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FEDERAL ELECTION COMMISSION

11 CFR Parts 9034, 9036, and 9037

[Notice 1992-3]

Matching Fund Submission and Certification Procedures for Presidential Primary Candidates

AGENCY: Federal Election Commission.

ACTION: Final rule: Correction to announcement of effective date.

SUMMARY: This document corrects the effective date for the final rules setting forth procedures for matching fund submissions by Presidential primary candidates at 11 CFR 9034.1, 9034.5, 9036.2, 9036.4, 9036.5, 9036.6, 9037.1 and 9037.2. The announcement of effective date was published Wednesday, November 6, 1991 at 56 FR 56570. These regulations implement portions of the Presidential Primary Matching Payment Account Act. 26 U.S.C. Chapter 96. The Commission announces that these rules are effective as of November 7, 1991.

EFFECTIVE DATE: November 7, 1991.

FOR FURTHER INFORMATION CONTACT: Ms. Susan E. Propper, Assistant General Counsel, 999 E Street NW., Washington, DC 20463, (202) 219-3690 or toll free (800) 424-9530.

SUPPLEMENTARY INFORMATION: A correction to the effective date for the matching fund submission regulations is being made to ensure that these rules will appear in the 1992 Code of Federal Regulations. Accordingly, the publication on November 6, 1991 of the Announcement of Effective Date, which was the subject of FR Doc. 91-26755 is corrected as follows:

1. On page 56570, in the third column, under **SUMMARY:** in the last two lines of the paragraph, "November 6, 1991" is corrected to read "November 7, 1991".

2. On page 56570, in the third column, under **EFFECTIVE DATE:** "November 6, 1991" is corrected to read "November 7, 1991".

3. On page 56571, in the first column, under "Announcement of Effective Date", line 5, "November 6, 1991." is corrected to read "November 7, 1991."

Dated: February 21, 1992.

Scott E. Thomas,

Vice Chairman, Federal Election Commission.

[FR Doc. 92-4435 Filed 2-26-92; 8:45 am]

BILLING CODE 6715-01-M

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 39

[Docket No. 92-NM-15-AD; Amendment 39-8180; AD 92-05-01]

Airworthiness Directives; Boeing Model 747 Series Airplanes

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Final rule; request for comments.

SUMMARY: This amendment supersedes an existing airworthiness directive (AD), applicable to certain Boeing Model 747 series airplanes, which currently requires repetitive inspections of the engine number two and engine number three upper strut wing leading edge compartments to detect chafing of the fuel supply tube and the electrical power feeder cables; repetitive inspections of the strut drains to verify that the drains are not obstructed; corrective action, if necessary; and a submission of a report of inspection findings. The amendment changes the applicability to delete Model 747-200 and 747-300 series airplanes, and to include additional Model 747-400 series airplanes. This amendment also deletes the requirement for inspections of the strut drains, deletes the required reporting of inspection findings, and adds an optional terminating modification. This amendment is prompted by the results of inspections required by the existing AD and the development of a modification that eliminates the need for the required inspections. The actions specified in this AD are intended to prevent fire in the number two and three enging struts.

DATES: Effective March 13, 1992.

The incorporation by reference of certain publications listed in the regulations is approved by the Director of the Federal Register as of March 13, 1992.

Comments for inclusion in the Rules Docket must be received on or before April 27, 1992.

ADDRESSES: Submit comments in triplicate to the Federal Aviation Administration, Transport Airplane Directorate, ANM-103, Attention: Rules Docket No. 92-NM-15-AD, 1601 Lind Avenue SW., Renton, Washington 98055-4056.

The service information referenced in this AD may be obtained from Boeing Commercial Airplane Group, P.O. Box 3707, Seattle, Washington 98124. This information may be examined at the FAA, Transport Airplane Directorate, 1601 Lind Avenue SW., Renton, Washington; or at the Office of the Federal Register, 1100 L Street NW., room 8401, Washington, DC.

FOR FURTHER INFORMATION CONTACT: Mr. Jon Regimbal, Seattle Aircraft Certification Office, Propulsion Branch, ANM-140S; telephone (206) 227-2687. Mailing address: FAA, Northwest Mountain Region, Transport Airplane Directorate, 1601 Lind Avenue SW., Renton, Washington 98055-4056.

SUPPLEMENTARY INFORMATION: On January 3, 1992, the FAA issued AD 91-20-51, Amendment 39-8152 (57 FR 3928, February 3, 1992) to require repetitive inspections for damage of and adequate clearance between engine fuel supply tubes and power feeder cables in the number two and three engine struts, and to require repetitive inspections of the strut drains to verify that the drains are not obstructed. That action was prompted by a fire that occurred in the number two engine strut on a Boeing Model 747-400 series airplane. Although the investigation is continuing, the fire appeared to have been caused by electrical arcing between the engine number one electrical power feeder cable and the engine number two fuel feed line in the upper strut wing leading edge compartment of engine strut number two. Arcing could result from chafing or other damage to the electrical power feeder cables. Arcing in this location can create a hole in the fuel tube and provide a simultaneous ignition source. This condition, if not

corrected, could result in a fire within the engine strut.

Since issuance of that AD, the FAA has received new data that indicate certain changes to the applicability and requirements of the existing rule are necessary:

The results of the inspections required by AD 91–20–51 have revealed that no chafing/clearance problems have occurred on any Model 747–200 or Model 747–300 series airplanes. The FAA has reconsidered the applicability of the existing rule with respect to these airplanes and, due to certain design differences of the subject area, has determined that the addressed unsafe condition does not exist with respect to these series airplanes. The applicability of the rule has been revised to delete these airplane series.

Even though provisions were made during the production of later airplanes in the Model 747–400 series to increase the clearance between engine fuel supply line and electrical power feeder cable, some operators have reported that the clearance on these planes has been found to be less than that required by AD 91–20–51. In light of this, and the fact that the later-produced Model 747–400 series airplanes are similar in design to the earlier-produced airplanes, the FAA has determined that the potential unsafe condition exists with respect to these airplanes. The applicability of the rule, therefore, has been expanded to include these later Model 747–400 series airplanes.

An inspection of the engine strut number two on the incident airplane after the strut fire, revealed that the flammable fluid drains in the strut were blocked. The blockage could allow fuel to collect within the strut and increase the fire risk. For this reason, AD 91–20–51 required repetitive inspections of the strut drains for blockage. However, further investigation by the operator and the manufacturer has revealed that the drain on the subject airplane actually was blocked by fire debris; the drains were not blocked prior to the fire. Based on this information, the FAA has determined that repetitive inspections of the strut drains, as required by AD 91–20–51, are no longer necessary. This final rule has deleted that requirement.

Reports obtained from operators, in response to the requirement in AD 91–20–51, have supplied the FAA with sufficient data to determine how widespread the identified problems are with respect to the Model 747 fleet. The FAA, therefore, has determined that the continuing submission of such reports is no longer necessary; accordingly, the requirement for such reporting has been deleted from this final rule.

The FAA has recently reviewed and approved Boeing Alert Service Bulletin 747–24A2168, Revision 1, dated December 5, 1991, which describes procedures for inspection of the clearance between the power feeder cables and fuel tube. The service bulletin also describes procedures for a modification of the engine number two and engine number three upper strut wing leading edge compartments, consisting of the installation of a new cable support bracket. Once this modification is installed, repetitive inspections for clearance between the cables are no longer necessary. Additionally, the effectivity of the service bulletin has been revised to include additional Model 747–400 series airplanes.

The FAA has included the installation of the modification, described in the revised Boeing service bulletin, as an optional terminating action for the repetitive inspections required by this rule. This is considered interim action. The FAA intends to revise this rule to require modification of the electrical power feeder cable installation in engine struts two and three. However, the proposed compliance time for installation of the modification is sufficiently long so that notice and opportunity for prior public comment would not be impracticable.

Since a situation exists that requires the immediate adoption of this regulation, it is found that notice and opportunity for prior public comment hereon are impracticable, and good cause exists for making this amendment effective in less than 30 days.

Comments Invited

Although this action is in the form of a final rule that involves requirements affecting flight safety and, thus, was not preceded by notice and an opportunity for public comment, comments are invited on this rule. Interested persons are invited to comment on this rule by submitting such written data, views, or arguments as they may desire. Communications shall identify the Rules Docket number and be submitted in triplicate to the address specified under the caption **ADDRESSES.** All communications received on or before the closing date for comments will be considered, and this rule may be amended in light of the comments received. Factual information that supports the commenter's ideas and suggestions is extremely helpful in evaluating the effectiveness of the AD action and determining whether additional rulemaking action would be needed.

Comments are specifically invited on the overall regulatory, economic, environmental, and energy aspects of the rule that might suggest a need to modify the rule. All comments submitted will be available, both before and after the closing date for comments, in the Rules Docket for examination by interested persons. A report that summarizes each FAA-public contact concerned with the substance of this AD will be filed in the Rules Docket.

Commenters wishing the FAA to acknowledge receipt of their comments submitted in response to this notice must submit a self-addressed, stamped postcard on which the following statement is made: "Comments to Docket Number 92–NM–15–AD." The postcard will be date stamped and returned to the commenter.

The regulations adopted herein will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 12612, it is determined that this final rule does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

The FAA has determined that this regulation is an emergency regulation and that it is not considered to be major under Executive Order 12291. It is impracticable for the agency to follow the procedures of Order 12291 with respect to this rule since the rule must be issued immediately to correct an unsafe condition in aircraft. It has been determined further that this action involves an emergency regulation under DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979). If it is determined that this emergency regulation otherwise would be significant under DOT Regulatory Policies and Procedures, a final regulatory evaluation will be prepared and placed in the Rules Docket. A copy of it, if filed, may be obtained from the Rules Docket at the location provided under the caption **ADDRESSES.**

List of Subjects in 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Incorporation by reference, Safety.

Adoption of the Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration amends 14 CFR part 39 of the Federal Aviation Regulations as follows:

PART 39—[AIRWORTHINESS DIRECTIVES]

1. The authority citation for part 39 continues to read as follows:

Authority: 49 U.S.C. 1354(a), 1421 and 1423; 49 U.S.C. 106(g); and 14 CFR 11.89.

§ 39.13 [Amended]

2. Section 39.13 is amended by removing amendment 39–8152 (57 FR 3928, February 3, 1992), and by adding an airworthiness directive (AD), amendment 39–8180, to read as follows:

92–05–01. Boeing: Amendment 39–8180. Docket 92–NM–15–AD. Supersedes AD 91–20–51, Amendment 39–8152.

Applicability: Model 747–400 series airplanes, line numbers 696 to 843, 845 to 850, 852 to 870, 872 to 875, 877, 880 to 884 and 887; certificated in any category.

Compliance: Required as indicated, unless accomplished previously.

To prevent fire within the engine strut, accomplish the following:

(a) For airplanes having line numbers 696 through 734, inclusive: Within 10 days after February 18, 1992 (the effective date of AD 91–20–51, Amendment 39–8152), inspect the electrical power feeder cables and the engine fuel supply tube in engine struts two and three for damage or chafing and minimum clearance of 0.375 inch, in accordance with Boeing Alert Service Bulletin 747–24A2168, dated September 24, 1991, or Revision 1, dated December 5, 1991. If damage is found or if clearance is not within the specified limits, prior to further flight, repair any damage in accordance with that service bulletin, and relocate the electrical power feeder cables so that the clearance is more than 0.375 inch. Repeat this inspection at the following intervals:

(1) If the clearance is less than 0.75 inch, repeat this inspection at the intervals not to exceed 500 flight hours.

(2) If the clearance is 0.75 inch or greater, repeat the inspection at intervals not to exceed 1,000 flight hours.

(b) For airplanes having line numbers 735 to 843, 845 to 850, 852 to 870, 872 to 875, 877, 880 to 884, and 887: Within 30 days after the effective date of this AD, inspect the electrical power feeder cables and engine fuel supply tube in engine strut number three for damage or chafing and minimum clearance of 0.375 inch, in accordance with Boeing Alert Service Bulletin 747–24A2168, Revision 1, dated December 5, 1991. If damage is detected or if clearance is not greater than the specified limits, prior to further flight, repair any damage in accordance with that service bulletin, and relocate the electrical power feeder cables so that the clearance is more than 0.375 inch. Repeat this inspection at the following intervals:

(1) If the clearance is less than 0.75 inch, repeat the inspection at intervals not to exceed 500 flight hours.

(2) If the clearance is 0.75 inch or greater, repeat the inspection at intervals not to exceed 1,000 flight hours.

(c) Modification of the electrical power feeder cable installation in engine struts two and three, in accordance with Boeing Alert Service Bulletin 747–24A2168, Revision 1, dated December 5, 1991, constitutes terminating action for the inspections required by paragraphs (a) and (b) of this AD.

(d) An alternative method of compliance or adjustment of the compliance time, which provides an acceptable level of safety, may be used when approved by the Manager, Seattle Aircraft Certification Office (ACO), FAA, Transport Airplane Directorate. The request shall be forwarded through an FAA Principal Maintenance Inspector, who may concur or comment and then send it to the Manager, ACO.

(e) Special flight permits may be issued in accordance with FAR 21.197 and 21.199 to operate the airplane to a location where the requirements of this AD can be accomplished.

(f) The inspection and modification required by this AD shall be done in accordance with Boeing Alert Service Bulletin 747–24A2168, Revision 1, dated December 5, 1991. This incorporation by reference was approved by the Director of the Federal Register in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from Boeing Commercial Airplane Group, P.O. Box 3707, Seattle, Washington 98124. Copies may be inspected at the FAA, Transport Airplane Directorate, 1601 Lind Avenue SW., Renton, Washington; or at the Office of the Federal Register, 1100 L Street NW., room 8401, Washington, DC.

(g) This amendment (39–8180), AD 92–05–01, becomes effective March 13, 1992.

Issued in Renton, Washington, on February 11, 1992.

Darrell M. Pederson,

Acting Manager, Transport Airplane Directorate, Aircraft Certification Service.

[FR Doc. 92–4463 Filed 2–26–92; 8:45 am]

BILLING CODE 4910–13–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 172

[Docket No. 82F–0295]

Food Additives Permitted for Direct Addition to Food for Human Consumption; Acesulfame Potassium

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; denial of requests for a stay of effective date and for a hearing; confirmation of effective date.

SUMMARY: The Food and Drug Administration (FDA) is denying the request for a stay of the effective date of the amendment to the food additive regulations that provides for the safe use of acesulfame potassium as a nonnutritive sweetener in some foods. This request asked that the final rule be stayed until the issues raised in the objectives are resolved in a hearing. FDA is also denying the request for a hearing on the objections to this final rule. After reviewing the objections to the amendment and the request for a hearing, the agency has concluded that the objections do not raise issues of material fact that justify granting a hearing or revoking the regulation.

EFFECTIVE DATE: This document confirms July 28, 1988, as the effective date.

FOR FURTHER INFORMATION CONTACT: Laura M. Tarantino, Center for Food Safety and Applied Nutrition (HFF–333), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–254–9523.

SUPPLEMENTARY INFORMATION:

I. Introduction

In the **Federal Register** of July 28, 1988 (53 FR 28379), FDA issued a final rule permitting the use of acesulfame potassium as a nonnutritive sweetener. This regulation allows use of the additive as a table-top sweetener and as an ingredient in chewing gum, and in dry bases for beverages, instant coffee and tea, gelatins, puddings, pudding desserts, and dairy product analogs. This regulation, codified at § 172.800 (21 CFR 172.800), was issued in response to a food additive petition filed by American Hoechst Corp. (now Hoechst Celanese Corp.). Acesulfame potassium is the potassium salt of 6-methyl-1,2,3-oxathiazine-4(3*H*)-one-2,2-dioxide.

In the preamble to the final rule, FDA outlined major portions of its review of the petition and responded to safety questions raised in a letter dated September 23, 1987, to the agency from the Center for Science in the Public Interest (CSPI). These questions related to two long-term rat studies and a short-term study in rats made diabetic by treatment with streptozotocin. CSPI had examined the reports of these studies under the provisions of the Freedom of Information Act before writing its letter. After publication of the final rule, CSPI had an opportunity to review the reports on all major studies, as well as the FDA memoranda reviewing those studies.

II. Objections, Request for a Hearing, and Request for a Stay

Following publication of the final rule, CSPI filed timely objections (CSPI Obj.) to the regulation and requested a formal evidentiary public hearing on the issues raised in its objections. The objections sought revocation of the final rule on acesulfame potassium. CSPI also requested that the regulation be stayed

until these issues are resolved in a hearing.

III. Standards for Granting a Hearing and a Stay

Under section 409(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(e)), a request for a hearing on the issuance of a food additive regulation does not automatically stay or delay the effectiveness of that regulation. That section does, however, grant the Secretary of Health and Human Services the discretion to stay the effectiveness of the regulation (21 U.S.C. 348(e)). The Secretary's authority has been delegated to the Commissioner of Food and Drugs (21 CFR 5.10). In its stay request, CSPI argues that it has justified a discretionary stay of the food additive regulation for acesulfame potassium and requests a stay until a hearing is held to resolve the objections.

Section 409(f) of the act (21 U.S.C. 348(f)) provides that any person adversely affected by a final food additive regulation may file objections, specifying with particularity the provisions of the order "deemed objectionable, stating reasonable grounds therefor," and may request a public hearing based upon such objections. FDA 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. Specific criteria for determining whether a hearing has been justified are set forth in § 12.24(b) (21 CFR 12.24(b)). A hearing will be granted if the material submitted shows the following:

(1) There is a genuine and substantial issue of fact 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 person. A hearing will be denied if the Commissioner concludes that 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 Commissioner concludes that the action would be the same even if the factual issue were resolved in the way sought * * *.

A party seeking a hearing is required to 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) *reh. den.*, 445 U.S. 947 (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. *U.S. E.P.A.*, 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 judgment as a matter of law. (See Rule 56, Federal Rules of Civil Procedure.) The same principle applies in administrative proceedings.

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 Association* 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, the agency need not grant a hearing. *Dyestuffs and Chemicals, Inc.* v. *Flemming*, 271 F.2d 281 (8th Cir. 1959), *cert. denied*, 362 U.S. 911 (1960). FDA need not grant a hearing in each case where an objector submits additional information or posits a novel interpretation of existing information. (See *United States* v. *Consolidated Mines & Smelting Co.*, 455 F.2d 432 (9th Cir. 1971).) In other words, 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 (9th Cir. 1977). Finally, courts have uniformly recognized that a hearing need not be held to resolve questions of law or policy. (See *Citizens for Allegan County, Inc.* v. *FPC*, 414 F.2d 1125 (D.C. Cir. 1969); *Sun Oil Co.* v. *FPC*, 256 F.2d 233, 240 (5th Cir.), *cert. denied*, 358 U.S. 872 (1958).)

In summary, a hearing request should present sufficient credible evidence to raise a material issue of fact and the evidence must be adequate to resolve the issue as requested and to justify the action requested.

IV. Resolution of CSPI's Stay Request

The agency is responding to CSPI's objections in this document. Because FDA has determined, as set forth below, that a hearing need not be held, the question of a stay pending a hearing is moot.

V. Analysis of Objections and Response to Hearing Requests

CSPI raised four specific objections to the agency's final rule for acesulfame potassium, and requested a hearing on specific factual issues raised by each objection. In particular, CSPI filed objections to agency conclusions drawn from each of the three long-term safety studies of acesulfame potassium conducted in rodents.[1] In the preamble to the final rule (53 FR 28379, July 28, 1988), the agency addressed a number of the issues raised in these objections in responding to CSPI's letter of September 23, 1987. Below FDA addresses each of the four objections, as well as the data and information filed in support of each, comparing each to the standards for granting a hearing in § 12.24.

In addition to its four objections, CSPI observed that the chronic studies submitted to establish the safety of acesulfame potassium were performed over a decade ago, when approval of the sweetener was sought in Europe, and asserted "Test standards in these countries may not measure up to FDA standards." CSPI did not identify any specific evidence to support its assertion, nor did CSPI request a hearing on this point.

The agency has never condemned a laboratory solely on the basis of its location, and, in fact, has accepted many satisfactory studies from a variety of European laboratories in support of several food additives. Also, the agency has inspected many European laboratories under its good laboratory practice regulations without finding any difference in overall quality between these laboratories and laboratories in the United States. The agency reached its decision on the safety of acesulfame potassium only after concluding that the available studies were satisfactory to establish safety. CSPI has not presented any specific evidence to challenge that conclusion.

A. Adequacy of the Second Long-Term Rat Study

In concluding that acesulfame potassium had been shown to be safe,

[1] Among the studies submitted by the petitioner in support of the safety of acesulfame potassium were three long-term (chronic) toxicity and carcinogenicity studies performed in rodents: (1) a study in Swiss mice; (2) a study in CIVO-bred Wistar rats (hereinafter referred to as the "first" rat study); and (3) a study in CPB–WU Wistar rats (hereinafter referred to as the "second" rat study). The agency discussed its evaluation of these studies in the preamble to the acesulfame potassium final rule (53 FR 28379, July 28, 1988).

FDA reviewed a long-term study conducted in CPB–WU Wistar rats (the "second rat study"). In the preamble to the final rule, the agency concluded that this study was adequate for the evaluation of a food additive and that it demonstrated the safety of acesulfame potassium. (See 53 FR 28379, 28380, and Ref. 1.) Implicit in FDA's determination of the second rat study's adequacy was that the dosing levels in this study were appropriate.

In its first objection, CSPI contends that the dosing levels in the second rat study were not high enough. (See CSPI Obj., p. 2.) In particular, CSPI asserts that the highest dose in this study (3 percent acesulfame potassium in the diet) did not reach the maximum tolerated dose (MTD). The MTD is the dose in a chronic study that elicits signs of minimal toxicity without substantially altering the normal lifespan of the test species due to effects other than tumors.) CSPI claims that doses for this study were selected on the basis of a subchronic study in rats which showed no toxicity at 3 percent and minimal effects but no distinct toxicity at 10 percent test compound in the diet. Based upon the results of the subchronic study, CSPI claims that the MTD of acesulfame potassium is 10 percent and that the highest level of acesulfame potassium used in the long-term study (3 percent) is less than the MTD. (See CSPI Obj., pp. 2 and 3.)

To support its objection, CSPI cities FDA's "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food" (the FDA Redbook); an excerpt from a publication of the International Agency for Research on Cancer (IARC), "Long-Term and Short-Term Assays for Carcinogens: A Critical Appraisal" (the IARC Report); an FDA memorandum dated March 26, 1987; and data from the sub-chronic and second long-term studies in rats, which data were not specifically identified. (See CSPI Obj., pp. 4 and 5.)

CSPI's objection to the adequacy of dosing in the second rat study raises two separate questions: (1) Was the study required to use the MTD? (2) Was the study's 3 percent dose level sufficiently high for a proper assessment of the carcinogenic potential of acesulfame potassium?

As discussed in detail below, FDA is denying CSPI's request for a hearing on its first objection because the data and information identified by CSPI in support of this objection, even if established at a hearing, would not be adequate to justify resolution in CSPI's favor of the factual question about adequacy of dosing. (See § 12.24(b)(3).)

In particular, FDA is denying CSPI's first objection to the extent that it asserts that use of the MTD in a chronic study is required. The principal information cited by CSPI to support its contention that use of the MTD is required is the FDA Redbook (Ref. 2). (See CSPI Obj., p. 3) However, use of the MTD is not required by the FDA Redbook or any agency regulation.

The FDA Redbook contains general principles that serve as guidance for assessing the safety of direct food additives and color additives used in food; these principles are to be applied using good scientific judgment. The FDA Redbook represents the agency's best advice to manufacturers of food and color additives on how to satisfy that act's safety standard of "reasonable certainty * * * that a substance is not harmful." (See 21 CFR 170.3(i).) These general guiding principles are not binding requirements for manufacturers or for the agency.[2] Indeed, in a recent decision on FD&C Blue No. 2, the appellate court held that the criteria in the FDA Redbook are not binding and that deference to agency expertise is especially appropriate with respect to the selection of the MTD. (See *Simpson* v. *Young*, 854 F. 2d 1429, 1434–35 (D.C. Cir. 1988).)

None of the remaining data and information cited by CSPI, even if established at a hearing, would support a conclusion that use of the MTD is mandatory in a chronic study. In particular, the excerpt from the IARC report cited by CSPI discusses the consequence of selecting too low a dose for a chronic study; the report does not establish a requirement that the MTD be used (Ref. 3, p. 34). (See CSPI Obj., p. 4, 4. 11.) Likewise, the FDA memorandum dated March 26, 1987, discussed the apparent no-effect level for acesulfame potassium of 3 percent; it did not address the use of the MTD generally or discuss specifically the MTD for the second rat study. (See CSPI Obj., p. 4.) Finally, CSPI did not identify the data from the second rat study and the subchronic study on which they were relying; these data, however, even if identified, could not themselves answer the question of whether the MTD must be achieved in order for a chronic study to be valid.

FDA is also denying CSPI's request for a hearing on its first objection to the extent that the objection asserts that testing at the 3 percent dose level was not sufficiently high for a proper assessment of the carcinogenicity of acesulfame potassium. The sole basis for CSPI's objection to the dosing in this study is its claim that the MTD was not achieved. (See CSPI Obj., pp. 2 and 3.) As shown above, CSPI has provided no data or information establishing that the MTD must be reached in order for a chronic study to be valid. Thus, the data and other information cited by CSPI do not justify a conclusion that the dosing in the second rat study was not sufficiently high. (See § 12.24(b)(3).)

Finally, CSPI asserts that the FDA Redbook requires two rodent studies to establish the safety of a food additive such as acesulfame. (See CSPI Obj., p. 5.) CSPI further asserts that if the second rat study is determined to be inadequate, there will no longer be two rodent studies to support the safety of acesulfame potassium. Again, the data and information identified by CSPI, even if established at a hearing, would not be adequate to justify resolution of this issue in CSPI's favor. (See 21 CFR 12.24(b)(3).) The only information cited to establish that two rodent studies are required for approval is the FDA Redbook. (See CSPI Obj., p. 5.) As previously noted, the FDA Redbook does not establish binding requirements; instead, the FDA Redbook provides guidance to those conducting studies to assess the safety of direct food additives such as acesulfame potassium. Because the information cited is not sufficient to establish CSPI's factual assertion, a hearing need not be granted on this issue. (See § 12.24(b)(3).)

B. Adequacy of the Chronic Mouse Study

FDA relied upon the chronic mouse study of acesulfame potassium when it concluded that this sweetner had been shown to be safe. By relying on this study, FDA implicitly concluded that this study was adequate to assess the carcinogenicity of acesulfame potassium in that the study's dosing was adequate. (See 53 FR 28379, 28380, July 28, 1988 and Ref. 1.) In addition, in the final rule for acesulfame potassium, FDA explicitly addressed the adequacy of the length of the chronic mouse study. (See 53 FR 28379, 28380, July 28, 1988.) In particular, with respect to study duration, FDA considered the length of the mouse study and concluded that it was adequate because it had been conducted for the majority of the animals' lifespan (Ref. 1).[3]

[2] The principles set out in the FDA Redbook were not promulgated by notice and comment rulemaking and do not have the force and effect of law.

[3] The Agency found that at the time the study was conducted (mid 1970's), survival of the Swiss strain of mice tended to decline severely between 18 and 24 months of age. Accordingly, even if the mouse study had not been terminated when it was

Continued

CSPI's second objection asserts that, for two reasons, the chronic mouse study is not adequate to demonstrate that acesulfame potassium does not cause cancer in mice. First, CSPI asserts that doses in this study were not properly determined. (See CSPI Obj., p. 6.) Specifically, CSPI claims that, because there was no subchronic study in mice to determine the MTD, there is no assurance that the highest dose used (3 percent) was sufficient to assess whether acesulfame potassium causes cancer in mice. (See CSPI Obj., p. 7.) CSPI further asserts that, because FDA identified 3 percent as a no-effect level, this study did not meet FDA's own standards for long-term studies. (See CSPI Obj., p. 7.)

Secondly, CSPI claims that the mouse study was of insufficient duration in that this study lasted only 80 weeks and that FDA's Redbook requires chronic studies in rodents to be at least 104 weeks in duration. (See CSPI Obj., p. 7.) Accordingly, CSPI asserts that the mouse study was of insufficient duration to demonstrate that acesulfame potassium does not cause cancer.

In support of its second objection, CSPI identified the following data and information: the FDA Redbook; an excerpt from a publication of the National Toxicology Program, "Report of the National Toxicology Program Ad Hoc Panel on Chemical Carcinogenesis Testing and Evaluation" (the NTP Report); the IARC Report; and FDA memoranda dated March 26, 1987 and September 16, 1987. (See CSPI Obj., pp. 8 and 9.)

FDA is denying CSPI's request for a hearing on the adequacy of the chronic mouse study because the data and information identified by CSPI in support of its second objection, even if established at a hearing, would not be sufficient to justify resolution of the factual question in CSPI's favor. (See § 12.24(b)(3).)

First, FDA is denying CSPI's request for a hearing on this objection to the extent that it is based upon the mouse study's alleged failure to achieve the MTD. As with its first objection, CSPI relies principally upon the FDA Redbook to establish that the use of the MTD is required. (See CSPI Obj., p. 8.) As set forth in detail above, the FDA Redbook provides guidance for conducting tests of direct food additives such as acesulfame potassium; it does not establish requirements. The FDA memoranda cited by CSPI discussed the apparent no-effect level for acesulfame potassium and the use of rat studies to determine the Acceptable Daily Intake of the sweetener; they neither addressed the use of the MTD generally, nor discussed specifically the MTD for the mouse study. Thus, none of the information identified by CSPI is sufficient to justify the conclusion that the MTD must be used in all chronic studies. (See § 12.24(b)(3).)

FDA is also denying CSPI's request for a hearing on this objection to the extent that this request is based on an alleged requirement that the MTD be determined only by a subchronic study. Once again, CSPI relies upon the FDA Redbook and the IARC Report to support its assertion that a subchronic study is the only acceptable way of determining dosing levels. (See CSPI Obj., pp. 7 and 9.) However, as discussed above, neither the FDA Redbook nor the IARC Report establish requirements; both simply provide guidance for the conduct of chronic animal testing. In fact, in a comparable situation with FD&C Blue No. 2, the appellate court concluded that there are reasonable alternative approaches for determining the high dose in a chronic study.

> It is clear from the record that the pilot study is simply one accepted and efficient method to determine the MTD to be used in the main study, not an iron-clad prerequisite to the validity of the MTD actually selected * * *. Thus, the FDA justifiably rejected petitioners' argument that a pilot study was necessary to determine the Blue No. 2 MTD.
>
> (*Simpson* v. *Young, supra,* 854 F.2d at 1435.)

Accordingly, the only information identified by CSPI is insufficient to justify the conclusion that the MTD for a chronic study must be determined by a subchronic study in the same species. (See § 12.24(b)(3).)

The agency is also denying CSPI's request for a hearing on this objection to the extent that it is based upon the claim that the mouse study was of insufficient duration. In support of its allegation of insufficient duration, CSPI relies upon the FDA Redbook and the NTP Report. (See CSPI Obj., p. 8.) Neither of these documents supports CSPI's position.

First, as discussed in detail in this document, as a general matter, the FDA Redbook provides guidance for chronic animal testing; it does not establish requirements. Similarly, the NTP Report identified by CSPI does not establish an ironclad requirement that chronic rodent studies be 104 weeks long. To the contrary, the NTP Report recommends that experimental animals be allowed "to survive for most of their natural lifespan" (Ref. 4, p. 189).[4] Accordingly, the data and information identified by CSPI, even if established at a hearing, would not justify the conclusion that the mouse study was of insufficient duration. Thus, FDA is denying a hearing on this objection. (See § 12.24(b)(3).)

CSPI's objection to adequacy of the mouse study is based solely upon the alleged failure of the study to achieve the MTD and the study's alleged insufficient duration. (See CSPI Obj., pp. 6 and 7.) As shown above, CSPI has identified no data or other information to demonstrate that, for a chronic study to be adequate, the MTD must be achieved and that such study must be at least 104 weeks in duration. Accordingly, the data and other information identified by CSPI do not justify a conclusion that the mouse study was not adequate to assess the carcinogenicity of acesulfame potassium. (See § 12.24(b)(3).)

As with its first objection, CSPI asserts that the FDA Redbook requires two rodent studies to establish the safety of a food additive such as acesulfame potassium. (See CSPI Obj., p. 9.) CSPI further asserts that if the mouse study is determined to be inadequate, there will be no longer be two rodent studies to support the safety of acesulfame potassium. As shown above, the data and information identified by CSPI, even if established at a hearing, would not be adequate to justify resolution of this issue in CSPI's favor. (See § 12.24(b)(3).) Because the information cited is not sufficient to establish CSPI's factual assertion, a hearing need not be granted on this issue. (See § 12.24(b)(3).)

C. Results of the First Long-Term Rat Study

As discussed in the final rule in the **Federal Register** of July 28, 1988 (53 FR 28379), the petitioners submitted data from a long-term toxicity and carcinogenicity study conducted in CIVO-bred Wistar rats (the "first rat study"). The agency evaluated all of the data and information from this study and concluded that the data do not establish a carcinogenic effect of acesulfame potassium. However, because of deficiencies and confounding factors, the agency further concluded that the first rat study is "inadequate for

(at 80 weeks), termination would probably have been required a short time later because of increased, excessive mortality.

[4] FDA agrees with the NTP Report recommendation on study length. In this case, terminating the mouse study at 80 weeks was consistent with the NTP recommendation, given the average lifespan of Swiss mice: at the time of the study, their mortality declined severely between 18 months and 2 years.

assessing the carcinogenic potential of the test compound or for any other purposes of a safety evaluation" (53 FR 28379 at 28381; Ref. 1).

CSPI's third objection contends that the first rat study provides evidence that acesulfame potassium causes cancer in rats, citing increased incidences of lung lymphoreticular tumors and several types of other, rat tumors. The objection also disputes FDA's reasons for concluding that the study is inadequate for determining the safety of the sweetener.[5] CSPI makes six separate contentions in this objection. Each of these is addressed individually below.

1. Incidence of Rare Tumors

CSPI asserts that the first rat study demonstrates a carcinogenic effect of acesulfame potassium because increased incidences of several rare tumors (thymus lymphosarcoma, blood lymphocytic and monocytic leukemias, kidney carcinoma, chromophobe adenoma of the pituitary, and parafollicular cell adenoma of the thyroid) were observed in the treated animals. (See CSPI Obj., pp. 10 and 11.) In support of its assertion, CSPI cites an FDA memorandum dated "December 2, 1984" (Ref. 5; the memorandum referred to by CSPI is in fact dated December 3, 1984).

FDA is denying CSPI's request for a hearing on its third objection to the extent that it alleges that the incidence of rare tumors in treated animals of the first rat study provides evidence of the carcinogenicity of acesulfame potassium. The only evidence that CSPI cites in support of its allegation is the FDA memorandum dated December 3, 1984. This memorandum, even if its contents were established at a hearing, would not demonstrate that the rare tumors were attributable to dietary exposure to acesulfame potassium.

The December 3, 1984, FDA memorandum was merely a tabulation of the lesions and findings reported by the investigators of the first rat study. The memorandum was prepared by FDA scientists for the purpose of further evaluation of the study data.[6] It was not prepared for the purpose of drawing conclusions about whether the findings were effects that could be attributed to the test compound, and in fact, the memorandum does not draw any such conclusions. Thus, the data in the memorandum identified by CSPI do not justify a conclusion that the rare tumors observed in treated animals were attributable to acesulfame potassium. Accordingly, FDA is denying CSPI's hearing request on this point.[7] (See § 12.24(b)(3).)

2. Absence of Complete Histopathological Data.

In the preamble to the final rule, FDA explained its reasons for determining that the first rat study was not adequate to demonstrate safety. The agency stated:

> A major deficiency in the study is the fact that only 20 of the 60 rats in the control and high dose groups were subject to a complete histopathological examination, thereby limiting the proper interpretation of the results of the study.
>
> (See 53 FR 28379 at 28380).

In its third objection, CSPI asserts that FDA's reasoning on this point " is not persuasive, because there is no reason to suspect that more extensive histopathological examination would have distorted the dose-response trend observed * * *." (See CSPI Obj., pp. 11 and 12.) The only evidence CSPI identifies in making its assertion are FDA memoranda dated December 3, 1984, and August 15, 1986. (See CSPI Obj., p. 12.)

FDA is denying CSPI's request for a hearing on its third objection to the extent that it alleges that further histopathological examination of animals in the first rat study would not have distorted the alleged observed dose-response trend.[8] Because complete histopathological examination of tissues from all animals in the first rat study was not done and cannot be done now, any prediction of the results of such an examination is simply speculation. Speculation regarding data that do not exist cannot serve as the basis for a hearing. (See § 12.24(b)(2).)

Moreover, as discussed above, the December 3, 1984, FDA memorandum cited by CSPI (Ref. 5) was merely a tabulation of the findings reported by the investigators of the first rat study, prepared for the purpose of further evaluation of the study data. The August 15, 1986, memorandum (Ref. 6) was a statistical analysis of mortality and body weights of rats of the first study; it did not discuss the histopathological examination nor did it address tumor incidence or dose-response trends. Thus, the information in the FDA memoranda, even if established at a hearing, is not sufficient to establish CSPI's factual assertion. (See § 12.24(b)(3).)

3. Significance of Extensive Chronic Respiratory Disease

In discussing the agency's conclusion that the first rat study was inadequate to demonstrate carcinogenicity or safety of acesulfame potassium, FDA noted that "extensive, severe chronic respiratory disease in the lungs of rats of all groups confounded diagnosis and interpretation of lung lesions in these animals." (See 53 FR 28379 at 23830). The agency also noted that the particular lung tumors associated with the CIVO-bred Wistar strain of rat differed from those in other rat strains and were associated with extensive, severe chronic respiratory disease (CRD) in this strain of rat (53 FR 23879 at 23832, Ref. 5).[9] Moreover, the agency noted that the second rat study, conducted in a different rat strain, did not show lymphoreticular tumors in the lungs (53 FR 28379 at 28380).

In its third objection, CSPI disagrees with the agency's interpretation of these data. In particular, CSPI asserts that lymphoreticular tumors occurred in the absence of CRD in dosed male rats, and further that, despite CRD, the study results showed dose-related trends in tumor incidence, time-to-tumor, and time-to-death with tumor.[10] (See CSPI

[5] Many of the issues raised in this objection were raised previously by CSPI in its letter to FDA dated September 23, 1987, and were addressed by the agency in the preamble to the final rule (53 FR 28379, July 28, 1988).

[6] Specifically, the memorandum requested "that the Division of Mathematics perform statistical analyses of the tumor data for each of the 3 long-term feeding studies" (Ref. 5).

[7] In support of its third objection, CSPI also cited data regarding tumor incidence in the second rat study. Specifically, CSPI asserted that thymus lymphosarcoma was also found only in treated rats of the second rat study. This statement apparently is based on the initial pathology report of the second study. Before reaching a decision on the second rat study, however, the agency requested more detailed and consistent listings of the study results, which led to a reexamination of the slides and preparation of a new report (53 FR 28379 at 28380). No thymus lymphosarcomas were found in the treated animals following complete reexamination of the histopathology slides, as given in the later and more complete report (petitioner's submission dated March 20, 1986; see section D, below). Thus, the data from the second rat study do not support CSPI's contention concerning tumor incidence in the first rat study.

[8] FDA does not agree that the data establish an acesulfame potassium-dependent, dose-response trend in tumor incidence; see section V.C.4. of this document.

[9] The lung tumors common in this strain of rats were lung lymphoreticular tumors, that is, tumors of reticuloendothelial cells of lymphoid tissue in the lungs. Some of these tumors were classified as reticulum cellsarcomas, which are a type of malignant lymphoreticular tumor; that is, reticulum cell sarcomas are a subset of lymphoreticular tumors. Further, lymphoreticular tumors are tumors of the reticuloendothelial system (i.e., the "lymphatic" system). The lymphatic system is distributed throughout the body, and usually, these tumors are disseminated. In this strain of rats, (which had very high rates of chronic respiratory disease), the lymphoreticular tumors were localized to the lung. (See Ref. 1 and 53 FR 23879 at 23832, Ref. 5).

[10] In its objection, CSPI incorrectly claims that FDA said that CRD occurred in all study rats. (See

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Obj., p. 12.) In support of its assertion, CSPI cites an FDA memorandum dated June 19, 1986 (Ref. 7).

FDA is denying CSPI's request for a hearing on this objection to the extent that it disputes FDA's conclusion that the presence of extensive CRD confounded interpretation of the first rat study because the evidence identified in support of CSPI's objection, even if established at a hearing, would not be adequate to justify resolution of this issue in CSPI's favor. (See § 12,24(b)(3).)

The only evidence that CSPI cites in support of its allegation is the FDA memorandum dated June 19, 1986. This memorandum was a request for an evaluation of all of the data available regarding the carcinogenic potential of acesulfame potassium. The portion of the memorandum cited by CSPI is a tabulation of recently submitted data, in which it was noted that lymphoreticular tumors occurred in the absence of CRD in a few animals. Importantly, however, the memorandum did not conclude that the lymphoreticular tumors observed in the absence of CRD were attributable to acesulfame potassium. Thus, the data in the memorandum relied upon by CSPI are not sufficient to refute FDA's conclusion that the presence of CRD confounded interpretation of the first rat study. Furthermore, CSPI identified no other evidence to support its assertion. Accordingly, FDA is denying CSPI's hearing request on this point. (See § 12.24(b)(3).)

4. Incidence of Lymphoreticular Tumors in Male Rats

In the preamble to the final rule, the agency noted that, in the first rat study, there was a slightly higher incidence, and earlier appearance, of lymphoreticular tumors in dosed rats than in the concurrent control group. The agency concluded that under the circumstances of severe CRD, sampling limitations, and the very high rate of spontaneously-occurring lung tumors in this strain of rat, no conclusions should be made about any effect of acesulfame potassium on the lungs (53 FR 28379 at 28380).

In its third objection, CSPI challenges the agency conclusion and assets that "acesulfame potassium, not CRD, was responsible for the increased mortality [from lymphoreticular tumors] in males." (See CSPI Obj., p. 13.)

In support of its allegation, CSPI cites a table that CSPI constructed, titled "Cause of Death in Male Rats That Died or Were Killed When Moribund." (See CSPI Obj., p. 14.) CSPI assets that the table shows an acesulfame potassium dose-related increase in mortality, and that "This dose-related increase in mortality was due to lymphoreticular tumors, not CRD. Male treated rats died of lung tumors at a much higher rate, and of CRD at a much lower rate, than controls did * * *." (See CSPI Obj., p. 14.)

The table upon which CSPI relies contains three columns of data that CSPI abstracted from two separate documents. Column one purports to represent the percentage of deaths of control and dosed male rats attributed to CRD; column two, the percentage of deaths attributed to reticulum cell sarcoma; and column three, the percentage of deaths attributed to lymphoreticular tumors. The data in the first two columns were taken for original (uncorrected) report of the study; the third column lists data taken from a review memorandum of a subsequent (corrected) report.

FDA is denying CSPI's request for a hearing on this objection to the extent that it alleges that acesulfame potassium was responsible for increased mortality from lymphoreticular tumors in male rats of the first study, because a hearing will not be granted on the basis of mere allegations or descriptions of positions or contentions (§ 12.24(b)(2)).

To justify a hearing on this objection, CSPI must specifically identify reliable evidence that can resolve the factual issue in the way sought by CSPI. The table CSPI constructed, and the conclusions CSPI draws from it, are not reliable for several reasons. (1) The table misrepresents the meaning of the data. The study reports from which the data were drawn listed the number of animals found to have the listed conditions. Contrary to the title of the table, CSPI has presented no evidence to establish that for each animal, CRD, reticulum cell sarcomas, or lymphoreticular tumors were determined to be the cause of death. (2) Data are double counted. Specifically, "lymphoreticular tumors" is a general term for benign and malignant noeplasms of the reticuloendothelial cells of the lymph nodes. This category includes "reticulum cell sarcomas," which are malignant tumors of the lymphoid tissue. Thus, the animals identified in column two (deaths attributed to reticulum cell sarcomas) are also counted in column three (deaths attributed to lymphoreticular tumors). (3) A portion of the data are drawn from an unreliable source. That is, the data purporting to represent the percentages of deaths attributed to CRD (column one) and reticulum cell sarcomas (column two) were taken from the original report of the study, which had several inconsistencies in the data. This original report was superseded by a consistent and more accurate report. (4) The data in column three cannot properly be compared to data in columns one and two. Data in columns one and two were drawn from a study report that counted only animals that died or were killed when moribund; the data in column three, however, were taken from a latter report of the study that listed all animals examined, including those sacrificed at the end of the study as well as those that died or were killed when moribund.[11]

CSPI asserts that deaths were caused by lung tumors and that the lung tumors were caused by the test compound. However, the information CSPI has offered in support of its assertion is not reliable, as explained above. A hearing must be based on reliable evidence, not on mere allegations or on information that is inaccurate and contradicted by the record. (See § 12.24(b)(2).)

5. The use of Historical Control Data

In the preamble to the final rule, FDA discussed historical control data for CIVO bred Wistar rats. Specifically, the agency noted:

> Reticulum cell sarcomas are known to occur spontaneously in this strain of rat; incidents as high as 32 percent had been reported in untreated CIVO-bred Wistar rats * * *. These findings on the lymphoreticular neoplasms observed in treated and control rats from this study reinforce the agency's judgment that these neoplasms were not caused by acesulfame potassium treatment * * *.

(53 FR 28379 at 28380 and Ref. 5 of final rule).

The agency received from the petitioners historical control data on tumors in this strain of rat, as well as information about the factors taken into account by the testing laboratory in its selection of appropriate historical control data. The historical control data are from the same type of studies conducted in the same laboratory, with the same strain of rat, under similar conditions, with continuity of pathological standards, and are from the same time period as the first rat study (Ref. 8). The agency evaluated this information in reaching its conclusion that there was no evidence that the tumors observed in the first rat study

Obj., p. 12.) In fact, FDA stated that CRD was seen in rats in all groups in the study. (See 53 FR 28379 at 28380.)

[11] The data in column three are, therefore, inconsistent with the title of the table, which purports to compare causes of death in animals that died or were killed when moribund.

were attributable to acesulfame potassium.

CSPI objects to the agency's reliance on historical control data and makes three points about comparing the data in the first rat study to historical control data.

a. CSPI lists possible sources of variability in historical control data and asserts that "There is no evidence that FDA carefully evaluated the data for these sources of variability or that the laboratory conducting the study attempted to control the variability." (See CSPI Obj., p. 14.)

In support of its assertion, CSPI cites an Office of Science and Technology Policy (OSTP) report, "Chemical Carcinogens: A Review of the Science and its Associated Principles" (the OSTP report); a presentation by Dr. James S. Winbush to the Toxicology Forum (the Winbush statement); and unspecified "data from the petitioner's first long-term rat study, * * * evidencing the petitioner's failure to attempt to identify and control sources of variability in tumor rates among historical controls" (CSPI Obj., p. 16). CSPI cites the OSTP report as stating that the sources of variability in historical control data should be identified and, if possible, controlled (CSPI Obj., p. 14); CSPI cites the Winbush statement as listing the factors that can account for tumor rate variability among historical control groups (CSPI Obj., pp. 14 and 15).

FDA is denying CSPI's request for a hearing on this objection to the extent that it alleges that FDA did not evaluate historical control data for sources of variability, because the data and information identified by CSPI in support of the objection, even if established at a hearing, would not be adequate to justify resolution of this factual issue in CSPI's favor. (See § 12.24(b)(3).) With regard to the unspecified data from the petition, a hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of that hearing. The person seeking a hearing must meet a threshold burden of identifying specific evidence that suggests a need for a hearing. (See § 12.24(b)(2).)

The assertion that there is no evidence showing FDA evaluation of, or laboratory control of, variability in historical controls is contradicted by the record. The objection fails to acknowledge the information on this point that FDA evaluated. CSPI has identified no specific evidence to challenge FDA's evaluation. The only information that CSPI specifically identified in support of its assertion are the Winbush statement and the OSTP report. The Winbush statement and the OSTP report, even if established at a hearing, do not support a conclusion that the agency's consideration of the historical control data was inadequate. (See § 12.24(b)(3).) In fact, FDA agrees with and follows the principles set out in the OSTP report and in the Winbush statement.[12]

b. CSPI asserts that the incidence of lymphoreticular tumors in females of the high-dose group was twice the average of historical control groups (CSPI Obj., p. 15).[13]

FDA is denying CSPI's request for a hearing on its third objection to the extent that it alleges that the average incidence in historical control groups is the most appropriate reference for comparing experimental data. CSPI offers no evidence in support of this position.[14] A hearing will not be granted on the basis of mere allegations or descriptions of positions or contentions. (See § 12.24(b)(2).)

c. In discussing the mortality of dosed male rats, which was higher than the mortality of control male rats, CSPI asserted "Although the study authors attribute this difference in death rates to unusually low mortality in the controls, and state that test group mortality was still within the historical control range, the variability in historical controls is too great for the historical data to be used in determining significance. Indeed, the high mortality rates and high variability lead one to question the adequacy of conditions in this laboratory." (See CSPI Obj., p. 13.)

CSPI identifies no specific evidence in support of the foregoing allegation. Accordingly, FDA is denying CSPI's request for a hearing on its third objection to the extent that it alleges that the variability in mortality in historical controls in this laboratory is too great for historical data to be used in determining significance, because a hearing will not be granted on the basis of mere allegations. (See § 12.24(b)(2).)

Moreover, by questioning the adequacy of the testing laboratory because of high mortality rates and high variability in mortality rates, CSPI actually identifies the crux of the problem with the first rat study: during the time of the study, CRD was so extensive in this colony that the disease and associated conditions obscured whether there could have been possible effects caused by the test compound. Thus, CSPI's objection is consistent with FDA's conclusion that the study is not adequate for use in determining the safety of an additive. A hearing will not be granted on factual issues that are not determinative with respect to the action requested. (See § 12.24(b)(4).

6. Appropriateness of dose levels. In the preamble to the final rule (53 FR 28379 at 28380, 28381), the agency discussed its reasons for concluding that the first rat study was not adequate to demonstrate carcinogenicity of acesulfame potassium, and noted that this study was not relied upon to show the safety of the sweetener.

In its third objection, CSPI asserts that the high dose in the first rat study was too low for a proper assessment of carcinogenicity, and further alleges that "This flaw biased the study toward a negative finding on carcinogenicity. If this flaw was corrected, an even stronger carcinogenic effect would likely be found." (See CSPI Obj., p. 10.) CSPI identified no specific evidence in support of this objection.

FDA is denying CSPI's request for a hearing on this objection to the extent that it alleges that the high dose used in the first rat study was too low for a proper assessment of carcinogenicity, because a hearing will not be granted on the basis of mere allegations. (See § 12.24(b)(2).) In addition, CSPI's contention that a higher dose level would likely have produced an "even stronger" carcinogenic effect is speculation on the outcome of a study that was not done. Speculation regarding data that do not exist cannot serve as the basis for a hearing. (See § 12.24(b)(2).)

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[12] Moreover, FDA followed the principles set out in the OSTP report and in the Winbush statement in assessing the use of historical control data in this instance. In discussing the use of historical control data, the OSTP statement cited by CSPI goes on to state: "Obviously one has more confidence in the most recent historical control data from the same laboratory conducting the current study than in a complication of pooled older data from other laboratories" (50 FR 10372 at 10418, March 14, 1985). OSTP also states that "Historical control data can be valuable when used appropriately, especially when the differences in incidence rates between treated and concurrent negative controls are small and can be shown to be within the anticipated historical incidence." (See 50 FR 10372 at 10418.)

[13] In making this statement, CSPI ignored the fact that all incidences of lymphoreticular tumors in the first rat study, for treated as well as control groups, were within the range of incidences found in historical controls.

[14] The average incidence of historical control groups is not the most appropriate statistical reference point for comparing incidences among treated and historical or concurrent control groups: Information about the variability of the toxicologic end point under consideration is lost when incidences are averaged; the more variable the end point is among control animals, the more information is lost through averaging. In contrast, by comparing incidences in treated and control animals with the range of historical control incidences, information about the variability of the toxicologic end point is retained.

Finally, even if it were established that the dose used in the first rat study was too low for a proper assessment of carcinogenicity, this determination would not alter FDA's conclusion that this study was not adequate for determination of safety or carcinogenicity (53 FR 28379 at 28281). Thus, FDA is denying CSPI's request for a hearing on this point because a hearing will not be granted on factual issues that are not determinative with respect to the action requested. (See § 12.24(b)(4).)

D. Results of the Second Long-Term Rat Study

As discussed above, the petitioners submitted data from a long-term toxicity and carcinogenicity study conducted in CPB–WU Wistar rats (the "second rat study"). In the preamble to the final rule (53 FR 28379 at 28380), FDA explained that the original report of the second rat study contained inconsistencies in the criteria used to identify and diagnose lesions. Because of these inconsistencies, FDA requested more detailed and explicit listings of the results of the study. In response, the petitioner had the data and microscopic slides reviewed by a consulting pathologist, who prepared a new report. After a comprehensive review of all of the data, the agency concluded that the second rat study is adequate for the safety evaluation of a food additive and that there is no association between the occurrence of neoplasms and treatment with acesulfame potassium (Ref. 1; 53 FR 28379 at 28380 and 28381).

CSPI's fourth objection contends that the second long-term rat study demonstrates that acesulfame potassium causes cancer in rats.[15] CSPI discusses two bases for this contention.

1. Incidence of rare tumors. CSPI contends that the incidence of several types of rare tumors (lymphosarcoma of the thymus, hemangiosarcoma of the mesenteric lymph nodes, brain meningioma, spleen mesothelioma, and adenomatous polyps of the uterus) were elevated in treated animals. In support of this contention, CSPI cites an FDA memorandum dated December 2, 1984 (actually dated December 3, 1984) (Ref. 5).

FDA is denying CSPI's request for a hearing on this objection to the extent that it alleges that the increased incidence of rare tumors in treated animals in the second rat study provides evidence of carcinogenicity of acesulfame potassium. The data and information identified by CSPI in support of this objection, even if established at a hearing, would not be adequate to justify resolution of this factual question in CSPI's favor. (See § 12.24(b)(3).)

The only evidence that CSPI cites in support of its allegation is the FDA memorandum dated December 3, 1984. This memorandum, even if its contents were established at a hearing, would not demonstrate that the rare tumors were attributable to dietary exposure to acesulfame potassium. The memorandum was merely a tabulation of all lesions and findings reported in the second rat study, and was prepared for the purpose of further evaluation, including statistical analysis of the data (Ref. 5). It was not prepared for the purpose of drawing conclusions about whether the findings were effects that could be attributed to the test compound and, in fact, it did not draw any conclusion about whether the findings were attributable to acesulfame potassium.

Moreover, the memorandum cited by CSPI reflected the listing of the data in the first, inconsistent report of the study, a report that was subsequently revised and corrected. CSPI ignored the corrected data in the record when it formulated its objection. Unlike CSPI, FDA made its final determination on the basis of the entire record when it concluded that the data from the second rat study did not show an association between the occurrence of tumors and treatment with acesulfame potassium.

In summary, the data in the memorandum identified by CSPI do not justify a conclusion that the rare tumors observed in treated animals were attributable to acesulfame potassium. Accordingly, FDA is denying CSPI's hearing request on this point. (See § 12.24(b)(3).)

2. Incidence of mammary gland tumors. In promulgating the rule authorizing the use of acesulfame potassium, FDA specifically considered the differences in the incidence of mammary gland neoplasms in female rats in the second rat study. In the preamble to the final rule, FDA noted that most of the mammary tumors observed were fibroadenomas, and that there was an increased incidence of fibroadenomas in treated female rats. The agency also stated that tumors other than fibroadenomas were few in number and were distributed randomly among the different groups, and that the incidences of mammary gland hyperplasia were similar and uniformly high in all groups of treated and control females. (See 53 FR 28379 at 28380.)

After review of all of the data, the agency concluded that the occurrence of mammary gland neoplasms was not associated with treatment with acesulfame potassium. The final rule cited several reasons for this conclusion:

> (1) Fibroadenomas are a common old age tumor in this strain of rats and their incidence is variable.
>
> (2) The incidence of mammary fibroadenomas in female control rats from seven comparable studies, performed at this testing laboratory around the same time period as the acesulfame potassium study, is 250 of 452 or 55.3 percent * * *. This incidence is higher than the incidences for any of the treated groups in the acesulfame potassium study and is much higher than that for the concurrent control group. The concurrent control group had an unusually low incidence of these tumors.
>
> (3) In the treated groups, the lack of a dose response in incidences of fibroadenomas, as well as of all mammary tumors and of hyperplasia, is evidence that there is not a treatment-related effect of the sweetener on the incidence of fibroadenomas.
>
> (4) There was no evidence of progressive stages of mammary gland neoplasms (hyperplasia to malignant neoplasms) that would indicate a treatment-related induction of tumors.

(53 FR 28379 at 28381 and Ref. 6 of final rule).

In its fourth objection, CSPI challenges the agency's conclusion that the occurrence of mammary neoplasms was not associated with acesulfame potassium treatment. (See CSPI Obj., pp. 17 and 18.) CSPI further challenges the agency's reasons for its conclusion. (See CSPI Obj., pp. 19 and 20.) CSPA makes four separate points with regard to the occurrence of mammary tumors in the second rat study.

a. CSPI first asserts that the incidences of mammary gland neoplasms in female rats increased with increasing dose of acesulfame potassium up to the mid-dose,[16] and that this provides evidence of the carcinogenicity of the sweetener. (See CSPI Obj., p. 18.) CSPI further asserts that there were "increases in benign and malignant tumors associated with dosing of acesulfame potassium." (See CSPI Obj., p. 20.) In support of its assertions, CSPI identifies no specific evidence, referring only to unspecified and unidentified study data and FDA evaluations. (See CSPI Obj., p. 20.)

FDA is denying CSPI's request for a hearing on this objection to the extent

[15] Most of the issues raised in this objection were raised previously by CSPI in its September 23, 1987, letter to FDA, and were addressed by the agency in the preamble to the final rule (53 FR 28379, July 28, 1988).

[16] This is simply a restatement of the fact that the mid-dose animals had more tumors than the low-dose animals, but the high-dose animals did not have more tumors than the mid-dose animals.

that it alleges that the increased incidence of mammary neoplasms in the second rat study provides evidence of carcinogenicity of acesulfame potassium, because a hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of the hearing. The person seeking the hearing must meet a threshold burden of identifying specific evidence that suggests a need for a hearing. (See § 12.24(b)(2).)

b. CSPI makes two separate assertions regarding FDA's use of historical control data. First, CSPI asserts that the weight accorded to historical control data is inappropriate and that "[t]here is no evidence that FDA examined the data for sources of variability or to ensure that the historical studies conformed with Good Laboratory Practice Standards." (See CSPI Obj., p. 19.)

CSPI identifies no specific evidence in support of its assertion that FDA failed to examine adequately the historical control data. Thus, FDA is denying CSPI's request for a hearing on its fourth objection to the extent that it alleges that FDA did not examine the historical data for sources of varability, because a hearing will not be granted on the basis of mere allegations. (See § 12.24(b)(2).)

Moreover, CSPI's assertion that there is no evidence that FDA evaluated the variability in historical control data is not correct. CSPI's objection fails to acknowledge the information received from the petitioner concerning historical controls that FDA did evaluate.[17]

FDA is also denying CSPI's request for a hearing on this objection to the extent that it alleges that FDA failed to ensure that the studies that constitute the historical control data conformed with good laboratory practice. Once again, CSPI identifies no specific evidence demonstrating that FDA's alleged failure to do detailed examinations of the historical studies seriously undermines the utility of the historical data for comparison purposes. CSPI's objection identifies no relevant data that were overlooked by the agency, nor does it identify any specific problems that invalidate these data. Thus, FDA is denying a hearing on this point, because a hearing will not be granted on the basis of mere allegations. (See § 12.24(b)(2).)

Secondly, CSPI asserts that wide variability of tumor rates in the historical controls makes the historical control data less reliable than if the range of incidences was narrow.[18] CSPI identifies no specific evidence in support of this allegation. Accordingly, FDA is denying CSPI's request for a hearing on its fourth objection to the extent that it alleges that the variability in tumor rates in historical controls limits the usefulness of historical control data, because a hearing will not be granted on the basis of mere allegations. (See § 12.24(b)(2).)

c. In the final rule (53 FR 28379 at 28381), FDA noted that the lack of a dose response to acesulfame potassium in the incidence of mammary tumors was evidence that there was not a treatment-related effect of the sweetener. In challenging the agency's reasoning, CSPI asserts that it is not necessary to establish a positive dose response to conclude that a test substance is a carcinogen. (See CSPI Obj., p. 20.) In support of its assertion, CSPI cites an article, "Scientific Basis for Identification of Potential Carcinogens and Estimation of Risk" (Ref. 9).

FDA is denying CSPI's request for a hearing on this objection to the extent that the objection alleges that it is not necessary to establish a positive dose response to reach a conclusion of carcinogenicity, because resolution of this factual issue in CSPI's favor is not adequate to justify a finding that the second rat study showed a carcinogenic effect of acesulfame potassium. (See § 12.24(b)(4).)

FDA agrees that it is not always necessary to establish a positive dose response to reach a conclusion of carcinogenicity. The agency also agrees with the principles outlined in the article cited by CSPI. However, as stated previously, the agency reached its decision about the lack of association of the sweetener with mammary gland tumors based on the weight of all of the evidence; no single point provided complete proof in determining the question of carcinogenicity. As discussed above, CSPI has identified no specific evidence to support the conclusion that the second rat study demonstrates a carcinogenic effect of acesulfame potassium, even absent a dose response.

d. CSPI asserts that FDA's point on the lack of progressive stages of mammary gland neoplasms is "hardly proof" that tumors were not related to treatment. (See CSPI Obj., p. 20.) Again, CSPI identifies no specific evidence to contradict FDA's conclusion that the absence of progressive stages of mammary gland neoplasms supports the agency's conclusion that the mammary gland neoplasms were not treatment-related.

FDA is denying CSPI's request for a hearing on its fourth objection to the extent that it alleges that the lack of progressive stages of mammary gland neoplasms is not evidence that tumors were not treatment-related, because a hearing will not be held on the basis of mere allegations. (See § 12.24(b)(2).) Because CSPI has not submitted any new information to support its allegation that this study demonstrated that acesulfame potassium caused cancer in rats, and has not demonstrated that the agency overlooked significant information in reaching its conclusion of safety, a hearing is not required (See § 12.24(b)(2).)

VI. Summary and Conclusions

Under 21 CFR 170.3(i), safety of a food additive means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. FDA's regulations reflect the congressional judgment that the additive must be properly tested and the tests carefully evaluated, but the additive need not, indeed cannot, be shown to be safe to an absolute certainty. The House Report on the Food Additives Amendment stated:

> Safety requires proof of a reasonable certainty that no harm will result from the proposed use of the additive. It does not—and cannot—require proof beyond any possible doubt that no harm will result under any conceivable circumstance.

(H.R. Rept. No. 2284, 85th Cong., 2d Sess., 1958.)

Acesulfame potassium has been thoroughly tested for safety and the data have been reviewed by the agency. As discussed above, the agency has concluded that the studies conducted to establish the safety of this compound are adequate to demonstrate, to a reasonable certainty, the safety of acesulfame potassium for its intended uses.

The petitioner has the burden to demonstrate safety before FDA will approve the use of a food additive. Nevertheless, once the agency makes a finding of safety in a listing document, the burden shifts to an objector, who

[17] The agency noted in the final rule that the historical control data that the agency evaluated were "* * * from seven comparable studies, performed at (the same) testing laboratory around the same time period as the acesulfame potassium study * * *" (See 53 FR 28379 at 28381 and Ref. 6 of final rule).

[18] Historical control data are used to establish the background rates for tumor incidence. The variation in tumor rates among groups of test animals that is due to the spontaneous incidence of a tumor is the key information sought. Wide variations in the spontaneous incidence of a tumor show that tumor incidence can be expected to vary for reasons other than treatment with the test substance.

must come forward with evidence that calls into question FDA's conclusion (*American Cyanamid Co.* v. *FDA*, 606 F2d. 1307, 1314–1315 (D. C. Cir. 1979)).

CSPI has neither submitted new information to support its claim that FDA incorrectly concluded that acesulfame potassium is safe, nor has CSPI established that the agency overlooked significant information in reaching its conclusion. Indeed, CSPI presents no evidence that has not already been carefully reviewed and weighed by the agency. The agency has determined that the objections do not raise genuine and substantial issues of fact that would justify an evidentiary hearing on any of the objections raised. (See § 12.24(b).) Accordingly, FDA is overruling CSPI's objections and is denying CSPI's request for a hearing. In addition, CSPI's request for a stay of the effectiveness of the July 28, 1988, regulation until a hearing is held is moot because FDA is denying the hearing requests. FDA is thus confirming July 28, 1988, as the effective date of the regulation.

VII. References

The following references have been placed on display in the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD, 20857, and may be seen in that office by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Cancer Assessment Committee, Memorandum of Conferences, November 21, 1983, February 21, 1985, December 12, 1985, and June 17, 1986.

2. FDA, Bureau of Foods, "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food," 1982.

3. Feron, V.J., et al., "Basic Requirements for Long-term Assays for Carcinogenicity." in "Long-term and Short-term Assays for Carcinogens: A Critical Appraisal," International Agency for Research on Cancer, IARC Monographs, Supplement 2, 1980, pp. 21–83.

4. Board of Scientific Counselors, National Toxicology Program, "Report of the NTP Ad Hoc Panel on Chemical Carcinogenesis Testing and Evaluation," 1984, pp. 188–190.

5. Taylor, L.L., Food Additives Evaluation Branch, memorandum of December 3, 1984.

6. Chi, R.K., Experimental Design and Evaluation Branch, memorandum of August 15, 1986.

7. Taylor, L.L., Additives Evaluation Branch, memorandum of June 19, 1986.

8. De Groot, A.P., and V. J. Feron, CIVO Institute, "Statement on: Historical Control Data on Lung Tumors," food additive petition 2A3659, submission of April 23, 1986.

9. Interagency Regulatory Liaison Group, Work Group on Risk Assessment, "Scientific Bases for Identification of Potential Carcinogens and Estimation of Risks," *Journal of the National Cancer Institute*, 63:241, 1979, p. 252.

Dated: February 20, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 92–4425 Filed 2–26–92; 8:45 am]

BILLING CODE 4160–01–M

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of the Assistant Secretary for Public and Indian Housing

24 CFR Part 901

[Docket No. R–92–1520; FR–2897–O–04]

Public Housing Management Assessment Program; Announcement of OMB Approval Number

AGENCY: Office of the Assistant Secretary for Public and Indian Housing, HUD.

ACTION: Interim rule; Announcement of OMB approval number.

SUMMARY: On January 17, 1992 (57 FR 2160), the Department of Housing and Urban Development published in the **Federal Register**, an interim rule that established the Public Housing Management Assessment Program (PHMAP) in accordance with section 502 of the National Affordable Housing Act (approved November 28, 1990, Pub. L. 101–625, hereinafter, NAHA) as amended by the Departments of Veterans Affairs and Housing and Urban Development, and Independent Agencies Appropriations Act, 1992 (approved October 28, 1991, Pub. L. 102–139, hereinafter, 92 App. Act). PHMAP provides policies and procedures for the Department's use in identifying public housing agency (PHA) management capabilities and deficiencies, and allows HUD Field Offices to practice accountability monitoring and risk management.

In the supplementary information section, under the heading Paperwork Reduction Act, it was indicated that information collection requirements contained in the interim rule had been submitted to the Office of Management and Budget (OMB) for review under the Paperwork Reduction Act of 1980, and were pending approval of collections of information by OMB. It also indicated that the OMB control number, when assigned, would be announced by separate notice in the **Federal Register**.

The purpose of this document is to publish the OMB approval number for the section containing information collection requirements.

EFFECTIVE DATE: February 27, 1992.

FOR FURTHER INFORMATION CONTACT: Casimir R. Bonkowski, Director, Office of Management and Policy, Office of Public and Indian Housing, Department of Housing and Urban Development, 451 Seventh Street, SW., Washington, DC 20410, telephone (202) 708–0440. A telecommunications device for hearing or speech impaired persons (TDD) is available at (202) 708–0850. (These are not toll-free telephone numbers.)

SUPPLEMENTARY INFORMATION:

Paperwork Reduction Act

The information collection requirements contained in the regulatory section listed below have been approved by the Office of Management and Budget under the provisions of the Paperwork Reduction Act of 1980 (Pub. L. 96–511) and is assigned the control number listed.

List of Subjects in 24 CFR Part 901

Public housing, Reporting and recordkeeping requirements.

Text of the Amendment

Accordingly, part 901 of title 24 of the Code of Federal Regulations is amended as follows:

1. The authority citation for part 901 continues to read as follows:

Authority: Sec. 6(j), United States Housing Act of 1937 (42 U.S.C. 1437d(j); sec. 502, National Affordable Housing Act (approved November 28, 1990, Pub. L. 101–625); sec. 7(d), Department of Housing and Urban Development Act (42 U.S.C. 3535(d)).

§ 901.100 [Amended]

2. Section 901.100 is amended by adding at the end of the section, the following statement:

(Approved by the Office of Management and Budget under OMB control number 2577–0156).

Dated: February 21, 1992.

Grady J. Norris,

Assistant General Counsel for Regulations.

[FR Doc. 92–4476 Filed 2–26–92; 8:45 am]

BILLING CODE 4210–33–M

DEPARTMENT OF DEFENSE

Department of the Army

32 CFR Part 591

Procurement—General Provisions

AGENCY: Office of the Assistant Secretary of the Army (Research, Development and Acquisition), DOD.

ACTION: Removal of rule.