

Orphan Products Development

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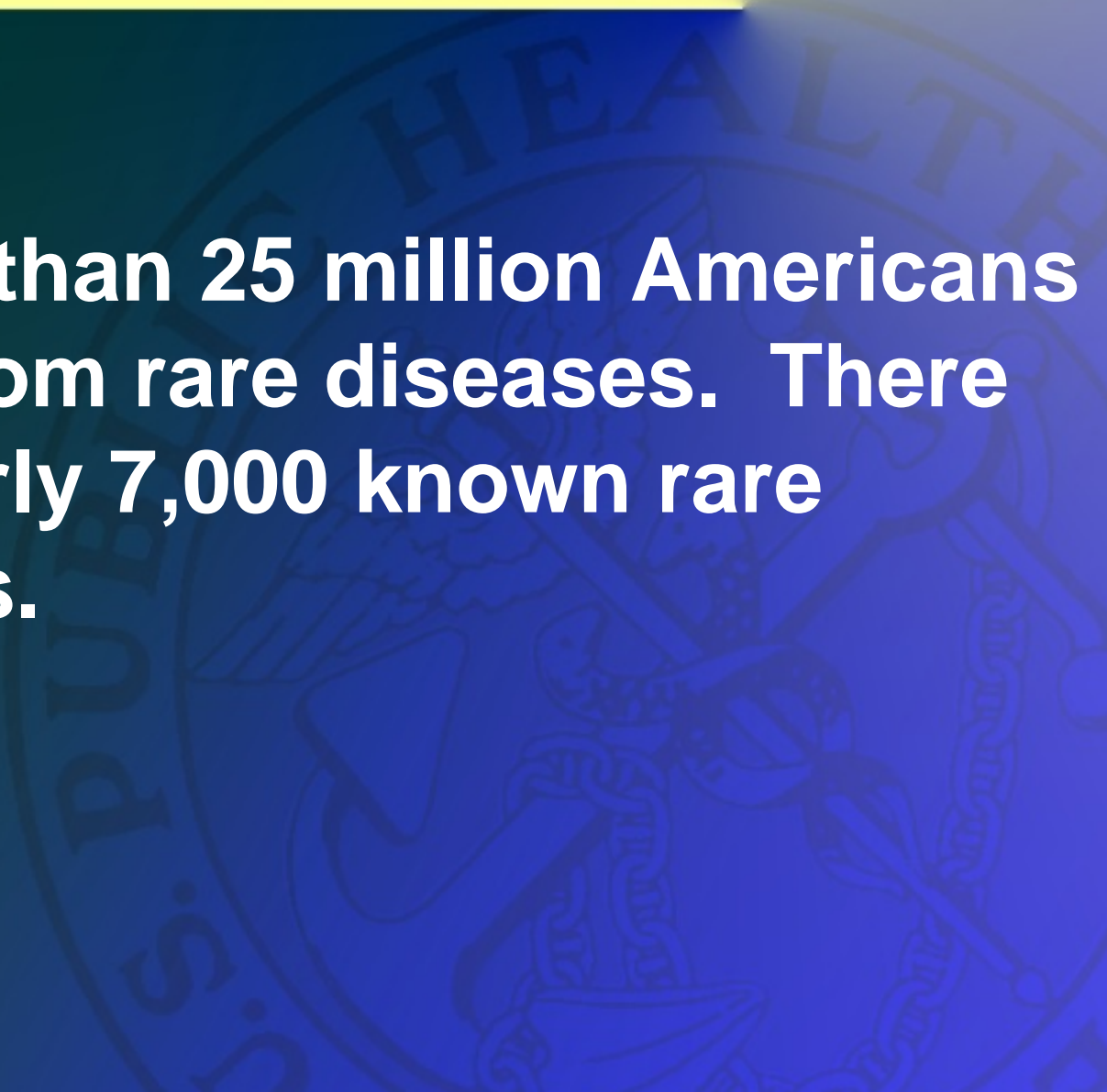
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Orphan Products

Greater than 25 million Americans suffer from rare diseases. There are nearly 7,000 known rare diseases.





History of the Orphan Drug Act

- Industry reluctant to invest in small markets
- National Organization for Rare Disorders (NORD) founded to provide patient services and lobby Congress
www.rarediseases.org
- Quincy, M.E. (1976-1983)



“Orphan-Drug”

- “They are like children who have no parents, and they require special effort.”
 - *Congressman Henry Waxman*

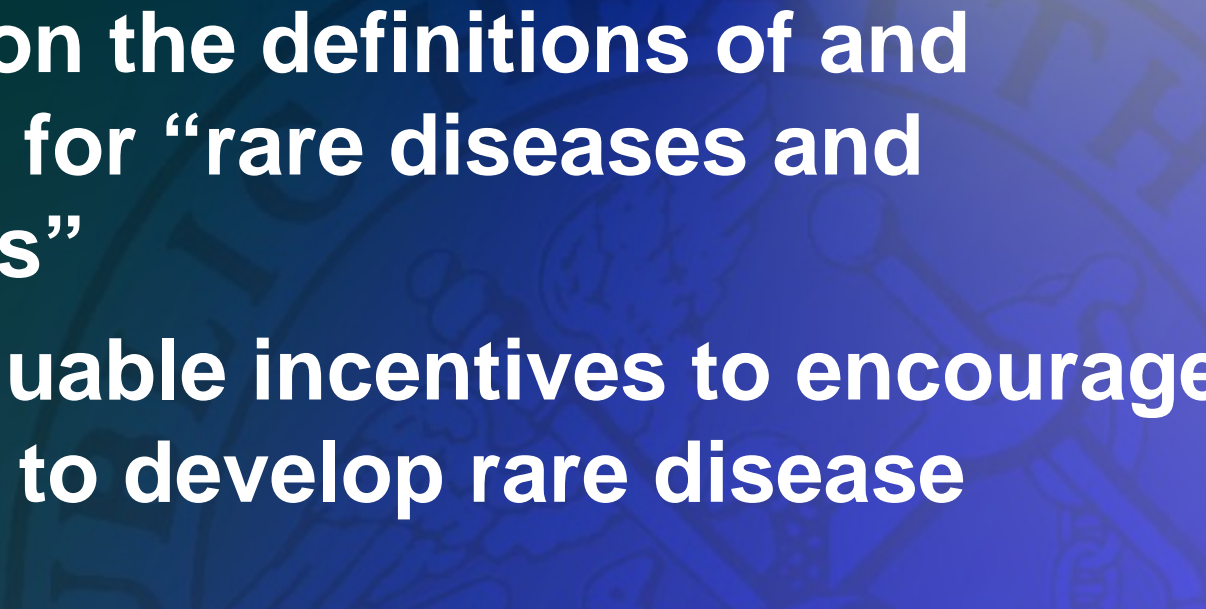


Orphan Drug Act (ODA)

- Signed into law January 4, 1983
 - FDA was given the added mission to promote the development of therapies for rare diseases
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Orphan Drug Act (ODA)

- Focus is on the definitions of and treatment for “rare diseases and conditions”
 - Offers valuable incentives to encourage sponsors to develop rare disease treatment
- 



Definition 1984 Amendment

- **Rare disease or condition**
 - ***Any disease or condition which (a) affects less than 200,000 persons in the U.S. or (b) affects more than 200,000 persons in the U.S. but for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such disease or condition will be recovered from sales in the U.S. of such drug***



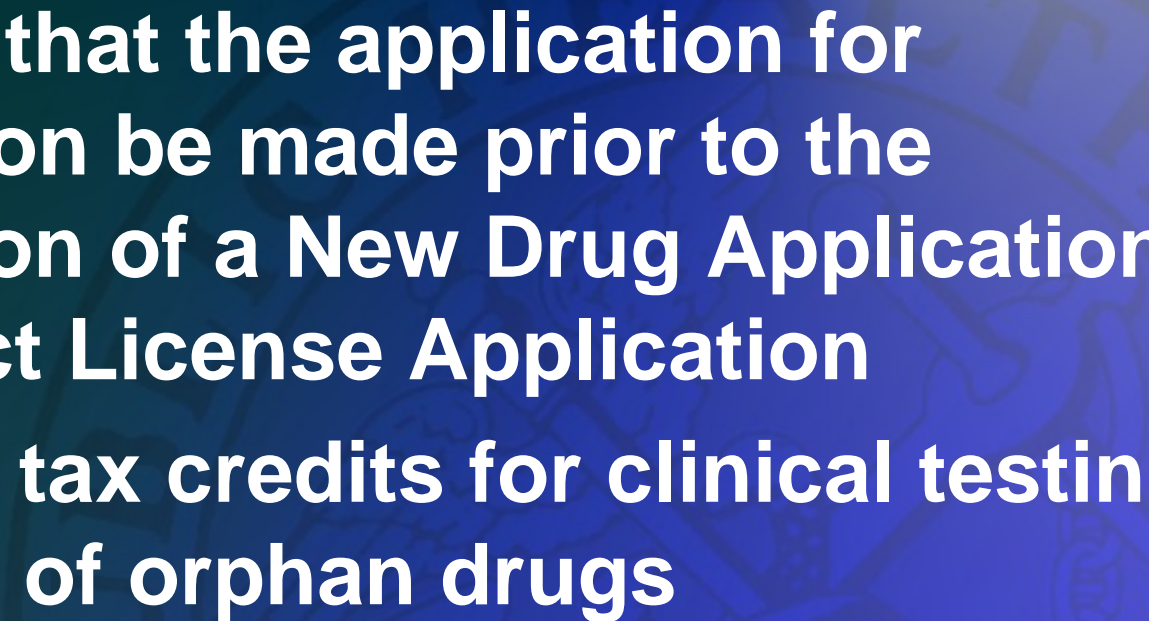
1985 Amendment

- Included patentable and non-patentable drugs and biologics





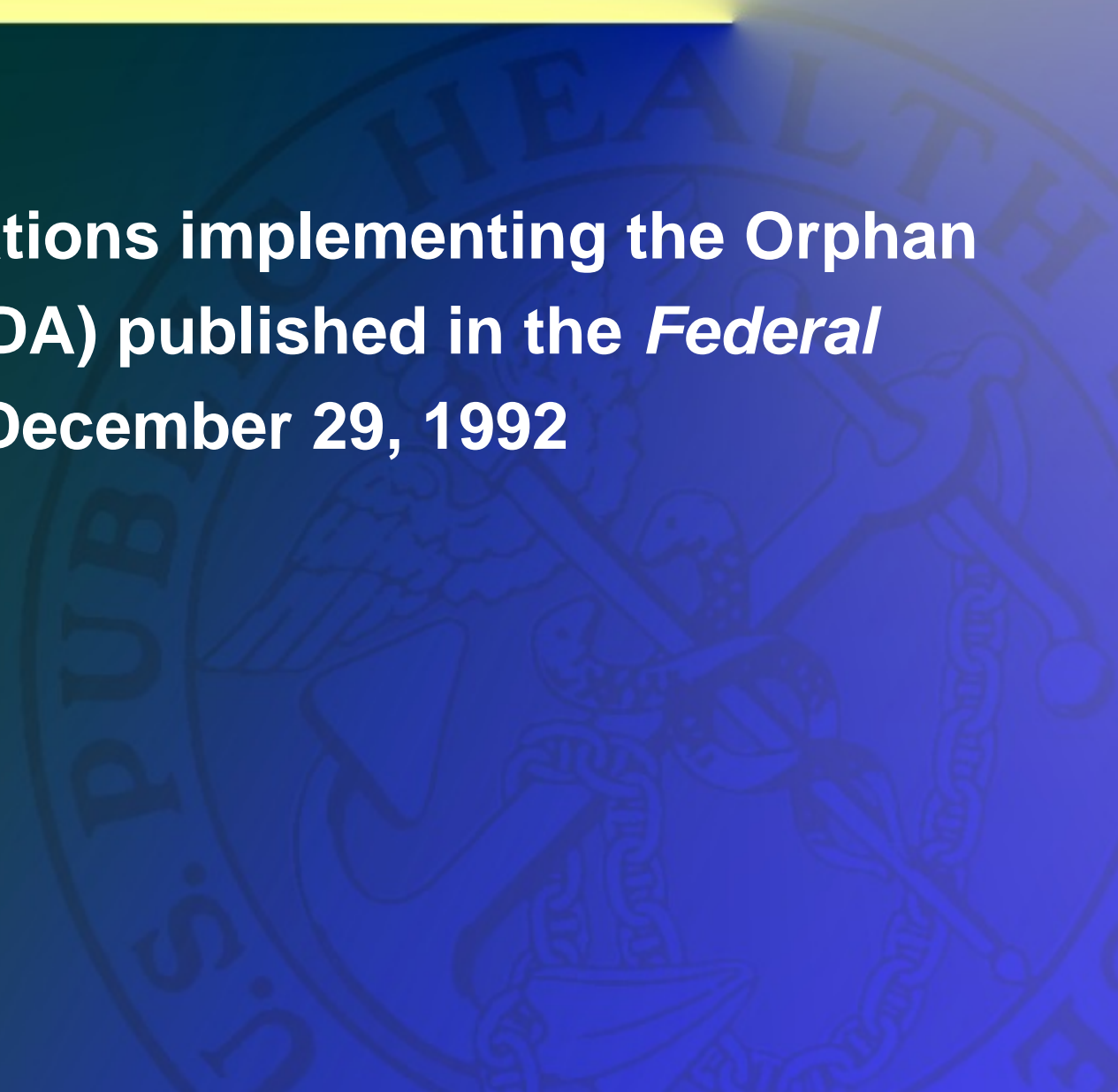
1988 Amendment

- Required that the application for designation be made prior to the submission of a New Drug Application or Product License Application
 - Extended tax credits for clinical testing expenses of orphan drugs
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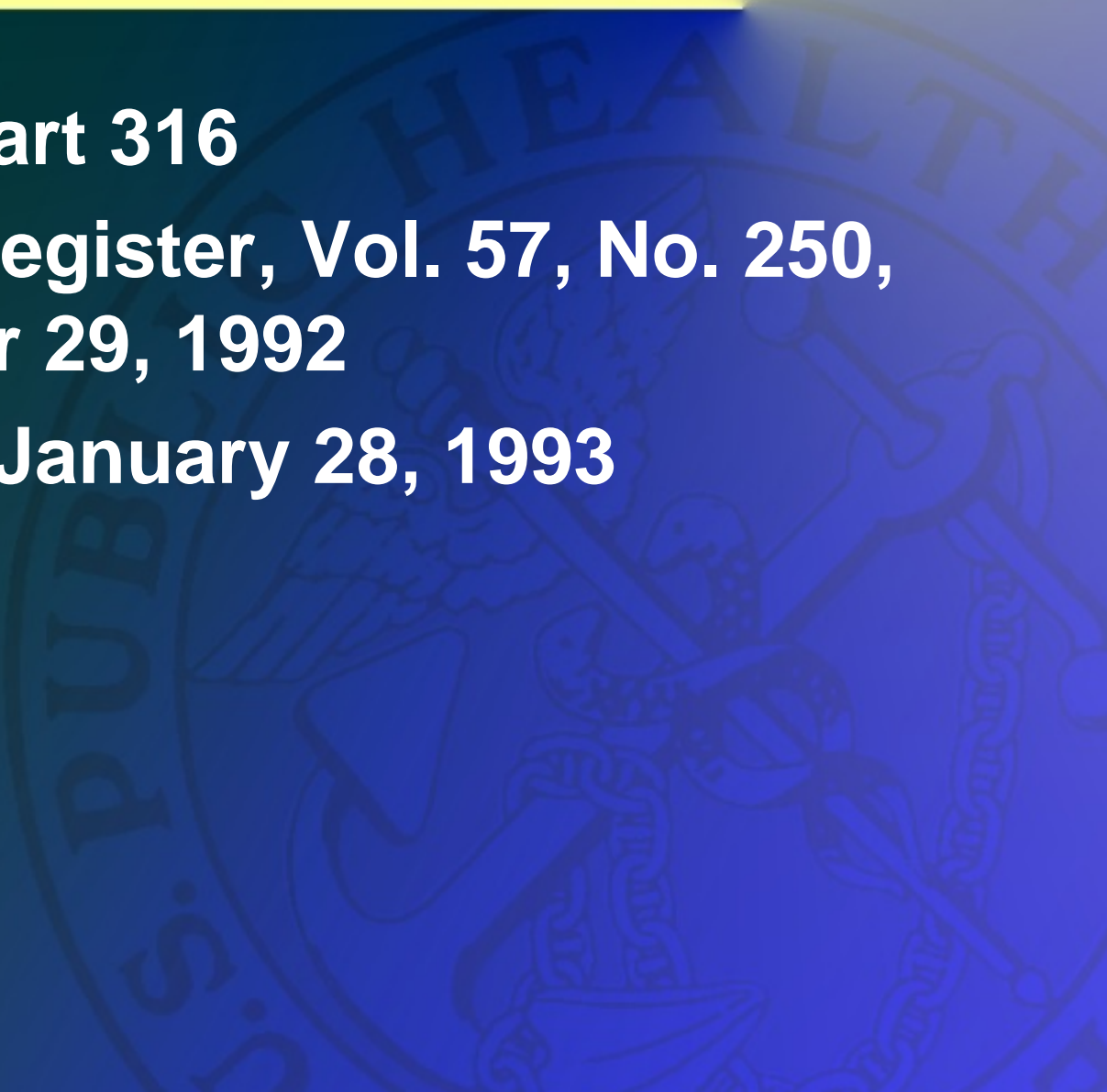
1992 Amendment

Final Regulations implementing the Orphan Drug Act (ODA) published in the *Federal Register* on December 29, 1992





Orphan Drug Regulations

- **21 CFR Part 316**
 - **Federal Register, Vol. 57, No. 250, December 29, 1992**
 - **Effective January 28, 1993**
- 



Office of Orphan Products Development (OOPD)

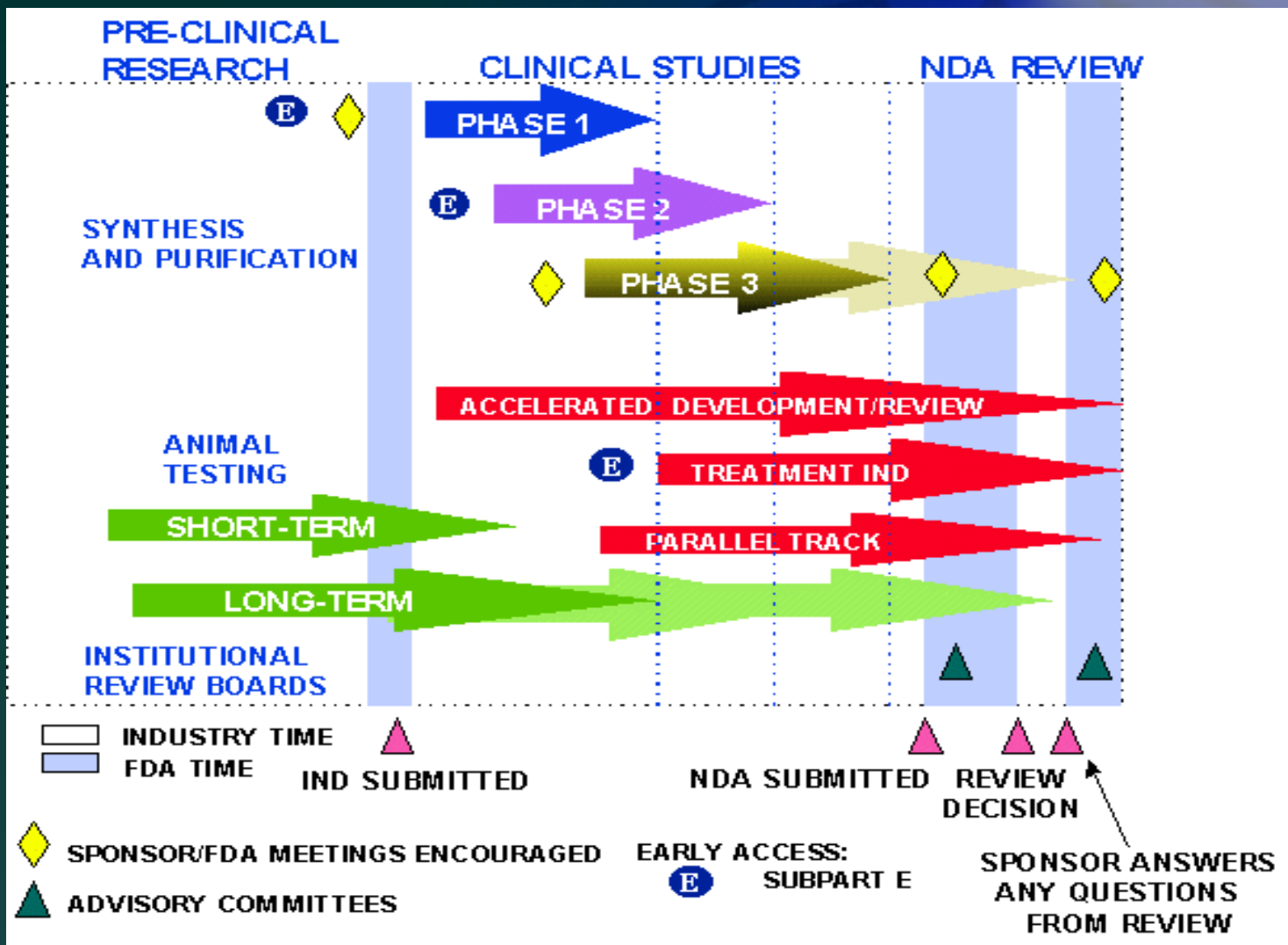
- **Responsibilities of OOPD**
 - Review requests for orphan product designation
 - Serve as liaison between sponsors and the FDA review division
 - Oversee the orphan products program



Office of Orphan Products Development (OOPD)

- **Responsibilities of OOPD**
 - Encourage sponsors to conduct clinical trials
 - Award grant funding to defray costs of qualified clinical testing incurred in connection with the development of drugs for rare diseases or conditions


The Drug Development Process





Clinical Trials Today

- **Two clinical trials**
 - *Exception for serious condition where no other therapy is available and other substantial evidence is available (FDAMA 1997)*
- **Well-controlled**
- **One trial must have a clinical endpoint**
 - *Accelerated approval can use surrogate endpoint*
- **Orphan drugs have same requirements**



Incentives of the Orphan Drug Act

- **Marketing Exclusivity**
 - **Research Grant Funding**
 - **Tax Credits for Clinical Research**
 - **Protocol Assistance**
 - **Waiver of PDUFA Application Fee**
- 



Marketing Exclusivity

- **Received upon FDA approval of a specific drug for a specific indication**
 - 7 years following FDA market approval
 - Additional 6 months for pediatric studies
- **FDA cannot approve same drug for same indication during exclusivity period**



Patents Versus Exclusivity

- Patents last longer but often occur early in drug development process. **Exclusivity begins after marketing approval**
- Easier to challenge a patent compared with **exclusivity**
- Patents are defended in court. **FDA protects exclusivity for the sponsor**



Research Grants

- **Funds clinical studies supporting the development of orphan products**
 - Products can be drugs, biologics, medical devices, and medical foods



Tax Credits

- Provides for a 50 percent tax credit for clinical research and testing expenses
- Can be applied to Federal taxes incurred in prior year (carryback) or applied for up to 20 years (carry forward) against future taxes
- Tax credit provisions made permanent from May 31, 1997



Protocol Assistance

- **Helps potential sponsors design research that conforms to FDA requirements**
- **Sponsors may receive both formal and informal guidance regarding preclinical or clinical requirements for product approval**



PDUFA Application Fee

Congress exempted designated orphan products from the user fee requirement

User fee

\$1,247,000 FY 09


\$1,178,000 FY 08

Establishment fee

\$425,700 FY 09

Product fee

\$71,520 FY 09



Three Types of OOPD Requests

- **Orphan Designation**
 - **Grants**
 - **Humanitarian Use Devices (HUDs)**
- 



Orphan Designation

- **Qualifies a product for special financial incentives**
- **Two criteria must be met:**
 - **Rationale must be consistent with accepted medical knowledge**
 - **The prevalence in the U.S. population must be less than 200,000**



Designation Statistics

Designation Requests

2753

Designated Products

1955

Approved Product

336

Recent Approvals of Designated Products



- **NeoProfen (ibuprofen lysine) – Patent Ductus Arteriosus**
- **Soliris (eculizumab) – Paroxysmal Nocturnal Hemoglobinuria**
- **Cyanokit (hydroxocobalamine) – Cyanide Poisoning**
- **Elaprase (idursulfase) – Mucopolysaccharidosis II**
- **Revlimid (lenalidomide) – Multiple Myeloma**
- **Kuvan (saproterin) – Hyperphenylalanemia**
- **Norditropin (somatropin) – Noonan Syndrome**
- **Myozyme (alpha-glucosidase) – Glycogen Storage Disease II**



Grants Program

- **Goal - To encourage clinical development of products for use in treatment of rare disease or conditions**
- **Applications solicited through Request for Applications (RFA) published in *Federal Register* annually**
- **Only clinical studies qualify**



Grants Program

- To date, FDA has provided more than **\$150 million** in grants to fund studies on an estimated **180 rare diseases**
- **Current budget - \$14.2 million**
 - *Grants may cover between \$200,000 to \$400,000 in total costs (direct plus indirect) per year for up to four years*
 - *Approximately \$10 million will fund non-competing continuation grants*
 - *Approximately \$4.2 million will fund 10 to 12 new grants per year (subject to availability of funds)*
 - *Applications for \$200,000 may be for Phase 1, 2, or 3 studies*
 - *Applications for \$400,000 must be for studies continuing in Phase 2 or 3 of investigation*
 - *A fourth year of funding is available only for Phase 2 or 3 clinical studies*



Grants Program Review Process

- **First review - OPD staff**
 - **Clinical trial to provide safety and/or efficacy data for one product for one indication**
 - **Study must be performed under an IND/IDE**
 - **Prevalence is < 200,000 U.S. patients**
 - **Budget is within program limits**
 - **Product availability**



Grants Program Review Process

- **Second review – Ad hoc panel of experts**
- **Third review - National Advisory Council**
 - **Ensure concurrence with first review**
- **Final awards determined by rank ordered priority scores**



Management of Funded Grants

- **Assignment of project officer**
 - **Liaison between grantee and FDA review division**
 - **Enrollment goals/achievement**
 - **Quarterly progress updates**
 - **Site visits**
 - **Sponsor acquisition**



Humanitarian Use Devices (HUDs)

- **June 26, 1996 - FDA issued final regulations to implement the HUD provisions of the Safe Medical Device Act of 1990**
- **Device intended for use in the treatment or diagnosis of a disease or condition affecting fewer than 4,000 individuals per year in the U.S.**



Humanitarian Use Devices (HUDs)

- **Humanitarian Device Exemption (HDE) -**
 - Exempts sponsors of devices from effectiveness requirements of medical device law provided that safety conditions are met
 - Procedures for HUD designation found in 21 CFR 814.102

Development of Orphan Products Throughout the World

Orphan Drug Acts:

Japan

1993

Australia

1998

European Union

1999

00PD Website

- <http://www.fda.gov/orphan>



Questions

