

DATES: Submit written comments on the collection of information by September 5, 2000.

ADDRESSES: Submit written comments on the collection of information to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Peggy Schlosburg, Office of Information Resources Management (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1223.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3520), Federal agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal agencies to provide a 60-day notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Affirmation of Generally Recognized As Safe (GRAS) Status (21 CFR 170.35(c)(1))—(OMB Control Number 0910-0132)—Extension

Under authority of sections 201, 402, 409, and 701 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321, 342, 348, and 371), FDA reviews petitions for affirmation as GRAS that are submitted on a voluntary basis by the food industry and other interested parties. Under section 409 of the act, the agency has the authority to regulate food additives. Section 201(s) of the act, defines "food additive" and expressly excludes from the definition substances GRAS for use in food.

Specifically under section 201(s) of the act, a substance is GRAS if it is generally recognized among experts qualified by scientific training and experience to evaluate its safety, to be

safe through either scientific procedures or common use in food. The act has historically been interpreted to permit food manufacturers to make their own determination that use of a substance in food is GRAS. To implement the GRAS provisions of the act, FDA has issued procedural regulations under § 170.35(c)(1) (21 CFR 170.35(c)(1)). These regulations establish a process by which a person may obtain FDA concurrence with a GRAS determination; this concurrence is referred to as "GRAS affirmation." These regulations set forth the information to be submitted to FDA to obtain agency concurrence that a substance is GRAS (§ 170.35(c)(1)).

GRAS petitions are reviewed by FDA to ascertain whether the available data establish that the intended use of the substance is GRAS based upon either a history of the safe use of the substance, or upon widely available safety data (scientific procedures). The GRAS affirmation process is a voluntary one, and there is some risk that FDA may not agree with the petitioner's GRAS determination. The GRAS petition process does provide a public procedure for coordinating GRAS determinations. The process reduces the potential for public health problems when substances are marketed based upon unwarranted safety determinations and allows a food manufacturer to rely on the lawful status of a substance that has been affirmed by FDA as GRAS.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

21 CFR section	No. of respondents	Annual frequency per response	Total annual responses	Hours per response	Total hours
170.35(c)(1)	1	1	1	2,614 (average)	2,614

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

FDA estimates that it may receive one GRAS petition annually. Although the burden varies with the type, size, and complexity of the petition submitted, GRAS petitions may involve analytical work, analysis of appropriate toxicological studies, and the work of drafting the petition itself. Since 1980, FDA has not received any petitions for affirmation of GRAS status under 21 CFR part 186—Indirect Food Substances Affirmed As Generally Recognized As Safe. Section 184.1(a) (21 CFR 184.1(a)) affirms the use of those substances affirmed as GRAS in 21 CFR part 184—

Direct Food Substances Affirmed As Generally Recognized As Safe, for use as indirect food ingredients.

Dated: June 27, 2000.

William K. Hubbard,

Senior Associate Commissioner for Policy, Planning, and Legislation.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00N-1224]

Agency Information Collection Activities; Submission for OMB Review; Comment Request; Guidance for Industry; Submitting and Reviewing Complete Responses to Clinical Holds

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that the proposed collection of information listed below has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Submit written comments on the collection of information by August 4, 2000.

ADDRESSES: Submit written comments on the collection of information to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Wendy Taylor, Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: Karen L. Nelson, Office of Information Resources Management (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1482.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Guidance for Industry: Submitting and Reviewing Complete Responses to Clinical Holds

On November 21, 1997, the President signed into law the Food and Drug Administration Modernization Act (the Modernization Act) (Public Law 105-115). Section 117 of the Modernization Act provides that a written request to

FDA from the applicant of an investigation that a clinical hold be removed shall receive a decision in writing, specifying the reasons for that decision, within 30 days after receipt of such request. A clinical hold is an order issued by FDA to the applicant to delay a proposed clinical investigation or to suspend an ongoing investigation for a drug or biologic. An applicant may respond to a clinical hold.

Section 505(i)(3)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)(3)(C)) requires that any written request to FDA from the sponsor of an investigation that a clinical hold be removed must receive a decision, in writing and specifying the reasons, within 30 days after receipt of the request. The request must include sufficient information to support the removal of the clinical hold.

In the **Federal Register** of May 14, 1998 (63 FR 26809), FDA published a notice of availability of a guidance that described how applicants should submit responses to clinical holds so that they may be identified as complete responses, and the agency can track the time to respond. FDA is now issuing a revised guidance.

The revised guidance states that FDA will respond in writing within 30 calendar days of receipt of a sponsor's request to release a clinical hold and a complete response to the issue(s) that led to the clinical hold. An applicant's complete response to an investigational new drug application (IND) clinical hold is a response in which all clinical

hold issues identified in the clinical hold letter have been addressed.

The guidance requests that applicants type in large, bold letters at the top of the cover letter of the complete response "Clinical Hold Complete Response" to expedite review of the response. The guidance also requests that applicants submit the complete response letter in triplicate to the IND, and that they fax a copy of the cover letter to FDA's contact, listed in the clinical hold letter, who is responsible for the IND. The guidance requests more than an original and two copies, i.e., three copies, of the cover letter in order to ensure that the submission is received and handled in a timely manner.

Based on data concerning the number of complete responses to clinical holds received by the Center for Drug Evaluation and Research (CDER) from July 1, 1998, to June 30, 1999, CDER estimates that approximately 48 responses are submitted annually from approximately 43 applicants, and that it takes approximately 284 hours to prepare and submit to CDER each response.

Based on data concerning the number of complete responses to clinical holds received by the Center for Biologics Evaluation and Research (CBER) in fiscal year 1999, CBER estimates that approximately 134 responses are submitted annually from approximately 110 applicants, and that it takes approximately 284 hours to prepare and submit to CBER each response.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

Complete responses to clinical holds	No. of respondents	No. of responses per respondent	Total annual responses	Hours per response	Total hours
CDER	43	approx. 1	48	284	13,632
CBER	110	approx. 1	134	284	38,056
Total					51,688

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

In the **Federal Register** of April 13, 2000 (65 FR 19911), the agency requested comments on the proposed collections of information. No significant comments were received.

Dated: June 27, 2000.

William K. Hubbard,

Senior Associate Commissioner for Policy, Planning, and Legislation.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Microbiology Devices Panel of the Medical Devices Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration

(FDA). At least one portion of the meeting will be closed to the public.

Name of Committee: Microbiology Devices Panel of the Medical Devices Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the agency on FDA's regulatory issues.

Date and Time: The meeting will be held on July 27, 2000, 10:30 a.m. to 5:30 p.m. and July 28, 2000, 8 a.m. to 5 p.m.

Location: Holiday Inn, Walker/Whetstone Rooms, Two Montgomery Village Ave., Gaithersburg, MD.