the review committee. Applicants should request a legibly dated U.S. Postal Service postmark or obtain a legibly dated receipt from a commercial carrier or the U.S. Postal Service. Private metered postmarks shall not be acceptable as proof of timely mailings.

Applications which do not meet the criteria in 1. or 2. above are considered late applications and will be returned to the applicant.

Where To Obtain Additional Information

All application procedures and guidelines are contained within the present announcement. Business management technical information may be obtained from David Elswick, Grants Management Specialist, Procurement and Grants Office, Centers for Disease Control and Prevention (CDC), 255 East Paces Ferry Road, N.E., Mailstop E–13, Atlanta, GA 30305, telephone (404) 842–6521.

Programmatic technical assistance may be obtained from Steven Adams, Project Officer, Radiation Studies Branch, Division of Environmental Hazards and Health Effects, National Center for Environmental Health, Centers for Disease Control and Prevention (CDC), 4770 Buford Hwy, N.E., Mailstop F–35, Atlanta, GA 30341–3724, telephone (770) 488–7040.

Potential applicants may obtain a copy of Healthy People 2000 (Full Report, Stock No. 017–001–00474–0) or Healthy People 2000 (Summary Report, Stock No. 017–001–00473–1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402–9325 (Telephone (202) 513–1800).

Dated: June 15, 1998.

John L. Williams,

Director, Procurement and Grants Office, Centers for Disease Control and Prevention (CDC).

[FR Doc. 98–16327 Filed 6–18–98; 8:45 am]

BILLING CODE 4163–18–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 97N–0384]

Knickerbocker Biologicals, Inc.; Revocation of U.S. License No. 458–001

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the revocation of the establishment license (U.S. License No. 458–001) and the product licenses issued to Knickerbocker Biologicals, Inc., for the manufacture of Whole Blood, Red Blood Cells, Plasma, and Source Leukocytes. Knickerbocker Biologicals, Inc., did not respond to a notice of opportunity for a hearing on a proposal to revoke its licenses.

DATES: The revocation of the establishment license (U.S. License No. 458–001) and the product licenses is effective June 19, 1998.

FOR FURTHER INFORMATION CONTACT: Astrid L. Szeto, Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–6210.

SUPPLEMENTARY INFORMATION: FDA is revoking the establishment license (U.S. License No. 458–001) and the product licenses issued to Knickerbocker Biologicals, Inc., doing business as Knickerbocker Blood Bank, 272 Willis Ave., Bronx, NY 10454, for the manufacture of Whole Blood, Red Blood Cells, Plasma, and Source Leukocytes.

An attempted inspection of the facility by FDA revealed that the facility was no longer in operation at the location listed on the license. A certified, returned-receipt letter from FDA dated November 14, 1996, notifying the Responsible Head of the unsuccessful inspection and requesting the status of the firm was returned to the agency as ''undeliverable; address unknown''. A later attempt by FDA to visit three other known addresses of Knickerbocker Biologicals, Inc., New York, NY, verified that the company was no longer in business at these locations. The respective post office for each location was also visited and each verified that no information regarding either a forwarding address or address change was available. Based on the inability of authorized FDA employees to conduct a meaningful inspection of the facility, FDA initiated proceedings for the revocation of the licenses under 21 CFR 601.5(b)(1) and (b)(2). A certified, returned-receipt letter, dated January 24, 1997, to the firm's Responsible Head providing notice of FDA's intent to revoke the licenses and its intent to offer an opportunity for a hearing on the proposed revocation was returned as undeliverable.

Under 21 CFR 12.21(b), FDA published in the **Federal Register** of October 6, 1997 (62 FR 52135), a notice of opportunity for a hearing on a proposal to revoke the licenses of Knickerbocker Biologicals, Inc. In the notice, FDA explained that the proposed license revocation was based on the inability of authorized FDA employees to conduct a meaningful inspection of the facility because it was no longer in operation and noted that documentation in support of the license revocation had been placed on file for public examination with the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857. The notice provided the firm 30 days to submit a written request for a hearing and 60 days to submit any data and information justifying a hearing. The notice provided other interested persons with 60 days to submit written comments on the proposed revocation. The firm did not respond within the 30-day time period with a written request for a hearing. The 30-day time period, prescribed in the notice of opportunity for a hearing and in the regulation, may not be extended. No comments were received from any other parties within the 60-day time period.

Accordingly, under 21 CFR 12.38, section 351 of the Public Health Service Act (42 U.S.C. 262), and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Biologics Evaluation and Research (21 CFR 5.68), the establishment license (U.S. License No. 458–001), and the product licenses issued to Knickerbocker Biologicals, Inc., are revoked, effective June 19, 1998.

Dated: May 28, 1998.

Kathryn C. Zoon,

Director, Center for Biologics Evaluation and Research.

[FR Doc. 98–16294 Filed 6–18–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Studies of Adverse Effects of Marketed Drugs; Availability of Grants (Cooperative Agreements); Request for Application

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA), Center for Drug Evaluation and Research, is announcing $1.4 million for cooperative agreements to study adverse effects of drugs marketed in Canada, the United States and its territories, subject to the availability of Fiscal Year 1999 funds. This amount is consistent with the level

of funding in the President's budget. FDA expects to make up to four awards for $300,000 per year for 3 years for general data bases and up to two awards for $100,000 per year for 3 years for special population data bases. The purpose of these agreements is to conduct drug safety analysis to the benefit of the public's health; respond expeditiously to urgent public safety concerns; provide a mechanism for collaborative pharmacoepidemiological research designed to test hypotheses, particularly those arising from suspected adverse reactions reported to FDA; and enable rapid access to multiple data sources to ensure public safety when necessary.

DATES: Submit applications by August 3, 1998.

ADDRESSES: Application kits are available from, and completed applications should be submitted to: Robert L. Robins, Division of Contracts and Procurement Management (HFA–520), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–7185.

Note: Applications hand-carried or commercially delivered should be addressed to 5630 Fishers Lane, rm. 2129, Rockville, MD 20852. Please DO NOT send applications to the Center for Scientific Review (CSR), National Institutes of Health (NIH). Applications mailed to CSR and not received by FDA in time for orderly processing, will be returned to the applicant without consideration.

FOR FURTHER INFORMATION CONTACT:

Regarding the administrative and financial management aspects of this notice: Robert L. Robins (address above).

Regarding the programmatic aspects of this notice: Thomas M. Conrad, Division of Pharmacovigilance and Epidemiology (HFD–730), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–3180.

SUPPLEMENTARY INFORMATION: Because of the reduction of funding throughout the U.S. Government and particularly in this program, continuation of funding will be evaluated annually to a higher degree than ever before. As stated later in this document, funding of the second and third years will be contingent upon: (1) Investigator's demonstrated success collaborating with FDA scientists, as well as with other investigators funded by this cooperative agreement program. Such demonstration may include suggestions for and design of a study, analysis of data sets, and publication of results among FDA and cooperative agreement investigators, and (2) the availability of Federal fiscal year appropriations. A points system has been established to quantitate the grantee's usefulness in the Government's collaborative efforts with non-Federal organizations to improve the health of the American public.

It is determined that these cooperative agreements are exempt from Protection of Human Subjects requirements in accordance with 45 CFR 46.102(b).

FDA's authority to fund research projects is set out in section 301 of the Public Health Service Act (the PHS Act) (42 U.S.C. 241). FDA's research program is described in the Catalog of Federal Domestic Assistance, No. 93.103. Applications submitted under this program are not subject to the requirements of Executive Order 12372.

I. Background

New drugs are required to undergo extensive testing before marketing. With the submission of adequate data on safety and effectiveness, FDA approves a new drug application (NDA) and that permits a manufacturer to market its product in the United States. Although the information provided before marketing is sufficient for approval, it is not adequate to anticipate all effects of a product once it comes into general use. This request for applications (RFA) is intended to encourage collaboration between FDA and researchers with pharmacoepidemiological data bases to address postmarketing issues confronting the agency.

FDA is also interested in the ability to measure and/or estimate incidence rates and test hypotheses based on signals of possible drug safety problems originating from reports of adverse reaction reports received by FDA.

II. Program Research Goals

FDA shall fund a variety of data bases representing, without overlap to each other or agency contracts, different patient populations and/or types of patient care settings.

The goal for these cooperative agreements is to collaborate with researchers with pharmacoepidemiological data bases, to investigate suspected associations between specific drug exposures and specific adverse events, and to estimate such risk. The specific objectives are to: (1) Provide immediate access to existing data sources with the capability of providing assessments of study feasibility; (2) respond to specific drug safety questions within a few weeks; and (3) provide a complete analysis to those questions deemed feasible within a few months.

Additional points will be awarded for the collaborative sharing of data sets with the agency and with other cooperative agreement recipients.

Databases

For the purpose of this RFA, all $300,000 awards will be to longitudinal data bases. Awards for data bases of special populations ($100,000 awards) may be either longitudinal or case control.

A. Longitudinal Data Bases

These data bases must be able to: (1) Provide exposure data on new molecular entities (those approved within the last 5 years in the United States); (2) perform feasibility studies of multiple drugs and/or multiple outcomes; (3) identify adverse drug events that occur infrequently (i.e., at rates lower than can be detected in clinical trials); and (4) provide data and preliminary analysis within a very short timeframe (2 to 4 weeks depending on the problem).

Data base characteristics of interest might include the ability to: (1) Estimate adverse event rates or relative risks for a specific event; (2) estimate the contribution of various risk factors associated with the occurrence of adverse events (e.g., age, sex, dose, coexisting disease, disease severity, concomitant medication); (3) determine adverse event rates for generic entities as well as for classes of drugs; (4) obtain data from laboratory results; (5) link to state vital statistics; (6) link to cancer registry; (7) determine inpatient exposure; and (8) follow patients long term after an exposure to a suspect drug.

In addition, FDA is interested in data bases capable of innovatively applying the objectives stated previously to general populations.

The ideal data source would: (1) Capture all drug exposures linked longitudinally to each patient regardless of health care delivery setting. Outcomes of interest could be either acute or chronic effects, all health provider encounters (i.e., medical records) would be captured whether in the ambulatory, emergency, chronic care or acute care setting; (2) have the statistical power to identify rare (<1 event per 1000 exposures) adverse events in the population of interest; (3) be automated with a computerized system available for linking each patient to all relevant medical care data including drug exposure data, coded medical outcomes, vital records, cancer registries and birth defect registries; (4) have a low patient turn-over, thereby permitting long-term longitudinal followup of most patients for delayed

adverse effects; (5) address effects from chronically used drugs (e.g., Framingham Study); and (6) address delayed effects resulting from drug use.

Additional points would be awarded for linkage of data bases to laboratory values and readily accessible medical records as evidenced by past performance in studies. The ability to retrieve medical records relevant to study questions posed by FDA is extremely important.

Submitted applications must include an indepth description of the data base and provide descriptive and quantitative information on diagnoses or drug exposures in the population.

The applicant shall also provide evidence that their data base has sufficient exposure to marketed drugs (as evidenced by listing their top 50 drug substances of exposure; including the drug and number of exposures). The quality and validity of the data should be described in detail.

B. Case-Control Data Bases

These data bases must be able to: (1) Provide exposure data in general and/or hospital populations; (2) perform feasibility studies; and (3) provide data and preliminary analysis within a very short timeframe (2 to 4 weeks depending on the problem).

The specific objectives are to: (1) Provide immediate access to existing data sources with the capability of providing assessments of study feasibility; (2) respond to specific drug safety questions within a few weeks; and (3) provide a complete analysis to those questions deemed feasible within a few months.

Characteristics of interest might include: (1) The use of standardized ascertainment and outcome methodology; (2) the ability to perform prospective and retrospective studies; (3) demonstrated validation of data; (4) estimate the contribution of various risk factors associated with the occurrence of adverse events (e.g., age, sex, dose, coexisting disease, disease severity, concomitant medication); (5) availability of large numbers of cases with validated outcomes of interest in drug safety and associated controls; (6) construct cases and controls for case-controlled and nested case-controlled studies (include sampling scheme); (7) determine odds ratios; and (8) determine attributable risks.

In addition, FDA is interested in data bases capable of innovatively applying the objectives stated previously to general and specifically defined populations.

The ideal data source would: (1) Capture all drug exposures for each patient regardless of health care delivery setting; (2) identify rare (<1 event per 1000 exposures) adverse events in the population of interest; and (3) be automated with a computerized system available for linking each patient to all relevant medical care data including drug exposure data, coded medical outcomes.

Additional points would be awarded for linkage of data bases to laboratory values and readily accessible medical records as evidenced by past performance in studies. The ability to retrieve medical records relevant to study questions posed by FDA is extremely important.

Submitted applications shall include an indepth description of the data base and provide descriptive and quantitative information on diagnoses and drug exposures in the population. The quality and validity of the data should be described in detail. The applicant shall also provide evidence that their data base has sufficient exposure to marketed drugs (as evidenced by listing their top 50 drug substances of exposure; including the drug and number of exposures) and demonstrate the prevalence of exposure in their control groups.

III. Reporting Requirements

Program progress reports will be required annually. These reports must be submitted 60 days prior to the last day of the budget period of the cooperative agreement. The Progress Report Summary required for Non-Competing Continuation Application is sufficient, if amended with the following information: (1) Publications, abstracts, presentations to professional organizations; (2) top 50 drug substance exposures for the previous year; and (3) summary of any changes in the demographics or capabilities of the data base over the last year.

Financial Status Reports (SF–269) will be required annually. These reports must be submitted within 90 days after the last day of the budget period of the cooperative agreement. Send the original and one copy each, of the Annual Progress and Financial Reports to the Grants Office at the address listed above. Failure to file the Annual Progress Report or the Financial Status Report (SF–269) in a timely fashion will be grounds for suspension or termination of the grant.

Program monitoring of the grantees will be conducted on an ongoing basis and written reports will be prepared by the Project Officer. The monitoring may be in the form of telephone conversations between the Project Officer and/or Grants Management Specialist and the Principal Investigator. Periodic site visits with appropriate officials of the grantee organization may also be conducted. The results of these reports will be recorded in the Official Grant File and may be available to the grantee upon request.

A final Program Progress Report, Financial Status Report (SF–269) and Invention Statement must be submitted within 90 days after the expiration of the project period as noted on the Notice of Grant Award. Send the original and one copy to the Grants Management Officer at the address listed above.

Up to two representatives from each cooperative agreement may be required, if requested by the Project Officer, to travel to FDA up to twice a year for no more than 2 days at a time. These meetings will include, but are not limited to, presentation on study design and findings and discussions with FDA staff involved in the collaborative research. At least one FDA employee may visit the cooperative agreement site at least once a year for collaboration and information exchange.

IV. Mechanism of Support

A. Award Instrument

Support of this program will be in the form of cooperative agreements. All awards will be subject to all policies and requirements that govern the research grant programs of the Public Health Service (PHS), including the provisions of 42 CFR part 52, 45 CFR parts 74 and 92 and PHS Grants Policy Statement.

B. Eligibility

These cooperative agreements are available to any public or private nonprofit organization (including State, local, and foreign units of government) and any for-profit organization. For-profit organizations must exclude fees or profit from their requests for support. Organizations described in section 501(c)4 of the Internal Revenue Code of 1968 that engage in lobbying are not eligible to receive grant/cooperative agreement awards.

C. Length of Support

The first year will be competitive and future support for the second and third years will be noncompetitive. Future support will be contingent upon: (1) Investigator's demonstrated success collaborating with FDA scientists, as well as other investigators funded by this cooperative agreement program. Such demonstration may include suggestions for and design of a study, analysis of data sets, and publication of

results from investigations performed by FDA and cooperative agreement investigators, and (2) the availability of Federal fiscal year appropriations.

D. Funding Plan

Up to four cooperative agreements may be funded with the intent that they will have large, general data bases with the ability to address a variety of questions in the field of pharmacoepidemiology. (If an application using case-control methods research is received, it will be placed in the special population data bases as described in the next paragraph.) These cooperative agreements have $1.2 million dollars budgeted per year.

Up to two cooperative agreements may be funded for special populations, such as acquired immune deficiency syndrome (AIDS), pregnant women, pediatrics, maternal-child linked data bases. The data base type for these awards may be either longitudinal or case control. These two cooperative agreements have $200,000 dollars budgeted per year.

These amounts are to include all direct and indirect costs. Federal funds for this program are limited; therefore, if two or more approved cooperative agreements are perceived as duplicative or very similar data sources with one another, FDA will support only the source with the best score. If any data source is perceived as duplicative or very similar to an existing FDA research contract, the contract will take precedence over the application.[1]

Applicants may compete for either type of cooperative agreement, but not both. An applicant can only be awarded one cooperative agreement under this RFA. Applicants must clearly label block No. 2 of the face page of their application either ''Large'' or ''Special''. If the application appears to be eligible for both areas of consideration and is not labeled, reasonable efforts will be made to contact the applicant to determine their preference. If reasonable efforts to contact the applicant fail, program staff shall determine in which area the applicant will compete.

V. Delineation of Substantive Involvement

Program support will be offered through cooperative agreements because FDA will have a substantive involvement in the programmatic activities of all projects funded under this RFA. Involvement may be modified to fit the unique characteristics of each application. Substantive involvement includes, but is not limited to the following:

1. FDA staff will participate in the selection and approval of the drug and medical events to be studied as predicated by the needs of FDA. The drug and medical events to be studied will be jointly agreed upon by the Principal Investigator and the FDA staff.

2. FDA scientists will collaborate with awardees in study design and data analysis. Collaboration may include sharing of the analysis data set, interpretation of findings, review of manuscripts, design of protocols and where appropriate, coauthorship of publications.

3. Because of the ad hoc and frequently urgent nature of the agency's request, we have decided to quantify the amount of requests we would ask of an awardee in one year's time. We expect that the grantee would perform at least one medium or large study in the course of each year. We also would expect that at least one large or one medium study, per year, result from requested feasibility studies. The following table illustrates our method to quantify work.

TABLE 1.—QUANTIFICATION OF WORK

Large Study[1]	30–60 points
Medium Study[2]	15–40 points
Other[3] (e.g., Data Base Search or Feasibility Study)	1–3 points

[1] Large Study—a large study is one that would involve extensive use of the data base (e.g., large studies with laboratory linkages) and, possibly, the retrieval of medical records.
[2] Medium Study—a medium study is one that might be a large data base search only or a smaller data base search with medical records retrieval required.
[3] Other—include feasibility studies and requests for information that may include a few tables describing demographics of the patients, drug exposures and denominator data.

The determination of the points per project will normally be determined by the grantee and the program before work begins; however, if circumstances dictate a change is needed after work has begun, it will be permissible, if agreed by both the grantee and the agency.

All grantees will receive requests for all feasibility studies made by the agency. This method will afford all grantees the opportunity to respond to requests.

An additional 10 points will be awarded to medium and large studies (after the above points have been negotiated) for sharing data sets with the agency and other cooperative agreements.

These points will be used in determining continued support of the cooperative agreement for the second and third years of the project period.

VI. Review Procedure and Criteria

A. Review Procedure

All applications submitted must be responsive to the RFA. Those applications found to be nonresponsive will not be considered for funding under this RFA and will be returned to the applicant. Again, this RFA is limited to data bases where data have been collected from drugs marketed in Canada, the United States and its Territories.

Responsive applications will undergo dual peer review. A review panel of experts, comprised primarily of non-Federal scientists, in the fields of epidemiology, statistics and data base management will review and evaluate each application based on its scientific merit. Responsive applications will also be subject to a second level review by the National Advisory Environmental Health Science Council for concurrence with the recommendations made by the first level reviewers, and funding decisions will be made by the Commissioner of Food and Drugs or his designee.

B. Review Criteria

Applications will be reviewed according to the following criteria, with each criteria being of equal weight within each major category, unless

[1] FDA Contracts include IMS America's National Prescription Audit, National Disease and Therapeutic Index, Provider Prospective, Retail Prospective (Contract No. 223–98–5520) and Mediplus (Purchase Order No. F–07396).

otherwise specified. All applications will be scored with a maximum of 100 points allowable.

Specific review data base size and characteristics apply to each type of data base (General Longitudinal or Special Populations, Case-Control or Special Populations, Longitudinal). Each applicant will be reviewed by the type of data base the applicant claims to be applying for. Separate scores will not be given for the same data base.

1. Size and Characteristics of the Data Base (General Longitudinal; Special Populations, Longitudinal; or Special Populations, Case-Control) (45 points—Total)

General, Longitudinal Data Base

The size and characteristics of the general, longitudinal data base should include the following:

a. Structure (10 points)

Common data structure and elements. With this, we would desire to have a data base that has unified and linked data that has common structure and data elements for critical variables (including, at a minimum, demographics, drug use and clinical outcomes.)

b. Size (10 points)

1. Patient population >3 million individuals enrolled annually (10 points).
2. Patient population >2 million individuals enrolled annually (7 points).
3. Patient population >1 million individuals enrolled annually (4 points).

c. Duration (10 points)

A long calendar time-period for which patient longitudinal data are available and linked.

- No points to data bases with less than 2 years of drug exposure and outcome data.
- 2 points for 2 years of drug exposure and outcome data.
- 2 points for each year greater than 2 years of drug exposure and outcome data.
- 10 points (maximum) for 6 years or more of drug exposure and outcome data.

d. General Data Base Features (15 points)

1. Ability to assemble and follow (retrospectively and prospectively) well-defined cohorts based on exposure or clinical diagnosis for the purpose of performing case-control or cohort studies.
2. Ability to access and to link to the patient, all health provider encounters and drug exposure information regardless of patient care setting.
3. Ability to detect rare (<1:1,000) adverse drug events in one or more specific target populations of interest (i.e., children, pregnant women, and the elderly).
4. Ability to detect and study, with sufficient power, birth defect and cancer outcomes related to drug exposure.
5. Ability to study all drug products, especially new molecular entities (NME's) approved by FDA since 1993.
6. Ability to ascertain patient enrollment and turnover rates as demonstrated by descriptions of the entry and dropout rates and the average length of enrollment.
7. A standard set of drug and disease classification systems.
8. Ability to successfully retrieve a high proportion of medical records (sufficient to address the issue presented) in a timely fashion. Documentation of a large proportion of medical records retrieved in a specified time period should be included.
9. Ability to link to cancer registry and to state vital statistics.
10. Ability to identify risk factors for drug-associated outcomes and assess potential confounders.
11. Ability to assess drug interactions.
12. A short lag time (<6 months) between patient events (hospitalization, etc.) and availability of clean data.
13. A listing of the data base's top 50 drug substances of exposure to include the drug and number of exposures at the time of the panel review.

Special Populations Data Base, Longitudinal

The size and characteristics of the data base should include the following:

a. Size (15 points)

Special population data bases shall demonstrate that their data base is representative of their special population as a whole. These special data bases can be awarded full points if sufficient evidence is submitted that demonstrates that their special population is adequately represented.

b. General Data Base Features (30 points)

1. Ability to assemble and follow (retrospectively and prospectively) well defined cohorts based on drug exposure or clinical diagnosis for the purpose of performing case-control or cohort studies.
2. Ability to access and to link to the patient, all health provider encounters and drug exposure information regardless of patient care setting.
3. Ability to study all drug products, especially NME's approved by FDA since 1993.
4. Ability to detect and study, with sufficient power, birth defect and cancer outcomes related to drug exposure (if applicable).
5. Ability to ascertain patient enrollment and turnover rates as demonstrated by descriptions of the entry and dropout rates and the average length of enrollment.
6. A standard set of drug and disease classification systems.
7. Ability to successfully retrieve a high proportion of medical records (sufficient to address the issue presented) in a timely fashion. Documentation of a large proportion of medical records retrieved in a specified time period should be included.
8. Ability to link to state vital statistics.
9. Ability to identify risk factors for drug-associated outcomes and assess potential confounders.
10. Ability to assess drug interactions.
11. A long calendar time period for which data are available and longitudinally linkable. *No points will be awarded to data bases with less than 2 years of history.*
12. A short lag time (<6 months) between patient events (hospitalization, etc.) and availability of clean data.
13. A listing of the data base's top 50 drug substances of exposure to include the drug and number of exposures at the time of the panel review.

Special Populations Data Base, Case-Control

The size and characteristics of the case controlled data base should include the following:

a. Size (15 points)

Investigators should be able to provide information on at least 500 cases of a specific disease or disorder and exposure primarily to new molecular entities.

b. Controls (15 points)

Evidence of past experience performing case-control studies, estimating sample size, exposure rates and proper use of controls as evidenced in literature and abstracts.

c. General Data Base Features (15 points)

1. Ability to provide information on a variety of diseases or disorders and drug exposures.
2. Ability to assemble and follow cases and controls based on drug exposure and clinical diagnosis.
3. Ability to access and to link to the cases, all health provider encounters and drug exposure information regardless of patient care setting.
4. Ability to study drug-induced risks in one or more specific target populations of interest (i.e., children, pregnant women, and the elderly).

5. Ability to study all drug products, especially NME's approved by FDA since 1993.

6. Ability to attain complete and unbiased ascertainment of cases and controls.

7. A standard set of drug and disease classification systems.

8. Ability to successfully retrieve a high proportion of medical records (sufficient to address the issue presented) in a timely fashion. Documentation of a large proportion of medical records retrieved in a specified time period should be included.

9. Ability to identify risk factors for drug-associated outcomes and assess potential confounders.

10. Ability to assess drug interactions.

11. A listing of the data base's top 50 drug substances of exposure to include the drug and number of exposures at the time of the panel review.

The Remaining Criteria Apply to General, Longitudinal; Special Populations, Longitudinal; and Special Populations, Case-Controlled Data Bases:

2. Identification of NME's (15 points)

NME's in a data base (as identified in the following list) with:

- at least 6,000 exposures will be awarded 3 points for each NME;
- at least 4,000 exposures will be awarded 2 points for each NME;
- at least 2,000 exposures will be awarded 1 point for each NME.

Applicant's may choose five NME's from the following list for evaluation and scoring by the panel.

NME's eligible for scoring with the previously described criteria are shown below in Table 2:

TABLE 2.—NEW MOLECULAR ENTITIES

Brand names	Approval year
Cedax	1995
Claritin	1994
Cognex	1993
Cozaar	1995
Effexor	1993
Felbatol	1993
Fosamax	1995
Glucophage	1994
Lamictal	1994
Lovenox	1993
Neurotin	1993
Propulsid	1993
Risperdal	1993
Serevent	1994
Ultram	1995

3. Information Systems and Software Capabilities (10 points)

Information systems and software capabilities should include the following (2 points each):

a. A well-defined and acceptable description of computer resources and the extent of automation and software capabilities.

b. Availability of computerized data elements (inpatient drugs, diagnostic procedures and diagnosis; outpatient drugs, diagnostic procedures and diagnosis; medical records) or progress toward automation of those data elements not yet available.

c. Existing software to calculate person-time at risk and time of event occurrence.

d. Ability to complete routine searches of the data base within a short time period of about 15 working days.

e. Ability to generate customized statistical, ASCII or other appropriate data sets to facilitate data transfer and research collaboration.

4. Personnel (20 points)

Personnel should have the following qualifications:

a. Scientific (10 points)—Extensive research experience, training and competence of all personnel. Special consideration will be given to teams with knowledge and previous experience in drug epidemiology. Applicants with strong acute and chronic disease epidemiology backgrounds and a demonstrated ability to draw on consultative expertise (particularly in the areas of postmarketing surveillance and epidemiology) are encouraged to apply. (If consultants are used, letters of intent or other contractual agreements, with beginning and end dates, shall be included in the application to fulfill this requirement.) Demonstrated ability to initiate, conduct, complete and publish epidemiology studies in a timely manner.

b. Support (10 points)—Project management and information systems expertise with previous experience in the organization and manipulation of large data sets and specific experience in data bases under agreement.

5. Data Sharing (5 points)

To provide study data sets (free of patient identifiers and in a format usable to the agency) with members of FDA for analysis and with other cooperative agreement holders in studies that would require data pooling.

6. Budget (5 points)

Reasonableness of the proposed budget. Special consideration will be given to methodology which is cost effective (e.g., well-structured medical records and/or records linkage) if otherwise scientifically acceptable.

VII. Submission Requirements

The original and five copies of the completed Grant Application Form PHS 398 (rev. 5/95) or the original and two copies of Form 5161 (Rev. 7/92) or Form PHS 398 for applications from State and local governments, with sufficient copies of the appendix for each application should be delivered to Robert L. Robins (address above). No supplemental material will be accepted after the closing date. The outside of the mailing package should be labeled ''Response to RFA–FDA–CDER–99–1''.

VIII. Method of Application

A. Submission Instructions

Applications will be accepted during normal working hours, 8 a.m. to 4:30 p.m., Monday through Friday, on or before August 3, 1998.

Applications will be considered received on time if sent or mailed on or before the receipt dates as evidenced by the legible U.S. Postal Service dated postmark or a legible date receipt from a commercial carrier, unless they arrive too late for orderly processing. Private metered postmarks shall not be acceptable as proof of timely mailing. Applications not received on time will not be considered for review and will be returned to the applicant.

Note: Applicants should note that the U.S. Postal Service does not uniformly provide dated postmarks. Before relying on this method, applicants should check with their local post office.

B. Format of Application

Applications must be submitted on Grant Application Form PHS 398 (Rev. 5/95). All ''General Instructions'' and ''Specific Instructions'' in the application kit should be followed with the exception of the receipt dates and the mailing label addresses. Do not send applications to the Center for Scientific Review, NIH. This information collection is approved under OMB control number 00925–0001. Applications from State and local governments may be submitted on Form PHS 5161 (Rev.7/92) or PHS 398 (Rev.5/95). The face page of the application must reflect the request for applications number RFA–FDA–CDER–99–1. This information collection is approved under OMB control number 0937–0189.

C. Legend

Unless disclosure is required by the Freedom of Information Act as amended (5 U.S.C. 552) as determined by the freedom of information officials of the Department of Health and Human Services or by a court, data contained in the portions of the application that have been specifically identified by page number, paragraph, etc., by the applicant as containing confidential commercial information or other information that is exempt from public disclosure will not be used or disclosed except for evaluation purposes.

Dated: June 9, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–16293 Filed 6–18–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98N–0192]

Agency Information Collection Activities; Announcement of OMB Approval

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a collection of information entitled ''Establishment and Product License Applications'' has been approved by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA).

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 the **Federal Register** of April 8, 1998 (63 FR 17183), the agency announced that the proposed information collection had been submitted to OMB for review and clearance under section 3507 of the PRA (44 U.S.C. 3507). An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. OMB has now approved the information collection and has assigned OMB control number 0910–0124. The approval expires on June 30, 1998.

Dated: June 9, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–16292 Filed 6–18–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 97N–0529]

Agency Information Collection Activities; Announcement of OMB Approval

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a collection of information entitled ''National Tobacco Retailer Tracking Study,'' has been approved by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA).

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

SUPPLEMENTARY INFORMATION: In the **Federal Register** of Tuesday, December 30, 1997 (62 FR 67876), the agency announced that the proposed information collection had been submitted to OMB for review and clearance under section 3507 of the PRA (44 U.S.C. 3507). An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. OMB has now approved the information collection and has assigned OMB control number 0910–0369. The approval expires on May 31, 2001.

Dated: June 11, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–16340 Filed 6–18–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98D–0401]

Draft ''Guidance for Industry: Content and Format of Chemistry, Manufacturing and Controls Information and Establishment Description Information for a Vaccine or Related Product''; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance document entitled ''Guidance for Industry: Content and Format of Chemistry, Manufacturing and Controls Information and Establishment Description Information for a Vaccine or Related Product.'' The draft guidance document would provide guidance to applicants on the content and format of the Chemistry, Manufacturing and Controls (CMC) and Establishment Description sections of the ''Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use''