2004, Critical Path Report,[1] the agency explained that to reduce the time and resources expended during early drug development on candidates that are unlikely to succeed,[2] tools are needed to allow developers to distinguish earlier in the process those candidates that hold promise from those that do not. This guidance describes some exploratory approaches that will protect human subjects while providing early information about candidate performance in humans.

Exploratory IND studies have a number of different goals. In some cases, an exploratory study can help developers gain an understanding of the relationship between a specific mechanism of action and the treatment of a disease. In other cases, a study can provide important information on pharmacokinetics, including, for example, biodistribution of a candidate drug. Whatever the goal of the study, exploratory IND studies can help sponsors identify, early in the process, promising candidates for continued development.

Existing regulations allow a great deal of flexibility in terms of the amount of data that need to be submitted in an IND application, depending on the goals of an investigation, the specific human testing being proposed, and the expected risks. But sponsors have not always taken advantage of that flexibility, and limited, early phase 1 studies, such as those described in this guidance, are often supported by a more extensive preclinical database than is needed.

This guidance applies to exploratory studies (i.e., early phase 1 clinical studies), involving IND and biological products, that assess feasibility for further development of a drug or biological product.[3] For the purposes of this guidance the phrase ''exploratory study'' is intended to describe clinical trials that occur very early in phase 1, involve very limited human exposure, and often have no therapeutic or diagnostic intent.

Typically, these exploratory studies are conducted prior to the traditional dose evaluation, safety, and tolerance studies that ordinarily initiate a clinical drug development program. The amount and type of preclinical information necessary to support an exploratory study will depend on the planned nature and extent of human exposure relative to the toxicity (or lack thereof) at the planned dose. The studies discussed in this guidance ordinarily do not have therapeutic intent. They are designed to evaluate whether a particular candidate should be entered into a drug development program.

FDA published a notice in the **Federal Register** of April 14, 2005 (70 FR 19764), announcing the availability of a draft version of this guidance. The agency was interested in soliciting input on the draft guidance. The comment period closed on July 13, 2005. A number of comments were received on the draft, and the agency considered them very carefully during finalization of the guidance. A number of clarifying changes were made during finalization of the guidance, but substantive changes were not made.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the agency's current thinking on exploratory IND studies. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collection of information has been approved under OMB control number 0910–0014.

III. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper 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 Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: January 3, 2006.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 06–354 Filed 1–12–06; 8:45 am]

BILLING CODE 4160–01–S

[1]Food and Drug Administration, ''Innovation or Stagnation, Challenge and Opportunity on the critical Path to New Medical Products,'' March 2004.

[2]A new medical compound entering phase 1 testing, often representing the culmination of upwards of a decade of preclinical screening and evaluation, is estimated to have only an eight percent chance of reaching the market, ''Critical Path Report,'' March 2004.

[3]This guidance applies to drug and certain well-characterized therapeutic biological products (e.g., recombinant therapeutic proteins and monoclonal antibodies regulated by the Center for Drug Evaluation and Research). The guidance does not apply to human cell or tissue products, blood and blood proteins, vaccines, or to products regulated as devices.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2005D–0286]

Draft Guidance for Industry on Investigational New Drugs; Approaches to Complying with Current Good Manufacturing Practice During Phase 1; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''INDs—Approaches to Complying with CGMP During Phase 1.'' This draft guidance is intended to assist persons producing drug and biological products (investigational drugs) for use during phase 1 development in complying with relevant current good manufacturing practice (CGMP) as required by the Federal Food, Drug, and Cosmetic Act (the FD&C Act). Controls for producing an investigational new drug (IND) for use in a phase 1 study are primarily aimed at ensuring subject safety. This guidance is being issued concurrently with a direct final rule and companion proposed rule published elsewhere in this issue of the **Federal Register**, which, if finalized, will specify that the particular requirements in the regulations need not be met for most investigational drugs manufactured for use during phase 1 development. Instead, the agency recommends the approaches outlined in this guidance for complying with the FD&C Act.

DATES: Submit written or electronic comments on the draft guidance by March 20, 2006. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or the Office of Communication, Training and Manufacturers Assistance (HFM–40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document. The guidance may also be obtained by mail by calling CBER at 1–800–835–4709 or 301–827–1800.

FOR FURTHER INFORMATION CONTACT: Monica Caphart, Center for Drug Evaluation and Research (HFD–320), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–9047, or Christopher Joneckis, Center for Biologics Evaluation and Research (HFM–1), 1401 Rockville Pike, Rockville, MD 20852, 301–435–5681.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''INDs—Approaches to Complying with CGMP During Phase 1.'' The FD&C Act specifies that drugs must be manufactured, processed, packed, and held in accordance with CGMP, or they are deemed to be adulterated. In September 1978, FDA implemented revised CGMP regulations for drug and biological products (see parts 210 and 211 (21 CFR parts 210 and 211)). These regulations were written primarily with commercial manufacturing in mind. Although the agency stated at the time that the regulations applied to all types of pharmaceutical production,[1] we indicated in the preamble to the regulations that we were considering proposing additional regulations governing drugs used in investigational clinical studies. This guidance makes recommendations for complying with CGMPs for certain phase 1 products.

This guidance applies to investigational new human drug and biological products (including finished dosage forms used as placebos) intended for human use during phase 1 development. Examples of investigational biological products covered by this guidance include investigational recombinant and nonrecombinant therapeutic products, vaccine products, allergenic products, in vivo diagnostics, plasma derivative products, blood and blood components, gene therapy products, and somatic cellular therapy products (including xenotransplantation products) that are subject to the CGMP requirements of section 501(a)(2)(B) of the FD&C Act. The guidance applies to investigational products whether they are produced in small- or large-scale environments because such studies are typically designed to assess tolerability or feasibility for further development of a specific drug or biological product. However, if an investigational drug has already been manufactured by an IND sponsor for use during phase 2 or phase 3 studies or has been lawfully marketed, manufacture of such a drug must comply with the appropriate sections of part 211 for the drug to be used in any subsequent phase 1 investigational studies, irrespective of the trial size or duration of dosing.

This guidance does not apply to human cell or tissue products regulated solely under section 361 of the Public Health Service Act; clinical trials for products regulated as devices; or already approved products that are being used during phase 1 studies (e.g., for a new indication).

This guidance (once finalized) and the regulation it complements (once finalized) represent the agency's effort to proceed with its plans to formally lay out an approach to aid manufacturers in implementing manufacturing controls that are appropriate for the stage of development. The use of this approach recognizes that some controls and the extent of controls needed to achieve appropriate product quality differ not only between investigational and commercial manufacture, but also among the various phases of clinical studies. Consistent with the agency's CGMP for the 21st Century initiative,[2] where applicable, manufacturers are also expected to implement controls that reflect product and production considerations and evolving process and product knowledge and manufacturing experience.[3]

The draft guidance describes FDA's current thinking regarding controls for special production situations (e.g., a laboratory setting, exploratory studies, multiproduct and multibatch testing) and specific product types (e.g., biological/biotechnology products, aseptically processed products) of IND products manufactured for use during phase 1 clinical trials as described in the scope section of the guidance. As the new rule will specify if finalized, the particular requirements in part 211 need not be met for most exploratory products manufactured for use during phase 1 clinical trials.

When finalized, this guidance will replace the 1991 ''Guideline on the Preparation of Investigational New Drug Products (Human and Animal)'' for the production of IND products for phase 1 clinical trials described in the scope section of the guidance. Phase 2 and 3 production will continue to be subject to those portions of parts 210 and 211 that are applicable.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on how to comply with CGMP during certain phase 1 clinical studies. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This draft guidance refers to collections of information that have been approved by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). OMB approved the collection of information under OMB control number 0910–0139.

III. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic

[1] Preamble to the 1978 CGMP regulation (43 FR 45076, September 29, 1978), comment #49, ''The Commissioner finds that, as stated in §211.1, these CGMP regulations apply to the preparation of any drug product for administration to humans or animals, including those still in investigational stages. It is appropriate that the process by which a drug product is manufactured in the development phase be well documented and controlled in order to assure the reproducibility of the product for further testing and for ultimate commercial production. The Commissioner is considering proposing additional CGMP regulations specifically designed to cover drugs in research stages.''

[2] See *http://www.fda.gov/cder/gmp/*.

[3] We are considering issuing additional guidance and/or regulations to clarify the agency's expectations with regard to fulfilling the CGMP requirements when producing investigational drugs for phase 2 and phase 3 clinical studies.

comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. Electronic Access

Persons with access to the Internet may obtain the document at *http://www.fda.gov/cder/guidance/index.htm*, *http://www.fda.gov/cber/guidelines.htm*, or *http://www.fda.gov/ohrms/dockets/default.htm.*

Dated: January 9, 2006.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 06–352 Filed 1–12–06; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Resources and Services Administration

Agency Information Collection Activities: Proposed Collection: Comment Request

In compliance with the requirement for opportunity for public comment on proposed data collection projects (section 3506(c)(2)(A) of Title 44, United States Code, as amended by the Paperwork Reduction Act of 1995, Public Law 104–13), the Health Resources and Services Administration (HRSA) publishes periodic summaries of proposed projects being developed for submission to the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995. To request more information on the proposed project or to obtain a copy of the data collection plans and draft instruments, call the HRSA Reports Clearance Officer on (301) 443–1129.

Comments are invited on: (a) Whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information shall have practical utility; (b) the accuracy of the agency's estimate of the burden of the proposed collection of information; (c) ways to enhance the quality, utility, and clarity of the information to be collected; and (d) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques or other forms of information technology.

Proposed Project: Voluntary Partner Surveys in the Health Resources and Services Administration—(OMB No. 0915–0212—Extension

In response to Executive Order 12862, the Health Resources and Services Administration (HRSA) conducts voluntary customer surveys of its ''partners'' to assess strengths and weaknesses in program services. An extension of a generic approval is being requested from OMB to conduct these customer or partner satisfaction surveys. HRSA partners are typically State or local governments, health care facilities, health care consortia, health care providers, and researchers.

Partner surveys to be conducted by HRSA might include, for example, brief surveys of grantees to determine satisfaction with a technical assistance contractor, or in-class evaluation forms completed by providers who receive training from HRSA grantees, to measure satisfaction with the training experience. Results of these surveys will be used to plan and redirect resources and efforts as needed to improve service. Focus groups may also be used to potential method to obtain input on services and training. Focus groups, in-class evaluation forms, mail surveys, and telephone surveys are expected to be the preferred methodologies.

The estimated response burden is as follows:

Instrument	Number of respondents	Responses per respondent	Hours per response	Total hour burden
In-class evaluations	40,000	1	.05	2,000
Surveys	12,000	1	.25	3,000
Focus groups	50	1	1.5	75
Total	52,050	1	.10	5,075

Send comments to Susan G. Queen, Ph.D., HRSA Reports Clearance Officer, Room 10–33, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857. Written comments should be received within 60 days of this notice.

Dated: January 9, 2006.

Tina M. Cheatham,

Director, Division of Policy Review and Coordination.

[FR Doc. E6–351 Filed 1–13–06; 8:45 am]

BILLING CODE 4165–15–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of Inspector General

Program Exclusions: December 2005

AGENCY: Office of Inspector General, HHS.

ACTION: Notice of program exclusions.

During the month of December 2005, the HHS Office of Inspector General imposed exclusions in the cases set forth below. When an exclusion is imposed, no program payment is made to anyone for any items or services (other than an emergency item or service not provided in a hospital emergency room) furnished, ordered or prescribed by an excluded party under the Medicare, Medicaid, and all Federal Health Care programs. In addition, no program payment is made to any business or facility, e.g., a hospital, that submits bills for payment for items or services provided by an excluded party. Program beneficiaries remain free to decide for themselves whether they will continue to use the services of an excluded party even though no program payments will be made for items and services provided by that excluded party. The exclusions have national effect and also apply to all Executive Branch procurement and non-procurement programs and activities.