# Promoting equity and preventing exploitation in international research: The aims, work and output of the TRUST project

Authors: Julie Cook, Kate Chatfield, Doris Schroeder (Centre for Professional Ethics, University of Central Lancashire, UK)

## Abstract (250 words max)

Achieving equity in international research is one of the pressing concerns of the 21st century. In this era of progressive globalisation, there are many opportunities for the deliberate or accidental export of unethical research practices from high-income regions to low and middle-income countries and emerging economies. The export of unethical practices, termed 'ethics dumping', may occur through all forms of research and can affect individuals, communities, countries, animals and the environment. Ethics dumping may be the result of purposeful exploitation but often arises from lack of awareness of good ethical and governance practice.

This chapter describes the work of the TRUST project towards counteracting the practice of ethics dumping through the development of tools for the improvement of research governance structures. Multi-stakeholder consultation informs all of TRUST's developments. Most importantly, this gives voice to marginalised vulnerable groups and indigenous people, who have been equal and active partners throughout the project.

At the heart of the TRUST project is an ambitious aim to develop a *Global Code of Conduct for Research in Resource-Poor Settings*. Uniquely, the Code provides guidance across all research disciplines in clear, short statements, focusing on research collaborations that entail considerable imbalances of power, resources and knowledge and using a new framework based on the values of fairness, respect, care and honesty. The code was recently adopted by the European Commission as a reference document for Horizon 2020 and Horizon Europe.

6 Key words

International Research, Ethics Dumping, Ethics Governance, International Justice, Global ethics

## Introduction

The progressive globalisation of research activities has resulted in an ever-increasing number of transnational studies (Gainotti *et al.*, 2016, Ravinetto *et al.*, 2016). Joint ventures between multiple stakeholders from different countries are commonplace in all forms of research, and a growing number of researchers from high income countries (HICs) are electing to conduct their research activities in low and middle income countries (LMICs) (Glickman *et al.*, 2009). A number of potential incentives and motivations for such collaborations have been proposed. For the LMIC partners, these include access to funding and other resources that might not be available otherwise (Bradley, 2016). For the HIC partners, co-operative ventures may convey operational and/or economic advantages (Dickson, 2006; Luna, 2009).

While such collaborations may yield benefits for both partners, they may also provoke sensitive ethical issues. Ethical review processes, compliance structures and follow-up mechanisms can differ greatly between partner countries. Consequently, there is a risk that research that is not permissible in a HIC will be exported to those LMICs where the legal and regulatory frameworks for research are not as rigorous. The European Commission (EC) has recently termed this practice 'ethics dumping' (EC 2016).[1] The challenges for cross-cultural research, undertaken in resource-poor settings by researchers from wealthier environments, have long been recognised (Molyneux *et al.*, 2009), but the practice of ethics dumping is receiving a growing amount of attention (Schroeder, Cook, Hirsch, Fenet & Muthuswamy, 2018; Novoa-Heckel, Bernabe & Linares, 2017). The European Union (EU) is currently funding actions to address the risk of ethics dumping from both public and private research (European Commission, 2016). One such action is the EU-funded project, TRUST.[2]

The goal of the TRUST project is to catalyse a global effort to improve adherence to high ethical standards in research around the world. In an interdisciplinary, global collaboration with 13 partners including multi-level ethics bodies, policy advisors, civil society organisations, funding organisations, industry, academic scholars from a range of disciplines, and representatives from vulnerable research populations, TRUST combines long-standing, highly respected efforts to build international research governance structures. The project's main strategic output consists of three tools to help counteract the practice of ethics dumping:

- A Fair Research Contracting on-line tool,
- A Compliance and Ethics Follow-up Self-Appraisal Tool, and
- A Global Code of Conduct for Research in Resource-Poor Settings.

The Fair Research Contracting tool is an interactive online tool that is designed to assist LMIC partners in making contractual demands on HIC partners without the need for their own specialist legal teams. It focuses on issues such as the fair distribution of post-research benefits, intellectual property rights, data and data ownership. The Compliance and Ethics Follow-up Self-Appraisal Tool is the component of TRUST's recommended approaches to ensuring compliance with research ethics requirements in LMICs beyond the ethics approval stage. The tool is intended to be practical, accessible, at little or no cost to the intended users.

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[1] The term was first used by the Science with and for Society Unit of the European Commission, which defines it as follows: "Due to the progressive globalisation of research activities, the risk is higher that research with sensitive ethical issues is conducted by European organisations outside the EU in a way that would not be accepted in Europe from an ethical point of view. This exportation of these non-compliant research practices is called ethics dumping" (European Commission, 2016).

[2] *Creating and enhancing TRUSTworthy, responsible and equitable partnerships in international research* is a 3 year (2015-18) project funded by the European Union's Horizon 2020 research and innovation programme, grant agreement No 664771. http://trust-project.eu/the-project/about/ [accessed 23.03.2018].

Both of these tools are vital components of TRUST's activities to counteract ethics dumping but in this chapter, we spotlight the development of the third tool, namely, a *Global Code of Conduct for Research in Resource-Poor Settings*. It is anticipated that researcher adherence to this innovative code will reduce the prospect of ethics dumping significantly. Crucially, funders can promote adherence to the code by adopting it as a requirement for funding of collaborative research that is undertaken in resource-poor settings.

Given its injurious and pervasive nature, the practice of ethics dumping is the central motivator for TRUST and, in keeping with the steps taken in our development of the Code, we begin with consideration of the nature and extent of ethics dumping, including real-world examples from LMICs.

## Ethics Dumping

> *"To be vulnerable means to face a significant probability of incurring an identifiable harm, while substantially lacking the ability or means to protect oneself."* (Schroeder & Gefenas, 2009, p. 117).

The term "dumping" has been traditionally used to describe predatory pricing policies (Investopedia, 2018). In this sense, it refers to the export by a country or company of a product at a price that is lower in the importing market than the price charged in the domestic market; the practice is intentional, with the primary purpose of obtaining a competitive advantage in the foreign market. In the context of research ethics, it has similar connotations and one can speak of ethics dumping in mainly two areas. First, when research participants and/or resources in LMICs are exploited *intentionally*, for instance because research can be undertaken in an LMIC that would be prohibited in a HIC. Second, exploitation can occur due to insufficient ethics awareness on the part of the researcher, ethics committees in their institutions, or low research governance capacity in the host nation.

For instance, a European researcher might accept a thumbprint on an informed consent document from an illiterate, indigenous research participant in a resource-poor setting and assume this is adequate. However, there may be an ethics infrastructure in the country from which ethics approval should be sought, and additionally the wider community may have already set up a protocol for community assent of research projects prior to any individual informed consent being sought. Even if it has not, it is likely to have its own customs or preferences for authorising such activities. Observance of such may not normally be required in European settings, or by European ethics approval systems, but it is often both practically and technically essential, as well as ethical, to obtain input from community leaders before enrolling highly vulnerable people in research studies.

Both extreme[3] and moderate[4] poverty increase the likelihood that communities and individuals will be exploited. The international debate on bioethics has long noted the existence of `double standards' (Macklin, 2004), and observed that advantage is being taken of vulnerable people in vulnerable nations. However, while there is global debate about exporting unethical business practices (e.g.

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[3] Where households cannot meet basic needs for survival (e.g. chronic hunger, no access to health care).

[4] Where households can only just meet basic needs for survival, with little left for the education of their children.

bribery and corruption, or tax avoidance) and unethical clinical trials, there is currently little global debate about research in general, or providing guidance to researchers from different disciplines.

The ethics of multidisciplinary research is complex as there are variances in vocabulary and the language of medical ethics is often transferred to other areas unsuccessfully. For example, the ethical implications of `incidental findings' in research are easily understood in the biomedical field. When unexpected, health-related information comes to light over the course of a study, researchers are confronted with ethical dilemmas about whether participants should be informed. However, in other fields, 'incidental findings' may have a completely different meaning, with distinctive implications and demand a different kind of ethical analysis.

Global and multidisciplinary collaborations can lead to confusion for all stakeholders about which governance structures and legal instruments are applicable to them. Whilst research involving clinical trials has received considerable attention for several decades, it is often unclear how non-medical research should be governed, especially in borderline areas (for example, food research involving human participants) or across cultural differences (for example, different views on animal welfare). Yet:

> *"... for vulnerable populations in developing countries it makes no difference whether they are exploited by an anthropologist or a genetic researcher. They all take something, they shouldn't have taken and then leave, whether it is knowledge, opinions or biological samples is irrelevant." (Anonymous consortium member from the South African San Institute).*

## Ethics Dumping Case Studies

> *"One can speak of exploitation when we treat ...[others'] vulnerabilities as opportunities to advance our own interests or projects. It is degrading to have your weaknesses taken advantage of, and dishonourable to use the weaknesses of others for your ends."* (European Commission, 2010, p. 127*).*

Multi-stakeholder engagement informs all of TRUST's developments and one of the first project activities was to identify and analyse real cases of ethics dumping. To this end, a fact-finding workshop was held in Mumbai in March 2016 with a range of participants with responsibility for ethics governance in health research across India. India has experienced many cases of ethics dumping, but also has a sophisticated and developing ethics oversight and governance system, so is ideally placed to identify input for TRUST. At this meeting, participants discussed more than 50 cases from India demonstrating the breadth of ethics dumping concerns including:

- a project to demonstrate the HPV vaccine in teenage girls with concerns about legitimate consent and serious adverse event (SAE) reporting,
- participants volunteering for clinical trials in order to obtain health care,
- lack of post-trial access to successful treatments for participants in clinical trials,
- NGO research undertaken without ethical governance due to lack of committee jurisdictions,

- genomics research carried out by teams from overseas amongst tribal populations without Indian ethical review which raised concerns about re-use of samples, commercial exploitation and benefit sharing, and
- problems with equity and authorship for Indian researchers in research publications.

In addition to this workshop, TRUST launched an international case study competition in December 2015 to collect global case studies of both ethics dumping in collaborative research and good practice to counter it. Some of the submissions have been included in the anthology *Ethics Dumping* (Schroeder *et al.*, 2017), and a selection of these cases, indicating key areas for concern, are summarised below.

### Cervical Cancer Screening in India[5]

Three clinical trials took place in India between 1998 and 2015 in urban and rural areas of India: Mumbai, Osmanabad and Dindigul. All the women recruited were poor and socially disadvantaged, without universal access to health care in areas where cervical cancer was known to be of high incidence and prevalence. The trials aimed to determine whether trained health care workers could conduct cervical cancer screening in the community using cheap methods of testing – primarily visual inspection of the cervix with acetic acid (VIA) – to reduce the incidence and mortality rate of cervical cancer.

The clinical trials were conducted on approximately 347,000 women, of whom about 141,000 were placed in the control arm (no screening). They were provided with so-called “usual care” or “standard care”, consisting of health education on cervical cancer symptoms, screening and treatment, and the availability of local facilities. The standard of care for testing of the disease in India has been cytology screening (Pap smear as per the international standard) since the 1970s, but screening for cervical cancer is not available universally under a government programme, although it is available in all major hospitals. The standard of care was therefore misconstrued to be no screening at all.

The women in the trial were observed (mainly retrospectively through medical records) to determine how many would get cervical cancer and how many would die, if they were never screened. This placed them at a known risk of developing invasive cervical cancer, and dying from it, because it was not detected and treated in time. 254 women in the no-screening arm of the trial died due to cervical cancer as per the latest published reports.

As these trials were non-drug related, prior permission from the Indian government in accordance with guidelines was not required at the time. The regulatory authorities involved were institution-based and unaccountable to legal oversight. A no-screening arm would not have been permitted in the USA, or in France, but was accepted for these clinical trials in India by the US sponsor (National Institutes of Health [NIH]), and the collaborator in France (the International Agency for Research on Cancer [IARC]), a specialized agency of the World Health Organization (WHO). US regulatory authorities claimed an inability to act on complaints regarding the Osmanabad and Dindigul trials as these were funded by a private foundation (Bill & Melinda Gates Foundation [BMGF]) and applied a retrospective waiver of the need for informed consent for the Mumbai trial.

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[5] Taken from Srinivasan, Johari & Jesani, 2017.

### An International Collaborative Genetic Research Project Conducted in China[6]

Between 1994-8 a research team from a renowned US university in receipt of substantial NIH and biopharmacy company funding collected blood and DNA samples from tens of thousands of farmers in the economically disadvantaged province of Anhiu in China, under the guise of free physical examinations. Three Chinese university and municipal partners co-operated in the study. The samples were exported to the US university's genetic bank for research into asthma (16,400 samples), diabetes, hypertension and other diseases. Following complaints and media attention, leading to an international controversy, an investigation by the US Department of Health and Human Services was subsequently reported to have found serious violations in multiple respects, yet their published results stated in 2003 that as no participant had been harmed, no action would be taken. This was despite the study recruiting 16,686 asthma participants when only 2,000 had been approved, and taking larger volumes of blood than agreed. The approved amounts of financial compensation for travel and loss of work were also reduced from USD10 per day to USD 1.50 – 3. It also emerged that many of the farmers had not provided consent as they were unaware this was a research study. 2003 regulations by the Chinese government to limit export of samples involving human genetic resources came too late to protect their samples. The US pharmaceutical company received major investment once it announced its possession of the samples. Several of the company's senior executives earned a net profit of over USD 10 million each through trade in stocks. The local residents who provided the samples received a free meal and an insignificant sum of money for expenses, many without knowledge of what was happening to them.

Equal partnerships with researchers from HICs are difficult to develop for countries like China. Loopholes and regulatory vacuums in host nations are easily exploited; it takes time to develop and introduce new systems and structures of research governance, but China's strengthening of its protection for IPR, genetic resources and ethical review are now having a positive impact on the exploitation of its resources.

### International Genomics Research Involving the San People[7]

In 2010 an international genomic research project entitled "Complete Khoisan and Bantu Genomes from southern Africa" was published in *Nature* amidst wide publicity (Schuster *et al.*, 2010). The research aimed to examine the genetic structure of "indigenous hunter-gatherer peoples" selected from Namibia, and to compare the results with "Bantu from Southern Africa" (ibid), including Nobel peace prize winner Archbishop Desmond Tutu. Four illiterate San elders were chosen for genome sequencing, and the published article analysed many aspects of the correlations, differences and relationships found in the single-nucleotide polymorphisms. A supplementary document published with the paper contained numerous conclusions and details that the San regarded as private, pejorative, discriminatory and inappropriate. The use of sensitive and problematic terms (such as "Bushmen" and "hunter-gatherers") demonstrated a lack of awareness and consultation, while discussion of marriage and other cultural practices, speculation about lactase persistence in adults, the claim that "Bushmen have better hearing than Europeans", and the selective survival advantages of different levels of skin pigmentation, was deeply problematic for the San people. The San leadership (via the Working Group of Indigenous Minorities in Southern Africa [WIMSA] ) met with the authors

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[6] Taken from Zhao & Yang, 2017.

[7] Taken from Chennells & Steenkamp, 2017.

in Namibia soon after publication. They enquired about the informed consent process and asked why San leaders (via any one of 3 legitimated representative advocacy groups) had not been approached for permission in advance in accordance with international guidelines regarding research with indigenous peoples, particularly as genomic research by its very nature speaks to collective issues. The authors refused to provide details, apart from stating that they had received video-recorded consents in each case (Hayes, 2011 p15). They defended their denial of the right of the San leadership to further information on the grounds that the research project had been fully approved by ethics committees/institutional review boards in three countries tasked with "protecting the rights and welfare of research subjects" and that they had complied with all relevant requirements to respect the "culture, dignity and wishes of subjects" (Ibid). The San leadership eventually wrote to *Nature*, expressing their anger at the inherent insult and lack of respect displayed by the whole process (Ngakaeaja, 2011).

### Seeking Retrospective Approval for a Study in Resource-Constrained Liberia[8]

In 2014, the Ebola Virus Disease (EVD) epidemic hit Liberia very hard. At the peak of the epidemic in October 2014, researchers were arriving in the country to conduct all forms of research, including social science, anthropological and clinical studies. As a result of the health emergency, the fully functional ethical research and oversight institutions were overwhelmed with investigators seeking information and guidance about the review process. Some investigators proceeded to conduct studies without approval of institutional review boards (IRBs). At the height of the EVD surge (November – December 2014) one study gathered information on the economic well-being of EVD survivors in several communities, to assess the economic impact of stigma and discrimination. Most of the participants were, at best, semi-literate. This study was therefore potentially distressing and traumatizing in itself and needed careful ethical consideration. However, the IRB did not receive an application until *after* the research was complete, when a junior research assistant representing the lead researcher (who had by then left the country) at a meeting revealed that approval was only being sought in order to disseminate the results. The IRB ruled that the research had been conducted unethically in contravention of clear national regulations and that the participants' autonomy had been breached. Approval was not given retrospectively, in a decision that took a stance on public policy and increasing compliance with mandated procedures.

## TRUST's Global Engagement Activities

It is an imperative for TRUST's developments that the voices and input of all relevant stakeholder groups are heard. From a 'top-down' perspective, this included a Funder Platform to engage members of research funding organisations around the world, who were brought together in a workshop in London in June 2017 to contribute to the development of the three TRUST tools. Funders are in a powerful position to demand adherence to high ethical standards, and to advise on their appropriateness, both ethically and in terms of compliance. Likewise, an Industry Platform was established to create a network of health sector industry representatives who share the vision of inclusive and fair research. Feedback from this network has informed TRUST's work, identified areas

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[8] Taken from Tegli, J.K., 2017

of (potential) exploitation in international research, and helped us to identify the necessary conditions by which industry might be willing to adopt the TRUST model for equitable partnerships in research worldwide.

In addition to the top-down input from a wide range of experts (Figure 1), TRUST sought to actively bring forth the experiences and opinions of vulnerable research populations. It can be challenging to reach relevant stakeholders when consulting in resource-poor settings. Hence, to ensure appropriate representation, TRUST included two highly vulnerable populations in the project, through Partners for Health and Development in Africa (PHDA), representing the interests of Nairobi sex workers, and the South African San Institute (SASI) which represents the San people of South Africa. Participation of these two groups has ensured influential input from some of the most vulnerable research participants in the world.

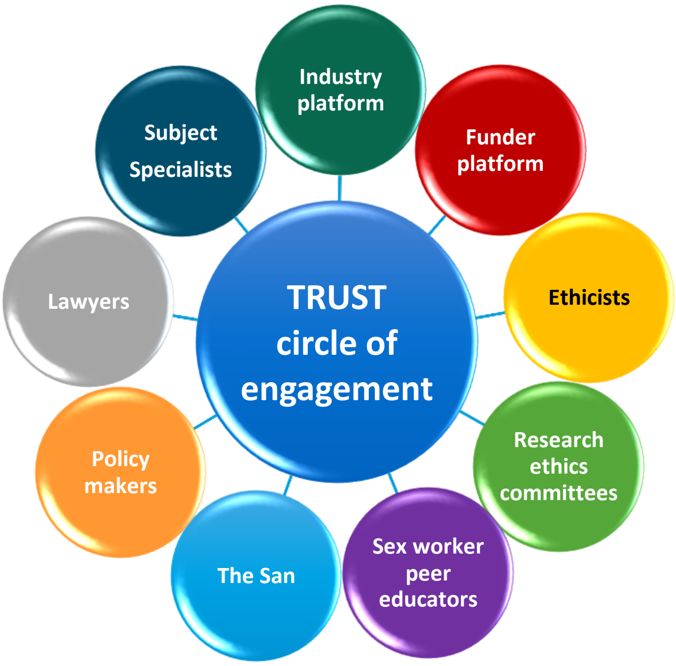
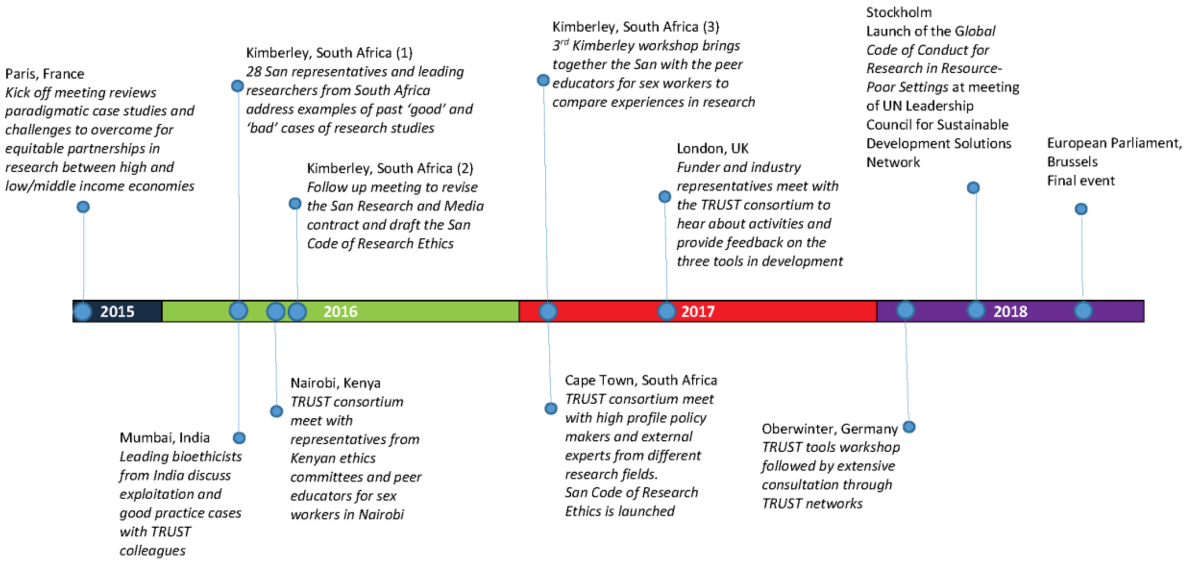


*Figure 1.*
*Engagement activities brought together a broad range of stakeholders who worked collectively to achieve the TRUST goals*

Stakeholder engagement has been ongoing throughout the project via all of the typical channels including email and online discussions, newsletters and social media. In addition, specific events were organised to engage with stakeholders in an in-depth, face to face manner, as mapped on the TRUST timeline (Figure 2).



*The TRUST project timeline October 2015 – September 2018*

**Figure 2:** The Trust Project Timeline (2015-2018)

Some of these events have been described above. Findings from others are captured below to illustrate the breadth of the subject areas and the richness of the information that was shared.

## Engagement with the San and the peer educators for sex workers

Three workshops were held in Kimberley, South Africa, where representatives from the San community came together to consider their past experiences in research and how they might improve ethical standards for the future. Indigenous communities in all parts of the world can be vulnerable to intrusive research and exploitation of their knowledge with little or no benefit to themselves. The San, being one of the most highly researched populations globally, have many such exploitative experiences to recount (Wynberg, Schroeder & Chennells, 2009). As a geneticist presenting at the first Kimberley meeting explained, genetic research with the San is highly valued because they have the oldest lineage of all living populations on earth. Additionally, their traditional knowledge and their customs can be of great interest; a linguist at the same meeting described the importance of threatened languages like those of the remaining 12 (out of a known 35) San languages.

Findings from the first workshop highlighted the following as major concerns for the San:

- a lack of appropriate informed consent procedures,
- the risks of not knowing or understanding the potential consequences of research,
- holding unrealistic expectations of participation,
- the vulnerability of individual participants, and
- a lack of negotiation with community leaders and mandated organisations to avoid confusion and conflict, and ensure respect for cultural requirements.

On the other hand, the San also described experiences of good practice where there has been clarity of intention of the researchers, effective informed consent strategies, respect for local research governance and negotiation with community representatives, a clear negotiation of benefits for research participants/communities, and the delivery of results and promised outcomes.

Looking forward, a need for capacity building was identified, especially pertaining to legal and contractual matters such as intellectual property rights, copyright law, and contracts. Other needs included consequences for those who do not abide by the existing San *Research and Media Contract*, which was felt to be in need of revision, and a formal code of research ethics for studies involving the San, which should be binding for researchers.

These themes were developed into outputs at the second consultative workshop in Kimberley, two months after the first. Here, 22 San representatives contributed to the drafting of the *San Code of Research Ethics* (South African San Institute, 2017), the first code of research ethics to be developed by an indigenous community in Africa. Additionally, revisions to the *Research and Media Contract* were suggested in line with the new Code and it was agreed that the San Council should be centrally responsible for research management.

The first major input from the Kenyan peer educators for sex workers came in Nairobi, May 2016. In Nairobi, PHDA runs the Sex Workers Outreach Programme, providing clinical and preventative services to sex workers who would otherwise find it difficult to access public health services because of discrimination and stigma. Those enrolled at the clinic for HIV prevention services are invited to participate in research studies concerning the epidemiology of sexually transmitted diseases and the host genetic factors that influence infectivity and disease progression (Andanda & Cook Lucas, 2007). Here, five representatives from the sex worker community spoke at length about their experiences of participating in clinical research studies and informed us about risk factors for their exploitation.[9] They expressed their community's concerns in the following areas:

- *Informed consent*
  Information needs to be fully accessible to those with low or no literacy, in appropriate languages, with clear and honest information about potential risks, including how those will be managed, and any benefits. Engaged communication is necessary as rumours can spread swiftly in close communities. Researchers must recognise that resource-poor people are at high risk of exploitation; most of them consent to participation because of the cash incentives and the possibility of health benefits.[10]
- *Feedback*
  The sex worker community needs feedback from research studies in simple and non-scientific language. In the past, results have been fed back in technical language that they can't understand: it puts people at risk when they don't understand the results.

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[9] Sex workers in LMICs are among the most vulnerable and frequently researched populations. Markers for their extreme vulnerability are the fact that they are 14 times more likely to contract HIV compared to other citizens in their countries and that they carry a very high burden of violence. http://www.jhsph.edu/news/news-releases/2012/baral-sex-workers.html [accessed 23.03.2018]; and http://www.ncbi.nlm.nih.gov/pubmed/24625169 [accessed 23.03.2018].

[10] See Cook Lucas et al., 2013.

- *Input into research design*
  There is a desire and willingness to participate fully in studies, right from the research design stage. Some of the community have suitable qualifications and this could help to broaden research literacy, as well as improve trust in the research and ease recruitment. Proper remuneration for such roles would be essential.
- *Specific sex worker concerns*
  Specific concerns such as mental health issues, addiction and alcoholism need to be considered, as well as the needs of those with HIV. Sex work is illegal in Kenya so there are always fears about confidentiality. There is more trust if researchers approach the community through the dedicated clinics, highlighting the importance of developing long-term relationships.[11]
- *Cultural sensitivity*
  Proper engagement with the community prior to the research is necessary to understand cultural sensitivities and take them into account. For example, there are concerns about the destinations of samples due to cultural beliefs, stigmatization of gay men, and general prejudice against sex workers.

In the third Kimberley meeting, the five peer educators from the Nairobi sex worker community joined with the San for a workshop to explore differences and similarities between their experiences. A dominant theme of this dialogue was that there are many common concerns across the different settings. As in many situations, where there is a serious power imbalance, this demands fully engaged dialogue and comprehensive consent. Many of the most vulnerable populations are marginalised both culturally and legally, which can also create ambiguities in the concept and practice of leadership. Furthermore, researchers' models of community engagement need to be appropriate, rather than just exported from other settings.

### A Kenyan research ethics committee perspective

In addition to the Kenyan participant and community perspective provided by the sex worker peer educators, the Nairobi meeting also heard an ethics committee and governance perspective from three of the most senior research ethics committee (REC) chairs in Kenya. These three professors provided direct insights into their considerable experience of the ethical challenges they have encountered when dealing with international, collaborative research. Together they revealed a broad range of challenges which allow for the potential exploitation of Kenyan research participants, Kenyan researchers and Kenyan resources.

The identified concerns and challenges are summarised into two categories: those that are largely issues of research governance and those that are more obviously issues of research ethics. By 'research governance' we mean the processes and systems that are used to ensure the regulation of research. For instance, one *process* or *system* by which the ethical acceptability of research can be achieved is double ethics review; approval from both the sponsor country and the local host. By 'research ethics' we mean the moral requirements that guide the conduct of research. For instance, the special protection that has to be given to vulnerable populations in research is a substantial

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[11] See Tukai, 2017.

requirement that refers directly to moral principles (protecting those who cannot protect themselves). Table 1 illustrates the breadth of the challenges that were described.

**Table 1. Primary concerns and challenges for Kenyan research ethics committees regarding international collaborative research**

| Research governance challenges | Research ethics challenges |
|---|---|
| • Different governance standards and procedures | • Exploitation of local researchers |
| • Unwillingness of Northern partners to abide by double ethics review | • No or little local relevance, or research outputs not affordable |
| • Ethics dumping potential due to REC oversight, capacity and training problems resulting from resource constraints | • Northern-type informed consent procedures ignoring literacy levels and community consent |
| • Unresolved issues in the ownership of biological samples | • Northern researchers show no or little cultural sensitivity |
| • Unresolved issues in the ownership of primary data | • Lack of feedback/dissemination |
|  | • Standards of care or placebo use differ between partners |

The concerns and challenges related to research governance are primarily associated with a need for more resources and tighter legal and regulatory systems. Neither are within the control of RECs. The research ethics challenges and concerns for Kenya echo what other authors have observed across LMICs.[12]

## A meeting of many minds

In Cape Town, a plenary meeting in 2017 broadened developing themes with the inclusion of perspectives from other fields in collaborative research: agriculture and biodiversity, technology transfer, and animal research. It brought together experts from these fields with people who are well-placed to influence funding agencies, national government departments and science councils, and the project partners, including representatives from the San and the Nairobi sex workers community. Attendees at this meeting were invited to consider and input directly into the emerging TRUST tools, providing invaluable insights that helped to steer subsequent developments. Contributions from these perspectives have been vital for ensuring that the tools are realistic and practicable across a range of research disciplines.

At the culmination of this meeting, representatives from various San communities in southern Africa came together with the TRUST team for the official launch of the *San Code of Research Ethics* (SASI, 2017). This Code has subsequently garnered much publicity and support, with enthusiastic interest

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[12] See for instance, Joseph, Caldwell, Tong, Hanson & Craig, 2016.

from journalists, researchers, ethics committees, funders, and other vulnerable populations around the world.[13]

## The Four TRUST Values

One of the outcomes of the Nairobi event was agreement that a set of values should guide the development of the Global Code of Conduct as well as TRUST's other outputs. The current international ethics framework is heavily influenced by an applied ethics approach that originated in the United States. This approach concerns the moral permissibility of specific actions and refers primarily to four principles (autonomy, beneficence, non-maleficence and justice) that represent the cornerstone of biomedical ethics (Beauchamp & Childress, 2009). These principles are widely applied beyond their origins in biomedical research, with varying degrees of acceptance and applicability. Through our engagement activities, it has become clear that these four principles have problems with global applicability and common global understanding[14]. Hence, rather than simply adopting this existing ethical framework, we have used an alternative approach that we believe resonates across borders and cultural contexts.

In TRUST we refer to values, rather than principles, as the foundation of our ethical standpoint in research. Values can be understood as the beliefs people have, especially about what is right and wrong and most important in life, that influence their behaviour. As such, they can inspire, motivate and engage people to discharge obligations or duties. The four TRUST values have been agreed as Fairness, Respect, Care and Honesty:

### Fairness

Fairness (or justice) can have a number of interpretations but the most relevant concepts for collaborative research ethics are *fairness in exchange*, and *corrective fairness*. In collaborations at least two parties are involved in a range of transactions, and issues that need to be considered for fairness in exchange might include the opportunities and allocation of benefits from the research for all parties. Corrective fairness is about how to right a wrong and includes considerations such as liability and accountability. This type of fairness is vital in collaborative ventures but can be challenging because it is dependent upon the availability and applicability of legal instruments and access to mechanisms to right a wrong (e.g. a complaints procedure, a court, an ethics committee).

### Respect

To show respect when engaging with communities requires an acceptance that their customs and cultures may be different from your own, and that you should behave in a way that does not cause offence. It means that one may need to accept a decision or a way of approaching a matter, even if one disagrees. Respect is therefore also a difficult value, as there is always the possibility that one *cannot* accept another's decision, especially when this creates a serious conflict of conscience. To find an appropriate route between imperialist-type imposition of approaches and careless acceptance of

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[13] http://trust-project.eu/san-code-of-research-ethics/

[14] For instance, often viewed as a liberalist ideal, Beauchamp and Childress' 2009 interpretation of 'autonomy' focuses on the rights of individuals to choose what happens to their bodies. However, this view can be at odds with cultural norms and practices in environments where the wellbeing of the community as a whole is more highly valued than that of any individual.

human rights violations may sometimes be challenging, but it is what researchers with integrity must sometimes address. And if they cannot address it, it may not be possible to undertake the research.

### Care

As a priority, care should be taken of those enrolled in research studies to the extent that their welfare is prioritised over any other goals. In line with the *Declaration of Helsinki* this means: *"While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects."* (World Medical Association [WMA], 2013. Article 8).

This care value applies across disciplines, not just in medical research and is also not restricted to human research participants. Article 21 of the *Declaration of Helsinki* extends the care for welfare to research animals (WMA, 2013. Art. 21). Likewise, care for environmental protection and sustainability is increasingly included in research ethics processes and frameworks for responsible research (Owen, Macnaghten, & Stilgoe 2012).

Researchers who take good care combine two elements: they care about research participants, in the sense that they are important to them, *and* they feel responsible for the welfare of those who contribute to their research, or might suffer as a result of it (including animals and the environment).

### Honesty

Honesty is a value that does not need complicated explanations or definitions. In all cultures and nations, 'do not lie' is a basic prerequisite for ethical human interaction. However, what does need explaining is the scope of the value of honesty in the context of global research ethics.

Lying is only one possible wrongdoing in the context of a broad understanding of honesty. For instance, in research ethics it is equally unacceptable to omit important information from an informed consent process. For this reason, research ethicists often use the terms *transparency* or *open communication* to ensure that all relevant information is provided so that research participants can make an informed choice about participating or not. Importantly, honesty is also related to research conduct other than interaction with research participants. Most prominently, the duties of honesty are described in *research integrity* frameworks (which are increasingly binding on researchers in institutions and via funders' requirements), which include issues such as credit for contributions, manipulation of data or misappropriation of research funds (World Conference on Research Integrity, 2010).

## Developing a Global Code of Conduct for Research in Resource-Poor Settings

Developing a Code of Conduct that has global applicability is no easy task. We have been mindful from the outset that there were specific traps to be avoided:

1. *Trying to reinvent the wheel*. There are a multitude of research ethics codes already in existence and it would be foolish to ignore them
2. *Building a conglomerate of existing codes*. While they may contain some relevant elements, most of the existing codes have been authored by people in high-income settings and are not directly focused upon the challenges that are associated with collaborative ventures in poor-resource settings
3. *Producing a 'we know it all' code*. Specialist expertise can be extremely helpful but may not capture all relevant vulnerabilities for ethics dumping. We wanted a systematic grounding for our code.

Before we could even begin to imagine what a code might look like, it was vital for us to understand what makes exploitation more likely to occur due to vulnerabilities that can be exploited, either knowingly or unknowingly. Investigation of this vast subject would be impossible from a traditional literature-based approach, or through investigation in a single geographical region. Many of these vulnerabilities are poorly represented in the literature and they can differ between countries, cultures and the nature of the research. For example, clinical trials, social science, animal experiments, environmental science, and research in emergency settings may pose a diverse array of risks that are largely dependent upon the local context in which they are undertaken. A creative approach to data collection was needed to try and capture as many risks and vulnerabilities as possible, hence our emphasis on wide ranging stakeholder engagement. Our Code is rooted in a broad based consultative exercise incorporating input from all of the aforementioned engagement activities.[15]

Individual vulnerabilities and risks of exploitation were extracted from the vast amount of information provided and the raw data were collapsed to group similar vulnerabilities together. For instance, there were many different examples of how people living in poor circumstances may be unfairly enticed to participate in research by the prospect of payment or reward. Such examples were grouped under the label of 'undue inducement'. Further thematic analysis resulted in distinctions between the various potential subjects, or levels of risk for exploitation (persons, institutions, local communities, countries, animals and the environment); in the final stage of the analysis the vulnerabilities were grouped according to the four values of fairness, respect, care and honesty.

This exercise resulted in an Exploitation Risk Table (Chatfield *et al.*, 2016) that contained 88 risks for exploitation in collaborative research. Importantly, care was taken to ensure that each individual risk was based upon real-world experience rather than hypothetical suppositions. The exploitation risk table clearly highlights the vulnerabilities that need to be taken into consideration when working in

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[15] This type of consultative exercise is of proven value in the development of ethical codes that are broadly representative and can have wide ranging impact; the principles of the 'Three Rs', which are globally accepted as a reasonable measure for ethical conduct in animal research, arose from a broad consultation with stakeholders undertaken in the 1950s. See Russell, Burch & Hume, 1959.

resource-poor settings in order to avoid ethics dumping. When risks were mapped against existing codes for research ethics, it was found that most (79) were addressed, at least to some extent, by an element in an existing code. However, no existing code addressed them all. Furthermore, it is not easy to spot the elements in existing codes that are of special significance to collaborative research in LMICs unless one is already aware of the challenges.

Our Global Code of Conduct for Research in Resource-Poor Settings consists of 23 articles, grouped according to the four values. Collectively, they address the 88 risks for exploitation that we identified. For example, under the Fairness value, Article 1 addresses risks to communities and institutions, as shown in Table 2.

| ***Article 1*** | ***Addresses risks of exploitation for:*** |
|---|---|
| *Local relevance of research is essential and should be determined in collaboration with local partners. Research that is not relevant in the location where it is undertaken imposes burdens without benefits* | **Communities:**<br>LMIC communities can be exploited in research when aims are driven by, and in the interests of, high income researchers/institutions with no real benefit to the local community. If the research is of no potential benefit to the local community, we must ask why is it being conducted there? |
| | **Institutions:**<br>Where LMIC partners are dependent upon funding and association with their high income partners for research, the research aims may be shaped by the high income partners and not tailored to the preferences, needs and skills of the local workforce. |

**Table 2.** Article 1: Global Code of Conduct for Research in Resource-Poor Settings addresses issues of fairness that affect communities and institutions

The Code does not repeat standard requirements for ethical research that apply wherever researchers work, across all settings. It lists only those that apply when people from high income settings are working in poor-resource settings. In this way, it offers a straightforward, quick and user-friendly means of ascertaining the ethical requirements for collaborative ventures with LMICs.

In summary, the Global Code of Conduct counters ethics dumping by:

- providing guidance across all research disciplines,
- presenting clear, short statements in simple language to achieve the highest possible accessibility,
- focusing on research collaborations that entail considerable imbalances of power, resources and knowledge and
- using a new framework based on the values of fairness, respect, care and honesty.

To ensure impact and longevity of the Code and going beyond the contract, a stand-alone website was created[16] that includes considerable learning materials in a Resource Hub, to support the Code.

The Code was launched in May 2018 at a meeting of the UN Leadership Council of the Sustainable Development Solutions Network, one of the most influential groups internationally working on global justice issues. One month later, in June 2018, it was distributed at a European Parliament event to members of parliaments, journalists, academics and the general public. In his speech, Wolfgang Burtscher, the European Commission's Deputy Director-General for Research announced:

> "As a concrete step forward, I would like to inform you that the Code developed by TRUST will be soon included in the Participant Portal of Horizon 2020 as a reference document to be consulted and applied by all relevant research projects and serve as an education tool for the younger generation of researchers".

The TRUST group was inspired by the multi-stakeholder approach to code building and its result. We hope the code will inspire researchers to build equitable research relationships between HICs and LMICs so that the benefits of innovative research will become available to all.

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[16] http://www.globalcodeofconduct.org/

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