Drug, and Cosmetic Act (the act) (21 U.S.C. 355(d)) to clarify that FDA, at its discretion, may make exception to the general requirement that there must be more than one adequate and well-controlled investigation to support an effectiveness determination. Section 115 of the Modernization Act provides in relevant part that ''[i]f the [agency] determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the [agency] may consider such data and evidence to constitute substantial evidence [of effectiveness].''

In clarifying the standard for substantial evidence, Congress acknowledged the agency's position that there have been major advances in the science and practice of clinical drug development since the effectiveness requirement was added to the act in 1962, and confirmed FDA's interpretation of the substantial evidence of effectiveness standard, as explained in the draft guidance document.

In addition to the provision on the evidence standard, the Modernization Act included section 403, ''Approval of Supplemental Applications for Approved Products.'' Section 403(a) of the Modernization Act requires FDA to publish in the **Federal Register**, within 180 days of enactment, standards for the prompt review of supplemental applications for drugs and biological products. These standards are included in a guidance document for which a notice of availability is published elsewhere in this issue of the **Federal Register**.

Section 403(b) of the Modernization Act requires that FDA, within 180 days of enactment, issue final guidances to clarify the requirements for, and facilitate the submission of data to support, the approval of supplemental applications for drugs and biologics. The guidance issued today fulfills this statutory requirement as it addresses the data requirements for both original drug and biological product applications and supplements to those applications.

In addition, section 403(b)(1) of the Modernization Act requires that FDA provide guidance to ''clarify circumstances in which published matter may be the basis for approval of a supplemental application.'' Section III of the guidance describes the circumstances in which a sponsor may rely in part, or entirely, on published reports of studies to support approval of a supplemental application.

Section 403(b)(2) of the Modernization Act requires that FDA provide guidance to ''specify data requirements that will avoid duplication of previously submitted data by recognizing the availability of data previously submitted in support of an original application.'' Section II of the guidance describes a range of circumstances in which existing data, whether or not previously submitted to an original application, may be used to support an application for a supplemental indication, thus permitting a sponsor to avoid developing unnecessary additional data.

The agency received 13 submissions commenting on the draft guidance, including comments from pharmaceutical and biological products companies and their trade associations, individuals and organizations in academic medicine and clinical pharmacology, patient advocacy organizations, and a consumer. The response to the draft guidance was generally favorable. The guidance was viewed as a significant step forward by the agency in clarifying and better articulating its quantitative and qualitative evidentiary standards for evidence of effectiveness. Comments observed that the principles espoused were scientifically reasonable, practical, and appropriately flexible. The agency has considered all of the comments in making revisions to the guidance document.

This guidance document is being issued as a Level 1 guidance consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). It represents the agency's current thinking on clinical evidence of effectiveness for human drug and biological products. 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.

Submit written requests for single copies of the guidance for industry entitled ''Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products'' to the Drug Information Branch (HFD–210), 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. Please send one self-addressed adhesive label to assist the offices in processing your request. The document may also be obtained by mail by calling the CBER Voice Information System at 1–800–835–4709 or 301–827–1800, or by fax by calling the CBER FAX Information System at 1–888–CBERFAX or 301–827–3844.

Interested persons may at any time submit written comments on the guidance to the Dockets Management Branch (address above). Requests and comments should be identified with the docket number found in brackets in the heading of this notice. A copy of the guidance and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 8, 1998.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 98–12901 Filed 5–14–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 97D–0214]

Guidance for Industry on Pharmacokinetics in Patients with Impaired Renal Function—Study Design, Data Analysis, and Impact on Dosing and Labeling; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled ''Pharmacokinetics in Patients with Impaired Renal Function—Study Design, Data Analysis, and Impact on Dosing and Labeling.'' The guidance is intended for sponsors planning to conduct studies to assess the influence of renal impairment on the pharmacokinetics of an investigational drug.

DATES: General comments on agency guidance documents are welcome at any time.

ADDRESSES: Copies of this guidance are available on the Internet at ''http://www.fda.gov/cder/guidance/index.htm'', or ''http://www.fda.gov/cber/guidelines.htm''. Submit written requests for single copies of ''Pharmacokinetics in Patients with Impaired Renal Function—Study Design, Data Analysis, and Impact on Dosing and Labeling'' to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food

and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or Office of Communication, Training and Manufacturers Assistance (HFM–40), 1401 Rockville Pike, Rockville, MD 20852–1448, or by calling 1–800–835–4709 or 301–827–1800. Submit written comments on the guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Shiew-Mei Huang, Center for Drug Evaluation and Research (HFD–850), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5671; or

Martin D. Green, Center for Biologics Evaluation and Research (HFM–579), 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–5344.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a guidance entitled ''Pharmacokinetics in Patients with Impaired Renal Function—Study Design, Data Analysis, and Impact on Dosing and Labeling.''

The pharmacokinetics (PK) and pharmacodynamics (PD) of drugs primarily eliminated through the kidneys may be altered by impaired renal function to the extent that the dosage regimen needs to be changed from that used in patients with normal renal function. Although the most obvious type of change arising from renal impairment is a decrease in renal excretion (or possibly renal metabolism) of a drug or its metabolites, renal impairment also has been associated with other changes, such as changes in hepatic metabolism, plasma protein binding, and drug distribution. These changes may be particularly prominent in patients with severely impaired renal function and have been observed even when the renal route is not the primary route of elimination of a drug. Thus, for most drugs that are likely to be administered to patients with renal impairment, PK characterization may need to be assessed in subjects with such impairment to provide appropriate dosing recommendations.

The guidance provides specific information on when studies of PK in patients with impaired renal function should be performed and when they may be unnecessary. It also addresses the design and conduct of PK studies in patients with impaired renal function, the design and conduct of PK studies in end stage renal disease patients treated with dialysis, the analysis and reporting of the results of such studies, and representation of these results in approved product labeling.

In the **Federal Register** of June 16, 1997 (62 FR 32617), FDA announced the availability of a draft version of this guidance, entitled ''Pharmacokinetics and Pharmacodynamics in Patients with Impaired Rental Function: Study Design, Data Analysis, and Impact on Dosing and Labeling.'' The June 16, 1997, document gave interested persons an opportunity to submit comments through August 15, 1997. All comments received through the end of September have been carefully reviewed and incorporated, where appropriate, in this revised guidance.

This guidance is being issued as a Level 1 guidance consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). It represents the agency's current thinking on conducting PK studies on patients with impaired renal function. 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 requirement of the applicable statute, regulations, or both.

Interested persons may, at any time, submit written comments on the guidance to the Dockets Management Branch (address above). Comments should be identified with the docket number found in brackets in the heading of this document. A copy of the guidance is available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 8, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–12898 Filed 5–14–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by agencies of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; *telephone* 301/496–7057; *fax:* 301/402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Molecular Computing Elements: Gates and Flip-Flops

TD Schneider, PN Hengen (NCI)
DHHS Reference No. E–170–97/0 filed Feb. 20, 1998
Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present invention is a method and apparatus for molecular computing which provides for molecular logic devices analogous to those of electronic computers, such as flip-flops, AND gates, etc. Coupling of the gates allows for molecular computing. The method allows data storage, the transformation of binary information and signal readout. Possible applications include encoding ''read only'' memory for microscopic identifiers, digital control of gene expression, and quantification of analytes. The computing elements also provide means for complex regulation of gene expression.

Lipooligosaccharide-Based Vaccine for the Prevention of Moraxella (Branhamella) Catarrhalis Infections In Humans

X–X Gu, JB Robbins (NIDCD)
Serial No. 60/071,483 filed Jan 13, 1998
Licensing Contact: Robert Benson, 301/496–7056 ext. 267

This invention is a vaccine for the prevention of disease caused by M. catarrhalis, which is the third most common causative agent of otitis media (middle ear infection) and sinusitis in children. The emergence of antibiotic resistant bacteria has caused concern that treatment of otitis media will become more problematic. This invention offers a new approach to managing otitis media. The vaccine is composed of lipooligosaccharide (LOS), isolated from the surface of strains of M. catarrhalis and detoxified by removing esterified fatty acids to produce detoxified LOS (dLOS), which is then conjugated to an immunogenic protein carrier such as tetanus toxiod. The conjugates have been shown to be nontoxic by the limulus amebocyte