

SIZE STANDARDS BY SIC INDUSTRY—Continued

[For all industries not specifically listed in this table, except for those in Divisions I and J of the SIC System, the size standard is \$5.0 million in annual receipts]

SIC (* = new SIC code in 1987, not used in 1972)	Description (N.E.C. = not elsewhere classified)	Size standards in number of employees or millions of dollars
8743*	Public Relations Services	\$5.0
8744*	Facilities Support Management Services	\$5.0
	Base Maintenance	\$18.0
8748*	Business Consulting Services, N.E.C.	\$5.0
Major Group 89—Services, Not Elsewhere Classified		
8999	Services, N.E.C.	\$5.0

¹ Megawatt hrs.

² Not Applicable to Government procurement of supplies. The nonmanufacturer size standard of 500 employees shall be used for purposes of Government procurement of supplies.

3. Section 121.601, Standard Industrial Classification Table, footnote 8 is revised to read as follows:

* Offshore Marine Services: The applicable size standard shall be \$18.0 million for firms furnishing specific transportation services to a concern engaged in offshore oil and/or natural gas exploration, drilling production, marine research; such services encompass passenger and freight transportation, anchor handling, and related logistical services to and from the work site.

4. Section 121.601, Standard Industrial Classification Table, footnote 12 is revised to read as follows:

¹² SIC code 5599: For retail firms whose principal line of business is the retail sale of aircraft, a \$10.0 million size standard shall apply.

5. Section 121.601, Standard Industrial Classification Table, footnote 15 is amended by revising the first sentence to read as follows:

¹⁵ Major Group 65—Leasing of building space to the Federal Government by Owners: For purposes of Government procurement, a size standard of \$18.0 million in gross receipts is established for owners of building space that is leased to the Federal Government. The standards for those procurements shall apply to the concern which owns the property and not to those acting as an agent for the owning concern. There is no size standard concerning the agent in a leasing arrangement. * * *

6. Section 121.601, Standard Industrial Classification Table, footnote 16 is revised to read as follows:

¹⁶ Division I—Services: For all industries not specifically listed in this division, the size standard is \$5.0 million.

Dated: July 15, 1993.

Erskine B. Bowles,
Administrator, U.S. Small Business Administration.

[FR Doc. 93-21365 Filed 9-1-93; 8:45 am]

BILLING CODE 8025-01-M

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Chapter I

[Summary Notice No. PR-93-14]

Petition for Rulemaking; Summary of Petitions Received; Dispositions of Petitions Issued

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of petitions for rulemaking received and of dispositions of prior petitions.

SUMMARY: Pursuant to FAA's rulemaking provisions governing the application, processing, and disposition of petitions for rulemaking (14 CFR part 11), this notice contains a summary of certain petitions requesting the initiation of rulemaking procedures for the amendment of specified provisions of the Federal Aviation Regulations and of denials or withdrawals of certain petitions previously received. The purpose of this notice is to improve the public's awareness of, and participation in, this aspect of FAA's regulatory activities. Neither publication of this notice nor the inclusion or omission of information in the summary is intended to affect the legal status of any petition or its final disposition.

DATES: Comments on petitions received must identify the petition docket number involved and must be received November 1, 1993.

ADDRESSES: Send comments on any petition in triplicate to: Federal Aviation Administration, Office of the Chief Counsel, Attn: Rules Docket No. —, 800 Independence Avenue SW., Washington, DC 20591.

The petition, any comments received, and a copy of any final disposition are

filed in the assigned regulatory docket and are available for examination in the Rules Docket (AGC-10), room 915G, FAA Headquarters Building (FOB 10A), 800 Independence Ave. SW., Washington, DC 20591; telephone (202) 267-3132.

FOR FURTHER INFORMATION CONTACT:

Mr. Frederick M. Haynes, Office of Rulemaking (ARM-1), Federal Aviation Administration, 800 Independence Avenue SW., Washington, DC 20591; telephone (202) 267-3939.

This notice is published pursuant to paragraphs (b) and (f) of § 11.27 of part 11 of the Federal Aviation Regulations (14 CFR part 11).

Issued in Washington, DC on August 26, 1993.

Danvers Long,

Acting Assistant Chief Counsel for Regulations.

Petitions for Rulemaking

Docket No.: 27375.

Petitioner: Professional Pilots Federation.

Regulations Affected: 14 CFR 121.383(c).

Description of Rulechange Sought: To modify § 121.383 by repealing subsection (c), thereby negating the present requirement that part 121 air carriers refrain from utilizing pilots who have reached the age of 60 and permitting pilots to operate in that capacity after reaching the age of 60.

Petitioner's Reason for the Request:

The petitioner feels that Federal law and policy; operational and regulatory developments since promulgation of the rule in 1960; together with the results of the recent FAA Civil Aeromedical Institute study that found no correlation between increased pilot age and increased accident rates; compel repeal of the rule.

Disposition of Petitions

Docket No.: 25850.

Petitioner: The Aviation Consumer Action Project and Victims of Pan AM Flight 103.

Sections of the FAR Affected: 14 CFR part 108.

Description of Rulechange Sought: To require U.S. air carriers to notify passengers of credible threats to flights and to establish a hotline to supply information about all threats.

Denial, August 10, 1993.

[FR Doc. 93-21394 Filed 9-1-1993-8:45 am]

BILLING CODE 4910-13-M

14 CFR Part 71

[Airspace Docket No. 93-AAL-2]

Proposed Modification of Class E Airspace; Kotzebue, AK

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of proposed rulemaking.

SUMMARY: This notice proposed to modify the Class E airspace at Kotzebue, AK. The proposed action would correct the legal description which inadvertently eliminated the Class E extensions during the Terminal Airspace Reconfiguration Amendment No. 71-16. Airspace Reclassification, which becomes effective September 16, 1993, will discontinue the use of the term "control zone," and airspace designated from the surface for an airport where there is no operating control tower will be Class E airspace. The intended effect of this proposal is to provide adequate Class E airspace for instrument flight rules (IFR) operators executing established standard instrument approach procedures (SIAP).
DATES: Comments must be received on or before October 14, 1993.

ADDRESSES: Send comments on the proposal in triplicate to: Federal Aviation Administration, Manager, Air Traffic Division, AAL-500, Docket No. 93-AAL-02, 222 West 7th Avenue #14, Anchorage, AK 99513-7587.

The official docket may be examined in the Office of the Assistant Chief Counsel for the Alaskan Region, Third Floor, Module B, Federal Building U.S. Courthouse, 222 West 7th Avenue, Anchorage, AK.

An informal docket may also be examined during normal business hours in the Office of the Manager, Air Traffic Division, at the address shown above.

FOR FURTHER INFORMATION CONTACT: Robert C. Durand, System Management Branch, AAL-531, Federal Aviation Administration, Module G, 222 West

7th Avenue #14, Anchorage, AK 99513-7587; telephone number: (907) 271-5898.

SUPPLEMENTARY INFORMATION:**Comments Invited**

Interested parties are invited to participate in this proposed rulemaking by submitting such written data, views, or arguments as they may desire. Comments that provide the factual basis supporting the views and suggestions presented are particularly helpful in developing reasoned regulatory decisions on the proposal. Comments are specifically invited on the overall regulatory, aeronautical, economic, environmental, and energy-related aspects of the proposal.

Communications should identify the airspace docket number and be submitted in triplicate to the address listed above. Commenters wishing the FAA to acknowledge receipt of their comments on this notice must submit with those comments a self-addressed, stamped postcard on which the following statement is made: "Comments to Airspace Docket No. 93-AAL-2." The postcard will be date/time stamped and returned to the commenter. All communications received on or before the specified closing date for comments will be considered before taking action on the proposed rule. The proposal contained in this notice may be changed in light of comments received. All comments submitted will be available for examination in the System Management Branch, Air Traffic Division, at Module G, Federal Building U.S. Courthouse, 222 West 7th Avenue, Anchorage, AK, both before and after the closing date for comments. A report summarizing each substantive public contact with FAA personnel concerned with this rulemaking will be filed in the docket.

Availability of NPRM's

Any person may obtain a copy of this Notice of Proposed Rulemaking (NPRM) by submitting a request to the Federal Aviation Administration, System Management Branch, AAL-531, Air Traffic Division, 222 West 7th Avenue #14, Anchorage, AK 99513-7587. Communications must identify the notice number of this NPRM. Persons interested in being placed on a mailing list for future NPRM's should also request a copy of Advisory Circular No. 11-2A, which describes the application procedure.

The Proposal

The FAA is considering an amendment to part 71 of the Federal Aviation Regulations (14 CFR part 71) to

modify the Class E airspace at Kotzebue, AK. This amendment would correct the legal description which inadvertently eliminated the control zone extensions during the Terminal Airspace Reconfiguration Amendment No. 71-16. These changes are needed to provide controlled airspace to the surface to contain IFR operations at the airport. Airspace reclassification, which becomes effective September 16, 1993, will discontinue the use of the term "control zone," and airspace designated from the surface, including any arrival extensions, for an airport where there is no operating control tower will be Class E airspace. The intended effect of this proposal is to provide adequate Class E airspace for IFR operators executing the VOR and NDB SIAP's at the Kotzebue Airport. The coordinates for this airspace docket are based on North American Datum 83. Class E airspace areas designated as surface areas for airports are published in Paragraph 6002 of FAA Order 7400.9A, dated June 17, 1993, and effective September 16, 1993, which is incorporated by reference in 14 CFR 71.1 in effect as of September 16, 1993. The Class E airspace designation listed in this document would be published subsequently in the Order.

The FAA has determined that this proposed regulation only involves an established body of technical regulations for which frequent and routine amendments are necessary to keep them operationally current. It, therefore—(1) is not a "major rule" under Executive Order 12291; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979); and (3) does not warrant preparation of a regulatory evaluation as the anticipated impact is so minimal. Since this is a routine matter that will only affect air traffic procedures and air navigation, it is certified that this rule, when promulgated, will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act.

List of Subjects in 14 CFR Part 71

Airspace, Incorporation by reference, Navigation (air).

The Proposed Amendment

In consideration of the foregoing, the Federal Aviation Administration proposes to amend 14 CFR part 71 in effect as of September 16, 1993, as follows:

PART 71—[AMENDED]

1. The authority citation for 14 CFR part 71 continues to read as follows:

Authority: 49 U.S.C. app. 1348(a), 1354(a), 1510; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963 Comp., p. 389; 49 U.S.C. 106(g); 14 CFR 11.69.

§ 71.1 [Amended]

2. The incorporation by reference in 14 CFR 71.1 of the Federal Aviation Administration Order 7400.9A, Airspace Designations and Reporting Points, dated June 17, 1993, and effective September 16, 1993, is amended as follows:

Paragraph 6002 Class E airspace areas designated as a surface area for an airport

* * * * *

AAL AK E2 Kotzebue, AK [Revised]
Kotzebue, Ralph Wien Memorial Airport, AK
(lat. 66°53'04"N, long. 162°35'56"W)
Kotzebue VOR/DME (lat. 66°53'08"N, long.
162°32'24"W)
Hotham NDB (lat. 66°54'05"N, long.
162°33'52"W)

Within a 4.3-mile radius of the Ralph Wien Memorial Airport and within 2.6 miles each side of the 039° bearing from the Hotham NDB extending from the 4.3-mile radius to 8.9 miles northeast of the airport and within 2.4 miles each side of the 091° radial from the Kotzebue VOR/DME extending from the 4.3-mile radius to 11.5 miles east of the airport and within 2.4 miles each side of the 278° radial from the Kotzebue VOR/DME extending from the 4.3-mile radius to 10.2 miles west of the airport. This Class E airspace area is effective during the specific dates and times established in advance by a Notice to Airmen. The effective date and time will thereafter be continuously published in the Supplemental Alaska (Airport/Facility Directory).

* * * * *

Issued in Anchorage, AK, on August 18, 1993.

Henry A. Elias,

Manager, Air Traffic Division, Alaskan Region.

[FR Doc. 93–21388 Filed 9–1–93; 8:45 am]

BILLING CODE 4910–13–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 207

[Docket No. 92N–0291]

Drug Listing Compliance Verification Reports

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend its drug listing regulations to codify FDA's current practice of periodically sending drug listing information to drug firms (manufacturers, repackers, and private label distributors) with a request that they review, correct, and return it to FDA within 30 days of its receipt. The proposal would help the agency maintain an accurate and complete list of currently marketed drug products.

DATES: Comments by November 1, 1993. FDA proposes that any final rule based on this proposal become effective 30 days after its date of publication in the **Federal Register**.

ADDRESSES: Written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Howard P. Muller, Center for Drug Evaluation and Research (HFD–362), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–295–8049.

SUPPLEMENTARY INFORMATION:

I. Background

The Federal Food, Drug, and Cosmetic Act (the act) requires a list of all drug products in commercial distribution be provided to the agency. Section 510 of the act (21 U.S.C. 360) requires the owner or operator of every drug establishment engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs to register the establishment with FDA and to submit to the agency a list of its drug products. The act also requires that this list be updated every 6 months (21 U.S.C. 360(j)(2)).

The Drug Listing Branch provides FDA with current information on many drugs in commercial distribution in the United States. Many of the agency's major drug regulatory projects, such as product recalls, depend upon complete and accurate drug listing information. Other Government agencies also use the drug listing information. For example, the Health Care Financing Administration uses the data base to identify reimbursable products for the Medicaid program.

A. Product Listing and Establishment Registration Forms

FDA's regulations in 21 CFR part 207 implement 21 U.S.C. 360. Under 21 CFR 207.21, the owner or operator of an establishment must register the establishment within 5 days of entering into the manufacture or processing of a

drug product and must list every drug product in commercial distribution. The establishment must use Form FDA–2656 for the initial registration, listing such information as its business name and address, and the type of ownership or operation (see 21 CFR 207.22 and 207.25). FDA then assigns an establishment registration number. In addition, each establishment is required to submit a list of drugs, including bulk drug substances, on Form FDA–2657 and to update this list each June and December (see 21 CFR 207.22, 207.25, and 207.30). (If a registered establishment reports on behalf of a private label distributor, 21 CFR 207.20 requires the use of Form FDA–2658.) Forms FDA–2657 and FDA–2658 are used to provide required information on each marketed drug, including: (1) The product trade name, (2) the package size and type, (3) a copy of the labels and package insert, (4) the quantity of an ingredient, and (5) the initial marketing date.

B. Compliance Verification Reports

FDA maintains a computer data base containing the establishment registration and drug product information submitted by drug establishments on Forms FDA–2656, FDA–2657, and FDA–2658. The computer data base has two major components: (1) A registration component containing the files on the registered establishments, and (2) a drug listing component containing drug product information in separate files for prescription, over-the-counter, and bulk drug products.

An internal Government study tested the accuracy of the prescription drug listing files by contacting many drug firms to determine whether the information contained in the data base corresponded to the products actually marketed by the firm. The study uncovered a substantial number of errors, due to a variety of causes. For example, some firms failed to list products or listed products inaccurately. Also, FDA has experienced some data processing problems, which the agency is working to correct.

FDA has a compliance program designed to increase the accuracy of the agency's computerized drug product files. The initial phase of the program is focusing on the prescription drug product file. As part of the compliance program, the agency periodically sends to each drug firm a hard copy printout of the agency's computer drug product files that lists the establishment's prescription drugs as reported on Form FDA–2657 or Form FDA–2658. This printout is known as the "Compliance

Verification Report." FDA attaches to the Compliance Verification Report a letter that asks each establishment to verify or correct the listed information and return it to the agency within 30 days. The letter explains that the drug listing information entered in the Compliance Verification Report will substitute for the corresponding portion of the next required updating of drug listing requirements and will not need to be resubmitted on Form FDA-2657. The letter contains instructions regarding other corrections that must be made on Form FDA-2657 or Form FDA-2658 rather than on the Compliance Verification Report.

II. Explanation of the Proposed Rule

FDA is proposing to amend 21 CFR part 207 to incorporate the Compliance Verification Report into the drug listing regulations. Current § 207.3 would be amended in paragraph (a)(3), § 207.31 would be redesignated as § 207.32, and new § 207.31 would describe the Compliance Verification Report and require that any establishment that receives a Compliance Verification Report review, correct, and return it to FDA within 30 days of its receipt. Information entered into the Compliance Verification Report that would fulfill an information requirement of any subsequent semi-annual drug listing requirement would not need to be resubmitted on Form FDA-2657. Drug products, in commercial distribution, which are not listed on the Compliance Verification Report, must be submitted by the establishment to FDA on a Form FDA-2657 or Form FDA-2658 in accordance with the regulations.

III. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(8) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IV. Economic Impact

The agency has carefully considered the economic impact of this proposed rule and has determined that it requires neither a regulatory impact analysis as specified by Executive Order 12291, nor a regulatory flexibility analysis as defined in the Regulatory Flexibility Act (Pub. L. 96-354). The agency believes that the proposed rule, if finalized, would generate costs that are well below the thresholds that would signify a

major rule. Therefore, the proposed rule does not require a regulatory impact analysis.

The proposed rule would revise the current reporting requirements, which will enable FDA to maintain a more accurate data base of drug listing information. Further, the proposed rule would provide a procedure for drug firms to verify, or correct, drug listing information related to their drug products. Much of the information that is entered into the Compliance Verification Report will substitute for current updating information requirements. No new information would be required by the proposed rule.

FDA believes that, if any costs result from the rule, the amount would be comparatively small in relation to the potential benefits. Accordingly, the agency concludes that the proposed rule is not a major rule as defined in Executive Order 12291. Further, the agency certifies that this proposed rule, if implemented, would not have a significant economic impact on a substantial number of small entities, as defined by the Regulatory Flexibility Act.

V. Paperwork Reduction Act of 1980

All reporting and recordkeeping requirements for the Compliance Verification Report as required by this proposed regulation have been approved by the Office of Management and Budget (OMB) under control number 0910-0045 "Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution."

The Compliance Verification Report does not solicit any new or additional information from drug establishments than is already required and approved under OMB No. 0910-0045. As explained elsewhere in this preamble, the Compliance Verification Report provides establishments with a summary of their marketed products as reflected in FDA files. Establishments are asked to update this information directly on the report, instead of on Form FDA-2657. Any new product information would continue to be listed on Form FDA-2657.

VI. Effective Date

FDA proposes that any final rule based on this proposal become effective 30 days after its date of publication in the Federal Register.

VII. Request for Comments

Interested persons may, on or before November 1, 1993, submit to the Dockets Management Branch (address

above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 207

Drugs, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 207 be amended as follows:

PART 207—REGISTRATION OF PRODUCERS OF DRUGS AND LISTING OF DRUGS IN COMMERCIAL DISTRIBUTION

1. The authority citation for 21 CFR part 207 continues to read as follows:

Authority: Secs. 301, 501, 502, 505, 506, 507, 510, 512, 701, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331, 351, 352, 355, 356, 357, 360, 360b, 371, 374); sec. 351 of the Public Health Service Act (42 U.S.C. 262).

§ 207.3 [Amended]

2. Section 207.3 *Definitions* is amended in paragraph (a)(3) by removing "§ 207.31(a)(2)" and adding in its place "§ 207.32(a)(2)".

§ 207.32 [Redesignated from § 207.31]

3. Section 207.31 is redesignated as § 207.32 and new § 207.31 is added to subpart C to read as follows:

§ 207.31 Compliance verification report.

(a) FDA periodically reviews the accuracy of its drug listing files by mailing to drug establishments a Compliance Verification Report, which is a copy of their individual drug listing file. The Compliance Verification Report contains information on some or all of the drug products listed by the establishment.

(b) An establishment that receives a Compliance Verification Report shall review and correct the information in the Compliance Verification Report and return it to FDA within 30 days of its receipt. Information supplied in response to the Compliance Verification Report that fulfills an information requirement under § 207.30 need not be resubmitted on Form FDA-2657.

(c) Establishments that have drug products in commercial distribution, which are not listed on the Compliance Verification Report, shall submit these drug product listings to FDA on Form FDA-2657 (and Form FDA-2658, when reporting for a private label distributor), in accordance with 207.20, 207.21, 207.22, 207.25, and 207.30.

Dated: June 30, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 93-21245 Filed 8-31-93; 8:45 am]

BILLING CODE 4160-01-F

21 CFR Part 334

[Docket No. 78N-036L]

RIN 0905-AA06

Laxative Drug Products For Over-The-Counter Human Use; Proposed Amendment to The Tentative Final Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking to amend the tentative final monograph for over-the-counter (OTC) laxative drug products to include conditions under which docusate salts, i.e., docusate calcium, docusate potassium, and docusate sodium, are generally recognized as safe and effective and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products (the Panel), public comments on the advance notice of proposed rulemaking that was based on those recommendations, and a comment submitted in response to the tentative final monograph for OTC laxative drug products that was published in the Federal Register of January 15, 1985 (50 FR 2124). This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by December 31, 1993. New data by September 2, 1994. Comments on the new data by November 2, 1994. Written comments on the agency's economic impact determination by December 31, 1993.

ADDRESSES: Written comments, objections, new data, or requests for oral

hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-5000.

SUPPLEMENTARY INFORMATION: In the Federal Register of March 21, 1975 (40 FR 12902), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC laxative, antidiarrheal, emetic, and antiemetic drug products, together with the recommendations of the Panel, which was the advisory review panel responsible for evaluating data on the active ingredients in these drug classes. The agency's proposed regulation, in the form of a tentative final monograph, for OTC laxative drug products was published in the Federal Register of January 15, 1985 (50 FR 2124).

In the advance notice of proposed rulemaking, the Panel recommended that docusate calcium¹, docusate potassium², and docusate sodium³ in the recommended dosages be classified in Category I (generally recognized as safe and effective) as OTC stool softener laxatives (40 FR 12902 at 12912). Subsequently, FDA became aware of information in animal studies implicating docusate sodium as a potential animal teratogen (Refs. 1, 2, and 3), thereby raising questions about the Panel's conclusions and recommendations for these laxative ingredients. Because evaluation of the animal studies had not been completed when FDA published the tentative final monograph on OTC laxative drug products in 1985, the agency did not discuss docusate salts and stated that a separate document would be published to address the status of these ingredients (50 FR 2124 at 2125). The agency has completed its evaluation of these animal studies and is now proposing that these

¹ The Panel designated this ingredient "dioctyl calcium sulfosuccinate." However, docusate calcium is currently the official name for this ingredient in the "USAN and the USP dictionary of drug names, 1992."

² The Panel designated this ingredient "dioctyl potassium sulfosuccinate." However, docusate potassium is currently the official name for this ingredient in the "USAN and the USP dictionary of drug names, 1992."

³ The Panel designated this ingredient "dioctyl sodium sulfosuccinate." However, docusate sodium is currently the official name for this ingredient in the "USAN and the USP dictionary of drug names, 1992."

docusate salts are safe and effective for OTC laxative use.

In response to the advance notice of proposed rulemaking, seven manufacturers, one university, and one individual submitted comments concerning docusate salts. These comments are also addressed in this document. Copies of the comments received are on public display in the Dockets Management Branch (address above).

The chemical name for docusate sodium is butanedioic acid, sulfo-, 1,4-bis(2-ethylhexyl)ester, sodium salt (Ref. 4). Docusate calcium, docusate potassium, and docusate sodium are chemically identical, with the exception of the substitution of a calcium or potassium salt for the sodium salt. The agency is unaware of any data demonstrating that the substitution of the calcium or potassium ion for the sodium ion in the docusate formulation would have a significant effect on the biological activity of the docusate anion. The agency believes that any toxicological effects are due to the organic portion of the molecule, and not to the calcium, potassium, or sodium portion.

Oral administration of docusate calcium and docusate sodium has been studied in pregnant rats (Ref. 1). Ingestion of docusate calcium at levels of 1,500 to 2,000 milligrams per kilogram (mg/kg) body weight or docusate sodium at levels of 2,000 mg/kg by pregnant rats throughout gestation days 6 through 15 resulted in increased fetal resorptions and produced significant incidences of fetal malformations, consisting primarily of exencephaly frequently associated with spina bifida and microphthalmia. However, 2,000 mg/kg of docusate calcium was not teratogenic when ingested for shorter periods of time (days 6 to 8, 8 to 10, or 10 to 12) during gestation.

In the same study, gavage dosing of docusate calcium at 750 mg/kg per day (mg/kg/day) during days 6 to 15 of gestation resulted in fetal resorptions and skeletal abnormalities, primarily incomplete ossification of cranial bones. In most instances, mean maternal weight gain was somewhat reduced after gavage doses of 750 mg/kg. Docusate calcium administered by gavage to pregnant rats at 1,000 and 1,500 mg/kg during various 3-day periods of gestation was not teratogenic but did cause fetal resorption and maternal deaths. The data from these teratology studies in the rat support a no-effect level of 500 mg/kg of docusate calcium, which is 100 times the human laxative dose of 300 mg/day.