

UAEM Solutions II:

~~Introduction to Neglected Disease Policy~~

Matthew Basilio, Arjun Suri, Serene Chen
Harvard University
September 29, 2007

The Problem

Drug development is *demand* based—not *need* based.

Disease with great “need” which are most poorly addressed by demand system are *neglected diseases* (NDs).

Between 1975 and 2004, of the 1,556 new chemical entities marketed globally, only 20 new drugs - a mere 1.3% - were for tropical diseases and tuberculosis, diseases which account for 12% of the total disease burden.

Drug Development for Neglected Diseases: a Deficient Market and a Public-Health Policy Failure Patrice Trouillier et al.
359 Lancet, 2188 (2002).

Examples of Currently Neglected Diseases

- Bacterial Infections
 - Trachoma
 - Leprosy
 - Buruli ulcer
 - Cholera
- Protozoan Infections
 - African trypanosomiasis
 - Visceral leishmaniasis (Kala-azar)
 - Malaria
- Viral
 - Dengue/dengue haemorrhagic fever
- Helminth Infections
 - Ascariasis
 - Trichuriasis
 - Hookworm infection
 - Schistosomiasis (urinary and hepatobiliary)
 - Lymphatic filariasis
 - Onchocerciasis
 - Dracunculiasis

Characteristics of Neglected Diseases

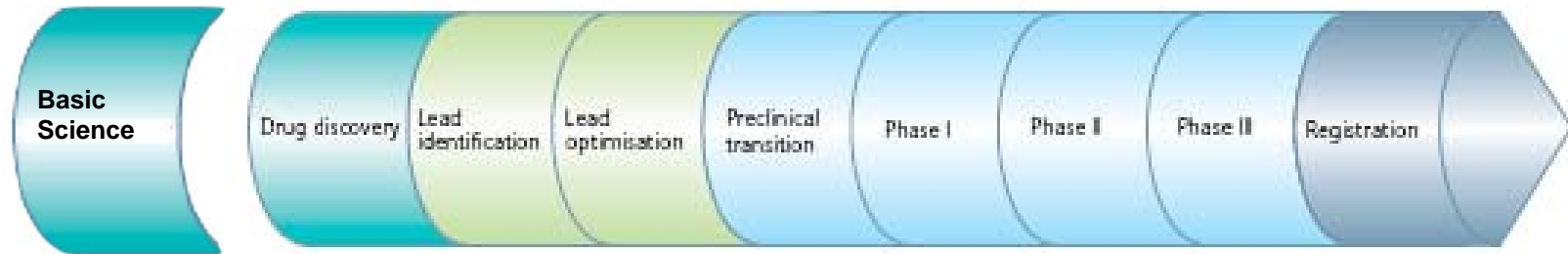
- Affecting world's poorest
- Disabling, disfiguring and stigmatizing
- Lacking safe and effective treatment



Areas of Much Needed Research

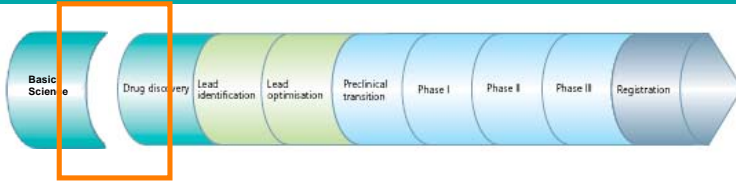
1. Basic knowledge on diseases
2. Basic knowledge on vectors
3. Drug & vaccinations
4. Diagnostics & monitoring devices
5. Vector control and interventions

The Research Pipeline



Modified from Wellcome 2005

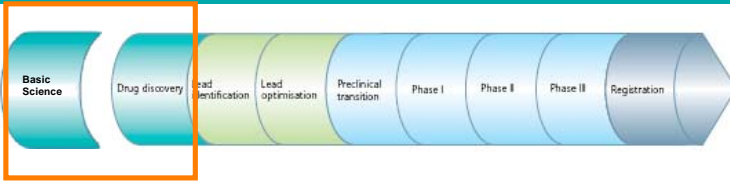
Lacking the “Push and Pull” in Basic Science



- Push: Historically lacked long-term, committed funding
- NIH
 - \$1.5 million grant for Binghamton University, State University of New York, research the rise of chloroquine-resistance.
- Other sources of public funding
 - Dept. of Defense
 - Dept. of Agriculture
 - NSF
- Pull: Picking up on basic science research

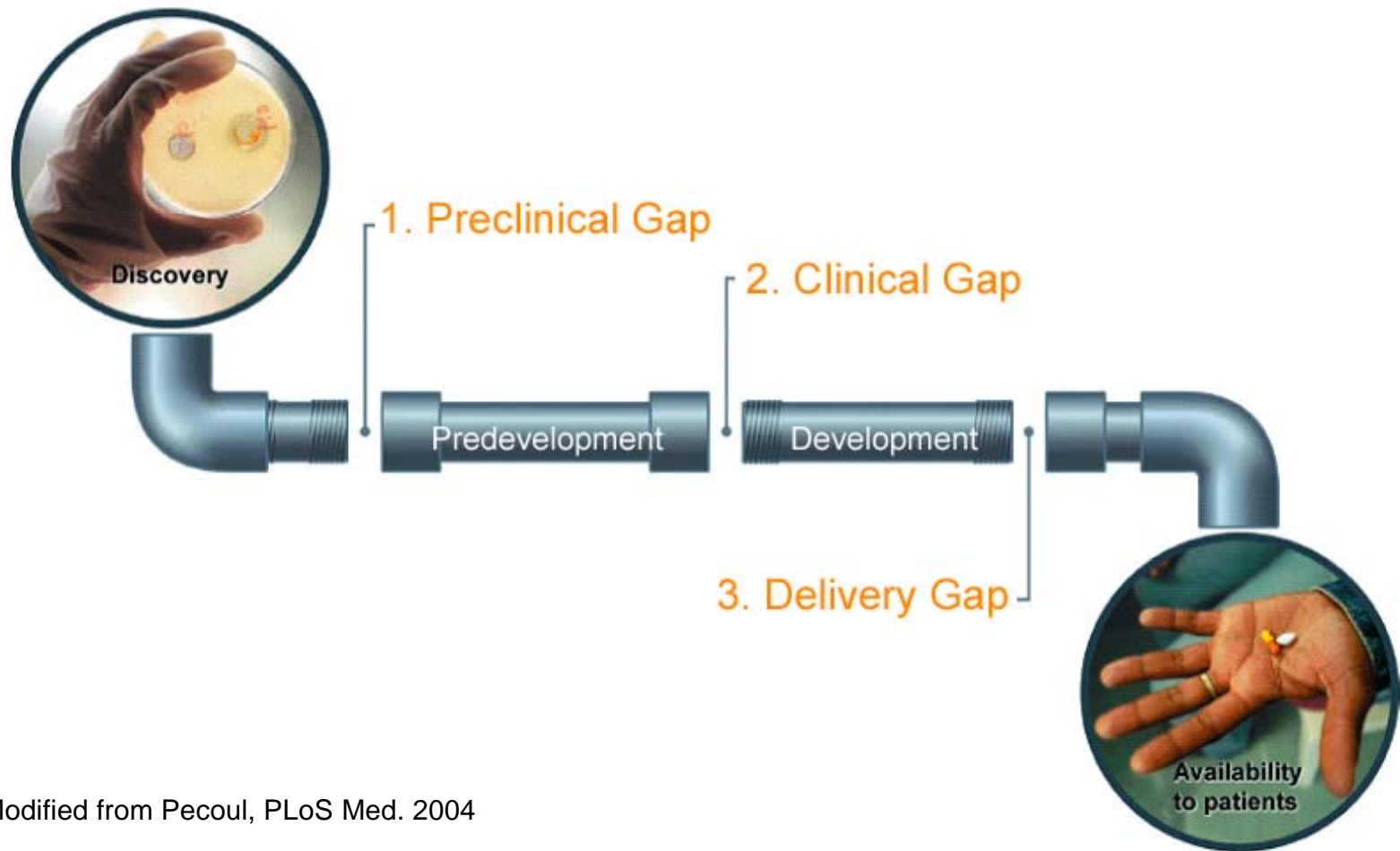
Data from **NIH**. Estimates of funding for various diseases conditions. 2005. And **Federal Funds for Research and Development: Fiscal Years 2002, 2003, 2004**. Arlington, VA: National Science Foundation Division of Science Resources Statistics; 2005.

Challenges in Increasing University ND Research



- Difficulty in setting research agenda
- Reward and incentive ends with publication
- Fear of zero-sum funding situation; funding paradox
- Lacking critical density of researcher; inherent separation of diseases

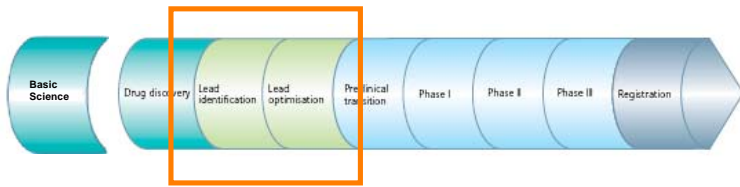
Gaps in the Research Pipeline



Modified from Pecoul, PLoS Med. 2004

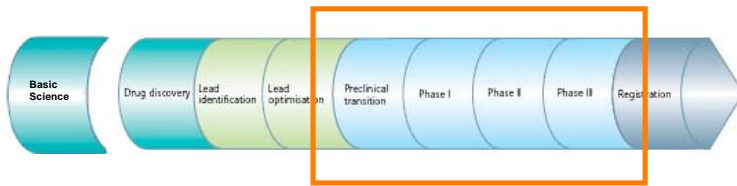
DOI: 10.1371/journal.pmed.0010006.g001

1. The Pre-clinical Gap



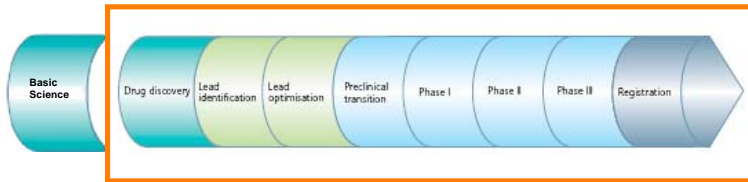
- Preclinical step: Identify physicochemical properties and safety of compound candidate.
- Two types of pre-clinical gaps:
 - Basic science knowledge not translated
 - Compound candidates not delivered to pre-clinical development
- “Push” incentives: governmental and philanthropic money

2. The Clinical Development Gap



- Moving validated drug candidates through clinical trials
- “Pull” incentives
 - transferable intellectual property rights
 - advanced purchase commitments
 - “pot of gold” \approx \$500 million/yr to justify investment

The Players in ND translational research



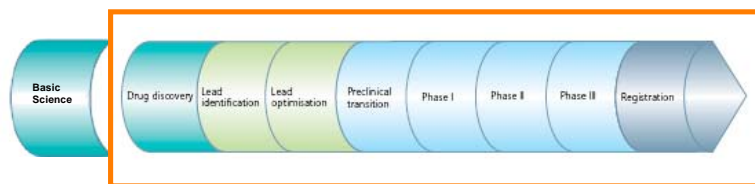
- **Public institutions**

- Academic institutions, research institutes, etc.
 - London School of Hygiene and Tropical Medicine
- Philanthropic and Governmental funding

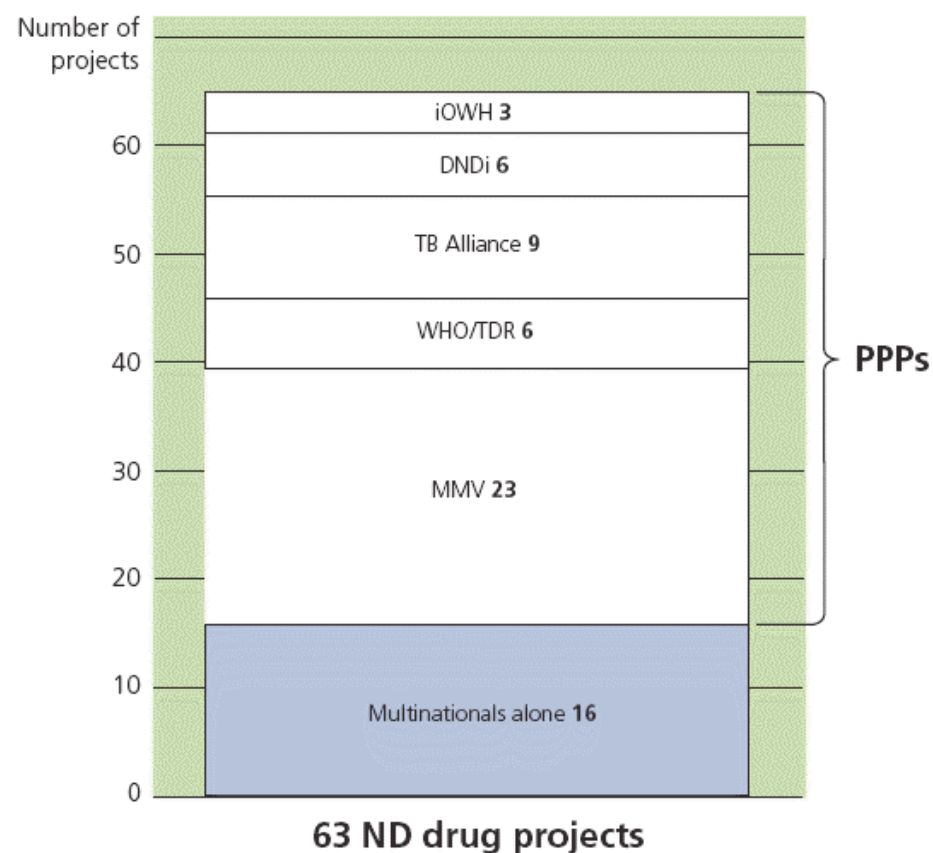
- **Industry involvement**

- Small-medium biotech
 - Niche marketing + outsourcing to Clinical Research Organizations
- Multinational pharmaceutical companies
 - GlaxoSmithKline, Novartis, AstraZeneca, and Sanofi –Aventis
 - Driven by “corporate social responsibility” or strategic marketing in developing countries

The Post-2000 landscape of ND research

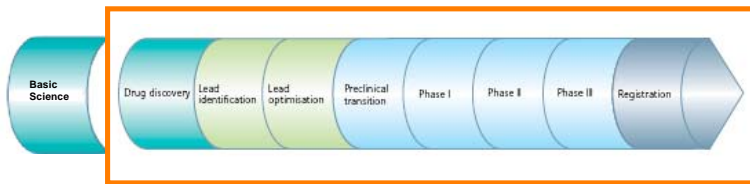


- 63 drugs in the ND pipeline
- 32 projects with large pharmaceutical companies
- 47 projects through Public-Private Partnerships



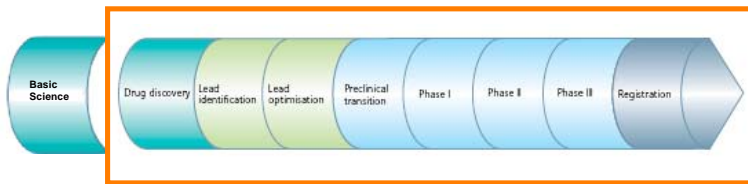
Modified from Wellcome 2005

Product Development Public-Private Partnerships (PD PPPs)

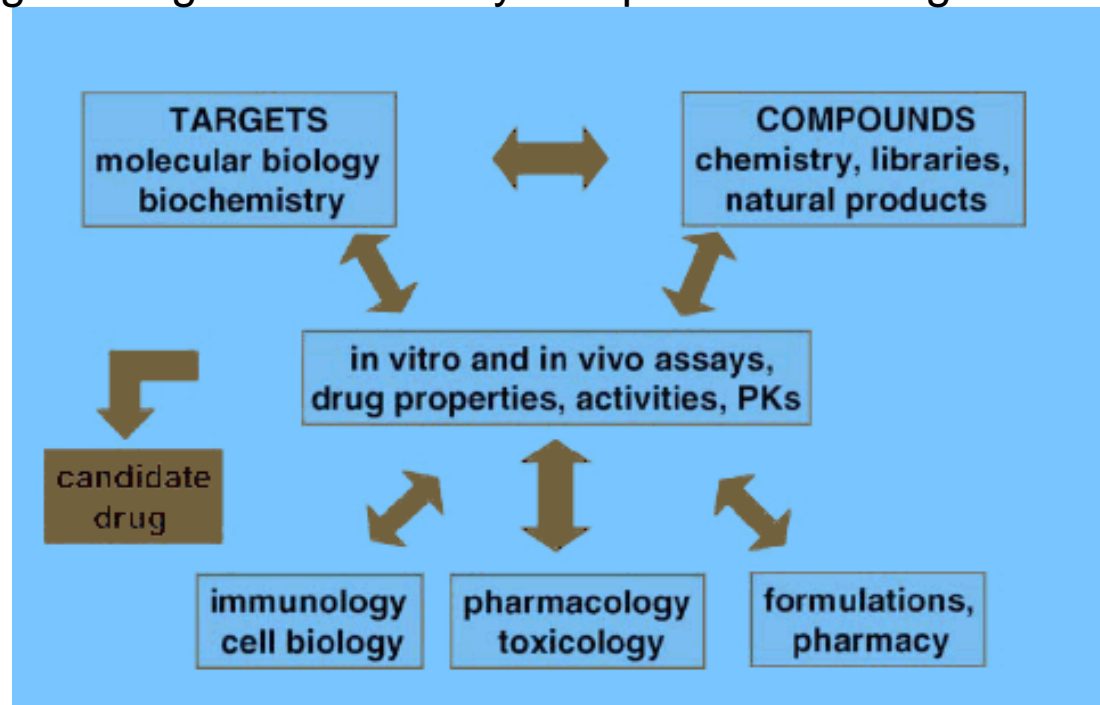


- PD PPPs are defined as “public-health-driven not-for-profit organizations that drive neglected-disease drug development in conjunction with industry groups” (Moran, 2005)
- Goal: efficiently coordinates multiple industry and academic partners and contractors along drug development pipeline

PD PPPs: Coordinating the Elements of Translational Research

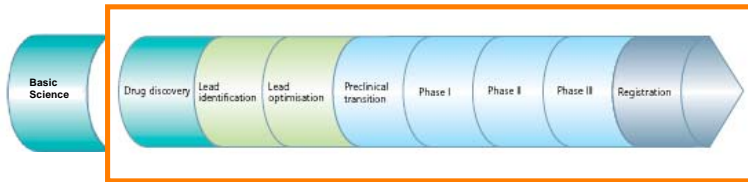


- *Innovation or Stagnation?* (FDA, 2004) concludes that a large proportion of the cost of drug development is due to the use of inadequate models to move things through the discovery and pre-clinical stages



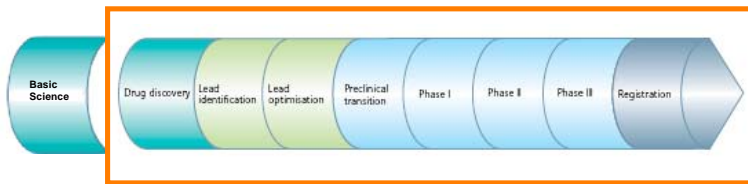
Croft 2005

Case Studies of PD PPPs



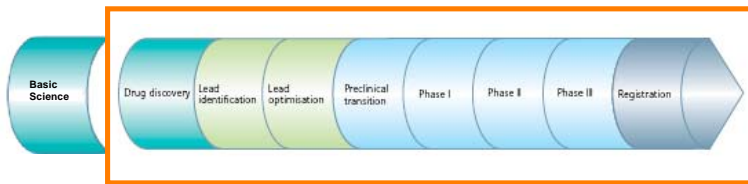
- Drugs for Neglected Diseases Initiative (DNDi)
- Institute for One World Health (IOWH)

Drugs for Neglected Diseases Initiative (DNDi)

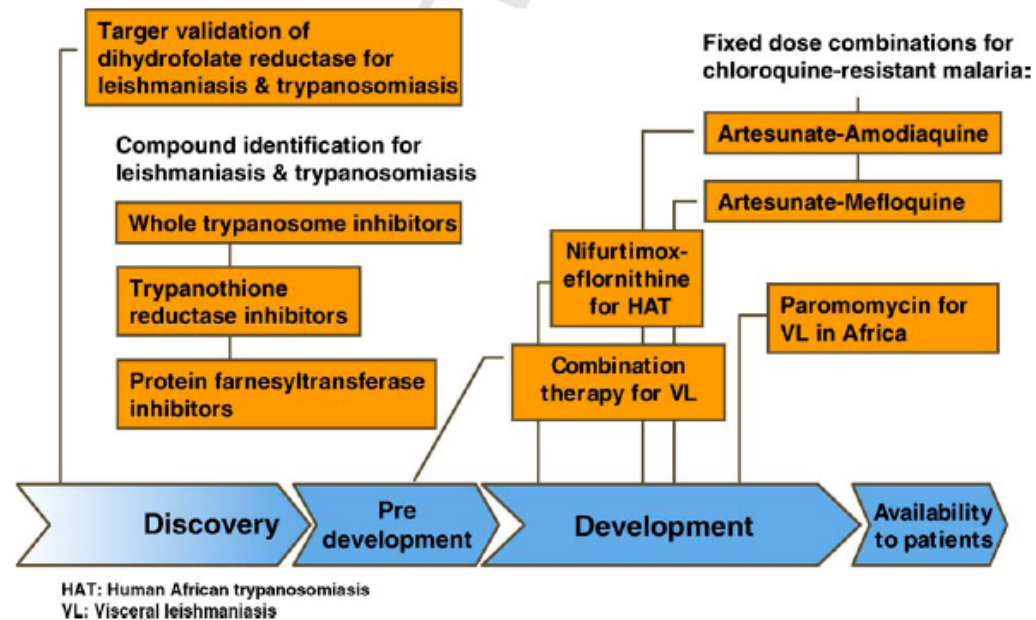


- Overseeing body that coordinates, supports and influences scientific collaboration in research on ND
- One international research organization
 - UNDP/World Bank/WHO's Special Programme for Research and Training in Tropical Diseases (TDR)
- One humanitarian organization
 - MSF
- Five public sector institutions
 - Oswaldo Cruz Foundation from Brazil
 - Indian Council for Medical Research
 - Kenya Medical Research Institute
 - Ministry of Health of Malaysia
 - France's Pasteur Institute

DNDi's projects

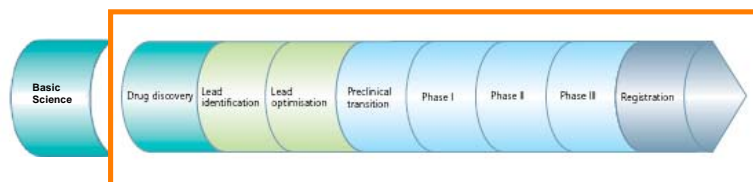


- Visceral leishmaniasis, Trypanosomiasis, Chagas, and Malaria



Croft 2005

Institute for One World Health (IOWH)



- Gates-funded not-for-profit pharmaceutical company
- Focus diseases: Leishmaniasis, Chagas disease, malaria, schistosomiasis and diarrheal diseases
- Licensing late-stage development candidates and drug development (not discovery)
 - Just completed Phase III for trials in India for paromomycin
- Originally for oral use against gut pathogens, now being tested for **visceral leishmaniasis**



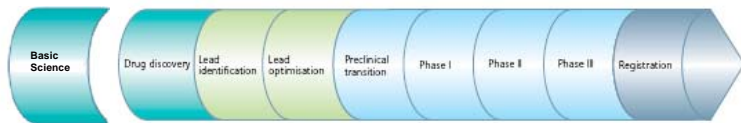
3. The Delivery Gap: Another 10 in the 10/90 Divide

- 10 million people die needlessly each year because they do not have access to existing medicines and vaccines
- Global Network for Neglected Tropical Diseases formed in 2006



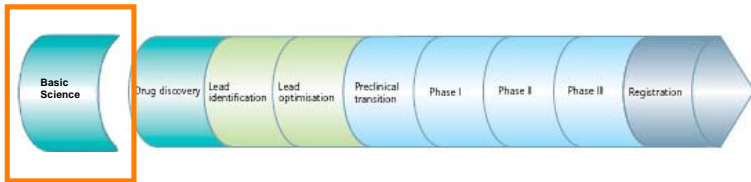
Patient treated for Sleeping sickness (MSF 2001)

Global Steps Forward



- **Basic Science**
 - Public (University and Non-University)
- **Drug Discovery**
 - Aligning Industry Incentives (pull mechanisms)
 - Developing Public Institutions (government, non-profit and public-private partnerships)

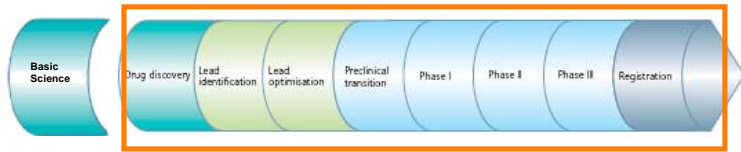
The Role of The University



- **Discovery**

- Faculty Development in Neglected Disease Research areas
 - Pre-Faculty
 - Instructors
 - Junior Faculty
 - Established Faculty
- Faculty Collaboration
 - Use of new technologies (i.e. genome mapping)
- International Collaboration
 - Building in-country capacity
 - Training US researchers in developing-country practices

The Role of The University



- Translational
 - Incubator Funds
 - Allow in-house or out-sourced development
 - Pre-clinical
 - Early-stage clinical
 - Development of In-House Capacity
 - Pre Clinical
 - Phase I
 - Expanding Tech Transfer linkages to Translational Institutions
 - Research Exemptions
 - Opening Compound Libraries

The Role of The University

Physical Interdisciplinary Center

Virtual Center

Incubator Fund	Physical Space	Faculty Development	Translational Linkages	International Research Network	Governing Body	Administrative Support
<i>To provide funding for pre-clinical testing of promising technologies</i>	<i>To provide a venue for collaboration</i>	<i>To hire professors and researchers of neglected diseases, to promote inter-disciplinary collaboration</i>	<i>To connect promising discoveries with public institutions, industry and PPPs seeking to bring technologies to market</i>	<i>To align global efforts through training of researchers at Harvard and abroad</i>	<i>To champion inter disciplinary neglected diseases projects</i>	<i>To oversee practical aspects of neglected diseases initiative</i>

The Role of The University

- Examples: Center for AIDS Research (CFAR)
 - Cores:
 - Administrative
 - Biostatistics
 - Clinical
 - Developmental
 - Immunology
 - Molecular Virology
 - Small Animal Containment

The screenshot displays the CFAR website's navigation menu and a section titled "Harvard University Center for AIDS Research Cores". The navigation menu on the left includes: Center for AIDS Research (CFAR), Cores, Administrative, Biostatistics & Computational Biology, Clinical, Developmental, Immunology, Molecular Virology / Biology, Small Animal Containment, Funding Opportunities & Awards, Members & Benefits, Scientific Programs, Acknowledging CFAR, Office of Int'l Programs (OIP), Community Programs, News & Events, Directory, Clinical Trials, and Education & Training. The "Cores" section features seven categories: Administrative, Biostatistics & Computational Biology, Clinical, Developmental, Immunology, Molecular Virology / Biology, and Small Animal Containment. Below this, a paragraph explains that these seven cores were identified through a strategic planning process to support the divergent needs of CFAR investigators and foster collaboration among AIDS investigators at Harvard.

The Role of The University

- Synergies with other UAEM Projects
 - Access-Minded Technology Transfer
 - Dual Use Technologies
 - Metrics
 - Human-indices would greatly favor ND technologies over current paradigms
 - More specific ND metrics have been proposed by Suk, et. al.

The Role of The University

- Gap 3: The Delivery Gap
 - Universities also have a role to play: Delivery Science
 - Jim Kim and Delivery Science at Harvard



Program in Global Health Delivery Science

- Invest in Research, Innovation and Training at the point of delivery in the poorest settings
- Support Scholarship that will help solve real problems in real time (IER, RE, DA, QI, Cases, VCA)
- Train and Nurture a new cadre of global health leaders – We need 1000's of master implementers
- Cultivate Communities of Practice that will achieve breakthrough results

The Role of The University

- Making it Happen
 - University Incentives
 - Funding
 - Prestige
 - General University Donors
 - Interested in what students want
 - ND Donors
 - Often like to see student-faculty collaboration

The Role of The University

PHILADELPHIA CONSENSUS STATEMENT *On University Policies for Health-Related Innovations*

PROMOTE RESEARCH AND DEVELOPMENT FOR NEGLECTED DISEASES

1. **Adopt policies promoting in-house ND research.** Universities should (a) adopt a classification system defining and prioritizing neglected diseases⁵; (b) support existing researchers engaged in ND work; (c) recruit talented ND researchers by establishing proper incentives and marketing their ND research programs; and (d) formalize annual review practices aimed at identifying new or currently shelved technologies with promising potential for application to ND end product development.
2. **Engage with nontraditional partners to create new opportunities for ND drug development.** Universities should actively seek out nontraditional partners (e.g., public-private partnerships, grantmaking organizations, nonprofits, and developing-world companies or research institutions) to facilitate development of technologies applicable to neglected diseases. Example interactions include: patent donation, dual-market licensing, and straightforward exclusive/non-exclusive licensing. In order to access novel funding sources for neglected diseases, universities should remove any barriers, such as intellectual property restrictions, to accepting research grants from nontraditional funders.
3. **Carve out an ND research exemption for any patents held or licenses executed.** Licensing terms should allow other non-profit institutions to conduct research for neglected diseases using the university's patented innovation.⁶ Similarly, for any out-licensed technologies, universities should retain the right to non-exclusively license use of its intellectual property for neglected disease research and for distribution of any resulting products in developing countries.