Certification of Coal-Tar Colors

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Use of toxic dyes in food was one of the public health problems which led to the passage of the original "pure food law" in 1906. Today, 50 years later, protection of the public from dyes that are harmful to health is still an important purpose of the Federal food and drug legislation.

The Federal Food, Drug, and Cosmetic Act of 1938 provides that coal-tar colors used to color any products subject to the act, except hair dyes, must be from batches certified for such use under regulations promulgated by the Secretary of Health, Education, and Welfare. It characterizes food, drugs, and cosmetics containing uncertified coal-tar colors as adulterated. The law applies both to products manufactured in this country and to imports.

The term "coal-tar color" as used for purposes of the law means any coloring matter that is or may theoretically be derived from coal tar. It has continued in the language since the days when coal tar was the only source of many organic chemicals that are now obtained from various sources, particularly petroleum. The word "color" is usually used instead of "dye" because, in the trade, the word "dye" refers only to soluble material; it does not include insoluble material such as that used to color face powder. However, the two words are frequently used without this distinction.

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Coal-tar colors are made from a number of chemical compounds called intermediates. If these intermediates have one thing in common, it is their high toxicity. Almost all dye intermediates are known to be poisonous.

Many of the thousands of known coal-tar colors are extremely toxic when taken internally. Some are irritants and sensitizers when applied to the skin. Some are carcinogenic. Actually, comparatively few colors have ever been tested to determine their safety for use in foods, drugs, and cosmetics. Colors need to be so evaluated, of course, only if such use is contemplated.

Dyes, like many other chemicals, are manufactured in reaction vessels from chemical compounds that, in turn, have been manufactured. In these processes, the dye may pick up such materials as lead, arsenic, mercury, cadmium, or chromium. For most uses, these do no harm, but in food, drugs, or cosmetics, they are likely to be a hazard to health.

From this brief description of coal-tar colors, it is obvious that food, drugs, and cosmetics should contain only thoroughly tested colors. The colors themselves must be nonhazardous, and they must be free from harmful quantities of contaminants. The provisions of the Federal Food, Drug, and Cosmetic Act that require certification of coal-tar colors were designed to make certain that only "harmless" dyes are used in products subject to that act.

The color certification program of the Food and Drug Administration is designed to carry out the provisions of the act pertaining to coal-tar colors. This program, which is one func-

tion of the Division of Cosmetics, is set up to do the following:

1. To list colors as certifiable when there is evidence to show that they are harmless and suitable for use, and that practical and accurate methods of analysis are available. New colors are added only on the basis of specific requests by manufacturers.

2. To conduct such analytical and investigative work as may be necessary to certify batches of coal-tar colors. Certificates are issued for individual batches on the basis of analyses of samples submitted by the manufacturer.

3. To conduct enforcement activities to insure compliance with the law.

Fees for certification based on the weight of the batches are paid by the manufacturer. These fees equip and maintain the certification service.

It is the aim of the Food and Drug Administration to achieve the following with respect to coal-tar colors:

1. Each color listed as certifiable must be completely characterized chemically. A sample of each batch manufactured must be completely analyzed chemically to make certain that it does not differ materially from the material submitted to pharmacological testing.

2. Each color listed as certifiable must have been thoroughly evaluated by pharmacological investigation. This investigation must show that the color is harmless and suitable for use.

Almost constant investigations are carried on in the attempt to realize this optimum state of affairs. When new techniques of analysis become available, they are applied to coal-tar colors.

History of Color Certification

Official recognition of the possibility of hazard to health in the use of synthetic dyes in food was evident as early as 1900. The appropriation for the Bureau of Chemistry of the Department of Agriculture, May 25 of that year, included funds "to enable the Secretary of Agriculture to investigate the character of proposed food preservatives and coloring matters, to determine their relation to digestion and health and to establish the principle which should govern their use. . . ." Several Food Inspection Decisions issued under this authority were in respect to foods offered for import into the United States. These decisions required notification of the addition of preservatives and colors to foods and freedom of such additives from deleterious properties.

Certification of colors used in food was begun in 1907, when the Federal Food and Drugs Act of 1906 became effective. Under this act, a list of colors permissible for use in food was adopted by the Board of Food and Drug Inspection, and certification of batches of these colors by the Department of Agriculture was optional with the manufacturer. Use of noncertified colors could not be a basis for regulatory action unless it could be shown that the food might be injurious to health by reason of harmful components of the colors used. It was not until 1939 that certification of batches of colors became mandatory and certification of colors used in drugs and cosmetics was begun.

The rules originally used in selecting colors for food, as stated in 1912 by Dr. Bernard C. Hesse in the Bureau of Chemistry Bulletin No. 147, were as follows:

Rule I: All colors which have not been physiologically tested either on man or animals shall not be permitted for use in foods.

Rule II: All colors which have been examined but with contradictory results shall not be permitted.

Rule III: All examined colors which are doubtful shall not be permitted.

Rule IV: Only those colors on the United States market in 1907 which are of definite composition and which have been examined with favorable results shall be permitted.

The adoption of colors today is based on the same principles. However, the tests applied are much more rigid and extensive than those used in 1907.

Under the original color regulations, certificates for individual batches of colors were issued by the Department of Agriculture on the basis of an affidavit of analysis by the manufacturer and a second affidavit of analysis by a competent scientist. These certificates were not based on analyses made by the Department; rather, they were approvals of the affidavits submitted by the manufacturer. Later actions set up a system of certification of batches based on

analyses made by the staff of the Department. This system made possible standardization of methods, and it is the basic system in use today.

From time to time, additional colors were added to the original list. Two colors, butter yellow (*p*-dimethylamino-azobenzene) and Sudan I (1 phenylazo-2-naphthol), were listed as certifiable and then withdrawn about 6 months later, on June 7, 1919. These colors were removed from the list because they produced a skin rash on persons handling them in quantity. The carcinogenic properties of butter yellow are now well known, but no hint of these properties was disclosed until several years after use of that color in food had been abandoned. In 1938, when the new law was passed, there were 15 colors listed as certifiable, all of which had been listed for at least 9 years.

Regulations Under the 1938 Act

When certification of colors for food, drugs, and cosmetics became compulsory, prompt adoption of lists of suitable colors was essential. After discussions with the dye manufacturers and representatives of the food, drug, and cosmetic industries, a number of colors were selected. They were tested chemically and submitted to such tests for toxicity as facilities permitted. Because it was necessary to adopt lists quickly in order to prevent a chaotic situation in the industries, the tests were considerably less than optimum. The chemical information was sometimes incomplete and sometimes, it was later learned, based on erroneous literature. The pharmacological information suffered from lack of data about the chronic toxicity of the dyes. The final step in the selection of colors was a series of hearings at which any interested party was permitted to testify and to cross-examine witnesses.

Following these hearings, regulations listing certifiable colors were adopted. These are substantially the regulations now in force. The colors are separated into three classes:

FD&C colors: Certifiable for use in coloring food, drugs, and cosmetics. These included all the colors that had been listed under the 1906 act.

D&C colors: Certifiable for use in coloring drugs and cosmetics, but not in food. These colors were all new to certification.

Ext D&C colors: Certifiable for use in coloring externally applied drugs and cosmetics, but not for food or for drugs or cosmetics applied to a mucous membrane. These also were colors not previously certifiable.

No colors are certified for use in the area of the eye, since no drugs or cosmetics intended for use in this area may be colored with any coal-tar color.

Shortly after the first regulations under the 1938 act were adopted, three additional colors were added to the FD&C list. Two of these were oil-soluble dyes, FD&C Orange No. 2 and FD&C Red No. 32, used principally in the external coloring of oranges. The other was FD&C Yellow No. 2, the potassium salt of 2,4-dinitrol-1-naphthol-7-sulfonic acid. (FD&C Yellow No. 1 is the corresponding sodium salt.) Oddly enough, no batch of FD&C Yellow No. 2 has ever been certified.

Later actions added one color to the list of Ext D&C dyes and placed one of the original D&C colors on the FD&C list as FD&C Violet No. 1.

The preparation and adoption of the coal-tar color regulations was a remarkable feat of cooperation between Government and industry. Both parties combined in the effort to make the regulations practical for the industry and effective for protection of the public. It is a tribute to their success that no basic changes in the regulations have been made except those dependent on information not available in 1938.

Recent Activities

It was realized in 1938 that the lack of data about chronic toxicity of coal-tar colors was a matter that required attention. Some studies were conducted, but the imminence of war and the war itself made it impossible properly to attack the problem until several years later.

Research in development of improved methods of chemical analysis was continued, but this work also was largely suspended during the war years. After the war, the availability of new apparatus, particularly spectrophotometric instruments, made progress much more rapid and results more certain.

Certification of FD&C Yellow No. 6

Specifications and procedures for FD&C Yellow No. 6 illustrate the requirements that colors must meet and the tests they must undergo in order to be certified.

General Specifications for All FD&C Colors

"No batch of a straight color listed . . . shall be certified under these regulations unless—

"(*a*) It is free from all impurities (other than those named in paragraph (*b*) or in the specifications set forth . . . for such color) to the extent that such impurities can be avoided by good manufacturing practice.

"(*b*) It conforms to the following specification: (1) In the case of a straight color listed in section 9.3 [i. e., an FD&C color]—

Lead (as Pb), not more than 0.001 percent.

Arsenic (as As_2O_3), not more than 0.00014 percent.

Heavy metals (except Pb and As) (by precipitation as sulfides), not more than trace."

Specific Requirements for FD&C Yellow No. 6

FD&C Yellow No. 6 is described as a "disodium salt of 1-*p*-sulfophenylazo-2-naphthol-6-sulfonic acid." It must meet the following requirements:

Volatile matter (at 135° C.), not more than 10.0 percent.

Water insoluble matter, not more than 0.5 percent.

Ether extracts, not more than 0.2 percent.

Chlorides and sulfates of sodium, not more than 5.0 percent.

Mixed oxides, not more than 1.0 percent.

Subsidiary dyes, not more than 5.0 percent.

Pure dye (as determined by titration with titanium trichloride), not less than 85.0 percent.

Analytical Determinations

Determination of total dye in the sample by titration with titanium trichloride, which quantitatively reduces the azo group.

Determination of the identity and quantity of dye by spectrophotometric procedures. Spectra in the visible, infrared, and ultraviolet regions are obtained and compared with spectra obtained from standard samples prepared in the FDA laboratories.

Determination of sodium chloride, sodium sulfate, insoluble matter, and volatile matter.

Determination of subsidiary dyes. Sodium salts of the following may be present: 1-phenylazo-2-naphthol-6-sulfonic acid, present if the sulfanilic acid used as an intermediate contains any aniline; 1-*p*-sulfophenylazo-2-naphthol-3,6-disulfonic acid and 1-*p*-sulfophenylazo-2-naphthol-6,8-disulfonic acid, present to some extent in all samples since it is almost impossible to prepare 2-naphthol-6-sulfonic acid entirely free from the disulfonated compounds; 1-(4 sulfophenylazo)-2-naphthol, present because some betanaphthol may be present in the sulfonated compound.

Determination of ether extracts, a measure of any organic tars or other ether soluble substances that may remain in the intermediates.

Determination of uncombined intermediates, present because of incomplete diazotization or coupling. Sulfanilic acid and 2-naphthol-6-sulfonic acid are the intermediates used for FD&C Yellow No. 6.

Determination of mixed oxides (iron, aluminum, etc.) that may be present. These usually get into the product because the processing equipment is attacked by reagents used in preparation of the dye.

Determination of lead and arsenic, usually present in the acids used in the sulfonation and nitration reactions carried out in the preparation of the intermediates.

Determination of heavy metals—copper, bismuth, tin, antimony, cadmium, and mercury. These also get into the dyes from processing equipment.

In addition, to meet the "good manufacturing practice" requirement in the general specifications, it must not contain more than traces of uncombined intermediates or of phenylazo-2-naphthol-6-sulfonic acid. Experience of many years has shown that it is practical to obtain almost complete removal of these impurities.

Certification or Rejection

If the sample is found to meet all the specifications, including the "good manufacturing practice" requirements, a certificate covering the batch is issued. If the sample fails to meet any one of the specifications, the batch is rejected.

Recent chemical investigations have shown that some of the colors do not have the exact composition or structure ascribed by earlier work. This information will probably not affect the status of the colors as certifiable, but it is of fundamental importance in establishing methods of analysis and standards that batches of the colors must meet in order to be certified.

Methods of analysis for coal-tar colors are a part of the program of the Association of Official Agricultural Chemists, and the results of the FDA's chemical investigations are usually published in the journal of that association. A mimeographed publication containing the methods of analysis used in the color-certification laboratory is also available.

Some of the recent pharmacological investigations have produced surprising results. Three colors, FD&C Orange No. 1, FD&C Red No. 32, and FD&C Orange No. 2, have been found to be considerably more toxic than was disclosed by earlier tests. These dyes act as gastrointestinal irritants. The toxicity of FD&C Orange No. 1 and of FD&C Red No. 32 has been confirmed by illness following ingestion of candy or popcorn containing these colors. In each case, the products contained very much more color than is customarily used.

As a result of the new tests, the Secretary of Health, Education, and Welfare issued a regulation removing the three colors from the lists of colors certifiable for use in food and drugs in November 1955. This regulation is now in effect with the exception of its application to FD&C Red No. 32 for coloring the outer skin of oranges. A stay issued by the Fifth Circuit Court of Appeals requires the continued certification of sufficient color for that use until the court has finally disposed of a petition to review the entire regulation. The colors were retained as certifiable for use in externally applied preparations since evidence is available to show that they are safe for such use.

Legal action against excessive use of certified colors is not authorized under the Federal Food, Drug, and Cosmetic Act. Section 406 (*b*) reads: "The Secretary shall promulgate regulations providing for the listing of coal-tar colors which are harmless and suitable for use in food, and for the certification of batches of such colors with or without harmless diluents." Sections 504 and 604 have almost identical wording with respect to colors for drugs and cosmetics.

The meaning of the word "harmless" is the cause of difficulty. The Food and Drug Administration believes the word to mean that the colors must be harmless per se, that is, without regard to the amounts of colors that would or could be consumed by the individual. This means, of course, that the colors must be without detectable physiological effect except that of inert or nonnutritive substances. The absolute harmlessness of any substance is virtually impossible to demonstrate.

The production of certified colors has increased steadily with the general expansion of the national economy. In 1941, about 2¼ million pounds of coal-tar colors were certified in 3,677 batches. In 1955, the amount was more than 5 million pounds in 4,675 batches. These figures include not only the highly concentrated "straight" colors, but also mixtures of the colors with various diluents, such as salt, sugar, or water. Such mixtures, which may contain two or more colors as well as diluents, are usually used instead of the straight colors in coloring food.

Certification of the 4,675 batches of coal-tar colors in 1955 required more than 25,000 analytical determinations, or about 100 per working day. An example of the certification requirements and procedures is given on page 584.

There have been very few regulatory actions against products containing uncertified colors in recent years. The requirements of the law are well known, and the food, drug, and cosmetic manufacturers generally make every effort to comply. In a few instances, products made in other countries have been denied entry into this country because they were found to contain uncertified colors.

Investigation of the production procedures used by the manufacturers of straight colors and mixtures has shown that few have failed to follow the regulations in every particular.

Program Needs

By law, the listing and certification of coal-tar colors is performed only upon payment of such fees as may be necessary to provide, main-

tain, and equip an adequate service for such purposes. Hence, the certification program is not handicapped by a lack of funds. But as demands for services increase, it is necessary to adjust facilities and personnel accordingly. Since the present program is the maximum that can be contained in the available laboratory and office space, relocation of the facilities is a matter for immediate attention. Recruiting and holding an adequate supply of personnel is a chronic problem, but at the moment at least all assigned positions are filled.
