Subject: Amendment of 73.202(b) Table of Allotments FM Broadcast Stations (Windthorst, Texas).

Number of Petitions Filed: 2.

Federal Communications Commission.

Magalie Roman Salas,

Secretary.

[FR Doc. 00–31174 Filed 12–6–00; 8:45 am]

BILLING CODE 6712–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Secretary's Advisory Committee on Genetic Testing

AGENCY: Office of the Secretary, DHHS.

ACTION: Request for public comment on a proposed classification methodology for determining level of review for genetic tests.

SUMMARY: The Secretary's Advisory Committee on Genetic Testing (SACGT) was chartered to advise the Department of Health and Human Services on the medical, scientific, ethical, legal, and social issues raised by the development and use of genetic tests. SACGT recently completed its first report, Enhancing the Oversight of Genetic Tests (available at *http://www4.od.nih.gov/oba/sacgt.html*). One of SACGT's major recommendations was that all new genetic tests be reviewed by the Food and Drug Administration (FDA) before they are used for clinical care or public health purposes through ''new and innovative oversight mechanisms that will not limit the development of new tests or inordinately delay their availability.'' SACGT also recommended that FDA correlate the level of review applied to each genetic test with the level of scrutiny warranted by the test.

To assist FDA in determining which tests warrant greater scrutiny, SACGT is developing a classification methodology. A SACGT Working Group on Genetic Test Classification, composed of SACGT members and ad hoc experts, met on August 3, 2000, to identify criteria for assessing the risks and benefits of genetic tests that could serve as the basis for a classification scheme. The full Committee endorsed the working group's approach on August 4, 2000. Due to further analysis of the proposed approach and concerns raised by professional genetics and laboratory organizations about its practicality, SACGT revisited the initial proposal at its November 2–3 meeting. SACGT modified the methodology and agreed that additional input from public and professional organizations should be gathered. It is now seeking public comments on the rationale and feasibility of the proposed test classification methodology and several specific questions.

DATES: The public is encouraged to submit written comments on the proposed classification methodology by January 25, 2001 in order for SACGT to consider the comments at its next meeting in February 2001. The following mailing address should be used: SACGT, National Institutes of Health, 9000 Rockville Pike, Building 1, Room 103, Bethesda, Maryland, 20892. SACGT's facsimile number is 301–496–9839. Comments can also be sent via e-mail to *hagas@od.nih.gov*. All public comments received will be available for public inspection at the SACGT office between the hours of 8:30 a.m. and 5 p.m.

FOR FURTHER INFORMATION CONTACT: Questions about this request for public comment can be directed to Dr. Susanne Haga, by e-mail (*hagas@od.nih.gov*) or telephone (301–496–9838). The methodology will also be posted on SACGT's website for review and comment.

SUPPLEMENTARY INFORMATION:

Background

Decades of genetics research have brought about many important medical and public health advances. The pace of discovery in this area has enabled scientists to make rapid progress in understanding the role of genetics in many common yet complex diseases and conditions, such as heart disease, cancer, and diabetes. It also has increased knowledge that may lead to the development of new tests to identify these disease conditions in individuals, sometimes before symptoms occur. According to GeneTests, a genetic testing laboratory directory, genetic testing is clinically available for more than 400 diseases or conditions in more than 200 laboratories in the United States, and investigators are exploring the development of tests for an additional 338 diseases or conditions. However, most of the current genetic testing is for single gene disorders such as Huntington disease and cystic fibrosis.

Genetic tests can be performed for a number of purposes. Moreover, a test can be used in more than one way, such as when a test used for diagnostic purposes is also used to predict risk of disease. SACGT included the following types of testing within its definition: (1) an analysis performed on human DNA, RNA, genes, and/or chromosomes to detect heritable or acquired genotypes, mutations, phenotypes, or karyotypes that cause or are likely to cause a specific disease or condition; and (2) the analysis of human proteins and certain metabolites, which are predominantly used to detect heritable or acquired genotypes, mutations, or phenotypes. The purposes of both these types of genetic tests include predicting risks of disease, screening of newborns, directing clinical management, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or populations. Not included in this definition are tests that are used primarily for other purposes, but that may contribute to diagnosing a genetic disease (*e.g.*, blood smear, certain serum chemistries), and tests conducted exclusively for forensic identification purposes.

In the past, many tests were developed to detect or confirm rare genetic diseases. More recently, tests have been developed to detect mutations that may be involved in or contribute to more common, complex conditions (such as breast, ovarian, and colon cancer and cardiovascular disease), the effects of which generally do not appear until later in life. Optimally, these tests are used to predict a person's predisposition to disease where there is a family history of the disease, and in general, such tests are not recommended for individuals without such a history. However, in the future, the use of predictive tests may expand and be offered to individuals without a family history of certain diseases and conditions, *e.g.*, common adult-onset disorders.

In Enhancing the Oversight of Genetic Tests, SACGT recommended that all new genetic tests be reviewed by the Food and Drug Administration (FDA) before they are used for clinical care or public health purposes. The Committee suggested that FDA's review be accomplished through ''new and innovative oversight mechanisms that will not limit the development of new tests or inordinately delay their availability.'' Determining the level of review required of a particular genetic test is crucial to ensuring that a test receives the appropriate level of review based on the characteristics of the test and its target disease or condition. In order to determine the appropriate level of review for genetic tests, SACGT concluded that a classification methodology was needed.

To assist FDA in determining the appropriate level of review, a working group on genetic test classification was convened in August, composed of SACGT members and ad hoc experts. The goal of the working group was to

develop criteria for assessing the risks and benefits of genetic tests that would serve as the basis for a classification scheme. In classifying genetic tests by the level of review warranted, the working group explored a number of factors that could be used, including test characteristics (analytical validity, clinical validity, and clinical utility), availability of safe and effective treatments, and the social consequences of a diagnosis or identification of risk status. They also considered whether the test would be for a common or an orphan (rare) disease or mutation; whether the test will be used for population-based screening or testing of individuals; whether the test is used to detect germline or somatic mutations; whether the test is primarily used for predictive or diagnostic purposes; the complexity of the test; the level of difficulty in interpreting test results; whether the mutation being tested for is highly or weakly penetrant (the likelihood of developing a disease or condition); and the availability of independent methods of confirmation to reduce the occurrence of false-positive test results.

Proposed Test Classification Methodology for Determining Level of Review for Genetic Tests

In SACGT's August draft of the classification methodology, the working group developed two levels of review and four criteria to be used in the determination of review level for genetic tests. The four criteria related to test volume; whether a test is to be used for population-based screening; the purpose of the test (predictive or diagnostic); and for predictive tests, the availability of an intervention, the predictive value of the testing process, or significant medical or social risks associated with the test. After further deliberation and discussion of the proposed test classification methodology, SACGT modified the methodology at its November meeting. The modified approach maintains the two levels of review initially proposed (Level I and Level II) but revises and reduces the number of criteria. The revised criteria relate to analytical validity, population-based screening, and frequency of disease. SACGT is seeking public comment on this revised test classification methodology.

Classification Structure and Levels of Review

SACGT determined that two levels of review would provide the most straightforward review process for all new genetic tests. In SACGT's proposed classification methodology, tests for rare diseases or conditions, with the exception of those used for population screening, would receive a Level I review and all other new genetic tests would receive a Level II review. While details of the review processes have yet to be fully defined, the Committee has outlined its expectations for each review level.

A Level I review would be a streamlined review process that would involve assurances of pre-test/post-test information according to a standard template and, possibly, data collection from existing resources. SACGT currently proposes that pre-test information include a description of the purpose of the test, the clinical condition for which the test is performed, the definition of the test (specific laboratory protocol), and evidence of analytical and clinical validity. Less evidence of data would be permitted in Level I. The Level II review process would include a detailed review of pre-test/post-test information and, possibly, new data collection initiatives.

SACGT suggests that both review levels consider the use of standards developed in consultation with professional organizations, consumer representatives, and other relevant groups; post-market adverse event reporting; and assurances for informed consent as appropriate. SACGT also suggests that, as appropriate, peer-reviewed literature could be used to substantiate claims of analytical and clinical validity.

Classification Criteria

The three criteria SACGT proposes to use in determining the level of review of a genetic test are analytical validity, population screening, and frequency of disease. The first criterion is an essential feature that all genetic tests should be able to demonstrate. The two other criteria classify genetic tests according to the number of people who may be affected by the disease or condition.

SACGT believes that all tests should be analytically valid and that no test should be considered for further review unless shown to be so. Analytical validity is defined as the ability of a test to measure or detect the analyte it is intended to measure or detect. An analyte is defined as the substance measured by a laboratory test, *e.g.,* DNA—mutation, allele, or chromosome, metabolites, or enzyme activity. Analytical validity includes analytical sensitivity (the probability that a test will detect an analyte when it is present in the sample) and analytical specificity (the probability that a test will be negative when an analyte is absent from a sample).

Population screening is the second criterion in the classification methodology. Population screening affects large numbers of people, most of whom are currently healthy. The risks of false-positive and false-negative test results need to be carefully evaluated. The type of follow-up for individuals who test positive must be clear and proven. In this schema, the definition of a population-based test is a test intended for use on a cluster of individuals who are identified as a group or population (>1000) on the basis of shared ethnicity, class, geographical location, gender, age, or other characteristics such as pregnancy, behavior (*e.g.,* smoking), physical traits (*e.g.,* baldness or height), or occupation in which the frequency of the disease allele or predispositional risk to be determined is higher than the frequency or risk in the general population. Carrier screening for Tay-Sachs disease in the Ashkenazi Jewish population would be considered a population-based test. Another example would be a test used for all newborns.

The third criterion SACGT proposes to include in the classification methodology is the frequency of the disease. This criterion would divide tests according to whether they test for a common disease or rare disease. SACGT proposes to define a rare disease or condition as having a prevalence of less than one in 2,000 individuals or an incidence less than one in 10,000 individuals.

There were a number of reasons why SACGT chose to divide genetic tests on the basis of whether it was for a rare disease versus a common disease. The Committee believes that tests for common diseases or conditions should receive a higher level of review for two reasons. First, the molecular and metabolic basis of common diseases is often complex. Recent findings have shown that the genetic etiology of common diseases and conditions is not as straightforward as traditional Mendelian disorders and likely involve the consideration of a number of other factors such as environment, lifestyle, and other genetic factors. For this reason, a higher level of review and larger clinical studies may be necessary to demonstrate the accuracy and validity of tests for common diseases or conditions. Second, tests for common diseases or conditions have the potential to affect a greater number of people.

The Committee wishes to make recommendations that will facilitate the continued development and availability

of tests for rare diseases and conditions. SACGT would not want to see the cost of, and time required for, review to become barriers to the provision of genetic tests for rare diseases, particularly those provided in the academic setting, given the limited financial resources and income of these laboratories.

Applying the Classification Methodology

These three criteria would be considered in a step-wise manner leading to a determination of the appropriate level of review warranted by a particular genetic test (see figure). When determining the level of review for a particular test, SACGT proposes that a test's analytical validity be ascertained first. If a test was shown to be not analytically valid, it would be automatically rejected. If a test was shown to be analytically valid, it would move on to the next criterion of population screening. In the Committee's view, tests used for population screening should receive a higher level of review because of the large number of people it would affect. If a test is to be used for population screening, it would receive a Level II review. If a test is not to be used for population screening, the third criterion would be applied. If the test is used to detect a rare disease or condition, it would receive a Level I review. Since it may take many years to gather large numbers of affected individuals for study, a Level I review would permit smaller data sets. Documentation would need to be provided to support the claim that a test is for a rare disease or condition. References may include peer-reviewed literature citations, specialized medical society proceedings, or governmental statistical publications. When no such studies or literature citations are available, the applicant may be able to demonstrate prevalence or incidence by providing credible conclusions from appropriate research or surveys. A rare disease test may sometimes warrant a Level II review. All other tests would receive a Level II review.

Questions on Which Comment Is Being Solicited

In order to ensure that a comprehensive and appropriate classification methodology is developed, SACGT would appreciate receiving public comment on the rationale and feasibility of the proposed test classification methodology. In addition, SACGT is interested in receiving input on the following specific questions:

1. Is the number of review levels appropriate? Should there be more than two levels? Should all genetic tests receive the same level of review?

2. Are the criteria of analytic validity, population screening, and frequency of disease appropriate for determining the proper review level? Should other criteria, such as the intended use of a genetic test (*e.g.*, diagnostic, predictive, carrier, prenatal, etc.) or clinical utility, be considered in the classification of tests? If so, how should they be incorporated into the methodology?

3. Are the proposed definitions for population and rare diseases appropriate?

4. SACGT has not proposed a specific threshold or minimum standard for analytical validity. Should a threshold for analytical validity be defined? If so, what should the standard be?

5. What characteristics of a rare disease test would raise the level of review from Level I to Level II?

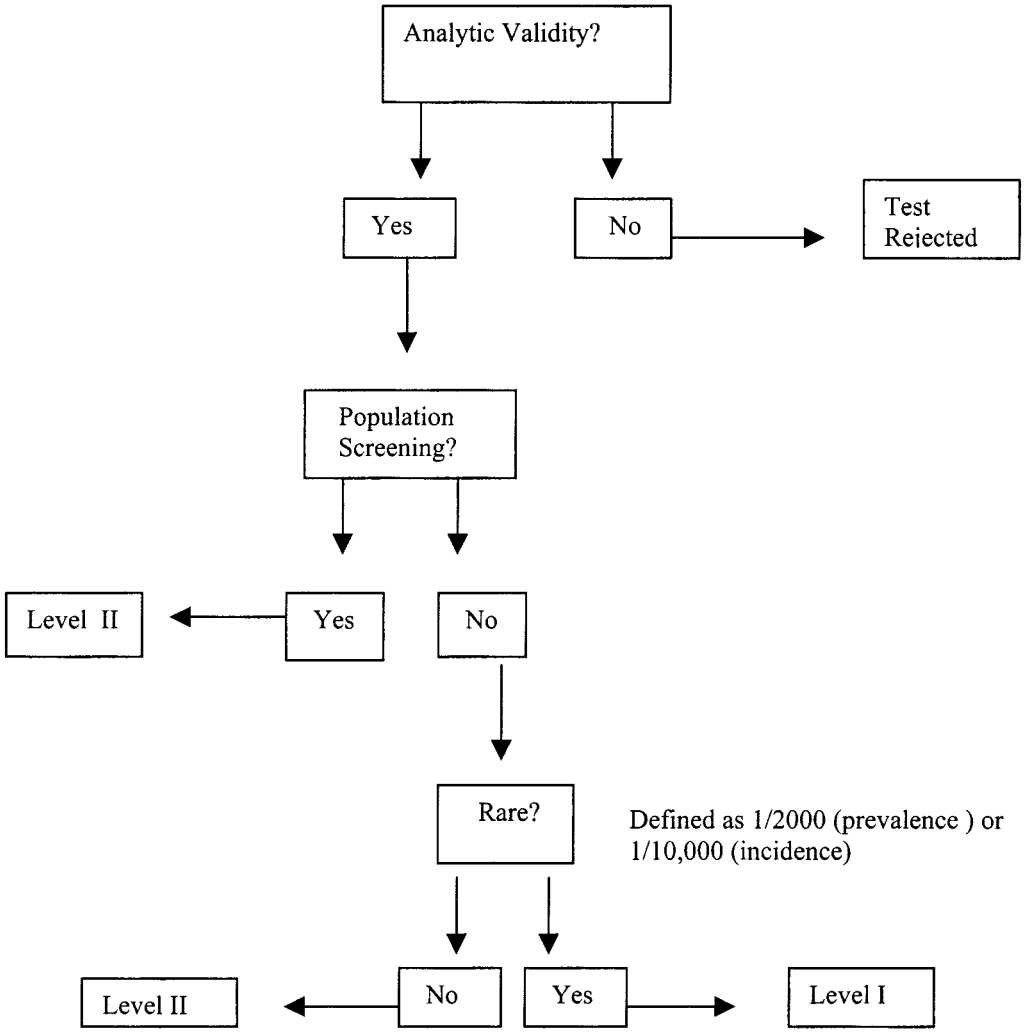
Dated: November 29, 2000.

Sarah Carr,

Executive Secretary, SACGT.

BILLING CODE 4140–01–P

Proposed Test Classification Scheme for Determining Level of Review of Genetic Tests



[FR Doc. 00–31218 Filed 12–6–00; 8:45 am]
BILLING CODE 4140–01–C

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Meeting of the National Human Research Protections Advisory Committee

AGENCY: Office of Public Health and Science, Office for Human Research Protections, HHS.

ACTION: Notice of first meeting.

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

The meeting will be open to the public, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the contact person listed below. Individuals planning on attending the meeting and who want to ask questions must submit their questions in writing in advance of the meeting to the contact person listed below.

DATES: The Committee will hold its next meeting on December 20–21, 2000. The meeting will convene from 8:30 a.m. to its recess at 4:30 p.m. on December 20th and resume at 9 a.m. to 3 p.m. EST on December 21st.

ADDRESSES: Bethesda Marriott-Pooks Hill, 515 Pooks Hill Road, Bethesda, Maryland 20814, (301) 897–9400.

FOR FURTHER INFORMATION CONTACT: Mr. Garey Rice, Administrative Officer, Office for Human Research Protections, 6100 Executive Boulevard, Room 310B (MSC 7507), Rockville, Maryland 20892–7507, (301) 402–6003. The electronic mail address is: *gr66s@nih.gov.*

SUPPLEMENTARY INFORMATION: The National Human Research Protections Advisory Committee was established on June 6, 2000 to provide expert advice and recommendations to the Secretary of HHS, Assistant Secretary for Health, the Director, Office for Human Research Protections, and other departmental officials on a broad range of issues and topics pertaining to or associated with the protection of human research subjects.