Brief project proposal

Generics across the ocean: Production, regulation, and export of Indian antibiotics for African markets

Summary

Antimicrobial resistance (AMR) is a threat to our common future. What shows up as a drug resistant strain of a microbe in human healthcare or animal husbandry is also the product of a multiplicity of contexts. Being a global problem, it has some particular local features, which currently is most notable the south-south flow of antibiotics. Poorly regulated production, export, sales and use in emerging economic powers, such as India, is connected to regions of escalating and largely under-regulated use, such as Africa. This indicates a gap in knowledge and arguably, practice: In Europe antibiotics policies are widely in place. By contrast, we know too little about regulation and control of production, quality, marketing and exportation of antibiotics of Asian origin. This proposed Postdoctoral project aims to map the conditions for the flow of antibiotics from India to eastern Africa, exploring regulation, production and export of antibiotics in India, on the one hand, and perceptions of resistance among Indian producers and regulating bodies, on the other. Through interviews with producers and regulators, as well as text analyses of policy and historical documents, we aim to produce novel insights into the growing concerns of unregulated markets for antibiotics, and inform international regulations of production and sale on the south-south axis.

Objective

The main objective of the study is to develop a broad social, economic and political understanding of regulation and production of Indian antibiotics, and deep insights to the dynamics and mechanisms of export of antibiotics to African markets. One possibility is to focus on fluoroquinolones, but this might change according to relevance. Sub-objectives are: 1) to explore regulation and production of antibiotics in India, 2) to investigate marketing and export of antibiotics for African markets by Indian producers, and 3) investigate perceptions of resistance among Indian producers and regulating bodies. Through the project we will establish a research group at Helsam with the tentative title *Forum for Antimicrobial Resistance (FAR),* which will serve as an organisational umbrella to bring together all research activities - national and international - on antimicrobial resistance across the departments at Helsam.

Background

Antimicrobial resistance (AMR) is one of the main challenges of our times, where knowledge of the problem in different sectors is incomplete or contradictory, affecting multiple levels of society. As the former secretary general of WHO, M. Chan has said, this “slow moving tsunami” threatens us with ”the end of modern medicine as we know it” (1). The consequences of rising rates of AMR for human and animal health, for economics and for the environment seem dire, endangering the future of societies at large (2). With rapidly increasing drug production and consumption in the global East and South, it is also a core issue in global health, adding new dimensions to a hazardous situation:

That of a fast growing, and poorly surveyed production and consumption of antibiotics where regulation, surveillance and other means of AMR policy are mostly absent (3, 4, 5).

There are two basic approaches to control AMR: technological solutions and curtailing consumption. Much attention has been given to efforts to produce technology, like novel antibiotics or rapid diagnostic tests. However, the most effective actions to reduce and control AMR will involve changes in social practices, including how farmers and regulatory systems manage livestock production; how public and healthcare professionals behave in relation to infection and use antibiotics, and how regulatory and financial structures incentivise or deter antimicrobial development, production and use. WHO has called for interdisciplinary action to tackle AMR (6), and new debates have arisen on how to combine basic and social science on the pressing issue of resistance (7, 8).

Production, regulating and marketing of antibiotics have undergone massive changes in the last generation. There is increasing concern within Europe and USA that their drug supply is dangerously relying on production in the global south, either by outsourcing production or by being totally dependent on importing active antibiotic ingredients (9). Today, emerging economic powers such as India or China are producing pharmaceuticals for export, increasingly dominating the markets in the global South, and particularly in Africa (9, 10, 11). There is a gap in knowledge and arguably, in practice of these new dominant producers: European production of antibiotics is regulated stringently, and policies are widely in place. By contrast, we know too little about regulation and control of production, quality, marketing and exportation of antibiotics of Asian origin. This Postdoc project focuses on Indian producers of antibiotics targeting African markets, and aims to map regulation, marketing and export, one the one hand, and their perceptions of antimicrobial resistance, on the other.

Specific aims

The project aims to develop a broad social, economic and political understanding of regulation and production of Indian antibiotics, through investigating the dynamics and mechanisms of export of these India produced drugs (possibly fluoroquinolones) to east African markets. Three main themes will be explored:

1) regulation and production of antibiotics in India,
2) marketing and export of antibiotics for African markets by Indian producers
3) perceptions of antimicrobial resistance among
    a. producers of antibiotics
    b. regulating agencies
    c. exporting businesses

Detailed description of the project

The proposed project will follow antibiotics from production in - and export from – India.
One suggestion is to focus on fluoroquinolones, as a well-established class of broad-spectrum antibiotics, extensively used since the 1980s in both veterinary and human medicine, with a known spectrum of drug resistance, named as a high priority for replacement due to resistance in WHO's respective list (www.who.int/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed). Fluoroquinolones came into widespread use in Africa in the 2000s after patents for these drugs had expired. This class of antibiotics became the drugs of

choice against enteric fever, severe gastroenteritis and salmonellosis, but resistance quickly appeared. Enrofloxacin in veterinary medicine and Ciprofloxacin in human medicine are the most widely known preparations with extensive records of resistances. However, the most relevant family of antibiotics to focus on can be decided according to empirical findings during fieldwork.

Over the last 30 years, Indian and Chinese pharmaceutical companies have developed into world leading producers of antibiotics. Research in global pharmaceuticals, and particularly generic medicine, has shown that India is the lead producer and exporter (10, 11), also to Africa (15). We know from previous research and observation in African markets that Indian antibiotics are commonly available, also over-the-counter. Recent studies have shown how the traditional trade routes along the shores of the Indian ocean have been - and continue to be - very important for the flow of drugs, last seen in the case of Ayurvedic medicine (16), from India. India has a long history of producing drugs for the global market. Already in 2005, the US International Trade Commission found that the Indian pharmaceutical industry was the fourth largest in the world, mostly due to its export of generic drugs (17), and according to a report by McKinsey, the Indian pharmaceutical market will grow to USD 55 billion in revenue by 2020 (18). Antibiotic consumption is massive in India; between 2000 and 2015, it increased with 103% (from 3.2 to 6.5 billion DDDS) (19). At the same time, awareness of microbial resistance is limited, both among the public and health professionals (20, 21, 22). In the National Action Plan on Antimicrobial resistance from 2017 (20), one of the five strategic priorities is to strengthen regulation, but the plan focuses primarily on reducing use in India, and less on production, quality and export (20).

This will be investigated through fieldwork in important hubs for the pharmaceutical industry and home to the major antibiotics producers (for instance Sun pharmaceutical industries and Aurobindo), such as New Delhi, Mumbai and Hyderabad. This is an explorative study utilizing qualitative methods, including in-depth interviews, informal conversations, and text analyses. An important focus in India will be the role of the Central Drugs Standard Control Organization (CDSCO, in New Delhi), the government agency responsible for registering, producing and distributing medicines, as well other drug regulatory agencies of relevance. India is categorized as an 'unregulated' market, i.e. with less elaborate regulatory systems for drug control (10), yet there are recent efforts to implement stricter policies concerning antibiotics (and resistance) (20, 23). Through long-term fieldwork, the Postdoc will aim to work closely with local actors in both the pharmaceutical industry and trade (small and larger entrepreneurs and businesses involved in Africa), as well as official regulators.

The Postdoc will start with a broad review of existing information and research about Indian drug producers, relevant policy and regulating documents that are available (Q1, Q2). The main data production will be through 6 months of fieldwork in important sites for pharmaceutical production(Q3 and Q4). S/he will track and collect local policy and regulation documents (past and present), interview people involved in regulation (n=approx. 7) of antibiotics, and people involved in the production and marketing of antibiotics, and fluoroquinolones in particular (n= approx. 20), as well as people involved in export (n= approx. 10). These interviews will also cover perceptions of resistance. Moreover, during fieldwork the researcher will follow public debate on AMR, and engage in dialogue with researchers and activists in places such as Mumbai and Hyderabad. In addition, s/he will, in close coordination with faculty in the department conduct a shorter fieldwork (3 weeks) in Tanzania, investigating the receiving ends of Indian export arrangements (Q6).

Possible student projects

We aim to recruit students from the MA program *International Community Health*, medical school (prosjektoppgave and forskerlinjen) as well as other programs of relevance at Helsam, to conduct related projects. Proposed topics are:

1. The history of India-WHO relations on regulating pharmaceutical industry
2. National efforts to reduce the use of antibiotics in public hospitals in India
3. Mapping and documenting Indian antibiotics available in markets in Tanzania
4. Perceptions of efficacy: Comparing Chinese and Indian antibiotics in Tanzania

These student projects will increase and expand the knowledge base and research activities on antibiotics between Asia and Africa in the institute. Moreover, collaborating as supervisors on these student projects will contribute to new platforms for collaborations across Helsam's departments.

Collaborative structure

Drug markets and drug regulations in India are complex and access might be a problem. However, there is increasing political attention, both nationally and globally, towards drug regulation in India within the context of AMR. We will therefore recruit a candidate with strong language skills (Hindi or other local languages is an advantage) and social science or humanities background, preferably holding previous research experiences with the pharmaceutical industry in India. We have some contacts at the Centre of Social Medicine and Community Health at the Jawaharlal Nehru University, and aim to develop (through colleagues at the Centre for Global health) workable relations with AMR researchers at the All India Institute of Medical Sciences (AIIMS) in New Delhi and Hyderabad.

The Postdoc will be guided by a team with backgrounds in anthropology, history and clinical medicine, in order to ensure that the inter-disciplinary potentials of this project are well exploited. The team, Anne Kveim Lie, Heidi Fjeld, Sigurd Høye and Christoph Gradmann, has broad experience in inter-disciplinary research in general, and collaborations between clinical medicine and social science and the humanities in particular. The institute of Health and Society has for a long time had leading experts within the research on AMR (ASP, history of medicine, HELED, Centre for global health). However, as is the case for most AMR research, individual research groups have been pursuing separate disciplinary strains in their research. We will use this common project to further develop and strengthen such a network into a Research group *Forum for Antimicrobial Resistance (FAR),* which will serve as an umbrella to join forces across the departments at Helsam.

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