The steps in the assembly of the expression construct should be described in detail. This description should include the source and function of the component parts of the expression construct, e.g., origins of replication, antibiotic resistance genes, promoters, enhancers, and whether or not the protein is being synthesized as a fusion protein. A detailed component map and a complete annotated sequence of the plasmid should be given, indicating those regions that have been sequenced during the construction and those taken from the literature. Other expressed proteins encoded by the plasmid should be indicated. The nucleotide sequence of the coding region of the gene of interest and associated flanking regions that are inserted into the vector, up to and including the junctions of insertion, should be determined by DNA sequencing of the construct.

A description of the method of transfer of the expression construct into the host cell should be provided. In addition, methods used to amplify the expression construct and criteria used to select the cell clone for production should be described in detail.

B. Cell Bank System

Production of the recombinant protein should be based on well-defined MCB and Working Cell Banks (WCB). A cell bank is a collection of ampoules of uniform composition stored under defined conditions, each containing an aliquot of a single pool of cells. The MCB is generally derived from the selected cell clone containing the expression construct. The WCB is derived by expansion of one or more ampoules of the MCB. The cell line history and production of the cell banks should be described in detail, including methods and reagents used during culture, in vitro cell age, and storage conditions. All cell banks should be characterized for relevant phenotypic and genotypic markers, which could include the expression of the recombinant protein or presence of the expression construct.

The expression construct in the MCB should be analyzed as described below. If the testing cannot be carried out on the MCB, it should be carried out on each WCB.

Restriction endonuclease mapping or other suitable techniques should be used to analyze the expression construct for copy number, for insertions or deletions, and for the number of integration sites. For extrachromosomal expression systems, the percent of host cells retaining the expression construct should be determined.

The protein coding sequence for the recombinant protein product of the expression construct should be verified. For extrachromosomal expression systems, the expression construct should be isolated and the nucleotide sequence encoding the product should be verified without further cloning. For cells with chromosomal copies of the expression construct, the nucleotide sequence encoding the product could be verified by recloning and sequencing of chromosomal copies. Alternatively, the nucleic acid sequence encoding the product could be verified by techniques such as sequencing of pooled c-DNA clones or material amplified by the polymerase chain reaction. The nucleic acid sequence should be identical, within the limits of detection of the methodology, to that determined for the expression construct as described in section III.A., and should correspond to that expected for the protein sequence.

C. Limit for In Vitro Cell Age for Production

The limit for in vitro cell age for production should be based on data derived from production cells expanded under pilot plant-scale or full-scale conditions to the proposed in vitro cell age or beyond. Generally, the production cells are obtained by expansion of the WCB; the MCB could be used to prepare the production cells with appropriate justification.

The expression construct of the production cells should be analyzed once for the MCB as described in section III.B., except that the protein coding sequence of the expression construct in the production cells could be verified by either nucleic acid testing or analysis of the final protein product. Increases in the defined limit for in vitro cell age for production should be supported by data from cells that have been expanded to an in vitro cell age that is equal to or greater than the new limit for in vitro cell age.

IV. Conclusion

The characterization of the expression construct and the final purified protein are both important to ensure the consistent production of a r-DNA derived product. As described above, analytical data derived from both nucleic acid analysis and evaluation of the final purified protein should be evaluated to ensure the quality of a recombinant protein product.

Glossary of Terms

Expression Construct

The expression vector that contains the coding sequence of the recombinant protein and the elements necessary for its expression.

Flanking Control Regions

Noncoding nucleotide sequences that are adjacent to the 5' and 3' end of the coding sequence of the product that contain important elements that affect the transcription, translation, or stability of the coding sequence. These regions include, e.g., promoter, enhancer, and splicing sequences, and do not include origins of replication and antibiotic resistance genes.

Integration Site

The site where one or more copies of the expression construct is integrated into the host cell genome.

In Vitro Cell Age

Measure of time between thaw of the MCB vial(s) to harvest of the production vessel measured by elapsed chronological time in culture, by population doubling level of the cells, or by passage level of the cells when subcultivated by a defined procedure for dilution of the culture.

Master Cell Bank (MCB)

An aliquot of a single pool of cells that generally has been prepared from the selected cell clone under defined conditions, dispensed into multiple containers, and stored under defined conditions. The MCB is used to derive all working cell banks. The testing performed on a new MCB (from a previous initial cell clone, MCB, or WCB) should be the same as for the MCB unless justified.

Pilot Plant Scale

The production of a recombinant protein by a procedure fully representative of and simulating that to be applied on a full commercial manufacturing scale. The methods of cell expansion, harvest, and product purification should be identical except for the scale of production.

Relevant Genotypic and Phenotypic Markers

Those markers permitting the identification of the strain of the cell line that should include the expression of the recombinant protein or presence of the expression construct.

Working Cell Bank (WCB)

The WCB is prepared from aliquots of a homogeneous suspension of cells obtained from culturing the MCB under defined culture conditions.

Dated: February 16, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–4064 Filed 2–22–96; 8:45 am]

BILLING CODE 4160–01–F

Advisory Committees; Notice of Meetings

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: This notice announces forthcoming meetings of public advisory committees of the Food and Drug Administration (FDA). This notice also summarizes the procedures for the meetings and methods by which interested persons may participate in open public hearings before FDA's advisory committees.

FDA has established an Advisory Committee Information Hotline (the hotline) using a voice-mail telephone system. The hotline provides the public with access to the most current information on FDA advisory committee meetings. The advisory committee hotline, which will disseminate current information and information updates, can be accessed by dialing 1–800–741–8138 or 301–443–0572. Each advisory committee is assigned a 5-digit number. This 5-digit number will appear in each individual notice of meeting. The hotline will enable the public to obtain information about a particular advisory committee by using the committee's 5-digit number. Information in the hotline

is preliminary and may change before a meeting is actually held. The hotline will be updated when such changes are made.

MEETINGS: The following advisory committee meetings are announced:

General Hospital and Personal Use Devices Panel of the Medical Devices Advisory Committee

Date, time, and place. March 11, 1996, 8 a.m., Holiday Inn—Gaithersburg, Ballroom, Two Montgomery Village Ave., Gaithersburg, MD. A limited number of overnight accommodations have been reserved at the hotel. Attendees requiring overnight accommodations may contact the hotel at 301–948–8900 and reference the FDA Panel meeting block. Reservations will be confirmed at the group rate based on availability. Attendees with a disability requiring special accommodations should contact Sociometrics, Inc., 301–608–2151. The availability of appropriate accommodations cannot be assured unless prior notification is received.

Type of meeting and contact person. Closed committee deliberations, 8 a.m. to 9 a.m.; open public hearing, 9 a.m. to 10 a.m., unless public participation does not last that long; open committee discussion, 10 a.m. to 5 p.m.; Janet L. Scudiero, Center for Devices and Radiological Health (HFZ–420), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–1287, or FDA Advisory Committee Information Hotline, 1–800–741–8138 (301–443–0572 in the Washington, DC area), General Hospital and Personal Use Devices Panel, code 12520.

General function of the committee. The committee reviews and evaluates data on the safety and effectiveness of marketed and investigational devices and makes recommendations for their regulation.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before March 4, 1996, 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 required to make their comments.

Open committee discussion. The committee will: (1) Discuss and make recommendations on the classification of two unclassified preamendments devices, percutaneously implanted long-term catheters, and implanted intravascular infusion ports; and (2) discuss a premarket notification submission for an antimicrobial coated latex examination glove.

Closed committee deliberations. FDA staff will present to the committee trade secret and/or confidential commercial information regarding present and future FDA issues. This portion of the meeting will be closed to permit discussion of this information (5 U.S.C. 552b(c)(4)).

Joint Meeting of the Antiviral Drugs Advisory Committee and the Dermatologic and Ophthalmic Drugs Advisory Committee (Ophthalmic Drugs Subcommittee)

Date, time, and place. March 14, 1996, 1 p.m., and March 15, 1996, 8:30 a.m., Holiday Inn—Gaithersburg, Whetstone and Goshen Rooms, Two Montgomery Village Ave., Gaithersburg, MD.

Type of meeting and contact person. Closed committee deliberations, March 14, 1996, 1 p.m. to 5 p.m.; open committee discussion, March 15, 1996, 8:30 a.m. to 11 a.m.; open public hearing, 11 a.m. to 12 m., unless public participation does not last that long; open committee discussion, 12 m. to 4 p.m.; Ermona B. McGoodwin or Liz Ortuzar, Center for Drug Evaluation and Research (HFD–21), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–5455, or FDA Advisory Committee Information Hotline, 1–800–741–8138 (301–443–0572 in the Washington, DC area), Antiviral Drugs Advisory Committee, code 12531.

General function of the committees. The Antiviral Drugs Advisory Committee reviews and evaluates available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of acquired immune deficiency syndrome (AIDS), AIDS-related complex (ARC), and other viral, fungal, and mycobacterial infections. The Dermatologic and Ophthalmic Drugs Advisory Committee reviews and evaluates data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of dermatologic and ophthalmic disorders.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before March 8, 1996, 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 required to make their comments.

Closed committee deliberations. On March 14, 1996, the Antiviral Drugs Advisory Committee will discuss trade secret and/or confidential commercial information relevant to pending new drug applications (NDA's). This portion of the meeting will be closed to permit discussion of this information (5 U.S.C. 552b(c)(4)).

Open committee discussion. On March 15, 1996, the Antiviral Drugs Advisory Committee and an ophthalmic drugs subcommittee of the Dermatologic and Ophthalmic Drugs Advisory Committee will meet jointly to discuss data relevant to NDA 20–638 Vistide™ (cidofovir, intravenous, Gilead Sciences, Inc.) for treatment of cytomegalovirus (CMV) retinitis in patients with AIDS.

Blood Products Advisory Committee

Date, time, and place. March 21 and 22, 1996, 8 a.m., Holiday Inn—Bethesda, Versailles Ballrooms II and III, 8120 Wisconsin Ave., Bethesda, MD.

Type of meeting and contact person. Open committee discussion, March 21, 1996, 8 a.m. to 9:10 a.m.; open public hearing, 9:10 a.m. to 9:40 a.m., unless public participation does not last that long; open committee discussion, 9:40 a.m. to 11:15 a.m.; open public hearing, 11:15 a.m. to 12:15 p.m., unless public participation does not last that long; open committee discussion, 12:15 p.m. to 3 p.m.; open public hearing, 3 p.m. to 4 p.m., unless public participation does not last that long; open committee discussion, 4 p.m. to 5 p.m.; open committee discussion, March 22, 1996, 8 a.m. to 11:30 a.m.; open public hearing, 11:30 a.m. to 12:15 p.m., unless public participation does not last that long; open committee discussion, 12:15 p.m. to 2 p.m.; closed committee deliberations, 2 p.m. to 3 p.m.; Linda A. Smallwood, Center for Biologics Evaluation and Research (HFM–350), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301–827–3514, or FDA Advisory Committee Information Hotline, 1–800–741–8138 (301–443–0572 in the Washington, DC area) Blood Products Advisory Committee, code 12388.

General function of the committee. The committee reviews and evaluates data on the safety and effectiveness, and appropriate use of blood products intended for use in the diagnosis, prevention, or treatment of human diseases.

Agenda—Open public hearing. Interested persons may present data,

information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before March 15, 1996, 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 required to make their comments.

Open committee discussion. On March 21, 1996, the committee will hear agency updates on Creutzfeldt-Jakob Disease and blood safety, peripheral blood hematopoietic stem cell products intended for transfusion, and a summary of regulatory issues related to human reproductive tissue. Labeling issues regarding testing for antibody to hepatitis C virus antigen by an ''HCV 3.0'' assay will be reviewed and discussed in the morning and in the afternoon, there will also be a discussion of clinical claims for the Roche Amplicor HIV Monitoring Test™. On March 22, 1996, the committee will review and discuss implications of non-lipid enveloped viruses in blood products.

Closed committee deliberations. On March 22, 1996, the committee will review trade secret and/or confidential commercial information relevant to current and pending products. This portion of the meeting will be closed to permit discussion of this information (5 U.S.C. 552b(c)(4)).

General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee

Date, time, and place. March 25, 1996, 8:30 a.m., Holiday Inn—Gaithersburg, Goshen Room, Two Montgomery Village Ave., Gaithersburg, MD. A limited number of overnight accommodations have been reserved at the hotel. Attendees requiring overnight accommodations may contact the hotel at 301–948–8900 and reference the FDA Panel meeting block. Reservations will be confirmed at the group rate based on availability. Attendees with a disability requiring special accommodations should contact John Sellman, Sociometrics, Inc., 301–608–2151. The availability of appropriate accommodations cannot be assured unless prior notification is received.

Type of meeting and contact person. Open public hearing, 8:30 a.m. to 9:30 a.m., unless public participation does not last that long; open committee discussion, 9:30 a.m. to 3 p.m.; closed committee deliberations, 3 p.m. to 4:30 p.m.; Gail G. Gantt, Center for Devices and Radiological Health (HFZ–410), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–3090, or FDA Advisory Committee Information Hotline, 1–800–741–8138 (301–443–0572 in the Washington, DC area), General and Plastic Surgery Devices Panel, code 12519.

General function of the committee. The committee reviews and evaluates data on the safety and effectiveness of marketed and investigational devices and makes recommendations for their regulation.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before March 18, 1996, 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 required to make their comments.

Open committee discussion. The committee will discuss and vote on a premarket approval application for a resorbable translucent membrane for use as an adjuvant in abdominopelvic surgery.

Closed committee deliberations. FDA staff will present to the committee trade secret and/or confidential commercial information regarding present and future FDA issues. This portion of the meeting will be closed to permit discussion of this information (5 U.S.C. 552b(c)(4)).

Each public advisory committee meeting listed above may have as many as four separable portions: (1) An open public hearing, (2) an open committee discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the specific meeting involved. The dates and times reserved for the separate portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather than a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairperson determines will facilitate the committee's work.

Public hearings are subject to FDA's guideline (subpart C of 21 CFR part 10) concerning the policy and procedures for electronic media coverage of FDA's public administrative proceedings, including hearings before public advisory committees under 21 CFR part 14. Under 21 CFR 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this Federal Register notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hearing's conclusion, if time permits, at the chairperson's discretion.

The agenda, the questions to be addressed by the committee, and a current list of committee members will be available at the meeting location on the day of the meeting.

Transcripts of the open portion of the meeting may be requested in writing from the Freedom of Information Office (HFI–35), Food and Drug Administration, rm. 12A–16, 5600 Fishers Lane, Rockville, MD 20857, approximately 15 working days after the meeting, at a cost of 10 cents per page. The transcript may be viewed at the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857, approximately 15 working days after the meeting, between the hours of 9 a.m. and 4 p.m., Monday through Friday. Summary minutes of the open portion of the meeting may be requested in writing from the Freedom of Information Office (address above) beginning approximately 90 days after the meeting.

The Commissioner has determined for the reasons stated that those portions of the advisory committee meetings so designated in this notice shall be closed. The Federal Advisory Committee Act (FACA) (5 U.S.C. app. 2, 10(d)), permits such closed advisory committee meetings in certain circumstances. Those portions of a meeting designated as closed, however, shall be closed for

the shortest possible time, consistent with the intent of the cited statutes.

The FACA, as amended, provides that a portion of a meeting may be closed where the matter for discussion involves a trade secret; commercial or financial information that is privileged or confidential; information of a personal nature, disclosure of which would be a clearly unwarranted invasion of personal privacy; investigatory files compiled for law enforcement purposes; information the premature disclosure of which would be likely to significantly frustrate implementation of a proposed agency action; and information in certain other instances not generally relevant to FDA matters.

Examples of portions of FDA advisory committee meetings that ordinarily may be closed, where necessary and in accordance with FACA criteria, include the review, discussion, and evaluation of drafts of regulations or guidelines or similar preexisting internal agency documents, but only if their premature disclosure is likely to significantly frustrate implementation of proposed agency action; review of trade secrets and confidential commercial or financial information submitted to the agency; consideration of matters involving investigatory files compiled for law enforcement purposes; and review of matters, such as personnel records or individual patient records, where disclosure would constitute a clearly unwarranted invasion of personal privacy.

Examples of portions of FDA advisory committee meetings that ordinarily shall not be closed include the review, discussion, and evaluation of general preclinical and clinical test protocols and procedures for a class of drugs or devices; consideration of labeling requirements for a class of marketed drugs or devices; review of data and information on specific investigational or marketed drugs and devices that have previously been made public; presentation of any other data or information that is not exempt from public disclosure pursuant to the FACA, as amended; and, deliberation to formulate advice and recommendations to the agency on matters that do not independently justify closing.

This notice is issued under section 10(a)(1) and (2) of the Federal Advisory Committee Act (5 U.S.C. app. 2), and FDA's regulations (21 CFR part 14) on advisory committees.

Dated: February 15, 1996.

Michael A. Friedman,

Deputy Commissioner for Operations.

[FR Doc. 96–4067 Filed 2–22–96; 8:45 am]

BILLING CODE 4160–01–F

[Docket No. 95N–0357]

Medical Devices; Investigational Devices; Interagency Agreement Between the Food and Drug Administration and the Health Care Financing Administration; Categorization of Investigational Devices for Coverage under Medicare; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of an interagency agreement between FDA and the Health Care Financing Administration (HCFA) and a list of all FDA-approved investigational device exemptions (IDE's) and their corresponding categorization determinations for possible Medicare reimbursement. This list was compiled in accordance with the categorization criteria set forth in the interagency agreement. The HCFA/FDA interagency agreement regarding investigational devices describes procedures by which FDA will assist HCFA in identifying nonexperimental/investigational devices that are potentially covered by Medicare under a final rule recently issued by HCFA extending coverage to certain devices and related services. FDA is making the interagency agreement and the list of FDA-approved IDE's and their categorization determinations available to IDE sponsors and the public.

DATES: The HCFA final rule ''Medicare Program; Criteria and Procedures for Extending Coverage to Certain Devices and Related Services'' became effective on November 1, 1995. The HCFA/FDA interagency agreement became effective on September 8, 1995.

ADDRESSES: Submit written requests for a copy of the interagency agreement and the categorization list to the Division of Small Manufacturers Assistance (HFZ–220), Food and Drug Administration, 1350 Piccard Dr., Rockville, MD 20850. Requests should be identified with the docket number found in brackets in the heading of this document. Send two self-addressed adhesive labels to assist that office in processing your request. Copies of the interagency agreement and the categorization list are available for public examination in the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857 between 9 a.m. and 4 p.m., Monday through Friday. Copies of a facsimile of this information are available from the Center for Devices and Radiological Health's (CDRH's) Facts on Demand (1–800–899–0381). This information may also be obtained from the electronic docket administered by the Division of Small Manufacturers Assistance and is available to anyone with a video terminal or personal computer (1–800–252–1366, 1–800–222–0185, or 1–301–594–2741). Requests for reconsideration of the categorization of an IDE should be submitted in the same manner as an IDE supplement and should reference the IDE number, and be submitted in triplicate to: IDE Document Mail Center (HFZ–401), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850.

FOR FURTHER INFORMATION CONTACT: John Ensign, Center for Devices and Radiological Health (HFZ–404), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–1190.

SUPPLEMENTARY INFORMATION: In the Federal Register of September 19, 1995 (60 FR 48417), HCFA published a final rule in which it announced that it would consider for Medicare coverage certain devices with an FDA-approved IDE that have been categorized as nonexperimental/investigational. An FDA-approved IDE application permits a device which otherwise could not be lawfully shipped without marketing clearance, to be shipped lawfully for the purpose of conducting a clinical trial in accordance with section 520(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360j(g)) and 21 CFR parts 812 and 813.

Under section 513 of the act (21 U.S.C. 360c), all devices must be classified into one of three regulatory classes: Class I (general controls), Class II (special controls), or Class III (premarket approval). For the purposes of consideration for reimbursement under the Medicare program and in accordance with the procedures set forth in the HCFA final rule published on September 19, 1995, FDA has categorized all FDA-approved IDE's into either Category A (experimental/investigational) or Category B (nonexperimental/investigational). An experimental/investigational (Category A) device refers to an innovative device believed to be in Class III for which ''absolute risk'' of the device type has not been established (that is, initial questions of safety and effectiveness have not been resolved, and the FDA is unsure whether the device type can be safe and effective). A nonexperimental/investigational (Category B) device refers to a device believed to be in Class I or Class II, or a device believed to be