§ 60.36 Standard of due diligence.

(a) In determining the due diligence of an applicant, FDA will examine the facts and circumstances of the applicant’s actions during the regulatory review period to determine whether the applicant exhibited that degree of attention, continuous directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period. FDA will take into consideration all relevant factors, such as the amount of time between the approval of an investigational exemption or research permit and the commencement of a clinical investigation and the amount of time required to conduct a clinical investigation.

(b) For purposes of this part, the actions of the marketing applicant shall be imputed to the applicant for patent term restoration. The actions of an agent, attorney, contractor, employee, licensee, or predecessor in interest of the marketing applicant or applicant for patent term restoration shall be imputed to the applicant for patent term restoration.

Subpart E—Due Diligence Hearings

§ 60.40 Request for hearing.

(a) Any person may request, not later than 60 days after the publication under §60.34(a) of FDA’s due diligence determination, that FDA conduct an informal hearing on the due diligence determination.

(b) The request for a hearing under this section shall:

(1) Be sent by mail, personal delivery, or any other mode of written communication to the Division of Dockets Management and filed under the relevant product file;

(2) Specify the facts and the action that are the subject of the hearing;

(3) Provide the name and address of the person requesting the hearing; and

(4) Certify that the requesting party has served a true and complete copy of the request upon the petitioner and the applicant by certified or registered mail (return receipt requested) or by personal delivery.

(c) The request shall state whether the requesting party seeks a hearing within 30 days or 60 days of FDA’s receipt of the request.

[53 FR 7305, Mar. 7, 1988, as amended at 67 FR 9585, Mar. 4, 2002]

§ 60.42 Notice of hearing.

Ten days before the hearing, FDA will notify the requesting party, the applicant, and the petitioner, orally or in writing, of the date, time, and location of the hearing. The agency will provide the requesting party, the applicant, and the petitioner with an opportunity to participate as a party in the hearing.

§ 60.44 Hearing procedures.

The due diligence hearing shall be conducted in accordance with this part, supplemented by the nonconflicting procedures in part 16. During the due diligence hearing, the applicant and the petitioner shall enjoy all the rights and privileges accorded a person requesting a hearing under part 16. The standard of due diligence set forth in §60.36 will apply in the due diligence hearing. The party requesting the due diligence hearing shall have the burden of proof at the hearing.

§ 60.46 Administrative decision.

Within 30 days after the completion of the due diligence hearing, the Commissioner will affirm or revise the determination made under §60.34(a) and will publish the due diligence redetermination in the Federal Register, notify PTO of the redetermination, and send copies of the notice to PTO and to the requesting party, the applicant, and the petitioner.
Subpart B—Packaging and Labeling

70.20 Packaging requirements for straight colors (other than hair dyes).
70.25 Labeling requirements for color additives (other than hair dyes).

Subpart C—Safety Evaluation

70.40 Safety factors to be considered.
70.42 Criteria for evaluating the safety of color additives.
70.45 Allocation of color additives.
70.50 Application of the cancer clause of section 721 of the act.
70.51 Advisory committee on the application of the anticancer clause.
70.55 Request for scientific studies.


SOURCE: 42 FR 15636, Mar. 22, 1977, unless otherwise noted.

Subpart A—General Provisions

§ 70.3 Definitions.

(a) Secretary means the Secretary of Health and Human Services.
(b) Department means the Department of Health and Human Services.
(c) Commissioner means the Commissioner of Food and Drugs.
(e) Color Certification Branch means the unit established within the Food and Drug Administration located in the Center for Food Safety and Applied Nutrition, charged with the responsibility for the mechanics of the certification procedure hereinafter described, and including the examination of samples of color additives subject to certification.
(f) A color additive is any material, not exempted under section 201(t) of the act, that is a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source and that, when added or applied to a food, drug, or cosmetic or to the human body or any part thereof, is capable (alone or through reaction with another substance) of imparting a color thereto. Substances capable of imparting a color to a container for foods, drugs, or cosmetics are not color additives unless the customary or reasonably foreseeable handling or use of the container may reasonably be expected to result in the transmittal of the color to the contents of the package or any part thereof. Food ingredients such as cherries, green or red peppers, chocolate, and orange juice which contribute their own natural color when mixed with other foods are not regarded as color additives; but where a food substance such as beet juice is deliberately used as a color, as in pink lemonade, it is a color additive. Food ingredients as authorized by a definitions and standard of identity prescribed by regulations pursuant to section 401 of the act are color additives, where the ingredients are specifically designated in the definitions and standards of identity as permitted for use for coloring purposes. An ingredient of an animal feed whose intended function is to impart, through the biological processes of the animal, a color to the meat, milk, or eggs of the animal is a color additive and is not exempt from the requirements of the statute. This definition shall apply whether or not such ingredient has nutritive or other functions in addition to the property of imparting color. An ingested drug the intended function of which is to impart color to the human body is a color additive. For the purposes of this part, the term color includes black, white, and intermediate grays, but substances including migrants from packaging materials which do not contribute any color apparent to the naked eye are not color additives.
(g) For a material otherwise meeting the definition of color additive to be exempt from section 721 of the act, on the basis that it is used (or intended to be used) solely for a purpose or purposes other than coloring, the material must be used in a way that any color imparted is clearly unimportant insofar as the appearance, value, marketability, or consumer acceptability is concerned. (It is not enough to warrant exemption if conditions are such that the primary purpose of the material is other than to impart color.)
(h) The exemption that applies to a pesticide chemical, soil or plant nutrient, or other agricultural chemical, where its coloring effect results solely
from its aiding, retarding, or otherwise affecting directly or indirectly, the growth or other natural physiological processes of produce of the soil, applies only to color developed in such product through natural physiological processes such as enzymatic action. If the pesticide chemical, soil or plant nutrient, or other agricultural chemical itself acts as a color or carries as an ingredient a color, and because of this property colors the produce of the soil, it is a color additive and is not exempt. (i) Safe means that there is convincing evidence that establishes with reasonable certainty that no harm will result from the intended use of the color additive.

(j) The term straight color means a color additive listed in parts 73, 74, and 81 of this chapter, and includes lakes and such substances as are permitted by the specifications for such color.

(k) The term mixture means a color additive made by mixing two or more straight colors, or one or more straight colors and one or more diluents.

(l) The term lake means a straight color extended on a substratum by adsorption, coprecipitation, or chemical combination that does not include any combination of ingredients made by simple mixing process.

(m) The term diluent means any component of a color additive mixture that is not of itself a color additive and has been intentionally mixed therein to facilitate the use of the mixture in coloring foods, drugs, or cosmetics or in coloring the human body. The diluent may serve another functional purpose in the foods, drugs, or cosmetics, as for example sweetening, flavoring, emulsifying, or stabilizing, or may be a functional component of an article intended for coloring the human body.

(n) The term substratum means the substance on which the pure color in a lake is extended.

(o) The term pure color means the color contained in a color additive exclusive of any intermediate or other component, or of any diluent or substratum contained therein.

(p) The term batch means a homogeneous lot of color additive or color additive mixture produced by an identified production operation, which is set apart and held as a unit for the purpose of obtaining certification of such quantity.

(q) The term batch number means the number assigned to a batch by the person who requests certification thereof.

(r) The term lot number means an identifying number or symbol assigned to a batch by the Food and Drug Administration.

(s) The term area of the eye means the area enclosed with in the circumference of the supra-orbital ridge and the infra-orbital ridge, including the eyebrow, the skin below the eyebrow, the eyelids and the eyelashes, and conjunctival sac of the eye, the eyeball, and the soft areolar tissue that lies within the perimeter of the infra-orbital ridge.

(t) The term package means the immediate container in which a color additive or color additive mixture has been packed for shipment or delivery. If the package is then packed in a shipping carton or other protective container, such container shall not be considered to be the immediate container. In the case of color additive mixtures for household use containing less than 15 percent pure color, when two or more containers of 3 ounces each or less, each containing a different color, are distributed as a unit, the immediate container for such unit shall be considered to be the package as defined in this section.

(u) The hair dye exemption in section 601(a) of the act applies to coal tar hair dyes intended for use in altering the color of the hair and which are, or which bear or contain, color additives derived from coal tar with the sensitization potential of causing skin irritation in certain individuals and possible blindness when used for dyeing the eyelashes or eyebrows. The exemption is permitted with the condition that the label of any such article bear conspicuously the statutory caution and adequate directions for preliminary patch-testing. The exemption does not apply to coloring ingredients in hair dyes not derived from coal tar, and it does not extend to poisonous or deleterious diluents that may be introduced as wetting agents, hair conditioners, emulsifiers, or other components.
in a color shampoo, rinse, tint, or similar dual-purpose cosmetic that alter
the color of the hair.

(v) The terms externally applied drugs
and externally applied cosmetics mean
drugs or cosmetics applied only to ex-
ternal parts of the body and not to the
lips or any body surface covered by mu-
cous membrane.

[42 FR 15636, Mar. 22, 1977, as amended at 61
FR 14478, Apr. 2, 1996]

§ 70.5 General restrictions on use of
color additives.

(a) Color additives for use in the area of
the eye. No listing or certification of a
color additive shall be considered to
authorize the use of any such color ad-
ditive in any article intended for use in
the area of the eye unless such listing or
certification of such color additive
specifically provides for such use. Any
color additive used in or on any article
intended for use in the area of the eye,
the listing or certification of which
color additive does not provide for such
use, shall be considered to be a color
additive not listed under parts 73, 74,
and 81 of this chapter, even though
such color additive is certified and/or
listed for other uses.

(b) Color additives for use in injections.
No listing or certification of a color ad-
ditive shall be considered to authorize
the use of any such color additive in
any article intended for use in injec-
tions unless such listing or certification
of such color additive specifically pro-
vides for such use. Any color additive
used in or on any article intended for use in
injections, the listing or certification of
which color additive does not provide for such
use, shall be considered to be a color
additive not listed under parts 73, 74,
and 81 of this chapter, even though
such color additive is certified and/or
listed for other uses.

(c) Color additives for use in surgical
sutures. No listing or certification of a
color additive shall be considered to
authorize the use of any such color ad-
ditive in any article intended for use as
a surgical suture unless such listing or
certification of such color additive spec-
ifically provides for such use. Any
color additive used in or on any article
intended for use as a surgical suture,
the listing or certification of which
color additive does not provide for such
use, shall be considered to be a color
additive not listed under parts 73, 74,
and 81 of this chapter, even though
such color additive is certified and/or
listed for other uses.

§ 70.10 Color additives in standardized
foods and new drugs.

(a) Standardized foods. (1) Where a pe-
tition is received for issuance or
amendment of a regulation estab-
lishing a definition and standard of
identity for a food under section 401 of
the act, which proposes the inclusion of
a color additive in the standardized
food, the provisions of the regulations
in part 71 of this chapter shall apply
with respect to the information that
must be submitted with respect to the
safety of the color additive (if such in-
formation has not previously been sub-
mitted and safety of the color additive
for the intended use has not been al-
ready established), and the petition
must show also that the use of the
color additive in the standardized food
would be in conformance with section
401 of the act or with the terms of a
temporary permit issued under §130.17
of this chapter.

(2) If a petition for a definition and
standard of identity contains a pro-
posal for a color additive regulation,
and the petitioner fails to designate it
as such, the Commissioner, upon deter-
mining that the petition includes a
proposal for a color additive regula-
tion, shall so notify the petitioner and
shall thereafter proceed in accordance
with the regulations in part 71 of this
chapter.

(3) A regulation will not be issued al-
lowing the use of a color additive in a
food for which a definition and stand-
ard of identity is established, unless its
issuance is in conformance with sec-
tion 401 of the act or with the terms of
a temporary permit issued under §130.17 of this chapter. When the con-
templated use of such additive com-
plies with the terms of a temporary
permit, the color additive regulation
will be conditioned on such compliance
and will expire with the expiration of
the temporary permit.

(b) New drugs. (1) Where an applica-
tion for a new drug is received and this
§ 70.11 Related substances.

(a) Different color additives may cause similar or related pharmacological or biological effects, and, in the absence of evidence to the contrary, those that do so will be considered to have additive toxic effects.

(b) Food additives may also cause pharmacological or biological effects similar or related to such effects caused by color additives, and, in the absence of evidence to the contrary, those that do so will be considered as having additive toxic effects.

(c) Pesticide chemicals may also cause pharmacological or biological effects similar or related to such effects caused by color additives, and, in the absence of evidence to the contrary, those that do so will be considered to have additive toxic effects.

(d) In establishing tolerances for color additives, the Commissioner will take into consideration, among other things, the amount of any common component permitted in other color additives, in food additives, and in pesticide chemical residues as well as the similar biological activity (such as cholinesterase inhibition) produced by such substance.

§ 70.19 Fees for listing.

(a) Each petition for the listing of a color additive shall be accompanied by a deposit of $3,000.00 if the proposal is for listing the color additive for use generally in or on foods, in or on drugs, and in or on cosmetics.

(b) If the petition for the listing is for use in or on foods only, the deposit shall be $3,000.00.

(c) If the petition for the listing is for use in or on drugs and/or cosmetics only, the deposit shall be $2,600.00.

(d) The provisions of paragraphs (a), (b), and (c) of this section shall be applicable, whether or not the proposal contemplates any tolerances, limitations, or other restrictions placed upon the use of the color additive.

(e) If a petition proposing the issuance of a regulation is withdrawn before it is finally accepted for filing, the deposit, less a $600.00 fee for clerical handling and administrative and technical review, shall be returned to the petitioner.

(f) If a petition proposing the issuance of a regulation is withdrawn within 30 days after filing, the deposit, less $1,800.00 if the petition is covered by paragraph (a) or (b) of this section, and less $1,600.00, if the petition is covered by paragraph (c) of this section, shall be returned to the petitioner.

(g) When a petition is withdrawn after filing and resubmitted within 6 months, it shall be accompanied by a deposit of $1,800.00 for a petition filed under paragraph (a) or (b) of this section, and $1,600.00 for a petition filed under paragraph (c) of this section. If a petition is resubmitted after 6 months, it shall be accompanied by the deposit that would be required if it were being submitted for the first time.

(h) When the resubmission pertains to a petition that had been withdrawn before acceptance for filing, a new advance deposit shall be made in full as prescribed in paragraph (a), (b), or (c) of this section.

(i) After a color additive has been listed, any request for an amendment or additional tolerance shall be accompanied by a deposit of $1,800.00 for use in the items specified in paragraphs (a)
Food and Drug Administration, HHS

§ 70.25 Fee schedules for services in listing dyes. (a) The fee for services in listing a diluent under §80.45 for use in color additive mixtures shall be $250.00. (b) The fee for services in listing a diluent under §80.35 for use in color additive mixtures shall be $250.00. (c) Objections and request for public hearing under section 721(d) of the act or section 203(d)(2)(C) of Pub. L. 86–618 (74 Stat. 404; 21 U.S.C. 379e, note) shall be accompanied by a filing fee of $250.00. (d) In the event of a referral of a petition under this section to an advisory committee, all costs related thereto (including personal compensation of committee members, travel materials, and other costs) shall be borne by the person or organization requesting the referral, such costs to be assessed on the basis of actual cost to the Government: Provided, That the compensation of such costs shall include personal compensation of advisory committee members at a rate not to exceed $75.00 per member per day. (e) In the case of requests of referrals to advisory committees, a special advance deposit shall be made in the amount of $2,500.00. Where required, further advance in increments of $2,500.00 each shall be made upon request of the Commissioner of Food and Drugs. All deposits for referrals to advisory committees in excess of actual expenses shall be refunded to the depositor. (f) All requests for pharmacological or other scientific studies shall be accompanied by an advance deposit of $5,000.00. Further advance deposits shall be made upon request of the Commissioner of Food and Drugs when necessary to prevent arrears in such cost. Any deposits in excess of actual expenses will be refunded to the depositor. If a request is denied the advance deposit will be refunded less such costs as are incurred for review of the request. (g) The person who files a petition for judicial review of an order under section 721(d) of the act shall pay the costs of preparing a transcript of the record on which the order is based. (h) All deposits and fees required by the regulations in this section shall be paid by money order, bank draft or certified check drawn to the order of the Food and Drug Administration, collectable at par at Washington, DC. All deposits and fees shall be forwarded to the Center for Food Safety and Applied Nutrition (HFS–200), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, whereupon after making appropriate record thereof they will be transmitted to the Treasurer of the United States for deposit in the special account “Salaries and Expenses, Certification, Inspection, and Other Services, Food and Drug Administration.”

(q) The Commissioner of Food and Drugs may waive or refund such fees in whole or in part when in his judgment such action will promote the public interest. (r) Any person who believes that payment of these fees will work a hardship on him may petition the Commissioner of Food and Drugs to waive or refund the fees.


Subpart B—Packaging and Labeling

§ 70.20 Packaging requirements for straight colors (other than hair dyes).

Straight colors shall be packaged in containers which prevent changes in composition. Packages shall be sealed so that they cannot be opened without breaking the seal. An unavoidable change in moisture content caused by the ordinary and customary exposure that occurs in good storage, packing, and distribution practice is not considered a change in composition. If the packaging material is a food additive it shall be authorized by an appropriate regulation in parts 170 through 189 of this chapter.

§ 70.25 Labeling requirements for color additives (other than hair dyes).

(a) General labeling requirements. All color additives shall be labeled with sufficient information to assure their safe use and to allow a determination of compliance with any limitations imposed by this part and parts 71, 73, 74, 80, and 81 of this chapter. In addition to
all other information required by the act, labels for color additives, except those in a form suitable for coloring the human body, shall state:

(1) The name of the straight color or the name of each ingredient comprising the color additive, if it is a mixture.

(2) A statement indicating general limitations for the use of the color additive, such as “for food use only”; “for food, drug, and cosmetic use”; “for use in drugs for external application only.”

(3) Where regulations issued impose quantitative limitations for a general or specific use of a straight color, the amount of each such straight color in terms of weight per unit/volume or percent by weight.

(4) An expiration date if stability data require it.

(b) Special labeling for color additives with tolerances. Where tolerances are imposed for a general or specific use of a color additive, the label shall in addition provide directions for use of the color additive which if followed will preclude the food, drug, or cosmetic to which it is added from containing an amount of the color additive in excess of the tolerance.

(c) Special labeling for color additives with other limitations. If use of the color additive is subject to other limitations prescribed in this part, such limitations shall be stated on the label of the color additive by a plain and conspicuous statement. Examples of such limitation statements are: “Do not use in products used in the area of the eye”; “Do not use for coloring drugs for injection.”

(d) Special labeling for color additives not exempt from certification. Color additives not exempt from the certification procedures shall in addition include in the labeling the lot number assigned by the Color Certification Branch, except that in the case of any mixture for household use which contains not more than 15 percent of pure color and which is in packages containing not more than 3 ounces there appears on the label, a code number which the manufacturer has identified with the lot number by giving to the Food and Drug Administration written notice that such code number will be used in lieu of the lot number.

Subpart C—Safety Evaluation

§ 70.40 Safety factors to be considered.

In accordance with section 721(b)(5)(A)(iii) of the act, the following safety factor will be applied in determining whether the proposed use of a color additive will be safe: Except where evidence is submitted which justifies use of a different safety factor, a safety factor of 100 to 1 will be used in applying animal experimentation data to man; that is, a color additive for use by man will not be granted a tolerance that will exceed 1/100th of the maximum no-effect level for the most susceptible experimental animals tested. The various species of experimental animals used in the tests shall conform to good pharmacological practice.

§ 70.42 Criteria for evaluating the safety of color additives.

(a) In deciding whether a petition is complete and suitable for filing and in reaching a decision on any petition filed, the Commissioner will apply the “safe-for-use” principle. This will require the presentation of all needed scientific data in support of a proposed listing to assure that each listed color additive will be safe for its intended use or uses in or on food, drugs, or cosmetics. The Commissioner may list a color additive for use generally in or on food, in or on drugs, or in or on cosmetics when he finds from the data presented that such additive is suitable and may safely be employed for such general use; he may list an additive only for more limited use or uses for which it is proven suitable and may safely be employed for such specific use or uses. This may allow the use of a particular dye, pigment, or other substance with certain diluents, but not with others, or at a higher concentration with some than with others.

(b) The safety for external color additives will normally be determined by tests for acute oral toxicity, primary irritation, sensitization, subacute dermal toxicity on intact and abraded skin, and carcinogenicity by skin application. The Commissioner may waive any of such tests if data before
§ 70.50 Application of the cancer clause of section 721 of the act.

(a) Color additives that may be ingested. Whenever (1) the scientific data before the Commissioner (either the reports from the scientific literature or the results of biological testing) suggest the possibility that the color additive including its components or impurities has induced cancer when ingested by man or animal; or (2) tests which are appropriate for the evaluation of the safety of additives in food suggest that the color additive, including its components or impurities, induces cancer in man or animal, the Commissioner shall determine whether, based on the judgment of appropriately qualified scientists, cancer has been induced and whether the color additive, including its components or impurities, was the causative substance. If it is his judgment that the data do not establish these facts, the cancer clause is not applicable; and if the data considered as a whole establish that the color additive will be safe under the conditions that can be specified in the applicable regulation, it may be listed for such use. But if in the judgment of the Commissioner, based on information from qualified scientists, cancer has been induced, no regulation may issue which permits its use.

(b) Color additives that will not be ingested. Whenever the scientific data before the Commissioner suggest the possibility that the color additive, including its components or impurities, has induced cancer in man or animals by routes other than ingestion, the Commissioner shall determine whether, based on the judgment of appropriately qualified scientists, the test suggesting the possibility of carcinogenesis is appropriate for the evaluation of the color additive for a use which does not involve ingestion, cancer has been induced, and the color additive, including its components or impurities, was the causative substance. If it is his judgment that the data do not establish these facts, the cancer clause is not applicable to preclude external drug and cosmetic uses, and if the data as a whole establish that the color additive will be safe under conditions that can be specified in the regulations, it may be listed for such use. But if, in the judgment of the Commissioner, based on information from qualified scientists, the test is an appropriate one for the consideration of safety for the proposed external use, and cancer has been induced by the color additive, including its components or impurities, no regulation may issue which permits its use in external drugs and cosmetics.

(c) Color additives for use as an ingredient of feed for animals that are raised for food production. Color additives that are an ingredient of the feed for animals raised for food production and that have the potential to contaminate human food with residues whose consumption could present a risk of cancer...
§ 70.51 Advisory committee on the applicability of the anticancer clause.

All requests for and procedures governing any advisory committee on the anticancer clause shall be subject to the provisions of part 14 of this chapter, and particularly subpart H of that part.

§ 70.55 Request for scientific studies.

The Commissioner will consider requests by any interested person who desires the Food and Drug Administration to conduct scientific studies to support a petition for a regulation for a color additive. If favorably acted upon, such studies will be limited to pharmacological investigations, studies of the chemical and physical structure of the color additive, and methods of analysis of the pure color additive and its identification and determination in foods, drugs, or cosmetics, as the case may be. All requests for such studies shall be accompanied by the fee prescribed in §70.19.