Dated: April 30, 1999.

Jane L. Browning,

Executive Director, PCMR.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99N–1010]

Agency Information Collection Activities: Proposed Collection; Comment Request; Investigational New Drug Regulations

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal agencies are required to publish a notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on requirements governing applications for FDA's approval to market a new drug.

DATES: Submit written comments on the collection of information by July 6, 1998.

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: Karen Nelson, Office of Information Resources Management (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–1482.

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 listed 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.

Investigational New Drug (IND) Regulations—21 CFR Part 312 (OMB Control Number 0910–0014—Extension)

FDA is requesting OMB approval for the reporting and recordkeeping requirements contained in FDA's regulation ''Investigational New Drug Application'' (part 312 (21 CFR part 312)). This regulation implements provisions of section 505(i) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(i)) to issue regulations under which the clinical investigation of the safety and effectiveness of unapproved new drugs and biological products can be conducted.

FDA is charged with implementing statutory requirements that drug products marketed in the United States be shown to be safe and effective, properly manufactured, and properly labeled for their intended uses. Section 505(a) of the act provides that a new drug may not be introduced or delivered for introduction into interstate commerce in the United States unless FDA has previously approved a new drug application (NDA). FDA approves an NDA only if the sponsor of the application first demonstrates that the drug is safe and effective for the conditions prescribed, recommended, or suggested in the product's labeling. Proof must consist, in part, of adequate and well-controlled studies, including studies in humans, that are conducted by qualified experts. The IND regulations establish reporting requirements that include an initial application as well as amendments to that application, reports on significant revisions of clinical investigation plans, and information on a drug's safety or effectiveness. In addition, the sponsor is required to give FDA an annual summary of the previous year's clinical experience. Submissions are reviewed by medical officers and other agency scientific reviewers assigned responsibility for overseeing the specific study. The IND regulations also contain recordkeeping requirements that pertain to the responsibilities of sponsors and investigators. The detail and complexity of these requirements are dictated by the scientific procedures and human subject safeguards that must be followed in the clinical tests of investigational new drugs.

The IND information collection requirements provide the means by which FDA can: (1) Monitor the safety of ongoing clinical investigations; (2) determine whether the clinical testing of a drug should be authorized; (3) ensure production of reliable data on the metabolism and pharmacological action of the drug in humans; (4) obtain timely information on adverse reactions to the drug; (5) obtain information on side effects associated with increasing doses; (6) obtain information on the drug's effectiveness; (7) ensure the design of well-controlled, scientifically valid studies; and (8) obtain other information pertinent to determining whether clinical testing should be continued and information related to the protection of human subjects. Without the information provided by industry in response to the IND regulations, FDA cannot authorize or monitor the clinical investigations which must be conducted prior to authorizing the sale and general use of new drugs. These reports enable FDA to monitor a study's progress, to assure subject safety, to assure that a study will be conducted ethically, and to increase the likelihood that the sponsor will conduct studies that will be useful in determining whether the drug should be marketed and available for use in medical practice.

The following two forms are required under part 312: Form FDA–1571 entitled ''Investigational New Drug Application.''A person who intends to conduct a clinical investigation submits this form to FDA. It includes: (1) A cover sheet containing background information on the sponsor and investigator; (2) a table of contents; (3) an introductory statement and general investigational plan; (4) an investigator's brochure describing the drug substance;

(5) a protocol for each planned study; (6) chemistry, manufacturing, and control information for each investigation; (7) pharmacology and toxicology information for each investigation; and (8) previous human experience with the investigational drug.

Form FDA–1572 entitled ''Investigator Statement.'' Before permitting an investigator to begin participation in an investigation, the sponsor must obtain and record this form. It includes background information on the investigator and the investigation, and a general outline of the planned investigation and the study protocol.

FDA is requesting OMB approval for the following reporting and recordkeeping requirements in part 312:

TABLE 1.—REPORTING REQUIREMENTS

21 CFR Section	Explanations
312.7(d)	Applications for permission to sell an investigational new drug.
312.10(a)	Applications for waiver of requirements under part 312. Only emergency requests are estimated under this section; other requests are included under §§ 312.23 and 312.31.
312.20(c)	Applications for investigations involving an exception from informed consent under § 50.24 (21 CFR 50.24). Estimates for this requirement are included under § 312.23.
312.23	IND (content and format).
312.23(a)(1)	Cover sheet FDA–1571.
312.23(a)(2)	Table of contents.
312.23(a)(3)	Investigational plan for each planned study.
312.23(a)(5)	Investigator's brochure.
312.23(a)(6)	Protocols—Phase 1, 2, and 3.
312.23(a)(7)	Chemistry, manufacturing, and control information.
312.23(a)(7)(iv)(*a*), (*b*), (*c*)	A description of the drug substance, a list of all components, and any placebo used.
312.23(a)(7)(iv)(*d*)	Labeling—copies of labels and labeling to be provided each investigator.
312.23(a)(7)(iv)(*e*)	Environmental impact analysis regarding drug manufacturing and use.
312.23(a)(8)	Pharmacological and toxicology information.
312.23(a)(9)	Previous human experience with the investigational drug.
312.23(a)(10)	Additional information.
312.23(a)(11)	Relevant information.
312.23(f)	Identification of exception from informed consent.
312.30	Protocol amendments.
312.30(a)	New protocol.
312.30(b)	Change in protocol.
312.30(c)	New investigator.
312.30(d)	Content and format.
312.30(e)	Frequency.
312.31	Information amendments.
312.31(b)	Content and format.
	Chemistry, toxicology, or technical information.
312.32	Safety reports.
312.32(c)(1)	Written reports to FDA and to investigators.
312.32(c)(2)	Telephone reports to FDA for fatal or life-threatening experience.
312.32(c)(3)	Format or frequency.
312.32(d)	Followup submissions.
312.33	Annual reports.
312.33(a)	Individual study information.
312.33(b)	Summary information.
312.33(b)(1)	Adverse experiences.
312.33(b)(2)	Safety report summary.
312.33(b)(3)	List of fatalities and causes of death.
312.33(b)(4)	List of discontinuing subjects.
312.33(b)(5)	Drug action.
312.33(b)(6)	Preclinical studies and findings.
312.33(b)(7)	Significant changes.
312.33(c)	Next year general investigational plan.
312.33(d)	Brochure revision.
312.33(e)	Phase I protocol modifications.
312.33(f)	Foreign marketing developments.
312.35	Treatment use of investigational new drugs.
312.35(a)	Treatment protocol submitted by IND sponsor.
312.35(b)	Treatment IND submitted by licensed practitioner.
312.36	Requests for emergency use of an investigational new drug.
312.38(b) and (c)	Notification of withdrawal of an IND.
312.44(c) and (d)	Opportunity for sponsor response to FDA when IND is terminated.
312.45(a) and (b)	Sponsor request for or response to inactive status determination of an IND.
312.47(b)	''End-of-Phase 2'' meetings and ''Pre-NDA'' meetings.

TABLE 1.—REPORTING REQUIREMENTS—Continued

21 CFR Section	Explanations
312.53(c)	Investigator information. Investigator report (Form FDA–1572) and narrative; Investigator's background information; Phase 1 outline of planned investigation; and Phase 2 outline of study protocol; financial disclosure information.
312.54(a) and (b)	Sponsor submissions concerning investigations involving an exception from informed consent under § 50.24.
312.55(b)	Sponsor reports to investigators on new observations, especially adverse reactions and safe use. Only ''new observations'' are estimated under this section; investigator brochures are included under § 312.23.
312.56(b), (c), and (d)	Sponsor monitoring of all clinical investigations, investigators, and drug safety; notification to FDA.
312.58(a)	Sponsor's submission of records to FDA on request.
312.64	Investigator reports to the sponsor.
312.64(a)	Progress reports.
312.64(b)	Safety reports.
312.64(c)	Final reports.
312.64(d)	Financial disclosure reports.
312.66	Investigator reports to Institutional Review Board. Estimates for this requirement are included under § 312.53.
312.70	Investigator disqualification; opportunity to respond to FDA. Estimates for this requirement are not included in the estimates for part 312.
312.83	Sponsor submission of treatment protocol. Estimates for this requirement are included under §§ 312.34 and 312.35.
312.85	Sponsors conducting phase 4 studies. Estimates for these postmarketing studies are not included in the estimates for part 312.
312.110(b)	Request to export an investigational drug.
312.120(b) and (c)(2)	Sponsor's submission to FDA for use of foreign clinical study to support an IND.
312.120(c)(3)	Sponsor's report to FDA on findings of independent review committee on foreign clinical study.
312.130(d)	Request for disclosable information for investigations involving an exception from informed consent under § 50.24.

TABLE 2.—RECORDKEEPING REQUIREMENTS

21 CFR Section	Explanations
312.52(a)	Transfer of obligations to a contract research organization.
312.57(a) and (b)	Sponsor recordkeeping.
312.59	Sponsor recordkeeping of disposition of unused supply of drugs. Estimates for this requirement are included under § 312.57.
312.62(a)	Investigator recordkeeping of disposition of drugs.
312.62(b)	Investigator recordkeeping of case histories of individuals.
312.160(a)	Records maintenance—shipment of drugs for investigational use in laboratory research animals or in vitro tests.
312.160(c)	Shipper records of alternative disposition of unused drugs.

TABLE 3.—ESTIMATED ANNUAL REPORTING BURDEN FOR HUMAN DRUGS[1]

21 CFR Section	No. of Respondents	No. of Responses Per Respondent	Total Annual Responses	Hours per Response	Total Hours
312.7(d)	7	1	7	24	168
312.10(a)	0	0	0	0	0
312.23(a) and (f)	1,601	1.25	1,996	1,600	3,193,600
312.30(a) through (e)	918	14.85	13,629	284	3,870,636
312.31(b)	760	8.87	6,738	100	673,800
312.32(c) and (d)	459	14.33	6,576	32	210,432
312.33(a) through (f)	1,841	2.35	4,318	350	1,511,300
312.35(a) and (b)	1	1	1	300	300
312.36	643	1.2	720	16	11,520
312.38(b)	621	1.24	773	28	21,644
312.38(c)	621	1.24	773	160	123,680
312.44(c) and (d)	710	1.10	780	16	12,480
312.45(a) and (b)	294	1.32	389	12	4,668
312.47(b)	252	1	252	160	40,320
312.53(c)	4,500	1	4,500	80	360,000
312.54(a) and (b)	4	1	4	48	192

TABLE 3.—ESTIMATED ANNUAL REPORTING BURDEN FOR HUMAN DRUGS[1]—Continued

21 CFR Section	No. of Respondents	No. of Responses Per Respondent	Total Annual Responses	Hours per Response	Total Hours
312.55(b)	4,500	1	4,500	48	216,000
312.56(b), (c), and (d)	5	1	5	80	400
312.58(a)	337	1	337	8	2,696
312.64(a) through (d)	8,200	1	8,200	24	196,800
312.110(b)	150	2	303	75	22,725
312.120(b) and (c)(2)	100	2	200	168	33,600
312(c)(3)	100	2	200	40	8,000
312.130(d)	4	1	4	8	32
Total Reporting Burden					10,514,993

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

TABLE 4.—ESTIMATED ANNUAL RECORDKEEPING BURDEN FOR HUMAN DRUGS[1]

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
312.52(a)	360	1	360	2	720
312.57(a) and (b)	4,000	2.05	8,200	100	400,000
312.62(a)	8,200	1	8,200	40	328,000
312.62(b)	8,200	12.2	100,000	40	328,000
312.160(a)	3,400	7.35	25,000	30 min	1,700
312.160(c)	3,400	2.35	8,000	30 min	1,700
Total Recordkeeping Burden					1,060,120
Human Drugs Total Burden Hours					11,575,113

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

TABLE 5.—ESTIMATED ANNUAL REPORTING BURDEN FOR BIOLOGICS[1]

21 CFR Section	No. of Respondents	No. of Responses Per Response	Total Annual Responses	Hours per Response	Total Hours
312.7(d)	9	1.3	12	24	288
312.10(a)	1	1	1	40	40
312.23(a) and (f) and 312.120(b), (c)(2), and (c)(3)	278	1.8	492	1,600	787,200
312.30(a) and (e)	975	6.5	6,411	284	1,820,724
312.31(b)	975	9.2	9,005	100	900,500
312.32(c) and (d) and 312.56(c)	602	6.7	4,034	32	129,088
312.33(a) and (f) and 312.56(c)	1,253	1.6	1,989	350	696,150
312.35(a) and (b)	1	1	1	300	300
312.36	22	5.5	122	16	1,952
312.38(b)	128	1.7	212	28	5,936
312.38(c)	128	1.7	212	160	33,920
312.44(c) and (d)	55	1.9	107	16	1,712
312.45(a) and (b)	74	1.4	105	12	1,260
312.47(b)	150	1.8	274	160	43,840
312.53(c)	672	6.6	4,421	80	353,680
312.54(a) and (b)	4	1	4	48	192
312.55(b)	374	6.1	2,288	48	109,824
312.56(b) and (d)	12	1.6	20	80	1,600
312.58(a)	10	1	10	8	80
312.64(a) and (d)	5,014	1	5,014	24	120,336
312.110(b)	10	1.3	13	75	975
312.130(d)	1	1	1	0.5	0.5
Total Reporting Burden					5,009,597.5

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

TABLE 6.—ESTIMATED ANNUAL RECORDKEEPING BURDEN FOR BIOLOGICS[1]

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
312.52(a)	27	2.5	67	5	135
312.57(a) and (b)	1,253	2	2,506	100	125,300
312.62(a)	5,014	1	5,014	40	200,560
312.62(b)	8,200	12.2	100,000	40	328,000

TABLE 6.—ESTIMATED ANNUAL RECORDKEEPING BURDEN FOR BIOLOGICS[1]—Continued

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
312.160(a)	3,400	7.35	25,000	30 min	1,700
312.160(c)	320	1	320	0.5	160
Total Biologic Recordkeeping Hours					655,855
Total Biologics Burden Hours					5,665,452.5
Total Human Drugs Burden Hours					11,575,113
Total Combined Burdens					17,240,565.5

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

Dated: April 29, 1999.

William K. Hubbard,

Acting Deputy Commissioner for Policy.

[FR Doc. 99–11310 Filed 05–05–99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98N–0811]

Agency Information Collection Activities; Submission for OMB Review; Comment Request; Guidance for Industry: Designation, Development, and Application Review for Products in Fast-Track Drug Development Programs

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 (the PRA).

DATES: Submit written comments on the collection of information by June 7, 1999.

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: Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: JonnaLynn P. Capezzuto, Office of Information Resources Management (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4659.

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: Designation, Development, and Application Review for Products in Fast-Track Drug Development Programs

Section 112(a) of the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Pub. L. 105–115) amends the Federal Food, Drug, and Cosmetic Act (the act) by adding section 506 (21 U.S.C. 356) and authorizes FDA to take appropriate action to facilitate the development and expedite the review of new drugs, including biological products, intended to treat a serious or life-threatening condition and that demonstrate a potential to meet an unmet medical need. The issuance of the guidance will be under section 112(b) of FDAMA, which requires the agency to issue guidance regarding fast-track policies and procedures within 1 year of the date of enactment of FDAMA, November 21, 1997. The guidance will discuss collections of information that are expressly specified under section 506 of the act, other sections of the Public Health Service Act (the PHS Act), or implementing regulations. For example, under section 506 of the act, an applicant who seeks fast-track designation must submit a request to FDA. Some of the support for such a request may be required under regulations, such as parts 312, 314, and 601 (21 CFR parts 312, 314, and 601), which specify the types and format of information and data that should be submitted to FDA for evaluation of the safety and effectiveness of investigational new drug applications (IND's) (part 312), new drug applications (part 314), or biological license applications (part 601). The guidance will describe three general areas involving collection of information: Designation requests, premeeting packages, and requests to submit portions of an application. Of these, designation requests, and premeeting packages in support of obtaining a fast-track program benefit will provide for additional collections of information not provided elsewhere in statute or regulation. Information in support of fast-track designation or fast-track program benefits that has previously been submitted to the agency, in some cases, may be incorporated by referring to them rather than by resubmission. In some instances, a summary of data and information may be submitted in support of fast-track designation or fast-track program benefits. Therefore, FDA anticipates that the PRA reporting burden under the guidance will be minimal.

Under section 506(a)(1) of the act, an applicant who seeks fast-track designation is required to submit a request to the agency. In order to receive a fast-track designation, the requester must establish that the product meets the statutory standard for designation, i.e., that: (1) The product is intended for a serious or life-threatening condition; and (2) the product has the potential to address an unmet medical need. In most cases, the agency expects that information to support a designation request will have been gathered under existing provisions of the act, the PHS Act, or the implementing regulation. Such information, if already submitted to the agency, may be summarized in a fast-track designation request.

The guidance will also recommend that a designation request include, where applicable, additional information not specified elsewhere by statute or regulation. For example, additional information may be needed to show that a product has the potential to meet an unmet medical need where approved therapy exists for the serious or life-threatening condition to be treated. Such information may include: Clinical data, published reports, summaries of data and reports, and a list of references. The amount of information and discussion in a designation request need not be voluminous, but it should be sufficient to permit a reviewer to assess whether the criteria for fast-track designation have been met. After the agency makes a fast-track designation, a sponsor or applicant may submit a premeeting