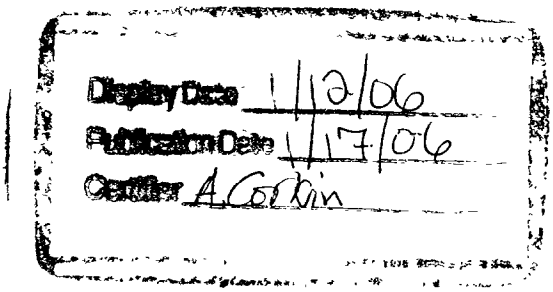
DDM



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Draft Guidance for Industry on Investigational New Drugs; Approaches to Complying with Current Good Manufacturing Practice During Phase 1; Availability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SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "INDs—Approaches to Complying with CGMP During Phase 1." This draft guidance is intended to assist persons producing drug and biological products (investigational drugs) for use during phase 1 development in complying with relevant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.

cd0438

2005D-0286

NAD 1

DATES: Submit written or electronic comments on the draft guidance by [*insert date 60 days after date of publication in the* **Federal Register**]. 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ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857,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 Submit written comments on the draft guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.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

---

[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."

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

---

[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.

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.

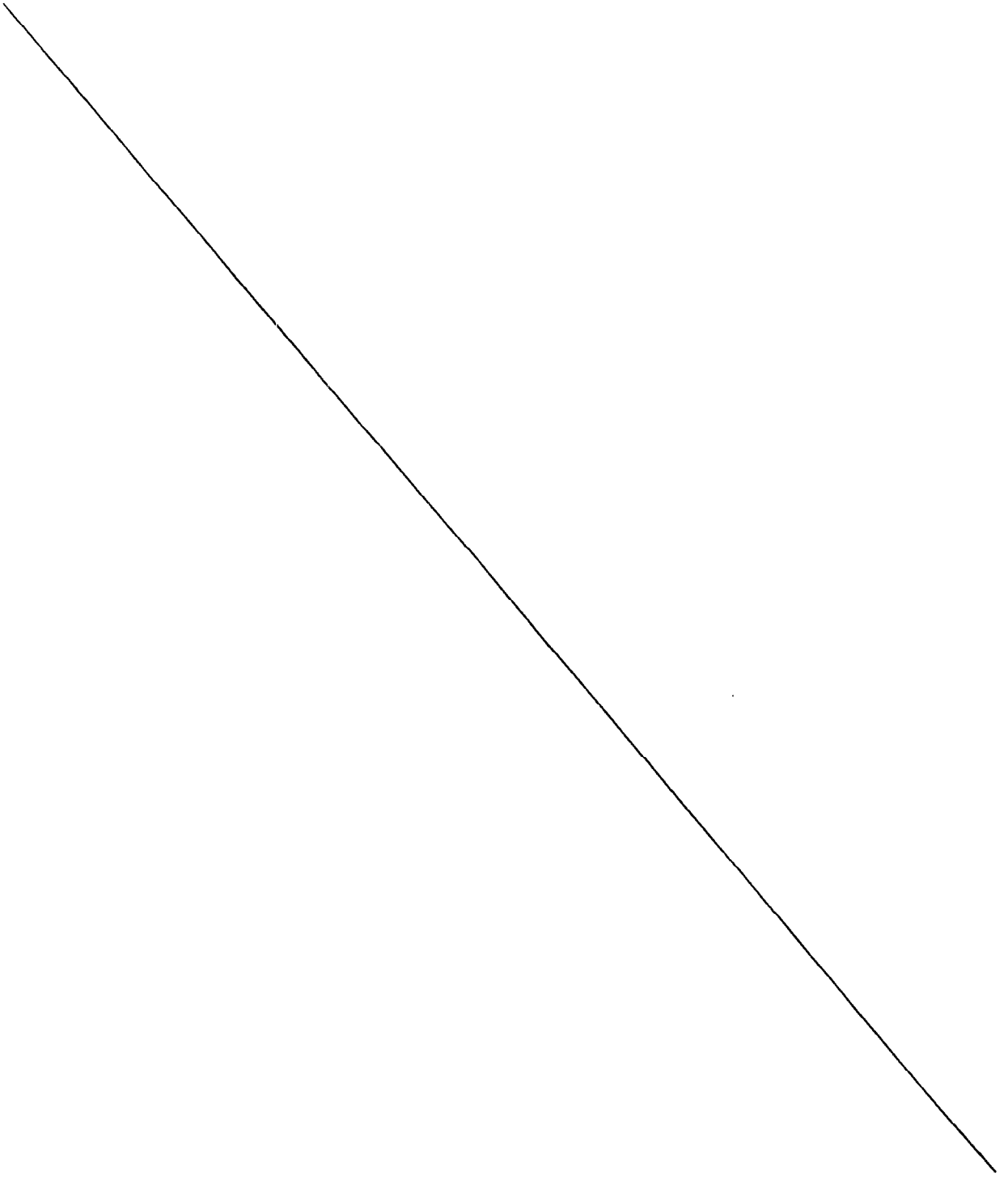
II. Paperwork Reduction Act of 1995

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 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: 1/9/06

January 9, 2006.

Jeffrey Shuren,
Assistant Commissioner for Policy.

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

BILLING CODE 4160–01–S