Cosmetic Science and Technology Series/Volume 2

The Cosmetic Industry

Scientific and Regulatory Foundations

edited by
Norman F. Estrin

THE COSMETIC INDUSTRY

COSMETIC SCIENCE AND TECHNOLOGY SERIES

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THE COSMETIC INDUSTRY

SCIENTIFIC AND REGULATORY FOUNDATIONS

Edited by

NORMAN F. ESTRIN

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ABOUT THE SERIES

The rapid growth of cosmetic science has made it virtually impossible for a single author or a single book to present a coherent review of the entire field. This series was conceived to permit discussion of the broad spectrum of current knowledge and theories of cosmetic science and technology. The series is made up of a number of books either written by single authors, or edited, with a number of contributors. Well-known authorities from industry, academia, medicine, and the government are participating in writing these books.

Our aim is to cover many facets of advances in the field of cosmetic science. Topics will be drawn from a wide spectrum of disciplines ranging from chemical, physical, analytical, and consumer evaluations to safety, efficacy, and regulatory questions. Organic, inorganic, physical and polymer chemistry, emulsion technology, microbiology, toxicology, dermatology and more—all play a role in cosmetic science. There is little commonality in the scientific methods, processes, or formulations required for the wide variety of cosmetics and toiletries manufactured. Products range from hair care, oral care and skin care products to lipsticks, nail polishes, deodorants, powders, aerosol products to over-the-counter products, such as antiperspirants, dandruff treatments, antibacterial soaps, acne creams, and suntan lotions. Thus cosmetics represent a highly diversified field with many subsections of science and art; for indeed, even today a lot of art and instinct are used and needed in the formulation and evaluation of cosmetics.

Since the early sixties, the regulatory climate has changed dramatically for the cosmetic industry. Under a modicum of control since the 1938 Federal Food, Drug, and Cosmetic Act, the passage of the 1962 Drug Amendments to this Act opened the door for a broad review of the

safety and efficacy of numerous cosmetics and toiletries, such as antiperspirants, baby creams, deodorant soaps, antidandruff products, oral care preparations, etc. Regulatory actions by the F.D.A. and other agencies soon followed, exemplified by the banning of tribromosalicylanilides, mercury compounds, bithionol, zirconium salts in aerosol products, hexachlorophene, chloroform, and chlorofluorocarbons as propellants for aerosols. These concerns have resulted in increased attention by industry to regulatory matters. Large departments have been staffed to deal with these problems; millions of dollars are spent annually on testing products to assure safety and efficacy and compliance to a host of regulations. The second book of this series entitled "The Cosmetic Industry: Scientific and Regulatory Foundations," edited by Norman F. Estrin, contains contributions by over fifty experts presenting the different points of view of government, industry, and trade associations regarding these important advances in the field of cosmetic science.

Finally, I want to thank all contributors and editors who are participating in the development of this series, the editoral staff at Marcel Dekker, Inc., and above all, my wife Eva, without whose editorial help and constant support I would never have undertaken this project.

Eric Jungermann, Ph.D.
Series Editor

PREFACE

This text is designed as a practical guide for individuals with scientific and regulatory responsibilities or interests in the cosmetic industry. The term "scientific" is used in this text particularly to note the relationship of science to regulatory decisionmaking. The vast body of knowledge contained under the heading "cosmetic science" is therefore not included in this text.

For ease of reference, the text is organized into three major sections. The first section, "The Regulatory Environment," summarizes the authority of various regulatory agencies and regulatory programs as they pertain to the cosmetic industry. Chapters are included for areas that have a direct and indirect impact on the cosmetic industry.

The second section, "Functioning in the Regulatory Environment," which comprises the major portion of this text, offers practical advice on how to operate within the regulatory environment outlined in the first section. This section is itself divided into two parts. The first part summarizes industry-wide activities that have been undertaken in response to existing regulations or to promote self-regulation. The second part contains practical advice on how to cope with the maze of regulations to which the cosmetic industry is subject.

The final section, entitled "Challenges for Tommorow," introduces scientific and regulatory issues that now, or in the future, are likely to have an impact on cosmetic manufacturers in this decade.

Authors of chapters appearing in this text were invited to submit chapters based on their knowledge or contributions in a specific area. Readers are encouraged to review source material cited in most chapters. Armed with the information contained in this volume, the reader should be in a better position to phrase the right questions in soliciting ex-

pert advice and consulting primary sources. We hope that this text will find use both in the United States and abroad, not only by individuals with scientific and regulatory responsibilities within the cosmetic industry, but also by those in government, those studying at academic institutions, and those preparing for a career in the cosmetic industry.

Norman F. Estrin, Ph.D.

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Part I

THE REGULATORY ENVIRONMENT

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REGULATION OF COSMETICS IN THE UNITED STATES—AN OVERVIEW

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I. BASIC PRINCIPLES

A. The Federal Food, Drug, and Cosmetic Act; the Fair Packaging and Labeling Act; and the Food and Drug Administration

In the United States, the composition and labeling of cosmetic products are governed primarily by the Federal Food, Drug, and Cosmetic Act (FDC Act)[1] and by the Fair Packaging and Labeling Act (FPLA).[2] These acts are enforced by the U.S. Food and Drug Administration (FDA), an agency of the Department of Health and Human Services (formerly the Department of Health, Education and Welfare).[3]

B. Definition of "Cosmetic"

The term "cosmetic" is defined by section 201(i) of the FDC Act as follows:

> (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, or introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles; except that such term shall not include soap.[4]

This definition is incorporated by reference in the FPLA.[5] If an article comes within this definition, it is subject to regulation as a "cosmetic" under the FDC Act and the FPLA.

II. COMPOSITION OF COSMETIC PRODUCTS

A. Prohibition of "Poisonous or Deleterious Substances"

Except for color additives (discussed in Sec. II.D), there is no official listing of ingredients "approved" for cosmetic use. Instead, section 601(a) of the FDC Act provides generally that a cosmetic shall be deemed to be "adulterated":

> If it bears or contains any poisonous or deleterious substance which may render it injurious to users under the conditions of use prescribed in the labeling thereof, or, under such conditions of use as are customary or usual....[6]

Accordingly, manufacturers are under a general duty to avoid use of any cosmetic ingredient that may render the finished product injurious to users under expected conditions of use.

B. Regulations Restricting Particular Ingredients

The FDA has published regulations explicitly prohibiting or restricting use of the following ingredients in cosmetic products: bithionol,[7] mercury compounds,[8] vinyl chloride,[9] halogenated salicylanilides,[10] zirconium in aerosol products,[11] chloroform,[12] chlorofluorocarbon propellants,[13] and hexachlorophene.[14] The FDA would consider violative products to be adulterated within the meaning of section 601(a) of the FDC Act.

These regulations prohibiting or restricting use of certain ingredients do *not*, however, purport to be a complete listing of all ingredients that should not be used in cosmetics. The FDA may initiate regulatory action (as described in Sec. IV.A) whenever it concludes that a particular ingredient used in a cosmetic product violates the standard of section 601(a) of the FDC Act.

C. Regulation Requiring Safety Substantiation

The FDA has published a regulation stating that manufacturers have a general duty to substantiate the safety of each ingredient and finished product prior to marketing:

> Each ingredient used in a cosmetic product and each finished cosmetic product shall be adequately substantiated for safety prior to marketing. Any such ingredient or product whose safety is not adequately substantiated prior to marketing is misbranded unless it contains the following conspicuous statement on the principal display panel:
>
> *Warning* – The safety of this product has not been determined.[15]

D. Color Additives

Pursuant to the Color Additive Amendments of 1960 to the FDC Act, color additives are regulated in a different manner than other cosmetic ingredients.[16] A color additive may not be used in a cosmetic product unless such use first has been approved by an FDA regulation.

The FDA has published numerous regulations listing particular colors authorized for use in cosmetics.[17] For certain of these colors, FDA approval ("certification") of each production batch of the color also is required.

E. Coal-Tar Hair Dyes

The general prohibition against use of a "poisonous or deleterious substance," established by section 601(a) of the FDC Act (discussed in Sec. II.A), does not apply to coal-tar hair dyes. Instead, section 601(a) requires that a specific caution appear on the label of a coal-tar hair dye product:

> Caution – This product contains ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should first be made. This product must not be used for dyeing the eyelashes or eyebrows; to do so may cause blindness.[18]

Coal-tar hair dyes also are exempt from the general requirement for FDA approval of color additives used in cosmetics.[19]

Assuming that a coal-tar hair dye product bears the foregoing cautionary statement, insofar as section 601(a) and the Color Additive Amendments are concerned, a manufacturer may use any coal-tar ingredient(s) in the product.

III. LABELING

A. Labeling Requirements – Generally

Pursuant to the FDC Act, the FPLA, and FDA regulations, cosmetic products generally are required to provide the following information on their labels:

1. A statement of the identity of the product
2. A statement of the net quantity of contents
3. A statement of the name and place of business of the manufacturer, packer, or distributor
4. A list of the ingredients included in the product; and for certain products
5. Cautionary or warning language

Before reviewing these various labeling requirements, it is important to note a distinction between requirements imposed pursuant to the FDC Act and requirements imposed pursuant to the FPLA: Generally, labeling requirements premised on the FDC Act must appear *both* on the immediate container of the cosmetic product *and* on the outside container or wrapper of the retail package.[20] Labeling requirements premised on the FPLA must appear *only* on the *outside* container or wrapper of the retail package.[21] Also, certain label statements are required by FDA regulations to appear on the "principal display panel,"[22] while other mandatory labeling information may appear elsewhere on the label.

A cosmetic product that fails to bear required labeling information is deemed to be "misbranded" and is subject to regulatory action by the FDA. (See Sec. IV.A concerning FDA enforcement.)

B. Statement of Identity

Pursuant to FDA regulations premised on the FPLA, the principal display panel of the outside container or wrapper of the retail package of a cosmetic product must bear a statement of the identity of the product.[23]

This statement must be in terms of the "common or usual name" of the product, or "an appropriately descriptive name," or, "when the nature of the cosmetic is obvious, a fanciful name understood by the public to identify such a cosmetic," or "an appropriate illustration or vignette representing the intended cosmetic use."[24]

C. Net Quantity of Contents

Pursuant to the FDC Act and FDA regulations premised on both the FDC Act and the FPLA, a statement of the net quantity of contents must appear both on the immediate container of the cosmetic product and on the principal display panel of the outside container or wrapper of the retail package.[25]

The quantity may be stated in terms of weight, measure, or numerical count.[26]

Customary English units of measure must be used (avoirdupois ounces, fluid ounces, etc.).[27] Metric measure may be declared in addition, but the net quantity of contents declaration may not be solely in terms of metric units.[28]

The regulations provide numerous specific requirements with respect to the format, type size, and placement of information about net quantity of contents.[29]

D. Name and Place of Business of Manufacturer, Packer, or Distributor

Pursuant to the FDC Act and FDA regulations premised on both the FDC Act and the FPLA, the name and place of business of the manufacturer, packer, *or* distributor must be declared both on the immediate container and on the outside container or wrapper of the retail package.[30] The information is not required to be on the principal display panel of the package.

Note the "or": The actual manufacturer (e.g., a contract manufacturer) need not be identified if the packer or distributor is identified.

E. Listing of Ingredients

Pursuant to FDA regulations premised on the FPLA, the outside container or wrapper of the retail package of a cosmetic product must declare the ingredients contained in the product.[31] The information is not required to be on the principal display panel.

Generally, ingredients must be declared in descending order of predominance, although ingredients present at concentrations of not more than 1 percent and color additives may be grouped separately and declared at the end of the ingredient listing without regard to order of predominance. The CTFA (Cosmetic, Toiletry and Fragrance Association, Inc.) *Cosmetic Ingredient Dictionary*, explicitly incorporated into the FDA regulations, is the most comprehensive source of approved nomenclature for cosmetic ingredient labeling.[32]

Ingredients that have been accepted by the FDA as having trade-secret status need not be identified by name, but are required to be designated in the ingredient listing by the phrase "and other ingredient(s)."[33]

F. Warnings or Caution Statements

Pursuant to the FDC Act or FDA regulations premised on that act, warnings or caution statements are required both on the immediate container and on the outside container or wrapper of certain cosmetic products. The coal-tar hair dye warning established by section 601(a) of the FDC Act has been discussed in Sec. II.E. The warning required by FDA regulations for products whose safety has not been substantiated has been discussed in Sec. II.C. In addition, the FDA has issued regulations requiring warnings for cosmetics in self-pressurized containers[34] and for feminine deodorant sprays.[35] A regulation requiring a warning for bubble bath products has also been published, but this requirement has been stayed pending reconsideration.[36]

G. Exemptions

The FPLA was passed by Congress to facilitate value comparisons by consumers when making purchasing decisions. Accordingly, cosmetic products intended for use solely as free samples, or otherwise not intended to be sold to consumers (e.g., products intended to be used in beauty salons or as theatrical makeup) are exempt from FPLA requirements.[37] This exemption is important particularly in the case of ingredient labeling, which is required only pursuant to the FPLA. Thus, for example, free samples or products intended for use solely in beauty salons are not required to bear cosmetic ingredient labeling.

H. Prohibition of False or Misleading Labeling

All cosmetics are subject to a general prohibition against false or misleading labeling. Section 602(a) of the FDC Act provides that a cosmetic shall be deemed to be misbranded:

> If its labeling is false or misleading in any particular.[38]

IV. FDA ACTIVITIES

A. FDA Enforcement

If the FDA believes that a cosmetic product is adulterated or misbranded because of violation of any of the requirements discussed earlier, the agency has several enforcement remedies.

The agency may send a *notice of adverse findings* or *regulatory letter* to the manufacturer or other responsible person.[39] These are formal warning correspondence. A notice of adverse findings usually states that the agency believes there has been a violation of law and requests a reply within 30 days that identifies "each corrective step taken or intended to be taken, including measures to prevent recurrence of the violation."[40] A regulatory letter is a more urgent document: It signifies that the "FDA is committed to initiate...administrative or legal action immediately if correction is not promptly achieved," and usually provides less time for response (often 10 days).[41]

In addition, if the FDA determines that a cosmetic is adulterated or misbranded, the agency may request the manufacturer to *recall* the product.[42] The FDA states that:

> A request by the Food and Drug Administration that a firm recall a product is reserved for urgent situations and is to be directed to the firm that has primary responsibility for the manufacture and marketing of the product that is to be recalled.[43]

When the FDA believes that a serious violation of law has occurred, the agency may request a U.S. attorney to institute a *civil seizure action*,[44] *injunction action*,[45] or *criminal prosecution in a U.S. district court*.[46] (Violations of FPLA requirements are not subject to criminal prosecution.)[47]

Because cosmetics generally present fewer risks than other products the FDA regulates, a relatively small portion of the agency's resources is applied to cosmetics regulation. For example, in fiscal year 1982, the FDA spent on cosmetics approximately $2.5 million, that is, less than 1 percent of the agency's total operating budget of approximately $321 million.[48] This allowed the FDA, among other activities, to conduct approximately 375 inspections of cosmetic manufacturers.[49]

B. Imports and Exports

Special provisions apply in the case of imports and exports.

With respect to imports, the FDA may request the U.S. Customs Service, within the Department of the Treasury, to detain any cosmetic product offered for import that "appears" to be adulterated or misbranded.[50] FDA regulations provide for an informal hearing if an importer wishes to challenge an import detention.[51]

With respect to exports, the FDC Act provides that a cosmetic intended for export "shall not be deemed to be adulterated or misbranded" if it:

> (A) accords to the specifications of the foreign purchaser,
>
> (B) is not in conflict with the laws of the country to which it is intended for export,
>
> (C) is labeled on the outside of the shipping package that it is intended for export, and
>
> (D) is not sold or offered for sale in domestic commerce.[52]

Thus, a cosmetic intended for export may, for example, include ingredients not permitted in the United States, or omit labeling required in the United States, *if* it complies with the foregoing criteria.

C. Voluntary Reporting Programs

Cosmetics are subject to three voluntary reporting programs established by FDA regulations. These include:

1. Voluntary registration of manufacturing and packing establishments.[53] More than 950 companies have registered with the agency.[54]
2. Voluntary reporting of cosmetic raw materials and cosmetic product ingredients.[55] More than 3,600 raw materials and more than 19,500 finished product formulations have been registered with the agency.[56]
3. Voluntary reporting of cosmetic product experiences, including information about adverse reactions.[57] More than 70 companies currently are participating.[58]

The FDA has issued standard reporting forms, available from FDA district offices or from the FDA's Division of Cosmetics Technology at FDA headquarters in Washington, D.C., for use by companies that participate in the voluntary reporting program.

V. OTHER MATTERS

A. The Cosmetic Ingredient Review

The Cosmetic, Toiletry, and Fragrance Association (CTFA)[59] has established a comprehensive industry-funded program for reviewing the

safety of cosmetic ingredients: the Cosmetic Ingredient Review (CIR).

Under the CIR program, an independent Expert Panel of scientists has been commissioned to evaluate the available literature, published and unpublished, on the safety of cosmetic ingredients. A permanent CIR staff is located in Washington, D.C. There is a liaison representative to the Expert Panel both from consumer organizations and from the cosmetic industry. In addition, the FDA has appointed one of its employees as a "contact person" to participate in Expert Panel proceedings.

Following peer review, panel reports assessing the safety of cosmetic ingredients are published by the CIR in a scientific journal.[60]

B. Cosmetic Drugs

Section 201(g) of the FDC Act defines a "drug" as including:

> articles intended for use in the...cure, mitigation, treatment, or prevention of disease in man...and...articles (other than food) intended to affect the structure or any function of the body of man....[61]

The "intended use" of an article may be determined by reference to the claims made for it in labeling or advertising.[62] Depending on the claims, a particular product may be subject to regulation as a cosmetic, a drug, or both.

Pursuant to section 201(g), certain cosmetic-type products have been subjected to regulation as drugs by the FDA. Examples include toothpastes represented to prevent tooth decay, antiperspirants, tanning products represented to prevent sunburn, and lip balm products represented to prevent chapping.

It is important to recognize that "drug" status entails significant consequences for a would-be cosmetic. Drugs are subject to different requirements with respect to manufacture, composition, and labeling, and to different FDA enforcement priorities. For example, drug manufacturers are required to register with the FDA their manufacturing establishments and each of their drug products.[63] The FDA has published regulations establishing minimum "current good manufacturing practice" (CGMP) requirements for drugs.[64] Labeling and composition may be subject to an applicable over-the-counter (OTC) drug monograph.[65] Active ingredients in drug products must be identified on the immediate container as well as on the outside container or wrapper.[66] Furthermore, drug establishments are likely to be inspected more often than are cosmetic establishments.[67]

For more information about cosmetic drugs, see Chap. 5.

C. Soap

The definition of cosmetic, quoted in Sec. I.B, explicitly excludes "soap."

The FDA has published a regulation interpreting the meaning of "soap" for the purpose of the cosmetic definition.[68] The FDA regulation takes the position that the "soap" exemption from the cosmetic definition applies only to articles that meet the following conditions:

> (1) The bulk of the nonvolatile matter in the product consists of an alkali salt of fatty acids and the detergent properties of the article are due to the alkali-fatty acid compounds; and
>
> (2) The product is labeled, sold, and represented only as soap.

If a product is a soap, it is exempt from the FDA's cosmetic regulations. Thus, for example, a soap may be manufactured with colors that are not approved for use in cosmetics, and a soap is not required to bear ingredient labeling.

Although exempt from cosmetic regulation under the FDC Act, soap products are subject to "consumer product" regulation by the Consumer Product Safety Commission (CPSC) and to labeling requirements established by the Federal Trade Commission (FTC). For more information about soap, see Chap. 4.

D. The Consumer Product Safety Commission

Cosmetics, as defined in the FDC Act, are explicitly excluded from regulation under the Consumer Product Safety Act[69] and the Federal Hazardous Substances Act,[70] the primary statutory authority of the Consumer Product Safety Commission (CPSC).

However, the CPSC has asserted authority over cosmetic-type products in a few respects: The CPSC has authority to regulate soap products, since "soap" does not come within the FDC Act definition of "cosmetic"; the CPSC asserts authority to regulate mechanical hazards presented by cosmetic product *containers*;[71] and the commission has authority under the Poison Prevention Packaging Act[72] to issue regulations establishing special packaging standards required to protect children from serious personal injury or illness.

E. Federal Trade Commission Regulation of Advertising

Advertising for cosmetic products (as distinguished from *labeling*) is regulated by the Federal Trade Commission (FTC), not the FDA. For information about the FTC, see Chap. 6.

F. Regulation by the States

In addition to federal regulation of cosmetics by the FDA, the individual states have the authority to regulate these products and to impose requirements that are not in conflict with federal provisions.

VI. CONCLUSION

In summary, the composition and labeling of cosmetic products offered for sale in the United States are regulated by the Federal Food, Drug, and Cosmetic Act, the Fair Packaging and Labeling Act, and regulations issued by the U.S. Food and Drug Administration. These requirements operate generally to prohibit the inclusion of harmful ingredients and to require informative labeling. Mandatory federal regulation is supplemented by a voluntary reporting program administered by the FDA, and by the industry-funded Cosmetic Ingredient Review evaluation of the safety of cosmetic ingredients. Products represented to affect the structure or function of the body, such as anticavity toothpastes or antiperspirants, are subject to regulation by the FDA as drugs. Soap is excluded from FDA cosmetic regulation and instead is subject to regulation by the Consumer Product Safety Commission and the Federal Trade Commission. Finally, the individual states have independent authority to establish regulatory requirements that are not in conflict with federal provisions.

NOTES

1 21 U.S. Code (U.S.C.) 301 et seq.
2 15 U.S.C. 1451 et seq.
3 The authority vested in the Secretary of Health and Human Services by the FDC Act and the FPLA has been delegated to the Commissioner of Food and Drugs, who directs the FDA. 21 Code of Federal Regulations (C.F.R.) 5.1(a).
4 21 U.S.C. 321(i).
5 15 U.S.C. 1454, 1456, 1459(a).
6 21 U.S.C. 361(a).
7 21 C.F.R. 700.11.
8 21 C.F.R. 700.13.
9 21 C.F.R. 700.14.
10 21 C.F.R. 700.15.
11 21 C.F.R. 700.16.
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13 21 C.F.R. 700.23.
14 21 C.F.R. 250.250.
15 21 C.F.R. 740.10(a).
16 21 U.S.C. 321(t), 361(e), 362(e), 376.
17 21 C.F.R. 73, 74, 81, 82.

18 21 U.S.C. 361(a).
19 21 U.S.C. 361(e).
20 21 U.S.C. 321(k).
21 15 U.S.C. 1459(b).
22 21 C.F.R. 701.10.
23 15 U.S.C. 1453(a)(1); 21 C.F.R. 701.11.
24 21 C.F.R. 701.11(b).
25 21 U.S.C. 362(b)(2); 15 U.S.C. 1453(a)(2); 21 C.F.R. 701.13.
26 21 U.S.C. 362(b)(2); 15 U.S.C. 1453(a)(2); 21 C.F.R. 701.13.
27 15 U.S.C. 1453(a)(3); 21 C.F.R. 701.13(j), (k), (o), (p).
28 15 U.S.C. 1453(a)(3); 21 C.F.R. 701.13(j), (k), (o), (p), (r).
29 See generally 21 C.F.R. 701.13.
30 21 U.S.C. 362(b)(1); 15 U.S.C. 1453(a)(1); 21 C.F.R. 701.12.
31 15 U.S.C. 1454(c)(3); 21 C.F.R. 701.3.
32 21 C.F.R. 701.3(f); 21 C.F.R. 701.3(c)(2).
33 21 C.F.R. 701.3(a).
34 21 C.F.R. 740.11.
35 21 C.F.R. 740.12.
36 21 C.F.R. 740.17, published in *Fed. Reg.* *45*:55172 (August 19, 1980). Notice of interim stay pending reconsideration published in *Fed. Reg.* *48*:7169, 7203-7204 (February 18, 1983).
37 15 U.S.C. 1451; FDA Inspection Operations Manual, section 694, Cosmetics, Exhibit 694.1-B, para. 1, Cosmetic Ingredient Labeling (TN 80-6), February 29, 1980.
38 21 U.S.C. 362(a).
39 FDA Regulatory Procedures Manual, part 8, Compliance, chaps. 8-10, Notice of Adverse Findings and Regulatory Letters, September 1980.
40 FDA Regulatory Procedures Manual, part 8, Compliance, chap. 8-10, Notice of Adverse Findings and Regulatory Letters, September 1980, p. 7.
41 FDA Regulatory Procedures Manual, part 8, Compliance, chap. 8-10, Notice of Adverse Findings and Regulatory Letters, September 1980, pp. 7-8.
42 21 C.F.R. 7.40-7.59.
43 21 C.F.R. 7.40(b).
44 21 U.S.C. 334.
45 21 U.S.C. 332.
46 21 U.S.C. 331, 333.
47 15 U.S.C. 1456.
48 FDA Talk Paper T80-52, "FDA Budget for FY 1981," December 18, 1980.
49 H. J. Eiermann, Cosmetic Regulatory Update – 1980, presented at Annual Educational Conference of the Food and Drug Law Institute, December 10, 1980, p. 13. (Mr. Eiermann is the Director of FDA's Division of Cosmetics Technology.) The number of inspections fluctuates from year to year. At the time of final edit-

ing of this chapter, it appears that the FDA may conduct more than 900 cosmetic establishment inspections in 1983, although more than half of these are planned to be fairly cursory "abbreviated inspections."

50 21 U.S.C. 381.

51 21 C.F.R. 1.94.

52 21 U.S.C. 381(d)(1).

53 21 C.F.R. 710.

54 Statistics for the Voluntary Cosmetics Registration Program, Division of Cosmetics Technology (FDA), October 1, 1980.

55 21 C.F.R. 720.

56 See note 54.

57 21 C.F.R. 730.

58 See note 54.

59 The Cosmetic, Toiletry and Fragrance Association (CTFA) is the national trade association representing manufacturers and distributors of cosmetic, toiletry and fragrance products in the United States. The CTFA's offices are at 1110 Vermont Avenue, N.W., Suite 800, Washington, D.C. 20005. The CTFA includes more than 250 companies that manufacture or distribute approximately 90 percent of the finished cosmetic products marketed in the United States. In addition, the CTFA includes more than 230 associate member companies from related industries, such as manufacturers of cosmetic raw materials and packaging materials.

60 See *J. Environ. Pathol. Toxicol.* 4(4):2ff (October 1980).

61 21 U.S.C. 321(g)(1).

62 For example, *United States v. "Sudden Change,"* 409 F.2d 734, 739 (2d Cir. 1969). "The manufacturer of the article, through his representations in connection with its sale, can determine the use to which the article is to be put." S. Rep. No. 361, 74th Cong., 1st Sess. (1935), quoted in C. W. Dunn, *Federal Food, Drug, and Cosmetic Act*, Stechert & Co., N.Y.C., 1938, p. 240.

63 21 U.S.C. 360.

64 21 C.F.R. 210, 211.

65 21 C.F.R. 330.

66 21 U.S.C. 321(k), 352(e)(1).

67 21 U.S.C. 360(h).

68 21 C.F.R. 701.20.

69 15 U.S.C. 2051 et seq. Section 3(a) of the Consumer Product Safety Act provides that the term "consumer product" does not include "cosmetics...as...defined in [the FDC Act]."

70 15 U.S.C. 1261 et seq. Section 2(f) of the Federal Hazardous Substances Act provides that the term "hazardous substance" does not apply to "cosmetics subject to" the FDC Act.

71 CPSC Advisory Opinion No. 229, December 15, 1975.

72 15 U.S.C. 1471. Section 2(2) of the Poison Prevention Packaging Act specifically includes "cosmetic" within the act's definition of "household substance."

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THE FDA's SCIENTIFIC AND REGULATORY PROGRAMS FOR COSMETICS

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I. INTRODUCTION

The primary mission of the cosmetic program at the Food and Drug Administration (FDA) is to enforce the provisions of the Food, Drug, and Cosmetic Act (FDC Act) and the Fair Packaging and Labeling Act

(FPLA). These laws are intended to protect consumers from unsafe or deceptively labeled or packaged cosmetics and to provide consumers with adequate label information to enable them to make value comparisons. The laws apply to cosmetics that are shipped in interstate commerce, a term that includes imports as well as commerce between states.

The FDC Act defines cosmetics as articles or their ingredients applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance without affecting the body's structure or functions. Soap is exempt from the provisions of the FDC Act. Articles promoted as cosmetics but also intended to treat or prevent disease, or to affect the structure or functions of the human body, are drugs as well as cosmetics. Some of the products that fall into this category are hormone creams, sunscreen preparations, anticaries toothpastes, antiperspirants, and antidandruff shampoos. These products must comply with both the drug and cosmetic regulatory requirements.

The FDC Act prohibits the introduction or receipt in interstate commerce of cosmetics that are adulterated or misbranded. A cosmetic is considered adulterated if it contains a poisonous or deleterious substance that may cause it to be injurious to users under customary conditions of use; if it contains a nonpermitted color additive or any filthy, putrid, or decomposed substance; or if it is manufactured or held under insanitary conditions. It is misbranded if its labeling is false or misleading, if it does not bear the required labeling information, or if it is deceptively packaged [1].

The FPLA is intended to ensure that packages and labels of consumer commodities provide accurate information on the identity of a product, the net quantity of contents, and the name of the manufacturer, packer, or distributor. The FPLA requires that the FDA publish regulations governing these requirements and authorizes the agency to promulgate other regulations necessary to prevent deception of consumers or to facilitate value comparisons [2]. In 1977, the agency, under the authority of the FPLA, required the listing of ingredients (other than those granted trade-secret status by the agency) in descending order of predominance (except flavor and fragrance ingredients) on cosmetic labels or packages [3]. It is important to note that under the FPLA the term "consumer commodity" is defined to include only those products customarily distributed for consumption by individuals in the home. Therefore products sold for use and consumption in professional establishments, such as beauty salons, are not required to bear a listing of cosmetic ingredients.

There is no statutory requirement that a cosmetic product be approved by the FDA before it is introduced into interstate commerce. A cosmetic manufacturer may, on his own responsibility, use essen-

tially any ingredient or market any cosmetic until the FDA can demonstrate that it may be harmful under customary conditions of use [4]. Some ingredients have been prohibited or their use restricted in cosmetics by FDA regulation [5]. Color additives are the only cosmetic ingredients that require prior approval by the FDA before use. Cosmetic firms are not required by law to register their manufacturing establishments, product formulations, or file consumer reports of adverse reaction with the FDA; however, voluntary programs for these activities have been established as discussed below.

The FDA can remove a cosmetic product or ingredient from the market upon showing that it may be injurious to users under customary conditions of use. When such proof is available, the agency may take direct action against products containing the harmful ingredient or may publish a notice of rule making in the *Federal Register* proposing to prohibit or restrict the use of the ingredient. Comments on the proposal are solicited from the public and evaluated by the FDA, and a decision in then made as to whether or not a final regulation should be published in the *Federal Register*. If the regulation is adopted, it becomes part of the *Code of Federal Regulations*.

II. MAJOR COSMETIC PROGRAM ACTIVITIES

The FDA's major cosmetic program activities involve the following elements:

Field inspection and compliance program activities
Consumer complaint and injury evaluation
Cosmetic registration activities
Chemical analysis and method development
Health hazard research
Regulation development
Public assistance and education

Some of these activities are reviewed in detail below. Others, such as health hazard research and regulation development, are the subject of periodic reports by FDA personnel and are published in cosmetic trade journals [6,7].

A. Compliance Programs and Enforcement Policy

The FDC Act authorizes the FDA to inspect any establishment where cosmetics are manufactured or held before or after introduction into interstate commerce. FDA investigators may examine any equipment, finished product, raw material, container, or label pertaining to cosmetics. The inspection of cosmetic establishments gives the FDA an opportunity to uncover insanitary or other conditions that may cause adulteration of products and harm to users. During inspections FDA

investigators frequently collect samples and product labeling for laboratory analysis and label review. The inspections are conducted by investigators from the FDA's district offices located throughout the United States.

To coordinate the inspectional activities of the district offices, appropriate headquarter units at the FDA each year issue a Compliance Program Guidance Manual for cosmetics. This manual, which is available to the public, provides background information for investigators on industry trends, products, and labeling issues that should be given emphasis during a given year. This information is frequently based on prevailing health hazard issues, pertinent scientific studies, and new regulations that may prohibit or restrict the use of an ingredient or require a warning statement on certain product labels. Often headquarters will designate some of the establishments to be inspected on the basis of past compliance problems, the types of product a firm is known to produce, or consumer reports of adverse reaction with specific products.

Some commodities under the FDC Act such as food, drugs, and medical devices are subject to established current good manufacturing practice regulations. No such regulation has as yet (1982) been established for cosmetics, although the authority to establish such regulations is incorporated in the FDC Act. Such regulations would benefit both the industry and the FDA by establishing the conditions under which a product would not be considered adulterated under section 601(c) of the FDC Act [1].

Enforcement actions may be taken against products that are found to be either adulterated or misbranded. The actions provided under the FDC Act include seizure of the product, injunction against the manufacturer or distributor to prevent further shipment of the product, or prosecution of an individual or the company responsible for the violation.

The most frequently used action to remove violative products from the market is product recall. Recall is a voluntary action on the part of a firm, but it is recognized that this action is an alternative to FDA-initiated court action against violative products. The FDA's policy regarding product recalls may be found in the *Code of Federal Regulations* [8]. The policy governs the practices, procedures, and guidelines for the voluntary retrieval or correction of violative products that have left the control of the responsible firm.

A cosmetic product being recalled or considered for recall because of a possible health hazard is evaluated by an ad hoc committee of FDA scientists who take into account a number of factors. Among them are the following assessments: (1) whether disease or injury has occurred from the use of a product; (2) whether any existing conditions could contribute to a clinical situation that might expose

individuals to a health hazard; (3) the hazard for various segments of the population; (4) the severity of the health hazard to which the population at risk would be exposed; (5) the hazard's likelihood of occurrence; and (6) the immediate or long-term consequences of the hazard. Based on this determination the FDA assigns a recall classification for the product as follows:

Class I. A situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious, adverse health consequences or death

Class II. A situation in which the use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote

Class III. A situation in which the use of, or exposure to, a violative product is not likely to cause adverse health consequences

The depth of a recall action is determined by the degree of hazard a product may represent and the extent of the product's distribution as follows: (1) consumer or user level, including any intermediate wholesale or retail level; (2) retail level, including any intermediate wholesale level; or (3) wholesale level.

Recalls may also be requested for misbranding violations.

Each week the FDA publishes an Enforcement Report [9], which contains information on prosecutions, seizures, injunctions, and recalls undertaken by the agency. These terms are defined as follows:

Prosecution: A criminal action filed by the FDA against a company or individual charging violation of the law.

Seizure: An action taken to remove a product from commerce because it is in violation of the law. The FDA initiates a seizure by filing a complaint with the U.S. District Court where the goods are located. A U.S. marshal is then directed by the court to take possession of the goods until the matter is resolved.

Injunction: A civil action filed by the FDA against an individual or company seeking, in most cases, to stop a company from continuing to manufacture or distribute products that are in violation of the law.

Recall: Voluntary removal by a firm of a defective product from the market. Some recalls begin when the firm finds a problem; others are conducted at the FDA's request. Recalls may involve the physical removal of products from the market or correction of the problem where the product is located.

B. Evaluation of Consumer Adverse Reaction Reports

A major responsibility of the FDA's cosmetic program is to evaluate consumer reports of adverse reactions. Most such reports deal with acute toxic effects such as skin or eye irritation, contact sensitization reactions, skin or eye infections, and photocontact sensitization reactions. Normally, chronic toxic effects of products or their ingredients cannot be identified from data accumulated from consumer adverse reaction reports due to the length of time between the use of the product and the onset of the toxic effect and the inability of physicians and consumers to identify the causative agents for such reactions.

The FDA's consumer complaint review activities are designed to identify products, ingredients, and product categories that may be associated with significant adverse reactions. In cases of severe adverse reactions or when a single product is associated with several reports of injury the FDA conducts follow-up investigations. These may include interviewing the complainant and the treating physician, obtaining medical records, and collecting samples. Depending on the facts in a given case, the follow-up investigation may include a visit to the firm that manufactured or distributed the product.

There are three basic sources of consumer cosmetic adverse reaction information available to the FDA. They are reports received by the agency directly from consumers, physicians, or their representatives; reports from selected hospital emergency rooms under the National Electronic Injury Surveillance System (NEISS); and reports directly from industry under the voluntary product experience reporting program. Additional reports from poison control centers and special surveys conducted by the FDA are also valuable sources of information.

Reports Received Directly from Consumers

Since 1970 the FDA's Division of Cosmetics Technology has maintained a computer-based information system to track reports of cosmetic adverse reactions received directly from the public. The information entered into the system includes the name of the product, name of manufacturer or distributor, product category, type of alleged injury, body part affected, and the formulation number if the formulation was voluntarily filed with the FDA. Table 1 summarizes some of the information received for the 10-year period 1970 through 1980.

The number of adverse reaction reports the FDA recives directly from consumers is small compared to the number reported to cosmetic firms. For example, during 1975 the FDA received 583 reports directly from consumers. During the same year 124 cosmetic firms voluntarily filed product experience reports with the FDA reporting 7,229 alleged adverse reactions from consumers. The number of product units estimated to have been distributed by the 124 firms reporting this year was 3.2 billion.

TABLE 1 Summary of Cosmetic Adverse Reaction Reports Received by FDA Directly from Consumers (1970 - 1980)

Product category[a]	Number of adverse reaction reports
Shampoos (noncoloring)	321
Other personal cleanliness products	223
Deodorants (underarm)	214
Bubble baths	195
Moisturizing creams and lotions	181
Hair permanent waves	169
Suntan gels, creams, and liquids	167
Hair dyes and colors (all types requiring caution statements and patch tests)	161
Mascara	158
Other manicuring preparations	149
Hair sprays (aerosol fixatives)	145
Hair straighteners	145
Bath soaps and detergents	128
Skin care creams and lotions for face, body, and hand (excluding shaving preparations)	123
Cleansing creams, lotions, liquids, and pads	119
Eye shadow	113
Dentifrices (aerosol, liquid, pastes, and powders)	113
Other makeup preparations	111
Other eye makeup preparations	107
Depilatories	104
Lipstick	102
Hair conditioners	90
Other skin care preparations	88
Feminine deodorants	78

TABLE 1 (Continued)

Product category[a]	Number of adverse reaction reports
Nail extenders	77
Other hair coloring preparations	73
Nail polish and enamel	70
Tonics, dressing, and other hair grooming aids	68
Skin lighteners	60
Makeup foundations	59
Other hair preparations	55
Eyeliners	52
Makeup base	49
Hair bleaches	48
Colognes and toilet waters	47
Baby shampoos	46
Paste masks (mud packs)	42
Bath oils, tablets, and salts	39
Rinses (noncoloring)	36
Night creams and lotions	34
Eye makeup remover	31
Makeup blushers (all types)	28
Aftershave lotion	28
Baby lotions, oils, powders, and creams	26
Hair preparations, wave sets	23
Shaving creams	23
Perfumes	22
Powder fragrance preparations (excluding aftershave talc)	22
Skin fresheners	22
Cuticle softeners	21

TABLE 1 (Continued)

Product category[a]	Number of adverse reaction reports
Other fragrance preparations	19
Wrinkle smoothing preparations	19
Indoor tanning preparations	18
Face powders	17
Mouthwashes and breath fresheners (liquid and sprays)	16
Hormone creams and lotions	16
Other oral hygiene products	14
Other shaving preparations	13
Foot powders and sprays	12
Hair rinses (coloring)	11
Other bath preparations	10
Personal cleanliness douches	9
Other suntan preparations	9
Manicuring preparations, basecoats and undercoats	8
Bath capsules	7
Makeup preparations, rouges	7
Nail polish and enamel removers	7
Eyebrow pencil	6
Hair lighteners with color	6
All other categories	27
	4,856

[a]Product categories listed in accordance with *Code of Federal Regulations*, section 720.4(c) [10].

Although the total number of adverse reaction reports received by the FDA directly from consumers is relatively small, several significant problems associated with consumer use of cosmetics have been uncovered under the program. For example, in 1978 the FDA received about 50 complaints of hair breakage and scalp irritation associated with a hair straightener. An investigation disclosed that a compounding error had resulted in one batch of the product containing 60 percent more than the intended level of free caustic (sodium hydroxide). During the course of the FDA investigation the firm recalled the product.

In 1974 consumer complaints of fingernail injuries associated with the use of certain nail extenders led the FDA to investigate the problem. It was determined that the methyl methacrylate monomer used in these products was causing the injuries. The FDA obtained a court order to seize the offending product and an injunction against further distribution of the product [11]. Similar products were voluntarily recalled by other distributors.

During 1976 and 1977, consumer complaints that a nail hardener had caused serious allergic and irritant effects were received. An investigation and subsequent laboratory analyses demonstrated that the product contained formaldehyde at a potentially harmful concentration. The product was seized in August 1977 [12].

During 1976—1978 a significant number of consumer complaints concerning one brand of suntan product were received. The ensuing investigation disclosed that the firm also had received many complaints. Many of the adverse experiences appeared to be a form of photocontact dermatitis. Research sponsored by the firm and investigations by the FDA identified 6-methylcoumarin, a fragrance ingredient in the product, as a potent photocontact allergen [13].

National Electronic Injury Surveillance System

Each year since 1974 the FDA has prepared a yearly analysis of cosmetic-related injury data reported into the National Electronic Injury Surveillance System (NEISS) data base. The system is operated by the Consumer Product Safety Commission. The goal of the NEISS program is reduction of risk of injury to individuals from association with consumer products. To achieve this goal, it is necessary to gather information on the factors involved in such injuries. Literally every consumer product is included in the system, and cosmetics is only one of hundreds of product categories that come under the NEISS review. The data come from selected hospital emergency rooms located throughout the country. NEISS data for cosmetic products include injury diagnosis, frequency of injuries by product categories, part of body affected, age and sex of patient, severity of injury, and the disposition of the case.

For calendar year 1979, 739 cosmetic-related injury cases were reported to NEISS [14]. Based on this number, NEISS estimates that

30,965 cosmetic-related injuries (a low estimate of 22,468 to a high estimate of 39,462 with a 95 percent certainty) were treated in hospital emergency rooms throughout the United States and its territories. Of the 739 injuries, 266 cases were associated with misuse of cosmetic products such as ingestion or aspiration of foreign objects. Of the 473 noningestion cosmetic-related product injuries, dermatitis was diagnosed in 51 percent of the cases; contusions/abrasions 16 percent; foreign body injuries 11 percent; and chemical burns 11 percent. Nearly half of the injuries, 49.5 percent, involved injury to the eyes. Other frequently affected body parts include the face (16 percent) and head (10 percent). The data for 1979 were based on a data collection network that included 74 selected hospital emergency rooms.

Because NEISS data are obtained from hospital emergency rooms, they are not good indicators of adverse reactions associated with customary use of cosmetics. The data are heavily weighted to the type of adverse reactions that would prompt a person to seek emergency medical treatment. These include primarily accidental injuries most frequently associated with the eye, face, or head. The type of reactions most often reported include dermatitis, contusions/abrasions, foreign body (e.g., broken glass as an accidental contaminant in a product), and chemical burns.

Voluntary Product Experience Reporting Program

In 1974 the FDA promulgated a regulation that provided for the voluntary submission of product experience reports to the FDA by cosmetic firms [15]. The program is designed to provide information to the FDA on the type and frequency of cosmetic adverse reactions reported by consumers to cosmetic firms. The program is voluntary because under law the FDA does not have the authority to require firms to provide such information. All cosmetic firms are invited to participate and file semiannual reports. Except for summaries of the data, the information provided under the program is confidential and not available to the public. Among the data requested are the name of the product, an estimate of the number of product units distributed during a given reporting period, and the number of adverse reactions reported to the firm. This program is intended to identify products and product categories with rates of adverse reactions significantly higher than the determined norm. This information could serve as a basis for further in-depth review by the FDA to determine the need for toxicological testing or other appropriate action to improve consumer safety in the cosmetic area.

Poison Control Center Data

Data from poison control centers in the United States are also a valuable source of information for the FDA concerning the potential of cosmetic products to cause adverse effects through misuses of the products, that is, accidental ingestion or aspiration. Poison control

center cases are not necessarily poisonings. The majority, in fact, are not. They usually are incidents of inappropriate exposure to chemical substances that were presumed to pose at least a potential threat to health at the time the control center was contacted. Whether or not poisoning resulted from the exposure would depend on such factors as the toxicity of the substance and the amount and route of exposure. Thus, the total number of cases involving specific products is primarily a measure of the frequency of accidental misuse, not poisoning. Cases that are reported with toxic signs or symptoms, a hospital visit, or death are classified as "toxic." The FDA uses the ratio of the "toxic" cases to the total number of cases reported to compare the relative harmfulness of various substances or products under conditions of accidental misuse [16].

.Poison control center data involving cosmetics at the FDA include the following information: total number of cases reported for all cosmetics and total cases broken down for 47 product categories. Within each category the cases are further subdivided into the total number and the number classified as "toxic." The data are provided for persons of all ages followed by totals for children under the age of 5 years. For example, for the years 1971 through 1978, 1.3 million cases were reported to poison control centers for all products, of which 83,000 were associated with cosmetics. Of these, 74,000 were cases involving children under the age of 5, of which 6,510 were "toxic" cases (approximately 6,000 cases had signs and symptoms, 500 resulted in a hospital visit, and none resulted in a fatality). The product categories having the highest number of cases reported to poison control centers were fragrance preparations, that is, perfumes, colognes, and toilet waters (28,400); creams and lotions (15,722); fingernail preparations (15,151); hair preparations (except shampoo) (6,801); and shampoos (6,621) [16].

FDA Consumer Survey

In 1975 the FDA reported the results of a three-month study of adverse reactions among a nationwide sample of 10,000 households [17]. The study, a cooperative effort by the FDA and the American Academy of Dermatology, was conducted in 1974 and involved 36,000 cosmetic users. This was the first attempt by the FDA to obtain cosmetic-related injury statistics from a large group of consumers. In the study, 703 consumer-perceived cosmetic reactions were reported, of which 589 (84 percent) were judged by dermatologists as definitely or probably product-related. Of these 589 cases, the vast majority, 505 (86 percent), were considered mild; 63 (11 percent) moderate; and 13 (2 percent) severe (in 8 cases the severity could not be determined) [18].

A follow-up report on the further analysis of the data and information collected during the above survey was completed in 1977 [19]. This report contains a summary of the consumer-perceived adverse

reactions during the three-month survey broken down into 43 cosmetic product categories. For each product category the number of person-brand uses and number of product users are tabulated as well as the incidence rates of adverse reactions per 10,000 person-brand uses. The product categories having the highest number of adverse reactions were deodorants and antiperspirants, soap, hair spray lacquers, moisturizer lotions, bubble baths, shampoos, mascaras, and colognes. The 589 adverse reactions were associated with 1.11 million person-brand uses in all product categories. The average incidence rate of adverse reactions per 10,000 person-brand uses for all categories was 5.3.

C. Voluntary Cosmetic Registration Program

In 1972 and 1974, the FDA established programs under which cosmetic firms are provided the opportunity to voluntarily register their manufacturing establishments, file product formulations, and report consumer adverse reaction information to the FDA. A detailed description of the regulations for the voluntary registration program may be found in the *Code of Federal Regulations* [10]. Firms interested in participating in these voluntary programs may obtain information, instructions, and the required forms by writing the Division of Cosmetics Technology, Food and Drug Administration, Washington, D.C. 20204.

The regulations were promulgated by the FDA as a result of petitions submitted to the agency by the Cosmetic, Toiletry and Fragrance Association. The programs have enjoyed the strong support of the association and many cosmetic firms. Most of the major cosmetic firms in the United States participate in one or more parts of the program. Some foreign cosmetic firms that export cosmetic products to the United States also file information under the programs.

Although participation in these programs has been less than anticipated at the time the programs were implemented, the registered data provide valuable information to FDA. As of July 1982, cosmetics firms have voluntarily registered 1,002 manufacturing establishments with the FDA. Currently the Division of Cosmetics Technology's total inventory of cosmetic manufacturers and packers contains 2,080 location addresses.

Since the start of the program 32,666 product formulations have been filed by 1,003 firms. Also, 8,652 amendments to filed formulations have been received and 12,536 notices that formulations had been discontinued have been filed. Thus the number of current formulations on file as of July 1982 was 20,130. In addition to the product formulations, 4,091 Raw Material Composition Statements have also been filed by 164 cosmetic raw material suppliers.

Product experience reports are filed on a semiannual basis. The number of firms participating in this program during the first seven years (14 reporting periods) ranged from 94 to 140. Data tabulated

for the four reporting periods of 1975 and 1976 indicate that 14,240 alleged consumer adverse reactions were reported to the cosmetic firms that participated in the program during this period (the number of participating firms ranged from 112 to 128). The estimated number of product units distributed by the reporting firms during this two-year period was 6.9 billion. The FDA estimates that the firms filing product experience reports represent 30 to 40 percent of U.S. cosmetic sales, although only 2 to 3 percent of the cosmetic firms participated in the program [20].

The information voluntarily provided by cosmetic firms on product formulations is entered into a computer information data base. The information in this system is not available from any other source and is widely used by the FDA, industry, and other institutions as a basis for establishing priorities for safety review programs and many other purposes. For example, the monographs published by the Cosmetic Ingredient Review Expert Panel, which is sponsored by the Cosmetic, Toiletry and Fragrance Association, utilizes information voluntarily submitted to the FDA by industry [21]. It is especially useful to the FDA and others for gathering information concerning the usage of ingredients in cosmetics whose safety may be questioned on the basis of new scientific information. The information can be used not only to identify the individual ingredients in a brand-name product but also permits the identification of ingredients used in specific product categories, their frequency of use, and use level. Some specific types of ingredients, such as preservatives, colors, fragrances, and flavors, are identified in the data base, and this information can be used to compile special types of ingredient use information. For example, data on the frequency of use of various preservatives in cosmetics have been published [22,23].

D. Chemical Analysis of Cosmetics

The FDA's Division of Cosmetics Technology is responsible for conducting analyses of cosmetic products when such analyses are deemed necessary for enforcement purposes. In addition, a major amount of effort is expended conducting research in the field of analytical chemistry. This research is directed toward the application of new instrumental analytical techniques to the analysis of cosmetics, determining the composition of complex cosmetic raw materials and fragrance ingredients, and, more recently, development of methods for the determination of potentially harmful trace contaminants of cosmetics, such as nitrosamines [24].

Most cosmetic samples analyzed by the FDA are collected by the agency either as the result of consumer adverse reaction reports or for surveillance purposes during inspections of cosmetic manufacturing establishments. The number of samples analyzed on an annual basis varies widely and usually is decided on the basis of both the need and

the amount of resources allocated to the cosmetic program in a given year. In recent years, a substantial amount of sample analysis and analytical methods research has been devoted to supporting toxicological and microbiological research conducted either under contract for the FDA or in the FDA's own laboratories.

Most of the analytical methods developed in FDA laboratories for the analysis of cosmetic products are reported in scientific journals. The majority are published in the *Journal of the Association of Official Analytical Chemists* (AOAC). The AOAC is a scientific organization whose primary purpose is to serve the needs of government regulatory and research agencies for analytical methods. Its goal is to provide methods that will perform with the necessary accuracy and precision under usual laboratory conditions [25]. A compilation of official methods for the analysis of cosmetics may be found in Chapter 35 of *Official Methods of Analysis of the AOAC* [26]. Additional analytical methods for the analysis of cosmetics have been compiled in *Newburger's Manual of Cosmetic Analysis* [27]. This manual provides general as well as specific methods for the chemical analysis of cosmetic products.

E. Microbiological Examination of Cosmetics

The ability of microorganisms to grow in some types of cosmetic products has been known for many years [28–30]. Many cosmetic formulations provide a good medium for the growth of bacteria and fungi. Some of these organisms may be pathogenic and therefore products contaminated with such microorganisms may constitute a health hazard to the consumer. Eye area cosmetics are of special concern because of the serious consequences of contaminated products coming into contact with a scratched or damaged cornea. Several cases of corneal ulceration resulting from the use of contaminated mascaras have been reported in the literature [31].

There is no need for cosmetics to be sterile. However, microorganisms found should be low in number, must be nonpathogenic, and must not cause the product to decompose during the expected shelf life of the product. It is important that cosmetics contain preservative systems that prevent microbial contamination not only during manufacture but also under normal conditions of product use. A cosmetic that is contaminated with pathogenic microorganisms may be deemed to be adulterated under section 601(a) of the FDC Act [1]. A cosmetic that contains microorganisms commonly identified with filth may be deemed adulterated under section 601(b) of the FDC Act [1].

Microbial contamination of a cosmetic can result in separation of the emulsion, product discoloration, or formation of gas or odor. Such product changes are relatively easy to detect; however, in many cases a cosmetic may show no visible evidence of contamination and still contain unacceptable types or densities of microorganisms.

A variety of bacteria have been isolated from cosmetic products by FDA laboratories. Some of the various genera noted have been *Acinetobacter, Citrobacter, Clostridium, Enterobacter, Escherichia, Hafnia, Klebsiella, Morganella, Proteus, Providencia, Pseudomonas, Serratia,* and *Staphylococcus.* Of these, the ones encountered most frequently have been *Staphylococcus* (especially *S. aureus*), *Pseudomonas* (notably *P. aeruginosa*), and *Klebsiella* [32].

The FDA has not established any quantitative bacterial or fungal limit or standard for cosmetic products. The assessment of the health hazard associated with a given microbiologically contaminated cosmetic is a judgmental decision made by an ad hoc committee of physicians and scientists in the Bureau of Foods [8,33]. Each case is evaluated individually, taking into account such factors as the intended use of the product and the number, type, and pathogenicity of the microorganisms found in the cosmetic [32].

Because of reports of eye injuries associated with consumer use of eye area cosmetics, the FDA published a notice in the *Federal Register* in 1977 [34]. In this notice the FDA expressed the importance of having mascaras and other eye area cosmetics adequately preserved to reduce the risk of microbial contamination during use and possible eye injury. Mascaras can become contaminated with microorganisms when the consumer uses the product and reinserts the applicator wand into the container after application of the mascara to the eye lashes. When microorganisms are introduced into a mascara that is inadequately preserved, they may multiply inside the container. If a contaminated applicator wand comes into contact with a scratched or damaged cornea, the eye may become infected. The FDA has received reports of corneal ulceration associated with the use of mascara products containing pathogenic microorganisms [31]. The majority of incidents involved mascaras in which the microorganism *P. aeruginosa* has been found. *P. aeruginosa* infections, if not recognized and treated immediately, can cause corneal ulceration that leads to partial or total blindness in the injured eye. Thus, particular attention should be given to the microorganism *P. aeruginosa* in developing an adequate preservative system for all cosmetics that may come in contact with the eye during intended or customary conditions of use. The agency believes that the preservative systems used in mascara and other eye-contact products should be adequate not only to prevent the further growth of microorganisms but also to reduce significantly the number of microorganisms introduced during use [34].

Because of concerns in the area of microbial contamination of cosmetic products in general and eye area products in particular, the FDA funded research studies at Emory and Georgia State Universities in Atlanta. These studies resulted in a series of published scientific papers dealing with microbial contamination of eye area cosmetics and their association with ocular infections [31,35–40].

The methodology used in FDA laboratories for the microbiological examination of cosmetic products is contained in Chapter 23 of the *FDA Bacteriological Analytical Manual* [41]. This chapter is available as a separate publication and may be obtained by writing: Director, Division of Microbiology, Food and Drug Administration, Washington, D.C. 20204.

F. Safety Evaluation of Cosmetics

The FDC Act does not require that cosmetic manufacturers or distributors test their products for safety prior to marketing. However, if the safety of a cosmetic is not adequately substantiated, it may be considered misbranded unless the label bears the following statement: "Warning—The safety of this product has not been determined" [42]. In regard to this requirement, cosmetic firms frequently request information from the FDA on cosmetic safety substantiation. The agency has advised that the safety of cosmetics can be substantiated through reliance on already available toxicological test data on individual ingredients and on product formulations that are similar in composition to a particular cosmetic and by the performance of any additional toxicological and other tests that are appropriate in the light of such existing data and information. Although satisfactory toxicological information may exist for each ingredient in a cosmetic, the agency believes that it is necessary to conduct some toxicological testing on the complete formulation to adequately assure the safety of a finished cosmetic product [43]. The agency has cited two papers in the scientific literature that describe reasonable approaches to safety evaluation and that contain references to appropriate testing procedures [44,45].

When cosmetic firms have requested additional guidance on cosmetic safety testing, the agency has provided such assistance when certain information about the product and its ingredients is made available. The type of information usually requested includes but is not limited to the following: the quantitative formulation, intended use of the product, anticipated human exposure, proposed labeling, information on safety data available on the individual ingredients, composition of the raw materials used to formulate the product, manufacturing and processing information, product stability data, and preservative efficacy testing data.

III. FDA ORGANIZATIONAL UNITS AND FUNCTIONS

A. Headquarters

The FDA is a component of the Public Health Service within the Department of Health and Human Services (formerly the Department of Health, Education and Welfare). The Commissioner of Food and Drugs reports to the Secretary of Health and Human Services through the

Assistant Secretary for Health and Surgeon General of the Public Health Service. The primary organizational units of the FDA are the bureaus, each of which has responsibility for one or more of the commodities regulated by the FDA. The six bureaus of the agency are Foods, Drugs, Veterinary Medicine, Radiological Health, Biologics, and Medical Devices.

The responsibility for cosmetics at the FDA is assigned to the Bureau of Foods. Within the Bureau of Foods the Division of Cosmetics Technology serves as the focal point for the FDA's cosmetic program. The division has two branches. The Product Composition Branch is charged with the responsibility of conducting chemical analyses of products, developing analytical methods for cosmetic ingredients and product contaminants, and supporting research conducted by other units of the FDA. The other branch, the Registration and Product Experience Branch, administers the voluntary cosmetic registration activities, monitors adverse reaction reports from consumers, and assists FDA field offices in areas such as inspections and by providing technical and program advice on cosmetics in general.

Other units of the Bureau of Foods that also provide scientific support to the cosmetic program are the Division of Microbiology and the Division of Toxicology. These units also conduct research studies and conduct testing in their respective areas. The Division of Regulatory Guidance is responsible for developing policy and implementing regulatory actions against violative cosmetic and food products.

B. Regional Offices

The FDA has District Offices in most of the major cities of the United States. There are 10 major Regional Offices, each of which has one or more District Offices. Most of the District Offices have laboratory units and all have a staff of investigators who conduct inspections of firms that manufacture, pack, or distribute commodities subject to the FDA's jurisdiction. In addition, many of the District Offices maintain offices known as Resident Posts in various cities in their districts.

IV. COSMETIC INFORMATION RESOURCES AT THE FDA

A. Publications

A variety of publications are available from the Bureau of Foods to assist the cosmetic, toiletry, and fragrance industries in complying with laws and regulations administered by the FDA. Information of general interest to consumers is also available to the public on request. The FDA maintains a comprehensive listing of available publications entitled "FDA's Catalog of Information Materials for the Food and Cosmetic Industries," [the catalog may be obtained by

writing: Food and Drug Administration, Industry Programs Branch (HFF-326), 200 C Street, S.W., Washington, D.C. 20204]. The catalog also provides addresses and phone numbers of some FDA headquarters units and Regional and District Offices as well as other U.S. governmental agencies that have informational materials which may be of interest to consumers and the cosmetics industry. Order forms, stock numbers, and costs (if any) of publications are also provided in the catalog. Most single copies of publications are available free of charge. Information is provided in the catalog for such official publications as the *Federal Register*, the *Code of Federal Regulations*, and the *FDA Consumer* magazine. These publications are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402 at a nominal cost.

The publications most frequently requested in the cosmetic area are the Food, Drug and Cosmetic Act, Fair Packaging and Labeling Act, Cosmetic Regulations—Reprint from Title 21, *Code of Federal Regulations*, and Requirements of Laws and Regulations Enforced by the U.S. Food and Drug Administration.

B. Corresponding with the FDA

Upon request, the FDA will be glad to reply to questions from firms concerning cosmetic laws and regulations. If comments on a specific product are needed, the inquirer should supply full information as to the identity and quantitative amount of each ingredient in the product, a copy of all labeling, and the dimensions of the container. Labeling may be submitted in draft form and need not be printed.

Questions concerning compliance issues should be sent to the Director, Division of Regulatory Guidance. Requests for scientific information in the fields of toxicology or microbiology may be sent to the Director, Division of Toxicology, or Director, Division of Microbiology. Questions relating to the use of color additives in cosmetics should be sent to the Director, Division of Food and Color Additives. Information requests in the field of chemistry or cosmetic science and technology or other matters related to the cosmetic program at the FDA may be directed to the Director, Division of Cosmetics Technology. The inquiries should be addressed to the appropriate division at: Food and Drug Administration, 200 C Street, S.W., Washington, D.C. 20204.

Questions relating to cosmetics that are drugs or inquiries relating to the classification of a product as such should be addressed to: Director, Division of Drug Labeling Compliance, Bureau of Drugs, Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20857.

Requests for records from FDA files under the Freedom of Information Act (FOI Act) should be addressed to: Public Records and

Document Center, HFI-35, Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20857. Any request for records must include a reasonable description of the record being sought so that it can be identified and located. The policy and procedures established for release of documents under the FOI Act may be found in the *Code of Federal Regulations [46].*

V. ACKNOWLEDGMENT

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3

THE TOXIC SUBSTANCES CONTROL ACT AND ITS POTENTIAL IMPACT ON THE COSMETIC INDUSTRY

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I. INTRODUCTION

The Toxic Substances Control Act [1] (TSCA) is a far-reaching statute. It empowers the Environmental Protection Agency (EPA) to regulate most synthetic and natural chemicals to reduce the risk of injury to human health or the environment. Under the statute

†Deceased

the EPA may promulgate regulations to govern the manufacture, distribution in commerce, processing, use, or disposal of chemicals if the agency finds that such activities present an unreasonable risk of injury to human health or the environment. Use of the term "manufacture" under TSCA includes manufacturing, production, or importing of chemicals.

Congress adopted a policy, embodied in TSCA, that adequate data regarding safety of chemicals in commerce should be acquired and that the acquisition of such data should be the responsibility of those who manufacture or process the chemicals. It was also the intent of Congress to establish authority for the EPA to take quick action to prohibit or restrict the manufacture or use of chemicals that are imminent hazards to health or the environment. The act cautions that regulation of chemicals under its purview should not be carried out in a manner that will impede technological innovation. Furthermore, the EPA is directed to carry out the act in a reasonable and prudent manner that will consider the environmental, economic, and social impact of any actions taken under authority of TSCA.

TSCA authorizes the EPA to gather information on existing chemicals, require testing of those that impose risks of injury, screen new chemicals to determine if they present a risk of injury to health or the environment, and control chemicals proven to present an unreasonable risk.

The Toxic Substances Control Act specifically excludes jurisdiction over pesticides, tobacco or tobacco products, nuclear materials, firearms and ammunition, and articles regulated under the federal Food, Drug, and Cosmetic Act. It is logical, therefore, for one to ask: "Why include a chapter on TSCA in a reference book devoted, among other things, to the regulatory foundations of the cosmetic industry?"

There are several reasons why the cosmetic scientists, regulatory affairs specialist, or purchasing agent should be aware of actions proposed or taken under TSCA authority with respect to chemicals used in cosmetics. First and foremost, if the EPA finds that exposure to a chemical poses a risk of injury to humans, there is a distinct possibility that the intimate bodily exposure often encountered in cosmetic applications of the chemical may also be hazardous. If the EPA should prohibit or severely restrict the manufacture or use of a chemical, there is a possibility that the Food and Drug Administration (FDA) would find that use of the chemical in a cosmetic would cause the product to be adulterated under section 601 of the federal Food, Drug, and Cosmetic Act. The chemical would certainly undergo scrutiny by the FDA, and its use in cosmetics might ultimately be prohibited. Reformulation of products to remove or replace an ingredient is usually disruptive of ongoing production, and may often by very costly and time-consuming.

Even if the FDA decided not to take regulatory action against an ingredient found by the EPA to be injurious to human health, there are other problems the cosmetic producer must face. For example, the

chemical may be produced primarily for use in TSCA-regulated applications, with purchases by the cosmetic industry amounting to a small fraction of the market. If use of the chemical is prohibited under TSCA, the producers may find it uneconomical to manufacture the relatively small amounts required by the cosmetic industry and choose to terminate all production, thus eliminating the source of the chemical.

Another consideration regarding a chemical given adverse publicity as a result of action taken by EPA under TSCA is the disclosure of that ingredient on the cosmetic labeling. This would undoubtedly dissuade many astute consumers from purchasing the cosmetic. It also might motivate public interest groups to discourage use of selected cosmetic products by means of adverse publicity. The negative impact of such publicity is often more expensive than the most costly reformulation or recall.

II. MAJOR PROVISIONS OF THE ACT

The Toxic Substances Control Act became effective January 1, 1977. It contains 31 sections, which deal with many major and minor provisions. This chapter will address itself primarily to eight sections of the act that should be of interest to the cosmetic industry. They are as follows:

Section 4:	Testing of existing chemical
Section 5:	Manufacturing notices
	New chemicals
	Significant new uses of existing chemicals
Section 6:	Regulation of hazardous chemicals
Section 7:	Imminent hazards
Section 8:	Records and reports
	Inventory
	Exposure
	Adverse reactions
	Substantial risks
Section 9:	Relationship to other laws
Section 14:	Disclosure of data
Section 21:	Citizens' petitions
	Public information
	Confidential information

TSCA divides the universe of chemicals in domestic commerce into two classes: "existing" (old) chemicals and "new" chemicals. This characterization is somewhat analogous to the FDA's definition of "old" drugs and "new" drugs. Under TSCA, an existing chemical is one that was manufactured for commercial purposes in the United States between January 1, 1975, and December 31, 1979. All other chemicals are considered to be new. A chemical may have been manufactured for commercial purposes in the past but been out of use for some time prior to 1975. That chemical would be classified as "new" if it were manufactured again after December 31, 1979.

A. Section 4: Testing of Existing Chemicals

Section 4(a) of TSCA authorizes the EPA to require testing of an existing chemical if the agency finds that its manufacture, distribution in commerce, processing, use, or disposal may precent an unreasonable risk of injury to human health or the environment. A finding by the agency that a chemical poses one of the aforementioned risks may be based on suspicion of adverse biological, biochemical, or physicochemical effects, taking into account the available test data and experience with the chemical. This may be coupled with reasonable expectations of the chemical's likely effects, based on correlation with the known effects of chemicals of similar structure (e.g., structure-activity relationships). Furthermore, the agency must establish that the information needed to resolve the issue is likely to be obtained through testing.

The EPA may also require testing of a chemical if it determines that it is or will be produced in substantial quantities and there is or will be substantial human or environmental exposure to the chemical. In such a case the agency need not find that a reasonable expectation of injury exists. All that is necessary is substantial production, substantial exposure, and the absence of sufficient data and experience on which to characterize the effects of the chemical on human health or the environment.

TSCA stipulates that the EPA shall promulgate rules governing the testing of chemicals meeting at least one of the criteria described in the two preceding paragraphs. The agency proposed its first testing rules under section 4 in July 1980 [2] and has continued to propose testing rules periodically since then. In some instances the EPA has accepted voluntary testing agreements in lieu of issuing testing rules. The agency also published an Advance Notice of Proposed Rulemaking governing phenylenediamines, a large group of chemicals, some of which are used extensively in the cosmetic industry [3].

Any testing of chemicals performed pursuant to an EPA-promulgated testing rule or negotiated testing agreement must be performed in accordance with good laboratory practices established by the agency. The results of these tests and all supporting test data must be submitted to the EPA and are considered to be public information. The act permits chemical firms to cooperate among themselves in conducting the required testing or designate an outside party, such as a trade association or independent testing firm, to conduct the testing. The act requires EPA to publish promptly in the *Federal Register* a notice of the receipt of test data submitted in accordance with the requirements of this section. The data are available for inspection by the public, and copies may be obtained from the EPA upon request, subject to the provisions of section 14 of TSCA.

Costs of testing may be distributed among the firms involved. The prorated sharing of costs would be based on proportionate shares of the total market held by the respective firms. In the event of a dispute over distribution of testing costs, the EPA administrator is authorized to determine what constitutes equitable sharing of costs by the firms manufacturing or distributing the chemical.

More than 55,000 chemicals were reported to be in domestic commerce during the period between January 1, 1975, and December 31, 1977, the base period for distinguishing between existing and new chemicals. Section 4(e) of TSCA established a committee to make recommendations to the EPA administrator respecting chemicals that should be given priority consideration by the agency for the promulgation of testing rules for existing chemicals. This committee is known as the Toxic Substances Control Act Interagency Testing Committee (ITC). The statutory mandate and operating procedures of the ITC are discussed in detail in Sec. III of this chapter.

Section 4(f) of the act requires the EPA to take appropriate action to control or regulate a chemical if it receives test data or other information leading to a conclusion that the chemical presents a significant risk of serious or widespread harm to humans from cancer, gene mutations, or birth defects. If such a conclusion is reached, the agency must take appropriate action under sections 5, 6, or 7 of the act. The available options are described later in this chapter.

B. Section 5: Manufacturing Notices

Section 5 of TSCA requires that a firm notify the EPA prior to starting manufacture or processing of any chemical that does not meet the definition of an "existing chemical." Section 5 also authorizes the EPA to promulgate rules governing significant new uses of existing chemicals and notification procedures. These two notifications are referred to as Premanufacturing Notices (PMNs) and Significant New Use Reports (SNURs), respectively.

Although manufacturers are not required to perform any premarket testing of a new chemical or an existing chemical being considered for a significant new use, they are required to submit to the EPA any test data or information in their possession regarding hazards. The EPA must publish in the *Federal Register*, within five working days, a notice of receipt of a PMN or SNUR. The notice must include a summary of pertinent data received. TSCA permits firms to assert claims of confidentiality regarding information submitted to the agency in PMNs and SNURs.

The act allows the EPA 90 days to evaluate the information received and notify a firm if it finds cause to delay, prohibit, limit, or restrict the manufacture of a chemical subject to either a PMN or SNUR. The agency may extend the evaulation period for an additional 90 days if it finds good cause to do so. Notice of an extension of the evaluation period and the reasons for it are sent to the firm and published in the *Federal Register*.

The EPA may require additional information or test data before it will permit the manufacture of a chemical subject to the rules of section 5 to proceed. If so, the firm must be notified of the requirements within the 90- or 180-day period mentioned in the preceding paragraph. If the firm is not notified within the period, it may proceed to manufacture the chemical. A Notice of Commencement of Manufacture must be sent to the agency at that time. Such notice may be sent by letter. No special form is required.

If, in its review of information provided under this section of the act, the EPA determines that the manufacture of a new chemical may harm human health or the environment, it may prohibit or regulate use of the chemical. The key provisions of TSCA concerning regulation of hazardous chemicals will be discussed later. When manufacture of a new chemical begins, it enters the universe of "existing chemicals."

A list of chemicals in commerce (e.g., existing chemicals), together with information on quantities produced, manufacturing sites, and other pertinent information is maintained by the EPA. This data base is known as the Toxic Substances Control Act Chemical Substance Inventory. The reader is directed to Sec. II.E of this chapter for a discussion of the Inventory and the statutory provisions governing it.

C. Section 6: Regulation of Hazardous Chemicals

The EPA may impose regulatory controls on a chemical if it concludes that the manufacture, distribution, use, or disposal of the chemical poses an unreasonable risk of injury to human health or the environment. Section 6 of TSCA contains the provisions governing the regulation of such chemicals. The agency is authorized to promulgate regulations imposing one or more of the following constraints on commericial use of a chemical if the evidence supports such regulation:

Prohibit entirely the manufacture or use
Prohibit the manufacture for specified uses
Impose a limit on the overall quantity produced
Impose a limit on the quantity produced for specified uses
Require that warnings and instructions for safe use accompany the chemical
Require that notice of unreasonable risk be given by manufacturers to their distributors, processors, or to the general public, depending on the nature and severity of the risk
Regulate the methods used to dispose of a chemical

TSCA does not contain a section authorizing the promulgation of rules governing current good manufacturing practices (GMPs) but it does present an interesting alternative. The alternative, which appears in section 6(b) of the act, authorizes the EPA to require a manufacturer or processor of chemicals subject to TSCA to submit a description of relevant quality control procedures used. This requirement may be

imposed if the EPA has a reasonable basis to conclude that the methods and controls used in producing a chemical cause the chemical to pose an unreasonable risk of injury to health or the environment.

If the agency determines that existing quality control procedures are not adequate, the EPA may order the firm to revise its procedures to the extent necessary to remedy the situation. By not stipulating quality control procedures in a GMP rule, the EPA and the regulated industry are in the enviable positions of not being locked into quality control standards that may become obsolete. Under this section of TSCA, the agency and industry may readily adapt to technological advances in manufacturing practices and their control.

A manufacturer may be required to notify distributors or processors of its chemicals if the deficiencies in quality control practices cause a chemical to pose an unreasonable risk of injury. Depending on the circumstances, including ultimate use of the chemical, a manufacturer may also be required to give notice of the risk to the general public. Finally, the agency may require the manufacturer of a chemical produced under inadequate quality control procedures to repurchase or replace chemicals in commerce that present a risk of injury that could have been reduced if adequate procedures were being used at the time of manufacture and distribution.

The EPA is required to consider several factors in supporting a regulation to control a hazardous chemical. The factors are prescribed in section 6(c) of TSCA, and the evidence must be included in a *Federal Register* Notice of Proposed Rulemaking. The first factor that must be addressed by the EPA is the effects of the chemical on health and the extent of human exposure to the chemical. Second, the agency is required to consider the effects of the chemical on the environment and the extent of environmental exposure to the chemical. The concept of benefit versus risk is included in a third factor, whereby the act requires that the agency consider and publish a statement regarding the benefits of the chemical for various uses and the availability of substitutes.

Finally, the statute requires the agency to include in its rulemaking record an analysis of the economic consequences of the proposed regulation. The agency must make every reasonable effort to predict these consequences after considering the impact on the national economy, small business, the environment, and public health. This section reiterates one of the policy statements of Congress written into the act: that the EPA shall consider the impact of proposed regulations on technical innovation. It also brings into focus the need to consider cost/benefit relationships, in addition to the benefit/risk assessment mentioned earlier. These should reduce the need for litigating such issues, as has been the case wih a number of rules promulgated under the federal Food, Drug, and Cosmetic Act, which does not address those issues.

D. Section 7: Imminent Hazards

An imminently hazardous chemical is one that presents an imminent (highly threatening) and unreasonable risk of serious or widespread injury to health or the environment. Such a risk is considered imminent under section 7(f) of the act if the EPA determines that its manufacture, use, or disposal in commerce is likely to result in injury to health or the environment before a Final Rule to regulate the chemical can be made effective under normal rule-making procedures.

If a chemical is found by the EPA to present an imminent hazard, the agency may propose a rule under section 6 of the act to prohibit or restrict its manufacture, use, or disposal and declare that rule to be effective immediately upon publication on the *Federal Register*. Regardless of whether or not a rule has been proposed under section 6, or testing initiated in accordance with section 4 of the TSCA, the EPA may proceed under section 7 to reduce or eliminate the risk of injury from an imminently hazardous chemical. The act authorizes EPA to seize a chemical or any article containing the chemical upon receipt of a court order authorizing the seizure. Publication of a *Federal Register* notice is not required. Consequently, action in the public interest can be taken more swiftly in situations where hazards are truly "imminent."

Whether or not a seizure order is received, the agency may seek relief in an appropriate district court to require recall of the chemical in question or articles containing the chemical. Other forms of relief available to the EPA include issuance of a mandatory order requiring the manufacturer of a chemical to notify purchasers of the risk, issue public notice of the risk, or replace or repurchase the chemical or articles containing it.

E. Section 8: Records and Reports

Section 8 of TSCA requires firms that manufacture chemicals for commercial purposes to maintain certain records and submit reports to the EPA in accordance with rules and procedures established by regulation.

Section 8(a) requires that manufacturers report to the EPA the following kinds of information, to the extent known, on selected chemicals:

Common name, chemical name, and molecular structure
Categories of use
Total amount of the chemical manufactured and the amount produced for each category of use
Description of the by-products resulting from the manufacture, use, or disposal
All existing data concerning health and environmental effects
Number of persons exposed to the chemical and duration of exposure in occupational areas
The manner of disposal

In June 1982 the EPA Issued its first Final Rule for section 8(a) reporting [4]. This rule covered about 250 chemicals that had either been recommended by the ITC for priority consideration, reported to EPA as presenting a substantial risk of injury to human health or the environment, or identified by the agency for other reasons. At the same time the agency proposed that 50 more chemicals recommended by the ITC be added to the list of those requiring section 8(a) reports [5]. This proposal includes a provision that all chemicals designated by the ITC in the future be automatically subject to reporting under section 8(a).

The information collected by the EPA under section 8 reporting rules is used, together with other information, in deciding which chemicals should be subject to testing requirements, regulatory controls, or other actions authorized by TSCA.

One of the highest-priority and most comprehensive undertakings required by TSCA was the compilation of a list of chemicals in commerce, the quantities produced during the initial reporting year, and the plant sites where those chemicals were manufactured. Section 8(b) of the act required the EPA to publish the initial list, known as the Toxic Substances Control Act Chemical Substance Inventory (the Inventory), and keep it current as new chemicals clear the Premanufacturing Notice process and are introduced into commerce. The Initial Inventory listed approximately 55,000 chemicals. By January 1984 the Inventory had grown to more than 60,000. All information in the Inventory is available to the public except for that which is claimed to be confidential business information.

Section 8(c) of TSCA authorizes the EPA to promulgate rules requiring manufacturers and distributors of chemicals to maintain records of significant adverse reactions to human health or the environment reported to have been caused by a chemical. The records referred to in this subsection include consumer allegations of personal injury or harm to health, reports of occupational disease or injury, and reports of adverse impact on the environment received from any source, whether or not such information qualifies for reporting in a Notice of Substantial Risk. These records are subject to inspection and copying by EPA investigators.

Section 8(d) requires manufacturers and processors of chemicals to submit to the EPA information or data concerning any health or safety studies known to them on chemicals designated by the agency. Most of the chemicals covered by the EPA rules are those recommended by the ITC and included in its Priority List. Information obtained under these rules will be used by the EPA to help make sound decisions on the need for testing rules governing the chemicals recommended by the ITC.

Finally, section 8(e) of TSCA requires that manufacturers or distributors of chemicals subject to TSCA report immediately to the

agency any information supporting a conclusion that a chemical presents a substantial risk of injury to human health or the environment. The kinds of information to be submitted include previously unreported test results indicating that a chemical is carcinogenic, mutagenic, or teratogenic. Data that show significant adverse acute or chronic health or environmental effects, and epidemiology or environmental monitoring data, must also be reported.

The EPA reviews promptly all Notices of Substantial Risk and judges whether the conclusions by the submitter appear to be valid. In many instances the agency requires additional information, and it communicates directly with the submitter. All Notices of Substantial Risk and the agency's evaluations are a matter of public record, except that a firm may request that portions of reports which are confidential business information be withheld from disclosure to the public. Information received in Notices of Substantial Risk may be used by EPA to support testing-rule or regulatory-control proposals.

F. Section 9: Relationship to Other Laws

Section 9 of TSCA should be of particular interest to the cosmetic industry. Under this section, if the EPA concludes that the manufacture, distribution, or use of a chemical is likely to present an unreasonable risk of injury to human health or the environment, and this risk may be controlled by another federal agency, the EPA is required to report the fact to the appropriate agency. The agency receiving such a report is required to evaluate the data, assess the risk, and report back to the EPA administrator what action, if any, it intends to take to reduce the risk. Both the EPA report to the other agency and the receiving agency's response must be fully documented in notices published in the *Federal Register*.

G. Section 14: Disclosure of Data

TSCA permits firms subject to the act to designate information disclosed to the EPA as confidential business information (CBI), provided that such information meets the appropriate standards of the Freedom of Information Act. TSCA does not require that CBI be subject to presubmission review. Under section 14 of TSCA, a firm may claim and be given confidential status for information on quantities of a chemical produced, manufacturing sites, name of the firm producing the chemical, and even the name or structure of the chemical if it believes the information is entitled to confidential treatment. If the specific identity of a chemical is claimed to be confidential, it is listed under a generic name in an appendix to the TSCA Inventory.

If the agency proposes to disclose to the public, or to a person not authorized to receive it, information that a submitter has claimed to be CBI, the EPA must notify the submitter by certified mail or other verifiable means of its denial of the claim and its intent to release the

information. The information may be released on the thirty-first day after the submitter is notified unless the EPA has first been notified that the submitter has begun an action in federal court to obtain judicial review and to prevent disclosure. Confidential information sought by any authorized Congressional committee must be released by the EPA upon written request after affected firms are provided 10 days' notice.

The EPA has developed strict security procedures to safeguard CBI. These procedures are described in the *TSCA Confidential Business Information Security Manual* [6]. TSCA imposes criminal penalties for wrongful disclosure of CBI.

H. Section 21: Citizens' Petitions

Section 21 of the act provides that any "person" (private citizen, firm, trade association, public interest group, etc.) may petition the EPA to issue, amend, or repeal a rule or order affecting the testing, regulation, recordkeeping, or reporting of information concerning chemicals subject to TSCA. The petition must be filed in the principal office of the administrator and must set forth the facts that are claimed by the petitioner to support the petition. The agency is authorized to hold a public hearing or conduct an investigation to determine if the petition should be granted.

The act requires the agency to either grant or deny the petition within 90 days after receipt. If the petition is granted, the EPA must initiate promptly proceedings to conform with the petitioner's request. If the petition is denied, the agency must publish in the *Federal Register* information about the petition and the reasons for denial. Denial of a Citizen's Petition is subject to review in federal court. The petitioner may challenge the denial in a U.S. district court within 60 days after the EPA's denial of the petition. The petitioner may also initiate a civil action to compel the agency to make a decision if it fails to act on the petition within 90 days after filing.

If the petitioner satisfies the court that the agency should be compelled to take the action sought in the petition, the court will order the agency to initiate the requested action. The court may award reimbursement of costs to the petitioner if it determines that an award is appropriate. The award may include costs of the suit and reasonable fees for attorneys and expert witnesses.

III. PRIORITIZING CHEMICALS FOR TESTING: THE TSCA INTERAGENCY TESTING COMMITTEE

A. Statutory Mandate

Section 4(e) of TSCA requires that a committee be established to make recommendations to the EPA administrator respecting chemicals to which the EPA should give priority attention for the promulgation

of the testing rules discussed previously. The committee was established and held its first meeting within five weeks after the effective date of the act. It adopted the name Toxic Substance Control Act Interagency Testing Committee, and is usually referred to as the TSCA/ITC or simply the ITC.

The ITC is composed of members from eight federal agencies, as prescribed in the act. The agencies are:

Council on Environmental Quality
Department of Commerce
Environmental Protection Agency
National Cancer Institute
National Institute of Environmental Health Sciences
National Institute for Occupational Safety and Health
National Science Foundation
Occupational Safety and Health Administration

The act stipulates that members be appointed by the heads of the respective agencies, and no person may serve as a member for more than four years. Strict provisions, regarding conflict of interest by appointed members and alternates, are set forth in section 4(e)(2)(C).

The EPA is required to provide administrative support services to the ITC as necessary to enable the committee to carry out its function. In this regard, the agency provides the services of a full-time executive secretary, clerical and legal support as required, access to available data processing programs and facilities, and funding for the services of a Technical Support Contractor. Technical support to the EPA members on the committee is also provided by the agency's Office of Toxic Substances. The other member agencies provide administrative support to their respective representatives.

Soon after it was established, the ITC became aware that several government agencies, not designated in TSCA to provide official members on the committee, possess expertise and active programs dealing with potentially toxic chemicals and related testing activities. Five such agencies and one national program accepted inviations from the ITC to provide nonvoting liaison representatives who regularly attend the ITC meetings and make substantial contributions to the committee's activities. The liaison representatives are from:

Consumer Product Safety Commission
Department of Agriculture
Department of Defense
Department of the Interior
Food and Drug Administration
National Toxicology Program

The statute requires the committee to issue, within nine months after the effective date of the act, an initial list of chemicals recommended to be given priority consideration for the promulgation of testing rules and to revise the list as it deems appropriate at least

every six months. The list, known as the Section 4(e) Priority List (Priority List), may contain individual chemicals or groups (categories) of chemicals. Categories may be established on the basis of similarities in chemical structure; in physical, chemical, or biological properties; in methods of use; or any other reasonable basis.

The committee is required to present its reasons for inclusion of each chemical or category on the Priority List. In practice the reasons have been presented in the form of scientific rationales, supported by data and information screened from the open literature and those provided voluntarily by industry, academia, various government agencies, and other sources. TSCA requires that the ITC recommendations and their supporting rationales be published in the *Federal Register*, affording interested persons opportunity to file written comments on them. While there is no limit to the number of chemicals that may be recommended on the Priority List, not more than 50 on the list at any given time may be designated for mandatory response by the EPA administrator within 12 months of their being added to the list. In response to an ITC recommendation, the EPA must either initiate a rulemaking proceeding to require the industry to perform the tests recommended by the ITC or present reasons for not initiating the proceeding.

Contrary to misconceptions that have arisen from time to time, the ITC is not part of the EPA. It is an independent committee, comprised of members from eight different agencies. The EPA is only one of those members, and it carries only one vote. The ITC recommends chemicals to be given priority consideration for promulgation of testing rules. The final decision on whether or not to require testing rests in EPA.

B. Criteria for Designating Chemicals to the Priority List

The ITC is required by law to consider all relevant factors in determining which chemicals to add to the Priority List. The committee is given broad discretion in selecting its criteria; however, section 4(e)(1)(A) of the TSCA specifies eight factors about chemicals that must be included. They are as follows:

- Quantity manufactured
- Amount that enters the environment
- Extent of human occupational exposure
- Extent of general population exposure
- Similarity to chemicals known to have adverse health or environmental effects
- Existence of data concerning effects on health or the environment
- Extent to which testing may provide data adequate to predict or determine the effects of a chemical on health or the environment
- Reasonably forseeable availability of facilities and personnel for performing the recommended testing

The act states that the committee must give special attention in establishing the Priority List to those chemicals that are known or suspected to be carcinogenic, mutagenic, or teratogenic. Other factors considered by the committee in its review include data on mammalian species with respect to acute toxicity (i.e., oral, dermal, ocular, and inhalation), reproductive effects other than teratogenicity, other subchronic or chronic effects (i.e., cardiovascular, behavioral, respiratory, and target organ effects), bioaccumulation potential in environmental species (especially aquatic organisms in the food chain), and general ecological effects (i.e., chemical fate, toxicology in aquatic, terrestrial, and avian species), and abiotic effects on the environment.

C. How Chemicals Are Screened and Scored

The TSCA Chemical Substance Inventory, currently containing more than 60,000 chemicals in commerce, provides the most comprehensive source list for chemicals to be screened by the ITC for selecting those that warrant in-depth review. The ITC makes its selections in a scoring procedure that is depicted schematically in Figure 1. The objective of the ITC scoring is to conduct a multistage screening of a large numbuer of chemicals to select a small number of candidates for detailed review.

In a typical scoring exercise, an Initial Listing of 2,000 to 3,000 chemicals from the TSCA Inventory is produced by applying various selection criteria in a computerized screening of the Inventory. The most widely used criterion is production volume. Other criteria may involve exclusion of "site-limited" chemicals (e.g., those that are manufactured and consumed as chemical intermediates in a single on-site process), high-molecular-weight polymers, chemicals of unknown or variable composition, complex reaction products, or biological materials.

The list of chemicals obtained from the Inventory is sometimes merged by computer with other lists of chemicals, including those maintained by other government agencies, to produce the ITC's Initial Listing. This is then screened manually by a panel to remove chemicals that have been scored previously, are already regulated under TSCA, are obviously well understood in terms of hazards (i.e., water, oxygen, many inorganic chemicals, etc.), and those that are so poorly characterized that they cannot be dealt with readily.

The committee had completed five scoring exercises by September 1983. In future exercises it intends to reexamine chemicals that were previously scored (some of them more than five years earlier) in the light of possible new information. The ITC intends also to begin to evaluate the poorly characterized chemicals mentioned previously.

The preliminary screening usually removes at least 75 percent of the chemicals from the Initial Listing. The remaining chemicals (usually 400 to 500) are then scored for human and environmental exposure by a panel of scientists with training and expertise in environmental chem-

SCREENING APPROACH:

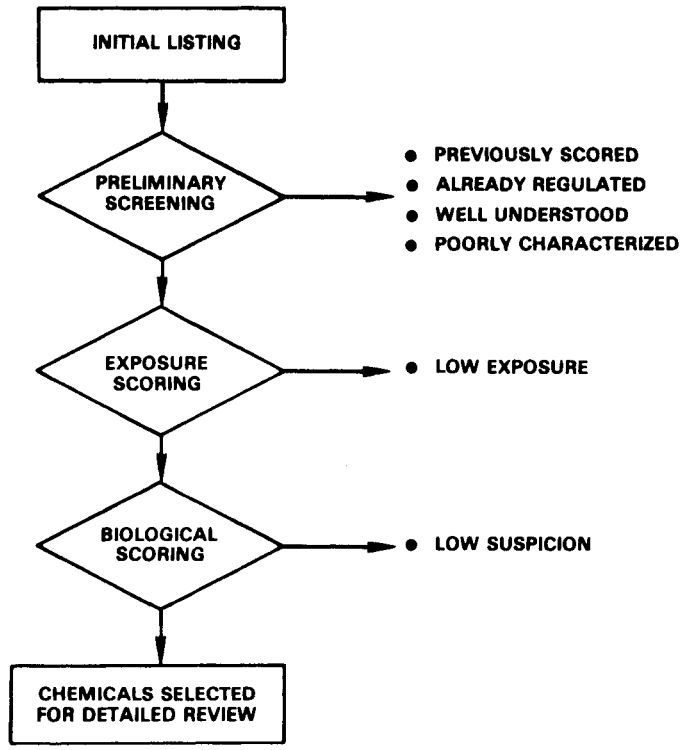

FIGURE 1 Flow diagram depicting the ITC screening and scoring approach leading up to detailed review by the full committee.

istry, chemical engineering, industrial hygiene, ecology, and computer science.

Exposure scoring is designed to rank the chemicals in terms of human and environmental exposure by computing three indices, an occupational exposure index, a general population exposure index, and an environmental exposure index. Ten factors are currently used in computing the indices. While the scope of this chapter does not permit a detailed description of these factors and the algorithms used in computing the indices, the factors are listed below:

Annual production
Fraction released in the plant
Number of workers exposed

Fraction released to the environment
Number of people exposed in the general population
Frequency of exposure
Intensity of exposure
Persistence in the environment
Penetrability in the host organism
Bioaccumlation potential

Numerical values for the factors are estimated by the exposure-scoring panel based on information obtained from existing data bases, reference books on industrial chemistry, chemical economics, chemical engineering and environmental chemistry, census data, and trade literature. Where data are lacking, the panel uses expert judgment to estimate the values for individual factors.

Upon completion of exposure scoring, the chemicals are ranked by computer in order of decreasing values of each of the three exposure indices and the ITC selects 200 to 250 chemicals with the highest exposure indices to be scored for likely biological effects. The objective of scoring for biological effects is to identify chemicals with high exposure that have the highest potential for causing harmful biological effects on human beings or the environment and for which adequate test data are lacking.

The general approach involves judgmental scoring and ranking of chemicals by experts using readily available toxicological data and extrapolating structure-activity relationships, where data are lacking. It must be appreciated that scoring is a priority-setting exercise. Its main purpose is to help improve the efficiency of the full evaluation by ITC by selecting the most likely candidates for attention first.

A consultant to the ITC once said: "A good exercise in priority setting involves some kind of compromise between completeness and speed. So almost be definition, the priority-setting exercise involves the use of incomplete data. Under ideal circumstances, expert judgment by the consultants would compensate for the paucity of data. But no situation is ideal. That's why selected chemicals are studied in depth by the full committee" [7].

In practice, a limited literature search is conducted by information specialists for each of the 200 to 250 chemicals being scored for biological effects. The information is summarized in a brief Information Profile. Abstracts of papers found in computerized data are appended to the profiles. Chemical and physical properties and structural formulas are obtained from standard handbooks and reference works.

A panel of 9 to 12 consultants with recognized expertise in various scientific disciplines is next engaged by the ITC to score the chemicals for eight biological effects. Those effects are

Carcinogenicity
Mutagenicity
Teratogenicity