other cases, it may be appropriate to record Tanner stages of pubertal development or obtain biological markers of puberty and examine data for any potential influence of pubertal changes.

2.5.5 Adolescents (12 to 16 to 18 years (dependent on region))

This is a period of sexual maturation; medicinal products may interfere with the actions of sex hormones and impede development. Pregnancy testing and, in relevant studies, review of sexual activity and contraceptive use become necessary.

This is also a period of rapid growth. Medicinal products and illnesses that delay or accelerate the onset of puberty can have a profound effect on the pubertal growth spurt and, by changing the pattern of growth, may affect final height. Evolving cognitive and emotional changes could potentially influence the outcome of clinical studies.

Many diseases are also influenced by the hormonal changes around puberty (e.g., insulin resistance increases in diabetes mellitus, seizures may recur around menarche, frequency and severity of migraine and asthma change). Hormonal changes may thus influence the results of clinical studies.

Within this age group, adolescents are assuming responsibility for their own health and medication. Noncompliance is a special problem, particularly when medicinal products (for example, steroids) affect appearance. In clinical studies, compliance checks are important. Recreational use of unprescribed drugs should be specifically considered and monitored.

The upper age limit was arbitrarily set and may vary among regions. It may be possible to include older adolescents in adult studies, although issues of compliance may present problems. Given some of the unique challenges of adolescence, it may be appropriate to consider studying adolescent patients (whether they are to be included in adult or separate protocols) in centers knowledgeable and skillful in the care of this special population.

2.6 Ethical Issues in Pediatric Studies

The pediatric population represents a vulnerable subgroup. Therefore, special measures are needed to protect the rights of pediatric study participants and to shield them from undue risk. The purpose of this section is to provide a framework to ensure that pediatric studies are conducted ethically.

To be of benefit to those participating in a clinical study, as well as to the rest of the pediatric population, a clinical study must be properly designed to ensure the quality and interpretability of the data obtained. In addition, participants in clinical studies are expected to obtain some direct or indirect benefit from the clinical study except under the special circumstances discussed in ICH E6 (''Good Clinical Practice,'' section 4.8.14).

2.6.1 Institutional Review Board/ Independent Ethics Committee (IRB/IEC)

The roles and responsibilities of IRB's/ IEC's as detailed in ICH E6 are critical to the protection of study participants. When protocols involving the pediatric population are reviewed, there should be IRB/IEC members, or experts consulted by the IRB/ IEC, who are knowledgeable in pediatric ethical, clinical, and psychosocial issues.

2.6.2 Recruitment

Recruitment of study participants should occur in a noncoercive manner. While reimbursement and subsistence costs may be covered in the context of a pediatric clinical study, coercive inducements (financial or other), either to the parents or to the child, are not appropriate.

When studies are conducted in the pediatric population, an attempt should be made to include individuals representing the demographics of the region and the disease being studied, unless there is a valid reason for restricting enrollment.

2.6.3 Consent

Pediatric study participants are dependent on their parents or guardians who take legal responsibility for the participants' welfare and safety; fully informed consent should be obtained from the legal guardian in accordance with regional laws or regulations. All participants should be fully informed about the study in language and terms they are able to understand. Participants should assent to enroll in a study (age of assent to be determined by IRB's/IEC's). Participants of appropriate intellectual maturity should personally sign and date either a separately designed, written assent form or the written informed consent. In all cases, participants should be made aware of their rights to decline to participate or to withdraw from the study at any time. A participant's wish to withdraw from a study must be respected. There may be circumstances in therapeutic studies where, in the opinion of the investigator, parents, and IRB/IEC, the welfare of a pediatric patient would be jeopardized by his or her failing to participate in the study; the patient's agreement or assent may be waived under such circumstances. Emancipated or mature minors (as defined by local laws) may be capable of giving autonomous consent.

Information that can be obtained in a less vulnerable, consenting population should not be obtained in a more vulnerable population or one unable to provide individual consent. Studies in handicapped or institutionalized pediatric populations should be limited to diseases or conditions found principally or exclusively in these populations, or where the disease or condition in these pediatric patients would be expected to alter the disposition or pharmacodynamic effects of a medicinal product.

2.6.4 Minimizing Risk

However important a study may be to prove or disprove the value of a treatment, participants may suffer injury as a result of inclusion in the study, even if the whole community benefits. Every effort should be made to anticipate and reduce known hazards. Investigators should be fully aware before the start of a clinical study of all relevant preclinical and clinical toxicity of the medicinal product. To minimize risk in pediatric clinical studies, those conducting the study should be properly trained and experienced in studying the pediatric population, including the evaluation and management of potential pediatric adverse events.

In designing studies, every attempt should be made to minimize the number of participants and of procedures, consistent with good study design. Mechanisms should be in place to ensure that a study can be rapidly terminated should an unexpected hazard be noted.

2.6.5 Minimizing Distress

Repeated invasive procedures may be painful or frightening. Discomfort can be minimized if studies are designed and conducted by investigators experienced in the treatment of pediatric patients.

Protocols and investigations should be designed specifically for the pediatric population (not simply re-worked from adult protocols) and approved by a competent and experienced IRB/IEC.

Practical considerations to ensure that participants' experiences in clinical studies are positive and to minimize discomfort and distress include the following:

- Personnel knowledgeable and skilled in dealing with the pediatric population and its age-appropriate needs, including skill in performing pediatric procedures
- A physical setting with furniture, play equipment, activities, andfood appropriate for age
- Conducting studies in a familiar environment such as the hospital or clinic where participants normally receive their care
- Using approaches to minimize discomfort of procedures, such as:

— Topical anesthesia to place IV catheters

— Indwelling catheters rather than repeated venipunctures for blood sampling

— Collection of some protocol-specified blood samples when routine clinical samples are obtained

IRB's/IEC's should consider how many venipunctures are acceptable in an attempt to obtain blood samples for a protocol and ensure a clear understanding of procedures if an indwelling catheter fails to function over time. The participant's right to refuse further investigational procedures must be respected.

Dated: April 5, 2000.

William K. Hubbard,

Senior Associate Commissioner for Policy, Planning, and Legislation.

[FR Doc. 00–9064 Filed 4–11–00; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Cardiovascular and Renal Drugs Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration

(FDA). The meeting will be open to the public.

Name of Committee: Cardiovascular and Renal Drugs Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the agency on FDA's regulatory issues.

Date and Time: The meeting will be held on May 1, 2000, from 8:30 a.m. to 5:30 p.m., and on May 2, 2000, from 9 a.m. to 5:30 p.m.

Location: National Institutes of Health, 9000 Rockville Pike, Bldg. 10, Clinical Center, Jack Masur Auditorium, Bethesda, MD.

Contact Person: Joan C. Standaert, Center for Drug Evaluation and Research (HFD–110), Food and Drug Administration, Woodmont II Bldg., 1451 Rockville Pike, Rockville, MD 20752, 419–259–6211, or John M. Treacy (HFD–21), 301–827–7001 or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572 in the Washington, DC area), code 12533. Please call the Information Line for up-to-date information on this meeting.

Agenda: On May 1, 2000, the committee will discuss new drug applications (NDA) 21–188, Vanlev® (omapatrilat) Bristol Myers Squibb to be indicated for hypertension, and NDA 19–901, Altace® (ramipril) Capsules, King Pharmaceuticals, Inc., to be indicated for significant reduction of mortality, myocardial infarction, stroke, revascularization procedures, and heart failure in high risk patients. On May 2, 2000, the committee will discuss NDA 20–807/S–004, Refludan® [lepirudin(-DNA) for injection] Aventis Pharmaceuticals, Inc., to be indicated for anticoagulation in adult patients with acute coronary syndromes (unstable angina and acute myocardial infarction without ST segment elevations on electrocardiogram (EKG).

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person by April 24, 2000. Oral presentations from the public will be scheduled between approximately 8:30 a.m. and 9:30 a.m. on May 1, 2000. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before April 24, 2000, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C., app. 2).

Dated: April 4, 2000.

Linda A. Suydam,

Senior Associate Commissioner.

[FR Doc. 00–9003 Filed 4–11–00; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Care Financing Administration

[Document Identifier: HCFA–482]

Agency Information Collection Activities: Proposed Collection; Comment Request

AGENCY: Health Care Financing Administration, HHS.

In compliance with the requirement of section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995, the Health Care Financing Administration (HCFA), Department of Health and Human Services, is publishing the following summary of proposed collections for public comment. Interested persons are invited to send comments regarding this burden estimate or any other aspect of this collection of information, including any of the following subjects: (1) The necessity and utility of the proposed information collection for the proper performance of the agency's functions; (2) the accuracy of the estimated burden; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) the use of automated collection techniques or other forms of information technology to minimize the information collection burden.

Type of Information Collection Request: Extension of a currently approved collection;

Title of Information Collection: Methodology for Estimating Waiver Costs of HCFA Demonstration Projects;

Form No.: HCFA–482 (OMB# 0938–0408);

Use: The information collected is intended to provide guidance to individuals responsible for the preparation of waiver cost estimates for HCFA demonstrations. These estimates are used in analysis of potential costs and benefits associated with implementing a proposed policy.;

Frequency: Other: On Occasion;

Affected Public: State, Local or Tribal Government, Individuals or Households, Business or other for-profit, and Not-for-profit institutions;

Number of Respondents: 25;

Total Annual Responses: 25;

Total Annual Hours: 2,000.

To obtain copies of the supporting statement and any related forms for the proposed paperwork collections referenced above, access HCFA's Web Site address at http://www.hcfa.gov/regs/prdact95.htm, or E-mail your request, including your address, phone number, OMB number, and HCFA document identifier, to Paperwork@hcfa.gov, or call the Reports Clearance Office on (410) 786–1326. Written comments and recommendations for the proposed information collections must be mailed within 60 days of this notice directly to the HCFA Paperwork Clearance Officer designated at the following address: HCFA, Office of Information Services, Security and Standards Group, Division of HCFA Enterprise Standards, Attention: Dawn Willinghan, Room N2–14–26, 7500 Security Boulevard, Baltimore, Maryland 21244–1850.

Dated: March 20, 2000.

John P. Burke III,

HCFA Reports Clearance Officer, HCFA Office of Information Services, Security and Standards Group, Division of HCFA Enterprise Standards.

[FR Doc. 00–9017 Filed 4–11–00; 8:45 am]

BILLING CODE 4120–03–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Care Financing Administration

[Document Identifier: HCFA–R–314]

Agency Information Collection Activities: Proposed Collection; Comment Request

AGENCY: Health Care Financing Administration, HHS.

In compliance with the requirement of section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995, the Health Care Financing Administration (HCFA), Department of Health and Human Services, is publishing the following summary of proposed collections for public comment. Interested persons are invited to send comments regarding this burden estimate or any other aspect of this collection of information, including any of the following subjects: (1) The necessity and utility of the proposed information collection for the proper performance of the agency's functions; (2) the accuracy of the estimated burden; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) the use of automated collection techniques or other forms of information technology to