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**The United States Food and Drug Administration
Orphan Drug Program as it Relates to
Orphan Drugs for Developing Nations (**)**

I am grateful for the opportunity to present the background and current status of the United States Food and Drug Administration orphan drug program, but I want to keep in mind the focus of this meeting: orphan drugs for developing countries. As I present this material, I hope you will consider these two questions:

First, what are the elements that need to come together to produce an orphan drug program? Second, how can the currently available incentives of the United States Orphan Drug Act be used to aid the international program you seek?

The FDA orphan drug program began over 10 years ago, when individuals at the agency recognized that certain drugs of perceived value, available elsewhere in the world, were not available in the United States. Though the pharmaceutical industry has always had a commitment to provide public service drugs, not all needed drugs were being developed. Many other groups recognized that there was a problem in the U.S. Some termed it a "drug lag" issue, and felt that FDA's extensive regulatory requirements for drug approval were the major reason for the lag, while others thought factors inhibiting drug development such as small market size, patentability problems, concerns over liability were the major issues. The Department of Health, Education and Welfare formed an inter-agency task force to study the matter, and in 1979 a report was issued that analyzed the subject and proposed solutions. Though the task force recognized that the problem was complex, they stated that the main reason for the problem

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was that "research, development and production are deemed too expensive relative to economic return". The solutions proposed were designed to mitigate the economic expense of development and increase potential economic return for pharmaceutical firms willing to undertake the development of these "significant drugs of limited commercial value".

The United States Congress, aware of the problem and the report, undertook its own survey. The 1982 report from the Committee on Energy and Commerce of the U.S. House of Representatives contained the results of that survey and concluded that:

- Orphan drugs are predominantly used in the treatment of rare diseases.
- They are not profitable.
- It is difficult to conduct human clinical trials to prove their effectiveness because there are so few people with any given disease.
- Many are not patentable.
- They cause more adverse side effects, on average, than drugs for common diseases.
- There are many drugs for rare diseases which are not approved and on the market.

Legislative proposal followed this survey, and with support from the media, voluntary disease-oriented organizations, academia, and government agencies, the Orphan Drug Act was passed and signed by President Reagan in January of 1983. This Act, as amended in 1984, provided various incentives to commercial sponsors of orphan drugs to facilitate their adoption. To qualify for these incentives, a drug had to meet this definition (tab. 1).

TABLE 1 - Provisions of Orphan Drug ACT. Definition of Orphan Drug.

A DRUG (OR BIOLOGIC) FOR A DISEASE OR CONDITION WHICH (A) AFFECTS LESS THAN 200,000 PERSONS IN THE UNITED STATES, OR (B) AFFECTS MORE THAN 200,000 IN THE UNITED STATES AND FOR WHICH THERE IS NO REASONABLE EXPECTATION THAT COSTS OF DEVELOPMENT AND DISTRIBUTION IN THE U.S. WILL BE RECOVERED FROM SALES IN THE U.S.

Drugs for rare as well as common diseases could fit under this definition, but clearly it is easier for drugs that would be used to treat a disease that affects 200,000 persons or less in the U.S. to qualify. This patient prevalence threshold refers to cases in the U.S., not worldwide. A disease common elsewhere, such as leprosy, could be rare in the U.S., and a drug for that disease could meet the statutory definition.

Once a sponsor has obtained designation for a drug for a specific indication, certain incentives are potentially available to that sponsor. Let me outline these for you (tab. 2).

Tab. 2 - Provisions of Orphan Drug Act.

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1. PROTOCOL ASSISTANCE
 2. ORPHAN DRUG DESIGNATION
 3. AVAILABILITY TO PUBLIC OF LISTS OF ORPHAN DRUG DESIGNATIONS
 4. SEVEN YEAR EXCLUSIVE MARKETING LICENSE FOR NONPATENTABLE DRUGS
 5. ENCOURAGEMENT OF TREATMENT INDS
 6. TAX CREDITS FOR CLINICAL TRIALS AFTER ORPHAN DRUG DESIGNATION AND PRIOR TO NDA APPROVAL
 7. ORPHAN PRODUCTS BOARD
 8. GRANTS AND CONTRACTS
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Some pertinent examples of orphan drug designation are shown in tab. 3 and FDA's orphan product grants for 1984 were as listed in tab. 4.

Although clofazamine as a treatment for leprosy is not news to any of you, it is the principle of that designation that I want to emphasize. Were there a new drug for a disease rare in the United States, but common elsewhere, it might obtain designation and that could lead to tax credits and seven years' exclusive marketing.

In approving the Orphan Drug Act, legislative comment on this issue was of interest.

"The term rare in the States is used to assure that the benefits of this bill apply to drugs for diseases or conditions which are rare here, even if prevalent in other countries. To the extent that this provision encourages the development of drugs for prevalent diseases in developing countries, the Committee believes it is sound public policy".

The tax credit portion of the law itself states that:

"No credit shall be allowed under this section with respect to any clinical testing conducted outside the United State unless such testing is conducted outside the United States because there is an insufficient testing population in the United States".

Very recently, FDA has adopted new regulations for approval of new drug applications, and this too is germane to this issue.

"Foreign data may serve as the sole basis for marketing approval of a new drug if (1) The foreign data are applicable to the U.S. population and U.S. medical practice; (2) the studies have been performed by clinical investigators of recognized competence; and (3) the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA is able to validate the data through an on-site inspection or

other appropriate means. Failure of an application to meet any of these criteria will result in the application not being approvable based on the foreign data alone. FDA will apply this policy in a flexible manner according to the nature of the drug and the data being considered*.

These bits of information may be useful in assessing how the U.S. Orphan Drug Act could be helpful in an international program.

TAB. 3 - Orphan Drug Designations.

Name of Drug/Biological Product	Proposed Use	Sponsor's Name and Address
<i>Generic-clofaximine</i> <i>Trade-Lamproene</i>	Treatment of leprosy resistant to Dapsone and the ENL and lepra reaction	Pharmaceuticals Division Ciba-Geigy Corporation 356 Morris Avenue Summit, New Jersey 07901
<i>Generic-hexamethylmelamine</i> <i>Trade-Hexantat</i>	Treatment of advanced adenocarcinoma of the ovary	Ives Laboratories 685 Third Avenue New York, NY 10017
<i>Generic-quinacrine HCl</i> <i>Trade-Not established</i>	For use in the prevention of recurrence of pneumothorax in patients at high risk of recurrence, e.g., patients with cystic fibrosis	LypkoMed, Inc. 2020 Ruby Street Melrose Park, IL 60160
<i>Generic-L-Carnitine</i> <i>Trade-not established</i>	Genetic carnitine deficiency	American McGaw Division American Hospital Supply Corporation 2525 McGaw Avenue Irvine, CA 92714
<i>Generic-L-Carnitine</i> <i>Trade-not established</i>	Primary and secondary carnitine deficiency of genetic origin	Sigma Tau, Inc. 723 North Beers Street Holmdel, New Jersey 07733
<i>Generic-L-5</i> <i>Hydroxytryptophan (L-5HTP)</i> <i>Trade-not established</i>	Treatment of postnarcotic intention myoclonus	Bolar Pharmaceutical Co, Inc. 130 Lincoln Street Copiague, NY 11726
<i>Generic-triethylene dihydrochloride</i> <i>Trade-Capsid</i>	Treatment of patients with Wilson's disease who are intolerant, or inadequately responsive to, penicillamine	Merck Sharp and Dohme Research Laboratories Division of Merck and Co., West Point, Pa 19486
<i>Generic-spiramycin</i> <i>Trade-Rovamycine</i>	For use in the symptomatic relief and parasitic cure of chronic cryptosporidiosis in patients with immunodeficiency	Rhono-Poulenc, Inc. 52 Vanderbilt Ave. New York, NY 10017
<i>Generic-pentamidine isethionate</i> <i>Trade-Pentam 300</i>	Pneumocystis carinii pneumonia	LypkoMed, Inc. 2020 Ruby Street Melrose Park, IL 60160
<i>Generic-pentamidine isethionate</i> <i>Trade-not established</i>	Pneumocystis carinii pneumonia	Rhono-Poulenc, Inc. 52 Vanderbilt Ave. New York, NY 10017

Tab. 4 - Grant Awards - Office of Orphan Products Development, Food and Drug Administration (September 1984).

CHILDREN'S HOSPITAL, Buffalo, New York, Clara Ambrus, M.D., Ph.D. Use of Enzyme-Reactors for Management of Phenylketonuria.
BOSTON UNIVERSITY, Boston, Massachusetts, Michael E. Oshrod, M.D. Treatment of Histiocytosis-X with Suppressin A.
THE WISTAR INSTITUTE, Philadelphia, Pennsylvania, Stanley A. Plotkin, M.D. Live Attenuated Cytomegalovirus Vaccine in Patients Receiving Renal Transplants.
BAYLOR COLLEGE OF MEDICINE, Houston, Texas, Earl J. Brewer, M.D. Methotrexate in Severe Juvenile Rheumatoid Arthritis.
UNIVERSITY OF FLORIDA, Gainesville, Florida, William N. Williams, Ph.D. Treating Palatal Insufficiency by Teflon.
A. L. LABORATORIES, INC., Englewood Cliffs, New Jersey, Bernard B. Brown, Ph. D. Bacitracin for Therapy of Pseudomembranous Colitis.
JAYE-BOERN LABORATORIES, INC., Northbrook, Illinois, Joel E. Bernstein, M.D. Topical Capsaicin Treatment of Post-Herpetic Neuralgia.

Before I conclude, I want to note incentives not provided in the legislation.

1. The standard for approval of orphan drugs was not changed from that required for other new drugs.
2. Medical devices, medical foods were not included in the definition of an orphan drug.
3. Support for preclinical studies during drug development was not provided.
4. No special liability protection for sponsors of orphan drugs was included.

In this brief overview, I have tried to use the history of the development of FDA's orphan drug program to give you some perspective on what you might expect in initiating an international program.

It takes the effort of many committed participants over a long period of time to make headway. Right now, however, the Orphan Drug Act is being used in the United States to aid the development of designated orphan drugs, and that law might provide immediate assistance toward your goal of providing orphan drugs for developing nations.

APPENDIX

An Act (*)

To amend the Federal Food, Drug, and Cosmetic Act to facilitate the development of drugs for rare diseases and conditions, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

Short Title; Findings

SECTION 1. (a) This Act may be cited as the "Orphan Drug Act". (b) The Congress finds that:

(1) there are many diseases and conditions, such as Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy which affect such small numbers of individuals residing in the United States that the diseases and conditions are considered rare in the United States;

(2) adequate drugs for many of such diseases and conditions have not been developed;

(3) drugs for these diseases and conditions are commonly referred to as "orphan drugs";

(4) because so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss;

(5) there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs; and

(6) it is in the public interest to provide such changes and incentives for the development of orphan drugs.

(*) Public Law 97-414, 97th Congress.

Amendments to the Federal Food, Drug, and Cosmetic Act

SEC. 2. (a) Chapter V of the Federal Food, Drug, and Cosmetic Act is amended by adding at the end the following:

SUBCHAPTER B - DRUGS FOR RARE DISEASES OR CONDITIONS

Recommendations for Investigations of Drugs for Rare Diseases or Conditions

SEC. 525. (a) The sponsor of a drug for a disease or condition which is rare in the States may request the Secretary to provide written recommendations for the non-clinical and clinical investigations which must be conducted with the drug before:

- (1) it may be approved for such disease or condition under section 505, or
- (2) if the drug is a biological product, before it may be licensed for such disease or condition under section 351 of the Public Health Service Act.

If the Secretary has reason to believe that a drug for which a request is made under this section is a drug for a disease or condition which is rare in the States, the Secretary shall provide the person making the request written recommendation for the nonclinical and clinical investigations which the Secretary believes, on the basis of information available to the Secretary at the time of the request under this section, would be necessary for approval of such drug for such disease or condition under section 505 or licensing under section 351 of the Public Health Service Act for such disease or condition.

(b) The Secretary shall by regulation promulgate procedures for the implementation of subsection (a).

Designation of Drugs for Rare Diseases or Conditions

SEC. 526. (a) (1) The manufacturer or the sponsor of a drug may request the Secretary to designate the drug as a drug for a rare disease or condition. If the Secretary finds that a drug for which a request is submitted under this subsection is being or will be investigated for a rare disease or condition and:

- (A) if an application for such drug is approved under section 505, or
- (B) if the drug is a biological product, a license is issued under section 351 of the Public Health Service Act,

the approval or license would be for use for such disease or condition, the Secretary shall designate the drug as a drug for such disease or condition. A request for a designation of a drug under this subsection shall contain the consent of the applicant to notice being given by the Secretary under subsection (b) respecting the designation of the drug.

(2) For purposes of paragraph (1), the term "rare disease or condition" means any disease or condition which occurs so infrequently in the United States

that there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under this subsection is made.

(b) Notice respecting the designation of a drug under subsection (a) shall be made available to the public.

(c) The Secretary shall by regulation promulgate procedures for the implementation of subsection (a).

Protection for Unpatented Drugs for Rare Diseases or Conditions

Sec. 527. (a) Except as provided in subsection (b), if the Secretary:

(1) approves an application filed pursuant to section 505 (b), or

(2) issues a license under section 351 of the Public Health Service Act for a drug designated under section 526 for a rare disease or condition and for which a United States Letter of Patent may not be issued, the Secretary may not approve another application under section 505 (b) or issue another license under section 351 of the Public Health Service Act for such drug for such disease or condition for a person who is not the holder of such approved application or of such license until the expiration of seven years from the date of the approval of the approved application or the issuance of the license. Section 505 (c) (2) does not apply to the refusal to approve an application under the preceding sentence.

(b) If an application filed pursuant to section 505 (b) is approved for a drug designated under section 526 for a rare disease or condition or a license is issued under section 351 of the Public Health Service Act for such a drug and if a United States Letter of Patent may not be issued for the drug, the Secretary may, during the seven-year period beginning on the date of the application approval or of the issuance of the license, approve another application under section 505 (b), or, if the drug is a biological product, issue a license under section 351 of the Public Health Service Act, for such drug for such disease or condition for a person who is not the holder of such approved application or of such license if:

(1) The Secretary finds, after providing the holder notice and opportunity for the submission of views, that in such period the holder of the approved application or of the license cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated; or

(2) such holder provides the Secretary in writing the consent of such holder for the approval of other applications or the issuance of other licenses before the expiration of such seven-year period.

Open Protocols for Investigations of Drugs for Rare Diseases or Conditions

SEC. 528. If a drug is designated under section 526 as a drug for a rare disease or condition and if notice of a claimed exemption under section 505 (i) or regulations issued thereunder is filed for such drug, the Secretary shall encourage the sponsor of such drug to design protocols for clinical investigations of the drug which may be conducted under the exemption to permit the addition to the investigations of persons with the disease or condition who need the drug to treat the disease or condition and who cannot be satisfactorily treated by available alternative drugs.

(b) Chapter V of the Federal Food, Drug, and Cosmetic Act is amended by inserting before section 501 the following:

SUBCHAPTER A - DRUGS AND DEVICES

Orphan Products Board

SEC. 3. Title II of the Public Health Service Act is amended by adding at the end the following:

SEC. 227. (a) There is established in the Department of Health and Human Services a board for the development of drugs (including biologics) and devices (including diagnostic products) for rare diseases or conditions to be known as the Orphan Products Board. The Board shall be comprised of the Assistant Secretary for Health of the Department of Health and Human Services and representatives, selected by the Secretary, of the Food and Drug Administration, the National Institutes of Health, the Centers for Disease Control, and any other Federal department or agency which the Secretary determines has activities relating to drugs and devices for rare diseases or conditions. The Assistant Secretary for Health shall chair the Board.

(b) The function of the Board shall be to promote the development of drugs and devices for rare diseases or conditions and the coordination among Federal, other public, and private agencies in carrying out their respective functions relating to the development of such articles for such diseases or conditions.

(c) In the case of drugs for rare diseases or conditions the Board shall:

- (1) evaluate: (A) the effect of subchapter B of the Federal Food, Drug, and Cosmetic Act on the development of such drugs, and (B) the implementation of such subchapter;
- (2) evaluate the activities of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration for the development of drugs for such diseases or conditions,
- (3) assure appropriate coordination among the Food and Drug Administration, the National Institutes of Health, the Alcohol, Drug Abuse, and Mental Health Administration, and the Centers for Disease Control in the carrying

out of their respective functions relating to the development of drugs for such diseases or conditions to assure that the activities of each agency are complementary,

(4) assure appropriate coordination among all interested Federal agencies, manufacturers, and organizations representing patients, in their activities relating to such drugs,

(5) with the consent of the sponsor of a drug for a rare disease or condition exempt under section 505 (i) of the Federal Food, Drug, and Cosmetic Act or regulations issued under such section, inform physicians and the public respecting the availability of such drug for such disease or condition and inform physicians and the public respecting the availability of drugs approved under section 505 (c) of such Act or licensed under section 351 of this Act for rare diseases or conditions,

(6) seek business entities and others to undertake the sponsorship of drugs for rare diseases or conditions, seek investigators to facilitate the development of such drugs, and seek business entities to participate in the distribution of such drugs, and

(7) recognize the efforts of public and private entities and individuals in seeking the development of drugs for rare diseases or conditions and in developing such drugs.

(d) The Board shall consult with interested persons respecting the activities of the Board under this section and as part of such consultation shall provide the opportunity for the submission of oral views.

(e) The Board shall submit to the Committee on Labor and Human Resources of the Senate and the Committee on Energy and Commerce of the House of Representatives an annual report:

(1) identifying the drugs which have been designated under section 526 of the Federal Food, Drug, and Cosmetic Act for a rare disease or condition,

(2) describing the activities of the Board, and

(3) containing the results of the evaluations carried out by the Board.

The Director of the National Institutes of Health and the Administrator of the Alcohol, Drug Abuse, and Mental Health Administration shall submit to the Board for inclusion in the annual report a report on the rare disease and condition research activities of the Institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration; the Secretary of the Treasury shall submit to the Board for inclusion in the annual report a report on the use of the credit against tax provided by section 44H of the Internal Revenue Code of 1954; and the Secretary of Health and Human Services shall submit to the Board for inclusion in the annual report a report on the program of assistance under section 5 of the Orphan Drug Act for the development of drugs for rare diseases and conditions. Each annual report shall be submitted by June 1 of each year for the preceding calendar year.

Tax Credit for Testing Expenses for Drugs for Rare Diseases or Conditions

SEC. 4. (a) Subpart A of part IV of subchapter A of chapter 1 of the Internal Revenue Code of 1954 (relating to credits allowable) is amended by inserting after section 44G the following new section:

Sec. 44H. Clinical Testing Expenses for Certain Drugs for Rare Diseases or Conditions.

(a) *General Rule.* There shall be allowed as a credit against the tax imposed by this chapter for the taxable year an amount equal to 50 percent of the qualified clinical testing expenses for the taxable year.

(b) *Qualified Clinical Testing Expenses.* For purposes of this section:

(1) *Qualified Clinical Testing Expenses.*

(A) *In general.* Except as otherwise provided in this paragraph, the term "qualified clinical testing expenses" means the amounts which are paid or incurred by the taxpayer during the taxable year which would be described in subsection (b) of section 44F if such subsection were applied with the modifications set forth in subparagraph (B).

(B) *Modifications.* For purposes of subparagraph (A), subsection (b) of section 44F shall be applied: (i) by substituting "clinical testing" for "qualified research" each place it appears in paragraphs (2) and (3) of such subsection, and (ii) by substituting "100 percent" for "65 percent" in paragraph (3) (A) of such subsection.

(C) *Exclusion for amounts funded by grants, etc.* The term "qualified clinical testing expenses" shall not include any amount to the extent such amount is funded by any grant, contract, or otherwise by another person (or any governmental entity).

(D) *Special rule.* For purposes of this paragraph, section 44F shall be deemed to remain in effect for periods after December 31, 1985.

(2) *Clinical testing.*

(A) *In general.* The term "clinical testing" means any human clinical testing: (i) which is carried out under an exemption for a drug being tested for a rare disease or condition under section 505 (i) of the Federal Food, Drug, and Cosmetic Act (or regulations issued under such section), (ii) which occurs: (I) after the date of such drug is designated under section 526 of such Act, and (II) before the date on which an application with respect to such drug is approved under section 505 (b) of such Act, and (iii) which is conducted by or on behalf of the taxpayer to whom the designation under such section 526 applies.

(B) *Testing must be related to use for rare disease or condition.* Human clinical testing shall be taken into account under subparagraph (A) only to the

extent such testing is related to the use of a drug for the rare disease or condition for which it was designated under section 526 of the Federal Food, Drug, and Cosmetic Act.

(c) Coordination with Credit for Increasing Research Expenditures:

(1) *In general.* Except as provided in paragraph (2), any qualified clinical testing expenses for a taxable year to which an election under this section applies shall not be taken into account for purposes of determining the credit allowable under section 44F for such taxable year.

(2) *Expenses included in determining base period research expenses.* Any qualified clinical testing expenses for any taxable year which are qualified research expenses (within the meaning of section 44F (b)) shall be taken into account in determining base period research expenses for purposes of applying section 44F to subsequent taxable years.

(d) Definition and Special Rules:

(1) *Rare disease or condition.* For purposes of this section, the term "rare disease or condition" means any disease or condition which occurs so infrequently in the United States that there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date such drug is designated under section 526 of the Federal Food, Drug, and Cosmetic Act.

(2) *Limitation based on amount of tax.* The credit allowed by this section for any taxable year shall not exceed the amount of the tax imposed by this chapter for the taxable year reduced by the sum of the credits allowable under a section of this subpart having a lower number or letter designation than this section, other than the credits allowable by sections 31, 39, and 43. For purposes of the preceding sentence, the term "tax imposed by this chapter" shall not include any tax treated as not imposed by this chapter under the last sentence of section 53 (a).

(3) Special limitations on foreign testing:

(A) *In general.* No credit shall be allowed under this section with respect to any clinical testing conducted outside the United States unless: (i) such testing is conducted outside the United States because there is an insufficient testing population in the United States, and (ii) such testing is conducted by a United States person or by any other person who is not related to the taxpayer to whom the designation under section 526 of the Federal Food, Drug, and Cosmetic Act applies.

(B) *Special limitation for corporations to which section 934 (b) or 936 applies.* No credit shall be allowed under this section with respect to any clinical

testing conducted by a corporation to which section 934 (b) applies or to which an election under section 936 applies.

(4) *Certain rules made applicable.* Rules similar to the rules of paragraphs (1) and (2) of section 44F (f) shall apply for purposes of this section.

(5) *Election.* This section shall apply to any taxpayer for any taxable year only if such taxpayer elects (at such time and in such manner as the Secretary may by regulations prescribe) to have this section apply for such taxable year.

(c) *Termination.* This section shall not apply to any amount paid or incurred after December, 1987.

(b) (1) Section 280C of such Code (relating to denial of deduction for portion of wages for which credit is claimed under section 40 or 44B) is amended by adding at the end thereof the following new subsection:

(c) *Credit for Qualified Clinical Testing Expenses for Certain Drugs:*

(1) *In general.* No deduction shall be allowed for that portion of the qualified clinical testing expenses (as defined in section 44H (b)) otherwise allowable as a deduction for the taxable year which is equal to the amount of the credit allowable for the taxable year under section 44H (determined without regard to subsection (d) (2) thereof).

(2) *Similar rule where taxpayer capitalizes rather than deducts expenses.* If:

(A) the amount of the credit allowable for the taxable year under section 44H (determined without regard to subsection (d) (2) thereof), exceeds

(B) the amount allowable as a deduction for the taxable year for qualified clinical testing expenses (determined without regard to paragraph (1), the amount chargeable to capital account for the taxable year for such expenses shall be reduced by the amount of such excess.

(3) *Controlled groups.* In the case of a corporation which is a member of a controlled group of corporations (within the meaning of section 44F (f) (5)) or a trade or business which is treated as being under common control with other trades or business (within the meaning of section 44F (f) (1) (B)), this subsection shall be applied under rules prescribed by the Secretary similar to the rules applicable under subparagraphs (A) and (B) of section 44F (f) (1).

(2) (A) The section heading of section 280C of such Code is amended to read as follows: *Sec. 280C. Certain expenses for which credits are allowable.*

(B) The table of sections for part IX of subchapter B of chapter 1 of such Code is amended by striking out the item relating to section 280C and inserting in lieu thereof the following: *Sec. 280C. Certain expenses for which credits are allowable.*

(c) (1) The table of sections for subpart A of part IV of subchapter A of chapter 1 of such Code is amended by inserting after the item relating to section

44G the following new item: *Sec. 44H. Clinical testing expenses for certain drugs for rare diseases or conditions.*

(2) Subsection (b) of section 6096 of such Code is amended by striking out "and 44G" and inserting in lieu thereof "44G, and 44H".

(d) The amendments made by this section shall apply to amounts paid or incurred after December 31, 1982, in taxable years ending after such date.

Grants and Contracts for Development of Drugs for Rare Diseases and Conditions.

Sec. 5. (a) The Secretary may make grants to and enter into contracts with public and private entities and individuals to assist in defraying the costs of qualified clinical testing expenses incurred in connection with the development of drugs for rare diseases and conditions.

(b) For purposes of subsection (a):

(1) The term "qualified clinical testing" means any human clinical testing:

(A) which is carried out under an exemption for a drug for a rare disease or condition under section 505 (i) of the Federal Food, Drug, and Cosmetic Act (or regulations issued under such section),

(B) which occurs: (i) after the date such drug is designated under section 526 of such Act, and (ii) before the date on which an application with respect to such drug is submitted under section 505 (b) of such Act.

(2) The term "rare disease or condition" means any disease or condition which occurs so infrequently in the United States that there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under this subsection is made.

(c) For grants and contracts under subsection (a) there are authorized to be appropriated \$ 4,000,000 for fiscal year 1983 and for each of the next two fiscal years.