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DEPARTMENT OF COMMERCE

National Institutes of Standards and Technology

15 CFR Part 290

[Docket No.: 210913–0184]

RIN 0693–AB68

Hollings Manufacturing Extension Partnership—Amendment to Venue for Publishing Notices of Funding Opportunities for Financial Assistance

AGENCY: National Institute of Standards and Technology (NIST), United States Department of Commerce.

ACTION: Final rule.

SUMMARY: NIST is issuing a final rule to amend the regulations governing the Hollings Manufacturing Extension Partnership (MEP) program to reflect the current requirements for publishing Notices of Funding Opportunities (NOFOs) for the establishment and operation of MEP Centers, consistent with the current MEP authorizing statute and Department of Commerce (Department or DOC) policy.

DATES: This rule is effective October 8, 2021.

FOR FURTHER INFORMATION CONTACT: J. Chancy Lyford, External Affairs, Performance and Support Division, Hollings Manufacturing Extension Partnership, National Institute of Standards and Technology, 100 Bureau Drive, Mail Stop 4800, Gaithersburg, MD 20899, 240–660–0324.

SUPPLEMENTARY INFORMATION:

I. Background

The Hollings MEP Program (Program) is a unique program, consisting of centers in each state and Puerto Rico with partnerships at the state, federal, and local levels. Prior to being amended by Section 501(b) of the American Innovation and Competitiveness Act (AICA), Public Law 114–329, the Program statute, 15 U.S.C. 278k(c), required that NIST publish in the **Federal Register** a description of each financial assistance program to establish an MEP Center. Section 501(b) of AICA removed the requirement that such notices be published in the **Federal Register**, which is consistent with the current policy of the Department of Commerce to publish all notices of funding opportunities (NOFOs) on *www.Grants.gov,* unless otherwise required by statute or regulation.[1]

NIST is amending the MEP regulations, specifically 15 CFR 290.7, to remove the requirement that NOFOs to solicit applications to establish a new MEP Center or to operate a pre-existing MEP Center be published in the **Federal Register**.

II. Statutory Authority

15 U.S.C. 278k was revised by section 501(b) of AICA to eliminate the requirement that solicitations for operators of MEP Centers be published in the **Federal Register**.

III. Regulatory Analysis

Because this final rule is a matter relating to public property, loans, grants, benefits, or contracts, 5 U.S.C. 553 does not apply. *See* 5 U.S.C. 553(a)(2). Therefore, prior notice and opportunity for public comment are not required under 5 U.S.C. 553, and there is no requirement for a 30-day delay in the effectiveness of this action under 5 U.S.C. 553(d).

Executive Order 12866

This final rule was determined to be not significant for purposes of Executive Order 12866.

Executive Order 13132

This final rule does not contain policies with Federalism implications as defined in Executive Order 13132.

Regulatory Flexibility Act

Because prior notice and opportunity for public comment are not required for this rule by 5 U.S.C. 553, or any other law, the analytical requirements of the Regulatory Flexibility Act, 5 U.S.C. 601 *et seq.,* do not apply.

[1] In addition, the Office of Management and Budget has encouraged Federal agencies to use *www.Grants.gov* since 2003. 68 FR 58146.

Paperwork Reduction Act

This rule contains no new collection of information subject to the Paperwork Reduction Act, 44 U.S.C. 3501 *et seq.*

National Environmental Policy Act

This final rule will not significantly affect the quality of the human environment. Therefore, an environmental assessment or Environmental Impact Statement is not required to be prepared under the National Environmental Policy Act of 1969.

List of Subjects in 15 CFR Part 290

Cooperative agreements, Grant programs, Science and technology.

For the reasons stated in the preamble, NIST is amending 15 CFR part 290 as follows:

PART 290—REGIONAL CENTERS FOR THE TRANSFER OF MANUFACTURING TECHNOLOGY

■ 1. The authority citation for 15 CFR part 290 continues to read as follows:

Authority: 15 U.S.C. 278k.

■ 2. Revise § 290.7 to read as follows:

§ 290.7 Proposal selection process.

Upon the availability of funding to solicit applications to establish a new Manufacturing Extension Partnership (MEP) Center or to operate a pre-existing MEP Center, the Director shall publish a notice of funding opportunity on *www.Grants.gov* requesting submission of competitive proposals from eligible organizations.

Alicia Chambers,

NIST Executive Secretariat.

[FR Doc. 2021–21976 Filed 10–7–21; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 73

[Docket No. FDA–2017–C–1951]

Termination of Listing of Color Additives Exempt From Certification; Lead Acetate

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; response to objections and denial of public hearing requests; removal of administrative stay.

SUMMARY: The Food and Drug Administration (FDA or we) is responding to objections and a public hearing request that we received from Combe Inc., on the final rule entitled ''Termination of Listing of Color Additives Exempt From Certification; Lead Acetate,'' which published on October 31, 2018. The final rule amended the color additive regulations to no longer provide for the safe use of lead acetate in cosmetics intended for coloring hair on the scalp. After reviewing the objections, we have concluded that the objections do not raise issues of material fact that justify a hearing. Therefore, the stay of the effectiveness for the repeal and delisting of the color additive regulation is now lifted, and we are amending the color additive regulations to no longer provide for the safe use of lead acetate in cosmetics intended for coloring hair on the scalp.

DATES: This rule is effective January 6, 2022.

ADDRESSES: For access to the docket to read background documents or comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

FOR FURTHER INFORMATION CONTACT: Shayla West-Barnette, Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740–3835, 240–402–1262.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of October 31, 2018 (83 FR 54665), we issued a final rule repealing the color additive regulation in § 73.2396 (21 CFR 73.2396) to no longer provide for the safe use of lead acetate in cosmetics intended for coloring hair on the scalp because new data available since lead acetate was permanently listed have demonstrated that there is no longer a reasonable certainty that no harm will result from the use of this color additive. We gave interested persons until November 30, 2018, to file objections and requests for a hearing on the final rule. The preamble to the final rule stated that the effective date of the final rule would be on December 3, 2018, except as to any provisions that may be stayed by the filing of proper objections (83 FR 54665 at 54673). On December 3, 2018, § 73.2396 was removed from the CFR. However, we had received objections and requests for a hearing on the objections from Combe Inc. (Combe), a manufacturer of hair dyes containing lead acetate. Under sections 701(e)(2) and 721(d) of the FD&C Act (21 U.S.C. 371(e)(2) and 379e(d)), the filing of objections operates to stay the effectiveness of our repeal until we take final action on the objections.

To implement a stay of effectiveness as required by sections 701(e)(2) and 721(d) of the FD&C Act, we published a final rule in the **Federal Register** of April 1, 2019 (84 FR 12081), reinstating § 73.2396 pending final FDA action on the objections to the October 31, 2018, final rule. We also stated that this action did not reflect any change in our determination that new data demonstrate that there is no longer a reasonable certainty of no harm from the use of this color additive.

FDA listed lead acetate in § 73.2396 in 1980 as a color additive for safe use in cosmetics intended for coloring hair on the scalp, subject to certain restrictions and labeling requirements, at levels up to 0.6 percent (weight to volume; equivalent to 6,000 parts per million (ppm)) lead in the cosmetic product (45 FR 72112). Lead acetate is used in progressive hair dyes that, when applied to gray hair, gradually change the color with repeated applications.[1]

II. Objections and Requests for a Hearing

Sections 701(e)(2) and 721(d) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) collectively provide that, within 30 days after publication of an order relating to a color additive regulation, any person adversely affected by such an order may file objections, specifying with particularity the provisions of the order deemed objectionable, stating the grounds therefor, and requesting a public hearing upon such objections. We may deny a hearing request if the objections to the regulation do not raise genuine and substantial issues of fact that can be resolved at a hearing (§ 12.24(b)(1) (21 CFR 12.24(b)(1)). (See also *Community Nutrition Institute* v. *Young,* 773 F.2d 1356, 1364 (D.C. Cir. 1985).)

Objections and requests for a hearing are governed by 21 CFR part 12 of our regulations. Under 21 CFR 12.22(a), each objection must meet the following conditions: (1) Must be submitted on or before the 30th day after the date of publication of the final rule; (2) must be separately numbered; (3) must specify with particularity the provision of the regulation or proposed order objected to; (4) must specifically state the provision of the regulation or proposed order on which a hearing is requested (failure to request a hearing on an objection constitutes a waiver of the right to a hearing on that objection); and (5) must include a detailed description and analysis of the factual information to be presented in support of the objection if a hearing is requested (failure to include a description and analysis for an objection constitutes a waiver of the right to a hearing on that objection).

Following publication of the final rule repealing the regulation in § 73.2396 to no longer provide for the safe use of lead acetate in cosmetics intended for coloring hair on the scalp, we received a submission from Combe, a manufacturer of hair dyes containing lead acetate, providing 19 objections and requesting a hearing on each of the objections. Combe provided the following numbered objections:

Objection 1: Combe objects to FDA's finding that there is no safe level of exposure for lead.

Objection 2: Combe objects to FDA's reliance on information about lead exposure in children (*e.g.,* recommendations from the Centers for Disease Control and Prevention (CDC)).

Objection 3: Combe objects to FDA's reliance on sources that discuss blood level of lead, not exposure levels (see, *e.g.,* National Toxicology Program (NTP) monograph).

Objection 4: Combe objects to the conclusions FDA draws from the Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Committee on Food Additives (JECFA) (2011).

Objection 5: Combe objects to FDA's reliance on the Environmental Protection Agency's (EPA's) goals for lead in drinking water.

Objection 6: Combe objects to FDA's conclusion that the 1980 Moore et al. study (Ref. 1, the Moore study) underestimated the exposure of lead.

Objection 7: Combe objects to FDA's criticisms of Moore.

Objection 8: Combe objects to FDA's finding that the lead in the Moore study could have been absorbed by other parts of the body than the blood.

Objection 9: Combe objects to FDA's reliance on a novel and unvalidated computer model.

Objection 10: Combe objects to FDA's treating an unvalidated computer model as more reliable than robust human data.

[1] For example, as indicated in a lead acetate-containing progressive hair dye product manufacturer's use direction (Ref. 10), after the initial application, users might apply the progressive hair dye daily until the desired color shade is achieved, and once or twice per week to maintain the hair color thereafter.

Objection 11: Combe objects to FDA's argument that the absorption percentage from the Moore study is invalid because it tested only a small patch of skin.

Objection 12: Combe objects to FDA's reliance on a ''permeability coefficient'' for lead instead of fractional absorption.

Objection 13: Combe objects to FDA's use of a permeability coefficient for lead acetate that EPA repudiated and replaced with a much lower estimate.

Objection 14: Combe objects to FDA's conclusion that lower median lead levels in blood since 1990 means that any lead contributed by lead acetate is less safe now.

Objection 15: Combe objects to FDA's entire analysis because it is missing two critical links—FDA never relates exposure from lead acetate to any change in blood levels, and thus it never relates it to any predicted harm.

Objection 16: Combe objects to FDA's whole argument as FDA never links exposure to lead from lead acetate to a change in steady-state blood levels.

Objection 17: Combe objects to FDA's conclusion about the effect of lead acetate on blood lead levels.

Objection 18: Combe objects to FDA taking a zero-tolerance approach for lead.

Objection 19: Combe objects to FDA's failure to consider reducing the permitted lead acetate level under § 73.2396 from 0.6 percent to 0.153 percent.

See Submission from Anthony M. Santini, Senior Vice President and General Counsel, Combe Inc., Peter Barton Hutt, Matthew J. Hegreness, and Richard F. Kingham, Covington & Burling LLP (Counsel for Combe Incorporated), to the Dockets Management Staff, FDA, dated November 30, 2018, at pages 25–58, available at: *https://www.regulations.gov/document/FDA-2017-C-1951-0233* (referred to as the Submission).

III. Standards for Granting a Hearing

Specific criteria for deciding whether to grant or deny a request for a hearing are set out in § 12.24(b). Under that regulation, a hearing will be granted if the material submitted by the requester shows, among other things, that: (1) There is a genuine and substantial factual issue for resolution at a hearing (a hearing will not be granted on issues of policy or law); (2) the factual issue can be resolved by available and specifically identified reliable evidence (a hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions); (3) the data and information submitted, if established at a hearing, would be adequate to justify resolution of the factual issue in the way sought by the requester (a hearing will be denied if the data and information submitted are insufficient to justify the factual determination urged, even if accurate); (4) resolution of the factual issue in the way sought by the person is adequate to justify the action requested (a hearing will not be granted on factual issues that are not determinative with respect to the action requested, *e.g.,* if the action would be the same even if the factual issue were resolved in the way sought); (5) the action requested is not inconsistent with any provision in the FD&C Act or any regulation particularizing statutory standards (the proper procedure in those circumstances is for the person requesting the hearing to petition for an amendment or waiver of the regulation involved); and (6) the requirements in other applicable regulations, *e.g.,* 21 CFR 10.20, 12.21, 12.22, 314.200, 514.200, and 601.7(a), and in the notice issuing the final regulation or the notice of opportunity for a hearing are met.

A party seeking a hearing must meet a ''threshold burden of tendering evidence suggesting the need for a hearing'' (*Costle* v. *Pacific Legal Foundation,* 445 U.S. 198, 214–215 (1980), citing *Weinberger* v. *Hynson, Westcott & Dunning, Inc,* 412 U.S. 609, 620–621 (1973)). An allegation that a hearing is necessary to ''sharpen the issues'' or to ''fully develop the facts'' does not meet this test (*Georgia Pacific Corp.* v. *EPA,* 671 F.2d 1235, 1241 (9th Cir. 1982)). If a hearing request fails to identify any factual evidence that would be the subject of a hearing, there is no point in holding one. In judicial proceedings, a court is authorized to issue summary judgment without an evidentiary hearing whenever it finds that there are no genuine issues of material fact in dispute, and a party is entitled to judgement as a matter of law (*see Rule 56, Federal Rules of Civil Procedure*). The same principle applies to administrative proceedings (see 21 CFR 12.28).

A hearing request must not only contain evidence, but that evidence should raise a material issue of fact ''concerning which a meaningful hearing might be held'' (*Pineapple Growers Ass'n* v. *FDA,* 673 F.2d 1083, 1085 (9th Cir. 1982)). Where the issues raised in the objection are, even if true, legally insufficient to alter the decision, an Agency need not grant a hearing (see *Dyestuffs and Chemicals, Inc.* v. *Flemming,* 271 F.2d 281, 286 (8th Cir. 1959)). A hearing is justified only if the objections are made in good faith and if they ''draw in question in a material way the underpinnings of the regulation at issue'' (*Pactra Industries* v. *CPSC,* 555 F.2d 677, 684 (9th Cir. 1977)). A hearing need not be held to resolve questions of law and policy (see *Citizens for Allegan County, Inc.* v. *FPC,* 414 F.2d 1125, 1128 (D.C. Cir. 1969); *Sun Oil Co.* v. *FPC,* 256 F.2d 233, 240 (5th Cir. 1958)).

Even if the objections raise material issues of fact, we need not grant a hearing if those same issues were adequately raised and considered in an earlier proceeding. Once an issue has been so raised and considered, a party is estopped from raising that same issue in a later proceeding without new evidence. The various judicial doctrines dealing with finality, such as collateral estoppel, can be validly applied to the administrative process (see *Pacific Seafarers, Inc.* v. *Pac. Far East Line, Inc.,* 404 F.2d 804, 809 (D.C. Cir. 1968), *cert. denied,* 393 U.S. 1093 (1969)). In explaining why these principles ought to apply to an Agency proceeding, the U.S. Court of Appeals for the District of Columbia Circuit wrote: ''The underlying concept is as simple as this: justice requires that a party have a fair chance to present his position. But overall interests of administration do not require or generally contemplate that he will be given more than a fair opportunity'' (*Retail Clerks Union, Local 1401* v. *NLRB,* 463 F.2d 316, 322 (D.C. Cir. 1972); see also *Costle* v. *Pacific Legal Foundation,* 445 U.S. 198 at 215–17).

IV. Analysis of Objections and Response to Hearing Requests

The submission from Combe contains 19 numbered objections, and Combe requests a hearing on each of them. We address each objection below, as well as the evidence and information filed in support of each, comparing each objection and the information submitted in support of it to the standards for granting a hearing in § 12.24(b). For purposes of clarity, we have grouped the numbered objections into categories of related subjects while maintaining the objection numbers assigned by Combe.

A. Category A: No Known Safe Level of Lead Exposure

Combe's numbered objections included in Category A are as follows:

1. Combe objects to FDA's finding that there is no safe level of exposure for lead.
2. Combe objects to FDA's reliance on information about lead exposure in children (*e.g.,* recommendations from the CDC).
4. Combe objects to the conclusions FDA draws from JECFA (2011).
5. Combe objects to FDA's reliance on EPA's goals for lead in drinking water.
18. Combe objects to FDA taking a zero-tolerance approach to lead.

Objection 1. Combe objects to ''FDA's finding that there is no safe level of exposure for lead.'' The objection asserts that, ''. . . the weight of the scientific evidence demonstrates that low levels of

lead are safe, especially for the population that uses hair dye containing lead acetate—older men with graying hair.'' See Submission, page 26.

(Response to Objection 1) Our determination that a color additive is 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 (§ 70.3(i)). The regulation in § 73.2396 permits the use of lead acetate (calculated as lead) at levels not to exceed 0.6 percent (6,000 parts per million (ppm; milligrams/kilograms (mg/kg))) as a color additive in cosmetics intended for coloring hair on the scalp. Combe did not provide scientific data to support its objection or to demonstrate that there is a level of exposure to lead that could be considered safe.

Following our full evaluation of data submitted in color additive petition (CAP) 7C0309 requesting repeal of § 73.2396 and other pertinent data and information (see September 18, 2018, memorandum from M.K. Wyatt to M. Harry, ''the Wyatt Memorandum'' (Ref. 2)), we have determined that there is no known level of exposure to lead that does not produce adverse effects. While Combe states that ''. . . lead does not pose a danger to adults at low levels . . .,'' Combe failed to provide in this objection the specific levels at which lead does not pose a danger to adults and any corresponding scientific evidence to support this statement. See Submission, page 27.

The objection failed to include new data or information that would refute our findings about the lack of a safe level of lead exposure. The objection merely alleges that low levels of lead are safe, without providing any scientific basis. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). The objector must, at a minimum, raise a genuine and substantial issue of fact for resolution at a hearing. Therefore, we are denying the request for a hearing on this objection.

Objection 2. Combe objects to ''FDA's reliance on information about lead exposure in children (*e.g.,* recommendations from the CDC).'' In this objection, ''Combe does not dispute the fact that lead exposure can harm a developing child,'' but states that this fact has ''no bearing on the use of lead acetate in a progressive hair dye for older men.'' See Submission, page 27. Combe also asserts that ''lead poses no danger at low levels to older adults.'' See Submission, page 28.

(Response to Objection 2) We acknowledge that Combe's products (*i.e.,* lead acetate-containing progressive hair dyes) are intended for use by adults and not by children. Our decision to repeal the regulation is based on the evidence of lead-related adverse health effects reported at low levels of lead in adults, such as adverse cardiovascular and kidney effects, cognitive dysfunction, and adverse reproductive outcomes (Ref. 3), and the lack of evidence of a safe level of exposure for lead. Currently, available data and information do not support the safe use of lead acetate intentionally added to cosmetics for coloring hair on the scalp of any age group or gender. Therefore, the use of lead acetate as a color additive no longer meets the safety standard of ''reasonable certainty of no harm.''

We also note that we did not rely on the toxicity information about lead exposure in children; rather, in the final rule, we referred to the CDC statement that there is no safe blood lead level in children to further demonstrate the risks of lead exposure and why there is a U.S. Government-wide effort to limit lead exposure to the public. We continue to work to limit consumers' exposure to lead in all FDA-regulated products, including cosmetics.

Combe failed to provide scientific data and information demonstrating that there is a safe level of lead exposure from the listed use of lead acetate as a color additive. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). The objector must, at a minimum, raise a genuine and substantial issue of fact for resolution at a hearing. Therefore, we are denying the request for a hearing on this objection.

Objection 4. Combe objects to ''the conclusions FDA draws from JECFA (2011).'' See Submission, page 32. In this objection, Combe cites JECFA's conclusion that ''it could not establish a new provisional tolerable weekly intake (PTWI) that would be considered health protective,'' and that JECFA instead established a ''negligible risk'' level for food. See Submission, at page 32. Combe alleges that ''FDA did not analyze the underlying scientific discussion in JECFA (2011).'' See Submission, page 32.

(Response to Objection 4) JECFA stated that ''because the dose-response analyses do not provide any indication of a threshold for the key effects of lead, the Committee therefore concluded that ''it was not possible to establish a new PTWI that would be considered to be health protective'' (Ref. 4). Notably, JECFA's statement about ''negligible risk'' was within the context of unavoidable lead exposure as an impurity in food, instead of intentionally added, avoidable exposures to lead in a cosmetic product. We are not aware of any statement by a competent, national regulatory authority or an international risk assessment body establishing a safe level of lead exposure that would support a determination that there is a reasonable certainty of no harm from the use of lead acetate as a color additive in hair dye. Instead, for example, the WHO has stated that ''[t]here is no level of exposure to lead that is known to be without harmful effects.'' (Ref. 5).

Contrary to Combe's assertion, JECFA's statement establishing a negligible risk level for lead as an unavoidable food impurity does not provide a ''safe harbor'' for any intentionally added lead in a cosmetic product. See Submission, page 33. Also, JECFA's negligible risk level for food does not support Combe's claim that the intended use of lead acetate in hair dye meets the safety standard of ''reasonable certainty of no harm'' set forth at § 70.3(i) (21 CFR 70.3(i)) because as JEFCA states, currently available data do not provide any indication of a threshold for the reported adverse effects from exposure to lead (Ref. 4).

The objection failed to include any new information or data that would change our findings about the lack of a safe exposure level of lead. The objection merely alleges that FDA did not analyze JECFA's conclusion and does not provide scientific information to support Combe's argument. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). The objector must, at a minimum, raise a genuine and substantial issue of fact for resolution at a hearing. Therefore, we are denying the request for a hearing on this objection.

Objection 5. Combe objects to ''FDA's reliance on EPA's goals for lead in drinking water.'' Combe states that the EPA goal in setting the maximum contaminant level for lead in drinking water at zero is based on the effect of lead in children. See Submission, page 33. Combe contends that EPA's goal for lead in drinking water ''in no way means, however, that lead is unsafe in a progressive hair dye for aging men with graying hair.'' Ibid.

(Response to Objection 5) FDA did not rely on EPA's goal for lead in drinking water; we referred to it to further document the adverse effects resulting from lead exposure. Adverse effects to the public more generally

resulting from lead exposure are the reason why there is a government-wide effort to limit lead exposure to the public. Our decision to repeal the regulation was based on the recognition that there is no scientific data demonstrating a safe level of exposure to lead and that the data currently available no longer demonstrate that there is reasonable certainty of no harm from the use of lead acetate as a color additive in hair dyes authorized under § 73.2396. Combe fails to show that there is a genuine and substantial issue of fact for resolution at a hearing. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). Therefore, we are denying the request for a hearing on this objection.

Objection 18. Combe objects to ''FDA taking a zero-tolerance approach to lead.'' Combe argues that ''FDA appears to draw a legal distinction between lead that is intentionally added and lead that is present as impurities. Although such a distinction can be legally drawn for food, FDA cannot do this for cosmetics.'' See Submission, page 54. Combe claims that the safety standard for cosmetics is the same, whether the lead is intentionally added or present as an impurity. Combe asserts that under section 406 of the FD&C Act (21 U.S.C. 346), FDA can only set tolerances for poisonous and deleterious substances for food, and not cosmetics. Combe further asserts that FDA is acting arbitrarily and capriciously by banning lead acetate in hair dyes, but not banning it in lipstick. See Submission, pages 55–56.

(Response to Objection 18) We disagree that the presence of lead as an impurity in some cosmetic products means that FDA must find that there is a reasonable certainty of no harm from the use of lead acetate in hair dyes at levels up to 6,000 ppm (mg/kg). The intended use of lead acetate is as a color additive and as such we are acting under sections 721(d) and 601(e) (21 U.S.C. 361(e)) of the FD&C Act. See 28 FR 13374 (December 10, 1963) (providing FDA's interpretation of sections 601(a) and (e) of the FD&C Act). We have concluded that intended use of lead acetate does not meet the safety standard of ''reasonable certainty of no harm'' set forth at § 70.3(i) for color additives. Combe has not demonstrated that the intended use of lead acetate meets this safety standard. Therefore, we are repealing the listing of lead acetate under section 721(d) of the FD&C Act, and its use adulterates a cosmetic under section 601(e) of the FD&C Act.

Our repeal of the listing of lead acetate as a color additive in hair dye and our recommendation to limit lead as an unavoidable impurity in lipstick and other cosmetics are not arbitrary and capricious actions, as Combe asserts. In our ''Draft Guidance for Industry: Lead in Cosmetic Lip Products and Externally Applied Cosmetics: Recommended Maximum Level'' (2016), we recommend lead not be present as an impurity (not an intentionally added ingredient) in cosmetics at levels exceeding 10 ppm (10 mg/kg) (Ref. 6).[2] Lead as an impurity may occur in any cosmetics due to its background presence in the environment. Lead as an impurity cannot be completely avoided, although we have concluded that limiting trace amounts of lead to less than 10 ppm (10 mg/kg) can be achieved through reasonable and practical approaches to control raw materials and through other good manufacturing practices (Ref. 7). The draft guidance does not apply to hair dyes that contain lead acetate as an ingredient (Ref. 6 at page 3).

By contrast, lead acetate as a color additive is an intentionally added ingredient in hair dye and must meet the safety standard for color additives. We believe that the available data demonstrate that exposure to lead acetate from the intended use may cause adverse effects (Refs. 3 and 4). Therefore, the use of lead acetate in hair dye products that would result in lead levels up to 6,000 ppm (6,000 mg/kg) in the final products does not meet the safety standard for color additives.

Because there is no factual issue Combe identifies in this objection that can be resolved by available and specifically identified reliable evidence, we are denying the request for a hearing on this objection (§ 12.24(b)(1)).

B. Category B: The Moore Study

Combe's numbered objections included in Category B are as follows:

6. Combe objects to FDA's conclusions that the Moore study underestimated the exposure to lead.

7. Combe objects to FDA's criticisms of Moore.

8. Combe objects to FDA's finding that the lead in the Moore study could have been absorbed by other parts of the body than the blood.

11. Combe objects to FDA's argument that the absorption percentage from the Moore study is invalid because it tested only a small patch of skin.

Objection 6. Combe objects to ''FDA's conclusions that the Moore study underestimated the exposure of lead.'' Combe asserts that the Moore study remains the best evidence of the absorption of lead from lead acetate, that the Moore study protocol was developed with guidance from FDA, and that FDA acknowledged as much because it used some of the figures derived from the Moore study in its own modeling. See Submission, pages 33–34.

(Response to Objection 6) FDA acknowledges that the Moore study has some scientific merit. As discussed in our responses to Objections 9, 12, and 13, the fractional absorption (the percentage of the total amount of lead applied that is absorbed through the skin) from this study was used to calculate EPA's permeability coefficient (*Kp*) value (the rate at which a chemical penetrates the skin), which we used in our assessment.[3] Additionally, the results generated by Moore et al. would be reliable for a situation where the experimental conditions reflected the intended use conditions. However as explained below, the intended conditions of use of the lead acetate-containing progressive hair dyes are different from the experimental conditions in the Moore study.

New scientific information and computational tools have become available since the Moore study protocol was developed in the 1970s to 1980. We considered newer scientific information, including peer-reviewed publications describing nonclinical and clinical studies that demonstrate that dermally applied lead acetate and other lead compounds penetrate human and animal skin (Ref. 2). Additionally, newer computational tools have shown that the surface area of the application site is an important factor for estimating dermal absorption of lead and other compounds. This includes the in silico (*i.e.,* via computer simulation, as opposed to in vitro or in vivo experimental studies) ConsExpo dermal absorption model that we used to predict the percentage of dermal lead absorption. Using a surface area that is representative of the actual application area is also consistent with our recent guidance for industry,[4] which provides recommendations for conducting in vivo absorption trials for topically applied active ingredients (Ref. 8). The

[2] The draft guidance, only when finalized, will represent the current thinking of the FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

[3] Objection 12 provides an additional explanation of fractional absorption and *Kp*.

[4] The Wyatt Memorandum (Ref. 2) refers to the draft guidance (Ref. 6), which has since been finalized.

guidance recommends, in part, that the test article should be applied to the part of the body and maximal skin surface areas that are consistent with the final product's intended skin surface area use (Ref. 8, page 6).

By contrast, the Moore study design—where the lead acetate formulation was applied to a small surface area on the forehead—did not reflect either where lead acetate hair dye is intended to be applied or the surface area of such application. Specifically, in the Moore study, the lead acetate formulation was tested on only a small fraction of the skin surface area (*i.e.,* 8 to 10 square centimeters (cm^2) on the forehead instead of approximately 580 cm^2 for the full scalp). Additionally, the test formulation was applied to an area of skin without many hair follicles, which may have further underestimated the amount of lead absorbed. Lead absorption was measured after 12 hours and 24 hours of exposure, and the test formulation was washed off after the first 12 hours. The study did not investigate the actual directions of use of this hair dye, which results in accumulation of lead on the hair and skin. [5] Therefore, the Moore study underestimated exposure to lead from the use of lead acetate hair dyes. Based on these flaws and the additional flaws we identified in the Moore study, specifically, the formulation used in the study contained 0.12 to 0.18 percent lead (instead of 0.6 percent), the ages of the eight male test subjects range from 20 to 35 years (instead of older adults), and the short duration of test article application, which were discussed in detail in the final rule that appeared in the **Federal Register** of October 31, 2018 (83 FR 54665 at 54668 through 54670), we stated that the Moore study results could no longer be relied on to make a safety decision for the use of lead acetate as a color additive in hair dye.

Therefore, considering the reported adverse effects at low levels of lead exposure (*e.g.,* increased blood pressure, hypertension, decreased glomerular filtration rate) (83 FR 54665 at 54668), and the absence of data showing a safe level of lead exposure, we believe that the safety standard of reasonable certainty of no harm is no longer met.

Because Combe has not provided new data that address the identified flaws in the Moore study, we conclude that Combe's argument on the Moore study is insufficient to justify a hearing (§ 12.24(b)(3)). Therefore, we are denying the request for a hearing on this objection.

Objection 7. Combe objects to ''FDA's criticisms of Moore.'' Combe states that in 1981, FDA concluded that Moore's radioactive tracking study demonstrated a miniscule amount of lead absorption from lead acetate hair dyes. See Submission, page 35. Combe further states that the Moore study result of 0.058 percent is supported by a subsequent study by Bress and Bidanset (Ref. 2), which estimated absorption of lead acetate as 0.05 percent. See Submission, at page 37.

(Response to Objection 7) We acknowledge that, based on the scientific information available 40 years ago, we considered the 1978 radioactive tracer skin absorption study sponsored by Combe (a petitioner for CAP 3C0107) and conducted by Moore et al. (published in 1980) to be the primary study supporting the approval of lead acetate as a color additive in 1980, and that it was applicable for studying human skin lead absorption at that time. However, as discussed in our response to Objection 6 and the October 31, 2018, final rule (83 FR 54665 at 54668 through 54670), we have since identified several flaws in the Moore study design and conduct, such as applying test formulation with a lower lead concentration, on a smaller surface area of skin, and for a short period of time, when compared to the intended conditions of use. For example, as discussed previously, Moore et al. applied the lead acetate-containing formulation to an 8 to 10 cm^2 surface area on the forehead without many hair follicles, which is not consistent with the intended condition of use for the hair dye product (on the full scalp with many hair follicles and a skin surface area of approximately 580 cm^2), thereby underestimating the exposure to lead from lead acetate-containing hair dye. In addition, the result of 0.058 percent was measured 12 hours after a single application of the hair dye, which was then washed off. Therefore, the result does not represent the accumulation of lead from daily use of the hair dye. Because of these identified flaws and others described in the response to Objection 6, the fractional absorption calculated from the Moore study does not accurately represent the actual dermal absorption under the intended conditions of use, and therefore does not support the safe use of lead acetate in progressive hair dyes.

We also reviewed the study published in 1991 by Bress and Bidanset (Ref. 2). While the results from this study are consistent with those from the Moore study, Bress and Bidanset also applied the lead compound to a small skin surface area; thus, their study is of similar limited utility as the Moore study because it may also underestimate the exposure to lead from the use of hair dye. The objection failed to provide new data that address the identified flaws in the Moore study and the limitation of the Bress and Bidanset study for estimating skin absorption of lead from the use of lead acetate hair dye, and the information discussed in this objection is insufficient to justify a hearing (§ 12.24(b)(3)). Therefore, we are denying the request for a hearing on this objection.

Objection 8. Combe objects to ''FDA's finding that the lead in the Moore study could have been absorbed by other parts of the body than the blood.'' Combe also states that the radioactive tracer skin absorption study conducted by Moore et al. measured whole body lead (including lead in the blood, other fluids, tissues, muscle, and bone) and that Moore et al. calculated that 40 percent of the lead absorbed by the whole body was absorbed into the blood. See Submission, page 38.

(Response to Objection 8) In a March 3, 1978, final rule postponing the closing date for the provisional listing of lead acetate for use as a component of hair colors (43 FR 8790), we stated that the radioactive tracer skin absorption study protocol submitted to FDA would measure whole body counts of lead absorption, and in addition, blood and urine samples would be analyzed for measurable levels of lead (43 FR 8790 at 8793). However, as further discussed in our response to Objection 12, the use of fractional absorption to express dermal absorption depends on the study design (*e.g.,* duration of exposure, how much of the test material is in contact with a given surface area, the concentration of the substance in the matrix). Also, as stated in our response to Objection 6, given its fundamental flaws, the Moore study underestimated exposure to lead from the use of lead acetate hair dyes. Therefore, we can no longer rely on this study's exposure estimate to assure the safe use of lead acetate in hair dye. Combe does not point to any other studies that have evaluated lead absorption across the full surface area of the scalp, nor does Combe point to other studies demonstrating an absorption estimate after correcting the flaw in the Moore study that could provide evidence that the use of lead acetate in hair dye is safe.

A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). Therefore, in

[5] The manufacturer's use directions state that after the initial application, users might apply the progressive hair dye daily until the desired color shade is achieved (usually takes 2–3 weeks), and then once or twice a week to maintain the hair color.

the absence of any other evidence, studies, or new scientific information addressing the flaws identified in the Moore study that would demonstrate that the use of lead acetate in hair dye is safe, we are denying the request for a hearing on this objection.

Objection 11. Combe objects to ''FDA's argument that the absorption percentage from Moore is invalid because it tested only a small patch of skin.'' See Submission, page 40. Combe acknowledges that the scalp has a larger surface area, but states that the use instruction for its hair dye product is to apply the dye to the hair while avoiding ''areas you want to keep gray'' and not to apply the product to the scalp. See Submission, page 41. Thus, Combe claims that its product ''would never touch the whole scalp.'' Ibid. Combe asserts that Moore's approach of applying the lead acetate formulations directly to skin on the forehead was a conservative approach that would substantially overestimate absorption. Combe further asserts that,

> Moore applied a small amount of hair dye to a small patch of skin and measured how much of that small amount was absorbed. Thus, Moore was able to estimate the percentage of the applied dye that enters the body. This fraction (0.058 percent) was then multiplied by the actual amount of hair dye that would reach the head, yielding the amount of absorption that can be expected from the whole application. By such multiplication, Moore took into account the application to more than just a small patch of skin. Moore considered the entire scalp.

See Submission, pages 41–42.

Combe also asserts that the way Moore estimated absorption ''remains the standard way that industry and regulators do it today.'' See Submission, page 42. Specifically, Combe states that FDA ''evaluated the dermal absorption of lead as a percentage of the amount applied to the skin'' in its 2016 draft guidance for lead as an impurity in cosmetic lip products and externally applied cosmetics, and that this approach is similar to the approach in the Moore study. Ibid.

(Response to Objection 11) Our criticism of the Moore study is not limited to its testing of only a small patch of skin; however, the size of the skin tested is one relevant factor.

We note that Combe asserts that lead acetate ''would never touch the whole scalp.'' See Submission, page 41. Yet, Combe failed to provide data showing how much of the scalp (by the percent area) is estimated to be exposed to the hair dye. Without such data, our assumption that the hair dye would be applied to the surface area of the scalp that would be expected to be treated with the hair dye product is consistent with the practices used in an appropriately designed dermal absorption study. For example, see the European Commission's Scientific Committee on Consumer Products' (SCCP's) guidance for testing and evaluating safety of cosmetic ingredients (Ref. 9). Page 44 of the SCCP guidance document states, ''Hence, when dermal absorption is expressed as a percentage, the absorbed amount resulting from *in vitro* tests has to be expressed as a percentage of the dose applied in real in use conditions, that can be estimated by the ratio of the default amount of formulation applied in real conditions and the respective default value of skin surface area per product type.''

In addition, it is likely that some users would apply the product to the whole scalp. For example, Combe's Grecian® Formula16® liquid and cream products use instructions state that the user should apply the lead acetate-containing hair dye ''to cover gray totally, until hair feels slightly damp;'' ''[c]omb hair as usual;'' ''if desired apply daily until hair reaches desired shade;'' and ''[t]o maintain your natural look, apply once or twice a week thereafter'' (Ref. 10). The pictures provided in the use instructions appear to indicate that the dye may be applied on the area of the head covered by hair (Ibid.). Accordingly, we expect that some users would follow these instructions and apply the dye and comb the damp hair such that the dye would widely reach the scalp.

Nonetheless, Combe asserts that Moore considered ''the entire scalp,'' by multiplying the percentage of the applied dye that enters the body (*i.e.,* the fractional absorption) by the ''actual amount of hair dye that would reach the head.'' See Submission, page 41. Experimental conditions can impact fractional absorption and are not independent of skin loading conditions, which can have dramatic effects on the results (Refs. 11 and 12). The experimental conditions in the Moore study were drastically different from the intended conditions of use, thus the fractional absorption measured in this experiment is not representative of the real fractional absorption under the intended use conditions. For example, a fractional absorption obtained by applying 0.1 milliliter (mL) of hair dye formulation containing 0.12 percent lead acetate to an 8 or 10 cm^2 area of skin on the forehead without many hair follicles and measured after 12 hours does not accurately reflect the actual use conditions where 0.18 mL of formulation containing up to 0.6 percent lead is applied to a 580 cm^2 area of scalp area with many hair follicles and is reapplied every 24 hours until the hair reaches the desired shade (Refs. 1 and 2). Thus, the relative dermal loading of the hair dye was 0.01 mL/cm^2 (0.1 mL/10 cm^2) in the Moore study versus 0.00031 mL/cm^2 (0.18 mL/580 cm^2), which is a 32-fold difference that influences dermal absorption. We do not consider a study design, in which the test formulation (with lower lead acetate concentration) was applied to a small surface area on the forehead (instead of the full scalp) and washed off after an application period-to be a conservative approach as Combe asserts, nor do we consider it an accurate measure of lead exposure from the product use. Thus, we believe that the Moore study underestimated the total amount of lead that was absorbed.

With regard to FDA's 2016 draft guidance, as discussed in our response to Objection 18, this guidance is specific to lead present in certain cosmetics as an impurity. It is important to note the maximum permitted use level of 6,000 ppm lead acetate intentionally added to a hair dye is 600 times greater than the maximum recommended lead level of 10 ppm as an impurity. For the draft guidance, FDA evaluated the dermal absorption of lead as a percentage of the amount applied to the skin in order to assess exposure more generally. The draft guidance incorporated usage data for three representative cosmetic product categories (lipstick, eye shadow, and body lotion) and estimated whole body exposure to lead. The draft guidance considered average daily usages of lipstick, eye shadow, and body lotion to make generalizations for lead as an impurity in all categories of cosmetics covered by this guidance, rather than in each specific category.

By contrast, for our review of lead acetate, we considered specifically how much lead would be absorbed from a hair dye to ensure that this intended use of lead acetate meets the safety standard for color additives. Because use of lead acetate as a hair dye is associated with a specific usage scenario limited to only the scalp, the intended conditions of use, including the surface area of application, were important in calculating absorption. Because of study design limitations with the Moore study, we used a published *Kp* value (see response to Comment 12 that addresses the *Kp* value) in a ConsExpo model to estimate exposure and predict potential percentages of dermal lead absorption for this specific usage scenario.

A hearing will not be granted on the basis of mere allegations or general descriptions of positions and

contentions (§ 12.24(b)(2)). Therefore, in the absence of any other evidence, studies, or new scientific information addressing the flaws identified in the Moore study that would demonstrate that the use of lead acetate in hair dye is safe, we are denying the request for a hearing on this objection.

C. Category C: ConsExpo In Silico [Computer] Modeling

Combe's numbered objections included in Category C are as follows:

9. Combe objects to FDA's reliance on a novel and unvalidated computer model.

10. Combe objects to FDA's treating an unvalidated computer model as more reliable than robust human data.

Objection 9. Combe objects to ''FDA's reliance on a novel and unvalidated computer model.'' Combe states that FDA failed to explain whether the model is validated and why it used this particular model. See Submission, page 39. Combe further claims that FDA never explained the details of the model, ''how the math works, or why FDA's inputs to the model are reasonable.'' Ibid.

(Response to Objection 9) Contrary to Combe's contention, the ConsExpo dermal absorption model is not novel. The ConsExpo dermal absorption model is a mathematically based modeling program that enables general estimation of human exposure to chemicals found in consumer products via inhalation, skin absorption, and oral intake. The description of the basis of the ConsExpo dermal absorption model was first published in 1996 (Ref. 13). The program was developed by the Netherlands National Institute for Public Health and the Environment (RIVM) and is available to the public. The program updates are now released by RIVM in collaboration with other European counterpart institutes, including the French Agency for Food, Environmental and Occupational Health and Safety, the German Institute for Risk Assessment, the Federal Office of Public Health (Switzerland), and Health Canada. This model has been used by other regulators (*e.g.,* Health Canada) and has been cited in various scientific publications, as listed in Appendix 6 of the Wyatt memorandum (Refs. 2 and 14).

In the Wyatt memorandum (Ref. 2, Appendices 4 to 6), and in the October 31, 2018, final rule (83 FR 54665 at 54670), we explained our decision to use the in silico modeling to predict the percentage of dermal absorption of lead by the surface area of the full human scalp and all the parameters and inputs to the model. We chose to use in silico modeling because, as described in our response to Objection 7, we had identified several flaws in the Moore study design that resulted in the underestimation of lead exposure from this intended use.

Using EPA's *Kp* value for lead acetate,[6] we used the ConsExpo dermal absorption modeling software to estimate absorption based on the intended conditions of use (including the relevant lead concentration, surface area, and duration of application period). As stated in Appendix 4 of the Wyatt memorandum (Ref. 2), we also performed an internal validation by applying parameters identical to experimental conditions used in the Moore study into the ConsExpo dermal absorption model. The model successfully predicts Moore's experimental results using Moore's study parameters from experimental conditions, which can be taken as evidence of validation of the model. We believe that no further validation is needed for the purpose of using the model to fill gaps in experimental data.

The objection failed to include any new information or data that would refute our conclusion that the ConsExpo dermal absorption model was appropriate to use in the manner that we applied it. A hearing will not be granted on the basis of general descriptions of positions and contentions (§ 12.24(b)(2)). The objector must, at a minimum, raise a material issue concerning which a meaningful hearing might be held. Therefore, we are denying the request for a hearing on this objection.

Objection 10. Combe objects to ''FDA's treating an unvalidated computer model as more reliable and robust than human experimental data.'' In this objection, Combe insists that the computer model is not needed because human data are available and that ''it is unscientific for a computer model to be used to trump robust human data.'' See Submission, page 40.

(Response to Objection 10) FDA agrees that human studies, when scientifically well-designed and conducted, provide more robust and reliable data than computer modeling in the safety evaluations of color additives. As discussed in the Wyatt memorandum and in the October 31, 2018, final rule (83 FR 54665 at 54668 through 54672), we reevaluated the Moore study and identified significant scientific flaws. Based on this reevaluation, our current thinking regarding the radioactive tracer skin absorption study conducted by Moore et al., is that it is no longer possible to rely on this human data because of these significant flaws. Consequently, we no longer consider it scientifically sound to continue the use of the experimental fractional absorption number derived from this study when the experimental conditions are not consistent with the intended conditions of use for the hair dye product. We believe that the flaws in the Moore study may have resulted in underestimating the exposure to lead from lead acetate-containing hair dye. We also believe that it is scientifically valid and appropriate to use the in silico computer model to extrapolate and predict the absorption to fill the data gaps created by the absence of data from human experimental studies designed and conducted to simulate the intended conditions of use for lead acetate-containing hair dye.

In this objection, Combe did not provide any information to address the significant flaws in the Moore study that we identified. This objection also failed to identify any other human studies that we could consider in lieu of the in silico computer model. Therefore, we are denying the request for a hearing on this objection.

D. Category D: Skin Permeability Coefficient

Combe's numbered objections included in Category D are as follows:

12. Combe objects to FDA's reliance on a ''permeability coefficient'' for lead instead of fractional absorption.

13. Combe objects to FDA's use of a permeability coefficient for lead acetate that EPA repudiated and replaced with a much lower estimate.

Objection 12. Combe objects to ''FDA's reliance on a 'permeability coefficient' for lead instead of fractional absorption.'' Combe argues that FDA has not demonstrated that the ConsExpo dermal absorption model has been validated for inorganic substances such as lead, and that FDA does not explain how the permeability coefficient for lead acetate was derived and whether it is appropriate for use in the model. See Submission, page 44. Combe further asserts that we are relying on an outdated permeability coefficient from EPA. See Submission, pages 43–44. Because this last argument is also the subject of Objection 13 (see Submission, page 45), we will respond to this assertion in our response to Objection 13 below.

(Response to Objection 12) There are two ways to calculate skin absorption for exposure assessments: (1) The use of

[6] *Kp* is a chemical-specific absorption-related constant that is independent of the surface area, concentration, etc. (see further description of *Kp* in our response to Objection 12).

the *Kp* and (2) the use of fractional absorption. *Kp* is a constant (*i.e.,* the rate at which a chemical penetrates across the stratum corneum (the outermost layer of the skin, *e.g.,* centimeters per hour (cm/h) or meters per second (m/s)). The fractional absorption is the percentage of the total amount of lead applied that is absorbed through the skin and depends on the study design (*e.g.,* duration of exposure, how much of the test material is in contact with a given surface area, the concentration of the substance in the matrix, etc.). Thus, the extension of an experimental fractional absorption number is only scientifically valid when the experimental conditions are similar, if not identical, to the intended condition of use. As discussed previously, the experimental conditions in the Moore study are significantly different from the intended conditions of use for the lead acetate-containing hair dye. For example, as mentioned in our response to Objection 9, Moore's study was conducted with formulations containing 6 millimole per liter (mmol/L) or 9 mmol/L lead acetate (equivalent to 0.12 or 0.18 percent lead respectively), which are three to five times lower than the maximum use level (0.6 percent lead) in hair dyes. Second, the test formulation(s) were reportedly applied to a skin surface area of 8 to 10 cm^2 on the forehead, an area of the skin without hair follicles, while lead acetate-containing hair dye is intended to be applied to the full scalp that has many hair follicles and a skin surface area of approximately 580 cm^2. Third, the 12-hour application period in the Moore study may be too short to assess the full extent of percutaneous absorption of lead under the intended conditions of use, which in some cases could remain on the scalp for 24 hours or longer and may accumulate due to repeated applications. Therefore, application to the small surface area, use of a formulation with a lower lead concentration, and a shorter exposure period used in the Moore study all resulted in an underestimation of the fractional absorption number of lead acetate.

Therefore, we believe it is appropriate to use the *Kp* (which allows the incorporation of parameters, such as the surface area, concentration, and duration of exposure) in the modeling to determine dermal absorption. We note that *Kp* is often the preferred, more reliable, and commonly utilized parameter to quantify percutaneous absorption of chemicals from solutions (Refs. 15 and 16).

We also note that the ConsExpo dermal absorption model can be applied to an organic or inorganic compound because the underlying basis for the model is the well-known Fick's law, which describes the transport of mass, through diffusion, from a region of higher concentration to a region of lower concentration. The Fick's law-based equation for the ConsExpo dermal absorption model is described in the user manual as follows (Ref. 17):

$$A_{abs} = A_{skin} \times (1 - \exp(-P \times S \times t/V))$$

Where:

A_{abs} = Amount of substance absorbed (kg)
A_{skin} = Amount of substance on the skin (kg)
P = Permeability of the skin (m/s) (Equivalent to *Kp* in the context)
V = Volume of the substance on the skin (m^3)
S = Exposed skin area (m^2)
t = Exposure time (s)

As shown in the equation above, the only physicochemical property related to the chemical itself is the *Kp;* chemical composition is not a part of the equation. Thus, this Fick's law-based approach, which is not dependent on chemical composition, does not need to be specifically validated according to whether the substance is organic or inorganic because the permeability *(Kp)* is a set number. As discussed above in our response to Objection 9, we used the ConsExpo dermal absorption model to fill in the existing experimental data gaps (*i.e.,* related to the small surface area, lower lead concentration, and shorter duration of exposure) in order to address the differences between the experimental conditions and the approved intended conditions of use.

Because the objection failed to provide new data that would change our conclusion, and the information discussed in the objection is insufficient to justify a hearing (§ 12.24(b)(3)), we are denying the request for a hearing on this objection.

Objection 13. Combe objects to ''FDA's use of a permeability coefficient for lead acetate that EPA repudiated and replaced with a much lower estimate.'' See Submission, page 45. Combe states that FDA used a permeability coefficient for lead acetate from, ''an internal report that EPA has since repudiated.'' Ibid. Combe further states: ''FDA's reliance on this figure is particularly unsupportable given that EPA in 2004 actually published a permeability coefficient for lead acetate that is an order of magnitude lower than the internal interim 1992 estimate.'' Ibid.

(Response to Objection 13) We acknowledge that we used the permeability coefficient in EPA's 1992 interim report (Ref. 18) (the larger *Kp* value of 4×10^{-6} cm/hr), rather than in EPA's 2004 final guidance (Ref. 19) (the smaller *Kp* value of 0.0005×10^{-3} cm/hr, which is 5×10^{-7} cm/hr), entitled ''Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual.'' The *Kp* values in EPA's 1992 and 2004 documents were both based on the same data set (the Moore study) and they are both valid. Specifically, the fractional absorption reported by the Moore study was in a range between 0 to 0.3 percent (Refs. 18, 19, 21, and 22). While the *Kp* value in EPA's 1992 document was based on the upper limit of the reported range (namely a fractional absorption of 0.3 percent), the *Kp* value in EPA's 2004 document [7] was based on the mean of the reported data range (minus the highest value for injured skin (''dry and scratch'' in the Moore study)) (namely a fractional absorption of 0.058 percent, instead of 0.3 percent). Using a higher *Kp* value—the upper limit of the reported range—is more conservative because it results in higher predictions of dermal absorption. FDA's use of this more conservative *Kp* value is consistent with ensuring there is a reasonable certainty of no harm from the use of this color additive.

Had FDA used the smaller *Kp* value from EPA's 2004 guidance, the predicted fractional absorption number would have been 3.8 percent (acknowledged by Combe in Objection 13; see Submission, page 47). The 3.8 percent fractional absorption is more than 10 times higher than what had been reported in the Moore study as the highest absorption value. This discrepancy in fractional absorption supports our conclusion that the Moore study underestimated the amount of lead absorbed and therefore was flawed. In addition, as stated in the Wyatt memorandum (Ref. 2, p. 19), FDA did not rely on the predicted levels of transdermal absorption from modeling to quantify the extent of lead acetate absorption. Rather, FDA used the predictions from modeling to show that the Moore study, which was relied on for the listing of lead acetate as an approved color additive in 1980, may have significantly underestimated exposure to transdermally absorbed lead from the use of lead acetate hair dyes (Ref. 2).

The objection failed to provide new data that would change our conclusion that there is no longer reasonable certainty that no harm would result from the listed use of lead acetate in hair dye, and the information discussed in their objection is insufficient to

[7] We disagree with Combe's characterization of EPA ''repudiating'' the prior Kp value in the EPA 1992 document. We also note that in its 2004 document, FDA did not independently derive the Kp value of 0.0005×10^{-3} cm/hr for lead acetate and instead cited Hostynek et al. (1998).

justify a hearing (§ 12.24(b)(3)). Therefore, we are denying the request for a hearing on this objection.

E. Category E: Lead Exposure and Blood Lead Levels

Combe's numbered objections included in Category E are as follows:

3. Combe objects to FDA's reliance on sources that discuss blood levels of lead and not exposure levels (see, *e.g.,* NTP monograph).

14. Combe objects to FDA's conclusion that lower median blood levels in lead since 1990 mean that any the lead contributed by lead acetate is less safe now.

15. Combe objects to FDA's entire analysis because it is missing two critical links—FDA never relates exposure from lead acetate to any change in blood lead levels, and thus it never relates it to any predicted harm.

16. Combe objects to FDA's whole argument as FDA never links exposure to lead from lead acetate to a change in steady-state blood lead levels.

17. Combe objects to FDA's conclusions about the effect of lead acetate on blood lead levels.

Objection 3. Combe objects to ''FDA's reliance on sources that discuss blood levels of lead and not exposure levels (see, *e.g.,* NTP monograph).'' Combe asserts that the NTP monograph does not support that lead is harmful at low levels in adults. See Submission, pages 30–32. Combe argues that the NTP showed increased risk of potential health effects (heart and kidney) associated with blood lead levels of 5–10 micrograms per decaliter (µg/dL), while noting that the current mean blood lead level in U.S. adults is 0.92 µg/dL. See Submission, at pages 30–31. Combe asserts that there is no evidence that the use of lead acetate-containing hair dye can raise blood lead levels to >5 µg/dL. See Submission, page 31.

(Response to Objection 3) With regard to the NTP monograph, the evaluation found sufficient evidence for an association of adverse effects on kidney function with blood lead levels of less than 5 µg/dL in adults (Ref. 3, page 87). A recent literature review by FDA found that ''the overall body of evidence . . . suggests that some adverse effects may occur at a blood lead level of 3 µg/dL . . . in adults'' (Ref. 20). In addition, as discussed in our response to Objection 2, there is a lack of evidence of a safe level of exposure for lead. For example, JECFA has stated that ''because the dose-response analyses do not provide any indication of a threshold for the key effects of lead, the Committee concluded that it was not possible to establish a new PTWI that would be considered to be health protective'' (Ref. 4, page 212). Furthermore, Combe fails to provide any data that shows the impact of the use of lead acetate-containing hair dye on blood lead levels.

Combe has not provided scientific evidence to support its contention that the intended use of lead acetate is safe. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). Therefore, we are denying the request for a hearing on this objection.

Objection 14. Combe objects to ''FDA's conclusion that lower median blood levels in lead since 1990 mean that any [of] the lead contributed by lead acetate is less safe now.'' Combe asserts that because blood lead levels in the U.S. population are lower now, any amount of lead contributed by lead acetate ''is safer now because of the overall lower levels of lead.'' See Submission, page 48.

(Response to Objection 14) In the October 31, 2018, final rule, we concluded that any increase in exposure to lead resulting from use of lead acetate containing hair dye can no longer be considered insignificant in terms of public health (83 FR 54665 at 54671). Given that there is no known safe exposure level for lead, we disagree that any amount of lead contributed by lead acetate-containing hair dye is safer now. The decrease in blood lead levels since 1990 resulted from the actions taken by multiple regulatory and public health agencies to reduce lead exposure in order to minimize potential adverse effects. For example, we have taken measures to reduce exposure to lead from our-regulated products to the lowest level that is technically feasible to protect the public health. Such measures include (but are not limited to) prohibiting the use of tin-coated lead foil capsules for wine bottles (21 CFR 189.301) and prohibiting the use of lead-soldering in food cans (21 CFR 189.240). The decrease in blood lead levels in the U.S. population, resulting from these measures, does not mean that the use of lead acetate in hair dye is safe.

To the contrary, as the science has evolved, more sensitive endpoints have been identified at lower blood lead levels than known in the 1970s. A growing body of evidence indicates that adults may experience adverse health impacts from exposure to lead levels lower than those previously believed to be harmful. For example, in 2012, the NTP provided evidence of adverse effects in adult humans (*e.g.,* increased blood pressure, hypertension, decreased glomerular filtration rate) at blood lead levels less than 10 µg/dL, based on epidemiological evidence (Ref. 3). Also see recent literature review by FDA that ''the overall body of evidence . . . suggests that some adverse effects may occur at a blood lead level of 3 µg/dL . . . in adults'' (Ref. 20). We further note that any additional lead exposure would contribute to the occurrence of the reported adverse effects of lead.

Combe has not provided data to demonstrate that the intended use of lead acetate-containing hair dyes would not elevate the lead level in blood and other tissues. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). Therefore, we are denying the request for a hearing on this objection.

Objection 15. Combe ''objects to FDA's entire analysis because it is missing two critical links—FDA never relates exposure from lead acetate to any change in blood levels, and thus it never relates it to any predicted harm.'' See Submission, page 49. Combe argues that FDA, in its conclusion in the final rule that ''we no longer can conclude that exposure to lead from lead acetate-containing hair dye has no discernible effect on the steady-state blood lead level,'' did not link exposure to lead from lead acetate to any change in steady-state blood lead levels. See Submission, page 49.

(Response to Objection 15) To satisfy its burden that would justify its request for a hearing, it is the objector's responsibility to provide data and scientific information that calls into question our conclusions. It is not enough to just make an allegation; the objection needs to contain scientific information to demonstrate the safety of the color additive under the intended conditions of use. We evaluated the data and information submitted in the petition (CAP 7C0309) along with comments submitted in response to the petition and other available information (including published literature) to arrive at our conclusion. Based on currently available data, we conclude that there is no known safe exposure level for lead. This view is consistent with conclusions by other U.S. agencies responsible for ensuring public health (*e.g.,* CDC, EPA) and international bodies (*e.g.,* JECFA).

Combe has not provided data showing that use of lead acetate-containing hair dyes would not increase the lead level in blood or in other tissues (including bones). Because a hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)), we are denying the request for a hearing on this objection.

Objection 16. Combe ''objects to FDA's whole argument as FDA never

links exposure to lead from lead acetate to a change in steady-state blood levels.'' See Submission, page 50.

(Response to Objection 16) Combe's argument in Objection 16 is essentially the same as its argument in Objection 15. We reiterate that our determination is based on whether the currently available scientific evidence shows that there is a reasonable certainty of no harm from the use of lead acetate-containing hair dye.

A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). Therefore, we are denying the request for a hearing on this objection.

Objection 17. Combe objects to ''FDA's conclusions about the effect of lead acetate on blood lead levels.'' See Submission, page 51. Combe argues that ''the amount of lead that lead acetate contributes to daily intake (*e.g.,* 0.3 µg) is less than 1 percent of the amount contributed daily by food, and thus the effect on steady-state blood lead levels would be expected to be extremely small—on the order of 0.01 µg or less.'' See Submission, page 52.

(Response to Objection 17) We reiterate that, in lead acetate-containing hair dyes, up to 6,000 ppm (mg/kg) lead acetate (calculated as lead) is intentionally added as an ingredient to achieve a coloring effect; as such, the lead acetate must meet the safety standard of a reasonable certainty of no harm. There is no lead-containing compound approved for use as a food additive or color additive in food. Thus, dietary exposure to lead results from lead that is present as an impurity in raw materials that manufacturers are unable to avoid through good manufacturing practices.

The objection failed to provide new data that changes our conclusion that the scientific evidence does not support any level of lead intake that is safe. Therefore, the information discussed in this objection is insufficient to justify a hearing (§ 12.24(b)(3)), and we are denying the request for a hearing on this objection.

F. Category F: Permitted Lead Acetate Levels

Combe's numbered objection in Category F is as follows:

Objection 19. Combe objects to ''FDA's failure to consider reducing the permitted lead acetate level under 21 CFR 73.2396 from 0.6 percent to 0.153 percent.'' Combe states, ''Since 1998, Combe's lead acetate hair dyes have contained only 0.153 percent lead, approximately a quarter of the permitted 0.6 percent under 21 CFR Section 73.2396.'' Submission, page 56. Combe asserts that ''the Agency refused to account for this fact in its Final Rule.'' Ibid.

(Response to Objection 19) We addressed this consideration in the final rule in our response to Combe's comment (see 83 FR 54665 at 54672). Combe states that it reformulated its lead acetate-containing products in 1998. See Submission Appendix A, page 1. Reformulating the hair dye product by reducing the lead content from 0.6 percent to 0.153 percent may reduce the exposure, but it does not establish a safe level of exposure to lead from lead acetate when used as a color additive in hair dye. We reiterate that we are not aware of data demonstrating that any level of lead is safe. We note also JECFA's concluding statement that it was not possible to establish a new PTWI for lead that would be considered health protective.

Moreover, a color additive regulation is not manufacturer or sponsor-specific and, as such, any manufacturer can use a listed color additive within the limitations of the regulation. Therefore, it is appropriate for FDA to conduct its evaluation associated with the repeal of § 73.2396 based on the maximum permitted use level of 0.6 percent (6,000 ppm; mg/kg) of lead acetate (calculated as lead) in hair dyes.

Combe has not provided data that demonstrates with reasonable certainty that no harm would result from the use of 6,000 ppm (mg/kg) lead acetate (calculated as lead) as a color additive in cosmetics for coloring hair on the scalp. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (§ 12.24(b)(2)). Therefore, we are denying the request for a hearing on this objection.

V. Summary and Conclusions

Section 721 of the FD&C Act requires that a color additive be shown to be safe prior to marketing. Under § 70.3(i), a color additive is safe if there is convincing evidence that establishes with reasonable certainty that no harm will result from the intended use of the color additive. When new scientific evidence comes to light that calls into question the safety of an approved color additive, we will evaluate the new evidence and determine if the color additive continues to be safe under the condition of use.

In our October 31, 2018, final rule, we stated that, following a full evaluation of the data submitted in support of CAP 7C0309 and other pertinent data and information, we concluded that the data currently available no longer demonstrate that there is a reasonable certainty of no harm from the use of lead acetate as a color additive in hair dyes authorized under § 73.2396. This conclusion was based on the recognition of the current consensus that there is no safe exposure level for lead; our reevaluation of the 1980 skin absorption Moore study that may have resulted in an underestimation of exposure to lead from its use in hair dye; and the fact that blood lead levels in the United States have dropped significantly since 1980, so we no longer could conclude that exposure to lead from lead acetate-containing hair dyes has no discernible effect on the steady-state blood lead level. Therefore, we issued a final rule repealing § 73.2396.

Our responsibility in listing a color additive for safe use in a regulated product is to evaluate the currently available scientific data and other pertinent information to determine with reasonable certainty that the color additive is not harmful under the intended conditions of use. Considering all the scientific information currently available, we have not changed our conclusion that the current data no longer support the safe use of lead acetate as a color additive in cosmetics intended to color hair on the scalp.

The burden is on the objector to provide pertinent evidence that calls into question our conclusion. Despite all its objections, Combe has not provided any new scientific data or information that establish with reasonable certainty that there is a level of lead exposure that could be considered safe and health protective. Combe has also not provided any new data demonstrating that no harm would result from the use of up to 6,000 ppm of lead acetate (calculated as lead) as a color additive intentionally added to cosmetics for coloring hair on the scalp.

Therefore, we have determined that the objections do not raise any genuine and substantial issue of fact that can be resolved by an evidentiary hearing (§ 12.24(b)). Accordingly, we are denying the requests for a hearing. Furthermore, after evaluating the objections, we have concluded that the objections do not provide any basis for us to reconsider our decision to issue the final rule amending § 73.2396 to no longer authorize the use of lead acetate as a color additive in cosmetics intended for coloring hair on the scalp.

Under sections 701(e)(2) and 721(d) of the FD&C Act, the filing of objections operates to stay the effectiveness of our repeal of § 73.2396 until we take final action on the objections. Section 701(e)(3) of the FD&C Act further stipulates that, as soon as practicable, the Secretary shall, by order, act upon such objections and make such order

public. We have completed our evaluation of the objections and conclude that a continuation of the stay is not warranted.

In the absence of any other objections and requests for a hearing, we conclude that this document constitutes final action on the objections received in response to the October 31, 2018, final rule as prescribed in section 701(e)(2) of the FD&C Act. Therefore, under sections 701 and 721 of the FD&C Act, notice is given that the objections and the requests for a hearing filed in response to the final rule that appeared in the **Federal Register** of October 31, 2018, do not form a basis for further stay of the effectiveness of the final rule. Accordingly, we are ending the stay of the final rule and we are repealing the listing for lead acetate in § 73.2396 as a color additive in cosmetics intended for coloring hair on the scalp as of January 6, 2022.

In the October 31, 2018, final rule, we stated our intention to exercise enforcement discretion for a period of 12 months from the effective date of the final rule regarding marketed hair dye products that contain the color additive lead acetate to provide an opportunity for industry to deplete the current stock of hair dye products with lead acetate and reformulate products prior to enforcing the requirements of the final rule. We also stated that we had taken into consideration the fact that bismuth citrate, which is listed in § 73.2110 for use in cosmetic hair dye products at a level up to 2.0 percent weight/volume, was already being used as an alternative for lead acetate in hair dye products marketed both in the United States and other countries. Therefore, our intent is to exercise enforcement discretion for a period of 12 months from the effective date of the final rule for those hair dye products containing the color additive lead acetate that comply with the requirements of § 73.2396, including the specifications, uses and restrictions, and labeling requirements.

VI. References

The following references marked with an asterisk (*) are on display with the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at *https://www.regulations.gov.* References without asterisks are not on public display at *https://www.regulations.gov* because they have copyright restriction. Some may be available at the website address, if listed. FDA has verified the website addresses, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

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*3. HHS, National Toxicology Program, ''NTP Monograph on Health Effects of Low-Level Lead,'' June 2012. *https://ntp.niehs.nih.gov/ntp/ohat/lead/final/monographhealtheffectslowlevellead_newissn_508.pdf.*
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*19. EPA (July 2004). ''Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment) Final.'' EPA/540/R/99/005, OSWER 9285.7–02EP, PB99–962212.
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List of Subjects in 21 CFR Part 73

Color additives, Cosmetics, Drugs, Foods, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 73 is amended as follows:

PART 73—LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION

■ 1. The authority citation for part 73 continues to read as follows:

Authority: 21 U.S.C. 321, 341, 342, 343, 348, 351, 352, 355, 361, 362, 371, 379e.

§ 73.2396 [Removed]

■ 2. Remove § 73.2396.

Dated: September 30, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2021–21892 Filed 10–7–21; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 878

[Docket No. FDA–2019–N–1250]

General and Plastic Surgery Devices; Reclassification of Certain Surgical Staplers

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is issuing a final order to reclassify surgical staplers for internal use (formerly regulated under the classification for ''manual surgical instrument for general use'' and assigned the product code GAG) from class I (general controls) into class II (special controls) and subject to premarket review. FDA is identifying the special controls for surgical staplers for internal use that the Agency believes are necessary to provide a reasonable assurance of the safety and effectiveness of the device. FDA is issuing this reclassification on its own initiative based on new information. As part of this reclassification, FDA is also amending the existing classification for ''manual surgical instrument for general use'' to remove staplers and to create a separate classification regulation for surgical staplers that distinguishes between surgical staplers for internal use and external use.

DATES: This order is effective October 8, 2021.

FOR FURTHER INFORMATION CONTACT: George Gibeily, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4660, Silver Spring, MD 20993, 301–796–0276, *george.gibeily@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended, establishes a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513(d)(1) of the FD&C Act, devices that were in commercial distribution before the enactment of the 1976 amendments (Medical Device Amendments of 1976, Pub. L. 94–295), May 28, 1976 (generally referred to as ''preamendments devices''), are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the Panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution before May 28, 1976 (generally referred to as ''postamendments devices''), are automatically classified by section 513(f)(1) of the FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval, unless, and until: (1) FDA reclassifies the device into class I or II or (2) FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the FD&C Act and part 807, subpart E of the regulations (21 CFR part 807).

On July 9, 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112–144). Section 608(a) of FDASIA amended section 513(e) of the FD&C Act, changing the process for reclassifying a device from rulemaking to an administrative order. Section 513(e)(1)(A)(i) of the FD&C Act sets forth the process for issuing such a final order. Specifically, prior to the issuance of an administrative order reclassifying a device, the following must occur: (1) Publication of a proposed reclassification order in the **Federal Register**, (2) a meeting of a device classification panel described in section 513(b) of the FD&C Act, and (3) consideration of comments to a public docket. The proposed reclassification order must set forth the proposed reclassification and a substantive summary of the valid scientific evidence concerning the proposed reclassification, including the public health benefits of the use of the device, and the nature and incidence (if known) of the risks of the device.

Section 513(e)(1)(A)(i) provides that FDA may, by administrative order, reclassify a device based on ''new information.'' FDA can initiate a reclassification under section 513(e) or an interested person may petition FDA. The term ''new information,'' as used in section 513(e) of the FD&C Act, includes information developed as a result of a reevaluation of the data before the Agency when the device was originally classified, as well as information not presented, not available, or not developed at that time (See, *e.g., Holland-Rantos* v. *U.S. Dep't of Health, Educ. & Welfare,* 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); *Upjohn Co.* v. *Finch,* 422 F.2d 944 (6th Cir. 1970); *Bell* v. *Goddard,* 366 F.2d 177 (7th Cir. 1966)).

Reevaluation of the data previously before the Agency is an appropriate basis for subsequent regulatory action where the reevaluation is made in light of newly available regulatory authority (see *Bell,* 366 F.2d at 181) or in light of changes in ''medical science'' (see *Upjohn,* 422 F.2d at 951). Whether data before the Agency are old or new, the ''new information'' to support reclassification under section 513(e) of the FD&C Act must be ''valid scientific evidence,'' as defined in section 513(a)(3) of the FD&C Act and 21 CFR 860.7(c)(2) (See, *e.g., Gen. Med. Co.* v. *FDA,* 770 F.2d 214 (D.C. Cir. 1985); *Contact Lens Mfrs. Ass'n* v. *FDA,* 766 F.2d 592 (D.C. Cir. 1985), cert. denied, 474 U.S. 1062 (1986)).

FDA relies upon ''valid scientific evidence'' in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the ''valid scientific evidence'' upon which the Agency relies must be publicly available. Publicly available information