

# **Access to health products: which priorities and what role for MSF ? Workshop report**

Michaël Neuman  
Natalie Roberts

Edited by Madoulika Cordier, Marc Le Pape, Michaël Neuman and Natalie Roberts

# ACCESS TO HEALTH PRODUCTS: WHICH PRIORITIES AND WHAT ROLE FOR MSF?

WORKSHOP REPORT

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# GENERAL PRESENTATION OF THE CAHIER

The Covid-19 epidemic has brought back to the fore recurrent debates on the barriers to access to medicines, diagnostic tests and vaccines. MSF has been involved in these debates since 1996, leading the association to first launch the Campaign for Access to Essential Medicines (initially known as the CAME, now renamed the MSF Access Campaign) in 1999, and then to support the creation of the Drugs for Neglected Diseases initiative (DNDi) in 2003.

For some in the association, global systems, notably rules around intellectual property, are primarily responsible for the inequalities in access to medicines. Over the last decade MSF's public communications on the subject, led by the Access Campaign, have largely reflected this analysis. However, others question the impact of this approach, and the potential of a predominant focus on campaigning for changes to global systems of patents and drug pricing to effectively address the problems faced by MSF teams and other practitioners in the places where MSF works.

It is in this context that the CRASH organised a two-day online workshop on 3rd and 4th February 2022, aimed principally at the directors and operational managers of MSF Operational Centre Paris, as well as members of the Access Campaign based in the Paris office, to help enlighten our colleagues on current debates, and to determine together which elements of the discussion would be the most relevant to resolve to support the advancement of MSF OCP's operational projects. Is Access to Medicines the same issue today as it was when MSF first became interested in the mid-1990s? Rather than just concentrating on the obstacles to accessing medicines, should the debate be broadened to encompass what are now called 'health products' or even further, towards access to care and thus largely structural problems of human resources, financing, or the absence of national health insurance policies?

We aimed to address these questions via four roundtables that each examined an important issue we want to tackle together, selected from current and future struggles felt to be priorities in our practice and our operational portfolio: vaccines for tuberculosis, malaria and beyond; the approach to tuberculosis and antibiotic resistance; the management of cancer patients; and issues in nutrition, malaria and paediatric health in general. To begin each roundtable we invited a small panel of people with a particular viewpoint of the subject to first provide their perspectives on the landscape, experiences and possibilities upon which MSF could develop, before opening the discussion more widely to the operational managers and other participants via Zoom. Although for reasons of manageability of an online discussion we had to limit the number of participants able to interact directly via their camera and microphone chiefly to OCP's operational managers, we extended an invitation to colleagues from the MSF OCP medical department, the Access Campaign, Epicentre, and other



Operational Centres to observe the workshops via a live stream, and to engage in the debate via the Live Chat function.

During the workshop we suggested to start each round table by defining therapeutic indications: for what purpose do we want to prescribe, and for whom? We then attempted to discuss what prevents us from doing so, illustrated by obstacles encountered in particular situations. To help frame those reflections we established a non-exhaustive typology of possible obstacles, which was circulated to participants in advance of the workshops. Finally, we requested participants to propose or conceptualise some solutions that could be envisaged for these problems, notably via the actions of MSF. The discussions were held in French and English, with simultaneous translation.

Prior to the workshop we organised a series of video interviews to solicit the views of experts external to MSF on the evolution of the pharmaceutical landscape and the circumstances of the development of drugs and health products today. The resulting video, with subjects that range from pre-development to distribution, via patents and quality-related issues, was circulated in advance to all workshop participants. We extend our grateful thanks to those experts for taking the time to describe their work to us; their in-depth knowledge and clear presentations make comprehensible even complex subjects that were previously unfamiliar to many of us. We highly recommend watching the video, which is available on the CRASH website, before reading this cahier:  
<https://msf-crash.org/en/conferences-debates/doing-drugs-video-briefing-access-medicines>

We find the workshop discussions extremely rich, in their density and complexity, as well as in the range of experiences and perspectives of the participants. Twenty-five years after MSF first became interested in the subject, a healthy debate continues about how best to address barriers to accessing medicines, tests and vaccines via our medical humanitarian practice. We hope these discussions will inspire and encourage practitioners from MSF and beyond to reflect on their work and the work of the association.

**Natalie Roberts**  
**Michaël Neuman**  
**Jean-Hervé Bradol**

## DIFFERENT OBSTACLES TO ACCESSING MEDICINES ENCOUNTERED BY MEDICAL HUMANITARIAN PRACTITIONERS

This is an attempt to outline a non-exhaustive typology of the obstacles encountered by practitioners in accessing medicines and vaccines:

1/ Useful, even indispensable, products, whose production has been halted because the market is too small. In the 1990s drugs prescribed against Human African Trypanosomiasis (HAT) and antibiotics for epidemic forms of meningitis saw their production and distribution abandoned - by the pharmaceutical company in one case, and by the manufacturer in the other. A similar contemporary situation is related to raw materials: some pharmaceutical companies have stopped manufacturing drugs for which there are generic versions, because they are not profitable. This means that they may also no longer produce the raw materials used to manufacture those products (China and India produce 80% of the world's active pharmaceutical ingredients), with the knock-on effect that they may also cease manufacturing other drugs that use the same raw materials, because they are in low demand or have low profit margins, but for which there are no generic versions.

2/ Useful, even indispensable, products whose prices are too high to prescribe them on the scale they are needed. This phenomenon is related to monopolies made possible by the globalization of intellectual property rules applied to the health product industry since the 2000s (an example of this is Sofosbuvir, and the way in which prices were set).

3/ Products that are necessary but non-existent because of a lack of necessary research into the treatment for diseases that affect the poorest people in particular. This category refers either to the absence of products for the treatment of neglected tropical diseases, or to the availability of products whose specifications (e.g. a cold chain of minus 80°) make their use difficult in the often precarious conditions of our work.

4/ Obstacles created by MSF's partners (usually ministries of health) or by MSF itself. This was the case when MSF rejected prescribing treatment for patients with extra-pulmonary tuberculosis or refused to modify its treatment or care protocols for malaria in Burundi, for trypanosomiasis in Angola, and more recently in the response to Ebola epidemics. The weakness and venality of some ministries of health should not be ignored here.

5/ Problems - complex requirements, slow procedures, lack of competences, influence of pharmaceutical companies - with the regulatory institutions that issue authorizations for the use of products at national or international (e.g. WHO prequalification) levels.

6/ The plethora of generic products, the quality of which is difficult, if not impossible, to determine, and for which prices can remain relatively high.

7/ Access to medicines is not a substitute for access to care. Some within MSF believe that access to medicines is just one of many barriers – and perhaps today far less crucial than others - to access to care, and that the real focus of the organisation should be to prioritise its influence and resources to improve “access” in a broader sense.

# INTRODUCTION

## by Jean-Hervé Bradol

My name is Jean-Hervé Bradol, and I'm a medical doctor. I've been working with Médecins Sans Frontières long enough to have been the Director of Operations in Paris when the Campaign for Access to Essential Medicines was launched in 1999, and as such I was a member of its first Steering Committee. I would like to take this opportunity to honour the memory of the Steering Committee colleagues with whom I worked at the time that are no longer with us. I am thinking, in particular, of Francine Matthys, Marcel Van Soest, and obviously Jacques Pinel. I would also like to take this opportunity to salute the other members who are still with us, people like Rafa Vilasanjuan and Jean-Marie Kindermans, with whom I worked for years on the issue of access to medicines.

### 1. INITIAL DIAGNOSIS AND ORIGINS OF THE CAMPAIGN

So how did MSF come to be involved in this issue? For reasons both good and not so good. For reasons both operational and institutional. It's not that institutional reasons are, in and of themselves, bad, but they are a little different. In the mid-1990s, our Cold War "refugee" programmes were in the process of closing, one after another. We had emerged from a global context of East-West confrontation, and the processes by which refugees were being produced were changing; you could say that MSF – and MSF France, in particular – was losing part of its operational "market" and so was looking for other areas of involvement. Responding to infectious diseases, both epidemic and endemic, was an obvious choice, because there were situations in the field that were starting to become really critical. One problem in particular was that there were some medicines that would have been very useful to us but were inaccessible due to very high prices. I'm thinking about antibiotics like second generation quinolones – Bayer's ciprofloxacin, for example. Those very high prices were obviously often locked in by patents, by intellectual property rules. For years there was little to no generic production for certain types of drugs, so they remained very expensive, and that prevented us from using them. At that time, we needed ciprofloxacin throughout the Great Lakes region and East Africa to deal with huge outbreaks of infectious bloody diarrhoea caused by a bacterium susceptible only to second generation quinolones. Patients were dying because we didn't have access to those types of drugs. In addition, new drugs that could have been produced through research weren't being developed; there was what we call a fatal imbalance – that is that most, say 90%, of the research energy and funding was going to diseases affecting rich countries, with a morbid competition between pharmaceutical companies. They were all trying to fill the same niches by copying their competitors' reference drugs. I'm thinking of the many copies of non-steroidal anti-inflammatory drugs that, even worse, turned out in the end to be toxic. So, as we said at the time,

there was no research at all happening for 90% of the world's population. Sometimes we were able to take advantage of veterinary research. Ivermectin, for example – which was a very useful drug in many fields at the time, in particular for river blindness, or onchocerciasis. Ivermectin was originally reserved for veterinary use and was donated by the manufacturer, Merck, in 1987. I'm also thinking of how we found new uses for older products – for example, using oily chloramphenicol to treat meningitis cases during outbreaks.

We also had to deal with the fact that useful, effective drugs were starting to disappear. For lack of a big enough market they were no longer being produced or distributed. With oily chloramphenicol, we realised at the time that the only manufacturer – who, if I remember correctly, was located in Lebanon – was in the process of halting production. The drug was therefore going to vanish at a time when it was the main antibiotic for controlling bacterial meningitis outbreaks. It was the same for the drugs used against sleeping sickness, melarsoprol and lomidine, which were also starting to disappear. The pharmaceutical company that distributed them didn't have a big enough market to continue. When stocks were being liquidated in the mid-1990s, the only way the pharmaceutical companies would agree to continue providing the drugs for sleeping sickness was if our logistics hub would take charge of the worldwide distribution.

There were also essential medicines that had become ineffective but weren't being replaced. During the 1990s and early 2000s there was a resurgence of malaria outbreaks, especially in Africa – in Sudan, Kenya, Ethiopia, and Burundi. The *plasmodium falciparum* responsible for the deadliest forms of malaria had become resistant to older drugs like chloroquine and Fansidar in a very high percentage of cases (one or two out of every three cases, depending on the situation). Yet no other treatment options were added to African national protocols until the mid-2000s. The same was true for antibiotics. We went from a world where co-trimoxazole – known by its brand name, Bactrim – was used for pretty much everything, from head to toe, for all types of infections, to falling victim to a lack of basic antibiotics once many organisms had developed resistance to co-trimoxazole. We found ourselves in a therapeutic stalemate for situations as simple as treating cystitis, i.e., bladder infections, in women.

There were also situations where medications that were essential were highly toxic and also losing their effectiveness. That was the case with the arsenic-based agents for sleeping sickness. Although the side effects were pretty dreadful, there were no other options at the time. We were killing from two to ten percent of our stage 2 sleeping sickness patients with melarsoprol. It was especially depressing in northern Uganda, when we – myself included – would inject dozens or even hundreds of patients with this type of drug and kill some percentage of them. And to make matters worse, as time went on the parasite – the trypanosome – became resistant to these arsenic derivatives, so the cost-benefit ratio of those highly toxic treatments was becoming worse and worse.

So, those were all situations we were starting to see at that time, and that we communicated to the outside world for the first time on MSF's 25th anniversary (1996), at a medical symposium on the

response to epidemics and infectious diseases. For the symposium's fourth session, we invited Patrice Trouiller, a pharmacist from the CHU (University Hospital) de Grenoble, to explain the mechanisms at work in creating the shortages that I have just summarised briefly.

## 2. DETERMINANTS OF THE MID-1990S PHARMACEUTICAL LANDSCAPE

When preparing this presentation, I tried to understand the major determinants that shaped this situation. I see four of them.

- a. The first determinant is that infectious diseases are caused by living organisms. In that sense they are special diseases; viruses, fungi, bacteria, and parasites adapt to the therapeutic response to them and develop resistance. In the 1990s there were emerging diseases – HIV, obviously, but also others, like Ebola. In addition, diseases that we had believed to be under control, like TB and dengue, were re-emerging. It is often said that it was a time when we thought we could put an end to infectious diseases. In reality, throughout history there have been people determined to end these diseases – not just for health and medical reasons, but for political and economic ones as well. Despite the remarkable triumph over smallpox, there have always been people who realised that victory in this area would be hard to achieve (again, because we are attacking living organisms that learn how to defend themselves). In fact, the people who led the effort to eradicate smallpox worldwide, who were then tasked by the World Health Assembly with determining whether such eradication would be reproducible for other infections and other endemic outbreaks, answered “no”. They felt that smallpox had unique characteristics without which a victory in the form of eradication on a global scale would be hard to imagine. Those characteristics included smallpox's very dramatic early clinical symptoms, the human-only reservoir for the virus, the existence of a particularly effective vaccine, and injection techniques well-suited to mass vaccination campaigns. The work's authors concluded that there was little chance of finding those conditions again and so of being able to eradicate other infectious diseases. Meanwhile, in the 1990s some very powerful institutions – I'm talking about the United States National Academy of Medicine (with regard to medicine and health), and the CIA (with regard to public safety) – produced a report on the public safety threat posed by the HIV epidemic. There was an awakening regarding the urgency of re-energizing the fight against infectious diseases.
  
- b. The second determinant was that at a time when there was little interest in finding new treatments for infectious diseases, and when the situation I described in the introduction was allowed to set in, what were we doing? We believed then in a big idea, in a definitive solution to health and medical inequality – the doctrine of health development. I think that as that period recedes further and further into the past it's hard to conceive of what that might have been, but it was really very ambitious. At the 1978 Alma-Ata conference, the various healthcare actors present set a goal of “health

for all by the year 2000". A list of diseases and populations was prioritised according to epidemiological burden and possibilities for prevention and treatment, and a list of essential medicines was drawn up. The term "essential medicines" refers to the WHO's effort to create a standardised list of medicines and the protocols for using them, which was a truly remarkable step forward. At the time, in France, the official dictionary of medicines, the VIDAL – the big red dictionary that many of us used – contained six thousand references. The WHO's list of essential medicines has only a few hundred. So it was a much-welcome rationalisation that had a tangible, practical impact on prescription quality. There was also the aim of immunisation for all of the world's children with the same six vaccines, which began in 1975 and expanded significantly in the 1980s. While MSF initially participated in that in some countries, such as Yemen, we soon realised we weren't the best organisation for those types of development programmes. The experience did, however, help us incorporate and learn how to manage mass vaccination campaigns – something that might be useful in emergencies. The human resources most important to the health development objective were health workers – that is, health technicians, rather than nurses or doctors. Financing for the worldwide effort to reduce inequality came both from public funds and cost recovery. It was a time when governmental authorities no longer wanted to finance social and healthcare spending, so users were asked to cover some or all of the costs – something they had trouble doing in health programmes where patients were only half convinced of the utility. By the mid-1990s, that "health utopia", as Rony Brauman put it, yielded both valuable working tools and frequent setbacks and failures. There were, for example, health systems where ineffective malaria drugs were being prescribed without any serious diagnosis. Most prescriptions for infectious diseases called for drugs that had become ineffective as resistance developed. So, there's your answer: if we didn't take an interest in the lack of health products and medicines effective against infections sooner, it was because we were busy with other things. We were busy participating in a massive development effort that was ultimately, at least in part, an illusion. We still believed in it, I'd say, when we were working in the field in the '80s and '90s. Some teams continued to believe in it into the early 2000s. I'm thinking about MSF teams in the DRC and Sierra Leone, who put respect for the standardisation sought by the national health authorities and the WHO above adopting new malaria treatment protocols. Even when we tried – like during the 2002 malaria epidemic in Burundi – to request exemptions from standardised protocols because of a massive deadly outbreak and the ineffectiveness of the current treatments, we were refused not just by the governments and international organisations like the WHO, but by our own colleagues as well. We faced a lot of reluctance from the latter because they felt that it side-tracked them from their primary goal, which was finding the solution to health inequality on a global scale, which was supposed to be health development in all its various components.

- c. The third determinant was the triumph of liberalism and globalisation in the late '80s and early '90s. With the Cold War over, one economic system had achieved total victory over the other and there was a kind of euphoria among the international economic organisations. I'm thinking of the International Monetary Fund and World Bank's "structural adjustment" policies, which bled

entire sectors dry – healthcare, social assistance, education, and culture. It was felt that private initiatives should cover the expenditures in these sectors. All government and national organisation budgets for those sectors were scaled back, which was catastrophic for hospitals and clinics. Jean-Pierre Olivier de Sardan and Yannick Jaffré wrote a book about the impacts of those policies, entitled *Une médecine inhospitalière*, which describes these phenomena in West Africa. Those policies could also be seen in the globalisation of intellectual property rules for the pharmaceutical industry. The mechanisms that enabled generic drug production irrespective of patents were ending. We were, however, able to make generic antiretrovirals with some large Indian generics companies – for example CIPLA, with whom we had a very productive partnership in this area. All the opportunities, the exemptions, the small openings were coming to an end, as some powerful governments and multinational pharmaceutical companies were trying to globalise the intellectual property rules. It was a completely strategic objective for them, as U.S. Trade Representative Robert Zoellick said at the time, when ordering forty or so pharmaceutical companies suing the government of South Africa for failure to respect intellectual property rights to stop. He told them, if you do this you will create so much more hostility in the world that we won't be able to globalise intellectual property rights. They had to agree to be a bit flexible with a few drugs, in order to achieve their aim of generalising the intellectual property rules for the pharmaceutical trade.

It was also a time of simplistic ideas about public health and its economy. I view three as having acted as ideological drivers.

The first was that *an ounce of prevention is worth a pound of cure*. That old adage was singularly disproven by the experience with HIV, where there was no conflict between curing the disease with a curative treatment and preventing it, as had previously been the case with other diseases. Thus far, with HIV, looking for a treatment that, if not curative, is at least suspensory, has been a good idea because the attempt to halt disease progression has in many cases also interrupted virus transmission – between sex partners, in particular.

Another big idea that often slowed public health progress was that *it's better to be done with it once and for all*. That's the eradication fantasy. If national and international health authorities were to be believed, measles should have been eradicated by 2015. The corollary of that idea is that you must choose areas where you can envisage “being done with something once and for all”, and that those should take precedence.

The last big idea was that *it's better to limit health spending*. Free-market thinking likens such spending to social assistance, which supposedly makes people dependent and lazy. But health care budgets had to be increased, for example, to treat malaria in sub-Saharan Africa by switching from chloroquine and Fansidar to a new generation of drugs, the artemisinin-based combination therapies. The cost of one treatment rose from a few dozen cents to a few euros. It took time to accept that increasing malaria-fighting budgets was essential. Bigger budgets were needed not



just for the drug itself, but also for pairing effective treatment with effective diagnosis, which meant paying for rapid diagnostic tests. And then – even though it obviously couldn't replace treatment – prevention (like distributing insecticide-treated mosquito nets) was still useful. All of that added to the budgets that had to be allocated to medical activities and public health, in a context where those expenditures were deemed harmful to the economy and the prevailing economic model.

- d. The final determinant that I observed with regard to access to medicines was the negligence, and subsequent mobilisation, of the healthcare actors. In my opinion, we ourselves were our own biggest enemy to ensuring an array of effective medicines for the principal treatment indications of our medical practice. I give this example fairly often. In 2000, all the MSF medical directors issued a resolution that was published and sent to all field teams in three languages (English, French, and Spanish), where they claimed that antiretroviral use wouldn't be possible in Africa – maybe not forever, but in the immediate future – despite the fact that sub-Saharan Africa was where the HIV pandemic was growing the fastest. The situation in southern and central Africa was dire. I'm just summarising, but you can see that the biggest enemy was us, in that situation. Many of us resigned ourselves to the shortage by saying “we aren't working for the short term anyway, we're working toward a comprehensive solution” – that is, the global health development plan. But at the same time, that negligence by the usual actors was accompanied by new forms of mobilisation and new alliances with new actors that made an enormous contribution. To fight HIV, we (it couldn't hurt just this once) built and maintained productive relationships with patient, researcher, practitioner, and human rights organisations – LGBT rights organisations, in particular. We also renewed our alliances with people and organisations that had historically worked on access to medicines issues. I'm thinking of Ellen 't Hoen, my eminent colleague from Health Action International – people who were working on these issues and who educated us about the mechanisms that lead to shortages. This determinant, which I would call subjective – our own beliefs, attitudes, and alliances – functioned both as a set of obstacles and advances. With sleeping sickness, for example, once we had alternatives to arsenic-based treatments it still took a huge amount of pressure to get our teams in Angola to accept them. They didn't have much problem with prescribing melarsoprol, even though they killed some of their patients while trying to cure them of the parasitic infection. But again, we also got the opportunity to meet new partners who taught us how to advocate.

### 3. CONCLUDING REMARKS

To finish, I'm going to offer a few points designed to stimulate reflection by mentioning some of the comments made at the time. I remember that when the Access Campaign's sponsors and creators came to present it to the Board of Directors in Paris, some board members remarked that perhaps

it would be better to talk about “neglected patients” than about “neglected diseases”. I think that intuition was a good one. Neglected patients and countries are one thing, but we don’t often think about the fact that, in absolute numbers, most of the world’s poor live in so-called “middle” countries in terms of income and economics. Members of the middle class can have very little access to the distribution networks for drugs that are absolutely essential to their lives and their survival. I’m thinking of cancer drugs right now. When we question our fellow doctors in middle-income countries, they all report how difficult it is – even when they have the budget for it – to access cancer drugs. I’m also thinking of specific patient populations for which we’ve always had to make a special effort – like drug users, where access-to-care issues due to their social situation are a more important consideration than anything disease-related. The same is true for people who engage in stigmatised sexual practices, including sex work, for whom we really have to mobilise because they often have significant health problems. It would be better to identify them by their social situation and the discrimination they face than as people with neglected diseases.

MSF’s Access Campaign still has some blind spots:

- Criminality in the pharmaceutical trade (poor quality, trafficking): The big pharmaceutical companies understand this well, since they play the “white knight” in this area.
  
- Drug safety: There’s a problem with liability – legal liability in case of an accident with the drugs. During the COVID-19 epidemic, the big pharmaceutical companies forced countries and private operators like us to assume legal liability in case of accidents with some of their products. How to respond? That’s a question we’re going to have to drill down into in the future, though this isn’t a new problem. During the H1N1 epidemic in 2010, countries like Poland didn’t buy any vaccines because they refused to assume liability in case of serious accidents.
  
- “Humanitarian marketing”: There have been efforts to develop certain products. Some products, however, need more social and political marketing. I’m thinking of products that haven’t been used enough – like Epicentre’s Africa-specific rotavirus vaccine, newer generation TB drugs, and therapeutic foods for malnutrition.

I’m going to end with the Campaign for Access to Essential Medicines itself. We created a new kind of institution, a totally worthwhile, productive innovation in the Médecins Sans Frontières universe. But it poses a problem that isn’t new – is this a never-ending campaign? Because a campaign is understood as something that’s time-limited, towards a specific objective. I believe that the people who started the campaign were thinking about a period of a few years – four or five years – which for many was the 2000-2005 Campaign. That ended long ago, and it’s impossible to have a permanent ongoing campaign without becoming a political actor proposing comprehensive, partisan solutions. One of the difficulties in how the campaign has evolved has been in accepting that we can’t have institutional sustainability without relying on an ideology that has little to do with addressing concrete problems – for which in many cases we have now found pragmatic solutions.

Yet I think that we're shifting in the direction of ideological activity; we saw this with COVID, where according to MSF and the Access Campaign the lack of vaccines in the Global South was caused by intellectual property rules. That claim, as it turned out, was totally unfounded. Know-how, not patents, was the most critical factor. Fairly early on, Moderna offered not to protect the patents for its COVID vaccine. MSF and the Access Campaign's quasi-automatic reflex was to blame intellectual property, while a different mechanism was at work in that case. And then there was the almost automatic reaction that if a new product comes out, the whole world, the poorest – Africans, in particular – should get it on a large scale, unless they only needed it for limited categories of at-risk people. For once, a demographic inequality was working in their favour; their population is, on average, much younger than that of Western Europe or North America, which meant that the COVID epidemic in those countries took a completely different form and was far less severe. We would hear MSF and its Access Campaign saying in the media that it should only take a year to vaccinate 70% of the entire world with two doses. That was a ridiculous proposition, as it was neither desirable nor feasible. Furthermore, no one was asking the people in poor countries their opinion, despite the fact that many were reluctant to get vaccinated. When you're trapped in an ideology, in automatic thinking, it's hard to recognise and admit those kinds of errors. So, I'm ending on a slightly controversial note. But I would justify that by the fact that for MSF and the Access Campaign, controversy has always been a driving force.

# SESSION 1

## Vaccines for tuberculosis, malaria and beyond

The session is moderated by **Dr Emmanuel Baron**, General Director of Epicentre.

### PANELISTS

#### **Dr Gerald Voss**

Scientific Director of the TuBerculosis Vaccine Initiative (TBVI) and the Executive Director of SciPeo Srl, Science & People. Gerald previously served as the Interim Director of the Global HIV Vaccine Enterprise. In the past, he was with GSK vaccines overseeing the R&D portfolio for Diseases of the Developing World, where he established and lead Product Development Partnerships in HIV, TB and malaria with the International AIDS Vaccine Initiative, Aeras, the Malaria Vaccine Initiative and the Bill & Melinda Gates Foundation.

#### **Dr Natalie Roberts**

Medical doctor, a director of studies at MSF Crash and a programme manager at La Fondation MSF. Previously Emergency Cell manager for MSF Operational Centre Paris, in 2019 she led MSF OCP's involvement in a large clinical trial of an Ebola vaccine during the epidemic in Nord Kivu, DRC. She is also a member of the Steering Committee of the MSF Access Campaign.

#### **Dr Rebecca F. Grais**

Director of Research at Epicentre. Her primary areas of research focus on prevention of infectious diseases and emerging infections. She has particularly focused on population-based studies of the effectiveness of public health interventions and efficacy trials of novel vaccines and therapeutic agents. Her works focuses on research in conflict and epidemic settings.

**Introduction by Emmanuel Baron:** “The aim of the session is to give some perspective to this audience, people from MSF and outside, and in particular the MSF decision-makers, about what MSF could reasonably do to improve access to vaccines in the places where our teams work.

The panelists will try to better describe the landscape, experiences and possibilities upon which MSF could develop to improve access to vaccines, and to elaborate further the action for access to better new or more adapted vaccines in the areas where MSF works. First there will be a presentation of the landscape of research and development of vaccines. Who decides which vaccines will be developed and which diseases will be targeted? Who sets the priorities, how is a vaccine developed, what are the different steps, and who are the different actors in this ecosystem? Then we’ll move onto the reality of the situations and the contexts where MSF works. What vaccines are needed, and why? Finally, we’ll address how clinical research, including that of MSF, has and can improve access to vaccines.”

**Gerald Voss:** “The development of new vaccines or drugs can be divided into discrete stages, starting with discovery, moving through pre-clinical then clinical development, and finally, registration and launch. As you move along this pathway, from very early stages to discovery, on to clinical development, and then launch, the technical and scientific risk decreases. If you’re working in a lab and researching an entirely new vaccine from scratch, there’s initially a very high risk of failure, both scientific as well as technical. But as you move into clinical trials and late clinical trials to investigate the efficacy of a new vaccine, the risk diminishes. On the other hand, the further you move along the development pathway, the more expensive the process becomes. The early stages can be achieved with a relatively limited budget but, for example, large-scale efficacy clinical trials are a substantial investment, financially as well as in terms of other resources. So, the gradient of risk diminishes as the gradient of investment increases.

There are discrete points and times in the development of new vaccines where it is necessary to stop and review all the data and information about the vaccine, to decide whether to make investments into the next stage. So, in the development of new vaccines, we make a series of investments at risk. If all goes well, you can move on to the next stage. In most cases, unfortunately, the approach doesn’t work, and the investment made up until then is lost.

In terms of who is deciding, and on which criteria it is decided that we should work on a particular target, there are a number of considerations. One is the medical need, which I think is the overriding consideration. If there is an infectious disease which causes big unmet medical needs, it makes sense to try to develop a vaccine against that. In the early stages, the main actors are academic laboratories, small biotech companies, and to some extent larger pharmaceutical companies, but currently the process is being driven mainly by academic laboratories. Moving along the development pathway, towards initial human clinical studies, often there is a handover from these early players to more experienced vaccine developers that will usually license these early-stage programs and prototypes before investing in them and developing them further.

If the target is an infectious disease that has a global medical burden, then it's a straightforward endeavor because the eventual market is global, so it includes rich countries who are interested in, and who can afford to buy, the final product. It becomes much more difficult if the target is an infectious disease that affects disproportionately low and middle-income countries, in which case the usual business model doesn't really work. That's why for HIV, malaria or TB vaccines, for example, there are other business models called product development partnerships, where institutions like IAVI (the International AIDS Vaccine Initiative), DNDi (the Drugs for Neglected Diseases initiative), or other institutions that invest philanthropic and public money partner with more experienced development partners, sometimes really big pharmaceutical companies, to develop together new vaccines or drugs that don't have attractive commercial markets. That is a model that has worked, to some extent.

To summarize: vaccine development is a process that is staged and takes a long time. As you move along the stages you diminish the risk but must increase the investment. And there is unfortunately ultimately a high degree of failure.”

**Emmanuel Baron:** “The vaccine against tuberculosis, the BCG vaccine, is about 100 years old. What are the limitations of BCG? How come we have a century-old vaccine for a disease which is extremely prevalent and very deadly around the world? Are there any other vaccines in the pipeline against tuberculosis, and what are the obstacles today to a new vaccine against tuberculosis?”

**Gerald Voss:** “The TB vaccine, BCG, is the most widely used vaccine in the world. It is an old vaccine and was actually discovered and developed in France at the Institut Pasteur in Lille. It is used very widely, but unfortunately has limitations. The main limitation being that it works well against extra-pulmonary tuberculosis in infants but there are conflicting data in older populations like adolescents and adults. It is a puzzle that nobody has really understood, but the efficacy of the vaccine given to those older populations is less than optimal. Some studies show that there's no effect at all. One of the underlying reasons might be that from the original BCG strains, there have been many derivatives and different strains are used throughout the world now. The assumption is that these different strains are not equal. Maybe one of the causes of this discrepancy in terms of data may come from the use of these different strains, which are produced by different local manufacturers in many different places.

There are definite limitations to BCG, but it must also be recognized that BCG has unintentional benefits. There are many studies that indicate that vaccination with BCG at birth provides better general immune health, which also helps fight other infectious diseases in the young and vulnerable. That's one of the reasons why BCG vaccination at birth, at least for the foreseeable future, will still be common practice. But there's also a consensus that we would like to have better TB vaccines. I think the underlying problem is that it is a big scientific challenge. *Mycobacterium tuberculosis* is an intracellular bacterium and the immune responses required to fight or eradicate the bacteria are

quite complex. The determinants of the bacteria that must be targeted by a vaccine-induced immune response remain unknown. There are many scientific obstacles that have prevented the development of a new vaccine.

There is, however, at least one vaccine in development, called M72, which was initially developed at the pharmaceutical company GSK. That vaccine was tested in an advanced clinical trial in South Africa.<sup>1</sup> The outcome was that it was able to reduce the development of disease, or pulmonary tuberculosis, in latently infected people by about 50%. These initial efficacy signals in a controlled clinical trial were very encouraging. After that the vaccine was handed over to the Gates Medical Research Institute, which committed to further develop this vaccine with funds from the Gates Foundation. GSK has made a commitment to supply one of the important components of the vaccine, the adjuvant. There is also one other modified BCG vaccine that is currently in trials in India and in South Africa, that was developed by an academic institution in Germany and now has been licensed to the Serum Institute of India, who is producing the vaccine and is responsible for the clinical trials. We will see what the outcome will be. So, while we have some encouraging signs, there's still a long way to go and scientific obstacles remain.”

**Emmanuel Baron:** “BCG is the most used vaccine in the world. I heard 100 million doses per year are used, but I don't know if that's accurate. Why does MSF need another vaccine for tuberculosis? What would be the best characteristics of this new vaccine in order to make it easy to use, to make it efficient and scalable? How do we see that from the experience of MSF and tuberculosis?”

**Natalie Roberts:** “I checked with my colleagues in the medical department how many doses MSF uses of the BCG vaccine. Last year MSF administered 44,000 doses of BCG. Probably we're administering them to comply with national programs, mainly at birth, as recommended by the World Health Organization (WHO). Still, only 44,000 doses, if we think about how 100 million are given each year, is a small drop in the ocean.

I think the question is not only do we at MSF need a new vaccine, but would we even use a new vaccine, and who for? We don't use the vaccine we have now very much. Yet the incidence of TB is massive in many of the countries where we work. In 2016 the largest incidence of TB in the world, over 300 cases per 100,000 per year, was in countries in Central and Southern Sub-Saharan Africa, including the Central African Republic, the Democratic Republic of Congo, and Kenya. They have some of the highest incidence rates in the world and of course, along with that incidence comes huge morbidity and huge mortality. So, if we consider the massive global incidence and prevalence of TB, then there's obviously a global interest in developing new vaccines, as well as new products to treat TB. Gerald explained that medical need is an overriding consideration for which products

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1. Van Der Meeren, Olivier, et al. “Phase 2b controlled trial of M72/AS01E vaccine to prevent tuberculosis.” *New England Journal of Medicine* 379.17 (2018): 1621-1634.  
<https://www.nejm.org/doi/full/10.1056/NEJMoa1803484>

will be developed. MSF is not a global health actor in that way, meaning we're not responsible for global public health, but given that there's such high incidence in the places we have chosen to work, it seems that there should be some specific interest for MSF to see the situation improve for the people living there. Would that situation improve without a better vaccine? TB is a disease of poverty, like cholera. We can get rid of cholera in places where there's a major investment in sanitation, but that investment often doesn't arrive, so we can only avoid large epidemics by using the cholera vaccine. TB rates also decrease when people aren't living in overcrowded, poorly ventilated conditions. If we think about the places where we work, do we really believe the living circumstances of the population are going to improve anytime soon, or are we going to just continue to see this catastrophically high incidence at the general population level in some places, or in specific locations such as camps, detention centers and slums? As these circumstances seem unlikely to improve, I think we do need an effective TB vaccine, just like we needed to use the cholera vaccine.

But if MSF did have access to a new TB vaccine, would we use it, and who for? Are we not using BCG much because it's a bad vaccine, because it's not useful for our patients since it's only useful in infants? Or because in MSF we generally focus more on treatment than on prevention of infectious diseases, so we don't invest much in terms of preventive vaccination? Or because we're aware of our limits in terms of our impact on global public health issues? If we put the concept forward that prevention is better than cure, then even if we might not be aiming for an impact on a global scale, shouldn't we put resources into trying to prevent cases on a local scale in places with ultra-high incidence where we're already working? Where we're already putting large resources into trying to diagnose people with TB and treat them, maybe we'd be more efficient and effective if we also started trying to prevent TB, or at least limit the number of cases. If we had a new vaccine, we could start reflecting on targeting certain defined populations, hotspots, in countries such as the Central African Republic or the DRC where even if there are national vaccination programs, they are usually inefficient. But if we wanted to target specific populations for whom the situation is catastrophic and unlikely to improve any time soon, we'd have to think about how that would work. What vaccine would we need? Although BCG is not a great vaccine for adults, it's relatively easy to use logistically, it's not complicated to store, it's not too difficult to administer. If there was a new vaccine that was more effective in adults, ideally it wouldn't have a cold chain or it would need only a simple cold chain, because we would want to target those places where we know that national vaccination programs are weak. And of course, as TB is such a massive global problem, any vaccine would need to be able to be produced cheaply and at large scale. Then finally, it's always difficult to convince national authorities and regulators to incorporate new vaccines into their programs. That could be also a role that MSF could play if we wanted to target certain populations, to start discussing with the national authorities in those countries about how we could support them to integrate a new vaccine."

**Gerald Voss:** "I think there is an important concept behind that, and that is that BCG is used in infants, but as you say, Natalie, some of the populations that you are working with are not infants. It could be refugee camps, slums, et cetera. It's adolescents, it's adults. I think that the new TB



vaccines should precisely be targeting those populations, which are by the way, also the engine of the TB epidemic. It is adolescents and adults that are driving the epidemic, and BCG is not effective for them. A new TB vaccine would need to be able to target these different populations.”

**Emmanuel Baron:** “We are going to switch to another example, malaria. It seems now there is something occurring after years of failure. Is there a vaccine now? What’s the story of the RTS,S vaccine? Who decided what and when? And are there any other vaccines in the pipeline?”

**Gerald Voss:** “The malaria vaccine, RTS,S, is a striking example of vaccine development. In fact, the work on that vaccine started 35 years ago in the US, in a collaboration between the US army laboratories and the predecessor of what is now GSK. In the 1990s, this vaccine got a big push in terms of its development because of something quite unique, that for malaria we have at our disposal the human challenge model. We can basically, under controlled circumstances, infect vaccinated people with *Plasmodium falciparum* and then investigate the outcome. If there’s an established infection despite vaccination, we can then treat with chloroquine, because the strain used in the studies is sensitive to chloroquine. So, the model is safe for volunteers and has a huge advantage in that we can test vaccines on humans at a very early stage of their development. In the 1990s, there was the first sign in a study done at the US Army Walter Reed Institute<sup>2</sup> that the RTS,S vaccine in combination with an ingredient, an adjuvant, was able to prevent infection with *Plasmodium falciparum*. That was a huge, huge positive for the vaccine.

But it still took 20 years to further develop this vaccine. The problem was, again, that malaria vaccine was not really a commercially viable target. Initially, it was thought that there could be a market amongst travelers, but it turned out quickly that wasn’t the case. The primary focus was really infants and young children in Sub-Saharan Africa. To enable the further clinical development of this vaccine there was again a public-private partnership developed with the Malaria Vaccine Initiative and GSK, who executed a quite complex clinical development plan, carefully moving from the first clinical studies in adolescents, then into the field first in adolescents and older children and then younger children. This was complex research and took some time. Finally, a big field study confirmed the efficacy of the malaria vaccine at about 50%,<sup>3</sup> which is not what everyone had hoped for, but it was a substantial signal. There was also some economic and health modeling that indicated that the use of this vaccine in countries in Sub-Saharan Africa would have a significant public health benefit. The vaccine was then submitted to the European Medicines Agency (EMA) for regulatory approval, which was granted in 2015. On that basis, WHO prequalification and policy recommendation were sought. However, at the WHO Strategic Advisory Group of Experts on Immunization (WHO SAGE)

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2. Stoute, José A., et al. “A preliminary evaluation of a recombinant circumsporozoite protein vaccine against *Plasmodium falciparum* malaria.” *New England Journal of Medicine* 336.2 (1997): 86-91. <https://www.nejm.org/doi/full/10.1056/NEJM199701093360202>

3. RTS,S. Clinical Trials Partnership. “Efficacy and safety of RTS, S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial.” *The Lancet* 386.9988 (2015): 31-45. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(15\)60721-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)60721-8/fulltext)

at the time there was a bit of a roadblock. They took the position of, ‘We are not going to provide a universal recommendation, we want to have demonstration studies in selected countries.’ These demonstration studies were set up and were executed but took again several years. Eventually, the vaccine received a prequalification from WHO as well as policy recommendations, but it took five or six years between the first regulatory approval and the moment where this vaccine could actually be used. It’s an interesting example of how sometimes different actors don’t seem unanimously aligned in accelerating new interventions.”

**Emmanuel Baron:** “It seems this vaccine was not what MSF wanted or expected. Natalie, what was MSF’s attitude toward this vaccine and how do you see it being used in MSF programs?”

**Natalie Roberts:** “As far as I understand MSF also wasn’t particularly interested in this vaccine for a long time, and we also made that clear very publicly.<sup>4</sup> I think that stems from being unimpressed with the initial studies that Gerald mentioned, as it wasn’t looking like it was going to be a very effective vaccine, so some people in MSF started thinking it wasn’t going to be worth the effort. There is also the problem that four doses are supposed to be administered to children at a timing of around 6, 7, 9, and 24 months. When we consider how difficult it is in many places that we work for children to receive just one or two doses of the measles vaccine, it’s not that surprising that many in MSF said, ‘Well, if the vaccine is not going to be very effective and it needs a lot of effort to administer, we’re not interested in investing time or resources into demonstration studies or into accelerating its development.’

However, now we have understood that when this vaccine is used and combined with other interventions, notably seasonal malaria chemoprophylaxis (SMC) and bed-net distributions, both of which are activities that MSF already implements in many fields, then we see far more convincing results, particularly in those hotspots where malaria is such a huge problem today. For example, some of the demonstrations showed that when this vaccine was used together with SMC in Burkina Faso or in Mali,<sup>5</sup> there was a much bigger impact than when either was given alone, eventually resulting in up to a 70% reduction in hospitalization and mortality due to malaria. In fact, there was even a 50% reduction in all-cause mortality in these locations when the vaccine and SMC were given together. That’s a huge reduction in all-cause mortality, and it’s because in these hotspots a huge proportion of all deaths are due to malaria. So alone, it’s not a great vaccine, but when combined with other actions that we’re already doing, we could have quite a large impact in selected locations.

Ideally a better vaccine would emerge, and better vaccines probably will emerge. From MSF’s side, we’re starting to reflect now about whether we should get over the fact it’s not a great vaccine and

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4. Press Release: MSF response on WHO guidance on malaria vaccine RTS,S (2015). <https://msfaccess.org/msf-response-who-guidance-malaria-vaccine-rtss>

5. Chandramohan, Daniel, et al. “Seasonal malaria vaccination with or without seasonal malaria chemoprevention.” *New England Journal of Medicine* 385.11 (2021): 1005-1017. <https://www.nejm.org/doi/full/10.1056/NEJMoa2026330>

start supporting its use in malaria hotspots. In places such as in the Sahel and in South Sudan, every year our teams see huge catastrophic peaks of malaria incidence and mortality. Every year we open hundreds and hundreds of beds in our facilities, and recruit extra staff, and yet we are still very aware that many kids with malaria arrive to us too late, or don't arrive at all. In those places, we've already for some time been doing SMC and bed-net distribution. Collaborating with local health authorities to design and implement a complimentary vaccination strategy would seem worth the extra effort to try and reduce the number of hospitalizations and reduce the mortality. It's not the best vaccine in the world and we've been quite clear about that, but it is the only vaccine we have right now, and it does seem that it could be useful if we use it in the right way. But we're coming in at quite a late stage, so now the question we must ask is, even at this late stage, can we get our hands on this vaccine and start collaborating with authorities in some places we work to try and make it useful?"

**Emmanuel Baron:** "Rebecca, there were several studies of this vaccine. What were they and how did they increase access to the vaccine? Should or could MSF have been more involved? Do you see a place for MSF to engage in the different phases of clinical development of a new malaria vaccine?"

**Rebecca Grais:** "I do. Gerald briefly went over what some of the studies were. They happened in the clinical development phase, and then also after the rollout. When we talk about a vaccine being good or bad, there's a couple of things to keep in mind. Everyone agrees that a perfect vaccine would induce an immune response that is not only durable, but also broad enough to protect against any type of evolution or mutation.

RTS,S is not only the first vaccine against a parasite, which is an amazing achievement and something which we tend to underestimate, but it's also a product that is going to take much effort and many different groups to improve upon over time. Malaria is a parasite, it's not a virus, so comparing the malaria vaccine to what we've experienced with COVID is problematic. The parasite is a fully independent organism which needs only a few little things to survive, whereas a virus invades a cell and can't replicate on its own. The parasite people argue about whether malaria is 'alive' or not, but it's got everything it needs, it's been able to evolve over millennia and has become very advanced. So, the development of a vaccine for malaria is inherently difficult. When an infected mosquito bites a human, the malaria parasite migrates to the liver, where it replicates, and then infects further via the blood. The trick is to prevent it from getting to the liver, which means it cannot replicate. The RTS,S vaccine and another one in development, called R21, instead of targeting the parasite itself, target a protein that helps the parasite find the liver. Targeting this specific protein aims to prevent replication from happening, rather than infection, which would be far more difficult or impossible. So, this vaccine for malaria is not 100% efficacious, it's not that perfect vaccine that I described, but it can have an incredible impact.

The other vaccine in development, R21, is based on the same idea as RTS,S. It is essentially a cheaper version of RTS,S, and so probably will perform the same as RTS,S. Natalie was explaining the oper-

ational relevance of a malaria vaccine and how that could also potentially reduce burden on programs, but more importantly reduce the burden of disease in the populations where we have programs, so it is in our interest to increase access to the vaccines, and there are many places for MSF and all of its entities to intervene in this process of clinical development of this other vaccine, R21. A key point I'd like to make is that access isn't just about the final price. There's lots and lots of work done by many different groups that intervene at many points in this process. One can intervene at the beginning, in developing what is called a Target Product Profile (TPP). That's an important moment for MSF to raise its voice and establish the needs. What should a vaccine look like? What is it that we want it to do? What characteristics need to be considered as desirable or mandatory for the vaccine to be useful? The second part is during the process of development, during those phases that Gerald mentioned with the different stage-gate points and with an understanding that the overall risk in terms of a scientific risk may decrease over time, but the investment does need to increase.

There, MSF and Epicentre can participate during the development to intervene in that process, not only actively participating by conducting trials and participating directly, but also in terms of weighing in and ensuring that things happen, and different factors are considered. There's a couple of good examples of how things that seem minor are actually quite major for the people that we hope will eventually benefit. One is in the definition of who is included in a trial, even during late-stage development. For example, in pediatric vaccines, such as the rotavirus vaccine, do you include children that are malnourished? Do you include children that are HIV positive? That clinical efficacy phase of a study has a real impact in terms of how the vaccine is then licensed and can be used later. Including those people, raising our voices about who should benefit from the final product, and also actively participating in studies, is important.

Another example of where MSF can intervene even after licensure is our recent study on yellow fever vaccines.<sup>6</sup> The WHO recommendations were a little too narrow for the vaccine to be used by MSF more widely, and not just MSF, everybody else too. That study dealt with the possibility of using fractionated doses. The same approach could be applied to all the WHO prequalified vaccines to try to increase the number of available doses, and in addition, to ensure that HIV-positive individuals and young or malnourished children are included in vaccination programmes. I think it is important to remember in the post-licensure phase to keep looking at the use of the products as well as following-up on investments, so analysing products to propose how they could be adapted to make them more suitable for the populations where we work. MSF should be participating in that process and ensuring that there is follow-up and advocacy on the use of all products even after the development phase and after licensure.”

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6. Juan-Giner, Aitana, et al. “Immunogenicity and safety of fractional doses of yellow fever vaccines: a randomised, double-blind, non-inferiority trial.” *The Lancet* 397.10269 (2021): 119-127.  
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32520-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32520-4/fulltext)

**Gerald Voss:** “Let me just reemphasize two things that Rebecca said. Overall, I think it depends on MSF’s ambition, where do you want to be in this space? When it comes to early development, there are two considerations. MSF has been conducting clinical trials, which have a great value. As well as yellow fever, there’s also the example of the recent large Ebola vaccine study in the Democratic Republic of Congo,<sup>7</sup> which would not have been possible to execute without substantial support from MSF and Epicentre. If MSF’s ambition is to facilitate clinical development in these environments, then I think you’re being quite successful, and I hope that you continue to be active in that space.

When it comes to early development, the other key consideration is the TPP, or Target Product Profile. There may be a role for MSF to influence and provide input into the TPP. I see this in collaboration, for example, with WHO who are setting up target product profiles for a number of infectious diseases that are a priority for WHO, including TB. Defining the TPP, or what WHO sometimes calls preferred product characteristics, provides the framework and guidance to developers on what is expected in terms of product properties so that it will be suitable to be used and implemented in low and middle-income countries. There is a role for MSF with its connection to operations in these settings to provide input on how the characteristics of such a vaccine should look. It could be about things like thermal stability so that it’s suitable for the cold chain. It could be certain methods of administration that are more suitable than others. There are people thinking about vaccine patches, could they ultimately replace administration by syringe or is that just a dream that will never arrive? That type of input from MSF as an important player in the overall environment would be welcome and useful. So, contributing to the clinical development and to the TPP are two major areas for MSF to contribute.”

## Q+A AND DISCUSSION

**Cathy Hewison, doctor, MSF OCP medical department, leader of the MSF TB Working Group:** “Just to give a point of view from the medical department and the TB working group about a TB vaccine. We say yes, we would like one and yes, we will implement it and yes, we’d give input into a TPP. I think even a vaccine that could have an effect by reducing the number of people that are infected with TB, meaning those with latent TB, who then go on to have active TB would be a massive improvement on what we have now, where we are trying to treat latent TB with drugs. BCG is a great vaccine for preventing severe forms of TB in young kids, and it is very widely used, but just not by MSF because national TB programs are very good at doing it and the coverage with BCG today is better than any other vaccine. So, MSF doesn’t need to get involved in that, we just use it in our maternities because it’s given at birth. It is great for that group, but what we want is a vaccine

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7. Watson-Jones, Deborah, et al. “Protocol for a phase 3 trial to evaluate the effectiveness and safety of a heterologous, two-dose vaccine for Ebola virus disease in the Democratic Republic of the Congo.” *BMJ open* 12.3 (2022): e055596. <https://bmjopen.bmj.com/content/12/3/e055596>

that will prevent those 10 million cases per year. Many are HIV patients, but they're still the minority, nine million people who are not HIV positive develop TB around the world every year. They are adolescents and adults, who are the main drivers of transmission as well. So absolutely, there's a massive need for a new vaccine and national programs would jump at it because diagnosing and treating TB is a nightmare still."

**Gerald Voss:** "I completely agree with that. It is really about adolescents and adults. 50% efficacy may already have a big impact, against the backdrop of what you've also said, that TB treatment is very cumbersome and heavy. If you connect that also to drug-resistant TB, it becomes even worse. Treating multi-drug resistant or extremely drug-resistant strains, can take up to 2 years and you have a lot of side effects. There's also a line of research that looks at potentially combining TB vaccines with treatment to shorten the treatment course, increase its efficacy or reduce toxicity."

**Natalie Roberts:** "I think that's one of the discussions that we must have: isn't it worth MSF investing more in vaccination because the treatment is such a problem for TB, as well as the diagnosis? The same as in other diseases. We can compare TB with Ebola, a very different disease, but it's also an absolute nightmare to find, diagnose, and treat people with Ebola in time to save them. The discussion we needed to have in MSF was whether to invest more in preventive vaccination against Ebola, knowing that it will always be really difficult to diagnose and treat the disease."

**Cathy Hewison:** "I think not just within MSF there should be that conversation, but the conversation must be with everybody else involved. I think that's something that should be done, MSF participating in the process with all the actors and within the ecosystem that Gerald described earlier."

**Emmanuel Baron:** "Another question, from Evgenia Zelikova (doctor, deputy cell manager MSF OCP operations department). Are there any limitations in the production capacity of the malaria vaccine? And how to overcome those difficulties?"

**Gerald Voss:** "I think there were some limitations, although I admit that I'm not aware of the latest. In the past, in order to get to scale, GSK converted an old Hepatitis B production facility to produce the malaria vaccine. The underlying reason is a very technical one because the Malaria vaccine is based on the same technology as the Hepatitis B vaccine. That was the earlier solution to get at least to some scale, and I think that did work. I don't know about the future demand and production provisions, but I think right now production capacity does not seem to be the major hurdle. Then again, if there are uncertainties about when a vaccine might be used and at what scale, do you invest in ramping up production? It becomes a risk, not only for a commercial entity, also for a philanthropic vaccine-manufacturing plant it would be the same. You need some certainty and some reliable forecasts in order to make investments to scale up production. Scaling up also takes time because it is also about quality, and if you build a new production facility, it needs to go through a

validation process to ensure good manufacturing practice. It needs to get approval by the authorities to ensure the quality of the product. It is complex.”

**Emmanuel Baron:** “You mentioned about TB, the scientific challenge that it represents to develop a new vaccine, but when there is a strong political willingness and financial incentives, it seems we can get somewhere. For example, the COVID vaccines were developed so quickly, so it can be done quickly, it’s just a matter of political support. Is that true, and how come we got access so quickly to a vaccine for COVID?”

**Gerald Voss:** “I’m going to be a little bit polemic. I think in terms of COVID, the world was extremely lucky because it was a straightforward endeavor to develop a vaccine. Basically, the first shot on goal was successful, and then this was repeated multiple times. We now have many different vaccines out there that seem to be very good. In terms of immunology, it was a straightforward thing to do as the protection that we are seeing today is mostly based on antibodies, which are easy to induce, or relatively easy. When it comes to TB, which is an intracellular bacterium, or plasmodium falciparum malaria, they’re more complex organisms. In the case of malaria, the parasites have a complex life cycle and so targeting those with effective immune mechanisms is a huge challenge. The fact that a relatively simple vaccine like the RTS,S malaria vaccine provides 50% efficacy is somewhat of a miracle. It was certainly not something which was built on a very rational scientific investigation. I think we need to understand that depending on the organisms we’re targeting, the scientific and sometimes technical challenges, are very different.”

**Emmanuel Baron:** “I would like to bring in one member of the audience, Alain, a pharmacist at the Access Campaign. Alain, you have an opinion about one of the main actors in research and in global health about whom we have not spoken so far, Bill Gates. Gates has a model for supporting the development of new vaccines, therefore, increasing access somehow. Can you describe it?”

**Alain Alsalhani, pharmacist MSF Access Campaign:** “Before giving you my opinion on the Gates Foundation, one thing that wasn’t mentioned in the briefing video was the difference between the chemical molecules which form drugs, and vaccines. Some existing vaccines are quite new, they were only invented at the turn of this century. It’s important to consider that, because contrary to what is possible for drugs, you don’t have this notion of generics in vaccines, you can’t just copy a vaccine. Even if you try to copy a vaccine, you must go again through the entire lengthy development process, which explains why there’s such a long time between the marketing of a new vaccine and the time when we see the equivalent vaccines manufactured, usually in India, the largest vaccine producer in the world. 70% to 80% of vaccines used in Africa come from India. Likewise, MSF buys from India. Some of the new vaccines should really be included in immunization programs, but in the ‘global south’, their introduction usually depends on price. For example, the conjugated pneumococcal vaccine was introduced in Europe in 2000, 2001. The first equivalent vaccine from India was put on the market in 2020, so 20 years were needed to reproduce a technology that already

existed. If you consider rotavirus or the conjugated meningococcal vaccine, essential vaccines in our fields, and look at the delay for a 'generic equivalent', well, it's between 15 and 20 years. Those are 15 to 20 years during which a single pharma company has the monopoly, or there is a duopoly, which can lead to high prices and sometimes supply issues.

There are different approaches to reducing this delay, one is to set up consortiums. One example is one of the first projects of the Gates Foundation, the Meningitis Vaccine Project. It was noted that there were repeated epidemics of meningitis in Sub-Saharan Africa, so it was decided to develop a single product that would be tailored for this context. Instead of having various multivalent products, one vaccine would be developed that responded exactly to the needs in Sub-Saharan Africa. This is where the problem of price came into play. The countries that would need to deploy the vaccine said that they couldn't pay more than 50 cents a dose, but all the Western pharmaceutical companies said that price was too low, they couldn't deliver that with their business model. There was just one lab in India, the Serum Institute, that would accept, but they didn't have the conjugation technology needed. The Gates Foundation, with WHO and PATH (a non-profit organization which specializes in the development of new health technologies for use in low- and middle-income countries), were able to get the technology from the US NIH (National Institutes of Health), which is a public body and so publicly funded, to transfer to the Serum Institute of India. This was a true collaboration whereby instead of taking 10 to 15 years, they could wrap it all up in 7 years. The work started in 2002, they completed it in 2009, and the Canadian regulatory body even came to support the Indian authorities. So, when there's a true collaboration and a real transfer of technology, it is possible to shorten the delay, which can have a huge impact. Prevenar, the pneumococcal vaccine, costs €50 today in France, the price that has been negotiated by the French health authorities, but the Indian equivalent is only €2. The pricing approach is different to drugs, but there is also R&D to consider. It's not the same, simple, approach as for producing generic drugs, but the impact on price is not the same either.

Just to finish by talking about COVID, I agree we were fortunate when it comes to COVID vaccines but also again the Serum Institute of India benefited from a rapid tech transfer from AstraZeneca, so regulatory approval was granted at almost the same moment for the AstraZeneca and the Serum Institute versions. Oxford University developed the original vaccine and ensured it was the object of a tech transfer. COVID is not an example to generalize, but it shows how the involvement of the vaccine developer can help shorten the timeline.”

**Julien Potet, policy advisor MSF Access Campaign:** “We see that the funding model for new vaccines for neglected diseases and tropical diseases is based essentially on GAVI and on the Gates Foundation, so on philanthropic funding and charities. That model has limits, and I wanted to know if there were other projects or models to fund research on neglected diseases and vaccines against leishmaniasis, TB, et cetera?”



**Gerald Voss:** “A short answer is that there are few other opportunities for the time being, but there are still two things to be said here. It could be argued that governments in middle income countries also have a responsibility to finance the research and development of new vaccines. For now, it’s mainly countries in Europe and the USA, particularly the NIH and the European Commission, that make funds available, but we could ask other governments to develop similar mechanisms in the interests of vaccinating their populations. The other opportunity is to rely on manufacturers in India or maybe Brazil that function with a different business model, and who can develop vaccines and manufacture at a more affordable price, as the clinical development process also costs less in these countries. So, there is philanthropy, governments, but not only those of the developed countries, and the involvement of pharma companies and laboratories in India and other emerging economies. To me, these are the three different possible axes.”

**Michaël Neuman, Director of Studies at MSF Crash:** “There were a few discussions earlier about MSF’s involvement with developers to make sure that there is a better alignment between the needs that MSF identifies and the development of vaccines. I’m making also reference to the rotavirus vaccine, perhaps also the cholera vaccine. There are questions about the development of vaccines and their utilization by MSF, and a certain discrepancy between the two. How to reduce that?”

**John Johnson, vaccine referent, MSF OCP medical department:** “In complement to the question of our role in discussions about Target Product Profile, I just wanted to note that it’s not just about the vaccine profile, but also how it’s used in the field. The same vaccine used differently, in different contexts, can have a very different result. What is the role of MSF and Epicentre in trialing new techniques in vaccine usage? It’s not always possible, because sometimes it depends on a regional or national advisory discussion, but what role can we play in developing new techniques in rolling out vaccination?”

**Rebecca Grais:** “To go back to Michaël’s question, there is a lot of participation of MSF in various forums. Gerald mentioned one of the central forums, which is the normative group for the planet, the WHO. MSF participates in those discussions via working groups, via medical departments, via internal experts in the subject who participate in the relevant sessions. Often, the TPPs that are formulated in those spaces are what developers use to then advance the development. They use them as a guide, and so MSF participating in those initial discussions is important, but as John mentioned, there are many other points where we can intervene. TPPs are tough to deliver on, and are usually an aspirational goal, and so sometimes the end-product may meet only the minimum requirements and not the optimal ones. Participating in the entire process along the way during those development phases is also important. I think that there is a role for MSF and its satellites to play in the development of those products, to ensure that, for example, the end use of the product is one which is adapted to the field. A counter example is one that Natalie and Gerald mentioned, the rVSV vaccine manufactured by Merck for Ebola Zaire. The only way that that vaccine could be trialed was during an epidemic, and it is extremely difficult to study clinical efficacy during an

epidemic, but it was trialed using a strategy called the ring strategy.<sup>8</sup> Its final use was then determined by how the vaccine was trialed, but the operational protocol which is based on the ring strategy is quite restrictive, makes it difficult to deploy the vaccine usefully, and deserves to be challenged. Again, not to belabor this point, but it is extremely important for MSF to participate further in that whole process, either more passively by weighing in on the terms of the design of trials and by participating in discussions to outline the design, or actively in terms of actually doing the trials, often via participating in a consortium. We must also ensure that there is a form of public component, which expresses the needs and desires not only of MSF, but most importantly the populations themselves.”

**Gerald Voss:** “I think this is a good discussion, but one thing that maybe we didn’t touch upon is that, if you think about new vaccines being rolled out or vaccines that are relatively new, it is not only about cold-chain or vaccine purchase, but there can be other obstacles as well. I’m talking about things like vaccine hesitancy and other societal factors, which need to be addressed as well.”

**Natalie Roberts:** “We talk about starting with the TPP, but how do you actually generate a TPP? I think within MSF, we must start by deciding together who we want to vaccinate, for what, and why. Our discussions should not necessarily aim at deciding what vaccines should exist in the world, as we’re not a global public health agency like the WHO, we are a particular organization, assisting specific populations. Once we determine which new vaccines we would need for our own practice, then we move onto what our desired criteria are, knowing that they might not ever arrive because there’s plenty of risks in developing new vaccines, so we might not get in the end the precise vaccine we want. But we should first be very clear between ourselves about what vaccines we would want to use and for who and why. Then we should start working on understanding what we would need to do that. That part we can’t do alone. Of course, we need to have discussions amongst ourselves, but then we must also engage with those people who will develop those vaccines and who will finance the development of those vaccines. Being part of the whole process from start to end to make sure that in the end, the vaccine we get is adapted to what we wanted. I think the Ebola rVSV vaccine is a very good example of where this hasn’t happened, because we’ve emerged with a vaccine which has some good qualities, but we’re not able to use it in the way we want to use it today, for the populations that we think most need protection against Ebola. It’s difficult to know if we could have done more during the development process, but now we must consider if and how we can continue to work with that vaccine to be able to use it in the way that we want. The diseases are different, the vaccines are different, but it’s now important for us to reflect on those diseases, on the patients we’re targeting, and to engage in all the different stages of the process so that eventually we achieve access to the vaccines that we want.”

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8. Henao-Restrepo, Ana Maria, et al. “Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!).” *The Lancet* 389.10068 (2017): 505-518.  
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(16\)32621-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)32621-6/fulltext)

**Emmanuel Baron:** “There is a last question from Felix Kouassi (doctor, deputy cell manager MSF OCP operations department) about the production capacity in Africa, which is something very much discussed in the previous months and will continue to be discussed in the future. Are there limitations on the African continent in vaccine production capacity, how to overcome them, and is it something we want to happen? It may not be so obvious.”

**Gerald Voss:** “There’s Africa and then there’s South Africa. South Africa is very different to the rest of the continent, as the country that is most developed with potential capacities. With that distinction, on the African continent, production capacity for biologicals and vaccines is very, very limited and even in South Africa is limited. I should say that the pandemic has provided a big push to think about this further. There are concrete efforts to, for example, establish more capabilities and capacities at the Institut Pasteur de Dakar. There are also initiatives in South Africa. I just saw the news where it said that, I think, one of the institutes in South Africa had basically cracked the Moderna mRNA code and will now be able to make and market the vaccine, with the previous commitment from Moderna to not pursue any patent litigation. That’s maybe a specific way forward for one vaccine, but in general, the capacity is not there, and I think it will be a long process because you don’t want to compromise quality. It’s not only about building a plant, but also about having the human resources and the technical expertise that is needed to put all this in place. If you look back to India and the manufacturers there, it took them decades to get where they are now. I think the message was needed, something’s being done about it and the pandemic has provided new motivation, but it won’t happen tomorrow.”

**Emmanuel Baron:** “It’s not only production, also a lot about regulation on the African continent as well. To know more about regulation do watch the introductory film that was made with the support of the DNDi. It’s extremely interesting on this point.”

## SESSION 2

# Tuberculosis and antibiotic resistance

The session is moderated by **Dr Christopher Mambula**, doctor and Deputy Cell Manager in charge of medicine at MSF OCP's Cell 5 (DRC, Kenya, Uganda and Malawi).

### PANELISTS

#### **Dr Cathy Hewison**

Medical doctor, working with Médecins Sans Frontières (MSF) since 1997, and since 2005 as a tuberculosis advisor in the MSF Operational Centre Paris medical department. Leader of the MSF TB working group since 2020. She has a particular interest in new drugs for drug resistant tuberculosis (DRTB) treatment and is involved in the endTB project.

#### **Dr Jennifer Cohn**

Dr Jennifer Cohn leads global access strategy development and implementation at GARDP (the Global Antibiotic Research and Development Partnership, of which MSF is a partner). Jennifer is an infectious disease physician and served as Senior Vice President at Resolve to Save Lives, Senior Director of Innovation at the Elizabeth Glaser Pediatric AIDS Foundation, and as the Medical Coordinator for the MSF Access Campaign.

#### **Dr Bern-Thomas Nyang'wa**

Dr Bern-Thomas Nyang'wa is the medical director for MSF Operational Centre Amsterdam (OCA). Bern completed his studies in Blantyre and was the first Malawian doctor to work for MSF. After working in Nigeria, Chad and CAR, Bern took up a post as TB implementer at MSF UK's Manson Unit. Bern was project manager then Chief Investigator for the TB-PRACTECAL clinical trial. Sponsored by MSF, the study is evaluating new approaches to combat multidrug-resistant tuberculosis.

**Introduction by Christopher Mambula:** “The topic of this discussion is Tuberculosis and Antibiotic Resistance. We will consider where we have come from, where we are now, and in what direction we could possibly go in the future. Cathy will start by providing the background of how MSF has approached tuberculosis and how we’ve been involved in managing TB in the last few years.”

**Cathy Hewison:** “I’d say the question of access to medicines is a bit like a puzzle, a complicated long puzzle with lots of pieces. It’s not a short campaign. It’s a long process, and it involves many actors, researchers, campaigners, operations, networking with the outside world, with manufacturers, with the WHO. I’ll try to discuss a few of the access issues in TB, how we worked on them and how we’ve moved forward.

TB is a bit different than for example HIV was in the initial days of the Access Campaign, where the issue was that there were drugs existing, but they were too costly and not available where we were. In TB, the number one issue is diagnosing the disease. Even today, we don’t have a point of care test that works for all forms of TB and for all populations affected by TB, and that doesn’t rely only on sputum. Teams in the field have been complaining about that since the early days of MSF’s work on TB. In 2005 the Access Campaign wrote a report called *Running Out of Breath*<sup>9</sup> which was an important moment to say, ‘The test we use, microscopy, is too insensitive. It relies on sputum. It requires lots of human resources. It’s not good enough.’ This report galvanized not just MSF but other partners to also say, ‘This is not good enough.’ But it still took a long time for everyone to accept that it wasn’t okay to ignore half the people with TB. MSF teams were then part of an important movement and included in an important survey to identify which Target Product Profiles for TB diagnosis should be developed. This action was led by clinicians in the field, working in the operations. Then, once things started moving in product development, determining the diagnostic tests that might or might not work was important. MSF, the Access Campaign, and Epicentre all played important roles there. To take the example of TB LAM, a point of care test that uses urine, not sputum, but which only works for small proportion of people who have TB, that is HIV patients with low CD4 counts. MSF and Epicentre were fundamental in doing the basic research that not only showed the impact on mortality for that population but also demonstrated how to use that test and the feasibility of using it in our fields. We’ve again done that with FujiLAM, the new form of TB LAM. Those studies were fundamentally important in getting the test included into WHO guidelines. The work doesn’t stop there, there’s also introducing the test, paying for it, getting it into the field, and getting it registered in the countries we work. Every two years MSF contributes to a report called *Step Up for TB*.<sup>10</sup> Lots of MSF fields are involved, as well as Stop TB and other partners, and it shows where different countries are with not only adopting the new recommendations by WHO but also implementing them. It pushes politically countries to step up, to register this test and to

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9. Médecins Sans Frontières. “Running out of breath? TB care in the 21st century.” Geneva (2005). <https://msfaccess.org/running-out-breath-tb-care-21st-century>

10. Médecins Sans Frontières and Stop TB Partnership. “Step Up for TB 2020: Tuberculosis Policies in 37 Countries. A Survey of Prevention, Testing, and Treatment Policies and Practice”. Geneva (2020). <https://www.msf.org/step-tb-report-2020>

work with the Global Fund. Most countries must include TB LAM in their Global Fund application because it's an expensive test. Even then, registration for TB LAM has only just happened in India. So, getting a new product registered and getting it into countries takes a lot of time, even when the WHO recommends it, and the Global Fund will pay for it.

Sometimes things don't work out. There are a few examples of getting in there early, identifying promising products, trying them out and then having to admit that they don't work. We also play an important role of showing what is not viable and what doesn't work in the field. But when, for example, GeneXpert came along it blew our minds. We couldn't believe that there could be this small machine with a cartridge which could diagnose TB and determine Rifampicin resistance so quickly. Before that we were often waiting three months; sending samples outside of the country to get a culture and drug susceptibility testing (DST) done. When GeneXpert came along, MSF operations entered the market immediately and bought, I think, all the machines. MSF was the biggest user of GeneXpert initially. The money was put on the table by MSF to deploy GeneXpert on our fields, and we did important feasibility studies and gave feedback on troubleshooting and early implementation. However, cost is still a real issue. It costs \$10 today to buy one GeneXpert TB cartridge, \$20 for an XDR (extensively drug-resistant TB) cartridge. Now we're running a campaign, five for five, to push Cepheid (the manufacturer of GeneXpert) to reduce the price of all their cartridges, for COVID, Ebola, hepatitis, and HIV as well as TB. We are also pushing for transparency. Manufacturers only say how much their product costs to purchase, but don't provide the data to explain that price in terms of research costs, or commercialization. Now, we push for research funding contracts to stipulate that the final pricing of the product is transparent from the beginning.

On TB treatment, I think most people think having access to first-line TB treatment is normal today. It's cheap, it's great quality. It wasn't always like that, it was a big work to get quality drugs sold through the Global Drug Facility (GDF), a facility created in 2001 as part of the Stop TB Partnership to act as a one-stop procurement and supply mechanism to provide global access to TB diagnostics and treatments. The GDF was initially supplying non prequalified drugs to countries. MSF lawyers entered a battle about quality, and there is an excellent system today where the GDF uses prequalification and receives millions of orders and can therefore provide cheap and good quality drugs globally. But in the past, the GDF was not performing adequately, and it was difficult for countries to source affordable, quality TB drugs. Once a country is no longer eligible for Global Fund funding, like Armenia, they are supposed to be able to pay for their own first-line drugs, but nobody was interested in supplying a couple of hundred drug regimens to Armenia at an affordable price. They finally got a couple of offers for single drugs, rifampicin and isoniazid, but at 11 times the cost. Then, antibiotic resistance started happening, but at that time nobody wanted to hear about antibiotic resistance and TB. We were transporting specimens out of the country, across the world, just to try to prove that patients had resistance and that countries like Armenia didn't have the range of drugs to treat them. WHO did not want to hear about it, they said that if TB was treated properly

then there wouldn't be resistance, so the fault was the clinicians', and especially the patients'. It took lots of risks from operation teams and investment from MSF to not only diagnose but also to start treating patients with antibiotic resistance. We were importing illegal drugs into Thailand in suitcases, getting kicked out of Siberia because they refused to let us use quality drugs. The problem of drug-resistant TB (DRTB) is that there are different manufacturers for each individual drug, and it requires a super expensive, long treatment, requiring a combination of five, seven drugs which are often toxic. To address some of those problems, MSF Logistique became the supplier for the whole world, pooling the drugs and trying to get them out to patients, the few patients that were identified. The market wasn't there initially, because there is no point identifying DRTB if you can't treat it, but the treatments were not being developed or made available because there were no patients identified. Finally, that role was taken over by the GDF. Our interest in drug-resistant TB came from that time. Once it was clear there was a need for them, we could finally see new drugs coming, even though there had been no new drugs for TB for 60 years. Bedaquiline and delamanid were developed and even before the phase two studies, MSF and the Access Campaign in France started talking to Johnson and Johnson, the manufacturer of bedaquiline, about compassionate use and about the countries that were going to need these drugs straight away. Knowing how many years it would take to complete studies and get the drug registered in those countries, compassionate use of bedaquiline was vital. It took years to convince the company, then another two years to convince WHO to put it in their guideline, and then another few years to convince countries, Armenia and Georgia, for example, to introduce it into their national programs. But the day it became available, Armenia was the first country to use it under compassionate use. It was two years until it became widely available on the market, so they gained two years and saved lots of people's lives. We got the MSF medical directors to pay for an entire batch of linezolid so that we could start using it in combination with bedaquiline, so we had to put the money on the table. There was only one linezolid manufacturer then. Now there are ten manufacturers, a 1,000% decrease in price, but we had to create the market. We had to use the drug to get the prices down. *Under the Microscope*<sup>11</sup> is a publication that comes out every couple of years, detailing the cost of all the drugs, and it has become the bible for national programs, for WHO, for everybody, in terms of transparency in drug prices. It has also helped bring down the prices, because not all countries can use the GDF. GDF shapes the global market to ensure good prices and good quality, but not everybody can use it.

To return to bedaquiline, the drug became widely available using this model of bringing individual products to market. But you don't need just one drug for TB, you need a combination, a regimen, so MSF invested in looking at multidrug resistant (MDR) TB regimens using different combinations of these new drugs. Bedaquiline's patent should expire in 2023, and some Indian manufacturers are ready to start putting generic versions on the market. But there is a risk of evergreen patents, the company changing the formula a little bit and filing a new patent for a more useful version of the

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11. Médecins Sans Frontières. "DR-TB and TB-Prevention Drugs Under the Microscope", 7th Edition. » Geneva (2020). <https://msfaccess.org/dr-tb-and-tb-prevention-drugs-under-microscope-7th-edition>

product. For example, it could be very interesting to have a long-acting bedaquiline treatment, a slow-release version, but that will lead to a new patent. There also are some potential Pan-TB regimens coming up, meaning there's no need to prescribe different treatments for drug-susceptible and drug-resistant TB, one single regimen would cover everything. They all include bedaquiline, so there'll probably be another patent. We're working to try to block those new patents, while also trying to avoid blocking the development of useful new products. It's a difficult balance. Today, there are a couple of new molecules in the pipeline. Unfortunately, some that seem promising nobody is interested in, because the clinical development is very long and risky. But there are some molecules being developed at GSK and AstraZeneca and we're already trying to push them to avoid taking out restrictive patents before they even do phase two trials, realizing the later we come in, the harder it is. My last point is that when we finally have new drugs or new regimens, we have got to be involved in rolling them out. There could be short regimens of only four months for drug-susceptible TB treatment in children. Nobody has rolled these new shorter regimens out because demonstrating and documenting them is difficult. We've got a real role there to play."

**Christopher Mambula:** "I would like to ask Jennifer to draw some parallels with bacterial antibiotic resistance, even if there is a discrepancy around the acute versus the chronic, disease courses that are rapidly evolving and patients who need very quick solutions, as opposed to diseases that develop more slowly and treatments that last longer."

**Jennifer Cohn:** "I am an Access leader from GARDP, which is a not-for-profit organization, developing new treatments for drug-resistant infections that pose the greatest risk to health. We appreciate the support that MSF has provided to GARDP both financially and operationally and look forward to strengthening our collaboration to address the silent pandemic of drug-resistant infections. I'm also a member of the MSF family, as a doctor and a former Medical Coordinator for the Access Campaign. I'm also a practicing infectious disease physician."

Everything Cathy said also applies to antibiotic resistance. MSF's commitment to prioritize and support innovation on behalf of those who really need it and who are most neglected has set it apart. It's also been set apart by this kind of multi-modal working through Operations, through Epicentre, through the Access Campaign, through advocacy, through communications. That is the critical coalition that antimicrobial resistance needs. Antibiotic resistance is growing globally in both the poorest and wealthiest countries. There was a recent publication, the Gram Study<sup>12</sup> from *The Lancet*, and the numbers in there are just stunning. The human toll of antibiotic resistance is extremely high, and it's growing. In 2019 there were an estimated 1.27 million people that died as the direct result of antimicrobial-resistant infections, and 5 million deaths associated with drug-resistant infections. With respect to children and especially neonates, we are only now starting to understand

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12. Murray, Christopher JL, et al. "Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis." *The Lancet* 399.10325 (2022): 629-655.  
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02724-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext)



their full impact. This year GARDP will publish results from an observational study that we conducted with Penta and St. George's University in London, called the NeoOBS study.<sup>13</sup> It looked at over 3,200 newborns at 19 sites across 11 countries, one of the largest ever observational studies on the care of babies with sepsis. The study showed that mortality rates reached up to 25% in some settings, and highlights the challenge with appropriate and timely diagnostics, and with antibiotic prescribing practices. It points to the urgent need to develop novel antibiotic treatments that use both new and existing antibiotics to provide appropriate empiric and tailored regimens for neonatal sepsis to save lives. It also points out that we don't have the necessary tools, not only the diagnostics and the drugs, but also the operational models to combat these infections on the ground. Antibiotics are a critical tool, both to respond to bacterial infections that are pandemics and epidemics within themselves, but also to respond to future pandemics, including viral pandemics. We've seen in previous influenza epidemics and the current COVID epidemic, they frequently result in bacterial secondary infections, which also act as multipliers for antimicrobial resistance, as necessary antibiotics are used for critically ill patients. Timely access to antibiotics is critical to save lives but providing the right antibiotic at the right time will also slow resistance and reduce mortality. Appropriate use also supports long-term access by preserving antibiotic effectiveness.

GARDP works to tackle drug-resistant infections in four ways. It develops new medicines for the greatest public health needs. It generates evidence to guide treatment use and inform policies. It ensures treatments are available to all who need them, and it shares knowledge networks and expertise. We're specifically focused on developing treatments to address several unmet needs: serious bacterial infections in hospitalized people, sepsis in newborns, and sexually transmitted infections such as drug-resistant gonorrhea. Our focus is on developing new and improved treatments using both existing and new antibiotics, particularly those in late-stage clinical development, but we also have a big focus on ensuring responsible and sustainable access. We believe that access combined and supported by appropriate use of new and existing antibiotics sits at the heart of addressing antimicrobial resistance. There are huge challenges to access for antibiotic and antimicrobial medications. First, some needs are just not being addressed. The latest WHO review of the antibiotic pipeline shows that it is nearly empty when compared to the needs as defined by the WHO priority pathogen list. This situation is aggravated by the fact that even when an antibiotic completes clinical trials, market failures often lead to the antibiotic not actually remaining in the market. Second, many new drugs, even if they're developed, are not registered where they're most required. Third, there's insufficient or no clinical evidence to guide their use, whether for specific populations such as children and neonates, or in low- and middle-income countries. There is also a lack of up-to-date surveillance data which should guide the sequencing of treatments to slow antibiotic resistance and address the most problematic pathogens. Our clinical care is also hindered

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13. Russell, Neal, et al. "Analysis from the NeoOBS Global Neonatal Sepsis Prospective Observational Cohort Study Across 19 Hospitals in 11 Countries; Clinical Presentation, Treatment, Mortality Outcomes and Development of the NeoSEP Sepsis Severity Score." [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3864901](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3864901)

by the fact that we don't have appropriate diagnostics widely available. Fourth, many antibiotics are undersupplied. Shortages have become the norm, not only in low and middle-income countries but also in Europe and the US. Unlike in TB, given that there's no Global Fund or GDF for antibiotics, the market is fragmented. There is very little organization, and I don't suspect we'll see a dedicated global fund for anti-microbial resistance (AMR). There may be some increases in investments from Global Fund and others, but we could also look at innovative solutions that involve local or regional solutions to pool demand and so organize the market for sustainable access. Fifth, some antibiotics are too expensive, due in large part to prices set by pharmaceutical companies that have exclusive rights to these products. Then finally, there's been chronic underinvestment in strengthening systems. Evidence-based interventions are needed, and political and financial support needs to be mobilized to support best practices in on-the-ground use of antibiotics. I also note that failures in the antibiotic market are not just because of neglect of specific patients or countries. It's also because we're stuck with an R&D (research and development) model of developing antibiotics that doesn't address the actual needs and depends on financial incentives for pharmaceutical companies to invest in R&D. It guarantees that they will focus on blockbuster drugs for chronic diseases, so that new R&D is not defined by the types of drugs that are needed for antibiotic resistance, nor the needs of low- and middle-income countries.

MSF, given its unique position of having medical expertise, extensive operations, deep relationships with health systems and other key stakeholders, and dedicated units on innovative research and access issues can address antibiotic resistance in a holistic way. First, MSF can be a trusted and independent voice in highlighting the need for public health-oriented R&D and reliable access to both new and old antibiotics and diagnostics to ensure that clinicians and patients have the necessary tools to appropriately fight bacterial infections and maintain antibacterial effectiveness in the long run. Second, MSF can help develop, document, and disseminate critical evidence to improve how we address AMR. This evidence can range from improving surveillance data to developing and testing operational models for appropriate introduction and use of new products. Given MSF's respected reputation, this evidence can also be converted to advocacy campaigns to change policies, guidelines, and funding prioritization more widely. Third, MSF can highlight the difficult systemic issues around R&D systems, incentives funding, medication pricing, and registration and supply chains that may prevent access and appropriate use. MSF can serve as an advocate for solutions for these crosscutting issues that require closely coordinated input from a range of actors. Fourth, MSF can be early adopters for new products, like Cathy mentioned for bedaquiline. accelerating access to populations that need these lifesaving medicines and building best practices even before a product is introduced on the market. Finally, there's a lack of international or even regional actors to support late-stage product development and the use of antibacterials. MSF could help fill this critical gap.”

**Christopher Mambula:** “Someone has asked if MSF is working with the TB Alliance on the new regimens that Cathy has talked about? Also, it seems that there are certain parallels in both diag-

nostics and in treatment, in that there are gaps and there are limits. The products that are available are relatively expensive and not very accessible to many different populations. When they are available, there are issues with children and neonates, for tuberculosis and antimicrobial resistance. Bern, how do you see the future as far as MSF is concerned?”

**Bern-Thomas Nyang’wa:** “We do work with the TB Alliance. One of the clinical trials that just showed amazing results on shorter treatment for drug-resistant TB includes a drug that the TB Alliance is developing, and they are collaborators in that process. I’m sure there’s more that we can do to work together, but from the perspective of developing clinical trials and implementing and ensuring that there are adequate supplies for it, we work with the TB Alliance.

TB and AMR are good examples of discussions around access. For diagnosis, treatment, prevention, we need new tools, we need to improve the current tools, and we need to improve access to the current tools, in TB and in AMR. Specifically on diagnosis, there are tools that are available that we’re not using adequately. There’s TB LAM that we can use to diagnose TB in a limited group of patients that can surely benefit, a group of patients that have high risk of death. Yet we are not always using it ourselves, and we’re not encouraging the Ministries of Health and others in the areas that we work to use it. The low-hanging fruits around diagnosis are first around making sure that there’s access to, and use of, the current tools. However, I also have to say, this morning I tested both my kids, aged seven and nine, for COVID, and it was so easy. This is a disease that two years ago we did not know what it was, but now there are easy, reliable tests. That is not possible for TB today. There are some complex processes and there still has to be a functioning lab. There is a question of lack of urgency and outrage. We’re too used to TB being difficult to diagnose. Let’s be outraged about the absence of an easy diagnosis; let’s be outraged that half the population that has TB cannot be diagnosed today. We should not accept that. Forget about the global perspective, already in your project and in your particular clinic, it’s happening. Patients that could have TB are not able to be diagnosed because we do not have the right tools to do that.”

**Christopher Mambula:** “That also would beg the question regarding treatments, whether they have already been produced or are still in the pipe, for which there are issues of access in terms of production, in terms of cost, in terms of registration in different countries. Where do you think MSF should concentrate its energy?”

**Bern-Thomas Nyang’wa:** “With regards to TB, the current treatment course for drug-susceptible TB used in most situations takes six months. It’s relatively efficacious if properly supported and if patients can complete it. There are recent studies and recommendations looking at the possibility of having a shorter treatment regimen, especially in children. We don’t have to change much, we would just have to identify the right patients to treat for four months instead of six months. Is four versus six a significant change? Maybe not on paper, but for a child taking treatment daily, if they must take it an extra two months it makes a big difference. So, there is the basic treatment for

drug-susceptible TB with isoniazid, rifampicin, pyrazinamide, and ethambutol that we need to think about and see how it can be improved.

For drug-resistant TB on the other hand, currently the treatment lasts 9 to 24 months. In most situations, patients take 15, 20 pills a day if they're not coinfecting with other illnesses, when they might take more than that. The treatment outcomes are still not as good as we would like. Globally, we're only around 60% in terms of treatment success for drug-resistant TB. With some of the work that has been done such as the TB-PRACTECAL trial,<sup>14</sup> the ZeNix trials<sup>15</sup> from the TB Alliance, and ongoing studies in End TB, we are demonstrating that we can improve on that. We've seen in the TB-PRACTECAL trial, with a six-month regimen that uses a maximum of five pills a day, that it is possible to achieve a cure rate similar to that of a drug-susceptible TB regimen. This is great progress. It is important to consider also the adverse events profile that you see with some treatment regimens. We have reached a watershed moment in DRTB, where we are really moving forward and not accepting that DRTB treatment needs to be much more complex than for drug-susceptible TB, in terms of not only the duration and the pill burden but also in terms of the toxicity of the treatment. But while it is great to have completed a nice clinical trial, and to get nice study results, we must ask ourselves where patients can get access to this regime and when they are going to benefit from it. Will it be the same as happened with bedaquiline, or with drug-susceptible TB when we pushed to change the treatment course from 8 months to 6 months? It took us close to 10 years to make sure those changes were implemented. There is a question around how quickly we react, how urgent we feel this is, and where we want to invest in trying to make a difference in patient's lives."

## Q+A AND DISCUSSION

**Christopher Mambula:** "Two questions have been put forward: does GARDP tackle pharmaceutical regulation in limited-resource settings to modify the way people can access drugs? And how does GARDP practically deal with systemic or massive problems that are beyond single countries, that impact globally?"

**Jennifer Cohn:** "Clearly GARDP can't address these alone. They go beyond antibacterial resistance, and they need to be coordinated with a huge number of stakeholders. Nevertheless, we are trying to take a few different approaches. One, we're trying to utilize existing mechanisms. Using the WHO prequalification process, for instance, which has been extensively used for HIV and for vaccines but has been underutilized for other products on the WHO Essential Medicines List (EML). We think

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14. Berry, Catherine, et al. "TB-PRACTECAL: study protocol for a randomised, controlled, open-label, phase II–III trial to evaluate the safety and efficacy of regimens containing bedaquiline and pretomanid for the treatment of adult patients with pulmonary multidrug-resistant tuberculosis." *Trials* 23.1 (2022): 1-16.  
<https://link.springer.com/article/10.1186/s13063-022-06331-8>

15. Conradie, Francesca, et al. "High rate of successful outcomes treating highly resistant TB in the ZeNix study of pretomanid, bedaquiline and alternative doses and durations of linezolid." *Journal of the International AIDS Society* 24.S4 (2021): 70-71.

that this is a way that we can help to reduce burden on countries and on companies, and really speed up registration in individual countries that may not have strong regulatory agencies. There are also other more regional harmonization approaches. When we're thinking about developing regulatory strategies, we look not only at the countries that have the biggest burden and so interest to target for early registration, but also those countries that may be national regulatory authorities of regional reference, such as is the case for certain PAHO (Pan American Health Organization) countries. We would support the strengthening of these regulatory harmonization and streamlining efforts, maintaining the quality, but reducing some of the administrative burden that can hinder access. For instance, we are working on a product which is a medication for very resistant gram-negative infections, essentially carbapenem-resistant infections. There are heavy burdens of these infections in Eastern Europe and in South Asia, but they are also growing in Sub-Saharan Africa and PAHO and the Middle East region. This product is approved by the US and European regulatory authorities, and it's on the WHO EML. It has no other registration. We are very interested in supporting wide registration access but that may take time. It may also take time to find a second manufacturer that will provide a cheaper product before we introduce it more fully on the market. During that period, we'll try to work with several countries on compassionate use or pre-registration early access programs, so that we can not only speed up getting the drug to where it's most needed but also learn lessons on how best to use it, so that once the product is fully registered in those countries it can be scaled rapidly. The lessons learned from early access use can be applied in other countries too, once the product is more widely available."

**Natalie Roberts, doctor, Director of Studies MSF Crash:** "I have two questions, the first being about whether MSF could play a stronger role in drug-sensitive TB. We've been very focused on drug-resistant TB (DRTB) but is there now a need for MSF to engage more with drug-sensitive TB (DSTB)? Secondly, Bern talked about how MSF as practitioners, we have demonstrated new regimens for treatments, particularly for multidrug resistant (MDR) TB. We've also heard about how we see patients, we document things, so that we can advocate, we can speak out based on our clinical experiences. As the practitioners that we are, is there also a bigger role for us on the ground via our operations, and what is that role in antibiotic resistance? Is it in diagnosing earlier, in treating earlier, in getting involved in developing new products, in doing the clinical trials? Are we going in the right direction, or do you think there are opportunities we're missing?"

**Cathy Hewison:** "I think everybody agrees it would be great to see shorter DSTB regimens rolled out. The shorter regimen for children is the same treatment even, just a shorter course. The drugs are available, they're cheap, there are children's formulations, they taste good. Everything's there, you just give them for two months less. So, it would seem straightforward. But in fact, the study done was only for non-severe TB, meaning pulmonary TB but not bilateral and with no cavities and no extrapulmonary TB except lymph node TB. They used x-ray to exclude severe TB. For us, the question is, can we roll this out without an x-ray to exclude severe TB? On one hand, we should be pushing for an x-ray, everybody should have an x-ray machine available to them, now there are

cheap digital x-rays and teleradiology. On the other hand, we still don't have x-ray everywhere. So, we need an operational research project to show how to roll this out safely and identify properly the children who can benefit from a four-month course. In MSF, there is a certain interest in doing that, but we have few projects who are involved with drug-susceptible TB. We might diagnose, if we have that capacity, but then we refer to national programs for treatment. So, we would have to invest in developing field operations where we could do this research. I think that at least a couple of projects should get involved and I'm pushing for that.

Just a point about registration. One thing that we've done in Eastern Europe is pool registration because most Eastern European countries no longer can use the Global Fund, which used a waiver to get these drugs introduced into national programs. These countries all have different languages and different alphabets, and no companies were interested in submitting separate dossiers for registration in each country. MSF and others at WHO suggested pool registration, which makes it easier for the company to submit one dossier for the whole region. Lots of countries benefited from it, but it's a real work."

**Bern-Thomas Nyang'wa:** "The Gram study paper that Jen referred to is the first time that we know the burden that antimicrobial resistant bacteria and antimicrobial resistance has around the world. DRTB is one of them, as TB is a bacterial infection. In each of our missions, our projects, we need to take the same approach for AMR as we aimed to do for DRTB. We need to understand what resistance we are facing, and we need to be able to identify drugs that are efficacious in treating the patients that we have. Just because there was a survey in Kampala at a particular lab 10 years ago, that doesn't mean that in every project in Uganda we need to utilize the same antibiotics, never mind in other countries. We need to know what's happening where we are working, which means we need to be able to do those tests because, for some time, we've considered microbiology as something complex, something more for use in specialized settings. We have hospitals where we treat a lot of patients, where we use a lot of antibiotics, and we are not sure what the results are, whether we're prescribing the right treatments. So, the first step is to try to ensure that our projects, our missions, have access to the diagnosis so that we can tell the world how bad things are, or maybe even how great they are, in terms of antibiotic resistance. There is not a dichotomy around access and stewardship. They are complementary, we need to be able to give the patients the drugs that we know will cure them, not the ones that we suspect might cure them because of a survey that was done 10 years ago somewhere else. No-one else will be able to show the resistance to, let's say, quinolones in Central African Republic, and if we don't do it, I don't think anyone will. It is important to be able to see what's happening to the patients in front of us, to really understand the epidemiology in those difficult places that we work in."

**Christopher Mambula:** "We've at least in OCP, in the last 10 years, tried to push that cursor forward. I think that OCA has done this as well. We've used different resources to create MSF microbiology labs, either setting them up ourselves or supporting existing labs in different countries to improve or stabilize their quality, to provide access to microbiology. Then also trying to plug into existing

systems within the WHO, to make sure that sensitivity but also resistance patterns are captured.

Jennifer, can you tell us about your developmental production model at GARDP? How does your work interface with manufacturers, knowing that we don't produce necessarily vaccines or drugs themselves? What alliance of partnerships do you have to move the subject forward?"

**Jennifer Cohn:** "Just first to return to Natalie's question. I absolutely agree with what Bern said, better surveillance data, better local antibiograms, better sequencing of products, knowing which diagnostics are needed most so that you can do that lab strengthening, all of that is critical. But there are some clinical research questions that I think would also be interesting for MSF, because as we saw in the Gram Study, the same types of bacteria may not be predominant in the US and Europe as elsewhere. For example, *Acinetobacter* has a heavier impact in South Asia and Southern Africa, as opposed to the US and Europe. We don't know how to treat *Acinetobacter* very well. Combination therapy is recommended but there's virtually no evidence on which combination therapy, in part because the prevalence of severe *Acinetobacter* infections in the high-income countries where most clinical trials are done is much lower than in many of the contexts in which MSF works. I think MSF could develop more innovative diagnostic strategies, for example triaging diagnoses so that when a person comes in with a severe infection in a region with high carbapenem-resistant organisms, we would use a carbapenem-resistant lateral flow assay that works on sputum. The state of operational research for antimicrobial resistance (AMR) really needs strengthening. There are huge networks of implementers and implementation scientists working on HIV or TB, but not for AMR, and where it exists, it's quite siloed.

With regards to the GARDP model on working with manufacturers, it's usually tailored to the drug, if it's an old drug that's already patent-expired, a generic, or a new drug whose patent the manufacturer may only be aiming to approve in Europe or the US. The model differs, but one approach we may take is to support collaborative research to speed or strengthen regulatory data for neonates, for example, which is a requirement for most drugs, but often it takes a long time to get that data. Long delays are allowed by the regulatory agencies, but we want to get that data quickly, so we have the drugs needed to treat the huge burden of neonatal sepsis demonstrated in our study. Or we may work with the manufacturer to license a medication, and then work on getting it licensed to other manufacturers, to distributors, et cetera, so that we can have an affordable version registered widely. Finally, we are interested also in older drugs, and in supporting studies to look at how older drugs that may be underutilized today can be used to preserve some of the more advanced drugs for extensively resistant bacteria. We work with generic suppliers, or even some of the original companies where there's only a single manufacturer, to think about a supply strategy or registration strategy, or about bringing in additional suppliers when needed."

**Christopher Mambula:** "We've been talking a lot about the science, about things that we could do or what others, such as the manufacturing industry and the different regulatory bodies around the

world, could do. But there are people involved, and human behavior drives these things forward. Andrea Bussotti, MSF France Director of Communications, is asking about the relative weight of social or cultural factors in tuberculosis and in AMR fields, regarding the overconsumption of antibiotics, beliefs about the effectiveness or lack of effectiveness of some antibiotics over others, and practitioners that are reluctant to prescribe new DRTB drugs, for example, because of a lack of trust in patients. How do you see this? What role do you think MSF has in dealing and engaging with communities, with patients, and with persons who we want to take these drugs that we're talking about today?"

**Bern-Thomas Nyang'wa:** "In TB we've made progress with a person-centered approach, talking to patients, discussing with them and their communities on how they can be supported through this disease. In reflection on that, it's important to understand that it's not the patients' fault or problem. For antibiotics, we know that even in the West, there are a lot of prescriptions that are not appropriate because if somebody has a fever and a cough, they go to a general practitioner and they want to get something out of it. There's a need to work with patients and with clinicians on how to handle those expectations. Maybe it's not as obvious for short treatments as when we think of a patient that we are asking to take 20 pills every day for nine months."

**Cathy Hewison:** "We were faced with that problem when we were so excited about bedaquiline. Some patients didn't want to take it, and certainly, clinicians were scared to use it. For the clinicians, what was important was evidence and creating their evidence themselves, so implementation under operational research conditions was hyper-important. I call it evidence-based advocacy. This I think is our strongest tool in TB. Secondly, on the patients, I think we've come a long way. With bedaquiline, it was very much patient-to-patient support that helped a lot. It's important to invest in getting patients involved at fundamental levels, so that patient groups are involved in the protocol stages of the clinical trials, for example."

**Jennifer Cohn:** "I hundred percent agree that we must have patient input into clinical trials, particularly for community-based medicines or medicines that may be taken for longer period. For instance, we are working on an oral therapy for drug-resistant gonorrhea. We need to know how it might be perceived as compared to an injectable, and it could be dichotomous. Some people might say, 'Get me away from that needle.' Others will say, 'No, no, no, the injection is stronger. I don't want tablets.' The human element is key. For HIV, we worked on treatment literacy. I think it's also been done for TB, but less for antibiotic resistance. Part of this is awareness of when and when not an antibiotic might be helpful, which contributes to the broader appropriate use of antibiotics. Patients and communities have a role to play in demanding that they receive appropriate treatment, and sometimes that means not receiving an antibiotic."

**Mohammed Musoke, doctor, deputy cell manager MSF OCP operations department:** "I wanted to reiterate one of the points that you mentioned, because I just came back from Somaliland, where



we have some new molecules and we're working with shorter regimens. The dilemma we have right now is that much of our cohort is refusing to take the short course regimens. People prefer to take a regimen of two years compared to one that is less than one year. We're talking to the patients and their families to understand why. We just assumed that people would want this regimen, so even the clinicians who are prescribing it really did not have the right information to give them. I would suggest that when a new drug or regimen is being introduced, we work within the context, putting more into operational research, patient feedback, our explanations to the MOH and the patients about how these molecules work. You would expect anyone would choose a shorter regimen compared to a longer one, but this is not what we're seeing. There are actions that we should consider whenever these new molecules are introduced, and we shouldn't assume that this activity is covered by our existing budgets."

**Felix Kouassi, doctor, deputy cell manager MSF OCP operations department:** "I was wondering whether there is a policy, a strong-willed desire to work with the ministries, rather than just sharing study outcomes with them, or just informing the MOH and the countries where we work. If, whenever we want to use a new drug, we don't work with the ministry, then it's very likely that there is going to be reluctance. Is there a real strong will in MSF to work with them and not just share the outcome of our research?"

**Cathy Hewison:** "This is a point that is fundamental and goes back to investment. You must invest in relationships of trust, with patients, with clinicians, and with the Ministry of Health, that take time to build up. It requires technical know-how, but also political know-how, to involve them from day one. It's no good coming with protocols and saying, 'Hey, we've done this research, and we're going to introduce this.' Everything that's been successful depended on these relationships. We didn't do our clinical trials in places we'd never set foot in, they happened after 20 years of working together with authorities on DRTB. Sometimes, we try to impose. We assume everyone will agree that shorter is better and less side effects is better and no injectables is better. But if you think about being diagnosed with cancer, people expect to have a long treatment that gives them lots of side effects. If you say, 'I'll give you a week's treatment with no side effects, and it is oral', they might not be convinced that the cancer would not come back. It's important to respect people's decisions."

**Bern-Thomas Nyang'wa:** "A direct experience that we had in the TB PRACTECAL trial was exactly that. We ran a sub study on patient-reported outcomes and how they felt. They all felt much better, but the clear message was also, 'But I want to keep coming. It's good to only take treatment for six months, but can I get a follow-up for the remainder of the usual time?' We should not consider that all patients are the same. Some would want six months and then disappear; others would want to stay around. Maybe the comprehension around whether they prefer shorter regimens or longer regimens could be that it's not necessarily about the treatment. It's about the care. They know that if they finish treatment, they might not be able to access medical care anymore. This person-centered and patient-centeredness is quite critical in delivering new innovations."

**Léon Salumu, doctor, cell manager MSF OCP operations department:** “I have two questions. The first to Cathy. It’s impressive what happened with the new tools, new drugs, new treatments but sometimes, as you say, it takes two, three years in order to be able to use them in the field. You just gave the example of bedaquiline in a compassionate setting, and countries being reluctant to change. Don’t you think that we should change this so that we take direct responsibility for introducing a new product? Also, listening to you all, we’ve been asking for new tools and new molecules for many, many years now, and progress is just incremental. Should we continue with the same policy, or should we do things differently, because we’ve been pleading for the same thing for so long? We can’t really see any improvement or major improvement, let’s say.”

**Cathy Hewison:** “It might seem that we’re not getting far, but there have been huge transformations compared to 20 years ago. That’s why I’m trying to emphasize that it’s a really long process. We’ve gone from having microscopy as a diagnostic, to GeneXpert with two cartridges which provides almost the whole resistance profile. We have come a long way, but to your question about where it’s blocked, TB-LAM is a good example. TB-LAM is lifesaving, it reduces mortality of that very specific risk group, and in all MSF projects we now use TB-LAM. The problem is outside of MSF projects, also understanding the flow of the patients and where the patients interact with somebody able to do that test. In South Africa, you must be a laboratory technician to do the test. Whereas, in other countries, like Malawi, anybody can be trained to use it, you don’t need to be a health professional. It’s a very easy test. If we look at FujiLAM, MSF has done an important study in four projects,<sup>16</sup> Homa Bay being one of them. In some focus groups, the issues that came up were about feasibility. It could be more sensitive than microscopy, but how do we fit it into the flow of patients? Who is going to do the test, and which patients will be eligible? That consideration of who does a test and who gets a test is something we should work more on. As to whether we should change our approach, I think we still need to stick to long-term investment, on the ground. But I would also say that we should go straight to the best technology. We must start using whole-genome sequencing for diagnosing sensitivities and resistance in TB, and for AMR. If you said that to me five years ago, I’d reply, ‘Come on, in our fields?’ We’ve only just started introducing basic microbiology labs. But we can easily send sputum samples, which don’t need to be packaged in UN packaging or sent via a cold chain. Now, two days later you can get your whole sequencing done. And with the advances in technology, in a few years, small machines will be able to sequence a sample on dry filter paper. Adopting only basic science isn’t the best approach, we should go right to the top in terms of investing in new technology.”

**Christopher Mambula:** “Jacob Burns (Director of Studies at MSF Crash) is asking about R&D, and whether the model we have today is a good model. Is it functional? Or is it broken? If yes, then as MSF or GARDP or others who are working on this, how can we move this forward and try to help restructure or be a part of that debate?”

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16. Huerga, Helena, et al. “Diagnostic Accuracy of the Novel FujiLAM Assay to Detect Tuberculosis in HIV-Positive Ambulatory Patients from Four African Countries.”  
[https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=4175222](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4175222)

**Jennifer Cohn:** “This is a huge question. I think fundamentally the R&D system serves the companies that can commercialize, can get the products out there, which are usually for-profit companies. There are a few that are either social enterprises or publicly held companies, but the vast majority are for-profit companies, so their bottom line is profit. When they look at the potential return on a drug, they look at what profit this drug is going to make. But new antibiotics are only necessary for small segments of the population. In general, most people still have bacteria that can be treated by generic, low-cost drugs. The new drugs that will be patented, they can charge very high prices for as they’re going to be used by small segments of the population, in general, for shorter periods of time. Part of what I, as an infectious diseases physician, want to do both for the patient, and the pathogen, is to not treat for any longer than I have to. The longer I treat the more risk of resistance developing in that individual. Maybe not of the target pathogen that I’m trying to treat, but we are all filled with bacteria, and all those different bacteria are also exposed to any drug I’m giving a patient. These companies are going to compare a niche antibiotic which will be given in a short treatment course to a cholesterol drug, a medicine for heart failure, a biologic for autoimmune disease, and they’re going to say, ‘Nope, I’m going to invest in the product that’s going to be a lifelong medicine that I can charge very high prices for.’ Markets place more value on basically value-based treatments, so small increments in effectiveness will buy you a large increment in price, as opposed to drugs that may be needed for public health purposes, especially in low and middle-income countries. That’s why things are not working well for anti-bacterials. It’s almost as if AMR is the poster child for the failures of the R+D system, but we’re getting down to the wire here, and we are going to have to address this urgently. Because of this urgency, the looming public health catastrophe, even pharmaceutical companies are beginning to engage in thoughts about different R&D models, questioning whether we shouldn’t have publicly owned companies or engage in different methods of payment of those companies who do commercialize, such as subscription-based payments that break the link between price and volume of the product that’s procured.”

**Christopher Mambula:** “I’m going to ask each panelist in 60 seconds to summarise the message you would like people to take home, knowing that we’ve discussed a whole lot of subjects over these last 90 minutes.”

**Bern-Thomas Nyang’wa:** “I’ll go back to what I said at the beginning. Outrage, urgency. We need to be outraged that while it’s great that we now have a six months’ treatment for drug-resistant TB, that’s just on paper. Our patients need it today, tomorrow, next week, but it might take five years to introduce widely if we are not feeling that this is urgent. We also still need to be outraged that the treatment is still for six months, which is a long duration to treat any disease. I would say, let’s keep going, push to do better. Dream big for our patients.”

**Cathy Hewison:** “I would add that it’s a marathon, not a sprint. It’s a long-term investment, on the field, identifying what is needed, what is missing, and passing that up the chain. Operations have

been great in investing in TB and that is the key to our evidence-based advocacy. It takes a team, not one person. We are lucky in TB, we've had the Access Campaign, Epicentre, operations and the medical department all working together towards agreed objectives. That is where you really make things happen when you connect with others and when others connect with you because you are all heading in the same direction."

**Jennifer Cohn:** "I absolutely agree with Bern. Outrage, urgency. That is what we need. AMR is growing. The burden is shocking. It is much higher than we thought. For anyone who hasn't read it, please read that *Lancet* article. It blew my mind. This is not going to stop. The more AMR grows in burden, the less effective will be almost any other medical intervention. Surgery, C-sections, maternal-child health, they are all going to be obliterated if we cannot treat the infections that necessarily come with many medical interventions. This is existential for us. I also agree with Cathy, and what's needed to further appropriate use, conserving antibiotics, using them appropriately, getting new antibiotics, is a multi-disciplinary approach. We need communications, we need operations, we need operational research, we need advocacy, to all come together to address this in an end-to-end way, which is the only way we're going to do everything that's needed for AMR."

**Christopher Mambula:** "For the panelists, thank you for your time. What I would also take away from this comes back to a patient-centered approach. Do not forget to include your patients in whatever kind of innovation, whichever change of treatments, whatever kind of change of duration, because in fact, they are the ones who take the treatment. They might have something really productive to say that will help all of us."



# SESSION 3

## Management of cancer patients

This session is moderated by **Pierre Mendiharat**, Deputy Director of Operations.

### PANELISTS

#### **Dr Fatoumata Sidibé**

Oncologist and hospital doctor at the university hospital CHU du Point G in Bamako, Mali, in the Department of Haematology and Medical Oncology. Graduate of the Université de Fès, the Université des Spécialistes in Lyon, and the Jules Bordet Institute in Brussels. Master's degree in Biology from the Université de Besançon.

#### **Dr Claire Rieux**

MSF Medical Director. Dr. Rieux has worked with MSF for more than twenty years. She specialises in clinical haematology. She ran the safety monitoring department at the university hospital CHU Henri Mondor in Créteil, France, for several years, and since 2017 has been helping MSF to initiate oncology programmes, creating a headquarters-based support team and facilitating an experts' network.

#### **Dr Jean-Paul Vernant**

Jean Paul Vernant is Professor Emeritus of Haematology at the Pitié-Salpêtrière Hospital. He was head of the haematological resuscitation unit and the bone marrow transplant unit at Henri Mondor Hospital from 1973 to 1997 before becoming head of the clinical haematology department at Pitié Salpêtrière until 2010. He was also head of the ORPHé (Oncology, Radiotherapy, Palliative Care and Haematology) unit from 2006 to 2011 and president of the hospital group's Transplantation Federation from 2010 to 2013. He wrote the recommendations for the 3rd French National Cancer Plan.

**Introduction by Pierre Mendiharat, Deputy Director of Operations, MSF-OCP:** “While cancer still represents a minority share of the morbidity and mortality in the low-income countries where MSF conducts most of its activities, that share is growing, and is catching up to the situation in high-income countries where together with cardiovascular disease, cancer accounts for the majority of the disease burden. According to the WHO, the largest increase in the number of cancer cases in the next 20 years is going to be in low- or middle-income countries.

In addition, cancer is one of the health fields where disparities in access to care are generally the greatest. To take one example, only 15% of low-income countries say that they are able to offer their population a full range of cancer treatment services, while among high-income countries that figure is 90%. When we talk about a full range of services, that means access not just to diagnosis and treatment, but also to prevention, since some cancers can be prevented, to a certain extent, thanks to dietary changes, smoking cessation, or vaccination.

For MSF, this is a very new field; there are only two cancer projects in the operational portfolio. These are in Mali and Malawi, where activities began in earnest in 2018 and 2019. Both are MSF France projects; MSF Switzerland has launched an effort to start a cervical cancer project in Kyrgyzstan. We had previously had activities that treated cancer patients, people with Kaposi’s sarcoma or precancerous cervical lesions, but they were not specialised programmes.

In Bamako, Mali, MSF is involved in screening, laboratory testing, chemotherapy, and palliative care. The number of patients in the programme is in the order of magnitude of several hundred. The programme in Malawi offers screening, treatment of precancerous cervical lesions, and surgery. Approximately one hundred women have received care thus far, and 9,000 children have been vaccinated. There is still no radiation or chemotherapy, however.

Hence access to cancer care is not just a matter of access to medicines, or even to health products. It’s a therapeutic field that requires a lot of tools and expertise, from screening to palliative care, including radiotherapy, surgery, chemotherapy, lab testing, and diagnosis. So, we’ll talk about those tools in general, and then about health product-related issues in particular.”

**Dr. Fatoumata Sidibé - Treatment practices and obstacles: the case of Bamako, Mali:** “I am going to describe my day-to-day reality and the day-to-day reality of Malian patients and practitioners in general, regarding care, especially in medical oncology.

#### *How care is organised in Mali*

Mali is 1,241,238 square kilometres and has a population of 20 million. It has several regions, going from the north, with Tombouctou and all of its current problems, to the south, passing through Bamako, Sikasso, and Kayes. The major concern in oncology is that once someone is

diagnosed, wherever they are in Mali, they have to go to Bamako for care. And not just anywhere in Bamako.

The public health facilities – and these are mainly what I’m going to talk about – are arranged in a pyramid; you start at the bottom, locally, and referrals go progressively up toward the top. The health districts are subdivided into health areas, and those health areas include what are called community health centres. These health centres have very little high-tech equipment. They often have just one general practitioner or one obstetrician-gynaecologist for the entire centre, and a few nurses. So, when they are overwhelmed, they refer patients to the referral health centres, which are a bit larger and have a lot more staff and higher tech equipment, but these also have their limits, and then on to tertiary care hospitals. In Bamako, you have the CHU du Point G, Gabriel Touré, Kati, Luxembourg, etc. There are also private health facilities, which can either be for-profit – from small clinics to high tech medicine – or not-for-profit, usually funded by NGOs or by community health organisations.

There are also quasi-public facilities that can be military infirmaries or National Social Insurance Institute (INPS) facilities. Lastly, I added the Pharmacie Populaire du Mali, which will come into play later when we talk about the importation and distribution of drugs. And we can’t forget traditional medicine, which is widely used even in Bamako, regardless of income, but especially for populations with limited resources, for whom hospital access is more difficult.

### *Cancer treatment*

There are several components to cancer treatment. Prevention is very important. That can range from healthy lifestyles to screenings, as well as treatment of precancerous lesions – like for cervical cancer – or immunisations. In Mali, we don’t have the resources. We screen for and treat precancerous cervical lesions, but for other cancers, like colon cancer, screening is not feasible in Mali. After prevention, there’s diagnosis. When cancer is suspected, it has to be confirmed by histological analysis and specimens can be collected by biopsy, surgery, or cytology and sent to a laboratory to confirm or rule out cancer. Once confirmed, the cancer has to be identified and staged. Where is it located? Has it metastasized elsewhere? Then comes staging, which can be done by imaging – the static imaging we’re all familiar with, standard radiographs, ultrasound, CT, or somewhat more specialised MRI. Yet there are very few MRIs in Bamako; in the private sector it’s expensive and thus inaccessible to most people. There are also bone scans and PET scans, which require a nuclear medicine department. We have a nuclear medicine department, but it hasn’t been operational for years, since 2010-2012. The department used to have a bone scan machine but it’s no longer operational, and we’ve never had a PET scanner. A PET scanner is really important, because it enables us to describe the dynamics of a lesion. In cancer it can be used – especially for treated patients – to see the lesion even after it’s dead, when it’s not in fact active. So, the PET scanner enables us to say whether the lesion is just a remnant or an active lesion that needs to be treated (or not). But we do



not have this equipment. Bone scans provide an image of the whole skeleton to determine if the cancer has spread to the bones, because taking X-rays or scans for each individual bone is irradiating for comparatively fewer results. We also do biological tests, which are after all quite accessible except for patients with very limited financial resources.

Once you have all that, you get to treatment. Roughly speaking, treatment is divided into local treatment, which is either surgery – surgery is available everywhere – or radiotherapy. Next there is systemic treatment, the number one being chemotherapy. The drugs that are used are mainly old cytotoxic molecules, which are often available in the pharmacies in Bamako. We also have targeted therapies. That is more complicated. It requires advanced technology to see whether or not to offer the treatment, and the cost of that treatment is also still very high. The most recent addition is immunotherapy, which is designed to restore patients' immune system so they can fight the cancer themselves. It's revolutionary, but these drugs are very expensive; they can cost from three to five thousand euros per injection and have to be given for several years. Finally, we come to palliative care, which is also used for the terminal stages we see in 80% of the cases because they are diagnosed too late.

How is it going now, in Mali? Once someone gets cancer, they have to come to Bamako, and here I'm referring mainly to public facilities, which are already complicated enough to access without considering the facilities that aren't accessible to everyone. The public hospitals that can currently treat cancer, either partially or totally, are the CHU de Kati, which is in Koulikoro region; the CHU du Point G, which is the most well-known and located near Koulouba, the presidential palace; the CHU Mère-Enfant, closer to downtown; and finally the Mali hospital, which was built recently. There are also some specialised facilities like the IOTA (African Institute of Tropical Ophthalmology), the odontostomatology centre, the dermatology hospital, and some private clinics. Histological diagnosis is done only at the CHU du Point G pathological anatomy and cytology lab, which is currently being renovated by Médecins Sans Frontières as part of our partnership. So even if the specimen is collected in Timbuktu or Sikasso, it has to be sent to the CHU du Point G. Some private labs now take samples, but they still have to send them to Point G. Staging can be done at any of the hospitals I listed. Chemotherapy, which is my daily practice, is done only at Point G and CHU Mère-Enfant, and the government gives us 280 million CFA a year. So, you see, that comes to about 426 thousand euros for all of the patients, annually. That's not close to enough. We have drug shortages all the time, and as a result the patients stop treatment because they can't buy the chemotherapy drugs themselves, and that leads to an enormous number of failures.

Now with MSF, since 2018-2019, they have really helped us out of a tight spot by taking over the management of localised breast and colon cancers, and by providing palliative care for other cases. In terms of treatment, there is chemotherapy, radiotherapy, and surgery. All of these complex treatments are essential to curing a cancer. Mali has only one radiotherapy machine, an older generation machine, which is far away at the Mali hospital, so patients have to wait from three to six months. Which means that sometimes, once people have finished their chemotherapy and need to have

radiotherapy, they wait so long that by the time it's their turn either they have a recurrence or their disease has progressed. As a result, they are disqualified from having that radiotherapy. Since there's no result, they come back to us to re-start with chemotherapies that no longer work. We'd like to also have other devices like VMAT (volumetric modulated arc therapy).

Now for distribution of the drugs, just to give you an idea, with this budget envelope we're always meeting with the DPM (Direction de la Pharmacie et du Médicament) or PPM to tell them our needs, but those requests are very limited because we know that we have to make do so that these products fit within the budget. If we want a drug that's outside the budget, we must drop it. If we ask for a quantity that is outside the budget, we also have to cut back. Then, once that small calculation is done, the PPM launches a call for tenders, buys and imports the products, and dispatches them to the CHU du Point G or CHU du Luxembourg or to the radiotherapy unit. Then if those drugs run out, the few patients who have the means can sometimes buy them at private pharmacies, but they aren't always available even there. Some pharmacies import, by buying abroad, in Morocco, but it's even more expensive and complicated and available only in dribs and drabs for the patient. This also results in vastly higher costs, because you must add customs and DHL.

Basically, I have talked about limitations. This is just a summary, but our current limitations are huge. We have only one pathology lab and the results take a month or more because they have to process all the biopsy samples, so it's not easy for them. They're also limited by the technology. They don't have molecular testing, either there or anywhere else in Mali, which means that certain targeted therapies like cetuximab – which has been revolutionary for colon cancer – can't be prescribed because you must know whether the drug is effective against the cancer before prescribing it, and you need molecular testing for that. We now have immunochemistry also, thanks to MSE, for breast cancer. As a result, we can prescribe trastuzumab if the cancer expresses that receptor. I spoke before about the limitations regarding nuclear medicine, radiotherapy, and the geographic situation in the country, which makes it so that everyone has to go to Bamako. What would be ideal would be to have a comprehensive oncology centre so that patients stop having to make the rounds in Bamako. But the biggest limitation is still the drugs. Aid must be increased, because the number of cancer cases has practically doubled here since 2018, from 8,300 to 14,000. We have twice the number of patients, while the budget envelope has stayed the same.

#### *Potential ways to improve treatment*

Here are a few suggestions for improving my day-to-day practice. The ideal would be for all patients to have access to the full range of treatments at a single site, in Bamako: that would mean building a national oncology centre that would have radiotherapy machines and chemotherapy and surgery departments, and in those departments, we would also have at our disposal the means for accessing targeted therapies such as trastuzumab and cetuximab, and also immunotherapy, which is very useful. It would also have palliative care units: we know that whatever we do, our patients will often

come in at later stages where they'll need to be cared for in a palliative unit. Care also needs to be decentralised so that patients in Tombouctou or Sikasso don't have to drop everything each time and come find lodging or stay with family. That usually ends poorly, because cancer can't be treated in a month. It's six months on average. It's often depressing for families to drop everything and come live in Bamako to complete the treatment.

To decentralise, to have all these technologies, we also need continuing and initial training for staff, including doctors and allied health professionals, because thus far we only have five oncologists and, for all of Mali, four radiation therapists and pathologists. We have only three surgical oncologists, but there are other specialist surgeons like gynaecologists and general surgeons who have been trained, either with a university degree from abroad or through on-the-job experience locally, who can treat cancers.

Awareness and prevention should not be forgotten either, at all levels. Mali should also start doing clinical or basic research so that we can provide figures, describe our population in terms of cancer, so that we can move more towards personalised medicine, because now we don't just treat the cancer, we treat the patient and her cancer. Personalised medicine yields much better outcomes than modelling care on what is done in the west or in developed countries. We don't necessarily have the same types of cancer.

**Dr. Claire Rieux - Cancer: MSF's experience:** "This is a very brief introduction to talk about discovering the situation in Mali as both a haematologist treating cancer patients and an MSF doctor deeply touched by the scale of the needs and by something I could relate to – that is, that there were doctors who were competent and motivated, who wanted to do things but were extremely frustrated by not being able to do them because their patients just couldn't afford the treatment. This often led to tailoring the protocols to what the patient could or could not afford, or according to "whether the radiotherapy machine was working or not". As Dr. Sidibé has told you about access, it's extremely complex. It's not just a question of vaccines or drugs – although those things are essential, absolutely necessary – but if you want to properly treat the vast majority of cancers, it's also a question of access to high quality surgery and radiotherapy, which is a major part of cancer treatment and a major bottleneck. Patients have to wait, and that wait is very clearly a lost opportunity for them. It's not just a question of equipment with radiotherapy, but also of highly specialised human resources. Radiotherapy involves several different professions: radiation therapists, medical doctors, and medical dosimetrists, not to mention the maintenance issues, which aren't just a problem in oncology.

The diagnosis is absolutely crucial: you can't treat this disease based only on symptoms. You can't even start treatment based on symptoms, because that leads to disaster, and you see that from time to time. Patients who didn't have cancer, who had an infection – tuberculosis, for example –, or benign tumours, and were treated with chemotherapy. Cancer drugs are extremely toxic with adverse effects.

The other thing that's hard for us is that we talk about "cancer", but really it isn't cancer, it's cancers. MSF projects today focus on the two most common cancers: cervical cancer and breast cancer. But I hope that we'll be much more open to other cancers in the future, and if we're trying to improve access – that is, create an initiative that is going to move beyond our actual projects – I think that will require some thinking; do we deploy tools for all cancers, or just certain cancers, given that, as you've seen, for everything having to do with treatment and everything having to do with management, there are a huge number of commonalities.

Another subject that we talked about yesterday: we must have high quality drugs, and we must have radiotherapy equipment. We need all that, but we also need them to be where the patients are, and be of good quality – that is, the implementation, the orchestration of all of these treatments is extremely important. We know that there are initiatives that have enabled the poorest countries – one by the American Cancer Society, for example, which is the largest patients' organisation, working with the Clinton Foundation, who negotiated agreements with Pfizer and CIPLA – to access much, much lower prices. And we're talking about conventional, basic chemotherapy drugs that are still used in more than 80% of cancers. But after that, how do we make sure that the drugs are distributed properly, monitored, and get to the right patient?

A third point, specific to cancer, is that treatments are sequenced; if the time between chemotherapy rounds is too long, that's a major lost opportunity for the patient. Waiting six months for radiotherapy is a major lost opportunity. These are extremely complex systems in which people can get completely lost, so I really want to stress the importance of care pathway coordination, which has really resulted in better cancer treatment. But we must ensure that there are people who can deal with that, and make sure that the patient gets all her treatments on time. This includes checking to see why a patient didn't come in, i.e., money, misunderstandings, etc.

Nevertheless, I think we're in a fairly good period for two major reasons: first, even if it's still in the early stages, a fair number of countries are beginning to develop universal medical coverage and so are trying to ensure that treatment of some of these diseases are reimbursed. Second, there are number of innovations that can facilitate access, namely telepathology and telehealth, which can be used to fill gaps in local expertise, though much more is needed, and it needs to be done in connection with international experts. Also, something that has really improved the prognosis for patients in France and other countries is what we call the multidisciplinary team (MDT) meeting. It's not one doctor making a treatment decision, it's a group of doctors – including the oncologist, the surgeon, the radiation therapist, the pathologist, the radiologist, etc. – looking at the patient's record and developing a treatment plan. So, when there's a complicated case – some of our African colleagues already do this – we can call an MDT meeting to request an opinion. The same can be done for mammography and, to take it even further, the artificial intelligence that's currently being developed can be used to initially screen the results of some tests and fill the human resource gap.”

**Pierre Mendiharat:** “Jean-Paul Vernant isn’t online yet, but he told me what he was going to say. There are two kinds of problems with cancer drugs. First, 85% of the drugs that are still used in France are off-patent, but some are in short supply precisely because they are off-patent, because they are (wrongly) no longer of interest to the pharmaceutical companies that manufacture them. Second, quite often there’s a price problem with innovative oncology products – as we know, the prices set by the pharmaceutical companies often have absolutely nothing to do with the cost of research, whatever that cost may have been.”

## Q+A AND DISCUSSION

**Isabelle Defourny, MSF-OCP Director of Operations:** “Dr. Fatoumata explained clearly how complex cancer care is, and the difficulties that practitioners in Bamako face. That said, they’re getting lots of things done anyway. Under difficult conditions, the practitioners are still managing to treat a not insignificant number of patients. Claire did a good job of explaining the pressure points. Radiotherapy is really a bottleneck that we’re working on right now. Setting up a second radiotherapy machine in Mali isn’t simple either, but it’s something we’re working on.

There are two points I wanted to stress. First, the coordination of care. While it’s true that there are more than a few centres available, patients are getting completely lost in the care pathway. It’s a complex care pathway where timing is very important. So, supporting patients by making sure that they finish their treatments is a really crucial aspect where we can offer some real added value. But there is a second area that we haven’t talked about much, though Dr. Fatoumata did mention it: prevention and early diagnosis. In my opinion, not much work is being done on the HPV vaccine, which protects against cervical cancer. It’s hard to understand why it is used so little. I think MSF recognises this, but it’s not a strong enough focus for us. I think work should be done on this in parallel with treating sick patients. The other focus that seems too weak but seems really fundamental to me if we want to have successful cancer projects is everything diagnosis-related – meaning early diagnosis. Dr. Fatoumata said it: 80% of the patients who come in are arriving too late and going directly to palliative care. For cervical cancer, we know what to do. We know what needs to be improved in screening for precancerous lesions. We need to use the HPV test, for example, on a larger scale. But there’s a strategy still to be put in place. For breast cancer, there’s really not much being done. So the two points – let’s say, except for radiotherapy – that seem super important to me are the care pathway and becoming much more involved in prevention. Prevention means the vaccine or early diagnosis. If we don’t put any energy into that in our projects, I think the results will continue to be quite poor. On that point, I would have been interested to hear what Dr. Fatoumata thought about that aspect of the work, what she thinks is feasible.”

**Dr Fatoumata Sidibé:** “For HPV vaccination, the data is there. The vaccine is available, but the patient has to pay for it. One shot costs about 100,000 to 150,000 CFA francs, depending on the

pharmacy; that's 150 to 200 euros for a country whose annual minimum wage is 45,000 CFA francs, so it's not at all feasible. They held strategy meetings without anyone who's involved in screening, or even doctors. Since then, we've been trying desperately to get the powers-that-be to listen and understand that this vaccine is truly essential, and that it would fix part of the problem. The other thing is that in Mali, as soon as you start talking – a bit like everywhere else in the world – when you start talking about vaccines, people immediately get afraid. Straightaway there are common misconceptions, negative messages like 'these are products' – and I'm using the language of the general public – 'these are products that the westerners, the Whites, developed to make us infertile, sterile, so the population stops growing'. It's a major effort to get them to accept, to get them to understand, and accept the vaccine. That effort is even more essential than free treatment, because even if it's free, without an awareness-raising campaign you won't get anyone to come. The vaccination rate will be very low and that won't fix the problem.

In terms of breast cancer, we convey awareness-raising messages about breast self-exam, but breast cancer screening is mainly mammography. In Bamako, we don't have many mammography machines. There was one at Point G that was being refurbished for several years. It's operational now. Another one is available at Gabriel Touré. Those are the two public facilities that have mammography machines. There are mammography machines at other facilities like the reference centres and other places that have never been used, because unfortunately the machines got there before the specialists. They fought to get the machines but didn't have any qualified radiologists who could read the images. In a lot of regions like Sikasso, there were machines given by the government that just sat in the rooms unused. So, we need to train radiologists, because as in all countries, screening via mammography is special. Mammograms have to be read twice. It requires experienced radiologists who are accustomed to reading that type of mammogram, so that we don't get a lot of false negatives or false positives, and the machines must be available and affordable. At Point G, which is public, it costs from 10,000 to 20,000 but privately it costs 30,000 CFA francs to do a mammogram. So again, not everyone can access it. We can't mount a campaign for that unless we're sure that screening will be free and that the test will be read correctly.”

**Pierre Mendiharat:** “Two questions from the audience: There is one general question: what are the barriers to access for the HPV vaccine? And a more specific question: does it really cost 150 euros for the HPV vaccine, per vaccine dose?”

**Dr Fatoumata Sidibé:** “The HPV vaccine injection, per dose, costs about 150 euros, and you must have two or three doses. They are sold at the private pharmacies, and not in the public pharmacies. Not in the Point G hospital pharmacy, for example.

And I was talking about common misconceptions. Those are the barriers: these common misconceptions, because the target population for the HPV vaccine is, first, girls before they become sexually active or right after they have a screening test – either a VIA/VILI or HPV test – to make sure they

don't have the virus. Some countries say that even if the test is positive, you can vaccinate at a later age. But if that is the target population, meaning girls and women who are a little older and more likely to be sexually active, a common misconception is that we want to inject substances to make them less fertile.

And the other barrier is that the Ministry of Health, the decision-makers, do not feel it necessary to pay for the vaccine, to make it free and add it, for example, to the immunisation schedule for girls and older women, despite the fact that cervical cancer is either the most, or second most, common type of cancer in Mali.”

**Pierre Mendiharat:** “One comment regarding a WHO-prequalified Chinese vaccine – some information from Delphine Pautis. This is something new; but it will be less expensive, it's WHO-prequalified, and should be available in a country like Mali.”

**Delphine Pautis, pharmacist, MSF Logistique:** “It is prequalified. I didn't ask about price or availability, but it is prequalified and so it should be possible to get access to it.”

**Alain Alsalhani, pharmacist, MSF Access Campaign:** “Don't forget that Mali receives Gavi assistance, so this is also something that should be discussed with Gavi. I took a quick look at the data. It looks as if there was actually a pilot project at one point, but it didn't last long, where Gavi gave 350,000 euros to buy the HPV vaccine. I think the correct response is to discuss, a propos of what Dr. Fatoumata was saying, with the Ministry of Health regarding the type of negotiations it has had with Gavi about introducing this vaccine into routine immunisation programmes. Right now, if the Chinese vaccine is indeed prequalified, it can also be supplied via Gavi or bought with Gavi money.”

**Pierre Mendiharat:** “When I was involved in Malawi at the start of the programme, that was exactly our problem; the HPV vaccine was supposed to be accessible via Gavi but there were all sorts of problems and so in the end the vaccine was used very little.”

**Julien Potet, MSF Access Campaign:** “Malawi introduced it and is going to get Gavi support, which is not the case with Mali, according to what Fatoumata says. The Malian authorities decided not to add it to the immunisation schedule yet. The other problem with Gavi was that the HPV vaccine supply was inadequate relative to the anticipated demand and the anticipated distribution capacities for the African continent. But the latest news is fairly reassuring with the arrival of new HPV vaccines. So, in terms of global supply, there will surely be enough doses for Gavi to be able to supply more countries. In terms of advocacy, if we think that cervical cancer is a priority in Mali, I think the target is both the Malian authorities and Gavi.”

**Isabelle Defourny:** “It seems to me that the strict minimum should be to offer the vaccine to the daughters of our patients, or other female members of their families. I think that should be part of

our care. We're not obliged, at the outset, to find a comprehensive solution for all of Mali, but to at least offer this vaccine to our female patients' daughters; that would at least be a start."

**Félix Kouassi, doctor, Deputy Cell Manager MSF OCP Operations Department:** "Is it a priority for the government, the health authorities, in these countries? We can talk about mobilising so that girls get vaccinated, but I think that first it must be seen as a priority for the governments, for the health authorities who, once it's a priority, will have to acquire the means."

**Pierre Mendiharat:** "One comment on the price and on the fact that in India, MSF is working on this issue of off-patent drugs."

**Leena Menghaney, Access Campaign South Asia:** "Those drugs that are no longer being made, it's a completely deliberate move by the pharmaceutical industry. For example, for multidrug-resistant TB in India, we talked to the manufacturers about what could be done to resume production with prequalification and quality assurance and encouraged the setting-up of a pooled procurement system, which has happened for older generation antibiotics. I get the impression that could be done for other older drugs or cancer drugs, working with manufacturers and encouraging them to find sources for these drugs and set up a quality assurance system in order to encourage them to produce more at a lower price, for a guaranteed market. That can be done for a lot of diseases with medicines that are fairly old. In India, we had quite a few problems with drugs that are no longer being made once it stops being profitable."

And the second thing I wanted to say – I know a lot about Asia, but very little about Africa – but as far as the HPV vaccine and support from feminist movements are concerned, it should obviously be a part of sex education for women and girls, and perhaps be promoted via school programmes and sexual health education. But some stakeholders are reluctant to make it part of sexual health. Also, we expect governments to adopt a new vaccine, but even if it's a few dollars, it's sometime too expensive for them to afford. We need to work on lowering the price of the HPV vaccine. We saw that for the pneumococcal vaccines as well."

**Jean-Paul Vernant - From a shortage of older drugs to the high price of new ones:** "We have some big problems even in wealthy countries like ours, and I can imagine what it might be like in developing countries. There are two types of problems. First, we have older drugs that have been around for 40 or 50 years that are in the public domain and so are of absolutely no interest to the industry. That is to say that they don't bring in enough money, unlike innovative therapies. What do they do? In order to get at least some profit, they outsource production of active ingredients to India or China and then subcontract the manufacturing. But why did these manufacturing countries change their technique? Quite simply because 20 to 30 years ago, the pharmaceutical companies that were working well started gobbling each other up, and so we went from having over a hundred firms to now only 12 to 15 Big Pharma companies setting all the rules. And those Big Pharma companies are



now financed by pension funds and investment funds so have to make big profits. So, the old drugs no longer interest them, yet these old drugs still account for 80% of the ones used for cancer treatment. All those drugs are still needed. But because their manufacturing is extremely complex – partly in Asia and partly by subcontractors – shortages are very common and those shortages are deeply troublesome both to us and to the patients, who suffer on account of them. So, we have to try to fix this problem of shortages in older drugs, a problem that is exponentially increasing.

As for innovative therapies, they bring in huge amounts of cash, and that's what interests the pharmaceutical companies, and so we've gone from the principle of earning lots of money by making inexpensive drugs that are prescribed to lots of people to that of manufacturing expensive niche drugs. Before, there were three types of lung cancers; now there are 10-15 types depending on the molecular abnormality, and only a few patients will be treated, but they'll get treatments costing 50, 100, or even 200 thousand euros a year. And so obviously these innovative therapies threaten the financial balance and social safety net, even in wealthy countries.

Question: why is it so expensive and how are prices determined? For a very long time, the old pharmaceutical companies, 30 to 40 years ago, would market authorised drugs at reasonable prices based on what they had spent on research and development. But they're not the ones doing new product research and development anymore. In fact, the research is done mainly by academic researchers in France, Germany, Japan, or the United States; and everywhere, it's public funds that finance the work but it's the industry that profits from that work. That's the first thing. Also, development that used to take 10 to 15 years to get a drug to market now takes only three or four years. It's a lot faster. So, there's little justification for drugs being very expensive based on R&D costs. We know that research and development now account for at most 15% of a pharmaceutical company's total budget, while 25% goes to marketing and 20 to 23% is profit. I read something absolutely incredible yesterday. Roche's turnover in 2021 was 62.8 billion Swiss francs. Profit was 23.7% of turnover. No other industry produces such enormous profits for their shareholders. They no longer charge high prices due to research and development; they charge high prices under the pretext of services rendered. But in fact, what defines the price of a drug is what they think the market will bear. And that's how the United States has ended up with drugs like Imatinib that are put on the market at 30,000 dollars per patient per year, and even up to 60, 90, 120 thousand dollars. Simply because the market can bear it. We're not going to be able to afford these innovative therapies forever, and of course they are unaffordable in developing countries.”

**Dr. Jean-Hervé Bradol, Director of Studies, MSF CRASH:** “Some of the blame lies with Gavi and the governments, which set public health priorities that only partially address their populations' needs, but I think we also have to take care of ourselves to some extent, and we also have to try to be more consistent. I know it's not easy, but this morning's session showed fairly clearly that those of us who are involved in the issue of treating female cancers each have a small fragment of the information and it's hard to put together a big picture containing all the information. The HPV

vaccine is a good example. It's been four years, or something like that, that we've been working on cancer in Mali and Malawi, cervical cancer, and between us we should have much better-consolidated information. As for Pr. Vernant and his discussion of the drug problem, the older drugs that will be abandoned, for example, that was one of the first problems we faced twenty years ago with the Access Campaign. That led us to become worldwide distributors of certain classes of drugs, since there was no one else to do it. I'm thinking of the drugs used to treat human African trypanosomiasis, or sleeping sickness. But what strikes me is the fragmentation of information within the MSF network that deals with that. Though we have almost all the information we need, it isn't consolidated, or isn't consolidated very much. This, it seems to me, is a clear indication to MSF Directors of the coordination work they have to do. I include myself among the managers that sometimes have trouble coordinating the operations they're implementing. But frankly, after listening to you this morning, the diagnosis is fairly clear."

**Isabelle Defourny:** "I agree completely with Jean-Hervé's diagnosis. There's a problem of coordination and information-gathering in the movement and even within OCP. Questions of this kind on the HPV vaccine – I also have a whole series of them on a lot of other diseases, a lot of other topics where I think the answers exist in various places in the movement. And it is indeed this working together to make progress on certain identified issues that we're going to have to do quickly."

After that I had another question. We talked about it a bit, and this is also for Dr. Fatoumata. It seems that with cancer, you need chemotherapy. Yet there are some that are really expensive, such as immunotherapy, but there are some that are not really expensive, older chemotherapies that are available as good quality generics. We talked about the problem of some older drugs going out of production, but I got the impression that in Mali and in various West African countries another problem for the government and for practitioners was knowing how to procure and how to identify those quality generic chemotherapies that are still produced. Is that still a problem?"

**Dr Fatoumata Sidibé:** "Yes, that's still problematic because when we tried to investigate, it was fairly complicated. The authorities have their supply networks that they don't want to abandon, and their own way of doing things that often isn't explicit and doesn't work for us, the practitioners. The people who decide these things are usually not practitioners. They aren't the ones who work with patients. They're doing administrative work and have trouble coming to us, and vice versa. They put out calls for tender. It changes every year because, due to transparency issues, they aren't allowed to pick the same supplier, which would actually be better for us. For example, I already talked to the MSF people, they know that there are labs in India or even France that manufacture these drugs at lower cost; we could establish partnerships so that with the same funding envelope MSF could find us the drugs, even just the cytotoxic agents and older drugs, on an ongoing basis and supply them to Mali. We tried to approach the manufacturers several times for that, even in India. After that, we would only have to ascertain the quality of those products, do some testing, and then import them. We proposed all that to the authorities. That can be part of the solution to

our problem, in any case. I won't talk about immunotherapy or targeted therapy, which are innovations that are still out of reach for all the generics makers. But still every year, there are just new calls for tender. Private or public entities come and state their prices and, depending on the price, the government buys their drugs. You get the feeling that there aren't even big negotiations involved. So, we keep seeing drug shortages and drugs that go a whole year without being available free of charge. And specifically, we identified some Indian pharmaceutical companies where the suppliers are in Senegal; meaning the patients can buy the drugs themselves. It's still less expensive than via some suppliers, but it's done on an individual basis, that is, the Point G hospital isn't going to say, 'Ah, there's no product, we'll ask for bids and buy in bulk.' No, it's patient X who needs the product and buys two or three vials, or who buys for each treatment round. And each time there are DHL costs and all the other costs that are added each time a small individual purchase is made. It's less advantageous."

**Julien Potet:** "It's really interesting to see the dichotomy between the older drugs that are no longer patented, that don't cost anything and have availability problems. It reminds me of penicillin G and certain older antibiotics that have similar supply problems; this is not an issue we've dealt with head-on in recent years at the Access Campaign, but I think it's really important. It doesn't cost much to maintain a supply of older drugs. The situation with the BCG vaccine is somewhat similar. So that's a first issue we could work on in MSF, not just for cancer but maybe antibiotics as well. I'm sure there are things to be done in that area, as well, with older antibiotics. The second issue is the new therapies – the more recent cancer therapies and monoclonal antibodies in particular. So, just to let you know that we at the Access Campaign are finally really getting into monoclonal antibodies. We're going to have a first in-house meeting to learn more about this subject in the coming weeks, inviting outside people, probably inviting biosimilar manufacturers. You should know that today, the supply is growing enormously in India. Serum Institute is getting deeply into manufacturing monoclonals, with a business model that consists of slashing the prices of trastuzumab and other blockbuster cancer drugs. I think we're going to have a small revolution, like we saw with certain drugs, by the Indian pharmaceutical industry, with the aim of a very major price cut for these drugs. That's something we have to be ready for, I think it will be in a few years, and it could potentially be very useful for countries like Mali."

**Pierre Mendiharat:** "Ellen 't Hoen was supposed to speak. She wanted to tell us about the difficulties of the WHO Essential Medicines List Committee to define a position on medicines that have a clear therapeutic value but are very expensive and so could overwhelm the financial capacity of low-income countries. The committee's experts recommended that the Medicines Patent Pool should first work on the intellectual property rights and prices of the medicines concerned. And she wanted to stress the fact that right now groups of cancer patients are organising and growing and that, according to her, is an opportunity to make progress on these advocacy issues."

# SESSION 4

## Nutrition, malaria, and children's health

This session is moderated by **Marie-Hortense Koudika**, doctor and Deputy Cell Manager in charge of medicine at the MSF OCP Dakar cell.

### PANELISTS

#### **Kevin Phelan**

With a Masters degree in nutrition science, Kevin is currently the nutrition advisor for ALIMA. He provides technical support to the organisation's teams and contributes to operational and clinical research in the areas of nutrition and health. Before joining ALIMA, Kevin Phelan worked with Médecins Sans Frontières for over ten years, in a variety of positions.

#### **Adeline Lescanne**

Adeline Lescanne is the Executive Director of Nutriset group. She holds degrees in agronomy and development studies. Her first field experience was at a health programme in Malawi, after which she joined Nutriset group, which was founded by her father. She worked to create and expand the international network of therapeutic food manufacturers under the PLUMPYFIELD label.

#### **Philippe Duneton**

Philippe Duneton is a physician specialising in infectious diseases and public health. He is currently Executive Director at Unitaid, an international purchasing and medicines organisation charged with centralising the procurement of medical treatments in order to get the best possible prices, for developing countries in particular.

**Marie-Hortense Koudika - Overview of malnutrition and malaria care:** “Nutrition and malaria are fundamental issues for MSF, since malaria and malnutrition are still diseases that MSF teams deal with every year in the countries where we work, and more specifically, in the Sahel today. To give you some numbers, for example, in 2021 nearly 32,000 children were treated for severe acute malnutrition in OCP projects alone, in the four countries monitored by OCP’s Dakar cell. And regarding malaria, nearly 260,000 children were treated for malaria last year. We know that there has been a fair amount of progress over the years in developing not just diagnostic tools and treatments, but also strategies and care models. In terms of nutrition, for example, there was all the effort around standardising the diagnostic tools that enabled the stratification of malnutrition with all the tables: weight-for-height, etc. There was also the advent of ready-to-use therapeutic foods, which revolutionised malnutrition management in the 2000s and thus facilitated ambulatory treatment of children and the decentralised, community-based care we are talking about now. As for screening, which used to be done only at health care facilities by qualified health workers, we are now talking more and more about having the families do the screening by giving the mothers a MUAC tape. There have been a fair number of studies to find good inclusion criteria and adapt the protocols. There has also been progress regarding combined strategies with, for example, the comprehensive prevention package for preventing malnutrition in infants to reduce morbidity and mortality. And as far as malaria goes, we still remember the era of chloroquine and quinine, before we moved on to artemisinin derivatives and then combination therapies. We went from presumptive diagnosis by the practitioner to routine diagnostic confirmation via the rapid diagnostic tests we use today. And thanks to those rapid diagnostic tests, we see how it’s now possible for non-medical workers – that is, in the community – to treat children with malaria. Seasonal malaria chemoprevention (SMC) has been shown to be up to 80% effective. That efficacy, however, seems to be undermined by difficulties with follow-up in the field, adherence, and certain issues that we will elaborate upon throughout this session.

One observation is that MSF, which has long been a major player in developing such improvements, now seems to be absent from discussions on managing acute malnutrition, including prevention, while it is other players like Alima that are now heavily involved in all those discussions.

What are our objectives for the future? What are the potential obstacles to access nutritional products suitable for treating and preventing acute malnutrition in children? What should be the model or strategy for malaria prevention and early treatment? Which solutions might we consider given those obstacles? These are the questions we’ll be discussing throughout this session.”

**Kevin Phelan - Alima’s experience at the childhood malnutrition treatment camp:** “Over the past ten years, Alima has treated more than 100,000 children in the Sahel and in central Africa for severe acute malnutrition, and now we understand that the system has problems. Diagnosis is delayed because we rely on community health workers and health workers. Treatment is delayed because families only get access to nutritional support when the children reach the most severe stage

of malnutrition. Attempts at prevention don't consider the fact that families suffer a significant lack of access to diets that meet the needs of their children in terms of quantity and quality. So, at best our attempts at prevention remain wishful thinking, and at worst malnutrition is blamed on the parents.

Alima was a pioneer in teaching mothers how to use the little MUAC bracelets so they could screen their children at home for early diagnosis. We also tried to develop simplified protocols that would make it possible to start treatment sooner, and then we promoted nutritional safety nets for children. Those last two efforts relied on specialised nutritional products, that is, ready-to-use therapeutic foods. In 2005, almost no children were treated for malnutrition because they had to be hospitalised for six weeks, and there was no access to clean water. RUTF enabled us to really scale up, and now approximately four million children receive the treatment as outpatients. They are treated at home, come in for a consultation once or twice a month, and we manage to get a satisfactory nutritional status in about six weeks. We haven't, however, managed to meet all the needs; there are still twenty million severely malnourished children, who are at a ten times higher risk of death than those who are adequately nourished. So, we have failed and must try to find some way to solve this problem. Especially since even the progress so far is fragile, as it is heavily dependent on precarious funding, without even mentioning the growing needs. In many parts of the Sahel malnutrition is a structural emergency, and not just the result of conflict, population displacement, or drought. While access to a healthy diet isn't the only thing a child needs to avoid malnutrition, it is still a prerequisite.

Over the last decade a new, lipid-based nutritional supplement tool, SQ-LNS, which is similar to RUTF but given in smaller quantities, has been developed and tested in randomised clinical trials. We give it as a daily supplement for 12 to 18 months. It can reduce acute malnutrition, wasting, anaemia, and even mortality, and has a positive impact on outcomes in terms of children's growth. *The Lancet* voiced support for the tool in some articles as an intervention for children with malnutrition or in countries where, in my opinion, such programmes are needed.<sup>17</sup> Alima has run some very small-scale programmes using SQ-LNS in Niger, Chad, and Cameroon, and I can tell you that the children love it and so do the mothers, because they can see with their own eyes how it helps their children. But again, at \$25 per child per year, we face a funding problem; that cost is considered well beyond the funding capacity of the governments of those countries. Another funding tool is needed – whether by Gavi, or a special Global Fund for nutritional products, or the World Bank – to ensure that these nutritional safety nets for children exist in areas where malnutrition is truly endemic. It might also require access to other sources of food, protein, with foods that are appropriate to the local culture, as we have to make sure that in addition to the SQ-LNS, these children will be fed, because we're still going to have more and more children who will become malnourished and die before we can give them nutritional support.”

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17. Keats, Emily C., et al. “Effective interventions to address maternal and child malnutrition: an update of the evidence.” *The Lancet Child & Adolescent Health* 5.5 (2021): 367-384.  
[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30274-1/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30274-1/fulltext)

**Marie-Hortense Koudika:** “You’ve told us an enormous amount about malnutrition; we know that there’s a kind of vicious cycle right now between malaria and malnutrition. What’s your conclusion today about malaria diagnosis, treatment, and prevention?”

**Kevin Phelan:** “Like everyone, we are facing this problem, this vicious cycle. But there’s one thing I’d like to say, with regards to the nutritional safety net for children; we showed that it facilitates and encourages the uptake of medical treatments for other diseases. When we combined SMC with nutritional product distribution we found, during the ‘1,000 Days’ programme, that the vaccination rates also went up for yellow fever, measles, etc. Unfortunately, that programme is no longer being funded. And speaking of the vicious cycle between malnutrition and malaria, there’s a new malaria vaccine that, despite its relatively low efficacy, will probably be part of the solution. If we encourage uptake of these vaccines or SMC via the nutrition programme, that means all the children’s daily needs could be covered. But first we need funding.”

**Adeline Lescanne - Development of therapeutic nutritional products: research, partnership, and local production:** “When the Nutriset group was created 35 years ago, the idea was to help fight malnutrition by offering commercially-manufactured nutritional products, which didn’t exist at that time. The idea was to be the link between the researchers – who had a fairly clear view of the needs, or were at least doing research on the nutritional requirements within a product – and the mouths of the children who needed a product that was good, enjoyable, and edible, because even malnourished children need a good product, and we have always been committed to that idea. And also, to work on the entire supply chain in order to simplify every step along the chain. That’s why we focused right from the start on products to treat severe acute malnutrition, which was the most visible type of malnutrition at the time. With the development of Plumpy’Nut we demonstrated that we were capable – collectively, not just Nutriset – of reaching many more children, and we were able to then take the time perhaps at that point to start to focus more on prevention and work on other types of malnutrition. If we’ve gotten to the point of having to treat a child for severe acute malnutrition, then we’ve already failed. There are two major aspects of prevention. On one hand, there’s the question of nutrition and which types of products to use, with huge research efforts on SQ-LNS in particular, and on the other, the socioeconomic aspects and the country’s economic development.

In addition to research, Nutriset’s capability and knowledge is in the development of private manufacturing companies. In 2005 we created the Plumpyfield network in the hopes of ensuring a local manufacturing response to the recurring demand for the different malnutrition treatment products. Through this network we now have factories in Haiti, Guinea, Niger, Burkina Faso, Nigeria, Sudan, Ethiopia, Madagascar, and India. We are very proud of that network.

Regarding prices, I think that should be another discussion, because prices are not actually any lower with local production. However, such factories have very significant impacts and positive

aftereffects in terms of reinforcing the countries' quality industrial capacity, pharmaceutical lab development, and agricultural sector development, so they are able to handle problems like aflatoxin and other different subjects to help make the environment more conducive to what they hope to achieve in the future, including developing a wider range of prevention products that could be industrially produced using local raw materials and not necessarily just manufacturing products for nutritional intervention. This is a first essential step toward having the tools locally, to being able to develop new products. It also allows greater government involvement, since it's always more attractive and rewarding to manage a local problem using home-grown responses than by importing products. Besides that activity, we still have a large factory in France that enables us to respond to emergencies and in countries where we see no possibility of having a local industrial tool, at least in the medium- or short-term. It recently sent more than 50% of its production volume to Yemen, for example.

In terms of products, in the beginning – as I said – we really worked on malnutrition treatment with products for severe acute malnutrition and moderate acute malnutrition, and then began focusing more and more on vulnerable populations with specific needs, like pregnant and breastfeeding women. Now we have decided to work more on disease support, that is, helping ensure that every patient's nutritional status is good enough to fight their disease. In particular, this year we worked with MSF to develop a product called Nutri'Hope, a complete high-protein nutritional powder that has to be reconstituted with water. For that, we responded to a specific request from MSF regarding the management of adult patients who are at risk for or suffering from malnutrition when entering programmes for all kinds of diseases.

Getting back to malaria, for a really long time we wondered whether we could use nutritional interventions as an opportunity to administer other treatments, since malaria attacks happen during the lean season. It could be also that better nutrition enables the body, and thus the children, to better fight disease. Studies are underway to investigate the relationship between the administration of nutritional products and the incidence of malaria. We would therefore start to get into using nutrition to really help children fight the disease.

Over the past two days you've been talking about drugs, yet the economic dynamics are not at all the same here. Our work is in the food industry. There was a major effort recently with UNICEF, the WHO, and researchers all over the world to reduce the cost of RUTF, which raised big questions about protein; could plant protein be sufficient? Right now, we don't have any studies that could show that, and using dairy protein in the product is obviously very expensive. We have to be careful not to lower the quality of the products, which is a very big risk for very little gain, because we're still not going to be able to reduce the prices significantly. We prefer to focus on product quality, on having a better quality product that could reduce the overall cost of the programme and have quicker impact on the children.”



**Philippe Duneton - Unitaid's role in meeting the funding challenges:** "I'm taking part in this panel today, but actually all the other discussions are also very relevant to us at Unitaid because we work on access issues – that is, which drugs, tests, and health products are needed, their quality (we just talked about that), and obviously their price. We have a particular focus on malaria. I'm going to get back to that, in particular because we were the agency that pushed SMC a few years ago. I note that we owe that approach to Senegalese and Malian researchers – thinking about Professor Doumba, in particular, who sadly left us a few years ago. Generally speaking, Unitaid also enabled the introduction of all of the antiretrovirals that are used in Africa, and regarding paediatrics, we were at the origin of all of the paediatric formulations – for tuberculosis, in particular, but also for malaria and HIV/AIDS. That seems important to us because these are neglected populations, as you know, in terms of both access and formulations. For 50 years we have failed to take proper care of children who unfortunately were affected by tuberculosis. I say that because that is part of our role as funders, but also as influencers. It is one of the roles of Unitaid to demonstrate that a product works – and we obviously work with MSF and other actors such as Alima on this – and it's probably one of the most important aspects of financing. I'd like to add that when we started working on paediatric formulations for HIV – we were addressing this problem with MSF, Nutriset and Alima – we were ensuring that the issue of malnutrition would be taken into account, as it is well known that putting malnourished children on ARVs is dangerous.

Regarding financing, there is a critical weakness for nutritional programmes. There is obviously an issue of governments, since we believe that a large part of the financing should be done by the countries themselves, but obviously there's a need for special additional international aid. The estimated needs, globally, for this issue are purportedly seven billion dollars – but compared to what? We are talking about 20 billion dollars for the Global Fund. If we take the Covid response – which has unfortunately also had an impact on other diseases and access to treatments, including for malaria, and their financing – we're talking about 35 billion dollars for the Covid response in the Global South. There are mechanisms that were created specifically for nutrition – 'Power of Nutrition' and UnitLife – and so the facilities for global financing. But the funding is not as good as what we might hope for right now. There are also funds which are not dedicated but could form part of Global Fund and Gavi programmes, but they're not systematic.

There is a part of the ongoing operational research that makes it possible, both now and in the future, to consolidate the cases; for funding, there's a significant 'evidence-based' effect, as they say, that should be pursued. In fact, that's the case for all of the organisations, the Global Fund, Gavi, etc. Also, with regard to financing, the fact is that there's a tendency to work in silos, so there are vertical malaria programmes, TB programmes, etc. And so, we really don't manage to have a more comprehensive approach centred on people's needs. This is important, because a person doesn't just contract malaria, or a child doesn't just contract malaria: there are other infectious diseases, the nutritional context, etc. The international organisations probably need to direct their efforts at both the country level and the advocacy level. That's a bit what we try to do, especially with our ALIMA

colleagues, since we started discussions with them a few years ago about childhood fevers, including about some very specific points – for example, how can we monitor not just access to oxygen but access to simple pulse oximetry tools as well? We started this work before Covid, but then realised how it was completely strategic for the Covid response. But we're also working on oxygen access with ALIMA and others – this time in the context of Covid. We know that there are so many public health benefits that it's worth negotiating agreements with companies that produce oxygen, as we did recently, but also to help countries make the diagnosis of what they need.

There is also the issue of anaemia, which is unfortunately a good indirect indicator for both nutrition and infectious diseases, including malaria. That should cover not just children but young women, as well – pregnant women, in particular. These are also avenues for discussion in terms of both anaemia testing and to see how we might get dietary supplements added to programmes for women and children.

And there is one specific aspect in the Sahel, for the previously-stated reasons, which is the multiplicative seasonal effect of both malaria and malnutrition. I think we need to consider combined programmes that can address malaria, nutrition, and anaemia prevention and treatment. There are even some complementary approaches, since it would involve also thinking about access to better quality antibiotics. We need a combination of things; just one thing is not going to solve all the problems. While there are obviously cost issues, I think it is still very important to ensure the efficacy question is prioritised.

One last word, perhaps, on SMC. I mentioned how important it was for us to have invested nearly 70 million dollars in a drug access project that was picked up by the Global Fund for seasonal malaria treatment. There is one issue that needs clarification, however, which is how SMC articulates with access to malaria vaccination. Unitaid co-financed the phase IV trials with Gavi and the Global Fund to show the value of such vaccination. It isn't a miracle, since the impact is modest; when you look at combining malaria vaccination with SMC, however, child mortality is further reduced. The problem is that there are availability issues, and there are production-related limitations at present. There may be a second vaccine manufacturer, but not for at least five years. One of the questions for the WHO, in terms of recommendations, is whether this tool should indeed be combined with SMC in the Sahel region or whether we should instead be thinking about introducing it in endemic, high-transmission countries. I don't have an answer to that. The WHO is working on it.”

**Marie-Hortense Koudika:** “Aside from financing, the most important point that you brought up – which could be one of the limitations – is that there is still work to be done on an integrated approach in our responses. And that refers to the idea of a patient-centred approach. I still recall the many programmes we had in countries where in any given week a mother might have to go back and forth to the health centre many times because there was one day for nutrition, one day

for vaccination, one day for something else. So, some of the care models in our practice still need rethinking, we should be working on integrating the different components of our programmes.”

## Q+A AND DISCUSSION

**Evgenia Zelikova, doctor, Deputy Cell Manager, MSF OCP Operations Department:** “I’d like to ask Kevin a question about Alima, regarding support for families of malnourished children and particularly psychosocial support.”

**Kevin Phelan:** “Clearly, we can always do better in providing psychosocial support for the families we meet in our programmes. But I would like to add something. With regards to mental health and the well-being of mothers, there is a lot of research in both the Global North and Global South showing that when mothers stop being stressed about food security for their children, their mental health and well-being inevitably improve. We’re in the process of testing that on a small scale in Ouagadougou.”

**Thierry Allafort, General Director, MSF France:** “We’ve made a lot of progress. Together we’ve learned how to treat malnutrition, and how to reconcile that with infectious diseases. There is still a lot of medical and technical progress to be made, for sure. Nonetheless, our ability to do that relies on products whose costs we haven’t managed to lower, and on funding that is on the decline. In the Sahel, among other places, we have to thank ECHO for having borne that expense for more than 15 years, but they are now cutting their funding. There is development funding coming in, but it falls far short of the target. So for you all, what is the solution?”

**Adeline Lescanne:** “We’re talking about a product – RUTF – that feeds a child for 75 cents a day. . . . Isn’t the work to then go seek funding by showing its effectiveness? There is no money for nutrition. I would find it super interesting to work together to convince people of the products’ effectiveness. We can be transparent about our numbers, if that would help you, and then support local production. But trying to cut programme costs would mean buying only in India and Pakistan.”

**Thierry Allafort:** “I didn’t say expensive, I said hard to make cheaper. And when you go to Niger where ECHO funding has already been drastically cut and you start talking about adding in coverage, for example, for prevention but that’s going to cost 200 to 300 million euros, it’s obviously hard to convince. People then turn instead to products that aren’t necessarily effective. So, you have an effective product whose cost we can’t bring down, on one hand, very little funding on the other. That’s what I wanted to stress – that we’re still having trouble finding solutions to this problem.”

**Philippe Duneton:** “There’s no miracle solution. On the overall question of funding, there are development-specific budgets and the question one might ask is whether there are other sources of funding.

There are innovative financing mechanisms that could be tried. We unfortunately know the fate of the airplane tax; it was suspended due to COVID, with the resulting crisis in aviation. We also worked really hard for implementation, and it worked in France but not in the other countries, of the TTF, or a tax on financial transactions, which is something that isn't well known; in France it brings in 800 million euros a year and helps finance a large portion of human development efforts including Global Fund, Gavi, and Unitaaid funding, the Global Compact on Education, and the Fonds Vert (Green Fund). There was a lot of discussion for a time in Europe, with eleven, and then five, countries that were supposed to institute it. Brexit put a halt to everything, because the countries wanted to position themselves on the financial markets and so didn't want to impose a tax at a time when they thought there would be companies that would move from the United Kingdom. A tax is never very popular, but it's the most popular one I know of. Taxing financial products that have zero economic impact and shouldn't pose problems for anyone – or not for individuals, at any rate – is another idea that should perhaps be back on the table, because at some point development money reaches its limit, and if we can't find additional funding mechanisms then we can't deliver these programmes.

You also have to remember that price wars can have a significant impact on quality. About twenty years ago, we had a situation with tuberculosis where products cost very little but were not good quality.”

**Adeline Lescanne:** “There's the example of SQ-LNS and how financing got triggered by publication of the results of those products in *The Lancet*. Last year, the World Bank budgeted 100 million dollars for two countries, Madagascar and Burkina Faso, for the use of those products. When you truly demonstrate effectiveness, money gets released. I'm not Unitaaid and I don't know everything, but I see it happening.”

**William Hennequin, Cell Manager, Operations Department, MSF OCP:** “It seems to me that – according to our practices and what we observe directly in the field – the needs of populations are clearly being underestimated, overall. In fact, you find – for example, in Moissala, Chad – that there are three times as many people as the population counted officially by the government and then reported to the institutional donors for supplying products for malaria, nutrition, etc. You often find that health facility managers don't understand how to order products or aren't good enough at it, so it isn't done properly. As a result, they don't receive the amount they should be requesting. It's done poorly, and so the system doesn't work very well. It often requires a lot of effort by our teams to make sure that it's done correctly. Unless that work is done properly in the field, it's hard to make it known at the national level that in fact they are often only supplying 10% – I say 10% but I don't think we're that far from the reality of what is really needed in a field project. They're often amazed at what MSF or other partners that run the facilities tell them when the facility is working: when we visit these facilities, there are few partners, few staff and few patients. As there are no drugs or treatments, people aren't coming in, which means that the needs and budgets are vastly underestimated. That's a major problem - although here I am setting aside all the discussions about the need

to boost funding or about innovations. But those are the practical realities I see right now in the countries where I practice. That the vast underestimation of real needs is also a problem.”

**Marie-Hortense Koukika:** “What can MSF do to improve that? We’ve talked about funding problems, but there may be something more than just a funding problem; there’s the whole model behind it that we certainly need to work on, including helping the different ministries of health with planning or scheduling needs. We know that, generally, data from MSF programmes is not often incorporated as such in Ministry of Health data. So actually, when we work like that, it becomes extremely difficult to for them to estimate the overall needs of the population and that ultimately makes it difficult to estimate the funding needs.”

**Michaël Neuman:** “I have to go back to the governments’ attitude, since the countries we’ve been talking a lot about since the beginning, are in the Sahel. These are not countries that are doing well, particularly in recent weeks – whether we’re talking about Chad, Mali, or Burkina Faso. Niger is a bit of an exception, but it’s also very complicated and so I’d like to go back to the problems in those countries, which are highly cyclical, and the impact that has on how we work with them around children’s access to nutritional health products, the malaria vaccine, and SMC. And more structurally as well, do we, the field actors, have the capacity to get those governments to work seriously with us on these issues? How will this collaboration with governments – especially at a really tense time like the present – ultimately play out?”

**Kevin Phelan:** “It’s true that *The Lancet* article provided momentum with a programme for 100,000 children in Burkina Faso and in Madagascar. But that momentum hasn’t reached Niger, for example, which is probably the world’s malnutrition hotspot right now, despite tens of millions of dollars being invested every year. The studies *The Lancet* talks about are absolutely incredible. They simply say that if you give children a good diet with all the nutrients children need, they do better! It took ten years for people to realise that. Now if it takes another ten years to consider how to intervene, that will be a monumental waste. When it comes to funding mechanisms, if we did it for TB, malaria, and HIV, we can do it for malnutrition. Otherwise, this will be one of the greatest moral and political failures of our time. In many cases large numbers of children are dying of hunger before we can implement a nutritional intervention.”

**Andrea Bussotti, Communications Director, MSF France:** “My question is really about what avenue we should take, and though I mean that partly as a provocative question, I hope there might also be some real, promising answers. Which avenues of operational research are still likely to really change the outlook? Because it’s easy to see that cost-wise, we’ve hit a wall; is there any way to work on other strategies for lowering programme costs?”

**Kevin Phelan:** “You call it operational research but what’s needed are just operations. From 2005 to 2010, Epicentre demonstrated the impact of combining different types of nutrients and food,

and food plus money. That was key in my thinking about this issue. So there is nothing new here. We can keep asking X operational research questions and speculate on whether these programmes help encourage families to get vaccinated, but the cost/effectiveness ratio has already been proven. It's now been proven, so it's not research anymore. We must bring this fully into the operations realm and set research aside for a bit. My recommendation is to try, for example, to do this on an industrial scale, in Niger, and that requires funding. We haven't even talked about the environmental impact. If we give supplements to 100,000 children a year, one a day, all of those little packets, it also creates a lot of waste in the environment. But in my opinion these questions should not be an obstacle to operations or programmes.”

**Isabelle Defourny:** “I'd like to respond to Michaël's question a bit. While the region is certainly super unstable, I still see two opportunities. First, there's the conflict in northern Nigeria, in Katsina, that's pushing a whole succession of children toward Niger. Oddly, that can be an opportunity, insofar as what interests the institutional donors in the region today are conflict zones. We may be able to combine the issues of malnutrition and conflict, because in the end, what we see are tens of thousands of children arriving in Niger from Nigeria in terrible shape. They arrive at much later stages of undernutrition and medical complications than do the children of Niger. They're not only fleeing from hunger – they're also fleeing from the security situation. There's a way to reframe this issue from that angle, to draw attention and funding. The other opportunity is that we are finally beginning to hear talk – fairly recently in Niger, from UNICEF, in particular – about the limits of treating four to five hundred thousand children with severe acute malnutrition every year. The number of malnourished children is only growing, because it is really, completely proportional to the demographics. Given the incredible congestion in the health system, there really is a feasibility problem. We are starting to hear that it's not going to work, from UNICEF especially – that we must tackle these malnutrition problems farther upstream. By returning on a larger, more proactive, scale to malnutrition prevention programmes, we might succeed in putting these nutritional response discussions back on the agenda.

And while I agree completely that we're no longer at the operational research stage, we must set up operations aimed at reducing malnutrition and improving children's nutrition, with the ultimate goal being healthy growth for children. I think there's still work to be done to totally convince ourselves of that goal internally. Because while everyone thinks that it's good that children grow properly at MSF projects, we are still focused on severe acute malnutrition and acute situations. Our paediatric projects aren't sufficiently focused on ensuring that children grow properly.

The other thing we must work on is that we must have a goal of scaling up to larger projects. We have to properly re-examine how different countries have managed to really reduce their malnutrition. Behind this 'small quantity' idea – large-scale distribution of small amounts of ready-to-use food – we get a glimpse of the whole problem. We are cutting the amounts as much as possible because there isn't any funding. That's not going to be enough.”

**Adeline Lescanne:** “What I’m asking myself is this: what has actually triggered funding for other diseases? What has triggered that funding we haven’t managed to trigger for nutrition? So maybe that’s another discussion we need to have: on the why. I imagine that you’ve had it, but I’m having a little trouble understanding why we haven’t managed to spur international interest around this topic, although we have clear evidence of products functioning.

On the optimisation issues, there is something we haven’t talked about – the new programmes that manage malnutrition using a single product and a single protocol against both severe acute malnutrition and moderate acute malnutrition. We are not moving forward on these programmes right now, although it would mean an incredible reduction in cost. We could treat many more children and it would be easy for the mothers. But UNICEF and the WFP can’t agree on who’s going to do what. It’s not normal that we aren’t making any progress.”

**Philippe Duneton:** “What I see is that it would be important to do what we call an ‘investment case’. It’s a matter of making something that is obvious to you, but isn’t really shared by the institutional donors, visible. So why? I don’t know for sure, but it could involve making the argument that if you treat a child, the effect isn’t just suspensory, but it has a multi-year impact on their development, and obviously that has direct ramifications in terms of general health and preventing death. I’m just not sure that at present there is the will to fund a specific organisation dedicated to nutrition. On the other hand, perhaps demanding that some portion of resources – increased, obviously – be dedicated to malnutrition issues would be worthwhile. We mentioned the FAO and UNICEF challenge also, but perhaps it would be useful to think in that direction if we want to build momentum and get funding.”

**Marie-Hortense Koudika:** “We’ve discussed all the issues regarding the limitations and difficulties related to access to the products used to treat malnourished children. We’ve also talked about the prevention issues and discussed, at length, the limitations due to funding that falls short of the needs. But we also said that it was important to consider different strategies.”

# FINAL THOUGHTS

**Michaël Neuman:** “Before we end, I would just like to go back to a question from Éric Goemaere, because it opens up some interesting perspectives. He wondered whether our discussion around funding issues doesn’t illustrate the contradictions at MSF, which has structurally reduced its operational institutional funding down to almost zero. He wondered whether it wasn’t time to re-examine those funding sources and whether MSF’s much sought-after financial independence in recent years hasn’t resulted in a major step backward in MSF’s operational goals, especially for these types of ambitious programmes and potential partnerships, including with UNITAID.

What we said to you in the beginning of these workshops was that it was really important for us to go back to the content of what we want to do, to start again from our work intentions – we put certain topics on the agenda, obviously not at random but which correspond to what we want to do – and that that should be the starting point. The prerequisite for these discussions is to want to do things. So methodically, what are we talking about? Stating our intentions, thinking about the overall landscape in which we work and then how we have tried to do things already, and describing the obstacles, sometimes very generally and a bit more specifically for MSF at other times, and then thinking about the actions that MSF wants and is able to undertake in the future. When we talk about actions, we’re talking about both operations and accompanying those field actions with analysis and campaigns.

I found the discussions extremely rich, really dense, and that density illustrates the participants’ work, their competence, but also the diversity of their viewpoints and experiences, and also how useful different points of view are to having quality conversations. We saw people who work on very different subjects and have very different points of view, with different experiences and personalities. That’s a good thing. Another point, obviously, is these are vast subjects. I don’t think MSF can hope to cover all of these subjects. I’m thinking, for example, of the dizzying session on oncology, but in spite of the complexity, the discussion enabled us to identify a few possible paths, with HPV vaccine access, for example. There were complex discussions containing a whole bunch of sub-issues, including price issues. We’ve talked a great deal about price issues these past few months at MSF, and I think the discussions have enabled us to add a little more detail to these issues beyond the questions of price, by also considering production capacity or quality issues. Also, questions have been raised about patient behaviours – we’ve talked about, or pointed a finger at, the role of patients in these access-to-care mechanisms. We’ve mentioned the importance of working with all the stakeholders – manufacturers, health officials, patients, and other stakeholders (including Alima, obviously) – to illustrate the necessity of working together on these issues. We also showed, I think, MSF’s limitations, particularly MSF’s limitations in working together successfully. What can also be



said is that in this landscape, MSF is never all alone, and to use an old metaphor, I would say that on these issues it should not abandon its stance of unfaithful but open partner, as long as we're able to find areas of agreement with partners and common goals, at least.

So, what does this all mean? That ideology is a bad counsel, which is also what I would like to take away from these discussions. To wrap up, we've seen how impressive the work done by everyone who participated in these discussions is, sometimes each person is working on their own, but despite everything, the work is there. A very impressive body of knowledge has been produced. It's true that it has yet to be articulated, and so the question I will end with is about our own internal ability at MSF to coordinate together to both identify and agree the right questions and then work on how best to get around those obstacles."

**Isabelle Defourny:** "I have found this all very inspiring. Lots of tangible work done, a huge amount of internal knowledge, and also we have easy and preferential access to a variety of specialists from outside MSF, so the context is favourable. I had said in the introduction that I think that the context internally, at OCP, is also favourable. We have a whole series of projects that are ready, within which there is a real opportunity to incorporate new tools and work on access issues. Before going into detail on those, one of the points I have taken away and that I think is very important is Jean-Hervé's introduction on the determinants of access, the different myths about 'health utopias' and the dangers for MSF in looking and advocating for comprehensive solutions. I'm basically talking to the Operations team here, because keeping that in mind and knowing the history is essential. Regarding access issues, there are some that are medium- and long-term: we talked about the tuberculosis vaccine, for example. But I'd especially like to discuss certain subjects that seem ripe to me, tools that we could use relatively quickly, but only with several conditions. We saw from the HPV vaccine example that we need to become much better organised internally to consolidate the knowledge that exists within ongoing field projects and ongoing studies, not just at the Access Campaign.

And then to my second point. In our approach, there's a certain imbalance between our desire to find comprehensive solutions to problems and our desire to use different or new practical tools – like the malaria vaccine, for example – in smaller projects. In several of our projects, it seems to me that we should be offering our patients certain already-existing tools – even if only on a small scale. Take the HPV vaccine, for example; while we aren't ready to introduce it throughout West Africa, and we aren't going to do it all by ourselves, making it available to the girls in our patients' families, at least, seems really essential to me. That's something we can do already in Mali and Malawi. Similarly, we talked about preventing malnutrition. At our N'Djamena project in Chad, where we treat children with severe acute malnutrition, the minimum would be preventing children from dying every year or becoming malnourished again every year and preventing their brothers and sisters from going through that, too. Ultimately, it's a matter of complementing our care with a responsibility to the patients we've hospitalised at extremely severe stages, who we know are at increased risk of death once they have reached the stage of severe acute malnutrition. In short, working with their

families to make nutritional support foods and malaria prevention available. Another example is the malaria vaccine, the RTS,S vaccine, only a limited number of doses of which have been produced. But still, 15 million doses isn't so bad. Our main action right now, if I understand correctly, is to advocate to make these vaccines available to countries that have major foci of malaria, but many don't have the means to conduct malaria vaccination. That's something I think we should do; but we shouldn't just be limiting our action to advocacy, but also really trying to procure these vaccines so we can use them in the major malaria foci where we work – in Niger, Mali, and South Sudan – and thereby help the governments make malaria vaccination a reality. Another subject we haven't talked a lot about in these sessions is Ebola. We've gotten to a stage now in OCP where we've identified the issues, we've identified the studies, and we've identified the 'proofs of concept' (demonstrations of feasibility) that would need to be put in place in order to be able to use, and ensure wider use of, the Ebola vaccines – the J&J vaccine, in particular – and monoclonal antibodies for prevention or post-exposure prophylaxis. So, improving the approach to Ebola is something we could move forwards fairly quickly just by getting organised amongst ourselves. It might require setting up one or another study again, contacting manufacturers, and then working on making those different tools available, but it's a concrete example that, in my opinion, we should proactively work on. Regarding oncology, there are a huge number of questions around access – some of them very complex, but others that are simpler. We see that with the HPV vaccine. The Access Campaign knows a lot about what's going on with the HPV vaccine but for reasons that are also, obviously, the fault of the operations team or our medical teams, that knowledge does not really exist in our projects, especially in the countries where we work. In Mali and Malawi, we have not managed to produce concrete examples of deployment of those vaccines. I think that by joining forces we will get there. In oncology, all of the issues are a bit complicated, but I think we should also work on making available generic chemotherapies and devices that are not particularly expensive but just don't exist in the countries where our projects treat cancer. There's also another subject we didn't talk about, but which was of interest to us a few years ago: the measles non-injectable vaccine, the Nanopatch. We know that the current measles vaccines have huge limitations. We will not be able to better prevent measles outbreaks and respond to measles epidemics with the current vaccines. Where are we at with the Nanopatch vaccine? Is there anything we can do to speed up its deployment? That's another concrete issue that we still haven't really worked on yet, and for which we have no response. Regarding multidrug-resistant TB, as you know, we have invested heavily in recent years in research. There's a large global research budget thanks to Unitaid, but right now multidrug-resistant TB is still missing from our operations, from our projects. So, we are investing heavily in research but not implementing the results. We are opening two projects that I hope will get a lot of patients, two multidrug resistant TB treatment projects in the Philippines and in Pakistan, but what we lack is a clear idea of the reality regarding the use of various drugs – bedaquiline, delamanid, and pretomanid – by different governments, and the obstacles to accessing these drugs. How do we make the Philippines and Pakistan concrete examples of much wider use of these drugs, and ultimately how do we reconcile the research issues, the operational issues, and the access issues? We also talked about nutrition. I find the 'investment case' idea interesting. I really think that's what we

should do. Finally, one last subject that we didn't talk about, but which is also important, is psychiatry and access to psychiatric drugs. We have one project, there's a project at MSF WaCA, and other sections are now going in that direction, too. Treating psychiatric patients in Africa – where there's a problem with access to drugs that aren't at all expensive – is another important focus, in my opinion.

I don't claim to have gone over all the issues here. Each would require its own working meeting to identify the issue beforehand, but it seems to me that we can address each of these issues by reorganising the work amongst ourselves, and eventually by including other people, for example some members of the Access Campaign who are very well-versed on these issues, to assist on each of our specific projects.”



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