Legal Aspects of cosmetic products

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Legal Aspect

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The Federal Food, Drug, and Cosmetic act and regulation of cosmetics

In June 1906, President Theodore Roosevelt signed the laws of Food and Drug Act, also known as the "Wiley Act". As per this act it prohibited, seizure of goods, interstate adulterated food transport, with referring to the addition of reduced quality or strength, formulation with additives which is injurious to health, or the/ use of grumpy, decomposed, or fetid substances. Misbranded food and drugs have been banned after approval of this act. The responsibility was given to Wiley's USDA Bureau of Chemistry for examination of food and drugs for adulteration and misbranding. In 1911 Supreme Court took decision and said that the 1906 act have not been applied for false claims of therapeutic efficacy, in response to which a 1912 amendment added "false and fraudulent" claims of "curative or therapeutic effect" to the Act's definition of "misbranded." In 1927, the Bureau of Chemistry's regulatory powers was reorganized under a new USDA body, the Food, Drug, and Insecticide organization which was shortened to the Food and Drug Administration (FDA) after three years (Source: https://www.drugs.com).

By the 1930s, it was widely assumed that the Food and Drugs Act of 1906 was obsolete. By 1937, most of the arguments had been resolved but Congressional action was stalled. Then came a shocking incident, deaths of more than 100 people after using a drug that was clearly unsafe.
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The incident hastened final enactment in 1938 of the Federal Food, Drug, and Cosmetic Act, the statute that today remains the basis for FDA regulation of these products.

A committee was passed Federal Food, Drug, and Cosmetic Act (FDCA) in 1938. The FDCA set up the Food and Drug Administration (FDA) to enforce this Act. The objectives of the FDCA were to ensure that foods are pure and not dangerous to eat, drugs and medical devices are to be safe and effective, and cosmetics may also be safe. It also regulates the labeling and packaging of foods, drugs, medical devices, and cosmetics. *Food and Drug Administration (FDA) is an agency of Department of Health and Human Services of the United States which is responsible for the safety of most types of foods, supplements, drugs, vaccines, biological products, medical devices, radiation-emitting devices, veterinary products, and cosmetics. The FDA enforces section 361 of the Public Health Service Act and its associated regulations. Time to time, FDCA has been amended and included more area related to food, drug and cosmetics (Source: www.fda.gov).*

The Food Additives Amendment of 1957 amended the FDCA to regulate food additives. The Delaney Clause of 1958 prohibited the use of substances in food if such substances, particularly food coloring agents, had been found to cause cancer in laboratory animals.

The Drug Amendments of 1962 also changed the FDCA. These amendments required drug manufacturers to show that their drugs are safe and effective. A new drug cannot be marketed
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except a new drug application (NDA) is effective. Congress passed the Medical Device Amendments to the FDCA in 1976.

Medical Device Amendments 1976 separate medical devices into three categories.

**Class I devices:** Which pose no unreasonable risk of illness or injury, and require only general manufacturing controls.

**Class II devices:** Which pose a greater potential risk of illness or injury and are subject to more stringent controls.

**Class III devices:** Which pose a potential unreasonable risk of illness or injury and are subject to the FDA's strictest regulation.

In 1997, Congress passed the Food and Drug Administration Modernization Act (Modernization Act), which amended the provisions of the FDCA relating to food, drugs, medical devices, and biological products. The goal of the Modernization Act was greater patient access to new medical products. One provision of the Modernization Act exempts compounded drugs from the FDA's standard drug approval requirements if the drug providers comply with several restrictions. One restriction was that the drug providers could not advertise or promote particular compounded drugs. In 2003, Congress passed the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Prescription Drug Act), which is also amended the FDCA. The Prescription Drug Act eliminates a new drug application holder's ability to obtain multiple stays
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to delay the marketing of a generic drug. The Prescription Drug Act provides for a Medicare-approved discount card to help pay for prescription drugs also.

The FDA regulation of cosmetics relate to adulteration and misbranding of cosmetics which is as given:

Subchapter VI: Section 361- Adulterated cosmetics

Section 362 - Misbranded cosmetics

Section 363 - Regulations making exemptions

Section 364 - Repealed

Section 361- Adulterated cosmetics: A cosmetic shall be deemed to be adulterated-

(a) If it bears or contains any poisonous or deleterious substance which may possibly reason for injury to consumers. This provision is not applicable to coal-tar hair dye.

(b) In case it may contain in whole or part of any filthy, fetid, or decomposed substance.

(c) In case it has been prepared, packaged, or held in not satisfactory conditions which may result in contamination with filth, or whereby it may cause injury to health.

(d) If the container as whole or partly is of any poisonous or deleterious substance which may cause injury to health of consumers.

(e) If it is not a hair dye and, or it contains, unsafe color additive.
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Section 362-Misbranded cosmetics:

(a) If the labeling is false or misleading

(b) If in package it contains a label containing either the name and place of business of the manufacturer/ packer/ distributor or specifications of the quantity of the contents by weight, measure, or numerical count within permitted variations.

(c) If any information required as per the act required to appear on the label is not placed

(d) If container is formed, made, or filled as to be mislead.

(e) If the colour or additive used is as per its packaging and labeling are in conformity with requirements. This is not applicable to packages of color additives which, with respect to their use for cosmetics, are marketed and intended for use only in or on hair dyes.

(f) If its packaging or labeling is in violation of any regulation.

Section 363-Regulations making exemptions: The Secretary shall promulgate regulations exempting from any labeling requirement of this Act. Cosmetics which are, in accordance with the practice of the trade, to be processed, labeled, or repacked in substantial quantities at establishments other than those which are originally processed or packed, on condition that such
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cosmetics are not adulterated or misbranded under the provisions of this Act upon removal from such processing, labeling, or repacking establishment. (Source: https://dash.harvard.edu)

The FDA has heavily relied on cosmetic industry for regulating itself with the intention of ensure consumers safety. But it was found that the system of self-regulation was ineffective, inefficient, and/or inappropriate.

The 1938 Act does not grant the FDA to authorize cosmetic manufacturers, submission of ingredient list, or submission of pre-market information or safety data for cosmetic products. The website section entitled “FDA Authority Over Cosmetics” notably features two subsections which clearly declare the respective roles of the FDA and cosmetics industry. A persistent safety issue in cosmetic is the distinction between drugs and cosmetics. The unlike outcomes of 1960s cases regarding “wrinkle remover” products claims established what would be an enduring difficulty in differentiating between drug and cosmetic claims in cosmetic labeling.

**Drug & Cosmetic Act, 1940**

A bill was introduced in 1937 in the Central Legislative Assembly to make effective the drugs enquiry committee for regulating the import of drugs into British India. The Drugs and Cosmetics Bill was passed by the Central Legislative Assembly, it received the consent of the Governor General on 10th April, 1940 and became the Drugs and Cosmetics Act, 1940 (23 of
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1940). It was passed by the Parliament of India on 10<sup>th</sup> April 1940 and applied all over India except Jammu and Kashmir. It regulates import, manufacture and distribution of drugs in our country. The prime intention of this act is to assure of drugs and cosmetics sold in India are safe, effective and authentic the quality standards. The related Drugs and Cosmetics Rules, 1945 contains provisions for classification of drugs under given schedules and there are guidelines for the storage, sale, display and prescription of each schedule. This act was originally known as the Drug Act and was passed in 1940. In 1930, the original act was prepared in agreement to the recommendations of the Chopra Committee. The related Drugs Rules was passed in 1945. Since 1940, the act has undergone several amendments and is now known as the Drugs and Cosmetics Act, 1940. The Section 16 of the act defines the standards of quality for drugs. The Section 17 defines "misbranding". A drug is considered misbranded if it claims more therapeutic value than it actually has. The manufacturer of such a drug may be asked to suspend manufacture of the drug under Section 18. Section 27 deals with fake and adulterated drugs. The act requires that ingredients of the drugs should be printed on the label. The Section 22 defines the powers of the drug inspectors and Section 23 defines the strict procedure which should be followed by the inspectors during any raids. But the Act lacks specific penalties for violation related to clinical trials. Time to time various amendments were added as follow:

LIST OF AMENDING ACTS AND ADAPTATION ORDERS

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2. The Adoption of Laws Order, 1950.


Legislation and regulations for perfumes and cosmetics

Various products used every day contain fragrances. Some of these products are regulated as cosmetics by FDA. If a product is intended to be applied to a person’s body to make the person more attractive, it’s a cosmetic under the law. Here are some examples of fragrance products that are regulated as cosmetics: Perfume, Cologne, and Aftershave. Fragrance ingredients are also commonly used in other products, such as shampoos, shower gels, shaving creams, and body lotions. Even some products labeled “unscented” may contain fragrance ingredients. This is because the manufacturer may add just enough fragrance to mask the unpleasant smell of other
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ingredients, without giving the product a noticeable scent. Some products are applied on to the body are also anticipated for therapeutic activities, such as to treat or prevent disease, or to affect the structure or function of the body. Products intended for this type of use are treated as drugs under the law, or sometimes as both cosmetics and drugs. Here are some examples of labeling statements that will cause a product containing fragrances to be treated as a drug: Easing muscle aches, soothing headaches, helping people sleep and treating colic.

Fragrance ingredients in cosmetics must meet the same requirement for safety as other cosmetic ingredients. The law does not need FDA approval prior to launch on the market, but they must be safe for consumers when they are used according to labeled directions, or as people customarily use them. Companies and individuals who produce or market cosmetics must have a legal responsibility to ensure that, products are safe and appropriately labeled. If a cosmetic is marketed on a retail basis to customers, such as in stores, on the internet, direct sell to consumers, it must have a full list of ingredients. But under U.S. regulations, flavor and fragrance ingredients can be listed as “Flavor” or “Fragrance” simply.

Nowadays safety is an increasing concern with fragrance chemicals. Increasingly, perfumes are the major cause for asthma, allergies, migraine, headaches, and other problems. The FDA does not require safety testing of ingredients that are used for cosmetics or perfumes. FDA must prove in court that the product is unsafe before it can require the product be removed from the market.
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marketplace. Many times, manufacturers will voluntarily recall a product that is in problem. The FDA does not require companies to register with the FDA, file the ingredients used, or even keep a record of injuries related to the use of their products. There is a voluntary data collection program if manufacturers wish to participate. The fragrance industry does come under the regulation of the FDA, but the regulation is extremely limited. Many of the ingredients used in fragrances have little or no safety testing done. FDA issues regulations to implement its statutory authority. The regulations can create binding obligations and have the force of law. Here are some regulations related to cosmetics, from Title 21 of the Code of Federal Regulations (21 CFR):

- 21 CFR Part 1- General Enforcement Regulations
- 21 CFR Part 2- General Administrative Rulings and Decisions
- 21 CFR Part 20- Public Information
- 21 CFR Part 250 Section 250- Requirements for Drugs and Cosmetics-Hexachlorophene
- 21 CFR Part 700 Subpart A (Section 700.3)- Cosmetics- General Provisions
- 21 CFR Part 700 Subpart B (Sections 700.11 Through 700.35)- Requirements for Specific Cosmetic Products
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- 21CFR Part 701 Subpart A-(Sections 701.1 Through 701.9) Cosmetic Labeling- General Provisions
- 21 CFR Part 701 Subpart B -(Sections 701.10 Through 701.19) Package Form
- 21 CFR Part 701 Subpart C-(Sections 701.20 through 701.30) Labeling of Specific Ingredients
- 21 CFR Part 710 -Voluntary Registration of Cosmetic Product Establishments
- 21 CFR Part 740 - Cosmetic Product Warning Statements

Safety testing and toxicology of cosmetics

In the different cosmetics regulations worldwide a cosmetic safety assessment for human health is completed for cosmetic products. In addition, cosmetic products should be correctly labelled and packaged with appropriate INCI (International Nomenclature for Cosmetic Ingredients) ingredients listing and warnings. A cosmetic safety assessment is an approach mandated in the EU, but also widely requested by buyers and authorities in North America, ASEAN Cosmetics Directive, Saudi Arabia and other countries like China which consider it as an alternative method. Cosmetic products which are in market must be safe and able to demonstrate the safety and to provide sufficient information to the authorities and consumers also. Safety of cosmetics
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is guaranteed through safety assessment and for that purpose, a unique dossier has to be composed. Several possible reasons may be given that suggest potential safety assessors of cosmetics must follow specific training in safety assessment.

The purposes of safety and toxicological testing are:

- Cosmetic preparation must be safe both for consumers as well as involved professionals like hairdressers or beauticians, etc.).
- Skin irritation and skin sensitization reaction may be avoided in case of skin preparations.
- Products applied on the scalp or the face may possibly come in contact with the eye. Thus, eye tolerance test has to be assessed for a cosmetic product.
- Systemic toxicity result from percutaneous absorption or from accidental (children) or sensibly foreseeable (e.g. oral hygiene products, lipsticks) oral intake should be considered.
- Ensuring the safety of cosmetic product requires a worldwide approach all over the life of the product from raw materials to the marketing.

Cosmetic ingredients are mostly chemicals and often mixtures of chemicals of synthetic origin or natural extracts. The careful selection of ingredients is key issue for ensuring the safety of the finished product. The toxicological profile of a raw material is obtained by
analyzing available data, concerning the raw material. These data include results of *in vitro*, *in vivo* and clinical testing and results of epidemiological studies also if available. *In vivo* studies make it achievable to investigate the toxicological outline of a cosmetic ingredient when apply to an animal by a route of exposure (topical, oral or by the inhalation route). They allow the determination of no-observed adverse effect levels (NOAEL), and also adverse effects at higher exposure.

**General toxicological requirements for cosmetics (Source: www.fda.gov)**

*It is mandatory to provide information when authorities demanded/requested on different tests as:*

- Acute toxicity
- Skin absorption
- Skin irritation
- Mucous membrane irritation
- Skin sensitization
- Sub-chronic toxicity
- Mutagenicity
- Phototoxicity and Photomutagenicity (in case of UV-light absorbing substances)
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- Human data (if available)
- Toxicokinetics
- Teratogenicity
- Reproduction toxicity
- Carcinogenicity and Genotoxicity
- Metabolism studies

ISO guidelines for cosmetics

The International Organization for Standardization (ISO) is an international standard-setting body composed of representatives from various national standards organizations. Current FDA’s thinking is concerned that what constitutes Good Manufacturing Practices (GMPs) for cosmetics. It is intended to aid industry to identify the standards and issues which may affect the quality of cosmetic products. In addition, as part of an international harmonization effort with the International Cooperation on Cosmetic Regulations (ICCR), FDA agreed to consider the current International Organization for Standardization (ISO) standard for cosmetic GMPs (ISO 22716:2007). ISO is a non-governmental organization which develops and publishes international standards. In September 2007, a met in Belgium of International Cooperation on Cosmetic Regulation (ICCR) was held. During this meeting, the regulators from the United States, Canada, the European Union, and Japan agreed that standardized scheme for GMPs
Legal Aspects of cosmetic products would be useful for the cosmetic industry. The regulators from this meet agreed to take ISO standards for cosmetic GMPs into consideration. GMPs are manufacturing guidelines which are used to ensure product quality control and an effective approach to risk management. These guidelines set out standards for product manufacturing, testing, storage, handling and distribution, to ensure that each step of manufacturing is acceptable for quality and safety of the product. GMPs do not provide specifics on how products are to be manufactured. Instead they outline the expected outcome of the processes. Each manufacturer, large or small, may have a unique means of achieving these outcome (source: www.fda.gov).

There are some important things which must be considered when manufacturing cosmetics to ensure they remain free of contamination, means safe and effective.

- Building and Facilities
- Equipments
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- Personnel
- Raw Materials
- Production
- Laboratory Controls
- Records
- Labelling
- Complaints (feedback)
Cosmetic and personal care companies are receiving increasing pressure from customers to provide solid scientific evidence to support product claims.

**Clinical and Efficacy testing**

Cosmetic products should provide evidences to support product claims. Various labels touting 80% stronger hair, 24 hour effective, reduces wrinkles, and the list goes on. But consumers are wise now, and companies are forced to change their tactics. Companies can no longer rely purely on their marketing claims. With the development of ways to measure cosmetic and personal care effects, they can now backup their claims. Until the 1950s most efficacy tests were subjective, but now instrumental methods have been created including *in vitro* and *in vivo* measurements on human volunteers. Instrumental evaluation is often used in an attempt to provide data to support claims commonly associated with the reversal of the signs of ageing due to intense scrutiny from both the regulators and competitors. A cosmetic scientist may have a different understanding of what is meant by the product claim than that of a consumer. Therefore, it is important to understand different terms and their scientific meaning when reading product claims. Studies must be relevant and analytical methods must be reliable and reproducible. Studies must follow an elegant and scientifically valid methodology as per good practices. The criteria applied for evaluation of cosmetics product performances must be accurate and precise. Studies conducted...
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on volunteers should be conducted as per the ethical guidelines and products tested should have undergone safety studies. Clinical studies should be conducted on the target population as per the inclusion/exclusion criteria. Tests can be open, single- or double-blind, depending on the aim of the study. The laboratories must have standardized operating procedures (SOPs). The maintenance of the equipment should be documented. The personnel conducting the study have qualifications, training and experience in the field of study, and ethical quality and integrity.

This section highlights the safety and efficacy of cosmetic products that are tested by validated in vitro methods that are substitute for the animal or human testing.

**Evaluation of antioxidant activity**

The ability of the cosmetic product to inhibit the formation of free radicals in cells exposed to oxidative stress, such as UVA irradiation and/or treatment with hydrogen peroxide, is to be analyzed for determining the anti-oxidant power. The cell viability is also to be assessed to highlight a potential protective activity of the given sample.

**Evaluation of the protection of DNA from oxidative stress**

The protective activity of a cosmetic product must be evaluated for its potential ability to reduce the damage caused by oxidative stress to DNA using specific markers. Assessment to detect
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variations of the nuclear morphology and, subsequently, the possible protection from part of the product against DNA after induction of the damage through irradiation with UV radiation.

**Evaluation of energizing**

For energizing action of a cosmetic product and/or raw materials on cell cultures of human keratinocytes, MTT assay and the analysis of the ATP content must be carried out. The MTT assay assesses *in vitro* viability of cells exposed to product and compared to untreated cells with varying concentration, in order to highlight the maximum non-cytotoxic concentration of the product to be used in the assay. The variation of the ATP content is to be analyzed in order to verify whether the product and/or raw material possesses an energizing activity.

**Evaluation of regenerating activity**

For regenerative action of a cosmetic product on cell cultures of human keratinocytes, MTT assay must be carried out, which evaluate the viability of cells *in vitro* exposed to product and to highlight, if it exists, the concentration can stimulate cell growth. The protein synthesis also needed evaluation in order to verify the product/raw material has regenerating activity or not.

**Evaluation of anti-inflammatory activity**

Inflammatory reactions generate pathologies by contact and they are a very important field of study to understand the effects of cosmetics on human skin and appendages. Tests may involve
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identification of the new markers intra/extracellular and quantification of cytokines released in the cells in contact with the cosmetic/ devices to be analyzed.

**Evaluation of pro-sensitizing potential**

The test must be able to evaluate the potential pro-sensitizing caused by raw materials/finished products for medical and cosmetic use by flow cytometric analysis of membrane antigens. Through the analysis of the expression of co-stimulatory molecules, the immunological reactivity of immune cells (monocytes) exposed to contact with the substance under examination, after having identified the non-toxic concentrations may be evaluated using MTT test.

**Evaluation of moisturizing activity**

The main effect of photo aging induced by ultraviolet radiation is the dehydration of the skin. To examine through alternative methods including *in vitro* study of the activity, it is possible to evaluate the expression of proteins capable of forming channels in the cell membrane in order to facilitate the transport of water, such as aquaporins, using western blotting technique. The functionality of these proteins influences the motility of keratinocytes, studied by the wound healing technique.

**Skin irritation evaluation on a 3D epidermis model**
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The assay may evaluate the potential irritant effect caused by the cosmetic product / medical device on an *in vitro* three-dimensional human skin model, according to the standard ISO 10993-10: 2010 reference.

**Mucoadhesion test**

Mucous membrane contact with harmful substances or irritants may be owed to its penetration, causes severe degenerative effects. The administration of substances with mucoadhesion property may add to protect the mucosa from aggression risk. To assess mucoadhesion of products, the binding inhibition of proteins (mucin) should be assessed.

**Antiplaque activity test**

The evaluation of antiplaque activity of a product is based on the ability of the product itself to inhibit the growth of the main bacteria responsible for dental plaque. Thus the products must be tested over specific bacteria and calculate their efficiency with respect to standard.

**In vitro evaluation of the barrier effect**

It is important to evaluate the possible barrier effect produced by the cosmetic product/medical device after damage induced by an irritating agent on a human epithelial three-dimensional model, according to validated protocols.
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(The content writer would like to declare that various official sources have been consulted and reproduced as per the official language).