

6.7.4 Removed lubricant from the system and/or the equipment shall be disposed of in accordance with applicable federal, state and local procedures and regulations.

6.8 The equipment must be capable of continuous operation in ambient [temperature] of 10 C to 49 C degrees and comply with 6.1.

6.9 The equipment should be compatible with leak detection material that may be present in the mobile air conditioning system.

7.0 For test validation, the equipment is to be operated according to the manufacturer's instructions.

8.0 This recommended practice will become a J standard one year after first publication.

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# federal register

Wednesday  
April 22, 1992

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## PART IV

### Department of the Interior

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#### Bureau of Indian Affairs

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#### 1992 Assessment Rates for Operation and Maintenance of the Salt River Indian Irrigation Project, Maricopa County, AZ; Notice

## DEPARTMENT OF THE INTERIOR

## Bureau of Indian Affairs

## 1992 Assessment Rates for Operation and Maintenance of the Salt River Indian Irrigation Project, Maricopa County, AZ

**AGENCY:** Bureau of Indian Affairs, Interior.

**ACTION:** Notice of rate change.

**SUMMARY:** The purpose of this document is to give the public notice of the current assessment rates for operating and maintaining the Salt River Indian Irrigation Project. The assessment rates are based on a prepared estimate of the cost of normal operation and maintenance of the irrigation project. Normal operation and maintenance is defined as the cost of all activities involved in delivering irrigation water, including pumped water and maintaining the facilities, for the year.

The Salt River Pima-Maricopa Indian Community Water Rights Settlement Act of 1988 became effective approximately December 9, 1991. That settlement changed the assessed acreage. No process was defined by the parties to the settlement, that the Area Director is aware of, to address his responsibility in accordance with 25 CFR part 171 to announce the annual assessment rate. Therefore, his staff has provided the Community a detailed estimate of the cost to operate the Salt River Project for the 1992 Calendar Year and the Community has responded with proposed assessment rates.

The assessment rate is \$50 per acre leased and entitles the payer to 3 acre feet of water per acre. The spill water rate is \$9 per acre foot. Excess water (beyond the 3 acre feet per acre when no spill water is available) rate is \$35 per acre foot. The acreage used to determine the assessment rate includes the total acreage leased for farming at this time, 7649 acres.

Enrolled Community members irrigating their own property will be charged \$10 per acre foot of water delivered to their property. They will not be charged the assessment rate.

The Settlement causes all sources of water to belong to the Community to be distributed wherever they direct below the Arizona Canal. The Community is expected to take over the operation and maintenance of the Project in the future, therefore this cooperative effort appears appropriate.

**DATES:** The rates stated in this public notice became effective January 1, 1992, and will remain in effect until the Community takes over the Salt River

Indian Irrigation Project or until changed by action of the Area Director.

**FOR FURTHER INFORMATION CONTACT:** Superintendent, Salt River Agency, Route 1, Box 117, Scottsdale, Arizona 85256, telephone COM (602) 640-2842.

**SUPPLEMENTARY INFORMATION:** The authority to issue this document is vested in the Secretary of the Interior by 5 U.S.C. 301 and the Act of August 14, 1914 (38 Stat. 583, 25 U.S.C. 385).

The 1991 basic operation and maintenance charges were calculated using the estimated operation and maintenance costs for calendar year 1991 and dividing that amount by the historic "assessable" acres. Additional sources of water beyond Bartlett Dam and the Kent Decree were delivered at actual cost. The year began with a serious drought situation. Nearly the highest amount of rain ever recorded for Phoenix in March occurred in 1991. As a result, more water was delivered for the assessment rate than anticipated (approximately 3 acre feet per acre) and most of the alternative sources were not required.

The basic 1991 assessment rate was \$38 per acre and included delivery of 2 acre feet per acre of water. The rate for the next 1.25 acre feet ordered beyond the 2 included in the basic assessment was \$43. The rate for delivery of Central Arizona Project water, if ordered, was \$48.41 for the first 0.7 acre foot and \$51.88 for the next 0.7 acre foot. Spill water was not charged against the apportionment and was delivered for \$9 per acre foot.

There was some confusion at the beginning of this year. There was no process identified in the Salt River Pima-Maricopa Indian Community Water Rights Settlement Act of 1988 for notification and declaration that the "Effective Date" had occurred. The last activity required in the Act was concluded December 9, 1991. At that time, the Community became entitled to a number of new sources of water (phased in) for use both north and south of the canal on all irrigable acres. The former "assessed" lands became history. In addition, nearly all available sources of water belong to the Community (they do not have to buy them at different rates like in 1991).

The decisions reported in this publication represent concurrence on the part of the parties involved that the leaseholders and Community members can farm and the Project can complete basic operation and maintenance with these rates in 1992. These decisions were agreed to April 1, 1992, at the Community headquarters. Participants included: Community leaders,

Community staff, BIA Area Office and Salt River Agency staff, leaseholders and Community farmers.

It was agreed at that meeting that funds collected beyond the minimum required to operate the Project would be used to install more canal measuring structures, replace obsolete maintenance equipment and improve the weed control process. It was also agreed that meetings between interested parties to the Project would continue at approximately monthly intervals to report on Project activities and finances; discuss potential improvements in operations and sources of other resources; begin setting rates for 1993; and establish a process for transfer of the Project to the Community when they are ready. The Superintendent will be responsible for arranging these meetings during 1992.

## Salt River Indian Irrigation Project 1992 Operation and Maintenance Assessment Rates

*Basic Assessment*

The basic operation and maintenance rate against the leased farmland in the Salt River Irrigation Project to which water can be delivered through the irrigation project works is hereby fixed at the rate of \$50 per acre for delivery of 3 acre feet of water. Irrigation water will not be delivered until the basic operation and maintenance assessments are made. Payment of the basic assessment may be made in two installments if the leaseholder's past accounts are in good standing. The first half (\$25 per acre) by May 1, 1992, and the second half by July 1, 1992.

The rate for excess water will be \$35 per acre foot. The rate for spill water will be \$9 per acre foot. Spill water will not be charged against the apportionment of three acre feet per acre this year. Since spill water is no longer "free" to the Community, as a result of the Act, in future years it may NOT be accounted for or charged in this manner.

*Community Members*

Enrolled members of the Community and their spouses who farm their own land will not be subject to the basic assessment rate. They may purchase water at the rate of \$10 per acre foot. They may purchase spill water, if available, for \$9 per acre foot. Payment will be required at the time of the order.

*Municipal and Industrial*

The rate for delivery of water for Municipal and Industrial purposes is hereby fixed at \$85 per acre foot.

*Interest and Penalty Fees*

Interest and penalty fees will be assessed, where required by law, on all delinquent operation and maintenance assessment charges as prescribed in the Code of Federal Regulations, title 4, part 102, Federal Claims Collection

Standards; and 42 BIAM Supplement 3, part 3.8, Debt Collection Procedures.

*Delivery of Water*

Delivery of water shall be made to all tracts of land for which the basic assessment is paid and water delivery rates are paid as set for the year 1992

and until further notice as long as the Bureau of Indian Affairs operates the Salt River Indian Irrigation Project.

Dated: April 8, 1992.

**Wilson Barber, Jr.,**  
*Phoenix Area Director.*

[FR Doc. 92-9314 Filed 4-21-92; 8:45 am]

BILLING CODE 4310-02-M



# **federal register**

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**Wednesday  
April 22, 1992**

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**Part V**

**Department of  
Health and Human  
Services**

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**National Institutes of Health**

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**Recombinant DNA Research: Actions  
Under the Guidelines; Notice**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institutes of Health**

**Recombinant DNA Research: Actions Under the Guidelines**

**AGENCY:** National Institutes of Health, PHS, DHHS.

**ACTION:** Notice of Actions Under the NIH Guidelines for Research Involving Recombinant DNA Molecules.

**SUMMARY:** This notice sets forth eight actions to be taken by the Director, National Institutes of Health (NIH), under the May 7, 1986, NIH Guidelines for Research Involving Recombinant DNA Molecules (51 FR 16958).

**FOR FURTHER INFORMATION CONTACT:** Additional information can be obtained from Dr. Nelson A. Wivel, Director, Office of Recombinant DNA Activities (ORDA), Office of Science Policy and Legislation, National Institutes of Health, building 31, room 4B11, Bethesda, Maryland 20892, (301) 496-9838.

**SUPPLEMENTARY INFORMATION:** Today eight actions are being promulgated under the NIH Guidelines for Research Involving Recombinant DNA Molecules. These eight proposed actions were published for comment in the *Federal Register* of July 2, 1991 (56 FR 30398), September 3, 1991 (56 FR 43686), November 4, 1991 (56 FR 56415), and January 3, 1992 (57 FR 316) reviewed and recommended for approval by the NIH Recombinant DNA Advisory Committee (RAC) at its meeting on February 10-11, 1992.

**I. Background Information and Decisions on Actions Under the NIH Guidelines**

**A. Addition of Appendix D-XXIV to the NIH Guidelines**

In a letter dated October 18, 1991, Dr. Gary J. Nabel of the University of Michigan Medical School, Ann Arbor, Michigan, indicated his intention to submit a human gene therapy protocol to the Human Gene Therapy Subcommittee (HGTS) and the RAC for formal review and approval. The title of this protocol is: "Immunotherapy of Malignancy by In Vivo Gene Transfer into Tumors." This request was published for comment in the *Federal Register* on November 4, 1991 (56 FR 56415).

The protocol was reviewed during the Human Gene Therapy Subcommittee (HGTS) meeting on November 21-22, 1991. Provisional approval was given with the following conditions: (i) Amend consent form regarding possibility of

sensitization to the human antigen; (ii) expand the clinical protocol regarding the number of biopsies; (iii) make available the nucleotide sequence analysis of the total construct of the vector; and (iv) provide clarification concerning the status of DNA integration in tumor cells. Dr. Nabel submitted the requested documentation to ORDA. The protocol was then forwarded to the RAC for consideration during the February 10-11, 1992, meeting. This request was published for comment in the *Federal Register* on January 3, 1992 (57 FR 316).

During the meeting on February 10, 1992, the RAC met to review the protocol and recommendations from the HGTS. A modification was requested to the patient's informed consent document in the Description of Treatment or Procedures to be Undertaken section. The revised wording in the consent form is to read as follows:

"By using techniques in the laboratory it is now possible to prepare large amounts of human DNA or genetic material and bacteria. This DNA will be mixed with fat bodies called liposomes, and we plan to transport the mixture into your tumor by a bacterial carrier or delivery system.

Also included in this package is a separate bacterial gene which helps us trace the location of the DNA liposome mixture. Once introduced into the tumor the DNA produces a protein which stimulates tissue rejection. This protein, known as HLA-B7, causes the cells which will contain it to be recognized as a foreign enemy by your immune system.

The purpose of our study is to determine whether this treatment will induce the cells of your immune system, known as lymphocytes, to attack and kill your tumor."

The RAC, by a vote of 13 in favor, 0 opposed, and 1 abstention, approved the protocol. The following section may be added to Appendix D:

**Appendix D-XXIV**

Dr. Gary J. Nabel of the University of Michigan Medical School, Ann Arbor, Michigan, can conduct gene therapy experiments on twelve patients with melanoma or adenocarcinoma. The patient population will be limited to adults over the age of 18 and female patients must be postmenopausal or have undergone tubal ligation or orchiectomy. The patient's immune response will be stimulated by the introduction of a gene encoding for a Class I MHC protein, HLA-B7, in order to enhance tumor regression. DNA/liposome-mediated transfection techniques will be used to directly transfer the foreign gene into tumor cells. HLA-B7 expression will be confirmed in vivo and the immune response stimulated by the expression of this antigen will be characterized.

These experiments will be analyzed for their efficacy in treating cancer.

I accept this recommendation and appendix D-XXIV of the NIH Guidelines will be added accordingly.

**B. Addition of Appendix D-XXV to the NIH Guidelines**

In a letter dated October 10, 1991, Dr. Kenneth Cornetta of Indiana University, Indianapolis, Indiana, indicated his intention to submit a human gene transfer protocol to the HGTS and the RAC for formal review and approval. The title of this protocol is: "Retroviral-Mediated Gene Transfer of Bone Marrow Cells During Autologous Bone Marrow Transplantation for Acute Leukemia." This request was published for comment in the *Federal Register* on November 4, 1991 (56 FR 56415).

The protocol was reviewed during the HGTS meeting on November 21-22, 1991. Provisional approval was given with the following conditions: (1) Amend the consent form regarding the possible benefit of the introduction of the gene; (ii) amend the consent form regarding compensation to the patient related to the research aspects of the protocol; (iii) demonstrate that the transduced leukemic cells will survive the freezing process; and (iv) add a statistical section that addresses the interpretation of recurrence of disease in labeled bone marrow specimens; it is important to determine how many cells contribute to a relapse. Dr. Cornetta submitted the requested documentation to ORDA. The protocol was then forwarded to the RAC for consideration during the February 10-11, 1992, meeting. The request was published for comment in the *Federal Register* on January 3, 1992 (57 FR 316).

During the meeting on February 11, 1992, the RAC met to review the protocol and recommendations from the HGTS. It was decided that the issues raised by the HGTS had been adequately addressed. The RAC, by a vote of 15 in favor, 1 opposed, and no abstentions, approved the protocol. The following section may be added to appendix D:

**Appendix D-XXV**

Dr. Kenneth Cornetta of Indiana University, Indianapolis, Indiana, can conduct gene transfer experiments on up to 10 patients with acute myelogenous leukemia (AML) and up to 10 patients with acute lymphocytic leukemia (ALL). The patient population will be limited to persons between 18 and 65 years of age. Using the LNL-6 vector, autologous bone marrow cells will be marked with the neomycin resistance gene. Gene marked and untreated bone marrow cells will be reinfused at the time of bone marrow transplantation. Patients will then be monitored for evidence of the neomycin resistance gene in peripheral blood and bone marrow cells in order to determine whether

relapse of their disease is a result of residual malignant cells remaining in the harvested marrow, or inadequate ablation of the tumor cells by chemotherapeutic agents. Determining the source of relapse may indicate whether or not purging of the bone marrow is a necessary procedure for these leukemia patients. Further studies will be performed in order to determine the percentage of leukemic cells that contain the LNL-6 vector and the clonality of the marked cells.

I accept this recommendation and Appendix D-XXV of the NIH Guidelines will be added accordingly.

#### C. Addition of Appendix D-XXVI to the NIH Guidelines

In a letter dated October 15, 1991, Dr. James S. Economou of the University of California, Los Angeles, indicated his intention to submit a human gene transfer protocol to the HGTS and the RAC for formal review and approval. The title of this protocol is: "The Treatment of Patients With Metastatic Melanoma and Renal Cell Cancer Using *In Vitro* Expanded and Genetically-Engineered (Neomycin Phosphotransferase) Bulk, CD8(+) and/or CD4(+) Tumor Infiltrating Lymphocytes and Bulk, CD8(+) and/or CD4(+) Peripheral Blood Leukocytes in Combination With Recombinant Interleukin-2 Alone, or with Recombinant Interleukin-2 and Recombinant Alpha Interferon." This request was published for comment in the Federal Register on November 4, 1991 (56 FR 56415).

The protocol was reviewed during the HGTS meeting on November 21-22, 1991. Provisional approval was given with the following conditions: (i) All data concerning vector safety and testing must be submitted; (ii) patient eligibility will be limited to those with at least one lesion that can be biopsied post therapy; (iii) the schedule for the post therapy assessment of cell trafficking is to be added; (iv) develop a statistical section for analysis of cell trafficking; (v) submit proportionality experiments demonstrating the limits of the ability to quantitate differences in ratio of the two vectors; (vi) submit data showing stable integration of the genetic markers in chronic cell cultures; (vii) modify the consent form so that the language concerning biopsies is moved from the biomodulator section to the viral marker section; and (viii) include a stopping rule in the protocol if the *in vivo* trafficking data is uninterpretable. Dr. Economou submitted the requested documentation to ORDA. The protocol was forwarded to the RAC for consideration during the February 10-11, 1992, meeting. The request was

published for comment in the Federal Register on January 3, 1992 (57 FR 316).

During the meeting on February 11, 1992, the RAC met to review the protocol and recommendations from the HGTS. It was decided that the issues raised by the HGTS had been adequately addressed. The RAC, by a vote of 15 in favor, 0 opposed and no abstentions, approved the protocol. The following section may be added to appendix D:

#### Appendix D-XXVI

Dr. James S. Economou of the University of California, Los Angeles, can conduct gene transfer experiments on 20 patients with metastatic melanoma and 20 patients with renal cell carcinoma. These patients will be treated with various combinations of tumor-infiltrating lymphocytes and peripheral blood leukocytes, including CD8 and CD4 subsets of both types of cells. These effector cell populations will be given in combination with interleukin-2 (IL-2) in the melanoma patients and IL-2 plus alpha interferon in the renal cell carcinoma patients. The effector cells will be transduced with the neomycin resistance gene using either the LNL6 or G1N retroviral vectors. This "genetic marking" of the tumor-infiltrating lymphocytes and peripheral blood lymphocytes is designed to answer questions about the trafficking of these cells, their localization to tumors, and their *in vivo* lifespan.

I accept this recommendation and Appendix D-XXVI of the NIH Guidelines will be added accordingly.

#### D. Addition of Appendix D-XXVII to the NIH Guidelines

In a letter dated October 8, 1991, Dr. Philip D. Greenberg of the University of Washington, Seattle, Washington, indicated his intention to submit a human gene therapy protocol to the HGTS and the RAC for formal review and approval. The title of this protocol is: "A Phase I/II Study of Cellular Adoptive Immunotherapy Using Genetically Modified CD8 + HIV-Specific T Cells for HIV-Seropositive Patients Undergoing Allogeneic Bone Marrow Transplant." This request was published for comment in the Federal Register on November 4, 1991 (56 FR 56415).

The protocol was reviewed during the HGTS meeting on November 21-22, 1991. Approval was given with the following requested changes in the patient consent form: (i) Reword the language regarding unforeseen problems; (ii) reword the language concerning the costs associated with the research aspects of the protocol and billing to the patients; (iii) clearly distinguish between the therapy and the gene modification portions of the protocol; (iv) use less technical terminology throughout the document;

and (v) provide hard copies of the helper-virus assay and vector testing slides presented during the HGTS meeting. Dr. Greenberg submitted the requested documentation to ORDA. The protocol was forwarded to the RAC for consideration during the February 10-11, 1992, meeting. The request was published for comment in the Federal Register on January 3, 1992 (57 FR 316).

During the meeting on February 11, 1992, the RAC met to review the protocol and recommendations from the HGTS. It was decided that the issues raised by the HGTS had been adequately addressed. The RAC, by a vote of 16 in favor, 0 opposed, and no abstentions, approved the protocol. The following section may be added to appendix D.

#### Appendix D-XXVII

Dr. Philip D. Greenberg of the University of Washington, Seattle, Washington, can conduct gene transfer experiments on up to 15 HIV seropositive patients undergoing allogeneic bone marrow transplantation for non-Hodgkin's lymphoma to evaluate the safety and efficacy of HIV-specific cytotoxic T lymphocyte (CTL) therapy. CTL will be transduced with a retroviral vector (HyTK) encoding a gene that is a fusion product of the hygromycin phosphotransferase gene (HPH) and the herpes virus thymidine kinase (HSV-TK) gene. This vector will deliver both a marker gene and a suicide gene in these T cell clones in the event that patients develop side effects as a consequence of CTL therapy. Data will be correlated over time, looking at multiple parameters of HIV disease activity. The objectives of these studies include evaluating the safety and toxicity of CTL therapy, determining the duration of *in vivo* survival of HIV-specific CTL clones, and determining if ganciclovir therapy can eradicate genetically modified, adoptively transferred CTL cells.

I accept this recommendation and appendix D-XXVII of the NIH Guidelines will be added accordingly.

#### E. Amendment to Appendix D-XV of the NIH Guidelines

In a letter dated December 20, 1991, Drs. R. Michael Blaese and W. French Anderson of the National Institutes of Health, Bethesda, Maryland, requested an action item concerning a major amendment to the protocol entitled, "Treatment of Severe Combined Immunodeficiency Disease (SCID) due to Adenosine Deaminase (ADA) Deficiency With Autologous Lymphocytes Transduced With a Human ADA Gene." This protocol was originally approved by the RAC at its meeting on July 31, 1990, and approved by the Director, NIH, published in the Federal Register on September 12, 1990 (55 FR 37565).

The requested amendment would use CD-34+ cells (the peripheral blood stem cell fraction) transduced with the gene coding for adenosine deaminase (ADA) as a supplemental therapy for patients with ADA deficiency. The request was published for comment in the *Federal Register* on January 3, 1992 (57 FR 316), and a correction notice published in the *Federal Register* on July 18, 1991 (56 FR 33174).

During the meeting on February 10-11, 1992, the RAC met to review this amendment to the protocol. The RAC, by a vote of 11 in favor, 3 opposed and 2 abstentions, approved the amendment to the protocol. The following section may be appended to appendix D-XV:

#### Appendix D-XV

In addition to the conditions outlined in the initial approval, patients may be given a supplement of CD 34+ enriched peripheral blood lymphocytes (PBL) which have been placed in culture conditions that favor progenitor cell growth. This enriched population of cells will be transduced with the retroviral vector, G1NaSvAd. G1NaSvAd is similar to LASN, yet distinguishable by the polymerase chain reaction (PCR). LASN has been used to transduce peripheral blood T lymphocytes with the ADA gene. Lymphocytes and myeloid cells will be isolated from patients over time and assayed for the presence of the LASN or G1NaSvAd vectors. The primary objectives of this protocol are to transduce CD34+ peripheral blood cells with the adenosine deaminase gene, administer these cells to patients, and determine if such cells can differentiate into lymphoid and myeloid cells in vivo. There is a potential for benefit to the patients in that these hematopoietic progenitor cells may survive longer, and divide to yield a broader range of gene-corrected cells.

I accept this recommendation and appendix D-XV of the NIH Guidelines will be amended accordingly.

#### *F. Amendment to Sections III-A and IV-C of the NIH Guidelines Regarding Notice of Meeting and Proposed Actions; Amendment to Introduction, Parts II, and V of the Points to Consider Regarding Review by the Human Gene Therapy Subcommittee*

During the HGTS meeting on July 30-31, 1991, a Working Group on the Future Role of the Recombinant DNA Advisory Committee was established to prepare a report about the feasibility of merging the HGTS and the RAC. This request was published for comment in the *Federal Register* on November 7, 1991 (56 FR 56415).

The HGTS received a report from this working group during its meeting on November 21-22, 1991, which recommended that: (i) All eligible HGTS members be added to the RAC as full voting members; or (ii) all of the HGTS

members be added to the RAC as non-voting members; or (iii) joint meetings would be held in which the HGTS would vote on the proposed action first, followed by the full RAC. During the meeting, the following motion passed by a vote of 11 in favor, 2 opposed, and no abstentions:

We move to recommend to the Recombinant DNA Advisory Committee, that its subcommittee, the Human Gene Therapy Subcommittee, be merged into the parent committee. The number of meetings per year of the Recombinant DNA Advisory Committee would increase to four per year. There would be a transition period of one year in which the Recombinant DNA Advisory Committee would begin to review proposed actions as the sole review group. The following provisions would apply: (i) The Human Gene Therapy Subcommittee would codify a set of guidelines for shortening the review process, and (ii) the eligible members of the Human Gene Therapy Subcommittee would be brought onto the Recombinant DNA Advisory Committee as full voting members in keeping with the nomination process for Federal Advisory Committees.

The HGTS forwarded the proposal to the RAC for consideration during the February 10-11, 1992, meeting.

In a letter dated December 23, 1991, Dr. Nelson Wivel, Director, Office of Recombinant DNA Activities, National Institutes of Health, Bethesda, Maryland, stated that amendments will need to be made to the NIH Guidelines in sections III-A and IV-C and to the Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA into the Genome of Human Subjects in the Introduction, Parts II, and V, in the event that the HGTS recommendations are accepted. If the recommendation on having more meeting dates to accommodate the expected increase in human gene transfer/therapy protocols is accepted, the Notices of Meeting and Proposed Actions will need to be changed from thirty days to fifteen days to allow expedited review. Changes are required in Sections III-A and IV-C of the NIH Guidelines. If the recommendation to have the HGTS merge into the parent committee is approved, all references to the HGTS will need to be deleted in the Points to Consider, in the Introduction, and Parts II, and V.

These requests were published for comment in the *Federal Register* on January 3, 1992 (57 FR 316).

During the meeting on February 10, 1992, the RAC met to review the requests of the HGTS and Dr. Wivel. The RAC, by a vote of 14 in favor, 0 opposed and no abstentions, approved: (1) To eliminate review of the human gene transfer/therapy protocols by the HGTS; this established sole review of

the protocols by the RAC; and (2) to change all references to thirty day Notice of Meeting and Proposed Actions to fifteen days. The RAC also recommended increasing the number of times the committee meets from three times a year to four times a year.

The following sections will be amended in the NIH Guidelines: Sections III-A, IV-C-1-b-(1), section IV-C-2, section IV-C-3-b-(1), section IV-C-3-b-(2). The amended sections will read:

#### Section III-A. Experiments That Require RAC Review and NIH and IBC Approval Before Initiation

Experiments in this category cannot be initiated without submission of relevant information on the proposed experiment to NIH, the publication of the proposal in the *Federal Register* for 15 days of comment, review by the RAC, and specific approval by NIH. The containment conditions for such experiments will be recommended by the RAC and set by NIH at the time of approval. Such experiments also require \* \* \*

Section IV-C-1-b-(1). Major Actions. To execute major actions, the Director, NIH, must seek the advice of the RAC and provide an opportunity for public and Federal agency comment. Specifically, the agenda of the RAC meeting citing the major actions will be published in the *Federal Register* at least 15 days before the meeting, and the Director, NIH, will also publish the proposed actions in the *Federal Register* for comment at least 15 days before the meeting.

In addition, the Director's proposed decision, at his/her discretion, may be published in the *Federal Register* for 15 days of comment before final action is taken. The Director's final decision \* \* \*

Section IV-C-2. Recombinant DNA Advisory Committee. \* \* \* All meetings of the RAC will be announced in the *Federal Register*, including tentative agenda items, 15 days in advance of the meeting with final agendas, if modified, available at least 72 hours before the meeting. No item defined as \* \* \*

Section IV-C-3-b-(1). Announcements of RAC meetings and agendas at least 15 days in advance; NOTE—If the agenda \* \* \*

Section IV-C-3-b-(2). Proposed major actions of the type falling under Section IV-C-1-b-(1) at least 15 days prior to the RAC meeting at which they will be considered; and

The following sections will be amended to the Points to Consider: The Introduction, Parts II, and V. This document was published in the *Federal Register* on March 1, 1990 (55 FR 7437), amended September 12, 1990 (55 FR 37565), and amended July 18, 1991 (56 FR 33174). The amended sections will read:

Introduction. (1) \* \* \* RAC consideration of each proposal will be on a case-by-case basis and will follow publication of a precis of the proposal in the *Federal Register*, and an opportunity for public comment. RAC's recommendation on each proposal will be

forwarded to the NIH Director for a decision which will then be published in the *Federal Register*.

Introduction. (4) \* \* \* The IRB and IBC may, at their discretion, condition their approval on further specific deliberation by the RAC. Consideration of proposals by the RAC may proceed simultaneously with review by any other Federal agencies provided that the RAC is notified of the simultaneous review. Meetings of the RAC will be open to the public except where trade secrets or proprietary information would be disclosed. The committee \* \* \*.

Introduction. (6) \* \* \* Part III summarized other requested documentation that will assist the RAC in their review of the proposals. Part IV specified reporting requirements.

Introduction. (7) The RAC will not at present entertain proposals for germ line alterations \* \* \*.

Introduction. (9) In their evaluation of proposals involving the transfer of recombinant DNA into human subjects, the RAC will consider whether the design \* \* \*. Accordingly, this document requests information that will enable the RAC to assess the possibility that the proposed experiments will inadvertently affect reproductive cells or lead to infection of other people (e.g., treatment of personnel or relatives).

Introduction. (10) In recognition of the social concern that surrounds the subject of gene transfer, the RAC will cooperate with other groups \* \* \*.

Introduction. (12) \* \* \* Investigators submitting proposals that employ essentially the same vector systems (or with minor variations), and/or that are based on the same preclinical testing as proposals previously reviewed by the RAC, may refer to preceding documents without having to rewrite such materials.

Part II. Special Issues. Although the following issues are beyond the normal purview of local IRBs, the RAC requests that the investigators respond to questions A and B below.

Part V. Minor Modifications. A minor change in a protocol approved by the RAC is a change that does not significantly alter the basic design of a protocol and that does not increase risk to the subjects. If the change has been approved by the relevant IRB and IBC, then the Chair of the RAC may give approval. It is expected that the Chair will consult with one or more members of the committee, as necessary. The Chair will report on any such approvals at the next regularly scheduled meeting of RAC.

I accept this recommendation to amend accordingly the NIH Guidelines in sections III-A and IV-C and to amend the Points to Consider in the Introduction, Parts II, and V.

*G. Amendment to Appendices B-I-B-1 and B-I-B-2 of the NIH Guidelines regarding the Bacterial Order, Actinomycetales*

In a written request dated April 15, 1991, Dr. Diane O. Fleming, representing the Mid-Atlantic Biological Safety

Association, requested that only pathogenic genera and species of the bacterial order, Actinomycetales, be included in Appendix B-I-B-1 of the NIH Guidelines.

It was proposed that the following pathogens be included in the list of Bacterial Agents in Appendix B-I-B-1 of the NIH Guidelines as follows:

Actinomadura madurae,  
Actinomadura pelletieri, Actinomyces bovis, Actinomyces israelii, Nocardia asteroides, Nocardia brasiliensis

In appendix B-I-B-2, the entry under Actinomycetes would be deleted.

This request was reviewed at the RAC meeting on May 30-31, 1991. Following a discussion there was agreement that Actinomyces should be removed from the list of fungi and reclassified as bacteria. There was disagreement, however, about the number of species to be listed as pathogens. Reviewers and committee members expressed concern that the number of possible pathogens may be larger than the six species proposed for inclusion. The RAC requested that Dr. Fleming consult with leading experts on Actinomycetales and develop a revised and expanded list of potential pathogens to be reviewed at the RAC meeting on October 7-8, 1991. This request was published for comment in the *Federal Register* on September 3, 1991 (56 FR 43686).

A second list of potential pathogens was submitted to the RAC. This included 63 organisms, a number that was reduced to 56 by clarification of taxonomic names and was reviewed by Dr. Lechevalier at Rutgers University, Dr. Blaine Beaman of the University of California at Davis, and Drs. Michael McNeil and Richard Knudsen at the Centers for Disease Control (CDC). Drs. McNeil and Knudsen presented a synopsis of their review at the RAC meeting of October 7-8, 1991.

During the October 7-8, 1991, RAC meeting, a motion was passed by a vote of 19 in favor, 0 opposed, and no abstentions to create an ad hoc working group within the RAC, plus outside consultants, to provide an amended list of pathogens.

On November 13, 1991, the RAC Working Group on Actinomycetales held a telephone conference call for the purpose of proposing a list of pathogens. Drs. B. Murray, D. Fleming, D. Krogstad, and M. Schaechter participated. Originally, a list of 19 organisms was developed; this included both the proven pathogens identified by the CDC and the suspected pathogens identified by the CDC that were also part of risk group 2 (BL-2) in the German classification, "Klassifizierung Der Bakterien Nach Den Im Ungang Mit Ihnen Auftretenden

Gefahren." These organisms are as follows:

Actinomadura madurae,  
Actinomadura pelletieri, Amycolata autotrophica, Dermatophilus congolensis, Gordona bronchialis, Gordona sputi, Nocardia asteroides, Nocardia brasiliensis, Nocardia otitidiscaviarum, Nocardia farcinica, Nocardia nova, Nocardia transvalensis, Nocardiosis dassonvillei, Rhodococcus equi, Rhodococcus aichiensis, Rhodococcus chubuensis, Rhodococcus rhodochrous, Rhodococcus ruber, Streptomyces Somaliensis.

Alternatively, a list of organisms representing only proven pathogens, as established by the CDC, would read as follows:

Amycolata autotrophica,  
Dermatophilus congolensis, Nocardia asteroides, Nocardia brasiliensis, Nocardia otitidiscaviarum, Nocardia transvalensis, Rhodococcus equi.

The request was published for comment in the *Federal Register* on January 3, 1992 (57 FR 316).

During the meeting on February 10, 1992, the RAC discussed the recommendations of the Working Group on Actinomycetales. The RAC, by a vote of 13 in favor, 0 opposed, and no abstentions, accepted the working group's recommendation to adopt the CDC classification of organisms with proven pathogenicity.

The following proven pathogens of the bacterial order, Actinomycetales, will be added to Appendix B-I-B-1, Bacterial Agents:

"Amycolata autotrophica,  
Dermatophilus congolensis, Nocardia asteroides, Nocardia brasiliensis, Nocardia otitidiscaviarum, Nocardia transvalensis, Rhodococcus equi."

The following organisms will be deleted from appendix B-I-B-2, Fungal Agents:

"Actinomycetes (including Nocardia species, Actinomyces species, and Arachnia propionica)[2]."

I accept this recommendation and Appendices B-I-B-1 and B-I-B-2 of the NIH Guidelines will be amended accordingly.

*H. Amend Appendices B-I-C-1 and B-I-B-1 in the NIH Guidelines Regarding Mycobacterium Avium*

In a letter dated December 18, 1991, Dr. William R. Jacobs, Jr., of the Albert Einstein College of Medicine, Bronx, New York, requested a lowering of the classification Mycobacterium avium from a Class III bacterial agent to a Class II bacterial agent. M. avium would move from Appendix B-I-C-1 to Appendix B-I-B-1 in the NIH

Guidelines. The request was published for comment in the Federal Register on January 3, 1992 (57 FR 316).

During the meeting on February 11, 1992, the RAC met to review this request. The basis of this request resides in the fact that CDC/NIH biosafety guidelines, that were published in 1984, recommended biosafety level 2 practices for *M. avium*. *M. avium* is ubiquitous in nature, a common contaminant in the soil, and there is no evidence that direct transmission occurs between humans. The RAC, by a vote of 14 in favor, 0 opposed, and no abstentions, approved the lowering of the classification of *Mycobacterium avium* from a Class III bacterial agent to a Class II bacterial agent. *M. avium* would move from Appendix B-I-C-1 to Appendix B-I-B-1 in the NIH Guidelines.

I accept this recommendation and Appendices B-I-C-1 and B-I-B-1 of the NIH Guidelines will be amended accordingly.

## II. Summary of Actions

### A. Addition of Appendix D-XXIV to the NIH Guidelines

The following section is added to appendix D:

#### Appendix D-XXIV

Dr. Gary J. Nabel of the University of Michigan Medical School, Ann Arbor, Michigan, can conduct gene therapy experiments on twelve patients with melanoma or adenocarcinoma. Patient population will be limited to adults over the age of 18 and female patients must be postmenopausal or have undergone tubal ligation or oophorectomy. The patient's immune response will be stimulated by the introduction of a gene encoding for a Class I MHC protein, HLA-B7, in order to enhance tumor regression. DNA/liposome-mediated transfection techniques will be used to directly transfer this foreign gene into tumor cells. HLA-B7 expression will be confirmed *in vivo*, and the immune response stimulated by the expression of this antigen will be characterized. These experiments will be analyzed for their efficacy in treating cancer.

### B. Addition of Appendix D-XXV to the NIH Guidelines

The following section is added to appendix D:

#### Appendix D-XXV

Dr. Kenneth Cornetta of Indiana University, Indianapolis, Indiana, can conduct gene transfer experiments on up to 10 patients with acute myelogenous leukemia (AML) and up to 10 patients with acute lymphocytic leukemia (ALL). The patient population will be limited to persons between 18 and 65 years of age. Using the LNL-6 vector, autologous bone marrow cells will be marked with the neomycin resistance gene. Gene marked and untreated bone marrow cells will be reinfused at the time of bone

marrow transplantation. Patients will then be monitored for evidence of the neomycin resistance gene in peripheral blood and bone marrow cells in order to determine whether relapse of their disease is a result of residual malignant cells remaining in the harvested marrow or inadequate ablation of the tumor cells by chemotherapeutic agents. Determining the source of relapse may indicate whether or not purging of the bone marrow is a necessary procedure for these leukemia patients. Further studies will be performed in order to determine the percentage of leukemic cells that contain the LNL-6 vector and the clonality of marked cells.

### C. Addition of Appendix D-XXVI to the NIH Guidelines

The following section is added to appendix D:

#### Appendix D-XXVI

Dr. James S. Economou of the University of California, Los Angeles, can conduct gene transfer experiments on 20 patients and with metastatic melanoma and 20 patients with renal cell carcinoma. These patients will be treated with various combinations of tumor-infiltrating lymphocytes and peripheral blood leukocytes, including CD8 and CD4 subsets of both types of cells. These effector cell populations will be given in combination with interleukin-2 (IL-2) in the melanoma patients and IL-2 plus alpha interferon in the renal cell carcinoma patients. The effector cells will be transduced with the neomycin resistance gene using either the LNL6 or G1N retroviral vectors. This "genetic marking" of the tumor-infiltrating lymphocytes and peripheral blood lymphocytes is designed to answer questions about the trafficking of these cells, their localization to tumors, and their *in vivo* lifespan.

### D. Addition of Appendix D-XXVII to the NIH Guidelines

The following section is added to appendix D:

#### Appendix D-XXVII

Dr. Philip D. Greenberg of the University of Washington, Seattle, Washington, can conduct gene transfer experiments on up to 15 HIV seropositive patients undergoing allogeneic bone marrow transplantation for non-Hodgkin's lymphoma to evaluate the safety and efficacy of HIV-specific cytotoxic T lymphocyte (CTL) therapy. CTL will be transduced with a retroviral vector (HyTK) encoding a gene that is a fusion product of the hygromycin phosphotransferase gene (HPH) and the herpes virus thymidine kinase (HSV-TK) gene. The vector will deliver both a marker gene and a suicide gene in these T cell clones in the event that patients develop side effects as a consequence of CTL therapy. Data will be correlated over time, looking at multiple parameters of HIV disease activity. The objectives of these studies include evaluating the safety and toxicity of CTL therapy, determining the duration of *in vivo* survival of HIV-specific CTL clones, and determining if ganciclovir therapy can eradicate genetically modified, adoptively transferred CTL cells.

### E. Amendment to Appendix D-XV of the NIH Guidelines

Appendix D-XV will read as follows:

#### Appendix D-XV

In addition to the conditions outlined in the initial approval, patients may be given a supplement of a CD-34+ enriched peripheral blood lymphocytes (PBL) which have been placed in culture conditions that favor progenitor cell growth. This enriched population of cells will be transduced with the retroviral vector, G1NaSvAd. G1NaSvAd is similar to LASN, et distinguishable by PCR. LASN has been used to transduce peripheral blood T lymphocytes with the ADA gene. Lymphocytes and myeloid cells will be isolated from patients over time and assayed for the presence of the LASN or G1NaSvAd vectors. The primary objectives of this protocol are to transduce CD 34+ peripheral blood cells with the adenosine deaminase gene, administer these cells to patients, and determine if such cells can differentiate into lymphoid and myeloid cells *in vivo*. There is a potential for benefit to the patients in that these hematopoietic progenitor cells may survive longer, and divide to yield a broader range of gene-corrected cells.

### F. Amendment to Introduction, Section II and V of the Points to Consider Regarding Review by the Human Gene Therapy Subcommittee; Amendment to Sections III-A and IV-C of the NIH Guidelines.

The following sections will be amended in the NIH Guidelines: Sections III-A, IV-C-1-b-(1), section IV-C-2, section IV-C-3-b-(1), section IV-C-3-b-(2)). The amended sections will read:

Section III-A. Experiments That Require RAC Review and NIH and IBC Approval Before Initiation.

Experiments in this category cannot be initiated without submission of relevant information on the proposed experiment to NIH, the publication of the proposal in the Federal Register for 15 days of comment, review by the RAC, and specific approval by NIH. The containment conditions for such experiments will be recommended by the RAC and set by NIH at the time of approval. Such experiments also require \* \* \*

Section IV-C-1-b-(1). Major Actions. To execute major actions, the Director, NIH, must seek the advice of the RAC and provide an opportunity for public and Federal agency comment. Specifically, the agenda of the RAC meeting citing the major actions will be published in the Federal Register at least 15 days before the meeting, and the Director, NIH, will also publish the proposed actions in the Federal Register for comment at least 15 days before the meeting. In addition, the Director's proposed decision, at his/her discretion, may be published in the Federal Register for 15 days of comment before final action is taken. The Director's final decision \* \* \*

Section IV-C-2. Recombinant DNA Advisory Committee. \* \* \*. All meetings of the RAC will be announced in the *Federal Register*, including tentative agenda items, 15 days in advance of the meeting with final agendas, if modified, available at least 72 hours before the meeting. No item defined \* \* \*.

Section IV-C-3-b-(1). Announcements of RAC meetings and agendas at least 15 days in advance; NOTE—If the agenda \* \* \*.

Section IV-C-3-b-(2). Proposed major actions of the type falling under Section IV-C-1-b-(1) at least 15 days prior to the RAC meeting at which they will be considered; and

The following sections will be amended to the Points to Consider: Introduction, parts II, and V. This document was published in the *Federal Register* on March 1, 1990 (55 FR 7437), amended September 12, 1990 (55 FR 37565), and amended July 18, 1991 (56 FR 33174). The amended sections will read:

Introduction. (1) \* \* \* RAC consideration of each proposal will be on a case-by-case basis and will follow publication of a precis of the proposal in the *Federal Register*, and an opportunity for public comment. RAC's recommendation on each proposal will be forwarded to the NIH Director for a decision which will then be published in the *Federal Register*.

Introduction. (4) \* \* \* The IRB and IBC may, at their discretion, condition their approval on further specific deliberation by the RAC. Consideration of proposals by the RAC may proceed simultaneously with review by any other Federal agencies provided that the RAC is notified of the simultaneous review. Meetings of the RAC will be open to the public except where trade secrets or proprietary information would be disclosed. The committee \* \* \*.

Introduction. (6) \* \* \* Part III summarized other requested documentation that will assist the RAC in their review of the proposals. Part IV specified reporting requirements.

Introduction. (7) The RAC will not at present entertain proposals for germ line alterations \* \* \*.

Introduction. (9) In their evaluation of proposals involving the transfer of recombinant DNA into human subjects, the RAC will consider whether the design \* \* \*. Accordingly, this document requests

information that will enable the RAC to assess the possibility that the proposed experiments will inadvertently affect reproductive cells or lead to infection of other people (e.g., treatment of personnel or relatives).

Introduction. (10) In recognition of the social concern that surrounds the subject of gene transfer, the RAC will cooperate with other groups \* \* \*.

Introduction. (12) \* \* \* Investigators submitting proposals that employ essentially the same vector systems (or with minor variations), and/or that are based on the same preclinical testing as proposals previously reviewed by the RAC, may refer to preceding documents without having to rewrite such materials.

Part II. Special Issues. Although the following issues are beyond the normal purview of local IRBs, the RAC requests that the investigators respond to questions A and B below.

Part V. Minor Modifications. A minor change in a protocol approved by the RAC is a change that does not significantly alter the basic design of a protocol and that does not increase risk to the subjects. If the change has been approved by the relevant IRB and IBC, then the Chair of the RAC may give approval. It is expected that the Chair will consult with one or more members of the committee, as necessary. The Chair will report on any such approvals at the next regularly scheduled meeting of RAC.

I accept this recommendation to amend accordingly the NIH Guidelines in sections III-A and IV-C and to amend the Points to Consider in the Introduction, parts II, and V.

*G. Amendment to Appendices B-I-B-1 and B-I-B-2 of the NIH Guidelines Regarding the Bacterial Order, Actinomycetales*

Appendix B-I-B-1, Bacterial Agents, the following organisms will be added:

Amycolata autotrophica  
Dermatophilus congolensis  
Nocardia asteroides  
Nocardia brasiliensis  
Nocardia otitidiscaviarum  
Nocardia transvalensis  
Rhodococcus equi

Appendix B-I-B-2, Fungal Agents, the following organisms will be deleted:

"Actinomycetes (including *Nocardia* species, actinomycetes species, and *Arachnia propionica*)[2]"

*H. Amend Appendices B-I-C-1 and B-I-B-1 in the NIH Guidelines Regarding Mycobacterium Avium*

Appendix B-I-C-1, Bacterial Agents, the following organism will be deleted: *Mycobacterium avium*

Appendix B-I-B-1, Bacterial Agents, the following organism will be added: *Mycobacterium avium*

OMB's Mandatory Information Requirements for Federal Assistance Program Announcements (45 FR 39592) requires a statement concerning the official government programs contained in the Catalog of Federal Domestic Assistance. Normally NIH lists in its announcements the number and title of affected individual programs for the guidance of the public. Because the guidance in this notice covers not only virtually every NIH program but also essentially every Federal research program in which DNA recombinant molecule techniques could be used, it has been determined to be not cost effective or in the public interest to attempt to list these programs. Such a list would likely require several additional pages. In addition, NIH could not be certain that every Federal program would be included as many Federal agencies, as well as private organizations, both national and international, have elected to follow the NIH Guidelines. In lieu of the individual program listing, NIH invites readers to direct questions to the information address above about whether individual programs listed in the Catalog of Federal Domestic Assistance are affected.

**EFFECTIVE DATE:** April 17, 1992.

**Bernadine Healy,**

*Director, National Institutes of Health.*

[FR Doc. 92-9368 Filed 4-17-92; 8:45 am]

**BILLING CODE 4410-01-M**

The following is a list of the members of the American Medical Association who have been elected to the office of Secretary for the year 1938. The members are: Dr. J. H. ...

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# federal register

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Wednesday  
April 22, 1992

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## Part VI

### Department of the Interior

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#### Fish and Wildlife Service

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#### 50 CFR Part 17

**Endangered and Threatened Wildlife and  
Plants; Status for Five Puerto Rican  
Trees and Two Fish, the Goldline Darter  
and Blue Shiner; Final Rules**

## DEPARTMENT OF THE INTERIOR

## Fish and Wildlife Service

## 50 CFR Part 17

RIN 1018-AB56

## Endangered and Threatened Wildlife and Plants; Determination of Endangered Status for Five Puerto Rican Trees

AGENCY: Fish and Wildlife Service, Interior.

ACTION: Final rule.

**SUMMARY:** The Service determines *Callicarpa ampla* (capá rosa), *Styrax portoricensis* (palo de jazmín), *Ternstroemia luquillensis* (palo colorado), *Ternstroemia subsessilis* (no common name) and *Ilex sintenisii* (no common name) to be endangered species pursuant to the Endangered Species Act (Act) of 1973, as amended. These species are endemic to Puerto Rico, with one possible exception, and are currently found only in the Luquillo Mountains within the Caribbean National Forest. All are extremely rare and potentially threatened by forest management practices, construction of communication facilities on high peaks, road construction and maintenance, hurricane damage, and collection. This final rule will implement the Federal protection and recovery provisions afforded by the Act for *Callicarpa ampla*, *Styrax portoricensis*, *Ternstroemia luquillensis*, *T. subsessilis* and *Ilex sintenisii*.

**EFFECTIVE DATE:** May 22, 1992.

**ADDRESSES:** The complete file for this rule is available for inspection, by appointment, during normal business hours at the Caribbean Field Office, U.S. Fish and Wildlife Service, P.O. Box 491, Boquerón, Puerto Rico 00622; and at the Service's Southeast Regional Office, suite 1282, 75 Spring Street SW., Atlanta, Georgia 30303.

**FOR FURTHER INFORMATION CONTACT:** Ms. Marelisa Rivera or Ms. Susan Silander at the Caribbean Field Office address (809/851-7297), or Mr. Dave Flemming at the Atlanta Regional Office address (404/331-3583 or FTS 841-3583).

**SUPPLEMENTARY INFORMATION:****Background**

The Luquillo Mountains are found in the extreme northeastern part of Puerto Rico. The majority of the area (11,300 hectares) is managed by the U.S. Forest Service as the Caribbean National Forest. Four forest associations have been identified in these mountains: tabonuco, palo colorado, dwarf and

sierra palm. The five species that are the subject of this rule are restricted to the palo colorado and/or the dwarf forests. The palo colorado association is found at elevations greater than 600 meters and covers approximately 17 percent of the Caribbean National Forest. It derives its name from the palo colorado tree (*Cyrilla racemiflora*) which is dominant in this forest type. The dwarf or elfin association is found on the summits of mountains at elevations greater than 750 meters and covers only 2 percent of the Forest. This forest is composed of dense stands of short, small diameter, twisted trees and shrubs and the forest floor is covered with mosses and epiphytes. Relative humidity ranges from 95 to 100 percent and annual precipitation from 313 to 450 centimeters. Temperatures range from 11.5° to 32.5° C throughout the year, with a mean annual temperature of 21° C (Brown et al., 1983).

*Callicarpa ampla* (capá rosa) was described by Schauer in 1847 from specimens collected in 1827 by Wydler at an unknown location in Puerto Rico (Schauer, 1847). Since then it has been collected only seven times: Six specimens are from Puerto Rico and one reportedly came from St. Thomas, U.S. Virgin Islands (Vivaldi and Woodbury, 1981). However, whether or not the specimen indicated as having been collected from St. Thomas actually came from there is questionable (Vivaldi and Woodbury, 1981). In Puerto Rico, this species has been collected in Barranquitas, Adjuntas, Utuado, Cayey, and the Luquillo Mountains. At present, the species is known only from the palo colorado forest association in the Luquillo Mountains. Only 14 trees in 5 sites have been located. In addition, 15 seedlings were observed at one population site during post-Hurricane Hugo surveys (C. Laboy, pers. comm.).

*Callicarpa ampla* is an evergreen tree which may grow to 50 feet (15 meters) tall. The young twigs are 4-sided and whitish. Leaves are opposite, entire, broadest at the middle and taper to both ends. They are 4 to 10 inches (10 to 25 centimeters) long, 1½ to 3 inches (3.3 to 7 centimeters) wide, green on the upper surface, densely white scurfy below, and borne on a petiole about 1 inch (2.2 centimeters) in length. The inflorescence is branched and has numerous, small, whitish flowers each with a 4-lobed corolla about ¼ inch (.3 centimeters) long. Fruits are white when young but become purplish upon maturity, and are ¼ inch (.5 centimeter) in diameter, with the calyx attached at the base (Vivaldi and Woodbury, 1981).

*Styrax portoricensis* (palo de jazmín) was collected for the first time in 1885

from the eastern mountains of Puerto Rico by Paul Sintenis and described by Krug and Urban in 1892 from those same specimens. Collected only twice, in 1935 and 1954, it was thought to be extinct until rediscovered by Roy Woodbury in November 1982 (George Proctor, pers. comm.). Only one immature tree is presently known and occurs in the palo colorado forest association of the Luquillo Mountains. It suffered slight damage from Hurricane Hugo in September 1989 due to wind-thrown trees. The trees that had fallen on it were subsequently removed by the U.S. Forest Service (Carlos Laboy, pers. comm.).

*Styrax portoricensis* is an evergreen tree which may reach 66 feet (20 meters) in height. Leaves are alternate, without stipules, entire with margins turned under, 2½ to 4 inches (6 to 10 centimeters) long and 1¼ to 2 inches (2.75 to 4.4 centimeters) wide, tapered at both ends and widest at the middle. They are shiny dark green above, pale green below, hairless, but occasionally with scattered star-shaped scales. The inflorescence is a 3 to 6 flowered raceme, each flower being borne on a curved pedicel ⅓ to ⅔ (.8 to 1.4 centimeter) long. Fruits are a one-seeded elongated drupe, about ½ inch (1.1 centimeter) in diameter, densely covered with scales and maintaining the cup-shaped calyx at the base (Vivaldi et al., 1981a).

*Ternstroemia luquillensis* (palo colorado) was described by Krug and Urban in 1896 on the basis of three specimens, two collected by Paul Sintenis and one collected by Eggers. It is known from both the palo colorado and dwarf forests of the Luquillo Mountains; however, two populations previously reported from the dwarf forest are no longer present. The largest was destroyed by the construction of communication towers on El Yunque peak, and the other nearby population was destroyed by a hurricane. Only six individuals in four locations, three of which are in the colorado forest type and one in the dwarf forest of Pico del Este, are presently known to occur (Vivaldi et al., 1981b). However, the two individuals of one population near Road #191 have not been relocated recently and indeed may have originally been misidentified.

*Ternstroemia luquillensis* is an evergreen tree reaching 60 feet (18 meters) in height. The leaves are alternate, thick and leathery, and widest at the middle but acute at both ends. They are up to 4 inches (10 centimeters) long and about 3 times longer than wide. Both surfaces are green and the

underside is black punctate. The flowers are showy, approximately 1 inch (2.5 centimeters) in diameter and the 5 petals are white or cream colored and concave. Fruits are ovoid capsules which are terminated by the persistent style. Seeds are red and about 3 millimeters in length (Vivaldi et al., 1981b).

*Ternstroemia subsessilis* was first collected in 1914 by J.A. Shaffer in the Luquillo Mountains and again in 1923 by Britton and Brunner at the summit of El Yunque. Although collected in the Maricao Forest in 1960 by Roy O. Woodbury, it is now apparently restricted to the palo colorado and dwarf forests of the Luquillo Mountains (Vivaldi et al., 1981c). One dwarf forest population was destroyed by the construction of communication facilities on El Yunque peak. Thirty-seven individuals in four populations, one in the dwarf forest near Pico del Este, are currently known (C. Laboy, pers. comm.).

*T. subsessilis* is an evergreen shrub or small tree which may reach 17 feet (5 meters) in height. Leaves are alternate, entire, stiffly coriaceous, obovate or oblanceolate, 1 1/4 to 3 inches (3 to 7 centimeters) long and 1/2 to 1 inch (1.5 to 2.8 centimeters) wide. Both leaf surfaces are dull green but the lower surface is black punctate. Flowers are solitary, white, 1/2 inch (1 centimeter) in diameter, sessile, and axillary at the ends of the branches. The fruit is an ovoid-conical capsule about 10 millimeters long and tapering to a sharp point. Ripe fruits were observed in May 1991.

*Ilex sintenisii* was first discovered by Paul Sintenis in the upper elevations of the Luquillo Mountains. This Puerto Rican endemic is found only in the Luquillo Mountains where it is restricted to the dwarf or elfin forest. The dwarf forest covers only approximately 225 hectares or 2 percent of the Caribbean National Forest. It is threatened by the potential for further construction and expansion of communication facilities on these high peaks. A total of 150 individuals in three populations have been reported.

*I. sintenisii* is a shrub or small tree which may reach 15 feet (4.5 meters) in height and 3 inches (7.6 centimeters) in diameter. Leaves are alternate, glabrous, obovate to elliptic, coriaceous, 3/8 to 1 1/4 inch (1 to 2.5 centimeters) long and 1/4 to 3/4 inch (.6 to 1.9 centimeters) wide, and notched at the apex with the edges turned under. The bark is gray, smooth, and usually covered with mosses and liverworts. The flowers are white, axillary on pedicels 1/4 to 3/8 inch (.6 to 1 centimeter) long, and 4 to 5 parted. Fruits and drupes are green when immature.

*Callicarpa ampla*, *Styrax portoricensis* and *Ternstroemia luquillensis*, and *T. subsessilis* were recommended for Federal listing by the Smithsonian Institution (Ayensu and DeFilippis, 1979). These tree species were included among the plants being considered as endangered or threatened by the Service, as published in the Federal Register (45 FR 82480) dated December 15, 1980; the November 28, 1983 update (48 FR 53680) of the 1980 notice; and revised of September 27, 1985 (50 FR 39526) and February 21, 1990 (55 FR 6184). These species were designated category 1 (species for which the Service has substantial information supporting the appropriateness of proposing to list them as endangered or threatened) in each of the four notices. *Ilex sintenisii* has been ranked as likely to go extinct in 5 to 10 years (Priority B) by the Center for Plant Conservation. It is considered to be a critical plant by the Natural Heritage Program of the Puerto Rico Department of Natural Resources.

In a notice published in the Federal Register on February 15, 1983 (48 FR 6752), the Service reported the earlier acceptance of the new taxa in the Smithsonian's 1978 book as under petition within the context of section 4(b)(3)(A) of the Act, as amended in 1982. The Service subsequently found that listing *Callicarpa ampla*, *Styrax portoricensis*, *Ternstroemia luquillensis*, and *T. subsessilis* was warranted but precluded by other pending listing actions of a higher priority, and that additional data on vulnerability and threats were still being gathered. The Service proposed listing these five species on April 19, 1991 (56 FR 16059), constituting the final finding under the petition process.

#### Summary of Comments and Recommendations

In the April 19, 1991, proposed rule and associated notifications, all interested parties were requested to submit factual reports of information that might contribute to the development of a final rule. Appropriate agencies of the Commonwealth of Puerto Rico, Federal agencies, scientific organizations, and other interested parties were contacted and requested to comment. A newspaper notice inviting general public comment was published in the San Juan Star on May 10, 1991. Four letters of comment were received and are discussed below. A public hearing was neither requested nor held.

The U.S. Army Corps of Engineers, Jacksonville District, reported that they did not have any actions proposed or under consideration that might affect any of these five species and did not

have any additional information on their status.

The Secretary of the Puerto Rico Department of Natural Resources supported the listing of the species. The Department's Terrestrial Ecology Division concurred with the determination and provided more accurate collection information for *Styrax portoricensis* and *Ternstroemia subsessilis*. Information for the final rule has been revised accordingly.

The U.S. Forest Service supported the listing of all five species and provided supplemental information based on recent survey and management activities conducted for these species. This additional information has been incorporated into the final rule as appropriate.

#### Summary of Factors Affecting the Species

After a thorough review and consideration of all information available, the Service has determined that these five trees should be classified as endangered species. Procedures found at section 4(a)(1) of the Endangered Species Act (16 U.S.C. 1531 et seq.) and regulations (50 CFR part 424) promulgated to implement the listing provisions of the Act were followed. A species may be determined to be endangered or threatened due to one or more of the five factors described in section 4(a)(1). These factors and their application to *Callicarpa ampla* Schauer, *Styrax portoricensis* Krug & Urban, *Ternstroemia luquillensis* Krug & Urban, *T. subsessilis* (Britton) Kubuski, and *Ilex sintenisii* (Urban) Britton are as follows:

##### A. The Present or Threatened Destruction, Modification, or Curtailment of Its Habitat or Range

Although all five of these species are found only within the Caribbean National Forest, which is managed by the U.S. Forest Service, forest management practices such as the establishment and maintenance of plantations, selective cutting, trail and road construction and maintenance, and shelter construction may affect these trees unless their protection is given adequate consideration. The destruction of the dwarf or elfin forests for the construction and/or expansion of communication facilities by the U.S. Navy and private entities also continues to be a potential problem. A proposal for expansion of the Navy facilities on Pico del Este is currently under consideration. Individual of *Callicarpa ampla* are found along Road #191, proposed for reconstruction and

reopening in the near future with funds from the Federal Highway Administration. In addition, the extreme rarity of all these species make the loss of any one individual even more critical. The Service notes, however, that the U.S. Forest Service has stated (*in litt.*, 1991) that it is Forest Service policy to protect these species from possible effects associated with any proposed land management activity. Recent survey and management actions by the Forest Service for these species further indicate a definite commitment to their conservation.

*B. Overutilization for Commercial, Recreational, Scientific, or Educational Purposes.*

Plant collecting is prohibited in the Caribbean National Forest; however, remote areas are difficult to monitor on a regular basis. The ornamental potential of these species may result in taking in the future.

*C. Disease or Predation*

Disease and predation have not been documented as factors in the decline of this species.

*D. The Inadequacy of Existing Regulatory Mechanisms*

The Commonwealth of Puerto Rico has adopted a regulation that recognizes and provides protection for certain Commonwealth listed species. However, *Callicarpa ampla*, *Styrax portoricensis*, *Ternstroemia luquillensis*, *T. subsessilis*, and *Ilex sintenisii* are not yet on the Commonwealth list. Federal listing would provide immediate protection and, if the species are ultimately placed on the Commonwealth list, would enhance their protection and possibilities for funding needed research.

*E. Other Natural or Manmade Factors Affecting Its Continued Existence*

Probably the most important factor affecting *Callicarpa ampla*, *Styrax portoricensis*, *Ternstroemia luquillensis*, *T. subsessilis*, and *Ilex sintenisii* in Puerto Rico is their limited distribution. Hurricane Hugo recently devastated the Caribbean National Forest, causing defoliation and breaking branches on numerous individuals. Because so few individuals are known to occur, the risk of extinction is extremely high.

The Service has carefully assessed the best scientific and commercial information available regarding the past, present, and future threats faced by these species in determining to propose this rule. Based on this evaluation, the preferred action is to list *Callicarpa*

*ampla*, *Styrax portoricensis*, *Ternstroemia luquillensis*, *T. subsessilis*, and *Ilex sintenisii* as endangered. Forest management practices such as establishment of recreation areas and plantations, road construction and maintenance, selective cutting, trail construction and maintenance have the potential to dramatically affect all these species. The impacts of hurricane damage could be devastating. The expansion of communication facilities would result in elimination of individual plants. Therefore, endangered rather than threatened status seems an accurate assessment of the species' condition. The reasons for not proposing critical habitat for this species are discussed below in the "Critical Habitat" section.

**Critical Habitat**

Section 4(a)(3) of the Act, as amended, requires that, to the maximum extent prudent and determinable, the Secretary propose critical habitat at the time the species is proposed to be endangered or threatened. The Service finds that designation of critical habitat is not prudent for these species at this time. The number of individuals of *Callicarpa ampla*, *Styrax portoricensis*, *Ternstroemia luquillensis*, *T. subsessilis*, and *Ilex sintenisii* are sufficiently small that vandalism and collection could seriously affect the survival of these species. Publication of critical habitat descriptions and maps in the Federal Register would increase the likelihood of such activities. The Service believes that Federal involvement in the areas where these plants occur can be identified without the designation of critical habitat. All involved parties have been notified of the location and importance of protecting these species' habitats, and the U.S. Forest Service, the only involved landowner, already has ongoing activities intended to conserve and protect these species. Protection of these species' habitats will also be addressed through the recovery process and through the section 7 jeopardy standard.

**Available Conservation Measures**

Conservation measures provided to species listed as endangered or threatened under the Endangered Species Act include recognition, recovery actions, requirements for Federal protection, and prohibitions against certain practices. Recognition through listing encourages and results in conservation actions by Federal, Commonwealth, and private agencies, groups, and individuals. The Endangered Species Act provides for possible land acquisition and cooperation with the Commonwealth,

and requires that recovery actions be carried out for all listed species. Such actions are initiated by the Service following listing. The protection required of Federal agencies and the prohibitions against certain activities involving listed plants are discussed, in part, below.

Section 7(a) of the Act, as amended, requires Federal agencies to evaluate their actions with respect to any species that is proposed or listed as endangered or threatened and with respect to its critical habitat, if any is being designated. Regulations implementing this interagency cooperation provision of the Act are codified at 50 CFR part 402. Section 7(a)(2) requires Federal agencies to ensure that activities they authorize, fund, or carry out are not likely to jeopardize the continued existence of a listed species or to destroy or adversely modify its critical habitat. If a Federal action may affect a listed species or its critical habitat, the responsible Federal agency must enter into formal consultation with the Service.

Potential Federal involvement for these five trees relates to activities to be conducted by the U.S. Forest Service, the U.S. Navy and the Federal Highway Administration in the Caribbean National Forest. A conference was conducted between the Federal Highway Administration and the Fish and Wildlife Service in order to evaluate the possible impacts of the reconstruction and reopening of Road #191 through the Caribbean National Forest. Additional surveys were conducted and measures were developed to minimize impacts and protect individuals known to be located close to the road.

The Act and its implementing regulations found at 50 CFR 17.61, 17.62, and 17.63 set forth a series of general prohibitions and exceptions that apply to all endangered plants. All trade prohibitions of section 9(a)(2) of the Act, implemented by 50 CFR 17.61, apply. These prohibitions, in part, make it illegal for any person subject to the jurisdiction of the United States to import or export any endangered plant, transport it in interstate or foreign commerce in the course a commercial activity, sell or offer it for sale in interstate or foreign commerce, or remove it from areas under Federal jurisdiction and reduce it to possession. In addition, for endangered plants, the 1988 amendments (Pub. L. 100-478) to the Act prohibit the removal, cutting, digging up, or damaging or destroying of endangered plants in knowing violation of any State (Commonwealth) law or regulation, including State

(Commonwealth) criminal trespass law. Certain exceptions apply to agents of the Service and Commonwealth conservation agencies. The Act and 50 CFR 17.62 and 17.63 also provide for the issuance of permits to carry out otherwise prohibited activities involving endangered species under certain circumstances.

It is anticipated that few trade permits for these five species will ever be sought or issued, since the species are not known to be in cultivation and are uncommon in the wild. Requests for copies of the regulations on listed plants and inquiries regarding Federal prohibitions and permits may be addressed to the Office of Management Authority, U.S. Fish and Wildlife Service, 4401 Fairfax Drive, room 432, Arlington, Virginia 22203 (703/358-2104).

**National Environmental Policy Act**

The Fish and Wildlife Service has determined that an Environmental Assessment, as defined under the authority of the National Environmental Policy Act of 1969, need not be prepared in connection with regulations adopted pursuant to section 4(a) of the Endangered Species Act of 1973, as amended. A notice outlining the Service's reasons for this determination was published in the Federal Register on October 25, 1983 (48 FR 49244).

**References**

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**Authors**

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**List of Subjects in 50 CFR Part 17**

Endangered and threatened species, Exports, Imports, Reporting and recordkeeping requirements, Transportation.

**Regulations Promulgation**

Accordingly, part 17, subchapter B of chapter I, title 50 of the Code of Federal Regulations is amended, as set forth below:

**PART 17—[AMENDED]**

1. The authority citation for part 17 continues to read as follows:

**Authority:** 18 U.S.C. 1361-1407; 16 U.S.C. 1531-1544; 16 U.S.C. 4201-4245; Pub. L. 99-625, 100 Stat. 3500; unless otherwise noted.

2. Amend § 17.12(h) by adding the following, in alphabetical order under Aquifoliaceae, Styracaceae, Theaceae, and Verbenaceae, to the List of Endangered and Threatened Plants:

**§ 17.12 Endangered and threatened plants.**

\* \* \* \* \*

(h) \* \* \*

Species		Historic range	Status	When listed	Critical habitat	Special rules
Scientific name	Common name					
Aquifoliaceae—Holly family:						
<i>Ilex sintenisii</i> .....	None.....	U.S.A. (PR).....	E	461	NA	NA
Styracaceae—Styrax family:						
<i>Styrax portoricensis</i> .....	Palo de jazmín.....	U.S.A. (PR).....	E	461	NA	NA
Theaceae—Tea family:						
<i>Ternstroemia luquillensis</i> .....	Palo colorado.....	U.S.A. (PR).....	E	461	NA	NA
<i>Ternstroemia subsessilis</i> .....	None.....	U.S.A. (PR).....	E	461	NA	NA
Verbenaceae—Verbena family:						
<i>Callicarpa ampla</i> .....	Capá rosa.....	U.S.A. (PR).....	E	461	NA	NA

(Final: Five Puerto Rican trees—endangered)

Dated: April 14, 1992.

Richard N. Smith,

Director, Fish and Wildlife Service.

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