



Industry Platform



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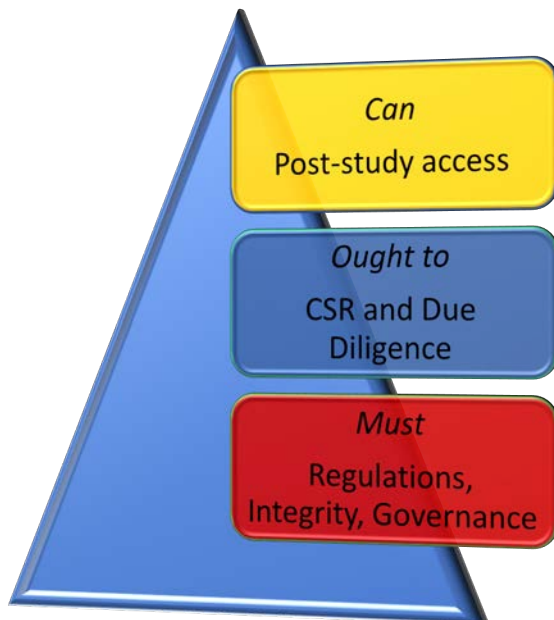
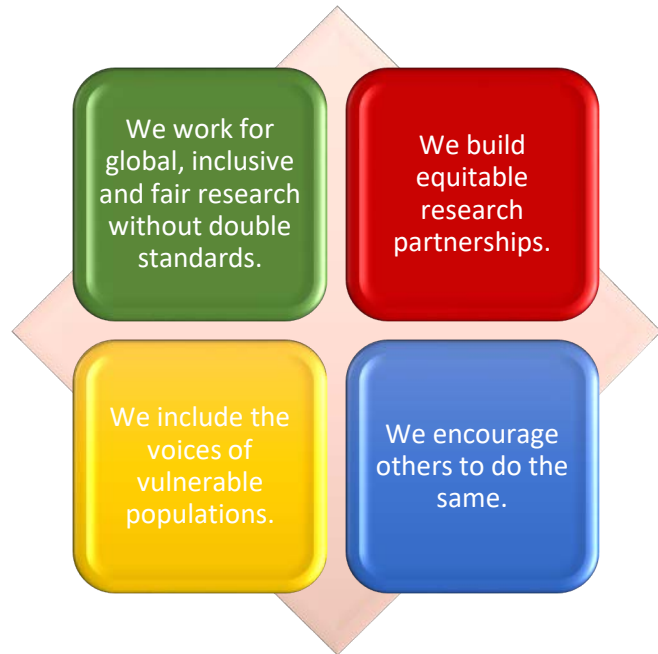
Executive Summary

The goal of the TRUST Project is to catalyse a global collaborative effort to improve adherence to high ethical standards in research around the world. The vision of the project is to:

- Work for global, inclusive and fair research without double standards,
- Build equitable research partnerships,
- Include the voices of vulnerable populations, and
- Encourage others to do the same.

Key to the fulfilment of this vision is the involvement of all relevant stakeholders including industry representatives and industry associations.

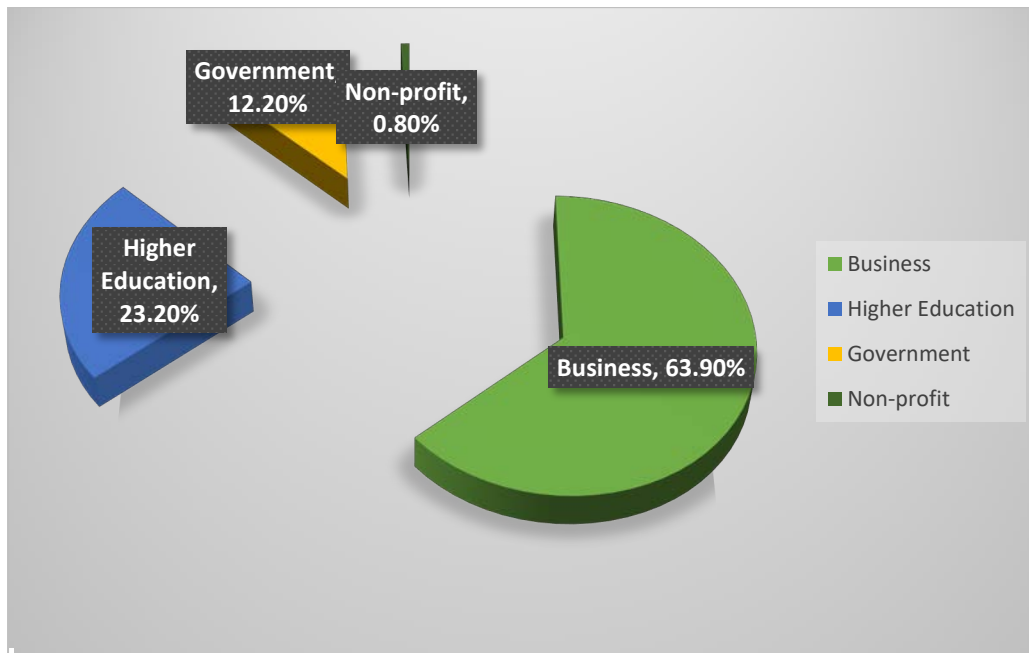
This report provides the context for the engagement of industry by the TRUST project, describes efforts at reducing exploitation in research partnerships with low and middle income countries (LMICs), and explains the two foci for TRUST lobbying: providing reasonable post-study access to successfully tested drugs for poor research participants with chronic diseases (“can”), and ex-ante due diligence (“ought to”) to identify, prevent and reduce actual and potential human rights risks in the context of LMIC clinical trials.



Introduction

In a global effort to achieve equitable research partnerships, consultation and cooperation with the business sector is indispensable. According to 2014 Eurostat data, the business sector is the largest source of Research & Development (R&D) investment in the European Union (EU). Of the four main institutional sectors - business enterprise, government, higher education and private non-profit - the business sector represents 63.9% (EUR 180.7 billion) of total R&D expenditure, followed by the higher education sector with 23.2% (EUR 65.6 billion).²

Diagram 1 - R&D expenditure by sectors of performance, EU-28 2014



Major societal challenges can only be addressed with effective research and innovation. The most ambitious societal reform program the International Community has ever approved, the *Agenda 2030 for Sustainable Development*,³ emphasizes that its implementation relies on successful research resulting in innovative technologies. Goal 9.5 reads:

Enhance scientific research, upgrade the technological capabilities of industrial sectors in all countries, in particular developing countries, including, by 2030, encouraging innovation and substantially increasing the number of research and development workers per 1 million people and public and private research and development spending.⁴



² http://ec.europa.eu/eurostat/statistics-explained/index.php/Europe_2020_indicators_-_research_and_development#How_much_is_the_EU_investing_in_R.26D.3F

³ <http://www.un.org/sustainabledevelopment/development-agenda/>

⁴ <https://sustainabledevelopment.un.org/post2015/transformingourworld>

Public acceptance of both the process and the outcomes of research and innovation cannot be taken for granted; they require a relationship of trust between multiple players. The precondition for societal trust is that research is undertaken with integrity and is based on fundamental values shared by the global community.⁵ The TRUST project can make a contribution to realize the EU ambition of a more inclusive and sustainable society using the principles of Responsible Research and Innovation (RRI).⁶

Being responsible for the highest investment in research, as noted above, industry must be considered a key stakeholder in the global implementation and dissemination of TRUST, as well as the promotion of RRI principles.⁷

For the industry engagement strategy within the TRUST project the pharmaceutical sector was chosen for the following reasons:

1. It was the only industry sector mentioned specifically in the earlier *Millennium Development Goals*. UN Millennium Goal 8, Target 4, notes that “in cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries.”⁸ The pharmaceutical sector’s importance in addressing global challenges was therefore acknowledged at the highest level of global policy making almost two decades ago.
2. The *Agenda 2030 for Sustainable Development* specifies in Goal 3, Target 3.8 the importance of achieving “universal access to safe, effective, quality and affordable essential medicines and vaccines for all.”
3. At the same time, the sector suffers from considerable mistrust amongst the general population,⁹ and especially in North-South collaborative research.
4. The pharmaceutical sector is the only sector that provides for a basic human right (access to health care) and is simultaneously supported by strong intellectual property rights systems.¹⁰
5. With the exception of the automobile industry, it is the largest single sector of R&D investment in Europe (see Diagram 2).

As the Director General of the European Federation of Pharmaceutical Industries and Associations (EFPIA), Richard Bergström, has noted:

Our industry is going through a period of unprecedented change, as well as coping with an economic crisis. In these times, it is all the more important that we demonstrate the value of our medicine to people’s lives, and the value of the industry to Europe’s economy. Also, we need to

We need to stay on course with our commitment to be more open, transparent and accountable in what we do.

Richard Bergström

⁵ <https://ec.europa.eu/programmes/horizon2020/en/h2020-section/science-and-society>

⁶ <https://ec.europa.eu/programmes/horizon2020/en/h2020-section/responsible-research-innovation>

⁷ <http://www.progressproject.eu/project-deliverables/>, see deliverables from WP4.

⁸ UN Millennium Goal 8, Target 4; available at <http://www.un.org/millenniumgoals/global.shtml>

⁹ Mark Kessel (2014) ‘Restoring the pharmaceutical industry’s reputation’, *Nature Biotechnology* 32, 983–990 (2014) doi:10.1038/nbt.3036.

¹⁰ Schroeder, Doris (2011) ‘Does the Pharmaceutical Sector have a Co-Responsibility to Secure the Human Right to Health?’, *Cambridge Quarterly of Healthcare Ethics*, Vol. 20:2, 298-308.

stay on course with our commitment to be more open, transparent and accountable in what we do.¹¹

Combining TRUST’s rationale for choosing to engage with the pharmaceutical sector with the statement of the Director General of EFPIA, one could argue that the sector faces a leadership opportunity, which TRUST hopes to support by promoting more equitable research partnerships globally.

Diagram 2 – R&D investment 2015, EU¹²



This report presents preliminary outcomes of interactions and conversations with industry representatives in the health sector, as well as conclusions regarding constraints and targets for the realisation of the TRUST model of respectful, fair and equitable research partnerships. The first section provides the context for the engagement of industry, the second section outlines what individual players are already doing to create more equitable research relationships with an emphasis on human rights, and the third and final section summarizes activities from the industry representatives in the TRUST consortium.

Pharma, Global Health and Ethical Research

As Paul Hunt, the former UN Special Rapporteur on the Right to Health has noted:

A pharmaceutical company that develops a life-saving medicine has performed a vitally important medical, public health and right-to-health function. By saving lives, reducing suffering and improving public health, it has not only enhanced the quality of life of individuals, but also contributed to the prosperity of individuals, families and communities. The company, and its employees, has made a major contribution to the realisation of the rights to life and the highest attainable standard of health.¹³

¹¹ <http://www.efpia.eu/our-work>

¹² The 2015 EU Industrial R&D Investment Scoreboard. <https://ec.europa.eu/assets/jrc/eu-scoreboard-2015>

¹³ *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Health*, Paul Hunt–Annex–Mission to GlaxoSmithKline 2009; 11, para 35; available at <http://198.170.85.29/Paul-Hunt-report-on-GSK-5-May-2009.pdf>

As indicated by Hunt, it is indisputable that the successful R&D investments of pharmaceutical companies have yielded substantial gains in life expectancy and Quality-Adjusted Life Years¹⁴ (QALYs) all over the world. This remains the single most important contribution of the pharmaceutical industry to humanity. As a result of its contributions to global health, the industry might be expected to enjoy high levels of respect for its undertakings. However, currently two major obstacles to such respect are:

- Clinical trials with conditions that violate human dignity and exploit vulnerable research populations, and
- High prices, which make access to the results of the research and innovation process unaffordable to many of those who most need it for their survival.

While there have been pharmaceutical innovation breakthroughs which are highly relevant to LMICs, e.g., for the treatment of Malaria or HIV, others, e.g., innovative medicines for the treatment of cancer, diabetes or Hepatitis C, have yielded only limited benefits for the local communities in which the research was undertaken. Due to the high prices of innovative medicines, poor people have had no or very limited access to these products. According to a World Health Organization (WHO) report:

Effective drugs exist to combat the principal components of the global burden of disease – HIV/AIDS, tuberculosis, malaria, and depression and suicide. However, ... half the world’s population is too poor to pay for many of the drugs they need from their own resources even at the lowest possible prices.¹⁵

At the same time, the pharmaceutical industry remains the most profitable industry globally (see Table 1).

Table 1 – 10 Most Profitable Industries, according to Factset¹⁶

Industry	Net Margin in 2016
Pharma: Generic	30.0%
Investment Managers	29.1%
Tobacco	27.2%
Pharma: major	25.5%
Internet Software/Services	25.0%
Biotechnology	24.6%
Savings Banks	24.0%
IT Services	23.0%
Regional Banks	23.0%
Major Banks	22.9%

¹⁴ The quality-adjusted life year (QALY) is a measure of disease burden, including both the quality and the quantity of life lived, i.e. capturing mortality and morbidity.

¹⁵ <http://apps.who.int/medicinedocs/en/d/Jh2951e/2.1.html>

¹⁶ <http://www.forbes.com/sites/liyanchen/2015/12/21/the-most-profitable-industries-in-2016/#515ee6917a8b>

The high profitability of the pharmaceutical industry is seen by many to be partly achieved through the “globalization of clinical trials”.¹⁷ One reason for relocations from the North to LMICs is the possibility to set up and run trials at much lower cost, in terms of materials, equipment, services, and staff. At the same time, the testing of experimental drugs in LMICs brings scientific gains to the pharmaceutical industry.¹⁸ LMICs have “large pools of ‘treatment-naïve’ patients, whereas in traditional research areas, the use of too much medication generates the risk of drug–drug interactions.”¹⁹ This makes LMICs highly attractive for pharmaceutical and medical research, as research participants who have had little or no previous exposure to drugs are generally regarded as more reliable for clinical testing.

When asked why India is such an attractive location for US or European trial sponsors, an Indian physician-researcher who established one of the first research ethics committees in India made the following observations (summarized in Diagram 3):

The reasons for the popularity of the developing world are the following: (a) Large population (b) Low cost (c) Legislative vacuum or infirmities (d) Ignorance about the legal and ethical issues of human trials among the public and even health care professionals and (e) Craze among the developing countries to link up with Western institutions and at any cost.²⁰

Diagram 3 – Reasons for relocating clinical trials to LMICs



As noted at the outset, the vision of TRUST is global, inclusive and fair research built upon equitable research partnerships. When undertaking clinical trials in resource-poor settings, two different fairness questions arise. These are linked to global distributive fairness, and fairness in exchange.²¹ Global distributive fairness asks the very broad question of what is owed to whom globally. For instance, Article 25 of the *Universal Declaration of Human Rights*

¹⁷ Ravinetto R. ‘Methodological and Ethical Challenges In Non-Commercial North-South Collaborative Clinical Trials’. 2015 Leuven University Press.

¹⁸ Ravinetto R. ‘Methodological and Ethical Challenges In Non-Commercial North-South Collaborative Clinical Trials’. 2015 Leuven University Press.

¹⁹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4428044/>

²⁰ Macklin R. (ed.). ‘Double standards in medical research in developing countries’ (Cambridge law, medicine and ethics). Cambridge University Press, 2004.

²¹ For a description of the difference, see Kate Chatfield, Doris Schroeder, Klaus Leisinger, Jaci van Niekerk, Ngayo Munuo, Rachel Wynberg and Paul Woodgate (2016), *Generic Risks of Exporting Non-Ethical Practices*, a report for TRUST, available: <http://trust-project.eu/deliverables-and-tools/>.

asserts that every human being “has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care”.²² In a world where people take this *Declaration* seriously, existing global as well as local resources would have to be distributed in a much fairer way to provide food, medical care and shelter to the poor. John Rawls’ “Theory of Justice” advocates such a system.²³

In the context of medical care and in response to a worldwide call for pharmaceutical enterprises to be more human rights aware and responsive, business leaders have tested a range of alternatives to redistribute the benefits of research. Most of these alternatives have focused on making medicines accessible and affordable to people in resource-poor countries. The following four main approaches can be distinguished:

1. Differential pricing and financing of essential drugs;
2. Negotiations followed by prior agreements before research is initiated;
3. International collaborative efforts and public-private partnerships;
4. Manufacturing of generic copies of patented drugs in LMICs and compulsory licensing.²⁴

However, the TRUST project cannot pursue questions of distributive fairness in its three years duration – instead it focuses on fairness in exchange.

If Indian research participants take risks and inconveniences to ensure that drugs can be marketed, then they have contributed to an enterprise from which they should benefit in return.²⁵ This is fairness in exchange. In the worst cases, research participants are exploited and could be left worse off than they were before entering the trial. An earlier TRUST report gives examples of cases of such exploitation.²⁶ For instance, patients may have been enrolled in a study by a contract research organisation represented by a general practitioner who did not inform them that they are part of a Stage IV clinical trial. Those who suffered serious side-effects would then not even know that they could have claimed compensation.²⁷ In another instance, research participants might have helped to bring a new drug to market – a drug that benefitted them considerably (for instance a new cancer drug). Yet, at the end of the trial, neither their national health system nor they as an individual can afford the drug. It may therefore be that they will die or suffer from considerable morbidity, even

The question arises: What is the moral responsibility of pharmaceutical companies vis à vis research participants after the trial is over?

²² <http://www.un.org/en/universal-declaration-human-rights/>

²³ John Rawls (1999): *A Theory of Justice* – Revised Edition, Oxford: Oxford University Press.

²⁴ For an overview of reform plans to increase access to medicines, see Doris Schroeder and Peter Singer (2008) *Intellectual Property Rights Reform Plans* - a report for Innova-P2, http://www.uclan.ac.uk/research/explore/projects/assets/cpe_innova_deliverable1_1.pdf. See also Leisinger K.M. (2012) ‘Poverty, Disease, and Medicines in Low- and Middle-Income Countries: The Roles and Responsibilities of Pharmaceutical Corporations.’ In: *Business & Professional Ethics Journal* 31:1 pp.135 – 185.

²⁵ It would be exploitative to demand of vulnerable populations in LMICs that they should contribute to the health care enterprise altruistically, to benefit the greater good.

²⁶ Schroeder D, Cook Lucas J, Fenet S, Hirsch F (eds) (2016) “*Ethics Dumping*” – *Paradigmatic Case Studies*, a report for TRUST, available: <http://trust-project.eu/deliverables-andtools/>.

²⁷ Case obtained during the TRUST case study competition. To be published in 2017.

though a drug they personally helped to bring to market could improve their health or well-being.

Exploitation of the first type (unethical behaviour in trials) should be eliminated completely in a world that tolerates no double standards in research. The “do no harm” principle reigns supreme. The moral responsibilities are clear in this case, and many international guidelines to promote non-exploitative research already exist. It is more difficult to address the second case, where a research participant will suffer if s/he is not given access to the experimental drug s/he has helped to bring to market. The question is: What is the *moral* responsibility of pharmaceutical companies vis à vis research participants after the trial is over.

Preventing exploitative research

The risks of exploitation in research are diverse and manifold. An earlier TRUST Deliverable²⁸ identified 88 risks:

- 18 risks for individuals, communities, countries, animals or the environment in the category of *fairness of exchange* (e.g. a mismatch with local research needs).
- 17 risks for individuals, communities, countries, animals or the environment in the category of *corrective fairness* (e.g. no capacity for local ethics review).
- 14 risks for individuals, communities, countries, animals or the environment in the category of *respect* (e.g. spiritual priorities ignored by Northern researchers).
- 17 risks for individuals, communities, countries, animals or the environment in the category of *care* (e.g. inadequate consideration of unintended consequences for local biodiversity).
- 12 risks for individuals, communities, countries, animals or the environment in the category of *honesty as transparency* (e.g. only partial information given in informed consent process).
- 10 risks for individuals, communities, countries, animals or the environment in the category of *honesty as integrity* (e.g. bribery on local ethics committee).

Contributions of industry to prevent exploitative research

There are many guidelines and standards addressing the ethical challenges posed by research, and many go through continuous cycles of revisions. For instance, the *Declaration of Helsinki* was amended 9 times between 1964 and 2013. Industry players have incorporated some guidelines and standards into their company policies (see Table 2).

Large and international pharmaceutical companies in particular have policies and guidelines for the most sensitive areas, and many of them undertake compliance monitoring (see Table 2).

However, in the context of North-South collaborations, a number of challenges remain, making it difficult for research actors and research participants to interpret and implement international norms appropriately.

²⁸ Kate Chatfield, Doris Schroeder, Klaus Leisinger, Jaci van Niekerk, Ngayo Munuo, Rachel Wynberg and Paul Woodgate (2016), *Generic Risks of Exporting Non-Ethical Practices*, a report for TRUST, available: <http://trust-project.eu/deliverables-and-tools/>.

Particular challenges relevant to industry are:

1. Local ethics review of clinical trials when structures do not exist or are inadequately resourced and/or its members are insufficiently trained.
2. The need for guidelines to allow for specific cultural and social aspects of LMICs or local communities to be considered/included.²⁹
3. Compliance mechanisms to ensure that research is undertaken according to the protocol approved by an ethics review.
4. Agreement on the precise, implementable obligations of pharmaceutical companies, ranging from accountability when contract research organisations are employed in LMICs, to post-trial access to successfully tested interventions for research participants.

Table 2 – Overview of company policies³⁰

Company	Codes on interaction with healthcare professionals	UN Global Compact	Guide for the care and use of laboratory animals	Guidelines for good clinical practice (ICH)	Declaration of Helsinki
AstraZeneca	✓	✓	✓	✓	✓
BASF		✓	✓		
Bayer	✓	✓	✓	✓	✓
GSK *	✓	✓	✓	✓	✓
J&J +	✓	✓	✓	✓	✓
Merck & Co	✓	✓	✓	✓	✓
Merck KGaA	✓	✓	✓	✓	✓
Monsanto		✓			
Novartis	✓	✓	✓	✓	✓
Novo Nordisk	✓	✓		✓	✓
Pfizer	✓	✓	✓	✓	✓
Roche		✓	✓	✓	✓
Sanofi	✓	✓	✓	✓	✓
Syngenta		✓			

* GlaxoSmithKline, + Johnson & Johnson

²⁹ Ravinetto R. 'Methodological and Ethical Challenges In Non-Commercial North-South Collaborative Clinical Trials'. 2015 Leuven University Press.

³⁰ Andanda P, Wathuta J, Leisinger K and Schroeder D, National and International Compliance Tools, a report for TRUST, available: <http://trust-project.eu/deliverables-and-tools/>.

Contributions of the EC to prevent exploitative research

The European Commission promotes and supports **corporate (social) responsibility (CSR)**, defined as voluntary policy measures that companies implement to adhere to international guidelines and principles, and to include social, environmental, ethical, consumer, and human rights concerns in their business strategy and operations.³¹

The European Commission Strategy on CSR³² is based on the following guidelines and principles:

- [United Nations Global Compact](#)
- [United Nations Guiding Principles on Business and Human Rights](#)
- [ISO 26000 Guidance Standard on Social Responsibility](#)
- [International Labour Organization Tripartite Declaration of Principles concerning Multinational Enterprises on Social Policy](#)
- [OECD Guidelines for Multinational Enterprises](#)

The *UN Guiding Principles on Business and Human Rights* (UNGPs), have been unanimously endorsed by the member states and receive wide recognition and support from the business and civil society communities. The EU recognises the UNGPs as “the authoritative policy framework”³³ in addressing corporate responsibility. It has therefore created a dedicated task force to support the implementation of its principles and identify potential gaps.

The UNGPs strive to “advise on appropriate methods, including human rights due diligence, and how to consider effectively issues of gender, vulnerability and/or marginalization, recognizing the specific challenges that may be faced by indigenous peoples, women, national or ethnic minorities, religious and linguistic”.^{34,35} An important part of the recommendations given by the UNGPs is that companies ought to go through a Human Rights Due Diligence process (Article 17 of the Guidelines):

In order to identify, prevent, mitigate and account for how they address their adverse human rights impacts, business enterprises should carry out human rights due diligence. The process should include assessing actual and potential human rights impacts, integrating and acting upon the findings, tracking responses, and communicating how impacts are addressed.³⁶

The due diligence element of responsible research and innovation will be taken up again below, in the actions of the TRUST industry platform.

³¹ https://ec.europa.eu/growth/industry/corporate-social-responsibility_en

³² *ibid.*

³³ *Implementing the UN Guiding Principles on Business and Human Rights - State of Play*. Commission Staff Working Document SWD (2015)144. http://ec.europa.eu/growth/industry/corporate-social-responsibility_it

³⁴ See http://www.ohchr.org/Documents/Publications/GuidingPrinciplesBusinessHR_EN.pdf, p.5

³⁵ Due diligence is an investigation process done by a company or a person prior to entering a business relationship or before committing to an agreement, transaction or action.

³⁶ See http://www.ohchr.org/Documents/Publications/GuidingPrinciplesBusinessHR_EN.pdf, p.17

Actions of the TRUST Industry Platform

As part of TRUST's engagement and co-ordination efforts, the TRUST Industry Platform is:

- Promoting the creation of a network of industry representatives who share the vision of globally inclusive and fair research;
- Assuring that industry feedback informs the work carried out by the TRUST consortium;
- Providing the TRUST consortium with identified areas of exploitation in international clinical trials, and
- Identifying necessary conditions according to which industry would be willing to adopt the TRUST model for equitable partnerships in research worldwide.

To co-ordinate and guide the efforts of its Industry Platform, TRUST relies on the active and committed involvement of Prof. Klaus Leisinger and Dr François Bompert.

Prof. Leisinger is the former, long-term president of the Novartis Foundation for Sustainable Development, senior advisor of the United Nations and founder of FGVA ([Foundation Global Values Alliance](#)), one of TRUST's partners.

Dr François Bompert, Vice-President, Deputy Head and Medical Director of the Access to Medicines department, [Sanofi](#), is a member of the TRUST Advisory Board. He currently chairs the meetings of the Global Health Initiative of EFPIA ([European Federation of Pharmaceutical Industries](#)).

TRUST Industry Platform Pyramid

Any work done on the TRUST Industry Platform needs to be sensitive to the fact that the pharmaceutical industry must generate profits in order to remain successful in its risky (R&D) endeavours, survive in a highly competitive environment, create productive employment, and reward its shareholders. The industry is:

[N]ow facing strategic issues that require an adjustment to the traditional business model. The increasing price and cost pressure, patent expirations on blockbuster drugs leading to aggressive generic competition, public policy and changes in how consumers access medicine contribute to an erosion of profit margins. Big pharma, like other industries, is not immune to the pressure of having to meet ... quarterly earnings expectations; indeed, today's companies are measured on how well their stock performs ... This has resulted in a greater emphasis on a return on investment from R&D and reducing the amount of capital it is allocated. In turn, this has increased offshoring, the elimination of in-house teams and the flight of scientific expertise into the biotech/biopharmaceutical sector.³⁷

At the same time, the pharmaceutical industry's reputation is poor among many stakeholders:

past scandals and heavy fines for big companies found guilty of unethical practices have coloured public perceptions. In Great Britain and Canada in particular, they find a very negative environment, partly caused by campaigns by NGOs such as

³⁷ <http://www.nature.com/nbt/journal/v32/n10/full/nbt.3036.html>

Oxfam and MSF, and films like *The Constant Gardener*. Pharmaceutical companies' names, it was felt, are virtually unknown unless through scandal or plant closures.³⁸

Many people in the industry believe that the poor reputation is unjustified considering not only the successes in the treatment of many diseases but also with regard to access to medicine programmes for patients living in absolute poverty. Meanwhile international NGOs such as Oxfam maintain that:

Until the fundamental tension between its existing business model and the obligations of developing countries to promote the right to health is resolved, Oxfam believes that the industry will engender serious reputational risks, jeopardise its licence to operate and potentially fail to deliver value.³⁹

Assuming a transformative leadership role with regard to the most important issues which people all over the world expect the pharmaceutical industry to address (prices, product safety, availability of medicines⁴⁰) is critical, and business behaviour in this regard should change more than just communication:

A pyramid reflecting the Dahrendorf⁴¹ model of norms was developed consisting of “must do” actions, “ought to do” actions and “desirable actions”. These actions focus on the need to ensure the ethical conduct of research studies (*must do* in terms of seeking compliance with guidelines, and *ought to do* in terms of additional safety mechanisms), and on access to medicines for poor research participants with chronic diseases (desirable).

The pyramid (see Diagram 4) forms the basis of interactions between TRUST and representatives of large multinational pharmaceutical companies, with the emphasis on two actions which would help achieve the overall TRUST aim (to catalyse a global collaborative effort to improve adherence to high ethical standards in research around the world): *ex ante*⁴² due diligence, and post-trial access.

Ex ante due diligence (*ought to*)

Ethical issues, and particularly human rights-related issues, do not play out in the realm of theory; they always occur in a specific context and are related to specific social, economic, cultural, political and other factors. Any effort to prevent or mitigate ethical issues must therefore be based on the specificity of the context. Inflexible guidelines, codes or policies for LMICs, or even for a specific country such as “India”, “Vietnam” or “China”, do not always adequately address the heterogeneity of different population segments and local settings.

³⁸ <http://www.globescan.com/component/edocman/?task=document.viewdoc&id=82&Itemid=0>

³⁹ <https://business-humanrights.org/en/documents/oxfam-report-investing-for-life-company-responses-oxfam-rejoinder>

⁴⁰ <http://www.globescan.com/component/edocman/?task=document.viewdoc&id=82&Itemid=0>

⁴¹ Dahrendorf R.: *Homo Sociologicus. Ein Versuch zur Geschichte, Bedeutung und. Kritik der Kategorie der sozialen Rolle*. Opladen 1977

⁴² Ex ante means that the action (due diligence) needs to be undertaken before the relevant activity takes place, e.g. before volunteers are enrolled for a clinical trial.

Diagram 4 – Corporate Responsibilities for Pharmaceutical Companies conducting Clinical Trials in LMICs



Human rights-related due diligence involves anticipating adverse human rights impacts that the business enterprise may cause or contribute to through its own activities, or which may be directly linked to its operations, products or services by its business relationships. The process will vary in complexity with the size of the business enterprise, the risk of severe human rights impacts, and the nature and context of its operations. But it should be ongoing, recognizing that the human rights risks may change over time as the businesses’ operations and operating context evolve.⁴³

The ex ante due diligence requirement is particularly salient in the context of clinical trials in LMICs. The rationale behind carrying out an ex ante due diligence process is that only responsible actors will be able to identify, prevent, mitigate and account for potential adverse / undesirable impacts on patients – and address them. To be able to do this, the risks must be known. Such a due diligence process includes assessing actual and potential vulnerabilities and impacts, integrating and acting upon the findings, tracking responses, and communicating how impacts are addressed.

Post-trial access to drugs (*desirable*)

Phase III trials are designed to assess the effectiveness of a new medicine and its value in clinical practice. However, the issue for medicines used for infectious diseases is different from issues around chronic diseases: infectious diseases can be cured, but chronic diseases can only be managed to a certain degree.

⁴³ See UN Guidelines on Business and Human Rights, http://www.ohchr.org/Documents/Publications/GuidingPrinciplesBusinessHR_EN.pdf

Trial participants living in absolute poverty and suffering from *chronic* diseases end up in a difficult situation: Companies will normally make the drug that was tested on trial participants “commercially available”, or assume that it will be provided by national health institutions. But in both cases the prices are usually too high for the patient (who is normally uninsured) as well as the government of a low- or even middle-income country. In practice this means that the patient – who may have felt the positive impact of the innovative medicine as a trial participant – ends up without access to the drug he or she needs.

From our point of view post-trial access of Phase III trial participants to the innovative medicines evaluated is a moral duty – and the duty bearer is the pharmaceutical company which benefits from the registration of a new drug.

From our point of view post-trial access of Phase III trial participants to the innovative medicines evaluated is a moral duty – and the duty bearer is the pharmaceutical company which benefits from the registration of a new drug. Registration is one of the consequences of successful trials.

Input into TRUST Deliverables

Inputs from the TRUST Industry Platform have already been incorporated into three main project Deliverables:

- TRUST Report on paradigmatic case studies
- TRUST Report on generic risks of exporting non-ethical practices
- TRUST National and International Compliance Tools

The TRUST *Report on paradigmatic case studies* includes a case study on healthy volunteers in clinical trials⁴⁴ analysed from the industry perspective. The text highlights:

- The issue of obtaining informed consent from participants who are illiterate or have low literacy levels, and who may neither understand the risks that healthy volunteers are exposed to in clinical studies nor which rights they have,
- The issue of poor and vulnerable individuals participating in multiple studies at the same time because of financial benefits, therefore potentially exposing themselves to medical risks due to unknown drug interactions, and
- Compromising the reliability of the data obtained in each of the studies due to multiple enrolment.

The authors of the case study recommend that creating national databases to record the volunteers involved in clinical trials could help tackle issues b) and c). A small working group on healthy volunteers in LMICs has been formed to produce a policy brief for Year 3. The group includes Prof. Leisinger and Dr Bompert, together with Dr Vasantha Muthuswamy (President

⁴⁴ Leisinger K., Bompert F., Schmitt K. ‘Healthy Volunteers in Clinical Studies’, in Schroeder D., Cook Lucas J., Fenet S., Hirsch F. (eds.) *Report on paradigmatic case studies* a report for TRUST, <http://trust-project.eu/deliverables/deliverables-and-tools/>

of the Forum for Ethics Review Committees in India (FERCI)), Dr Dafna Feinholz (UNESCO) and Prof. Doris Schroeder (TRUST Co-ordinator).

The authors recommend that creating national databases to record the volunteers involved in clinical trials could help prevent exposing them to unknown medical risks.

The TRUST *Report on generic risks of exporting non-ethical practices* introduced a detailed list of risks (see above) identified through themed and conceptual analysis by the TRUST consortium in a collaborative way. Thanks to the extensive experience of Prof. Leisinger and Dr Bompert and their knowledge of health research in LMICs, numerous risks and ethical concerns linked to the globalization of clinical trials have been taken into account and carefully discussed.

The TRUST *Report on national and international compliance tools* analysed the self-regulatory codes of 14 pharmaceutical and chemical companies with regard to three questions:

- Are compliance or auditing mechanisms in place to ensure that guidelines are followed?
- Are sufficiently robust mechanisms in place for informed consent?
- What approaches to post-trial access are taken?

Analysis indicated that compliance and auditing mechanisms are in place at the major pharmaceutical companies under consideration, and that informed consent mechanisms are adapted to challenges such as the illiteracy of many LMIC populations. However, there seems to be no consensus on the role and responsibilities of companies in relation to post-trial access to successfully tested medicines, which is therefore a good target for TRUST action.

Dissemination

In order to promote and disseminate the TRUST vision, on April 5, 2016, Prof. Leisinger and Dr Bompert introduced the TRUST project and discussed its goals during a meeting of the Global Health Working Group of EFPIA in Paris.

One-to-one meetings with representatives of major companies have already taken place, and others are scheduled for the midterm of the project. Prof. Leisinger and Dr Bompert aim to create an open and constructive discourse with the pharmaceutical industry as requests coming from the TRUST project constitute *voluntary actions on top of their legal requirements*.

To explain the thinking of the TRUST consortium further, and to exchange views and learn from each other, the Industry Platform will co-organize the *Funders and Industry TRUST workshop* to take place in London, in June 2017, at the Wellcome TRUST headquarters.

Concluding remark

These misunderstandings [about the right thing to do] are becoming rare as foreign scientists grow more sensitized to ethical issues, and as African scientists realize the need for clearer rules governing sample collection and export. Yet inequitable partnerships remain a problem.⁴⁵

Efforts to tackle gaps in international legislation and regulation have been made and further work is underway.⁴⁶ Nevertheless, the actual responsibility for implementing change falls directly on the shoulders of the individuals involved. All the world's policies, guidelines and codes are only as good as the **human beings** that

ultimately choose – or not – to apply them. As such, engaging organizations and corporations must be seen as a necessary but not sufficient condition. Whether or not guidelines are followed, whether or not any code of conduct is adhered to in a reflected and constructive manner depends on the personality and integrity of the human being(s) in charge.

There is more work to be done, and more targets to meet during the course of the TRUST project. Our hope at the moment is for the TRUST Industry Platform to become a source of inspiration for others “to do the same”.



⁴⁵ <http://www.nature.com/news/research-africa-s-fight-for-equality-1.17486>

⁴⁶ Ravinetto et al. (2016).