Globalisation of clinical drugs trials: who is benefitting and at what cost?

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Public Conference on Clinical Drug Trials, Geneva / Switzerland

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Globalisation of clinical trials

- Increasing trend to offshore drug trials in low & middle income settings (LMIC)
- Reducing trend to conduct clinical trials in high income countries (EU, USA, CH)
- Figures vary according to Drug regulatory authorities (DRAs) and units of measure

$\Rightarrow$ **At least 1/3 of international clinical trial participants are from LMIC**

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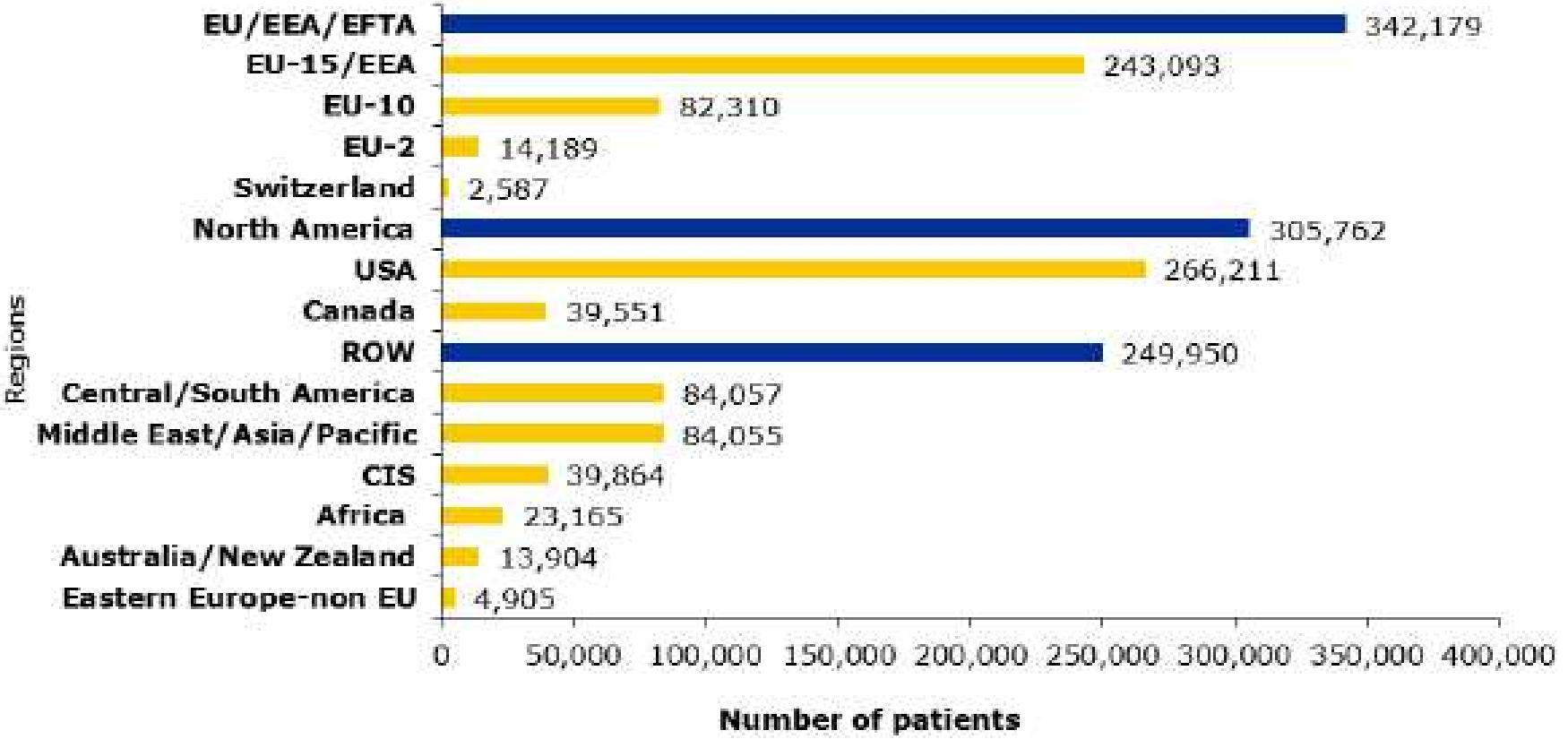
Source: European Medicines Agency (2013), Clinical trials submitted in marketing-authorisation applications to the European Medicines Agency: Overview of patient recruitment and the geographical location of investigator sites

Figure 1. Number of patients in pivotal trials submitted in MAAs to the Agency per region/sub-region during the period 2005-2011. The data are shown as three "global regions" – EU/EEA/EFTA, North America and ROW (Rest of the World) and then split into its component sub-regions.



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Number of patients in pivotal trials submitted in marketing-authorisation applications (MAAs) to the European Medicines Agency 2005-2011

- Previous chart represented an average figure (2005-2011), but data for 2011 alone show clear upward trend for LMIC & downward trend for EU
- Waiting for data of 2012 and beyond

	2010		2011		Total	
	Σ	%	Σ	%	Σ	%
EU/EEA/EFTA	**66,220**	**41.6**	**44,590**	**31.2**	**342,179**	**38.1**
EU-15/EEA	52,680	33.1	27,711	19.4	243,093	27.1
EU-10	11,358	7.1	13,449	9.4	82,310	9.2
EU-2	1,792	1.1	3,269	2.3	14,189	1.6
Switzerland	390	0.2	161	0.1	2,587	0.3
North America	**51,025**	**32.0**	**44,987**	**31.5**	**305,762**	**34.1**
Canada	6,811	4.3	5,078	3.6	39,551	4.4
USA	44,214	27.7	39,909	27.9	266,211	29.6
ROW	**42,105**	**26.4**	**53,384**	**37.3**	**249,950**	**27.8**
Africa	2,952	1.	2,298	1.6	23,165	2.6
Middle East/ Asia/Pacific	19,307	12.1	18,243	12.8	84,055	9.4
Australia/New Zealand	3,321	2.1	1,905	1.3	13,904	1.5
CIS	6,463	4.1	10,737	7.5	39,864	4.4
Eastern Europe-non EU	121	0.1	742	0.5	4,905	0.5
Central/South America	9,941	6.2	19,459	13.6	84,057	9.4
total	**159,350**	**100**	**142,961**	**100**	**897,891**	**100**

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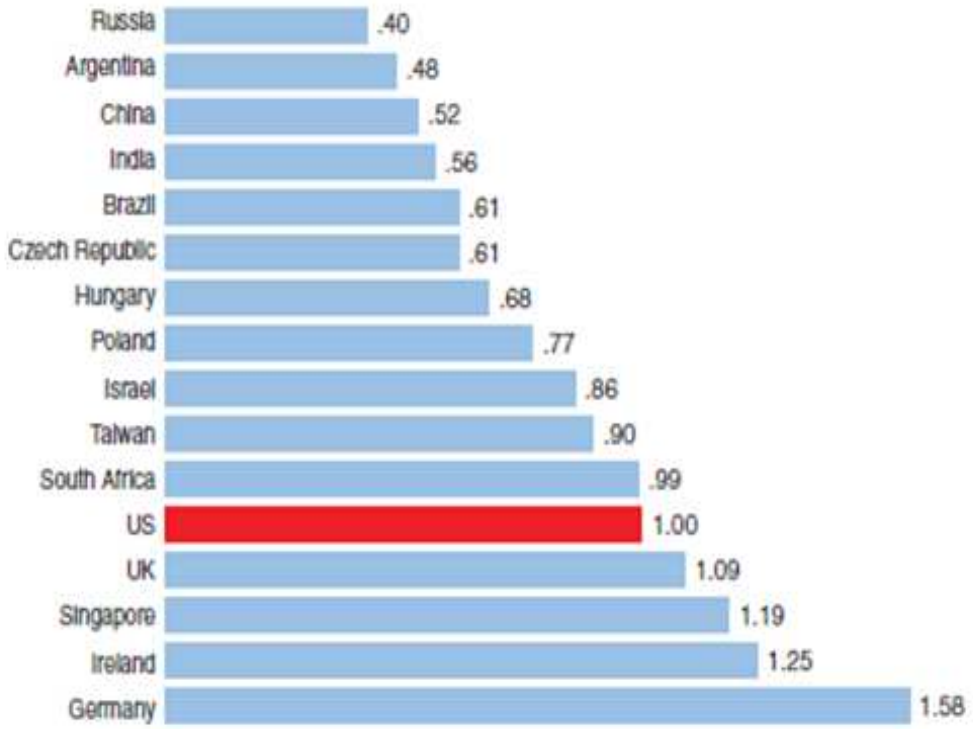
Reasons for offshoring CT



Source: SalaryExpert.com; WDI Database; Economist Intelligence Unit; CBRE Global Markets Rent 2005; A.T. Kearney analysis, Aug 2005; Clinical Trial Offshoring

Figure 5-3 Overall clinical trial costs

Reproduced with permission from Burrill & Company, "Biotech 2010 Life Science: Adapting for Success," BIO International Convention, Chicago, 4 May 2010.

+ Recruitment easier (subjects looking for access to free medicines)
+ Less Drop-out rates
+ Large pools of patients (also 'treatment-naïve')
+ Weaker regulatory environment
+ Less stringent ethical reviews
+ Local demand (trying to attract clinical trials)
+ Regulatory step

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Ethical concerns

NGO investigations, media reports & published literature have revealed **serious ethical issues related to industry-sponsored drug trials conducted in LMIC**

⇒ Relevance: meeting local health priorities?
⇒ Scientific soundness (design, placebo, standard therapy)
⇒ Issues with informed consent process
⇒ Lack of compensation in case of adverse events
⇒ Systemic oversight weaknesses & loopholes (authorization, monitoring, local ethics committees)
⇒ Limited Post-trial access to treatment

Benefits of trials in LMIC?

- Ethical guidelines deem **trials unethical and exploitative if product tested is not benefitting i.e. made available** to the population concerned
- Companies claim they do trials only in LMIC where they intend to apply for market approval
- Recent studies show that only about 40% (South Africa) to 60% (Latin America, India, Egypt) of the drugs that made it to a high-income market were effectively registered in the LMIC where tested
- Products registered in LMIC are mostly paid out-of-pocket and well above the monthly minimum wage or GNI per capita, hence unaffordable

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Unethical trials & safety issues

- Not only ethical/moral, but potentially also drug safety issues in unethical trials

- Concerning as the current trend is to shorten the duration and number of patients in trials in the context of accelerated-access schemes

Our campaign on drug trials ethics

- Field investigations on (CH) industry-sponsored drug trials in Russia, Ukraine, India, Argentina & Egypt
- Report on how Swissmedic verifies ethical (GCP) compliance of offshored trials during MA process in CH
- Dialogue with Swiss authorities – ongoing
- Intervention at Novartis' and Roche's AGMs, invitations to discuss the issue further (only Novartis followed up)
- Parliamentary initiatives, Revision of CH Medicines Law – consensus reached in March 2016, with 2 new articles on transparency (publication of results) & inspections abroad

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Transparency issues around trials

- New EU regulation requires publication of clinical study reports, strong political signal
- Jeopardised by more restrictive publication policy of EMA
- Jeopardised by the new EU directive on trade secrets
- Revised CH Medicines Law contains new article on publication of trials results (art. 67b), but still very vague and not yet operationalised

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The way forward

Regulatory authorities (High-income countries):

- ✓ Strengthen ethical control of trials used for market approval (‘no double standard’)
- ✓ Publicise entire clinical study reports (not summaries) for all these pivotal trials

Regulatory authorities (host countries):

- ✓ Establish a robust legislation system with independent control (oversight) system
- ✓ Improve transparency

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The way forward

Trial sponsors (transnational):

- ✓ Responsibility to respect human rights (UN Guiding Principles on Business & Human Rights) => identify risks, take measures to prevent & report about it
- ✓ Following the national laws is not enough, act with due diligence is necessary

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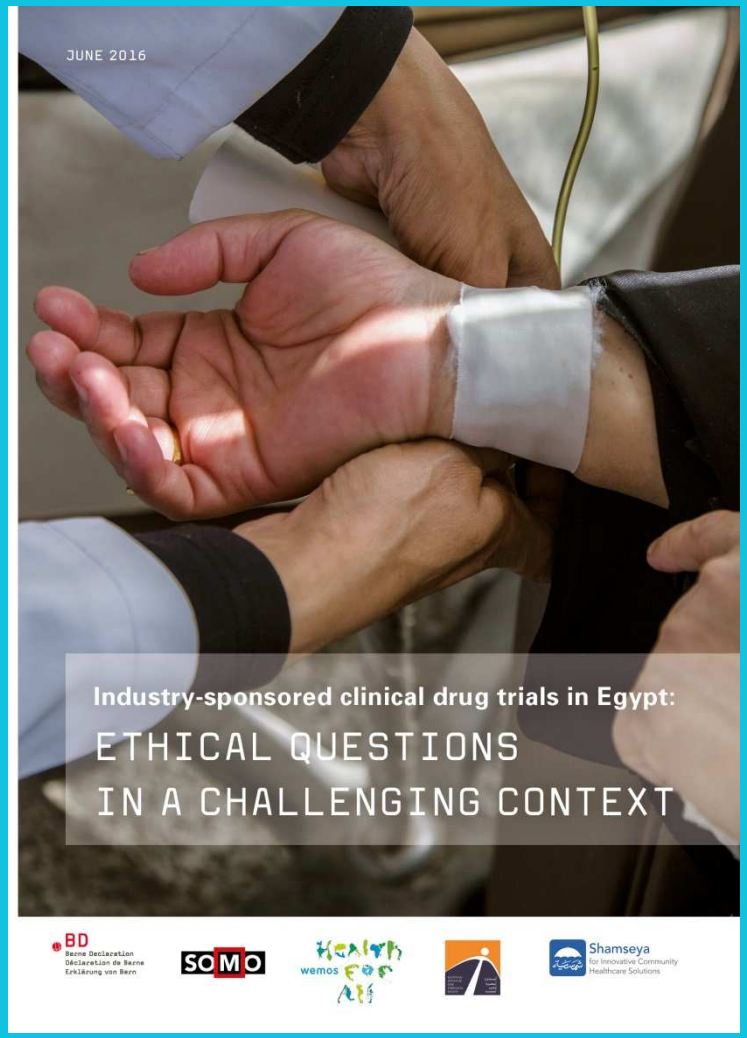

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Thank you

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