Innovation and Intellectual Property for Health and Diseases of Poverty

A Research Perspective

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Overview of Presentation

- Public health issues underlying need for innovation

- WHO 'historical' engagement in R&D linking innovation and IP, often through public private partnership
  - TDR (tropical diseases), HRP (human reproductive health), IVR (vaccines)

- Experiences and Perspectives
  - IP and related negotiations to secure appropriate R&D and affordable product access
  - Capability strengthening to enhance innovation and its exploitation, especially in developing countries
A vicious cycle

DISEASE

POVERTY
Leading causes of mortality, 2000

Total = 53.9 million

Premature mortality
(worldwide, 0–44 years)

- Infectious: 48%
- Non-communicable: 19%
- Injuries: 10%
- Maternal: 3%
- Perinatal: 2%
- Nutritional: 18%

Total premature mortality (worldwide, 0–44 years) = 53.9 million
Leading infectious causes of mortality, 2000 estimates

Deaths (millions)

- ARI: 3.5
- AIDS: 2.3
- Diarrhoea: 2.2
- TB: 1.5
- Malaria: 1.1
- Measles: 0.9

< 5 years old: Yellow
> 5 years old: Red
Many Other Significant Diseases

- Lymphatic filariasis
- Intestinal nematodes
- Leishmaniasis
- Schistosomiasis
- African Tryps.
- Onchocerciasis
- Dengue
- Chagas disease
- Leprosy

Million DALYs
African Trypanosomiasis
The classic disease of poverty
100% fatal unless treated

Currently available drugs
- Suramin 1920 Early stage only / Toxicity / Injectable
- Pentamidine 1950 Early stage only / Toxicity / Injectable
- Melarsoprol 1949 Toxicity / Resistance developing
- Eflornithine 1990 Cost / Toxicity / Tb gambiense only / Infusion
Infected and Affected

Patient as worker, provider, employee, employer

Carer as worker, provider, employee, employer

Big Picture Made up from numerous individual tragedies!
HIV/AIDS impacting on all other diseases and associated populations

- Western Europe 550,000
- North Africa & Middle East 500,000
- Sub-Saharan Africa 28.5 million
- North America 950,000
- Caribbean 420,000
- Latin America 1.5 million
- East Asia & Pacific 1 million
- South & South-East Asia 5.6 million
- Australia & New Zealand 15,000
- Eastern Europe & Central Asia 1 million
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Two main imperatives

- Work to ensure access by those in need to tools that are available

- Work to ensure that improved and new tools discovered, developed and made available to those in need
Factors Influencing Innovation and New Tool Development

Percentage Sales of Pharmaceuticals (by value)

- Low Income Countries
- Middle Income Countries
- High Income Countries

Source: UNIDO and Commodity Trade Statistics, ITSB, UN Statistics Division, NY

Public Sector
Reduction of Cost and Risk

Private Sector
Preferential Pricing

10 to 20 YEARS
100’s of millions of dollars

Biology/genomics
Target identification
Validation
Entry lead
Optimized candidate drug
Entry into humans
Registered drug

Launch Patent Expiry
WHO engagement in R&D - some concrete results

- TDR
  - UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases

- HRP
  - UNDP/UNFPA/World Bank/WHO Special Programme of Research, Development and Research Training in Human Reproduction

- IVR
  - Initiative for Vaccine Research

- Other activities
Research Strategy: Basic research to implementation

- Solutions for public health problems
- From Bench to Community
- Focus determined by scientific opportunity and control needs
## New Drugs for Parasitic Control - TDR

<table>
<thead>
<tr>
<th>Drug</th>
<th>Reg</th>
<th>Indication</th>
<th>Partners</th>
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<tbody>
<tr>
<td>Praziquantel</td>
<td>1980</td>
<td>Schistosomiasis</td>
<td>Bayer</td>
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<tr>
<td>Mefloquine</td>
<td>1984</td>
<td>Malaria</td>
<td>Hoffman La Roche, WRAIR</td>
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<td>Ivermectin</td>
<td>1987</td>
<td>Onchocerciasis</td>
<td>Merck</td>
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<tr>
<td>Halofantrine</td>
<td>1988</td>
<td>Malaria</td>
<td>Smith Kline Beecham, WRAIR</td>
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<tr>
<td>Eflornithine</td>
<td>1991</td>
<td>African Trypanosomiasis</td>
<td>Marion Merrel Dow</td>
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<tr>
<td>Liposomal amphotericin B</td>
<td>1994</td>
<td>Leishmaniasis (Kala azar)</td>
<td>NeXstar</td>
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<td>Artemether</td>
<td>1997</td>
<td>Malaria</td>
<td>Rhone Poulenc Rorer, Kunmig</td>
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<td>Artemether-lumefantrine</td>
<td>1999</td>
<td>Malaria</td>
<td>Novartis</td>
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<tr>
<td>Artemotil (beta-arteether)</td>
<td>2000</td>
<td>Malaria</td>
<td>Artecef, WRAIR, Dutch Min. Dev.</td>
</tr>
<tr>
<td>Miltefosine</td>
<td>2002</td>
<td>Leishmaniasis (Kala azar)</td>
<td>Zentaris, Indian CMR</td>
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<tr>
<td>Chlorproguanil-dapsone</td>
<td>2003</td>
<td>Malaria</td>
<td>Glaxo Smith Kline, DFID</td>
</tr>
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</table>
New organisations

- TDR - incubated initiatives
  - Global Forum for Health Research
  - Medicines for Malaria Venture
  - FIND

- TDR - partnered initiatives
  - THE GLOBAL ALLIANCE FOR TB Drug Development
  - DNDi
### Reproductive Health Tools - HRP

#### New drugs / applications

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<td>Mesigyna</td>
<td>1992</td>
<td>Fertility regulation</td>
<td>Schering</td>
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<tr>
<td>Cyclofem</td>
<td>1993</td>
<td>Fertility regulation</td>
<td>Aplicaciones Farmaceuticas, P.T.Tunggal, Pfizer</td>
</tr>
<tr>
<td>Norlevo</td>
<td>1999</td>
<td>Fertility regulation</td>
<td>HRA Pharma</td>
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<tr>
<td>Postinor-2</td>
<td>1999</td>
<td>Fertility regulation</td>
<td>Gedeon Richter / Schering</td>
</tr>
<tr>
<td>Mifepristone</td>
<td>1988</td>
<td>Medical abortion</td>
<td>Roussel Uclaf / Exelgyn</td>
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Development of New Vaccines - IVR

- Facilitation of Late stage development of advanced vaccine candidates with emphasis on Africa
  - HPV (GSK, Merck), Rotavirus (GSK, Merck), Pneumococcus (GSK)
- Discovery and Development
  - Meningitis group A for Africa (MVP)
  - HIV, malaria, TB, Dengue, Japanese Encephalitis, Leishmaniasis etc.
TDR - a 2-fold Mission

- To undertake research, development and evaluation of new and improved tools to fight major tropical diseases

- To strengthen research capabilities in countries where these diseases are endemic
Experiences and Perspectives to facilitate discussion

How to generate *affordable* products for diseases primarily afflicting poor populations where there is no market incentive / no scientific opportunity for investment
- Product development partnerships (core IP already exists)
- Innovation / discovery partnerships (core IP still to be created)

How to develop capacity for creation and utilisation of innovation, especially in developing countries
- Technology transfer
- Utilisation / protection of indigenous knowledge
- Stimulating and capturing innovation in developing countries

Reward systems to supplement existing practices?
IPR throughout the R&D process

Potential value → COSTS/RISKS → Real value
**IPR as a key issue**

- **Knowledge generation**
  - Knowledge can arise from many sources / places, it may or may not be patent protected

- **Development of knowledge into products**
  - Knowledge must be managed for translation into products. Inventors may need to transfer the knowledge to other institutions that can generate effective products

- **Compensation**
  - The generation of tools / products must balance both the needs for rational and equitable use driven by public health goals without neglecting the needs of the “owner and / or developer”
Experiences in Product Development

- Majority of new products for diseases of poverty over last 25 years have resulted from adapting use of existing compounds / drugs for alternative disease indications
- Where a need has been demonstrated, on the whole companies have engaged in, and supported development and manufacture
- Now moving to a new situation in which require innovation to sustain development pipeline – this brings different challenges
- There are also occasional examples of products generated through public sector investment only and need for non-standard approaches
Experiences in Product Development I

- IPR exists and owner wishes to co-develop
  - Negotiate preferential pricing and sustainable production once developed (miltefosine for visceral leishmaniasis with Zentaris)
  - Occasionally may result in donation (ivermectin for onchocerciasis with Merck)

- IPR exists and owner does not want to co-develop
  - Need for license to enable a third party to develop and register (some examples under discussion)
Experiences in Product Development II

- IPR expired, but a company wishes to co-develop
  - Negotiate Preferential pricing and sustainable production once developed (Lapdap for malaria with GSK)
  - Orphan Drug Legislation may assist by provision of additional market exclusivity (Mefloquine for malaria in USA with Hoffmann-La Roche)

ISSUE – MAY REQUIRE ADDITIONAL INCENTIVES
- Especially if company small
- Especially if there is a market of sufficient size to interest further generic producers
- Why should company invest if product immediately generic and available to competitors without investing?
Experiences in Discovery

- **IP (e.g. potential drug 'in field')** yet to be generated
  - Negotiate rights in field to continue project in case partner quits
  - Negotiate commitment to affordable pricing
  - Negotiate some payback (royalty) on any profits outside field
  - Several examples now exist (TDR, MMV, GATB, IAVI, others.....)

**ISSUES**
- Companies often prepared to give rights 'in the field', but wary of allowing reach into core technology for use 'outside the field'
- Universities often 'overvalue' their technology
- May sometimes delay 'hard' negotiation and just agree to move to next step along the discovery / development pathway
Issue of accessing compounds for 'testing' for drug discovery

- TDR has many confidentiality agreements with companies to enable testing of compounds, with agreement to further negotiate if tests justify further exploration

ISSUE

- If we proceed, companies are providing their 'secret' compound for use in field and thus making 'public' compound's structure
  - This is a 'risk' on their part as if such a compound later shown to be active for another indication, their ability to protect it is limited
Experiences of Public Sector IPR

- WHO / HRP development with partners of 'cyclofem', an injectable contraceptive
  - Creation of 'Concept Foundation' to manage licensing to local companies and to ensure coverage, quality and price
Question

- Are there ways of consolidating best practice and further 'facilitating' institutional access to information, tools and technologies of innovative value 'in the field' of diseases of poverty, whilst protecting the legitimate rights and commercial interests of IP owners (e.g. companies) 'outside this field'?
Capacity for Innovation (in Developing Countries)

- Requires the promotion of science and research as being of value to health (accepted in North – e.g. NIH, EC, national agencies)
- Requires national science policies, including for health research
- Requires promotion of concept of 'translational research' from academic research to 'use-inspired' research
- Requires culture of risk – taking within public sector
- For technology gap to be narrowed, require stepwise intro. of 'appropriate' IP systems in countries / regions
  - Encourage developing country scientists to appropriately exploit local knowledge, both traditional and new
- Requires policy balance between 'innovation' and 'access'
Examples of Capacity Building Activities

- Working with generic companies to develop capacity to undertake late stage R&D
- Working with DC scientists to take forward technologies into devt. with local companies
  - Malaria vaccines (Shanghai, Delhi)
  - Leishmania diagnostics, Delhi
- Special focus on Natural products for drugs and insecticides
  - Ensure best practices in line with IP and biodiversity conventions etc
Summary from R&D Perspective

- Negotiating product R&D partnerships and/or manufacture with industry broader than IP issue alone
- Existing IP mechanisms can be made to work, but additional 'supporting' elements to facilitate 'in field' access to IP and to limit risks to IP holders may be of value
- Promote research capacity and utilisation, including in Developing Countries, to bring about dynamism that generates innovation
- Action needed at country, regional and international levels
Other related issues

- Balance of policy for innovation and access
- Balance and type of public and private sector investment
  - Political commitment
  - Public vs. Private vs. Public-Private
  - Cross-cultural communication needed
- Balance of 'push' and 'pull' mechanisms for R&D
- Innovation / technology divide

Whatever policies / advice generated it needs to be reducible to practice
Innovative Essential Products

R&D

Access

Tomorrow’s Public Health

5 April, 2004

CIPIH Meeting