product-coding gene, fusion partners, or other appropriate cell lines. The level of DNA from the host cells can be detected by direct analysis on the product (such as hybridization techniques). Clearance studies, which could include spiking experiments at the laboratory scale, to demonstrate the removal of cell substrate-derived impurities such as nucleic acids and host cell proteins may sometimes be used to eliminate the need for establishing acceptance criteria for these impurities.

(b) Cell culture-derived impurities include, but are not limited to, inducers, antibiotics, serum, and other media components.

(c) Downstream-derived impurities include, but are not limited to, enzymes, chemical and biochemical processing reagents (e.g., cyanogen bromide, guanidine, oxidizing and reducing agents), inorganic salts (e.g., heavy metals, arsenic, nonmetallic ion), solvents, carriers, ligands (e.g., monoclonal antibodies), and other leachables.

For intentionally introduced, endogenous, and adventitious viruses, the ability of the manufacturing process to remove and/or inactivate viruses should be demonstrated as described in ICH guidance ''Q5A Viral Safety Evaluation of Biotechnology Products Derived From Cell Lines of Human or Animal Origin.''

6.2.2 Product-related impurities including degradation products

The following represents the most frequently encountered molecular variants of the desired product and lists relevant technology for their assessment. Such variants may need considerable effort in isolation and characterization in order to identify the type of modification(s). Degradation products arising in significant amounts during manufacture and/or storage should be tested for and monitored against appropriately established acceptance criteria.

(a) Truncated forms. Hydrolytic enzymes or chemicals may catalyze the cleavage of peptide bonds. These may be detected by HPLC or SDS–PAGE. Peptide mapping may be useful, depending on the property of the variant.

(b) Other modified forms. Deamidated, isomerized, mismatched S–S linked, oxidized, or altered conjugated forms (e.g., glycosylation, phosphorylation) may be detected and characterized by chromatographic, electrophoretic, and/or other relevant analytical methods (e.g., HPLC, capillary electrophoresis, mass spectroscopy, circular dichroism).

(c) Aggregates. The category of aggregates includes dimers and higher multiples of the desired product. These are generally resolved from the desired product and product-related substances and quantitated by appropriate analytical procedures (e.g., size exclusion chromatography, capillary electrophoresis).

Dated: August 11, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 99–21352 Filed 8–17–99; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99D–2636]

Draft Guidance for Industry on Levothyroxine Sodium; 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 ''Levothyroxine Sodium.'' The draft guidance is intended to answer questions concerning applications for orally administered levothyroxine sodium drug products.

DATES: Written comments on the draft guidance may be submitted by October 18, 1999. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Copies of this draft guidance are available on the Internet at ''http://www.fda.gov/cder/guidance/index.htm''. Submit written requests for single copies of the draft guidance for industry to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Dockets Management Branch (HFD–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Christine F. Rogers, Center for Drug Evaluation and Research (HFD–7), 5600 Fishers Lane, Rockville, MD 20857, 301–594–2041.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a draft guidance for industry entitled ''Levothyroxine Sodium.'' In the **Federal Register** of August 14, 1997 (62 FR 43535), FDA announced that orally administered levothyroxine sodium drug products are new drugs. The notice stated that manufacturers who wish to continue to market these products must submit applications as required by section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) and 21 CFR part 314. The notice stated that FDA is prepared to accept new drug applications for these products, including applications under section 505(b)(2) of the act. A number of questions have arisen with respect to applications for levothyroxine sodium. This draft guidance is intended to answer questions about submitting applications for orally administered levothyroxine sodium drug products.

This level 1 draft guidance is being issued consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). The draft guidance represents the agency's current thinking on issues concerning applications, including applications under section 505(b)(2) of the act, for levothyroxine sodium. 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 statute, regulations, or both.

Interested persons may submit written comments on the draft guidance to the Dockets Management Branch (address above). 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. The draft guidance and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: August 9, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 99–21353 Filed 8–17–99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Human Genome Research Institute; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of a meeting of the National Advisory Council for Human Genome Research.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and/or contract proposals and the discussions could disclose confidential