Fundamentals of Clinical Trials and Human Subjects Protection at USAID

Global Health Mini-University 2007

Lee Claypool
Cognizant Human Subjects Officer
USAID
Bureau for Global Health
Office of Population and Reproductive Health
Research, Technology and Utilization Division
lclaypool@usaid.gov

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Outline of Presentation

- What are clinical trials and why are they needed?
- How and why does USAID fund clinical trials?
- What is the product development process?
- How are human subjects protected in clinical trials, etc?
- What are USAID regulations re human subjects protection?
- What are key issues and concepts for international human subjects research?
- Questions and discussion

Clinical Studies or Trials

per International Conference on Harmonization

Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

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Scope of Health-Related Research and Development Activities at USAID

Report to Congress, Bureau for Global Health, May 2006

HIV/AIDS: Vaccines; Microbicides

Malaria: Vaccines; Drugs, formulations, approaches

Tuberculosis: Drugs; DOT performance, access

Reproductive Health and Family Planning: New & improved contraceptives

Maternal and Newborn Health: Healthy pregnancy and birth outcomes; Maternal mortality measurements; New pregnancy and birth interventions; Neonatal research and care

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Health-Related Research and Development, cont

Nutrition: Vitamin A for deficiency prevention and control; Zinc for diarrhea therapy and prevention; Iron for anemia prevention and treatment; Community therapeutic and emergency care

Acute Respiratory Infections: Community-based treatment of childhood pneumonia; Reducing exposure to indoor air pollution

Health Systems: Performance assessment and financing; Pharmaceutical management; Quality assurance

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Congressional Response to 2005 Report

"With its experience in the developing world, USAID does and should play a valuable role in facilitating international clinical trials, consolidating markets, and finding new opportunities to speed the discovery, development, and delivery of products to improve the lives of those in the developing world."

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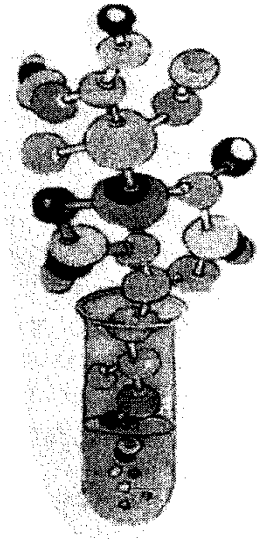
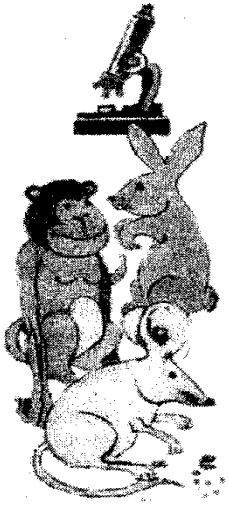
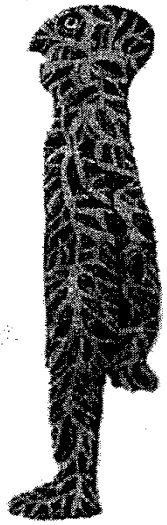
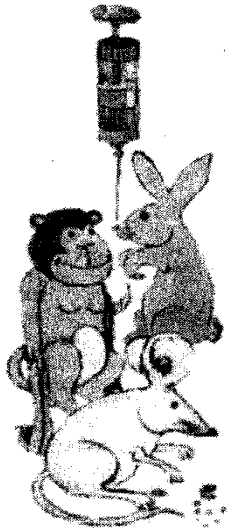
Product Development Process

Pre-Clinical		Phase I		Phase II
10 years	1-2 years	1-2 years	2 years	1-2 years
				
Years of laboratory testing and screening of many compounds may result in a promising contraceptive drug.	Any possible toxicity of the compound is thoroughly checked and its pharmacology is assessed in animals.	Lack of toxicity and minimum effective dose are assessed in groups of 10 to 20 volunteers in different countries.	Long-term toxicity studies begin in animals as well as studies on reproduction, mutagenecity and carcinogenecity.	The first check of efficacy in humans involves up to a few hundred volunteers; acceptability studies begin.

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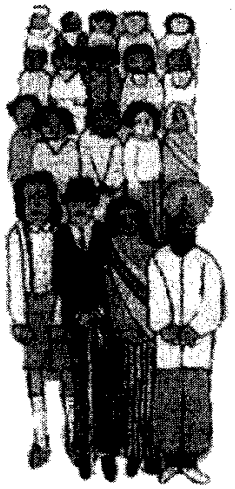
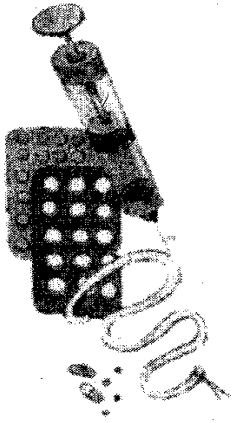
Product Development Process, cont

Phase III

Phase IV

2-3 years	1 years	1-3 years	Indefinitely	Indefinitely
				
Large-scale studies (1,000 subjects) start, lasting up to one year in various countries; acceptability studies continue.	Final arrangements are made for manufacture of the new contraceptive, and for its appropriate packaging.	All clinical and animal data are transmitted to national drug regulatory agencies, whose approval will be essential.	The finished product is supplied to family planning clinics, whose staff are trained in its delivery.	The drug becomes freely available: long-term surveillance guards against any rare adverse risks to health.

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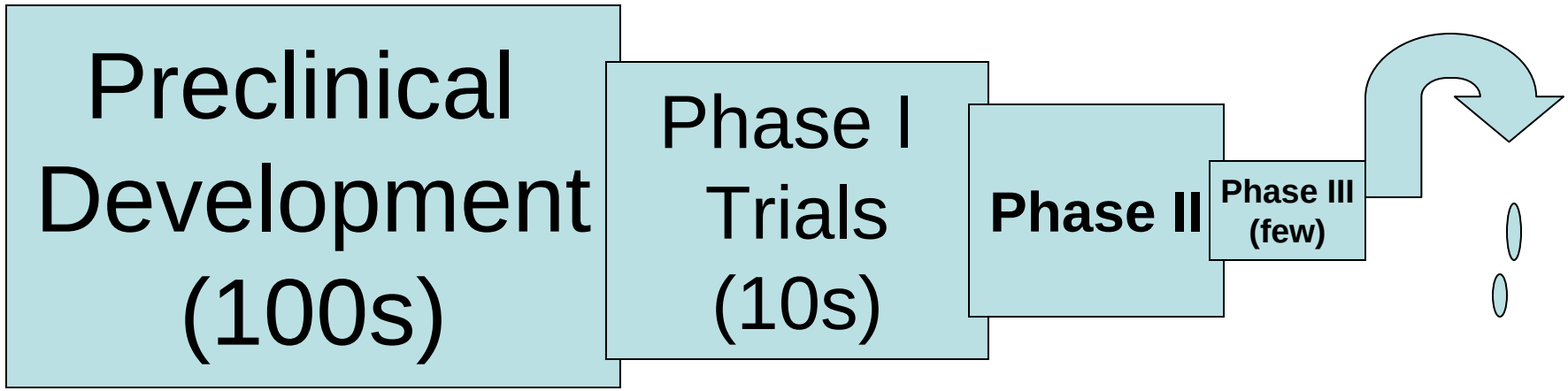
Product Development Pipeline



(Many in, few out)

Protection of Human Subjects in Research Supported by USAID

USAID Guidance, Bureau for Global Health

Revised 12/26/2006

(A Mandatory Reference for ADS Chapter 200)

This is an explanation of selected relevant issues in Human Subjects Protection and how to apply the agency regulations appropriately for USAID-funded activities

Code of Federal Regulations

Title 22 – Foreign Relations

Chapter II – Agency for International Development

Part 225 – Protection of Human Subjects

(Cite as 22 CFR 225)

This is the USAID statement of the Common Federal Policy for Protection of Human Subjects, and is often referred to as the “Common Rule”.

USAID Standard Provisions for NGO Recipients

Standard Provision: Protection of the Individual as a Research Subject (April 1998)

(a) Safeguarding the rights and welfare of human subjects involved in research supported by USAID ***is the responsibility of the organization to which support is awarded***. … (***CHSO has oversight***, guidance, and interpretation responsibility.)

(b) Recipient organizations must comply with USAID policy when humans are the subject of research … and ***must provide "assurance"*** … that they follow and abide by the procedures in the Policy. …

Basic Principles of Human Research Subjects Protection

Per the "Belmont Report" of the President's Commission for the Study of Ethical Programs in Medicine and Biomedical and Behavioral Research, 1979

Human subjects research rests on 3 pillars of protection

- Review of the research by a properly constituted ethical committee or Institutional Review Board (IRB)
- A meaningful assessment of the risks and benefits by the IRB, and
- A meaningful informed consent procedure for research subjects

Key Issues and Concepts in Human Subjects Protection

- Defining Research – the Common Rule defines Research as "… a ***systematic investigation*** including research development, testing and evaluation designed to develop or contribute to ***generalizable knowledge***."

  Research *can* include: Experiments, observation studies, surveys, tests, recording other data for generalizable knowledge

  Research generally does *not* include: Medical care, quality assurance or improvement, some public health practices such as outbreak investigations and disease monitoring, program evaluation, fiscal and program audits, journalism, fact-finding inquiries, etc

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Key Issues and Concepts, cont

- Defining Human Subjects – living individuals about whom an investigator obtains 1) data through intervention or interaction, or 2) identifiable private information
- Exempting certain research, e.g., 1) survey research, unless subjects can be identified and disclosure of responses places subject at risk, 2) collection or study of existing data or specimens, if sources are publicly available or if subjects cannot be identified, and 3) research on the process or outcomes of service delivery broadly

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Key Issues and Concepts, cont

- Achieving truly adequate informed consent
- Waiving or altering informed consent, e.g., when minimal risk
- Defining minimal risk
- Coordinating responsibilities for multiple-site research
- Ensuring continuing review and active oversight (compliance with USG requirements for IRBs)
- Promoting ethical behavior in research that is exempt

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Key Issues and Concepts, cont

- Ethics of research with children, prisoners, military personnel, persons with impaired decision-making capacity, and in emergency or disaster situations
- Coordinating all local regulations and guidance with USG requirements (HSP, importing, exporting, etc)
- Meeting FDA requirements for new product review and approval (re data needed, docs, GCP, etc)
- And many others …

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Additional Information

- **Reports to Congress** - Health-Related R&D Activities at USAID, June 2005 & June 2006
- **USAID Standard Provision**
- **USAID Guidance**
- **22 CFR 225 – the "Common Rule"**
- **OHRP Website**
- **Mini-U Presentation**
- **Reference List**
- **USAID Cognizant Human Subjects Officer**

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Discussion

- Questions
- Suggestions
- Comments
- Requests
- Further information
- Pearls