doi:10.2533/chimia.2023.613 Chimia 77 (2023) 613–615

Basel: A Hotspot for Drug Discovery and Development Against Poverty-related Diseases

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Abstract: In discussion with Lukas Meier from the Swiss Tropical and Public Health Institute (Swiss TPH), Lutz Hegemann, Head of Novartis Global Health and Sustainability and Marcel Tanner, President of the Swiss Academies of Arts and Sciences, give their opinions on the changes that occurred in drug discovery and development for poverty-related diseases over the past 30 years. They emphasise the power of public–private partnerships and provide their points of views on what needs to be done in the future to ensure that the poorest of the poor also have access to important therapies.

Keywords: Drugs · Leprosy · Malaria · Neglected tropical diseases · Novartis · Product development partnerships · Public–private partnerships · Research & development · Swiss Tropical and Public Health Institute

Lukas Meier obtained a PhD from the University of Basel, Switzerland in 2012 for a thesis entitled 'Swiss science, African decolonization and the rise of global health, 1940-2010'. He is Secretary General of the R. Geigy Foundation/Swiss Tropical and Public Health Institute (Swiss TPH).

Introduction

As far as healthcare innovations are concerned, Basel is a special place. From here, LSD slowly conquered the globe in 1943 and made the world a little bit more colourful. A year later, Ciba researcher Leandro Panizzon synthesised Ritalin, a blockbuster in the treatment of the attention-deficit hyperactivity syndrome (ADHS). On the eve of the Second World War, Paul Müller (J. R. Geigy AG) discovered the insecticidal effects of DDT, which would fundamentally change entire agricultural and ecological systems. And in 1983 Sandoz/Novartis launched the immunosuppressant Sandimmun, which actually enabled transplant medicine. The development of new drugs against neglected tropical diseases (NTDs) also has a long tradition in Basel. Ciba-Geigy, one of the predecessor companies of Novartis, was prominently involved in the fight against leprosy. In 1981, it launched a new multi-drug therapy (MDT), consisting of dapsone, rifampicin and clofazimine, which has since cured more than 16 million people of the disease.

With its resident industry, the oldest University in Switzerland and among the 20 oldest world-wide, academic research institutes and a burgeoning start-up scene, Basel is a unique life-science cluster. Major pharmaceutical companies, academic research organisations and product development partnerships are just next-door to each other. The pharmaceutical and chemical industry is significant to the regional labour market, a global leader in productivity, and second in patent density. In 2018, the region had a total of 205 new life sciences patent applications per million residents. In an international comparison, only Boston has a higher number of patent applications.[1]

While the development of drugs against NTDs and other poverty-related diseases (*e.g.* malaria, helminths, tuberculosis, and leprosy) was an integral part of the chemical and pharmaceutical companies until the 1980s, this important research and development (R&D) thrust rapidly decreased during the 1980s and 1990s. R&D of new drugs is cost-intensive and the returns on investment for products addressing the needs of the world's poorest populations were insufficient to finance the research and development of NTDs. Roche, who had been pioneering malaria drug and vaccine development for decades, abandoned malaria research in the mid-1990s. The drug pipeline for treating one of the most severe public health problems in the global South was in danger of drying out. Today, however, the «lost decade» of the 1980s is only faintly remembered. Since then, Basel and Switzerland more broadly have witnessed the creation of new models of cooperation between pharmaceutical companies, academic research organisations and global stakeholders, which have given a huge boost to the development of drugs against malaria and NTDs.

We asked ***Lutz Hegemann***, Head of Novartis Global Health and Sustainability and ***Marcel Tanner***, President of the Swiss Academies of Arts and Sciences, what has changed over the past 30 years and what needs to be done in the future to ensure that the poorest of the poor also have access to important therapies.

Marcel Tanner, with its powerful pharmaceutical companies, Basel has always been a hotspot for innovation as well as drug discovery and development. However, in the mid-1990 leading companies such as Roche abandoned their malaria research branches for economic reasons. R&D for drugs against poverty-related diseases was in danger of being discontinued. How could this be prevented?

Marcel Tanner*:* "The situation in the 1990s was stuck in the sense that we had some promising tools to efficiently control poverty-related diseases such as malaria, for instance, but that new forms of partnerships between industry and academic partners to further accelerate the innovation process were sorely sought for. The academia tended to just ask for money from the pharmaceutical industry and thought they could do everything on their own. And the companies argued that markets for drugs against

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diseases of poverty did not offer them clear returns on investments made. In the 1990s we could profit from this unique insight that we were all sitting in the same boat to contributing to solve major global public health problems. Specifically, we discussed new public-private partnership models, which brought the industry and academic partners together under new auspices. We set up a so-called, international 'Strategic Project Preparation Group' with 12 members from the public and private sectors. I had the privilege to act as secretary on behalf of the Swiss government. Originally, the project was intended to stimulate research and development of new drugs against various neglected diseases but later it was argued that the initiative should first prove itself in one disease before developing a portfolio across other infectious diseases of poverty and NTDs. This explains the creation of Medicines for Malaria Venture (MMV) in the late 1990s and its focus on malaria only. Five years later followed the creation of the Drugs for Neglected Diseases *initiative* (DND*i*), founded in the wake of the Nobel Prize awarded to Médecins Sans Frontiers (MSF), finally also the Foundation for Innovative Diagnostics (FIND) was created."

Lutz Hegemann, one of the still most effective drugs against malaria is Novartis' combination therapy artemether-lumefantrine (known as Coartem), which has been provided to people at cost price in endemic settings since 2009. What interest does Novartis have in investing in the development of therapies against poverty-related diseases?

***Lutz Hegemann**:* "I see malaria drug development as part of the DNA of Novartis. To date, we have delivered over 1 billion doses of Coartem to the world's population without any profit to the company. We have also developed a paediatric formulation together with MMV. The long tradition of Novartis in R&D against NTDs, starting with leprosy, is a great motivation to continue in this field. For me, it has always been a big priority to develop a successor to Coartem, in case Coartem loses its efficacy due to the development of resistance. At the moment we are testing a compound from our own research at the Novartis Institutes for Biomedical Research in a phase III trial, which was developed together with Swiss TPH among others."

Swiss TPH's collaboration with Novartis was already very pronounced during the development of Coartem?

***Marcel Tanner**:* "The development of Coartem has historically been independent of MMV, but derives from Ciba-Geigy's activities in the search for a new anthelminthic drug. After a visit to China in 1995, Ciba-Geigy employees by chance were made aware by the Chinese of the antimalarial properties of Coartem, the combination of artemether with lumefantrine. The Chinese had extensive data on how the drug worked in adults. But there were no children data. We were therefore able to work with the Ifakara Health Institute (IHI) in Tanzania and the London School of Hygiene and Tropical Medicine (LSHTM) in the United Kingdom and the MRC Center in the Gambia to jointly conduct important phase III trials in children in Tanzania and the Gambia to fill this gap and to reach the fast-track registration of Coartem. It is these examples of partnership that ultimately spurred the creation of MMV."

Lutz Hegemann, what is Novartis doing to propel the R&D process for NTDs beyond malaria drug development?

***Lutz Hegemann**:* "In 2022, the company signed the 'Kigali Declaration of Neglected Tropical Diseases' and committed to invest US$ 250 million over the next 5 years in R&D for new drugs against diseases of poverty. Besides malaria, the Novartis commitment also covers a series of NTDs, including leishmaniasis, Chagas disease, cryptosporidiosis or dengue fever."

***Marcel Tanner**:* "The difference between malaria and the NTDs is that for malaria we formulated a consistent R&D agenda in the course of the elimination strategy in 2007, that prioritizes the R&D research questions to be tackled. Such a generally supported agenda does not yet exist for NTDs. Thus, in the absence of these global R&D priorities, the Novartis Institute for Global Health Research (known until 2023 as Novartis Institute for Tropical Diseases, NITD) and other institutions in the field of NTDs still have to rely on their internal strategies that in turn may fragment coherent and effective progress."

The development of new therapies and the validation of their safety and efficacy in clinical trials is undoubtedly central. But equally important is the distribution and access of disadvantaged people to such therapies. What are the challenges here?

***Lutz Hegemann**:* "In the public discussion, pricing is often seen as the biggest barrier to people's ability to access a drug, and in many cases this is true. Leprosy, however, paints a different picture. Since 2000, Novartis has made its multi-drug therapy available free of charge to patients worldwide through the World Health Organization. And yet there are still patients who do not receive therapy. The problem lies in the robustness and performance of the health systems themselves. Especially in the case of diseases with strong stigma, we need to ensure that people are diagnosed, drugs are delivered even to the remotest corners of the country, and that medical follow-up examinations take place. All this cannot be taken for granted."

***Marcel Tanner**:* "The most important determinant of community effectiveness is the degree of decentralization of health systems. The more decentralized a health system is, and the more powerful local governments are, the better integrated control and elimination can be tailored to a given setting and thus, the better is people's access to essential medicines, care and prevention. It is important to see that the health system not only comprises the public system but the whole public-private mix, including non-governmental organizations and charities. Therefore, cooperation between the global public-private partnerships and all the different actors of the national health systems is essential in the distribution process."

How would you assess Basel and the greater region as an innovation hub for the development of new therapies for neglected tropical diseases? Do we need new forms of public-private partnerships today?

***Lutz Hegemann**:* "In Basel, the Swiss TPH is a central cooperation partner of Novartis. What is important in drug development is an iterative process along the entire value chain from innovation, to validation of new compounds, to implementation of the programmes. I have just returned from a visit to the Centre Suisse de Recherches Scientifques en Côte d'Ivoire (CSRS), a close partner of Swiss TPH. The CSRS and the Swiss TPH are very well placed to implement new innovations in health systems in the countries of the South."

***Marcel Tanner**:* "The CSRS is, after all, part of the European & Developing Countries Clinical Trials Partnership (EDCTP), another key player in R&D of neglected diseases. It is precisely through this collaboration between Novartis, the Novartis Foundation, the Swiss TPH, the EDCTPs and other public-private partnerships that the Basel innovation ecosystem has a much greater impact today than in the past. It doesn't matter where exactly the various players are headquartered. What is important is that they work together iteratively and that everyone assumes their role and responsibility. And this is what we now need to do more of for a coherent R&D portfolio for NTDs, so that further innovations

will emerge in Basel and we will not restrict ourselves to just looking at a new drug, but will contribute with innovative tools and approaches to the universal access and thus to the well-being of a society with the limited possibilities that are available to us."

Lutz Hegemann (born 1966) leads the Novartis Global Health and Sustainability unit and is responsible for integrating environmental, social and governance (ESG) matters into the core of the company's business, with a special emphasis on innovation and access. The Global Health and Sustainability unit focuses on transforming health in low- and middle-income countries with programmes targeting malaria, neglected tropical diseases and non-communicable diseases such as sickle cell disease. It also represents the company's business in sub-Saharan Africa. Before taking on his present role, Lutz was Group Head of Corporate Affairs and Global Health. He has held roles of increasing responsibility since joining Novartis in 2005 in the Consumer Health Division. He began his career as a public health physician and scientist. Lutz Hegemann is a Fellow of the Royal Society for Tropical Medicine & Hygiene and serves on the boards of the Novartis Foundation, the Swiss Alliance against Neglected Tropical Diseases, the Tanzania Training Centre of International Health, PATH, and the Swiss Tropical and Public Health Institute.

Marcel Tanner (born 1952) is President of the Swiss Academies of Arts and Sciences, Professor emeritus of Epidemiology/Public Health and Medical Parasitology at the Faculties of Science and Medicine of the University of Basel and Director emeritus of Swiss TPH. As a member of the Advisory Panel of the Swiss National COVID-19 Science Task Force, he played an important role in advising the Swiss government and the population in better controlling the pandemic in Switzerland. Since 1977 and closely linked to Swiss TPH and Africa and Asia, his research focus ranges from basic research on the cell biology and immunology on malaria, schistosomiasis, trypanosomiasis, filariasis and HIV/AIDS to epidemiological and public health research on risk assessment, vulnerability, health impact and district health planning. Besides research, he contributed considerably to capacity strengthening and North-South partnership as reflected in his thrive to develop the Ifakara Health Institute (IHI) in Tanzania and the CSRS in Côte d'Ivoire. He has published extensively in many fields (>800 original papers). He also acts as advisor on communicable diseases research and control, health systems strengthening and capacity strengthening in various national and international agencies/bodies and in boards/committees such as University Hospital Basel, WHO/SAG, DND*i*, FIND, INCLEN-Trust, Gebert-Rüf Foundation, Fondation Botnar and as High Representative North of EDCTP.

Received: July 12, 2023

[1] Interpharma, Ed. Pharmastandort Schweiz: **2022**, Basel.

The definitive version of this article is the electronic one that can be found at https://doi.org/10.2533/chimia.2023.613