Opportunities & Challenges in the Landscape of R&D for NTDs

South Centre, 31 March 2014

Dr Bernard Pécoul, Executive Director
Burden of Neglected Tropical Diseases

This map displays countries endemic for each of these diseases based on 2009-2010 data and international borders. (from: www.unitingtocombatntds.org)

Buruli Ulcer
Chagas disease (American trypanosomiasis)
Cysticercosis
Dengue/Severe dengue
Dracunculiasis (guinea-worm disease)
Echinococcosis
Fascioliasis
Human African trypanosomiasis
Leishmaniasis
Leprosy
Lymphatic filariasis
Onchocerciasis
Rabies
Schistosomiasis
Soil transmitted helminthiasis
Trachoma
Yaws

Number of NTDS Endemic per Country
1  2  3  4  5  6  7+
Neglected Diseases: Primarily Affect Developing Countries & Lie Outside the World Market

*Source: IMS Health
A Decade Ago, Pipeline Virtually Empty for Neglected Diseases

Health R&D (1975 – 1999)

- 1,393 total products approved
- 16 new drugs for neglected diseases (1.1%)

A Fatal Imbalance

From 1975-1999:

- 16 of 1,393 new products for neglected tropical diseases + malaria and TB (1.1%) despite these diseases representing 12% of global disease burden

- Approx. 10% of R&D dedicated to illnesses that affect 90% of global disease burden ('10/90 gap')

Source: Fatal Imbalance: The Crisis in Research and Development for Neglected Diseases, MSF, 2001
Fatal Imbalance Remains Despite Progress Over A Decade

- 3.8% of new products for neglected diseases (reformulations, combinations)
- 1.2% of NCEs for neglected diseases
- Only 1.4% clinical trials (of nearly 150,000 trials) focus on neglected diseases
- Only 1% of global health investment for neglected diseases*

756 products developed (excluding vaccines) (2000-2011)

NCEs: 395
Other products: 332
Other diseases: 4


*Source: 'Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory?' Rottingen et al. Lancet, May 2013
DNDi Focuses on Patient Needs

*Beginning With The End In Mind*

Definition of Target Product Profiles with experts and practitioners from endemic countries, researchers, clinicians, control programmes, patients associations, WHO, etc.

**TPP Criteria**
- Indications
- Population
- Clinical Efficacy
- Safety and Tolerability
- Stability
- Route of Administration
- Dosing Frequency
- Cost
### DNDi Portfolio: A Mix of Existing Drugs & NCEs

6 new treatments available and 12 new chemical entities in the pipeline

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- **HAT**
  - SCYX2035811
  - SCYX1608210
  - SCYX-7158
  - NECT: Nifurtimox-Eflornithine Combination Therapy

- **Leishmaniasis**
  - Nitroimidazole backup
  - VL-2098
  - Fexinidazole
  - Anfoleish (CL)
  - New VL treatments for Bangladesh
  - New VL treatments for Latin America
  - New VL treatments for Africa
  - SSG&PM: Sodium Stibogluconate & Paromomycin Combination Therapy for VL in Africa

- **Chagas**
  - Nitroimidazole
  - Biomarkers
  - Fexinidazole
  - New Benz Regimens
  - New Combos
  - Benznidazole Paediatric Dosage Form

- **Filaria**
  - Emodepside

- **Paediatric HIV**
  - Two ‘4-in-1’ LPV/r-based Fixed-Dose Combinations
  - RTV Superbooster for HIV/TB co-infection

- **Malaria**
  - ASAQ FDC: Artesunate-Amodiaquine Fixed-Dose Combination
  - ASMQ FDC: Artesunate-Mefloquine Fixed-Dose Combination

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Jan. 2014

★ New Chemical Entity (NCE); Fexinidazole (for HAT, VL and Chagas Disease) = 1 NCE
6 New Treatments Developed Since 2007

- **ASAQ** (Fixed-dose combination of artesunate + amodiaquine) 2007
- **ASMQ** (Fixed-dose combination of artesunate + mefloquine) 2008
- **NECT** (Nifurtimox-eflornithine combination therapy) 2009
- **SSG&PM** (Sodium stibogluconate & paromomycin combination therapy) 2010
- **NEW VL TREATMENTS IN ASIA** (SD AmBisome® / PM+M / A®+M /) 2011
- **Benznidazole** 12.5 mg Pediatric dosage form of benznidazole 2011

- Easy to Use
- Affordable
- Field-Adapted
- Non-Patented
But for Neglected Patients, 10 Years Later
Reality Remains the Same…

- Poorest of the poor
- Living in remote areas
- Socioeconomic burden on family and community
- Marginalized & voiceless patients
Neglected Diseases: Treatment Limitations 10 Years Ago

We Need Safe, Effective, Easy-to-Use Drugs

- Ineffective (resistance)
- Toxic
- Expensive
- Painful when delivered
- Difficult to use
- Not registered in endemic regions
- Restricted by patents

Melarsoprol  Eflornithine
Main Challenges for Sustainable R&D for Neglected Patients

- IP & Open Innovation Platforms
- Overcoming Regulatory Barriers
- Sustainable Financing & New Incentives for R&D
Towards sustainability – DNDi experience

- *Lesson 1:* Strong involvement of endemic country in R&D coordination
- *Lesson 2:* Increased and sustainable financing of R&D for developing countries
- *Lesson 3:* Open knowledge innovation, equitable access and affordability
- *Lesson 4:* Innovative regulatory pathways to expedite research and access
Endemic countries represented in DNDi
Board of Directors

Founding Partners

- Indian Council for Medical Research (ICMR)
- Kenya Medical Research Institute (KEMRI)
- Malaysian MOH
- Oswaldo Cruz Foundation, Brazil
- Médecins Sans Frontières (MSF)
- Institut Pasteur France
- TDR (permanent observer)
Involving endemic countries at all stages of R&D

Major Role of Regional Disease Platforms:

- Defining patients’ needs and target product profile (TPP)
- Strengthening local capacities
- Conducting clinical trials (Phase II/III studies)
- Facilitating registration
- Accelerating implementation of new treatments (Phase IV & pharmacovigilance studies)
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Global R&D Funding for Neglected Diseases

Neglected Diseases
$3.045 billion (US)

Kinetoplastids
$131.7 million (US)

=> 4.3% of the total!


Data 2011

*LMIC= Low- and Middle-Income Countries
**HIC= High-Income Countries
Cost of R&D for DNDi

- €10-40* Million per improved treatment (new formulation, combination of therapeutic switch of existing compound)

- €100-150* Million per new chemical entity (NCE)

⇒ €400 Million will be needed (total, by 2018)

* does not include manufacturing expenditures, specific contributions from partners, in-kind contributions, nor attrition rate.
Case Studies Regarding Impact on NTDs

Research
- Screen
- Hit to Lead
- Lead Opt

Translation
- Pre-clinical
- Phase I
- Phase IIa / PoC

Development
- Phase IIb/III
- Registn

Implementation

Outcomes
- ASAQ FDC for malaria
  - €12m
- NECT for HAT
  - €7m
- NCE for HAT SCYX-7158
  - €20m

Impact
- €38m

Support to WHO elimination Roadmap by 2020

280m treatments delivered since 2007

96% in DRC stage 2
Towards sustainability – DNDi experience

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Open knowledge innovation & Access

Need to support open innovation models to:

- Boost innovation for developing countries health needs
- Reduce R&D costs
- Ensure equitable and affordable access
- Enable technology transfer and local production
- Delink R&D costs from product price
Access to compounds, know-how and knowledge
Increase access to innovation
Ensure equitable access to all patients & affordable treatment

=> Medicines Patent Pool, WIPO Re:Search, open & equitable licensing....
Delinking R&D costs from product price

- Target price in ‘target product profile’ (TPP)
- Contractual commitment of manufacturer to make final product available at cost, plus a minimal margin, in all endemic countries
- Non-exclusivity enabling technology transfer, local production & potential competition
Delinking R&D costs from product price
Example of ASAQ

- Registered in 2007, prequalified by WHO in 2008
- Non patented product
- Registered in 30 sub-Saharan African countries, in India, Bangladesh and Colombia
- Only FDC with a 3 year shelf life
- Ambitious risk management plan (Pharmacovigilance) with MMV and Sanofi
- Transfer of technology to Zenufa (Tanzania)

Source: Sanofi

ASAQ Treatments distributed in million by 2013

Source: Sanofi
Towards sustainability – DNDi experience

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Overcoming Regulatory Barriers

- New Chemical Entities (NCEs): now being developed to respond to specific needs in endemic countries
- Need to strengthen regulatory agencies in endemic regions (regional collaboration)
- Regulatory assessment of new treatments through collaboration of endemic countries, WHO and stringent regulatory agencies
Global Framework for R&D for Neglected Diseases

- Coordination of efforts
- Leadership from endemic countries
- Central role of WHO
- WHA Resolution
Ongoing World Health Organization (WHO) member state-driven process to ‘take forward action in relation to monitoring, coordination and financing for health R&D’ : World Health Assembly (WHA) resolution 66.22, follow-up of the CEWG report.

Demonstration projects selection in Dec. 2013 by a panel of international experts for final decision by WHO Member States; final selection 10 March 2014 (from 22 to 8 to 4)

Next steps: Implementation; Report to the WHO on initial outcomes in 2016

To demonstrate that Health R&D can be foster through a) new mechanisms of coordination, b) new incentives for R&D (open source and IP management), c) new innovative sustainable financing mechanisms (pool funding)
Visceral Leishmaniasis Demonstration Project - WHO

- **DNDi VL Global Research & Access Initiative**, selected by EMRO, AFRO and initially supported by Sudan, France, Switzerland, Spain

- Guiding principles/CEWG: Sharing knowledge and open innovation, Sustainable funding; Exploring innovative incentives mechanisms; Equitable access; Coordination through a collaborative approach.

- 5-year project; Budget: 35 M €

- Research, clinical trials and access in 4 continents: cross-regional operationnal activities through collaborative coordination

- Multiples partners: MoH, Research Institutes, WHO, pharmaceutical partners etc.

- Political and financial involvement of various countries (endemic countries, traditional and new donor countries); Pool funding
Next steps: towards implementation

WHO process: a catalyzer to gather partners and mobilize resources

Ensure on-going political and funding support key MSs from all regions: AFRO, SEARO, EMRO, EURO, PAHO, WPRO

Coordination and partnerships with partners for the implementation: LEAP, KEMRI, OSDD, pharma, Academics, MoHs, etc.

WHO Stakeholders’ meeting in Geneva (7 May)
Report to the WHA (2016) on mid-term outcomes
Thank You!