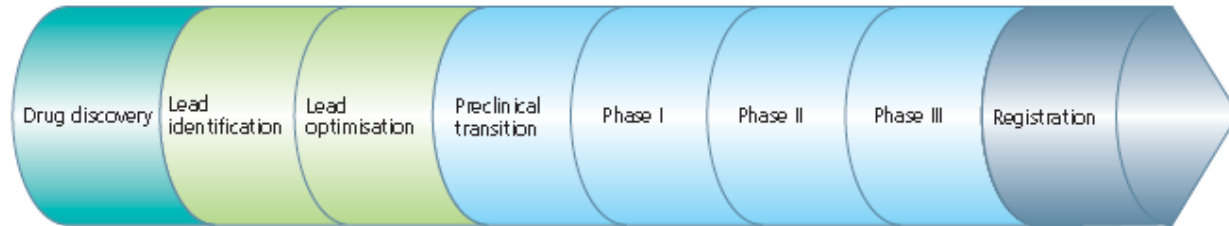


Multinational S&T Cooperation to Address Global Health Challenges

Dr Mary Moran
The George Institute for Global Health
OECD 25 March 2009

Global health S&T

Figure 1. The drug development pipeline ¹



Basic research

Applied research
(Product development)


Product dev't for global diseases

- Global diseases (HTn, diabetes, CVS)
 - Competitive, commercial R&D
- Limited scope for multinational cooperation
 - Pre-competitive research
 - Alignment of regulatory standards (ICH)
 - Private collaborations (North-South voluntary licencing/ joint ventures)

Transition product dev't

- DC-adaptations of global products
 - Generics
 - Novel fixed-dose combinations using generics (polypill ...)
 - Novel adaptations (heat-stable insulin/ non cold-chain vaccines)
- Downsized competitive, commercial model
- Some scope for multinational cooperation
 - Regulatory (WHO prequal; SADC regional harmonisation)
 - Private collaborations (South-South joint ventures e.g. Cipla India/Ugandan firm production plant)

Neglected disease product dev't

- Low-value IP  Much more non-competitive, non-commercial product development
- Much greater scope for multinational collaboration and cooperation
- Focus of remainder of presentation

Policy/ agenda coordination

Areas of coordination

- Priority setting
- Common product profiles (WHO-TDR/ biotech peak body BVGH/ PDPs/ pneumo vaccine AMC)
- Aligning standards (R&D, regulatory)
- R&D coordination (e.g. WHO/TDR – ANDI)

.... with varying degrees of success

Priority setting

Neglected Diseases	As defined by						
	<i>PLoS</i>	<i>WHO</i>			<i>Hotez 2007</i>	<i>WHO TDR</i>	<i>WHO IVR</i>
Leprosy	X	X			X	X	
Buruli ulcer	X	X			X		
Dengue fever		X				X	X



Dev't of shared standards

POLICY

Initiative on Optimising Malaria Vaccine
Lab Assays Evaluation (OPTIMALVAC)

Proposal for an Assay Harmonization
and Standardisation Initiative
WHO/IVR, EMVI and MVI

European Network for Harmonisation of
Malaria Vaccine Development (EURHAVAC)
Funded by EC FP6

T-cell assay meeting
Funded by MVI

Convened by WHO in November 2004, this group has addressed issues relating to assay standardisation, and recommended formation of an assay working group, the Malaria Vaccine Lab Assays Working group (MVLAW*)

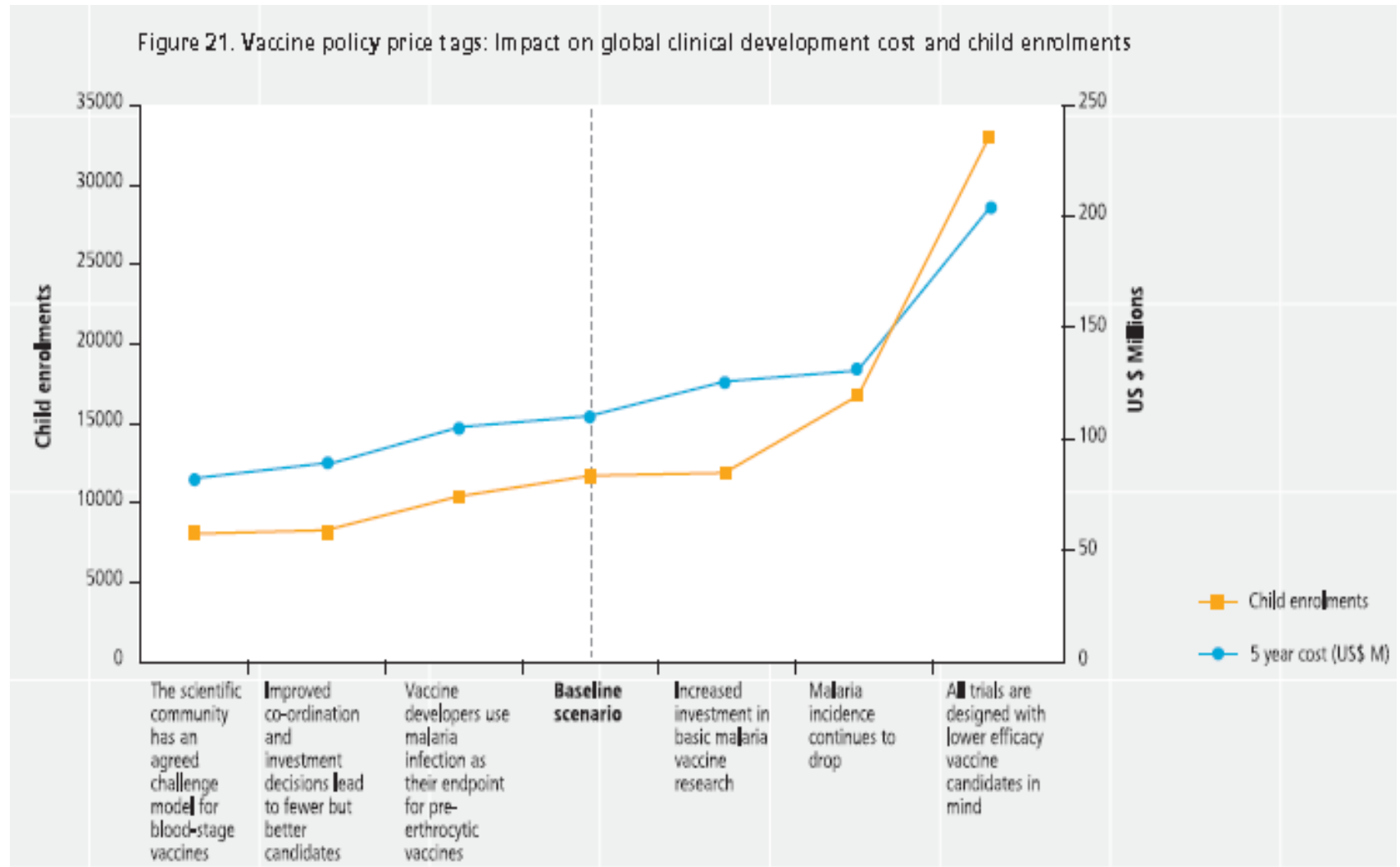
This group follows on from the proposed (but as yet unfunded) MVLAW group, which planned to cover humoral assay standardisation (e.g. ELISAs), functional assay standardisation (e.g. GIA and ADCI), and cell-mediated inhibition assays

This EMVI-led network aims to develop, optimise and standardise a range of reliable assays to be used in early pre-clinical, and clinical studies

To discuss a joint approach to T-cell assay development. Associated with the MVW Conference in London in September 2007

Costs of poor coordination

Figure 21. Vaccine policy price tags: Impact on global clinical development cost and child enrolments



**Who are the actors in multinational
neglected disease R&D?**

Variability across NDs

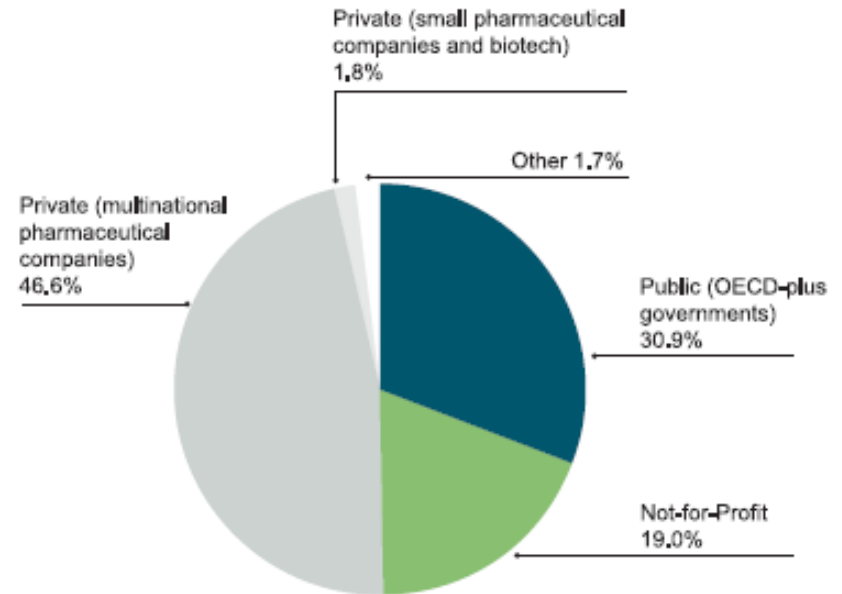
- Collaborative > competitive
- But depends on:
 - Disease
 - Product type (drug or vaccine)
- These 2 factors determine profit and cost i.e. feasibility for solo private activity Vs need for collaborative R&D

More commercial NDs

In diseases with commercial overlap, private firms play a bigger role:

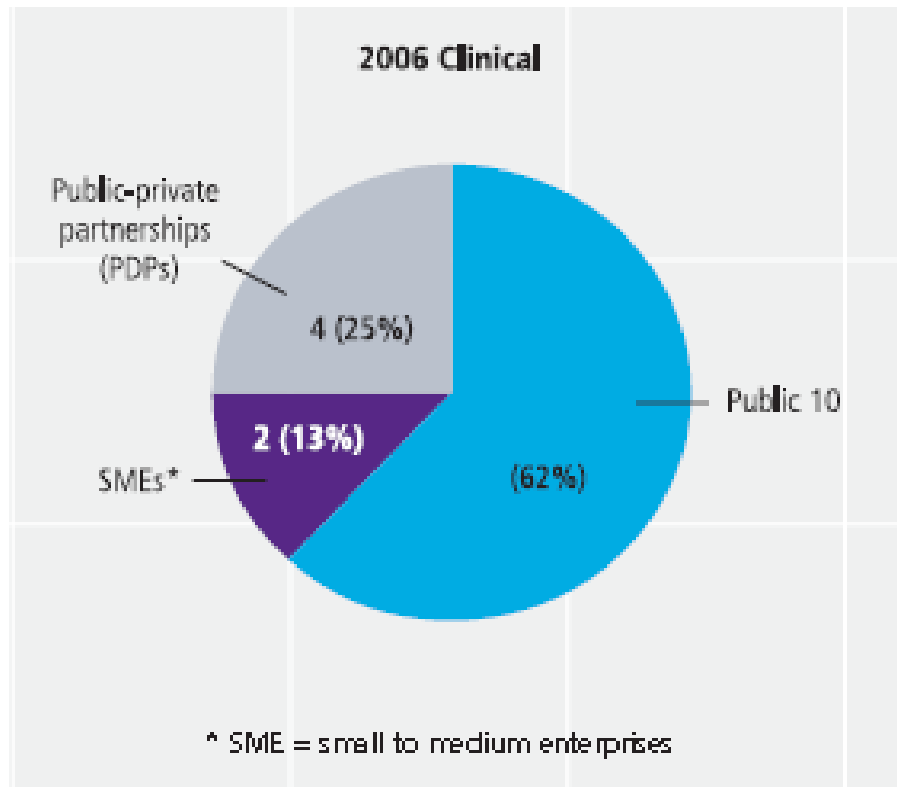
- Pneumonia / meningitis (48.4% of investment)
- Dengue (23.7%)
- Diarrhoeal illnesses (12%)

Bacterial pneumonia/meningitis



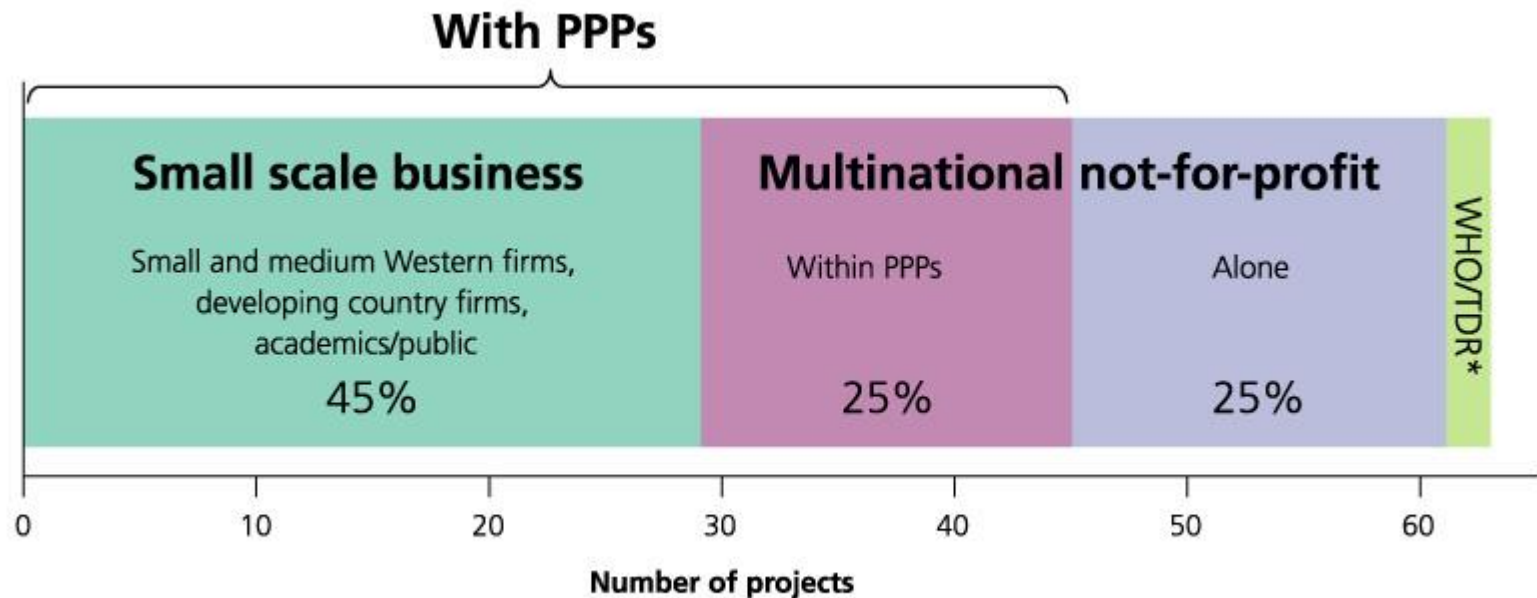
Low profit/ high cost NDs

Malaria vaccines in clinical development in 2006 by lead organisation type



Product Dev't Partnerships (PDPs)

Drug development 2004

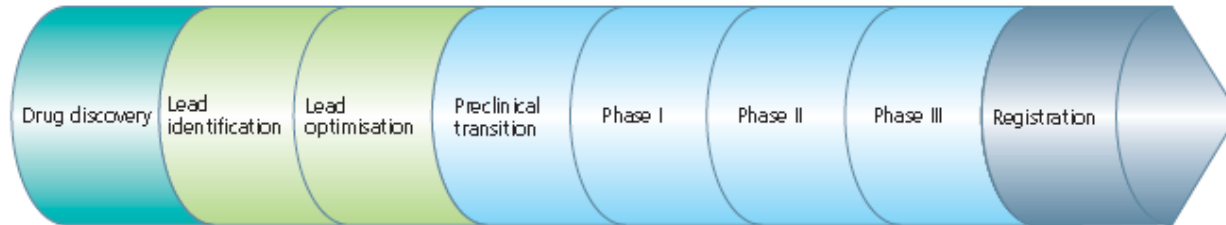


*Unable to verify details for three WHO/TDR projects.

PDP model

Classic collaborative multinational S&T model

Figure 1. The drug development pipeline ¹



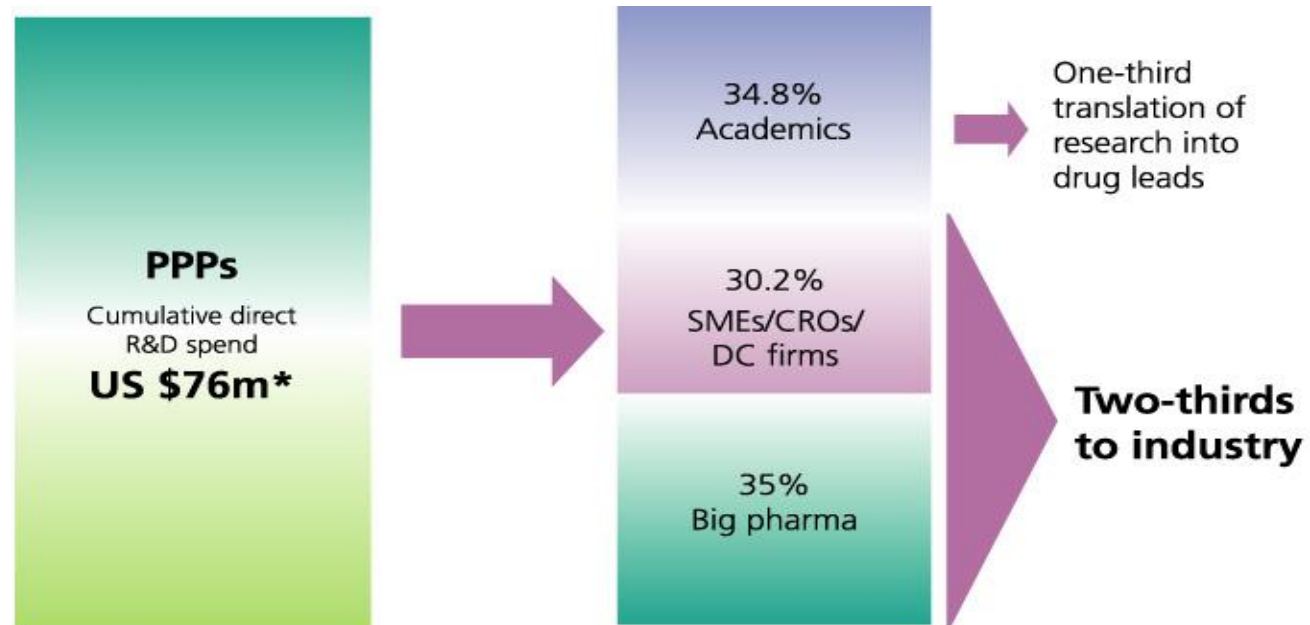
Leads from

- Companies
- Universities
- Public institutions

Dev't by:

- Public sector (trials/ trial sites)
- CROs (preclinical/ trials)
- Companies (regulatory)

Public-Private Partnerships



PDP model

- **Global portfolio**
 - Leads from multiple groups globally
 - Pool donor funding (core funding)
 - Minimise donor risk

- **Share IP and knowledge b/w PDPs**
 - Compounds (malaria/ sleeping sickness)
 - Medicinal chemistry

Funding

(G-FINDER 2008)

> \$2.5 billion invested in ND R&D in 2007

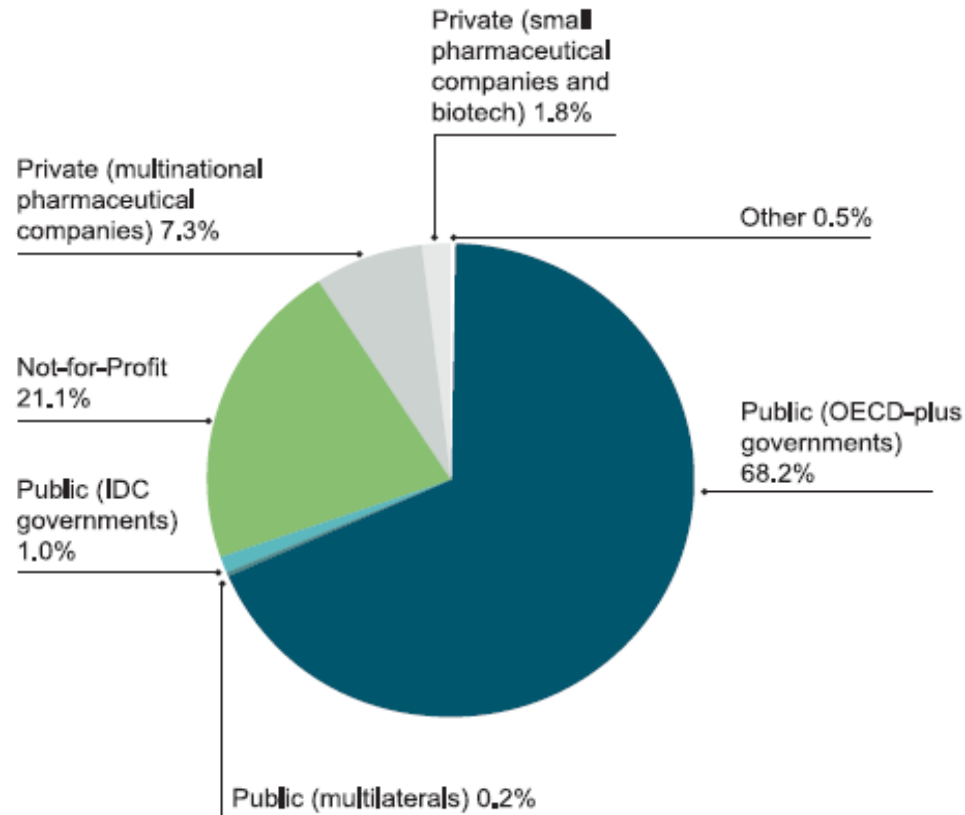
DISEASE	AMOUNT (US\$)	%
HIV/AIDS	1,083,018,193	42.3
Malaria	468,449,438	18.3
Tuberculosis	410,428,698	16.0
Kinetoplastids	125,122,839	4.9
Diarrhoeal diseases	113,889,118	4.4
Dengue	82,013,895	3.2
Helminths (Worms & Flukes)	51,591,838	2.0
Bacterial Pneumonia & Meningitis	32,517,311	1.3
Typhoid and Paratyphoid Fever	9,117,212	0.4
Leprosy	5,619,475	0.2
Buruli Ulcer	2,412,950	0.1
Trachoma	1,679,711	0.1
Rheumatic Fever	1,670,089	0.1
Core funding of a multi-disease R&D organisation	110,921,673	4.3
Platform technologies	9,997,189	0.4
Unspecified disease	51,619,120	2.0
Grand Total	2,560,068,749	100.0

R&D funding allocation

	Basic Research	Drugs	Vaccines (Preventive)	Diagnostics	Microbicides	Vaccines (Therapeutic)	Vector Control Products	Unspecified products	Total
HIV/AIDS	176.3	0.8	691.5	12.4	199.5		2.5	1,083.0	
Malaria									
<i>P. falciparum</i>	39.0	34.3	52.0	0.6		0.3	-	126.2	
<i>P. vivax</i>	2.0	0.1	1.8	0.2		-	0.3	4.4	
Other and/or unspecified malaria strains	71.9	179.7	34.6	0.8		17.4	33.4	337.9	
Diarrhoeal diseases									
Rotavirus			22.8				-	22.8	
Enterotoxigenic E.coli (ETEC)			11.9	0.2			0.2	12.3	
Cholera	11.3	0.1	6.1	-			0.4	17.9	
Shigella	1.7	-	9.4	-			3.4	14.5	
Cryptosporidium	5.3	2.6	-	-			-	7.9	
Enteroaggregative E.coli (EAggEC)			-	-			-	-	
Giardia				-			-	-	
Multiple diseases	-	10.4	16.3	7.1			4.7	38.4	

The 7:2:1 funding ratio

Total ND R&D funding by funder type



Funding organisations

RANK	FUNDER	AMOUNT (USD)	% TOTAL FUNDING
1	US National Institutes of Health	1,064,859,791	41.59%
2	Bill & Melinda Gates Foundation	452,102,715	17.66%
3	European Commission	121,366,882	4.74%
4	US Department of Defense	86,914,578	3.40%
5	United States Agency for International Development	80,600,336	3.15%
6	Wellcome Trust	59,985,371	2.34%
7	UK Medical Research Council	51,716,968	2.02%
8	UK Department for International Development	47,565,987	1.86%
9	Netherlands Ministry of Foreign Affairs	33,951,646	1.33%
10	Pasteur Institute	31,617,540	1.24%
11	Irish Aid	24,271,557	0.95%
12	Swedish International Development Agency	21,529,014	0.84%
	Sub Total	2,076,482,385	81.11%
	TOTAL R&D FUNDING	2,560,068,749	100.00%

- 12 organisations provided >80%
- 2 organisations provided ~ 60%

Public funding highly concentrated

Top 12 public funders

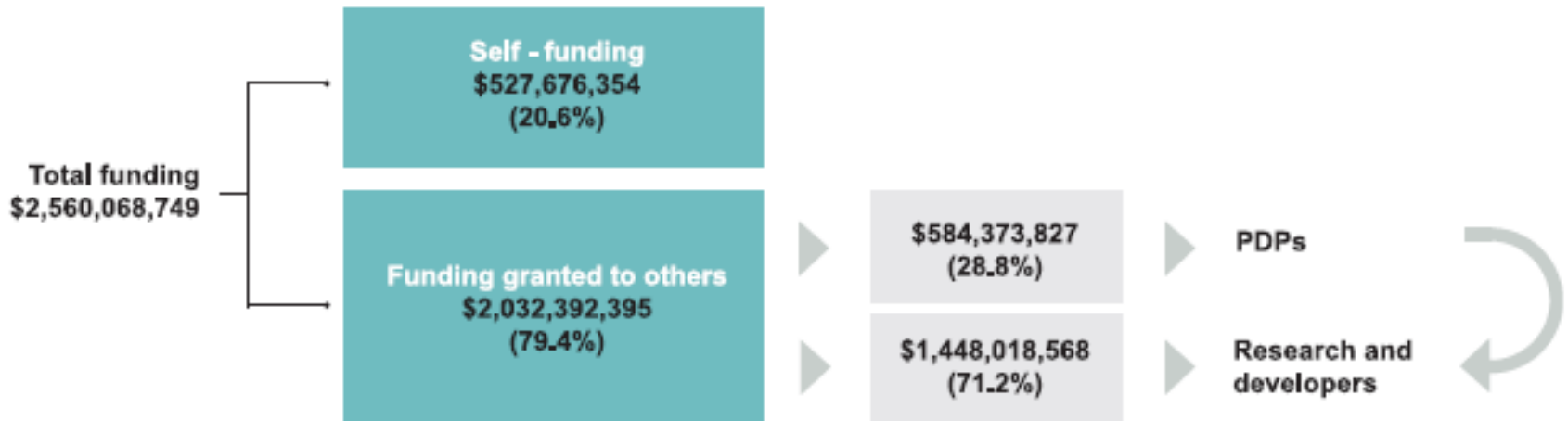
Rank	Country	Amount (\$)	%
1	United States of America	1,250,935,091	70.4
2	European Commission	121,366,882	6.8
3	United Kingdom	100,781,214	5.7
4	Netherlands	34,088,694	1.9
5	Ireland	24,271,557	1.4
6	Brazil	21,970,169	1.2
7	Sweden	21,566,527	1.2
8	Canada	19,134,610	1.1
9	Australia	18,166,780	1.0
10	Russia	16,666,666	0.9
11	Belgium	15,851,130	0.9
12	France	13,892,238	0.8
Subtotal		1,658,691,558	93.3
Total Public Funding		1,777,173,493	100

Philanthropic investment: very highly concentrated

Top philanthropic funders

FUNDER	AMOUNT (US\$)	%
Bill & Melinda Gates Foundation	452,102,715	84.0
Wellcome Trust	59,985,371	11.1
Médecins Sans Frontières	7,187,885	1.3
All other philanthropic organisations	16,970,326	3.2
Funds raised from the general public	2,064,283	0.4
Total philanthropic funding	538,310,580	100.0

Funding and PDPs



- ~ 30% of external funding
- ¼ of overall global R&D investments
- IF EXCLUDE NIH: Over half of all external public and nfp funding

Current opportunities
and
thoughts

Neglected disease product dev't

- The land of opportunity BUT
 - National sovereignty
 - EU-US divide
 - Academic independence
 - WHO's centralising role

Global coordination

- PDPs are main avenue at the moment
 - Pool funding
 - Pool candidate drugs and vaccines
 - Single set of in-house standards to rank/ progress/ terminate projects
- Large donors provide a degree of de-facto global coordination (b/w diseases; within product areas)
- Global leadership? CAN'T make people cooperate but CAN provide information to allow them to act cooperatively

Common technical standards

- Agree common technical standards
 - Agreed common assays, endpoints, markers, so can compare trial results for competing candidate products
 - Clinical trial protocols
 - Shared trial site audit templates

⇒ Allows global donors to compare like for like (a *de facto* global “portfolio”)

Regulatory

- “Pooling markets”
 - Accept scientific assessment from other regulatory authorities e.g. Singapore model
 - Reciprocal recognition (e.g. FDA-WHO prequalification)
 - Regional shared assessments (WADRAN/ SADC)
- Harmonise regulatory dossier content and format
 - Saves manufacturers having to prepare dozens of diff’t dossiers for diff’t countries
 - Allows regulators to share findings/ experience
 - ⇒ More rapid dissemination of new products
- RESEARCH REGULATORY COST/BENEFIT!

Information clearing house

Helpful for small companies, including info on:

- Drug targets (cf. BVGH)
- Desired product profiles
- R&D funding sources
- Clinical trial sites suitable for their product
- Other public services (e.g. batch manufacture/ free compound screening)

For policy-makers and funders

- Global portfolios (who's doing what)
- Global funding, so can see gaps, areas of concentration (G-FINDER)

IP approaches

- Taking advantage of low value IP
 - Open source drug discovery
 - Patent pools (starting)
 - Open compound access (PhRMA)
 - Optimise academic IP management