From Asia to East Africa: Antibiotic Trajectories Across the Indian Ocean (FAR)

1. Excellence

1.1. **State of the art, knowledge needs and project objectives**

Antibiotics are some of our most precious medical technologies. Introduced in the 1930s, they soon came to transform lethal diseases into treatable life events. Over the last decades, there has been increasing concern that this old and potent technology is losing its power to heal due to growing numbers of resistant microbes worldwide. Whereas few new antibiotics have been produced since the 1980s, the global markets for old school generic antibiotics are rapidly shifting. This project aims to explore antibiotic trajectories in the global South, following trade routes from Asia to the markets in eastern Africa.

Antimicrobial resistance (AMR) is a threat to our common future. Rising rates of AMR have enormous consequences for human and animal health, as well as for the environment, economics and the future of societies at large (WHO 2015). As microbes know no borders, this is a global problem that cannot be solved within national borders. Indeed, AMR has been described as 'a fast-evolving global public health crisis ranking with terrorism and climate change' (McCarthy 2013). In recent decades, the production, regulation and marketing of antibiotics have undergone massive changes. In Europe and the United States, concerns are increasing about national drug supplies that depend, in large part, on the outsourcing of production to economic powers in the global South, such as India or China (Zaman 2018). There is a lack of transparency in the global market and chain supply of antibiotics. Furthermore, in low and middle-income countries regulations are often poorly enforced, challenging national and global surveillance systems and the authority of nation states (Sosa et al. 2010; WHO 2014). India's drug industry is export oriented, and Chinese-origin ingredients are processed in India and then exported to Europe and the United States. At the same time, these antibiotics are increasingly dominating the markets in the global South, and particularly in Africa (Grace 2004; Mitsumori 2018). National governments and global actors are increasingly engaged in mapping and regulating the use of antibiotics in the global South, indicating both growing concern and efforts to address it (MoH Tanzania, 2017).

In global health and the medical sciences, there have traditionally been two basic approaches to control AMR: the production of new technologies and attempts to curtail use. Research on the latter often assumes that decisions about antibiotic use take place in the patient/clinician or animal/veterinarian encounter. However, studies within the social sciences have documented that such decisions involve complex and context-dependent negotiations, and frequently take place elsewhere, such as in informal drug shops, at local markets, on farms or via social networks (Chandler et al.2016). Therefore, effective actions to reduce and control AMR must be based on knowledge about social practices and the cultural perceptions and norms involved in such decisions, including with respect to how farmers and regulatory systems manage livestock production, how public and healthcare professionals behave in relation to infection and antibiotic treatment, and how regulatory and financial structures incentivize or deter antimicrobial development, production and circulation. Recognizing the need to better understand such social, economic, cultural and material dynamics, there is an increasing demand for interdisciplinary collaboration in tackling AMR (WHO, 2015). Leading medical journals, such as *The Lancet* and *Science,* have called for research contributions from the humanities and social sciences (Smith 2015; Chandler 2016, Roppe et al. 2019).

Given these important challenges to global biosecurity, there is a striking lack of knowledge about the regulation and control of production, marketing and export of Asian-origin antibiotics, and about their subsequent spread and consumption in the global South. This proposed project aims to fill this knowledge gap, contributing to a broader understanding of AMR by exploring the trajectories of antibiotics from China and India to Tanzania, and thus in three poorly regulated markets that are deeply interconnected via the Indian Ocean, their historical trade networks and an increasing and powerful Chinese presence in contemporary Africa.

This project aims to develop a theory of drug trajectories in the global South. Combining history, anthropology and biomedicine, the project has five secondary objectives:

1) to investigate the Chinese and Indian production, regulation, marketing and export of antibiotics for African markets

2) to analyze regulatory challenges and consumption drivers by exploring the circulation of Asian antibiotics in formal and informal Tanzanian markets

3) to challenge the single-species approach by exploring the factors that influence the use of antibiotics among humans, animals and in the fields in the Kilimanjaro region of rural Tanzania

4) to investigate the different roles of China and India as global health actors and the implications for power dynamics in the export and import of antibiotics

5) to deliver research-based contributions to antibiotic policies and regulatory processes and thereby contributing to the global policy conversation on AMR as a collective challenge

1.2. **Novelty and ambition**

The novelty of the project is three-fold: 1) This project brings the humanities and social sciences into a traditionally biomedical research field. 2) It highlights the role of medical technology in geopolitical and foreign affairs, as well as in relations between India and China, and between these two countries and Tanzania. 3) It employs a rigorous interdisciplinary methodology of 'following the drug' in South-South relations.

Through collaborative fieldwork between social scientists, historians, physicians and biomedical engineers, this project will challenge and expand the existing knowledge about AMR. It answers the call from both leading AMR research environments in the global North (*The Lancet*), and from our local collaborators in the global South, to bring the social sciences into the battle against AMR (see 2.1).

China's involvement and investment in Sub-Saharan Africa has intensified rapidly since the 1990s, and China is now recognized as the 'largest export and development partner' (Pigato & Tang, 2015). In the last decade, Chinese investment and business in the health sector has increased significantly (Anshan & April, 2013), Chinese hospitals and clinics have opened across Africa (Hsu, 2017), and China has sent thousands of medical professionals across the continent (Wang & Batemen, 2018; Lin et al., 2016). Through previous research undertaken by our team members about trade between China and Africa, we know that Chinese drugs travel with both African and Chinese entrepreneurs and companies engaged in the booming Chinese economic activities in Africa and that the quality of some of these drugs are questionable. So far, there is no research published on the role of pharmaceutical export in China's engagement in Africa, adding to the novelty of this project (see 2.1).

1.3. **Research questions and hypotheses, theoretical approach and methodology**

The project approaches antibiotics from within a broad sociocultural analytical framework. As most pharmaceuticals, antibiotics are not pure laboratory objects that exist independent of their social incorporations and interpretations but rather materials and technologies that come into being in relations with humans and nonhumans, with regulations, economics and environments (Hardon and Sanabria 2017). Numerous studies of the social lives of medicines (Whyte et al. 2002) have produced complex drug biographies, in which the pharmacological components of these drugs are merely some of the characteristics of their efficacy and meanings. Inspired by such biographical approaches to the study of pharmaceutical trajectories (Gaudillière 2005; Geest, Whyte, & Hardon 1996; Meier zu Biesen 2018), we follow antibiotics from inception to consumption, taking the sociocultural, economic and political dynamics to be crucial to their coming into being, and with respect to their circulation and use. Within this framework, we aim to develop a new theory of drug trajectories in the South-South axis, using antibiotics as a pertinent example.

Within this biosocial framework, the project has an explorative, ethnographic and historical design, focusing on trajectories and flows from parts of the world connected by the Indian Ocean.

Research questions: 1) What characterizes the production, regulation and marketing of antibiotics for African markets by Asian producers? 2) How do Asian antibiotics circulate throughout Tanzania, from import through regulations, distribution and sale? 3) Which factors influence the uses of antibiotics among humans, animals and in the fields of rural Tanzania, and how does the local population perceive antibiotic resistance?

Theoretical perspectives: In the recent anthropology of pharmaceuticals, a significant field of research that has been termed the 'market-state nexus' (Hardon and Sanabria 2017:120) has explored the commercial drivers of global industry and their effects on health and health understandings (Dumit 2012), thus providing critical perspectives on transnational regulations and their local implications (Banerjee 2016). This project expands the market-nexus approach to pharmaceuticals by taking antibiotics to be technologies of increasing Chinese power - both in African countries and in the field of global health.

Across the ocean, antibiotic circulation and consumption in Tanzania unfolds in the history and context of the pharmaceuticalization of the public health system. Since the 1980s, international donors have pushed the public health systems throughout Africa to focus on drug access and provision policies. Declining prices of antibiotics paved the way to a mass market in which antibiotics from China and India came to dominate, followed by concerns about both low drug quality and unregulated over-the-counter and street sales, leading to uncontrolled consumption by both humans and animals, particularly in industrial farming. Access to medicines is vulnerable to the political economy surrounding the production of pharmaceuticals today, both in the transnational market and in the national regulatory bodies of exporting countries, leading to complex connections between transnational and local (legal or illegal) trade, entrepreneurs and local drug markets. Analyzing antibiotic flows in Tanzania, and their potentially unequal and disruptive aspects, we take as a starting point the concept of 'living labyrinths' (Hardon and Sanabria 2017), in which technologies, materials and medicines act - not in controlled laboratories - but in messy social lives, informed by cultural, financial and political dynamics.

Much of the AMR research focuses on *either* human, animal or environmental aspects, producing disconnected knowledge bases in what can be described as knowledge silos. However, it is well-known that AMR is an outcome of the inextricable and complex interrelations between human, animal and environmental health. Intensive farming of animals has contributed considerably to the spreading of AMR, as the bulk of all antibiotics are being used as growth enhancers in meat production (McKenna 2018). This is also the case in east Africa, following the development of industrial farming over the last decades, helped in part by Chinese investments. In the global health agenda, it is increasingly recognized that AMR must be handled through an interdisciplinary and multispecies agenda, the *One Health One World* approach, focusing on the mutual advantages of improving human, animal and environmental health.

This implies a world getting smaller - compressed in terms of time and space - and conceptualized in terms like the 'global village' or 'single planet'; this is a world in which antimicrobial resistance developed in one location can be experienced almost immediately on the other side of the globe. However, the 'One World' agenda also implies a 'specific ontology' (Law 2011), in which products of knowledge as practiced in the global North are 'exported to other domains (Hinchcliffe 2017). Thus, we would also like to critically engage with this One World agenda and ask: whose health, whose economies and whose threats are being conceptualized within these frames. In global and national action plans, the possibility of a universal means to tackle AMR is often presupposed. However, health is constituted by locally situated sets of heterogeneous practices and challenges particular to their contexts. Thus, we also aim to employ a critical, post-colonial lens that is sensitive to local manifestations and negotiations of this challenging situation (Paige et al. 2014). Tackling AMR requires a recognition of the multiple dimensions of health, and of the challenges that local farms, laboratories and hospitals are facing as they try to mitigate disease and improve health. Thus, in this project, although we appreciate the global threat of AMR, we also pose fundamentally critical questions, such as: Whose health is being emphasized? Is this potentially reproducing or

perpetuating health inequity between the global North and South? Which economies are being secured? What priorities lead to emphasis on resistance, and what is at stake in this emphasis, particularly with respect to the considerably greater numbers of people who are dying from treatable infections due to lack of access to antibiotics than from infections with resistant microbes (Hinchliffe and Craddock, 2014)? No global AMR agenda will be possible without recognizing the need to understand the precarious conditions that many people in the global South are subjected to through their 'differential positioning or placement in social settings and economic markets' (Wallace, Bergmann et al 2014). Through long-term fieldwork engagements, conducted in native languages and in close collaboration with local partners, we will analyze perceptions, behaviors, documents and interactions, thus producing in-depth knowledge about the complex local, social and cultural settings in which antibiotics are made, circulated and used - and in which resistance is produced - providing alternative platforms for debates about the global agenda for tackling antimicrobial resistance.

1.4 **Project organization / work packages**

This project follows antibiotics from their regulation and production in China and India, to their crossing of the Indian Ocean, to their formal and informal ways of circulation, and to their consumption and resistance in people, animals and the environment in Tanzania. The analysis is organized into the following work packages, designed to mutually inform each other and contribute to the main research objectives above. To study the defined trajectory from China and India to Tanzania, we have organized the projects into three interconnected work packages, supervised by interdisciplinary teams. The research is organized into the following WPs, designed to mutually inform each other and contribute to the main research objectives.

WP 1: Production, regulation, and export of Asian antibiotics for African markets
Project group: Heidi Fjeld (PI), Heidi Østbø Haugen, Anne Kveim Lie, Lise Bjerke, Postdoc 1

This work package will investigate antibiotics from production in and export from India and China. The main objective of the study is to understand the production of antibiotics for animals and humans in India and China, their subsequent export to Africa, and to compare regulatory attempts, challenges and possibilities. Lise Bjerke is already working on a PhD project on the Indian case study. As the Indian case study has a similar and directly comparable research design, we here only describe the Chinese case.

The Chinese case will be investigated through document and trade registers analysis, combined with interviews. The four sub-objectives are: 1) to investigate how active pharmaceutical ingredients (APIs) and antibiotics are produced and marketed in China 2) to map how production has been regulated, with reference to both national and international guidelines, from the 1980s to today 3) to investigate how the export of antibiotics is organized and conducted from the hubs for export activities in Southern China and 4) to analyze China as a global health actor, through the case of antibiotic production and export.

India is a long-standing lead producer and exporter of generic medicines (Mitsumori 2018), also to Africa (Sudip, Maureen, & Phares 2010), and today, India and China manufacture the majority also of antibiotics in the world. The pharmaceutical relations between India and China are complex: China produces 80-90 percent of antibiotic active ingredients (EPHA 2016), which India also massively imports for its own production, and both countries compete in the same markets, such as eastern Africa. As in India, the Chinese pharmaceutical industry is booming and the combination of harmful waste from antibiotic production and broad use of these medicines by humans and in industrial livestock farming leads to growing concerns about resistance, threatening human, animal and environmental health. The Chinese government is struggling to effectively supervise both its production and use (Hao et al. 2015; Cui et al. 2017, Mitsumori 2018). In 2016, the Chinese government issued the *National Action Plan to Contain Antimicrobial Resistance 2016-2020*. This plan focuses primarily on regulating use and prescription nationally, with less attention to production, quality and export (Xiao 2017). An important focus in this WP is the role of the China Food and Drug Administration (CFDA), the government agency responsible for registering, producing and

distributing medicines, and attention will also be directed to other regulatory agencies of relevance for drug markets. This proposed project is the first to explore regulation of production and export of Chinese antibiotics.

The Postdoc will analyze policy, regulation and trade documents in the Chinese language, and, if possible, conduct two shorter fieldworks in South China. The Postdoc will map types of antibiotics, and antibiotic active ingredients, produced and exported, and will, if possible, interview local experts and people involved in the regulation, production, marketing and export of antibiotics. S/he will also follow public and political debates about AMR. In order to access antibiotic value chains from China to India, the Postdoc will conduct a shorter fieldwork in Mumbai, aiming to identify Chinese actors who will then be investigated. The Postdoc will also, in close coordination with WP2 and 3, conduct a shorter fieldwork in Tanzania, investigating the receiving ends of Chinese export arrangements.

WP 2: Import, regulation and circulation of Asian antibiotics in Tanzania
Project group: Christoph Gradmann (PI), Danstan Hipolite, Postdoc 2

This work package investigates the circulation of Asian antibiotics once they enter Tanzania. From the 1990s, the health services in Tanzania, like in other African countries, have undergone rapid pharmaceuticalization. With globalization, the markets shifted, and while there was previously a thin stream of antibiotics from the north to the south, there is now a flow of generic drugs from Asia, reviving old trade routes across the Indian Ocean for new products. At the same time, there has been a steep rise in what often is unregulated antibiotic distribution and consumption, thus increasing concern about inappropriate use of antibiotics and increased resistance as a probable consequence. Today, much research is being conducted by Tanzanian researchers on AMR (Blomberg 2007; Katakweba 2018). However, there has not been much focus on the flow of antibiotics from import to consumption, and this study fills this knowledge gap.

The main objective of this study is to document and analyze, at the national level, how Asian antibiotics travel in formal and informal networks and the affiliated regulatory efforts and challenges. Through close collaboration with the TFDA in Dar-es Salaam, a Postdoctoral fellow will conduct fieldwork in what will be identified as relevant sites across Tanzania, with respect to four objectives: 1) document how market access for antibiotics has been regulated in Tanzania, 2) identify drug circulating pathways and networks of formal and informal kinds, 3) document national efforts to register, administer and control antibiotics, and their consumption and use, and 4) investigate how regulatory officials in relevant government and non-government sectors conceptualize the possibilities and obstacles in the national efforts to battle AMR.

Regulatory and circulatory dynamics of antibiotics need to be framed historically. In many countries outside of Europe, antibiotics have not been subject to regulating policies until recently but arrived as powerful symbols of a technological modernity. Antibiotics were, with a few exceptions, not locally produced, and the supply of such medicines to health services was often controlled through international sponsors (Jennings, 2008). In Tanzania, market access has, since 2003, been subject to approval by a central registration authority, the TFDA. In this work package, we develop the history of national regulatory efforts on antibiotics, focusing on the initiatives preceding and leading up to the 2017 National Action Plan, and we aim to map the paths along which Tanzanian authorities (such as the Ministry of Health, the Ministry of Agriculture or the TFDA as well as national Veterinary Institutes) established themselves in a field dominated by foreign producers, NGOs and researchers. This work will build on work done on the transformation of the Tanzanian health system in the age of globalization, and on local medical research in Tanzania (Graboyes 2015).

Because Tanzania operates with a 20-year moving wall in archives, the National Archives are not rich for contemporary history. In this absence, we will thus employ a combination of methods that are commonly used in both contemporary history and social anthropology, such as document research with an emphasis on grey literature, such as reports or memoranda, as well as interviews and observation. We will work closely with the TFDA, and, together with them, we will identify significant persons to interview for this medical history. In addition, through participant observation,

we will learn about the pathways for and networks of Asian antibiotics in Tanzania, and we will follow the journeys that these actors and drugs make throughout the country. We will employ a Postdoctoral fellow with solid regional competence and language skills.

WP3: Consumption of antibiotics in Kilimanjaro region
Core project group: Anne Kveim Lie (PI), Ruth Prince, Mohammad Zaman, PhD student
This work package will focus on how people in the Kilimanjaro region in Tanzania adapt to disease, disease risk and the threat of AMR. Countering the tendency of social science investigations of AMR to focus exclusively on human behavior, we will consider the socially and economically embedded nature of human actions within a low-income setting. The main objective of this study is to analyze the social, cultural, economic and material dynamics that influence the use of antibiotics.

Our interest in antibiotics and associated resistance in rural Tanzania arises within the context of increasing use of antibiotics in intensive livestock farming in East African countries with a rapidly growing urban middle class and associated demand for animal products (Katakweba et al. 2015; Nonga et al. 2010). It also arises in the context of One Health concerns about pathways of resistance between animals and humans, in soil and water. The recruited PhD student will explore the social and economic conditions of antimicrobial use (such as poverty, food security, disease risks and antibiotic availability) among villagers and farmers in the Kilimanjaro region, which is an area with a booming meat industry. For this purpose, the PhD student will conduct ethnographic and historical research over a period of approximately one year, living and interacting with members of the local communities, including large-scale farmers, clinicians, pharmacists and dispensary staff, and others who come in contact with antibiotics. The study has four sub-objectives: 1) to explore how and why small and large-scale farmers employ antibiotics in their efforts to treat themselves, their families and their animals, 2) to analyze how people identify disease risks and relate to AMR in humans, animals and the environment, 3) to map for what, how and why people use which kinds of antibiotics in this area, 4) to map the availability of Asian antibiotics in the local hospitals, clinics, dispensaries and markets.

Participant observation and interviews will take place in two sites, an intensive industrial livestock farm and a rural community comprising small-scale livestock farmers, as well as in the settings in which these farmers live and act in their daily lives. This will enable us to look at AMR in locations that matter for its use and consequences: fields and livestock 'factories', families, markets and offices. The local collaborators in both human and veterinary medicine include the Kilimanjaro Christian Medical University in Moshi and Sokoine University of Agriculture in Morogoro. During this fieldwork period, the project members will meet with farmers, veterinarians and physicians in order to understand current disease challenges and assess possible strategies for change. The PhD student to be recruited should have a background in contemporary history, anthropology or other related disciplines and a familiarity with Swahili and eastern Africa.

3. Implementation

3.1 Project manager and project group

This proposed project is exploiting the synergies among the team members' national and international networks and ongoing research expertise in the fields of medicine, anthropology and medical history. The group, based at UiO's Department of Community Medicine and Global Health, Institute of Health and Society (HELSAM), has collaborated closely to develop the project over a period of one year. This has included seminars and meetings for the exchange of perspectives on and approaches to AMR. Project leader **Heidi Fjeld** (WP1, PI) is an associate professor at HELSAM with excellent leadership skills. She is the leader of the research group *Engaged Community Medicine,* which facilitates action-research between the social sciences, humanities and medicine. A social anthropologist, Fjeld has extensive experience from Asia, including ethnographic approaches to health systems in China and understandings of health, illness and treatments in Nepal and India. Professor **Christoph Gradmann** (WP2, PI) is a medical historian working on the global history of antibiotics and is currently writing about the history of drug resistant tuberculosis in Tanzania.

Associate Professor **Anne Kveim Lie** (WP3, PI) is a physician and medical historian, with extensive research experience on the recent history of antibiotic policy and regulation. Kveim Lie is also the PI of the SAMKUL-funded research project *Biomedicalization Inside Out*, and we are expecting collaboration and synergy effects between the two projects. Both Kveim Lie and Gradmann are members of ongoing interdisciplinary groups working on the *AMR: Antimicrobials in Society* project at the London School of Hygiene and Tropical Medicine and the *Antimicrobial Resistance – Historical Foresight* project at the University of Exeter. **Unni Gopinathan**, MD PhD is a global health policy researcher at the Norwegian Institute of Public Health, who in 2019 was at Harvard University as a Harkness and Fulbright fellow. He is part of York University's Global Strategy Lab at York University which takes a deep interest in antibiotics. Associate Professor **Ruth Prince** is a medical anthropologist with extensive experience from health system research in eastern Africa. She is also the PI of the ERC Starting Grant project *Universal Health Coverage and the public good in Africa: An anthropological study*, also providing important synergies with this proposed project. Heidi Østbø Haugen is a Professor of China studies at IKOS, UiO and will bring experience from her ongoing ERC Starting Grant and RNC Young Scholar project on Chinese business engagement in Africa. In addition, Lise Bjerke, who is working on the production and export of Indian antibiotics to Tanzania will be an important participant in the project group (WP1). **Muhammad Zaman**, professor in bioengineering and international health at Boston University, whose research focuses on how poor-quality antibiotics in the global south lead to resistance and will bring his expertise in global health innovation, drug quality assessment and AMR to the project.

The additional three members of the group will play advisory roles in particular WPs and in the opening and closing conferences. Kenneth Bo Nielsen, associate professor at the Department of Social Anthropology, UiO, will contribute with expertise on India, Indian agriculture and India in Africa. E. Kristian Rødland, MD in infectious medicine, is working on AMR in a 'One Health' perspective at the Norwegian Public Health Institute, and he will contribute with expertise from clinical medicine and surveillance. Sigurd Høye, MD is working on antibiotic prescription practices in Norway and is a leading actor at the Antibiotic Center for Primary Care (ASP) at UiO, thus securing a link to local relevance and concern in Norway. In addition, the project will be closely connected to INFRA, the Interdisciplinary Forum for Antimicrobial Resistance at Helsam (https://www.med.uio.no/helsam/english/research/network/INFRA/), and affiliated with Centre for Global Health at UiO (https://www.med.uio.no/helsam/english/research/centres/global-health/).

One Postdoctoral fellow will be recruited to WP1, to work together with a PhD student (Lise Bjerke) who is already employed through strategic funding from the UiO's Faculty of Medicine. One Postdoc will participate in WP2, and one PhD student will be employed for WP3. Cross-cutting interdisciplinary teams will participate and supervise all work packages, and we will facilitate close collaboration between the PhD students and the Postdocs, including the sharing of empirical material and co-authoring of articles. To develop further talent, we will recruit and supervise MA students (primarily from the M-phil. program *International Community Health*) as well as medical students doing their 20 ECTS research projects and one or two medical students at the MD PhD program ('forskerlinjen' at the Medical Faculty).