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Commentary/Commentario

Regulation of cosmetic safety in the United States

Regolamentazione della sicurezza dei cosmetici negli Stati Uniti

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Summary

Cosmetic products are very lightly regulated in the United States, even though cosmetic products may contain hazardous ingredients, including carcinogens. Cosmetic products associated with carcinogenic constituents include hair dyes and, in the past, hair sprays. Gaps in the basic law that controls cosmetics safety- the Federal Food, Drug and Cosmetic Act (FFDCA) are in large part responsible for the Food and Drug Administration (FDA) failing to act on behalf of consumers who use cosmetics. Eur. J. Oncol., 15 (2), 111-117, 2010

Key words: **cosmetics, carcinogens, Food, Drug and Cosmetic Act (FFDCA), Food and Drug Administration (FDA)**

Riassunto

Norme molto leggere regolano i prodotti cosmetici negli Stati Uniti, nonostante questi possano contenere ingredienti nocivi, agenti cancerogeni inclusi. I prodotti cosmetici associati a componenti cancerogeni includono le tinture per capelli e, in passato, gli spray e le lacche per capelli. Le lacune nella principale legge che controlla la sicurezza dei cosmetici, l'Atto Federale per gli Alimenti, i Medicinali e i Cosmetici (Federal Food, Drug and Cosmetic Act o FFDCA), sono in larga parte responsabili della mancata azione dell'Agenzia per gli Alimenti e i Medicinali (Food and Drug Administration o FDA) a tutela dei consumatori che usano cosmetici. Eur. J. Oncol., 15 (2), 111-117, 2010

Parole chiave: **cosmetici, cancerogeni, Atto per gli Alimenti, i Medicinali e i Cosmetici, Agenzia per gli Alimenti e i Medicinali**

Regulation of cosmetic safety in the United States

Regulation of cosmetic safety in the United States is essentially nonexistent. This is true even though cosmetics have long contained, and contain at this time, very hazardous constituents, including chemicals known to cause cancer in animals and/or humans.

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What is a cosmetic?

For purposes of regulation, Food and Drug Administration (FDA) has a very broad definition of "cosmetic" (Table 1) (1). People often think of cosmetics as beauty products used by women, but cosmetics, as defined for regulatory purposes, are used by women, men and children. The regulatory definition of cosmetic, from the Federal Food, Drug and Cosmetic Act (FFDCA) (2) is:

"Cosmetic: articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for beautifying, promoting attractiveness, or altering the appearance, and articles intended for use as a component of any such articles, except that such term shall not include soap".

The definition of cosmetic should be read in conjunction with the most pertinent definition of drug in the FFDCA (3):

"Articles…intended to affect the structure or any function of the body of man…".

Some products that would not ordinarily be thought of as cosmetics are, indeed, cosmetics (4). For instance, some soaps, some shampoos, and some toothpastes are cosmetics. Soaps are not cosmetics if they clean and only clean, but a soap that moisturizes is both soap and cosmetic. Shampoos that claim that they clean the hair and make no claims other than, perhaps, providing a fresh feeling and a pleasant fragrance, are cosmetics. However, shampoos that also claim to relieve the symptoms of dandruff and contain anti-dandruff ingredients are both cosmetics and drugs. A similar situation applies to toothpastes and mouthwashes, which are cosmetics if they make claims to sweeten breath and clean the teeth, but are both cosmetics and drugs if they claim to prevent cavities and gingivitis, and kill bacteria.

One particularly interesting category of cosmetics widely used by both men and women is deodorants/antiperspirants. Deodorants may include perfume (liquid) or a cream, gel or solid formulation. A deodorant's function is simply to cover up body odor. An anti-perspirant, on the other hand, is a drug because ingredients in the formulation affect production of sweat. Thus, deodorant/antiperspirant combinations are both drugs and cosmetics.

Some chemicals that provide cosmetics with their physical state (solid, liquid, gel) may be carcinogenic. Asbestiform talcs in talcum powders are good examples of potentially carcinogenic ingredients that establish the physical state of a product. Preservatives include chemicals, such as ethanolamines, that have been identified as precursors to animal carcinogens (nitrosamines). Formaldehyde, used as a preservative in some cosmetics, is a human carcinogen.

Many cosmetic products are marketed in spray formulations, so propellants are important constituents of cosmetics. Vinyl chloride, a human carcinogen, was used as a propellant in hair sprays.

Over the years, some exceedingly unusual ingredients have been used in cosmetics, most notably in "treatment" products. Ingredients used in the past have included female hormones (estrogens, known human carcinogens).

Table 1 - Cosmetics: regulatory scope of FDA authority (product categories) (1)

Skin moisturizers
Perfume (fragrance)
Lipstick
Nail polish, nail hardeners, polish remover
Synthetic nails
Eye make-up (mascara, eye shadow)
Face make-up (foundation, powder, blush, rouge)
Shampoo*
Permanent waves/setting lotion
Hair relaxers
Shaving products
Hair colors (coal-tar dyes and non-coal-tar colors, including metallic dyes)
Toothpaste*
Deodorant*
Soap (moisturizing)*
Bubble bath, bath oil
Cosmetics for children (baby lotion, skin cream, bubble bath, play make-up)

*See text for exceptions/notes

How are cosmetics regulated in the United States?

In an earlier paper (5) in this journal, the author discussed FDA's regulation of food additives. Regulation of food additives has been inadequate, but the situation is even worse for cosmetics, in large part because of the lack of statutory authority necessary for effective regulation of cosmetics.

Perhaps the most critical lack is that of pre-market safety clearance for cosmetic products and cosmetic ingredients (other than color additives). In fact, cosmetics constitute the only product category regulated by FDA for which pre-market safety clearance is not required. For both food additives, which are essentially cosmetics for food, and cosmetics, efficacy of the additive or cosmetic is considered irrelevant. For regulatory purposes, only safety matters, but there is no effective review by FDA of a cosmetic's safety before the product goes on the market.

Responsibility for regulating both food additives and cosmetics rests with the FDA's Center for Food Safety and Applied Nutrition (CFSAN). CFSAN is responsible for food safety, which has been of great concern in the United States in recent years. An emphasis on food safety is unlikely to be of much help to the cosmetics component of the Center, since it is unlikely that FDA would be willing to expend scarce resources on a program that is virtually unenforceable because of weak statutory authority.

Post-market removal of a cosmetic deemed unsafe depends on FDA's determination that a product is adulterated and/or misbranded. The concept of adulteration deals with the intrinsic safety of a cosmetic; if a product is unsafe, it is considered adulterated, and cannot be marketed. Misbranding deals with labeling, and if labels misrepresent required disclosures or characteristics of a cosmetic product, the product can be removed from the market.

Cosmetics companies are required to have on hand substantiation for the safety of their products. However, since the companies aren't even required to let FDA know that they are manufacturing/marketing cosmetic products and/or cosmetic ingredients, aren't required to report to FDA which ingredients are found in their products, and aren't required to report consumer injuries or illnesses, decisions to enforce against a product for adulteration or misbranding are, of necessity, very difficult to make.

Even when FDA attempts to enforce against a cosmetic product for adulteration or misbranding, the agency lacks authority to order that the marketer recall its unsafe products. Companies may choose to carry out voluntary recalls.

Although FDA lacks authority to do pre-market safety clearance, require submission of information on the identity of product manufacturers and the constituents of products, the agency has, to some extent, worked around these statutory gaps by setting up cooperative voluntary programs with the cosmetics industry. Thus, the Cosmetic Ingredient Review (CIR) (6) carries out reviews of ingredient safety. Prescription drug advertising labeling and advertising are regulated by FDA, and the agency can proceed against product marketers for misrepresentations. Labeling of over-the-counter (OTC) drugs is regulated by FDA, but advertising for OTC drugs is controlled by the Federal Trade Commission (FTC). Advertising for cosmetics is regulated by the FTC, which has tended to do very little enforcement against unjustified claims made for cosmetic products.

There have been occasional efforts to strengthen the law governing regulation of cosmetics by FDA. The last real success in improving cosmetics regulation came in 1960, with the passage of the Color Additive Amendments to the FFDCA (7) and application of the anti-cancer Delaney Clause (see below) to color additives. Unfortunately, the group of cosmetics about which there has likely been the greatest concern as regards possible carcinogenic effects, the coal-tar hair dyes, were not included in the structures of the Color Additives Amendment, although the dyes are subject to the Delaney Clause.

It is likely the most important statutory exemption to regulation of cosmetics is the one applicable to coal-tar hair dyes. Under provisions of the 1938 FFDCA, coal-tar hair dyes are exempted from enforcement as unsafe under the adulteration provisions of the FFDCA so long as packages of dyes meant for home use bear a prescribed warning against using the products in the area of the eyes and noting that the products can irritate skin and users should perform a patch test before using the color product on the scalp (8).

By 1938, the carcinogenicity in humans as well as animals of benzidine and related coal-tar dyes was well-known. However, that potential carcinogenicity was ignored when the exemption was granted, ensuring that products possibly unsafe in terms of being potentially carcinogenic, even if used according to directions, could be marketed. The reason for the labeling requirement and the exemption that made it possible for coal-tar hair dyes to stay on the market

was the horrifying results of the use of coal-tar dyes in the area of the eye. In one case in the 1930s, a woman died after using a coal-tar dye to permanently dye her eyelashes. In another case, coal-tar eyelash dye destroyed both of a woman's eyes (9).

Carcinogens in cosmetics; FDA's regulatory activities for specific carcinogens

Numerous chemicals found to be carcinogenic in animals and/or humans are used (or have been used) as ingredients in cosmetic formulations (Table 2) (10). Some of the chemicals are deliberately added to the formulations to impart desired qualities, while others, such as the nitrosamine N-nitrosodiethanolamine (NDELA), are formed during manufacture or storage by reactions between components of the cosmetic products.

Table 2 - Some cosmetic ingredients and contaminants evaluated by IARC (10)

Ingredient	IARC Group
CI Acid Orange	3
HC Blue No. 2	3
HC Red No. 3	3
HC Yellow No. 4	3
2-amino-4-nitrophenol	3
2-amino-5-nitrophenol	3
2,4-diamino-2-nitrobenzene (2-nitro-para-phenylenediamine)	3
D&C Red No. 9*	3
Acetaldehyde	2B
Formaldehyde	1
Vinyl chloride*	1
Talc containing asbestiform fibers	1
Talc-based body powder (perineal use)	2B
Chloroform**	2B
Benzoyl peroxide	3
Hydrogen peroxide	3
Lead compounds, inorganic	2A
Polyvinyl methacrylate	3
Resorcinol	3
Dichloromethane (methylene chloride)*	2B
Diethanolamine	3
Triethanolamine	3
Contaminants found in cosmetics	
Benzidine (1,1-biphenyl)-4,4'-diamine	1
N-nitrosodiethanolamine	2B

*Use in cosmetics in U.S. prohibited by FDA

** Use in cosmetics in U.S. prohibited other than residual amounts from use during processing or as byproduct in synthesis of chemical ingredient

Coal-tar hair dyes

Back during the early development of synthetic color chemicals, during the 19th and early 20th centuries, coal-tar colors were actually derived from the residue of destructive distillation of coal. Modern colors, although referred to as "coal-tar" colors, are derived from petroleum. When the color chemicals produced from petroleum are essentially identical to those from coal tar, FDA regulates those chemicals as coal-tar products.

Color chemicals reviewed by IARC (10) have, with rare exceptions, been assigned to Group 3 (potential carcinogenic effect cannot be determined). A search of Medline/Toxline databases in January 2010 established that few animal studies that would establish the carcinogenicity of coal-tar color chemicals have been carried out since the 1980s (11). The lack of test data makes it difficult for IARC to come to conclusions about hazard associated with the chemicals, but it also makes it difficult for FDA, Congress and the general public to weigh the necessity for regulation or, given the coal-tar dye exemption to the adulteration and misbranding provisions of the FFDCA, the need for Congressional action to revoke the coal-tar dye exemption.

Animal tests in the 1970s linked several important coal-tar color chemicals with cancer. The formulations of coal-tar hair color products changed in the 1970s and 1980s, with elimination of chemicals such as p-phenylenediamine. However, chemicals structurally similar to the chemicals no longer used are still being used in hair color preparations.

Volume 57 of the IARC Monographs reviewed several coal-tar hair colors and color feedstocks (12). The review covered both animal data and the epidemiologic studies available through approximately 1990. IARC concluded that there was evidence from animal and epidemiologic data that occupational exposure to products, including coal-tar hair colors, used in barber shops and beauty salons was "probably carcinogenic to humans". That finding

was based on "limited" epidemiologic data, including findings of elevated bladder cancer in male workers in barbershops. The association between exposure to coal-tar colors and bladder cancer had been noted in chemical industry workers by the turn of the 20th century.

Volume 99 (in press; January 2010) (13) of the IARC Monographs is an update of Volume 57. New data on barbers and hairdressers exposed to coal-tar dyes confirmed the increased incidence of bladder cancer in male barbers and hairdressers, and IARC maintained the classification for those exposures as Group 2A ("probably carcinogenic to humans").

Many women use coal-tar hair dyes at home. Epidemiology studies of consumers who used those colors at home were reviewed for both Volumes 57 and 99. In both cases, the epidemiologic data were considered "inadequate" to support a finding of carcinogenic effects of exposure to coal-tar hair dyes, and in both cases, personal use of coal-tar hair color products was classified as Group 3 ("cannot be evaluated as to its carcinogenicity").

Lead acetate: hair colors for men

Men have, for some time, used lead acetate-containing hair color products to cover graying or gray hair. Rather than producing a range of colors, lead acetate gradually darkens hair. The color must be applied every day, and development of a dark color is gradual (14).

Studies have demonstrated that lead acetate applied to the scalp can get into the bloodstream.

IARC has classified lead acetate at Group 2A, "likely carcinogenic in humans" (15).

The Delaney Clause

After World War II, people in the United States evidenced increased concern about cancer, a disease whose incidence rates were increasing. In 1958, Congress acknowledged the public concern by passing the Delaney Clause, an amendment to the FFDCA.

The Delaney Clause provides that any non-zero level of a chemical known to cause cancer in humans or animals renders the product in which the carcinogenic chemical appears adulterated.

The Clause was applied immediately to food additives and ingredients and to pesticides with residues that appear in food. In 1960, at the time the Color Additive Amendments to the FFDCA were passed, Congress expanded the coverage of the Delaney Clause to color additives, including the coal-tar hair dyes (16).

FDA has developed two principal methods for avoiding application of the Delaney Clause to various categories of carcinogenic chemicals, including color additives. Both of the avoidance methods result in cancer risks from use of hair color being considered trivial.

Vinyl chloride propellants in hair sprays

In the late 1960s and early 1970s, Italian scientists established the carcinogenicity in animals of vinyl chloride (VCM), one of the most widely used plastics monomers (17). Cases of angiosarcoma of the liver (ASL) were identified in workers in a B.F. Goodrich polyvinyl chloride (PVC) polymerization plant in Louiaville, KY (18). In 1974, the U.S. Occupational Safety and Health Administration (OSHA) set exposure limits for VCM (19), and the chemical has continued in use since the mid-1970s under tightly controlled conditions in PVC polymerization and other plastics plants.

One application of VCM in the 1960s that resulted in dispersive use of the monomer was as a propellant in hair sprays. Although development of cases of ASL in workers in the plastics industry has been well-documented, the first report of ASL in barbers/hairdressers was published only at the beginning of 2009 (20).

Two cases of ASL were reported in the paper by Infante *et al.* (20). Both cases, a male barber who did unisex work and a female hairdresser, were exposed to hairsprays and their VCM propellant for periods from the late 1960s through the mid-1970s. In 1974, FDA banned VCM for use in propellant formulations.

Estimation of possible exposures for the two cases was carried out for litigation purposes. In both cases, exposure levels could have come close to those

experienced by workers in PVC polymerization facilities.

Consumer exposures to VCM-propelled hairsprays may well have been significant during the period – 1960s through mid-1970s.

Discussion and conclusions

There is no debating the presence of carcinogenic chemicals in commonly used cosmetic products. There is also no debating FDA's failure to do anything much to reduce cancer hazard, or even inform the public about such risks. Although a good part of FDA's inaction can be attributed to the agency's lack of statutory authority to assess safety data for cosmetics before the products are marketed and to act effectively against cosmetics on the market once they have been determined to be hazardous, some of the agency's torpor is likely to be linked to Congressional and public disinterest.

What possibilities are there for improvement of this situation? There is a consortium of public interest groups in the United States that is making an effort to familiarize the public with cosmetics hazards (21). The group has also undertaken some cooperative projects with cosmetics companies in the U.S. and abroad to reduce hazardous ingredients in their products. It remains to be seen whether this effort can convince the public and Congress to improve the cosmetics laws, and convince FDA to regulate even with their limited authority as well as ask Congress for more authority over cosmetics.

The coal-tar hair color exemption merits particular attention, given the large number of women in this country who color their hair and the apparent use of such colors by young women, as opposed to older women who are covering gray hair. The principal question about the coal-tar colors is whether there are substitutes for the colors, and whether the color industry is developing alternatives to coal-tar colors. Would a clear statement by FDA as to the cancer risks of hair colors motivate women to demand safer colors? To date, IARC has had to classify consumer use of hair colors as "inadequate to assess risk", in large part because of lack of conclusive findings from epidemiology studies. Would publicizing the IARC conclusion that exposures of barbers and hairdressers constitute a "likely risk" (Group 2A) of increased incidence of bladder cancer suffice to motivate public pressure for increased control of coal-tar hair colors?

The puzzle of what to do about regulating cosmetics in the United States remains unsolved. What is clear is that without Congressional action to increase FDA's regulatory authority over cosmetics, the agency won't do more than it is doing now, which when it comes to cosmetics, is close to nothing. It is also clear that Congress won't provide more authority to FDA without there being clear public concerns about hazards, including cancer, associated with cosmetic use, and the public won't express concern to Congress without an effective campaign to acquaint the general public with cancer and other hazards of cosmetics.

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Note: The United States Food, Drug and Cosmetics Act is cited as 21 U.S.C. 321 (21 United States Code Part 321). The text of the Act can be found at: www.fda.gov, or www.law.cornell.edu/uscode/21usc

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