluate its safety..." the end product of which is no better or worse than that by FDA, but often more expeditious. The process and requirements for a successful GRAS determination are discussed and compared with that of the food additive petition (FAP) process. The future of the GRAS process is assured by its history of successful performance, bringing safe food ingredients to the consumer in a timely manner."[1]

[1] Burdock GA, Carabin, IG (2004) Generally recognized as safe (GRAS): history and description. *Tox Letts.* **150**:3-18

APPENDIX II. PRECLINICAL SAFETY EVALUATION

This comprises safety pharmacology, pharmacokinetic/toxicokinetic and toxicology studies.

A. Good Laboratory Practice (GLP)

GLP embodies a set of principles that provides a framework within which laboratory studies are planned, performed, monitored, recorded, reported and archived. These studies are undertaken to generate data by which the hazards and risks to users, consumers and third parties, including the environment, can be assessed for pharmaceuticals, agrochemicals, cosmetics, food and feed additives and contaminants, novel foods and biocides. GLP helps assure regulatory authorities that the data submitted are a true reflection of the results obtained during the study and can therefore be relied upon when making risk/safety assessments. Although fundamentally the same, a number of GLPs have been issued by different regulatory authorities. Links to some of the key ones are provided below:variations on

FDA: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=58

OECD:
http://www.oecd.org/document/63/0,2340,en_2649_34381_2346175_1_1_1_1,00.html

UK:
http://www.opsi.gov.uk/si/si1999/19993106.htm

B. International Conference on Harmonization (ICH)

In addition to the CMC guidance documents described above, ICH has also produced many guidelines for the preclinical assessment of pharmaceuticals. Copies of these documents are available at https://www.ich.org/page/safety-guidelines. Alternatively, ICH homepage can be used to find safety guidelines (https://www.ich.org/)

C. International Programme on Chemical Safety (IPCS INCHEM) (http://www.inchem.org/)

IPCS INCHEM is an invaluable tool for those concerned with chemical safety and the sound management of chemicals.

Produced through cooperation between the International Programme on Chemical Safety (IPCS) and the Canadian Centre for Occupational Health and Safety (CCOHS); IPCS INCHEM directly responds to one of the Intergovernmental Forum on Chemical Safety (IFCS) priority actions to consolidate current, internationally peer-reviewed chemical safety-related publications and database records from international bodies, for public access.

This program provides rapid access to internationally peer reviewed information on chemicals commonly used throughout the world, which may also occur as contaminants in the environment and food. It consolidates information from a few intergovernmental organizations whose goal it is to assist in the sound management of chemicals.

D. European Chemicals Agency

ECHA

E. Organization for Economic Co-Operation and Development (OECD) (http://www.oecd.org/home/0,2987,en_2649_201185_1_1_1_1_1,00.html)

The OECD groups 30 member countries sharing a commitment to democratic government and the market economy. With active relationships with some 70 other countries and economies, NGOs and civil society, it has a global reach. Best known for its publications and its statistics, its work covers economic and social issues from macroeconomics, to trade, education, development and science and innovation.

There are OECD guidelines for toxicity (safety) testing of chemicals. Unlike the ICH guidelines which specify under what circumstances and at what stage in development the various toxicity studies are required, the OECD guidelines indicate how the tests should be performed. A list of the guidelines is provided below:

F. Regional Guidance

In addition to the international guidance documents described above, some authorities have issued there own regional guidelines. Some key ones are available at the links provided below:

EMEA
http://www.emea.europa.eu/htms/human/humanguidelines/nonclinical.htm

FDA
http://www.fda.gov/cder/guidance/index.htm#Pharmacology/Toxicology

APPENDIX III. TRADE/REGULATORY ASSOCIATIONS

A. Cosmetics Europe (CE) (https://cosmeticseurope.eu/)

CE is the European Trade Association representing the interests of the cosmetic, toiletry and perfumery industry, and was set up in 1962.

- 23 national associations out of 25 EU member states
- 21 major international companies
- 7 associated or corresponding members

All in all, the European Association represents more than 2000 companies ranging from major international firms to small family-run organisations, often operating in niche markets. The cosmetic industry employs over 500,000 people within the European Union.

CE represents a wide range of products that go well beyond beauty aids. A significant part of the products we call cosmetics is made up of essential personal hygiene products such as deodorant, shampoo, toothpaste and

sunscreens, of which over 5 billion units are sold every year. Virtually every single person uses at least one of CE products every day and the average consumer spends the same amount on cosmetics and toiletries as he or she does for bread.

B. European Commission (EC)
(http://www.ec.europa.eu/)

The European Commission represents and upholds the interests of Europe as a whole. It is independent of national governments. It drafts proposals for new European laws, which it presents to the European Parliament and the Council. It manages the day-to-day business of implementing EU policies and spending EU funds. The Commission also keeps an eye out to see that everyone abides by the European treaties and laws. It can act against rule-breakers, taking them to the Court of Justice if necessary.

The requirements for pharmaceutical registration in the EU are controlled at three levels:

· Regulations – European law that must be adhered to

· Directives – legislative acts of the EU which require member states to achieve a particular result without dictating the means of achieving that result, i.e., the contents of the Directives need to be put into law by the individual member states

· Guidelines – guidance documents for the drug development process that do not have any legal authority

The Commission consists of 25 women and men — one from each EU country. They are assisted by about 24 000 civil servants, most of whom work in Brussels.

The President of the Commission is chosen by EU governments and endorsed by the European Parliament. The other commissioners are nominated by their national governments in consultation with the in-coming President and must be approved by the Parliament. They do not represent the governments of their home countries. Instead, each of them has responsibility for a particular EU policy area

The President and members of the Commission are appointed for a period of five years, coinciding with the period for which the European Parliament is elected.

Directorate General: Our job is to help make Europe's citizens healthier, safer and more confident.

Over the years the European Union has established EU laws on the safety of food and other products, on consumers' rights and on the protection of people's health.

The Health and Consumer Protection Directorate General has the task of keeping these laws up to date. It is national, regional or even local governments in EU countries who actually apply the EU's health and consumer protection laws. It is their job to make sure traders, manufacturers and food producers in their country observe the rules. Nonetheless, part of our job is to check that this is really happening and that the rules are being applied properly in all EU countries.

SCCP
http://ec.europa.eu/health/ph_risk/committees/04_sccp/04_sccp_en.htm

Questions concerning the safety of consumer products (non-food products intended for the consumer). In particular, the Committee will address questions in relation to the safety and allergenic properties of cosmetic products and ingredients with respect to their impact on consumer health, toys, textiles, clothing, personal care products, domestic products such as detergents and consumer services such as tattooing.

C. European Medicines Agency (EMEA)

European Medicines Agency (EMEA) is a decentralized body of the European Union with headquarters in Amsterdam. (https://www.ema.europa.eu/en)

- Its main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use. The EMEA coordinates the evaluation and supervision of medicinal

products throughout the European Union. The Agency brings together the scientific resources of the 25 EU Member States in a network of 42 national competent authorities. It cooperates closely with international partners, reinforcing the EU contribution to global harmonisation.

- The EMEA is headed by the Executive Director and has a secretariat of about 360 staff members in 2004. The Management Board is the supervisory body of the EMEA, responsible for budgetary matters.
- The EMEA began its activities in 1995, when the European system for authorising medicinal products was introduced, providing for a centralised and a mutual recognition procedure. EMEA has a role in both, but is primarily involved in the centralised procedure. Where the centralised procedure is used, companies submit one single marketing authorisation application to the EMEA. A single evaluation is carried out through the Committee for Medicinal Products for Human Use (CHMP) or Committee for Medicinal Products for Veterinary Use (CVMP). If the relevant Committee concludes that quality, safety and efficacy of the medicinal product is sufficiently proven, it adopts a positive opinion. This is sent to the Commission to be transformed into a single market authorisation valid for the whole of the European Union.
- In 2001, the Committee on Orphan Medicinal Products (COMP) was established, charged with reviewing designation applications from persons or companies who intend to develop medicines for rare diseases (so-called 'orphan drugs'). The Committee on Herbal Medicinal Products (HMPC) was established in 2004 and provides scientific opinions on traditional herbal medicines.
    - A network of some 3,500 European experts underpins the scientific work of the EMEA and its committees.

D. Food and Drug Administration (FDA) (http://www.fda.gov/)

FDA is an agency within the Department of Health and Human Services and consists of eight centers/offices, which are listed below.

FDA Center/Office Websites (http://www.fda.gov/)

Center for Biologics Evaluation and Research (CBER) https://www.fda.gov/about-fda/fda-organization/center-biologics-evaluation-and-research-cber

Center for Devices and Radiological Health (CDRH) https://www.fda.gov/about-fda/fda-organization/center-devices-and-radiological-health

Center for Drug Evaluation and Research (CDER) https://www.fda.gov/about-fda/fda-organization/center-drug-evaluation-and-research-cder

Center for Food Safety and Applied Nutrition (CFSAN) https://www.fda.gov/about-fda/fda-organization/center-food-safety-and-applied-nutrition-cfsan

Center for Veterinary Medicine (CVM) https://www.fda.gov/about-fda/fda-organization/center-veterinary-medicine

National Center for Toxicological Research (NCTR). https://www.fda.gov/about-fda/office-chief-scientist/national-center-toxicological-research

Office of the Commissioner (OC) https://www.fda.gov/about-fda/fda-organization/office-commissioner

Office of Regulatory Affairs (ORA)https://www.fda.gov/about-fda/fda-organization/office-regulatory-affairs

FDA-Affiliated Organizations

Joint Institute for Food Safety and Applied Nutrition (http://www.jifsan.umd.edu/)

National Center for Food Safety and Technology (https://www.ifsh.iit.edu/about/national-center-food-safety-and-technology-ncfst)

E. International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)

IFPMA is a non-profit, non-governmental organization representing industry associations from developed and non-developed countries. Clinical trial results are published at this site. http://clinicaltrials-dev.ifpma.org/

The International Federation of Pharmaceutical Manufacturers & Associations is a non-profit, non-governmental Organization (NGO) representing national industry associations and companies from both developed and developing countries. Member companies of the IFPMA are research-based pharmaceutical, biotech and vaccine companies.

In the research and development pipeline, the pharmaceutical industry is working on more than 700 new medicines and vaccines for infectious diseases including HIV/AIDS, cancer, heart disease and stroke, and diseases that disproportionately affect women, such as osteoporosis.

The main objectives of IFPMA are:

· to encourage a global policy environment that is conducive to innovation in medicine, both therapeutic and preventative, for the benefit of patients around the world.

· to contribute industry expertise and foster collaborative relationships and partnerships with international organizations, national institutions, governments and non-governmental organizations that are dedicated to the improvement of public health, especially in developing and emerging countries.

· to assure regular contact and experience-sharing and coordinate the efforts of its members towards the realization of the above objectives.

F. Personal Care Products Council (PCPC) (https://www.personalcarecouncil.org/about-us/)

PCPC provides a complete range of services that support the personal care products industry's needs and interests in the scientific, legal, regulatory, legislative, and international fields. PCPC strives to ensure that the personal care products industry has the freedom to pursue creative product development and compete in a fair and responsible marketplace. PCPC represents the industry's interests at the local, state, national, and international levels, promoting voluntary industry self-regulation and reasonable governmental requirements that support the health and safety of consumers.

PCPC has an ingredient database where information regarding chemicals may be found.

CIR (http://www.cir-safety.org/)

The Cosmetic Ingredient Review (CIR) was established in 1976 by the Cosmetic, Toiletry & Fragrance Association (CTFA), now known as PCPC, with support of the U.S. Food & Drug Administration and the Consumer Federation of America. Although funded by PCPC, CIR and the review process are independent from PCPC and the cosmetics industry. The Cosmetic Ingredient Review thoroughly reviews and assesses the safety of ingredients used in cosmetics in an open, unbiased, and expert manner, and publishes the results in the open, peer-reviewed scientific literature.

G. PhRMA (Pharmaceutical Research and Manufacturers of America) (http://www.phrma.org/)

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA companies are leading the way in the search for new cures.

PhRMA's mission is to conduct effective advocacy for public policies that encourage discovery of important new medicines for patients by pharmaceutical/biotechnology research companies.

The clinical trials database is accessible as is a synopsis of the drug review process.

H. WHO (World Health Organization)
(http://www.who.int/en/)

The World Health Organization is the United Nations specialized agency for health. It was established on 7 April 1948. WHO's objective, as set out in its Constitution, is the attainment by all peoples of the highest possible level of health. Health is defined in WHO's Constitution as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.

WHO is governed by 193 Member States through the World Health Assembly. The Health Assembly is composed of representatives from WHO's Member States. The main tasks of the World Health Assembly are to approve the WHO programme and the budget for the following biennium and to decide major policy questions.

http://www.who.int/topics/en/

The health topics link at the WHO website provides useful information and additional resources for many of the health issues of importance.

Spoke solves the solubility problem

Spoke Sciences builds regulatory strategy and compliance into our solutions. We do not simply solve the solubility problem for your favorite ingredients, we also incorporate regulatory intelligence to up-level your compliance. Please contact us if you would like to learn more.