

FALL 2015 | VOL. 16 NO. 3



ALERT



THE COST OF MEDICINE

A SPECIAL REPORT

HUMANITARIAN SPACE

Dear Friends,



My first mission was in Ivory Coast. My boss was a 28-year-old French nurse who was serving as project coordinator, hospital manager, and medical coordinator, all at

the same time. Her quiet, gentle manner belied a steely resolve. She knew every employee and many patients by name. Above all else, she was pragmatic, always seeking to do what was best for our patients, who were caught in a civil war.

I've always remembered her practical, patient-centered approach, because that's really what this work is about—the patients. But even our most dedicated, skilled field workers can only do so much if they don't have the right tools—the diagnostics, the medications, the vaccines—for the environments in which we work.

MSF's Access Campaign was founded to prod others to develop or provide these essential medical tools and to make sure they work in remote locations with few resources. The work the Access Campaign does is directly tied to our field experience and has profound consequences for the people with whom we work. It brings much-needed attention to pricing, policies, the research and development system, and other crucial elements of the process by which medicines and medical tools make it to the field—or don't, as the case may be.

And that's what this issue of *Alert* is about, the cost of medicine, and the processes that drive the development of some medicines over others. Our special report consists of four interrelated sections, three of which highlight a different challenge our field teams face, while the fourth looks at the root causes of the dynamics at play. The first, focused on

the \$1,000-per-pill price tag of a new hepatitis C treatment, covers medications that are unaffordable because of how and why they've been developed and marketed. The second shows what happens when too many vaccines are unadapted to the settings in which we work (and, in some cases, unaffordable as well). The third looks at how the Ebola outbreak showed the frustrations of trying to respond to a crisis where good treatment options are unavailable. And then, to bring it all together, we look at the prevailing research and development system, which neglects huge swathes of people and leaves them vulnerable to health issues and diseases for which they should have better options.

My boss back on my first mission could make decisions at the field level that improved the picture for patients, but other things were far beyond her control, like the funding and incentive mechanisms for research and development, and the lack of attention paid to neglected diseases that primarily affect poorer patients. That's why we think it's so important to highlight the work that the Access Campaign is doing and to understand the issues we are raising here.

And as we talk about innovation, pragmatism, and effectiveness, we dedicate this issue of *Alert* to Jacques Pinel, a longtime MSF staffer who recently passed away. In his distinguished career with MSF, Jacques helped develop some of the most innovative and effective tools our field teams have, kits and protocols still in use that demonstrate the spirit, ingenuity, and attention to the needs of patients to which we all aspire. You will be missed, Jacques, but your impact will be felt every day in MSF projects—and by patients—around the world.

Yours,

DEANE MARCHBEIN
President, MSF-USA Board of Directors

RIGHT: A man named Manoj, who was being treated by MSF for hepatitis C with pegylated interferon/ribavirin—and dealing with the intense side effects the drugs bring—sits near the shack in which he lives in Mumbai.
@Siddarth Singh/MSF

COVER: In Swaziland, a multidrug-resistant tuberculosis patient shows the pills she must take daily for her treatment regimen.
© Krisanne Johnson



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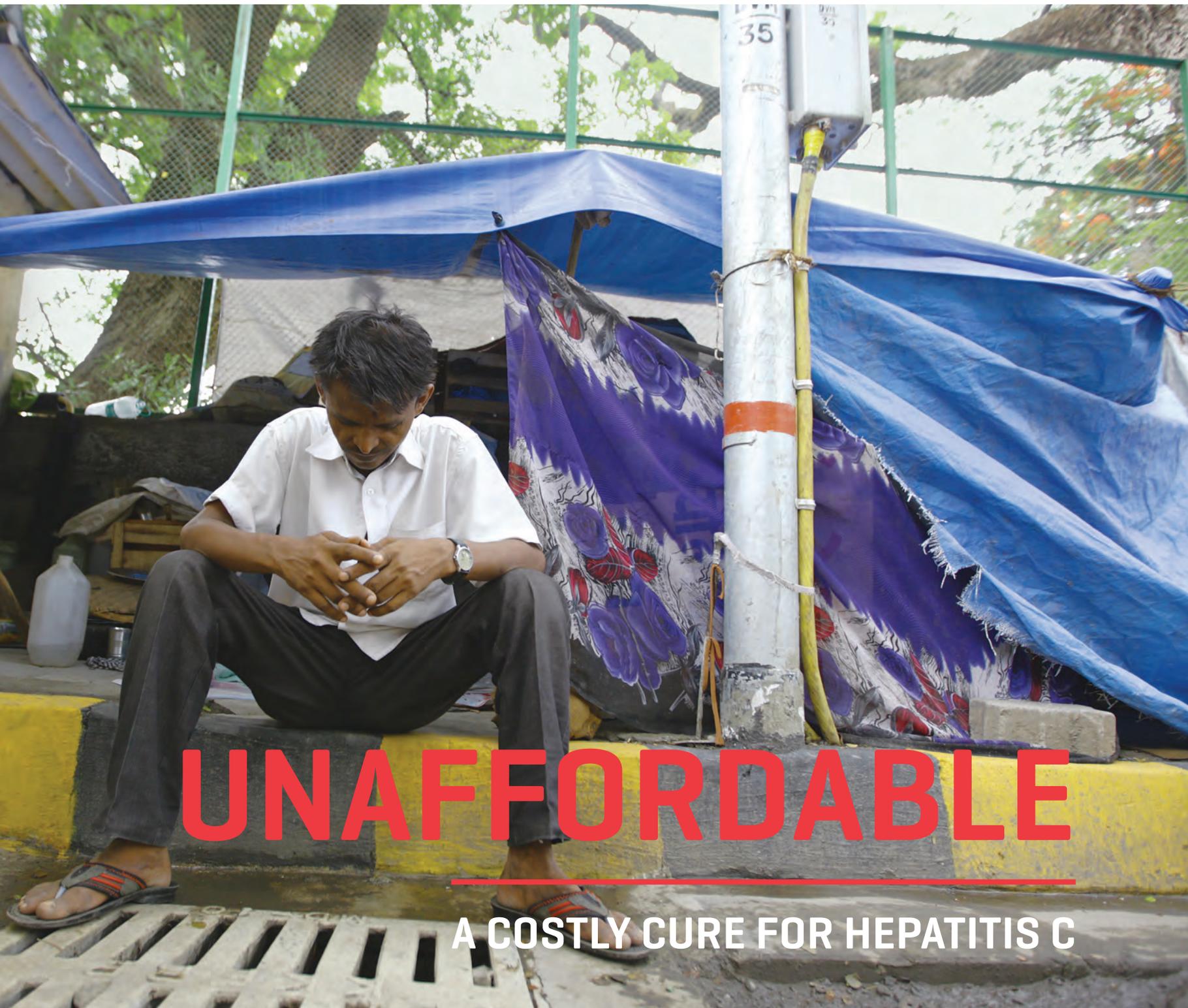
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UNAFFORDABLE

A COSTLY CURE FOR HEPATITIS C

LAST YEAR BROUGHT WHAT SHOULD HAVE BEEN PROMISING NEWS FOR THE ESTIMATED 130 TO 150 MILLION PEOPLE AROUND THE WORLD LIVING WITH CHRONIC HEPATITIS C INFECTION.

A class of drugs called direct-acting antivirals, or DAAs, started to become available to treat the disease. This was [and is] exciting because the standard treatment for hepatitis C previously involved six to twelve months of weekly injections, with side effects so toxic that some people would quit the regimen or avoid it altogether. And the cure rate was only between 35 and 80 percent.

DAAs, on the other hand, are faster—the regimen can be completed in three months—and more effective. For treatment providers, DAAs can also help simplify diagnostic and treatment protocols.

Yet instead of taking advantage of this new development, many people who have or who treat hepatitis C have been left waiting. From MSF clinics in countries like Pakistan, to doctors' offices in the US, access to DAA treatment is limited. The need is there. The will to treat is there. But the drugs often are not. One major obstacle is the cost.

THE \$1,000 PILL

One DAA called sofosbuvir is marketed as Sovaldi by the pharmaceutical company Gilead. It was introduced in the US with the shocking price tag of \$84,000 for a 12-week treatment course, which breaks down to \$7,000 per week, or \$1,000 per pill. And the total expense is even higher, because the full regimen requires that the drug be used in combination with at least one other antiviral medicine.

At this price, it would cost a total of \$226.8 billion to treat the estimated 2.7 million people living with chronic hepatitis C infection in the US alone, according the Centers for Disease Control and Prevention (CDC). US-based health insurance companies, some members of Congress, and various civil society and patient advocacy groups are challenging Gilead's pricing strategies, but, thus far, access to the

potentially revolutionary drug is limited to only the sickest or wealthiest patients, leaving millions behind.

MSF does not currently have medical operations in the US, but we are starting to treat hepatitis C in some of our projects and plan to scale up our work on the disease in more than half a dozen countries, with support in some projects from UNITAID. We want to use the best, most effective medications we can, but the prices being charged for new drugs like sofosbuvir make it extremely difficult to secure affordable access to the drugs.

INSUFFICIENT ACCESS

Gilead has enabled some access through a license that permits limited generic competition in 101 low- and middle-income countries with a high burden of hepatitis C. Generic competition will, over time and if allowed, help push prices down. But the license agreements exclude 38 developing and so-called “middle income countries,” or MICs, which is problematic because an estimated 75 percent of the world’s poorest people and over 70 percent of people with hepatitis C live in MICs, meaning many patients will still be priced out of care.

In a number of countries excluded from the voluntary licenses, Gilead is offering “tiered pricing,” a practice whereby companies seek to maximize profits by setting prices based on what a percentage of a population in any given country is willing to pay. Currently, the lowest available tiered price is \$900 for a three-month treatment course in the poorest of these countries (and in some additional developing countries, such as Egypt and India). This is the price MSF is now paying for sofosbuvir in countries deemed eligible by Gilead.

But in many of the countries that are locked out of the voluntary licenses, prices could range from \$2,000 to \$12,000 per treatment course. For example, in Brazil, Gilead currently charges about \$7,500 per three-month treatment course. At these prices, many patients would still have to go without, and care for others will still have to be rationed, with medical practitioners in effect forced to choose one patient over another.

WHY SO EXPENSIVE?

It’s possible to charge \$1,000 for a pill in the US because pharmaceutical monopolies allow companies to charge any price they want. Gilead and other pharmaceutical companies often claim pricing is linked to the cost of developing and manufacturing a new drug. This is misleading; the price is actually a function of the monopoly Gilead has on the manufacturing and sale of the drug. Peer-reviewed estimates¹ indicate that a full three-month treatment course of sofosbuvir could in fact be manufactured for approximately \$1.20 per pill.

We often hear that high prices are necessary for pharmaceutical companies to recoup the investments they make in the research and development (R&D) of drugs. While we don’t know the exact costs of drug R&D—because companies won’t provide transparent data—economist Jeffrey Sachs estimates total private R&D costs for sofosbuvir could be as low as \$300 million.

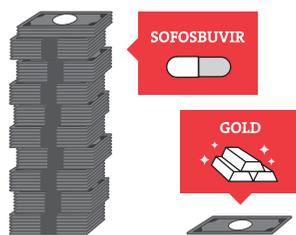
What’s more, Gilead did not develop the drug alone. It was initially developed by a smaller biotech company called Pharmasset that was founded by an Emory University professor whose work was supported by US government grants. Gilead paid \$11 billion for the company—and the sofosbuvir compound—speculating that it could charge extremely high prices for the cure, passing the acquisition costs on to patients.

Gilead also says its pricing takes into account the amount of money the drug will save others by obviating the need for future treatments, including liver transplants and hospitalization. Charging so much for the pill actually saves money, the argument goes, because other costly procedures are no longer necessary.

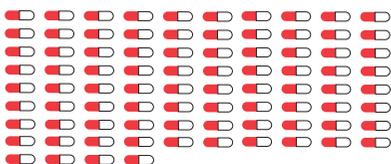
But for medical providers like MSF and other treatment programs trying to address the urgent needs of a growing and global patient cohort, Gilead’s “value” defense of their prices is difficult to accept. It’s akin to saying the price of treating one dental cavity should be based on the price of a root canal, or that the price to remove a pre-cancerous tumor should be based on the cost of chemotherapy for late-stage cancer. Beyond that, for the millions who cannot access the drug at this price, its value is precisely nothing.

SOFOSBUVIR/SOVALDI: THE \$1,000 PILL

GRAM FOR GRAM, SOFOSBUVIR IS PRICED AT **67X THE PRICE OF GOLD**



COST OF 12-WEEK TREATMENT COURSE: **\$84,000 (84 PILLS)**



COST: **\$1,000**
MANUFACTURING COST: **ABOUT \$1.20**

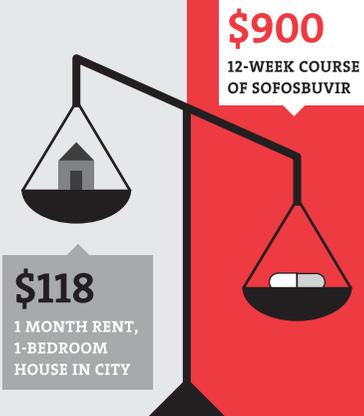
DRUG PRICING: A HIGH COST OF LIVING

BRAZIL



MORE THAN 22 MONTHS OF RENT IN A CITY = 12-WEEK COURSE OF SOFOSBUVIR

PAKISTAN



MORE THAN 7 MONTHS OF RENT IN A CITY = 12-WEEK COURSE OF SOFOSBUVIR

*price offered for government purchase

SOURCES: <http://scroll.in/article/741820/why-india-must-resist-pressure-from-big-drug-firms-and-their-backers-to-change-patent-laws>
http://www.numbeo.com/cost-of-living/country_result.jsp?country=Pakistan
http://www.numbeo.com/cost-of-living/country_result.jsp?country=Brazil&displayCurrency=USD

From a financial point of view, Gilead's strategy is working rather well for them. In Sovaldi's first year of sales, the company has taken in more than \$10 billion for sofosbuvir alone—or 34 times Sachs' estimated level of its R&D costs. Profits from sofosbuvir sales are in part responsible for the headline-making compensation package of Gilead's CEO, who has been dubbed the “\$600 million man.”

HOW TO INCREASE ACCESS?

Gilead's pricing strategy attempts to reap as much profit as possible under a system that allows unfettered profiteering, regardless of the repercussions for public health. Gilead can charge exorbitant prices because it has been granted patents that give it monopoly control over manufacturing and sales of the drug. Without competition, Gilead, accountable only to shareholders and its bottom line, can set whatever price it chooses.

But these patents are not valid under the laws of some countries that set the bar higher for what does and does not deserve patent protection. Ongoing legal challenges to several Gilead patent applications could open the door to the sort of generic drug competition that has been so crucial to getting treatment for other diseases to people, particularly in middle- and even high-income countries not included in Gilead's license. Even in countries that do grant the patents, there are other legal tools that can be used in the effort to allow price-lowering generic competition and thus broaden access to care.

Gilead's patent application on sofosbuvir has already been rejected by Egypt, for instance, which did not consider the medicine scientifically innovative. In India, the patent office rejected Gilead's application for one of sofosbuvir's key patents on the grounds that “there are a number of earlier compound structures that are very close to what Gilead is trying to get a patent for.”ⁱ Additional patent opposition efforts are ongoing in several other countries. As the medical aid group Médecins du Monde (Doctors of the World) explained when filing their patent opposition in Europe, “the improvement in the quality of life that [Sovaldi] offers to patients is a breakthrough, but the molecule that comprises the drug is not.”

DISTURBING ECHOES

We have been here before: in the early 2000s, MSF began treating patients with HIV with antiretrovirals (ARVs), drugs that transformed it from a death sentence into a manageable condition and that, like sofosbuvir, were relatively cheap to manufacture. But ARV prices were also prohibitively expensive initially, more than \$10,000 per patient per year.

Drug companies fiercely protected their patent monopolies and high drug prices. Developing country governments and donors couldn't pay. And thousands of people died for lack of access to treatment.

When more affordable generic ARVs were introduced, prices dropped dramatically, by 99 percent over a decade. Today, a course of treatment costs roughly \$100 per person per year,ⁱⁱ and more than 15 million people are now on HIV treatment globally.

We see similar challenges in treating hepatitis C. Robust generic competition is a proven path to lower prices. Lower prices means greater access. Greater access means more lives can be saved.

We shouldn't be comparing the cost effectiveness of DAAs to the cost effectiveness of liver transplants; instead, we should be testing and treating everyone in need, finding ways to balance the actual costs of bringing a drug like sofosbuvir to market with the human cost of putting profits over patients. Hepatitis C is an infectious disease, and reducing the reservoir of the virus in all communities should be a public health priority.

This is an adapted version of an article that originally appeared in Pharmafile in April 2015: <http://www.pharmafile.com/news/396162/pharmafocus-debate-price-new-hepatitis-c-treatments-fair>.

ⁱ Van de Ven N, Fortunak J, Simmons B, Ford N, Cooke G, Khoo S, et al. Minimum Target Prices for Production of Direct-Acting Antivirals and Associated Diagnostics to Combat Hepatitis C Virus. *Hepatology* [Internet]. 2015 [cited 2015 Aug 13]; 61(4): 1174-1182.

ⁱⁱ India Patent Controller. Decision in the matter of application no. 6087/DELNP/2005 [2014].

ⁱⁱⁱ MSF. Untangling the Web of Antiretroviral Price Reductions, 17th edition. July 2014. Available from: http://www.msfaccess.org/sites/default/files/MSF_UTW_17th_Edition_4_b.pdf



An MSF psychosocial counselor at MSF's clinic in Mumbai speaks with a hepatitis C patient about dealing with the side effects of the interferon/ribavirin treatment regimen. ©Siddarth Singh/MSF

UNAVAILABLE: MISSING ESSENTIAL MEDICAL PRODUCTS

A crucial, longstanding challenge that MSF medical teams face is that for some diseases and conditions, the tools we need to treat our patients simply don't exist. There is severe and chronic underinvestment in R&D for diseases and conditions that primarily affect developing countries. Neglected diseases such as sleeping sickness, leishmaniasis, tuberculosis, and Chagas disease represent more than 10 percent of the global disease burden, but fewer than 4 percent of new drugs approved across the world were indicated for neglected diseases between 2000 and 2011.^{iv}



ABOVE: In Guinea, an MSF worker collects a blood sample from a volunteer who received an experimental Ebola vaccine. © Yann Libessart/MSF

Because many of the patients are poor and cannot pay high prices, there are no incentives for pharmaceutical companies to develop products that do not contribute significant revenues to corporate bottom lines. This misalignment between public health priorities and existing investments and incentives for R&D doesn't just affect MSF and people in developing countries, however. Higher-income countries are also impacted.

For example, the emergence of drug-resistant bacteria and microbes—antimicrobial resistance (AMR)—is now occurring at an alarming rate globally, and the CDC and the WHO have both called antibiotic resistance one of the greatest threats to human health today. But pharmaceutical companies are pulling out of antibiotic development, largely due to low economic returns. Providing the sort of careful stewardship of antibiotics needed to avoid the development of resistance lowers potential sales volumes, as do short treatment courses.

FACING PAGE, LEFT TO RIGHT: MSF medical staff at the MSF Ebola treatment center at Donka Hospital in Conakry, Guinea. © Yann Libessart/MSF
An MSF staff member helps a young patient dress after his discharge from Bo Ebola Management Center in Sierra Leone. © Anna Surinyach
The experimental rVSV-EBOV Ebola vaccine. © Yann Libessart/MSF

According to the US President's Council of Advisors on Science and Technology,^v fewer than five of the 50 largest pharmaceutical companies have active antibiotic development programs, and the antibiotics pipeline is almost dry.

These examples are not the exception; they are representative of the failure of today's R&D system to meet critical public health needs. MSF is an advocate of new approaches to biomedical R&D that prioritize needs-based and public health-driven innovation and that ensure that products are made accessible to the populations who need them most.

^{iv} Pedrique B et al. The drug and vaccine landscape for neglected diseases (2000-11): a systematic assessment. *Lancet Global Health*, Early Online Publication, 24 Oct 2013.

^v Report to the President on Combating Antibiotic Resistance, September 2014



Q&A: EBOLA AS A CASE STUDY OF CRIPPLING PRODUCT UNAVAILABILITY

The Ebola crisis starkly illustrated how critically important it is to develop tools for infectious diseases before an outbreak occurs, as well as how challenging it can be to respond when adequate tools aren't available. This was not just an Ebola problem, though; it's an R&D problem, a systemic problem. And the consequences should really come as no surprise.

Ebola was discovered nearly 40 years ago, but only recently, after the outbreak that began last year devastated thousands of lives across West Africa and reached the US and Europe, were significant R&D efforts launched to deliver tools to prevent and treat the disease. MSF's neglected tropical diseases policy advisor Julien Potet describes how MSF experienced the shortcomings during the outbreak and how it is involved in the search for new solutions:

What were the challenges of R&D for Ebola that led to this situation?

Historically, Ebola has primarily affected rural populations in sub-Saharan Africa, and therefore the development of tools to prevent, diagnose, or treat the disease has not been a priority for pharmaceutical companies. Almost no R&D efforts were focused on Ebola until the mid 2000s, when the virus was identified as a potential bioterrorism threat in several countries. Thereafter, the US, Canada, and a few other governments began supporting some R&D projects for Ebola.

However, the primary objective was to protect citizens of the countries sponsoring the research, not necessarily to address the needs of people affected by the disease where it occurs, in Africa. Therefore crucial characteristics, such as product affordability or user-friendliness in resource-poor settings, were not really taken into consideration.

Moreover, some of the public funding for this research dried up due to national level budget cuts, and several potentially promising treatments and vaccines stalled in the early stages of development without a sponsor to take them forward. When the current outbreak in West Africa began escalating rapidly, MSF and other treatment providers had no tools at our disposal, despite the earlier public investments.

How did this affect MSF's ability to respond when the outbreak did occur?

Prior to this Ebola outbreak, there were no rapid diagnostic tests to aid with patient triage, no effective medicines to treat patients, and no vaccine to prevent infection. MSF's response therefore had to rely on traditional public health interventions, including infection control measures to contain the outbreak and supportive care to alleviate patients' symptoms and save lives.

Without effective treatment and vaccines for Ebola, the cornerstones of controlling an outbreak are timely diagnosis, isolation and management of cases, and epidemiologic surveillance. From the start of this Ebola outbreak, MSF relied on international mobile diagnostic laboratories deployed in the region to provide test results, but by the peak of the outbreak, it was clear that a rapid, point-of-care Ebola diagnostic test was urgently needed to speed up the time to diagnosis. Rapid diagnostic tests for Ebola are now in various stages of development, but none were commercially available in 2014.

What is the latest news in Ebola R&D?

The most encouraging news is that according to interim trial results, the Ebola vaccine being tested in Guinea [rVSV-EBOV] has proven highly effective in protecting people most at risk, including frontline workers and people who have come into contact with an infected person.

As one of the partners in the trial, MSF is administering the vaccine to 1,200 frontline workers in Guinea, including doctors, nurses, paramedics, laboratory staff, cleaning staff, and burial teams. More data is needed to tell us how efficacious this preventive tool actually is, however; for example, it is not clear how soon protection kicks in and how long it lasts. But with such high efficacy shown, all affected countries should immediately start using this vaccine to protect those most at risk of contracting the disease: contacts of infected patients and frontline workers.

The establishment of a stockpile is being considered to facilitate prompt distribution in response to future emerging outbreaks. Any

delayed rollout due to financial barriers could lead to another public health disaster, so it's important that this vaccine is affordable for use in resource-limited settings.

In addition: the development of this vaccine was heavily financed by public funding. Private investment has been small and arrived late in the process. Additional financial rewards are being offered for companies that successfully register a product in the US as well. The need to compensate is therefore minimal. In this situation, a fair price should be based on production costs and not on efforts to generate excessive profits.

What comes next?

MSF is participating in several landmark research studies for a diagnostic test, experimental treatments, and vaccine candidates. More user-friendly diagnostic tests are now being tested in the field. But none of the treatments being tested in patients with Ebola virus disease have yet been found to be safe and effective.

Unfortunately, some of the most promising treatments, including the drug called ZMapp, which is probably the best known, have been available in very limited quantities due to manufacturing constraints. Production should be scaled up, and MSF is calling for an open licensing approach of intellectual property so that more suppliers can produce the most effective treatments and make them available sooner and in greater quantities.

Moving forward, it's critically important that R&D efforts not be conducted in silos. Now that the number of Ebola patients has decreased, there is no other way to reach critical mass other than through collaboration. It is crucial to quickly share data from the clinical trials, in order to rapidly adapt protocols and prepare new partnerships.

All involved in Ebola R&D should commit to follow the R&D priorities set by the WHO and endemic countries, based on the needs of patients in West Africa. Bio-defense and any other objectives should be secondary.

UNADAPTED: GETTING VACCINES TO THOSE WHO NEED THEM MOST

For more than 40 years, MSF has been at the forefront of vaccine delivery in crisis contexts and in responses to outbreaks of vaccine-preventable diseases. We also conduct routine immunization in areas where health systems have failed. Vaccination is a cornerstone of MSF's work to reduce illness and death caused by preventable diseases. Vaccines prevent an estimated 2 million to 3 million deaths each year, but an estimated 18.7 million children still miss out on basic immunization.^{vi} While global immunization coverage reached 86 percent in 2014, vaccination rates in some places have stagnated, leaving behind children and adults chronically unimmunized and unprotected.



Porters carry sacks containing vaccination equipment over a bridge between Kitobo and Kitanga Villages during a 2014 vaccination campaign in Democratic Republic of Congo. © Phil Moore

ice packs go into a big cold box that is taken out to the vaccination sites. But even there, we then had to transfer the vaccines from the big cold box into smaller cold boxes, because at each single stage we had to protect the vaccines so that they remained effective. It was a nightmare.”

There is, however, a growing body of evidence, which includes MSF research, that shows some vaccines will remain stable beyond the standard 2–8°C [or 35.6–46.4°F] range for several days, or even weeks. Proper labeling and usage according to true temperature stability would result in an extended controlled temperature chain (ECTC) or “flexible cold chain,” whereby vaccines could be used outside the strict traditional cold chain.

ADVANTAGES OF ECTC

The clear benefits of ECTC in vaccination campaigns have yet to be fully realized. Only the meningitis A vaccine [MenAfriVac] has been relabeled and used in an ECTC for campaigns. [Tellingly, it was developed outside the prevailing industry R&D model, through a privately-funded consortium that worked with the Serum Institute of India and partnered with WHO and others while remaining committed to offering the vaccine at no more than 50 cents per dose.] In 2012, the Ministry of Health in Benin implemented the first ECTC pilot, using 155,000 doses of MenAfriVac in 150 remote villages. According to a March 2014 study, 98.7 percent of supervisors and 100 percent of vaccinators involved preferred the ECTC approach to a traditional cold chain-based immunization campaign.

Vaccination campaigns using ECTC could also dramatically reduce immunization costs. A 2014 study by the WHO, the Program for Appropriate Technology in Health [PATH], and Chad's Ministry of Health modeled the costs of implementing a MenAfriVac campaign in ECTC and compared it with the actual costs in a MenAfriVac campaign in three regions of Chad in 2011. Researchers found that ECTC implementation at the district level would

Whether vaccinating refugee children in South Sudan against pneumococcal diseases or pregnant women in Afghanistan against tetanus, MSF has committed itself to prioritizing vaccination as a core health service in its operations. While recent years have seen the introduction of several new vaccines that offer significant potential to reduce deaths, there has been little investment in adapting or optimizing vaccine products to resource-limited contexts.

Most vaccines, for instance, still need to be refrigerated in a rigid “cold chain” from the moment of manufacture to the point of injection, which poses an immense logistical challenge in places without reliable electricity. What's more, multiple doses are often needed to offer full protection, and bulky products complicate transport to remote areas.

COLD CHAIN CHALLENGES

Keeping vaccines cold remains a major constraint on their delivery, as half of the health care facilities in the world's poorest countries have no electricity supply and just 10 percent of them have reliable electricity.^{vii} Whether in a small village in rural Congo or a refugee camp in Iraq, vaccine delivery can be extremely difficult and costly to execute.

In a 2010 measles vaccination campaign targeting 500,000 people in Chad, MSF had to freeze 22,000 ice packs over the course of 11 days in order to keep the vaccines cold. In a recent measles vaccination campaign in Guinea, “We had 17 fridges full of the vaccines,” recalled MSF epidemiologist Sophie Dunkley. “We also had the 17 freezers to make and store the 5,000 ice packs we needed. The

have saved more than 20 percent of the cost of the vaccine doses for the campaign.

Considering this campaign was conducted in some of Chad's most densely populated and accessible districts, the cost savings of ECTC could be even greater in more remote regions. More generally, this suggests that an ECTC for vaccination outreach could reduce logistical burdens and allow teams to immunize more people.

TURNING RESEARCH INTO ACTION

MSF is also conducting research on the potential use of vaccines in ECTC. In 2013, MSF and Epicentre—the organization's medical research arm—worked with partners to carry out a two-phase study to determine the stability and continued efficacy of the tetanus toxoid vaccine produced by the Serum Institute of India under ECTC conditions. In the initial phase of the study, laboratory tests confirmed that the vaccine retained its chemical and biological properties when kept at ambient temperatures of up to 40°C (or 104°F) for up to 30 days.

The second phase was a clinical study undertaken in Chad's Moïssala District to see how effective the vaccine remained in practice under similar conditions. The participants—2,128 women of childbearing age—were each assigned to one of two groups and received two doses of the tetanus toxoid vaccine.

Women in the control group received vaccines kept in a strict cold chain; those in the second group received vaccines kept out of the cold chain (at up to 40°C for up to 30 days). Participants in both groups reached adequate levels of protection against tetanus. These results strongly suggest that the Serum Institute of India's tetanus toxoid vaccine maintains its efficacy under ECTC conditions.

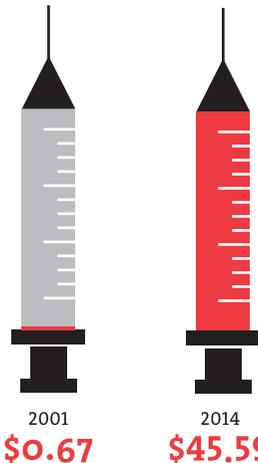
The challenge now lies in turning these findings into action. Campaigns with vaccines used in ECTC can increase immunization coverage and save lives—but the onus rests on the pharmaceutical companies that manufacture vaccines to relabel their vaccines for ECTC flexibilities. Many vaccine companies have data that would support doing so but have not acted on it, thus denying countries and medical providers like MSF the opportunity to implement simpler, more effective vaccination outreach.

^{vi} World Health Organization. Immunization, Vaccines and Biologicals. August 2015.

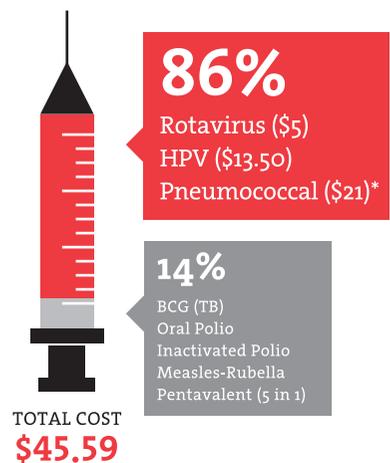
^{vii} GAVI Alliance. Report to the Program and Policy Committee: GAVI Alliance Report to the Programme and Policy Committee, GAVI's Supply Chain Strategy Framework. 2013 Oct 9.

THE COST OF VACCINES

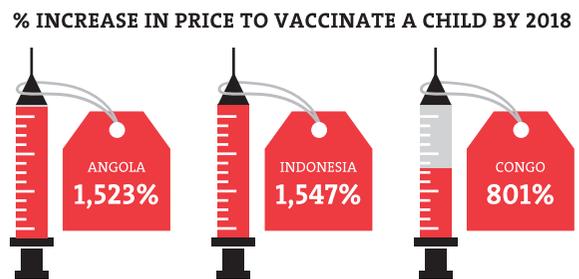
THE COST TO FULLY IMMUNIZE A CHILD IS NOW
68X MORE EXPENSIVE
THAN IT WAS IN 2001



JUST 3 NEW VACCINES
ACCOUNT FOR 86%
OF THE TOTAL COST TO VACCINATE A CHILD



WHEN POOR COUNTRIES
**LOSE DONOR
SUPPORT
TO PAY FOR
VACCINES**
THEY WILL BE STUCK WITH A
HEFTY PRICE TAG



SOURCE: www.msffaccess.org/rightshot2

* Some pneumococcal (PCV) doses procured under the first contracts for the Gavi Advance Market Commitment (AMC) are no longer receiving the AMC subsidy and are bought at \$3.30-\$3.50/dose. Based on awards made to date, 73% (1,095 million) of the AMC donor funds have been committed to GSK and Pfizer.

A FAIR SHOT

Cost is also a significant obstacle. At today's lowest global prices—which are available only to a small number of countries—the price to fully vaccinate a child is 68 times the price that it was just over a decade ago. In 2001, for instance, it cost a minimum of 67 cents to immunize a child against six diseases (tuberculosis, measles, diphtheria, tetanus, pertussis, and poliomyelitis); in 2014, it cost a minimum of between \$32.09 and \$45.59^{viii} to immunize a child against 12 diseases (tuberculosis, measles, rubella, diphtheria, tetanus, pertussis, hepatitis B, Haemophilus influenzae type b, poliomyelitis, pneumococcal diseases, rotavirus, and, for adolescent girls, human papillomavirus, or HPV).^{ix}

While it's an important advance that children can be protected against more deadly diseases, this price jump is unsustainable for many countries. It stems largely from a lack of competition in the new vaccines market, where there are only two manufacturers (a duopoly) for several new vaccines, including the pneumococcal vaccine (PCV), which is produced by GlaxoSmithKline and Pfizer only, and a severe lack of information on vaccine prices.

Without pricing information, making purchasing decisions for vaccines—finding the best price—is like shopping in the dark. This results in irrational pricing. In the retail market, for example, Lebanon and Morocco pay more for the pneumonia vaccine than France does.

On April 23, 2015, MSF launched a global campaign—"A FAIR SHOT"—calling on GlaxoSmithKline and Pfizer to slash the price of a full course of pneumococcal vaccine in developing countries to \$5 per child for all three doses, so more children can be protected from this childhood killer, and to disclose what they currently charge countries for the vaccine. To learn more and join the campaign, visit afairshot.org.

^{viii} \$32.09 is the price to immunize a boy in 2014; \$45.59 is the price to immunize a girl (includes the HPV vaccine).

^{ix} MSF. The Right Shot: Bringing down barriers to affordable and adapted vaccines. 2nd edition, Jan 2015 2013 Oct 9.

IN SEARCH OF THE RIGHT TOOLS: FUNDAMENTAL CHANGES NEEDED IN THE BIOMEDICAL INNOVATION SYSTEM

Imagine being a doctor without access to a new drug that is already available in wealthier countries and could save the life of the person with drug-resistant tuberculosis you're trying to treat. Or a pharmacist who cannot secure an affordable price for a lifesaving hepatitis C medicine. Or a project coordinator in a country where the outbreak of a disease with no known cure or vaccine is terrifying the population.



In Kyrgyzstan, an MSF staff member visits a tuberculosis patient at home.
© Pierre-Yves Bernard/MSF

Every day, MSF teams encounter situations that highlight the tools they don't have to prevent, diagnose, and treat many diseases that affect people in developing countries. It's understood from the outset that MSF teams work in resource-limited settings, and that staff will have to make do with the methods and tools they have. That's the nature of the work. But as people dedicated to saving lives and healing illnesses, it can be hard to reconcile the fact that someone could live or die because certain medicines, vaccines, or diagnostics that do exist are not available in countries where we work. And even when innovative tools do exist, they can be of limited use because they cost too much or can't be employed in a place where there might not be a consistent supply of electricity or qualified medical staff.

When vaccines, medicines, and tests are expensive or designed in ways that are unsuitable for the contexts in which MSF works, millions of people are denied the medical care they need. And yet, while the devastating human and economic consequences of these shortcomings are widely recognized, the reasons they exist—the reasons the prevailing models of R&D fail to address them—are rarely discussed or challenged.

INNOVATION FOR WHOM?

To understand why these gaps persist, it's important to look at how biomedical R&D is financed and incentivized today.

A primary driver of biomedical innovation is public funding coupled with the granting of patents and other intellectual property rights that give pharmaceutical companies exclusive domain to make and sell a new medicine or vaccine for a stipulated period of time. This in turn gives companies monopoly control over the market for that product, allowing them to charge high prices and inhibiting competition that would drive down costs.

Companies therefore decide where to allocate resources based on the revenues they believe a particular product could generate, not the public health burden they could address. What this means in practical terms is that public health priorities and needs rarely determine how corporate efforts are directed. In the current ecosystem, companies watching their profit margins and stock prices are effectively *dis-incentivized* from focusing resources and attention on diseases and conditions that primarily affect people in the developing world, people who don't represent a lucrative market.

From our vantage point, it's a broken system that is both inefficient and ineffective at responding to the most pressing global public health needs. And our field teams witness these costs on a daily basis.

FALSE ASSUMPTIONS

The logic behind the current R&D system is in part based on the false assumption that private companies carry all of the costs and risks involved in biomedical R&D. In fact, public funding—including research conducted by the US National Institutes of Health and universities, as well as tax credits and incentives funded with taxpayers' funds—contributes significantly to medical R&D. At least an estimated 30 percent of R&D funding comes from public sources, and an additional 10 percent comes from philanthropic contributions.^x In the earlier [and riskier] research, public contributions are even greater, up to 80 percent.^{xi}

Pharmaceutical companies then acquire the fruits of those investments by obtaining exclusive intellectual property rights, with the aim of developing commercial products that serve their bottom line. Through this approach, taxpayers essentially pay twice for R&D: first through public contributions to the R&D of these products, then again through the high purchase prices of the products themselves.

And though publicly supported entities contribute both research and funding, these contributions do not translate into guarantees on the use of that research in a commercialized product—to ensure, for example, that they are made affordable and available to patients.

In addition, there is a lack of transparency from the pharmaceutical industry, so we don't really know what the R&D costs are for specific products, what proportion of a given product was publicly financed, or how much it costs to manufacture. The accuracy of industry-funded estimates on the cost of developing a drug is questionable at best. Even Andrew Witty, the CEO of GlaxoSmith-Kline, has called a widely cited claim that it costs \$1 billion to develop and bring a new drug to market “a myth.” An industry-backed academic has since upped that figure,



Porters carry a cool-box used to safely store vaccines through the village of Kalungu II, Democratic Republic of Congo. © Phil Moore

We should ask how we can develop medicines and other products that meet public health needs without threatening to bankrupt our health care systems or exclude millions of people from affordable access.



An MSF worker administers a MenAfriVac vaccine during a meningitis A vaccination campaign in Mali. © Julie Damond

claiming today it now costs \$2.6 billion to bring a new drug to market.

In fact, we know from non-industry funded estimates and the experience of drug developers that a new drug can be developed for a fraction of the cost the industry often suggests, without any patents or high prices attached.

For example, utilizing up-front funding to develop an unpatented fixed-dose combination for malaria, the nonprofit public private partnership Drugs for Neglected Diseases initiative [DNDi], which MSF helped establish, was able to develop this treatment through a total investment of about \$13.2 million, and the treatment itself is now priced at less than \$1 for a three-day course. So far more than 250 million doses have been distributed in 31 African countries.

DNDi has estimated that development of a new chemical entity can cost as little as \$50 million per successfully developed drug; with attrition and failure rates taken into account, it's still as little as \$200 million. [DNDi recently announced plans to deliver 16 to 18 new treatments by 2023, for \$736 million total.]

NEW ROUTES TO INNOVATION

High prices have been a problem in developing countries for many years. MSF has actively campaigned for more than a decade to reduce the prices of medicines, starting with antiretrovirals to treat HIV/AIDS, and continuing today for medicines to treat tuberculosis (TB), hepatitis C, and other diseases; vaccines for pneumococcal disease; and diagnostic tests for HIV and TB.

More recently, exorbitant prices for hepatitis C and cancer treatments [see p. 4] have sparked public outrage in the US, leading to Congressional hearings, demonstrations, and coverage in mainstream media. But the question has usually been framed in terms of who will pay the high prices rather than why we have high prices in the first place.

We need to take this discussion to a deeper level, to question why we accept a biomedical R&D system that is heavily subsidized by the public sector but still allows companies to unilaterally determine research priorities and set high prices without any public health accountability. We should ask how we can develop medicines and other products that meet public health needs without threatening to bankrupt our health care systems or exclude millions of people from affordable access.

This means rethinking how we fund the costs and risks of biomedical innovation. In 2012, an independent group of experts convened by the WHO released a report calling for new models of financing biomedical research and fundamental changes to the way we incentivize innovation.^{xii} This would be accomplished by de-linking the cost of R&D from the price of the final product.

HOW TO IMPROVE BIOMEDICAL INNOVATION

Developing new medical tools is costly and risky, but a public health, needs-driven approach to R&D would put patients and access considerations at the center of the process. MSF and others are working to this end on a global level through several initiatives:

Demand Greater Transparency

One step in improving how R&D works is gaining a better understanding of the costs involved by promoting transparency from all entities conducting R&D. Some state and federal legislative bodies in the US have introduced proposals to increase disclosure of R&D and manufacturing costs. Although these measures have not yet passed, there is a growing call to better understand the costs and other factors contributing to investment and pricing strategies by pharmaceutical companies. For example, MSF is currently running a public campaign asking Pfizer and GlaxoSmithKline to disclose and reduce their pricing for PCV vaccines in developing countries. To learn more and join the campaign, see box on p. 9, and visit afairshot.org.

Fix Existing Incentives

Other limitations of today's R&D ecosystem could be addressed if we fixed and augmented existing incentive mechanisms introduced to promote R&D in neglected areas, such as the US Food and Drug Administration's priority review voucher (PRV) program. The PRV program rewards successful FDA registration of a product for certain neglected diseases with a "voucher" for accelerated review of a subsequent product that would not otherwise qualify for accelerated review.

A voucher is commercially valuable for companies [a recent voucher was purchased for \$350 million], so it compensates them for investing in an area with limited profit potential. Unfortunately, the PRV has loopholes; it has, for example, been awarded to a company that was registering a product that had already been registered outside of the US. And the PRV places no obligations on recipients to ensure the relevant medical tool is affordable and available.

In the US, MSF is calling on Congress to ensure that the PRV program functions as intended: to promote the development of new products for neglected diseases, and to make these products accessible to those who need them.

Create New Approaches to Incentivize Innovation

Additional strategies to incentivize public health-driven innovation are urgently needed, including initiatives that "de-link" the alleged costs of R&D from the price of the end product, in order to better ensure access and affordability.

MSF and partners have come up with a proposal to deliver affordable, effective new TB treatment regimens in a timely manner, something that is urgently needed because standard TB treatments are brutal and often ineffective. The so-called 3P Project [Push-Pull-Pool] for new TB regimens uses an open collaborative approach to drug development and novel approaches to financing and coordinating R&D.

The 3P Project seeks to **push** upfront funding to finance R&D activities [i.e. through grants]; **pull** or incentivize R&D through the promise of financial rewards if certain objectives are met [i.e. through prizes]; and **pool** intellectual property [IP] to ensure open collaborative research and fair licensing for competitive production and affordability of the final products.

Change the Global Biomedical Innovation System

Even if all of the strategies listed above are implemented, they will not resolve every shortcoming of the current R&D system. At the global level, we need a better-coordinated R&D framework for biomedical technologies that is sufficiently and sustainably funded, that is driven by public health needs and priorities, and that breaks with the reliance on high prices. We need to move beyond an ad hoc patchwork of limited, siloed efforts as well.

One way to start would be to improve coordination of public funding commitments to biomedical research and development, and to hold recipients accountable for ensuring that public investments lead to the development of affordable, accessible medical products.

Discussions on how to improve health R&D financing, coordination, priority setting, and outcomes are on the WHO's agenda and have been raised in other international forums. In these discussions, MSF is calling for the establishment of a sizeable, sustainably financed global R&D fund and mechanism that promotes coordination, collaboration, and utilization of new and innovative incentives to cover innovations of public health importance.^{xiii}

Medical innovation can only improve health if the people that need the products can access them. MSF believes that medical innovation should work for everyone, regardless of their economic situation or geographic location. To do this, we must push for alternative ways of conducting biomedical R&D and for reforms to today's global ecosystem.

^x Rottingen, J. et al. Mapping of available health research and development data: what's there, what's missing and what role is there for a global health observatory? [Online] *Lancet* 2013; 382(9900):1286. [Cited 2014 Dec 4].

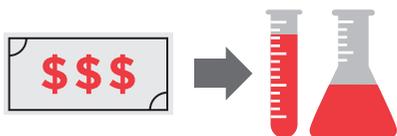
^{xii} Light D, Lexchin J. Pharmaceutical research and development: what do we get for all that money? *BMJ*. 2012;345:e4348.

^{xiii} World Health Organization. Research and development to meet health needs in developing countries: strengthening global financing and coordination. Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination Geneva; 2012

^{xiii} Balasegaram M, et al. [2015] A Global Biomedical R&D Fund and Mechanism for Innovations of Public Health Importance. [Online] *PLoS Med* 12(5): e1001831. doi:10.1371/journal.pmed.1001831 [Cited 2015 Sept 8].

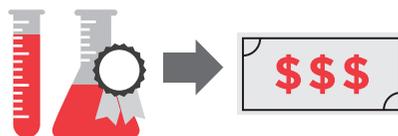


THE 3P PROJECT An Open Collaborative Approach to TB Regimen Development



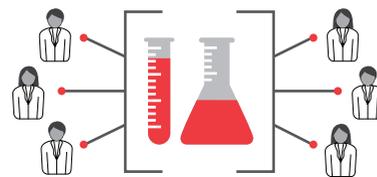
PUSH

Direct upfront funding to finance R&D activities (i.e. through grants)



PULL

Incentivize R&D through the promise of financial rewards if certain objectives are met (i.e. through prizes)



POOL

Share intellectual property (IP) to ensure open collaborative research and affordability of the final products.

PHOTO: Patients wait to receive PCV vaccines during an MSF vaccination campaign in Nyumanzi Settlement, Uganda. © Emily Gerardo



SUPPORTING MSF

MSF CORPORATE GIFT ACCEPTANCE POLICY

It is thanks to our donors that MSF is able to maintain the financial and operational independence that allows us to provide medical care to hundreds of thousands of people affected by conflict, privation, and disease in more than 60 countries around the world each year. The following outlines MSF practice and restrictions when it comes to corporate donations.

MSF Independence and Corporate Donations

It is our responsibility to ensure that the donations we receive are used in accordance with our guiding principles of independence, neutrality, and impartiality. That is why MSF cannot accept donations from corporations, foundations, or other entities whose core activities conflict with the goals of our medical humanitarian work or create conflicts of interest that may limit our ability to provide humanitarian assistance.

MSF has a policy to decline donations from companies that derive a substantial portion of their income from the production and/or sale of tobacco, alcohol, arms, or pharmaceuticals; or from mineral, oil, gas, or other extractive industries. This policy includes outright gifts of cash, corporate events, donations of goods and services (“in-kind” donations), sponsorships or partnerships, company matching gifts, or recognition gifts.

MSF Policy Towards Pharmaceutical Companies

As a consumer of pharmaceutical products that we try to procure at an affordable price and in appropriate quantities for our medical operations, MSF has frequent commercial relations with pharmaceutical companies. As we’ve explored in these pages, MSF’s operations are also profoundly affected by the pharmaceutical industry’s policies. Our medical teams are often unable to provide the best treatments for our patients because some of the medicines, diagnostic tools, or equipment needed for diagnosis and treatment are too expensive, no longer effective, poorly adapted to resource-poor settings, or simply nonexistent.

Primarily through the efforts of the Access Campaign and DNDi, MSF advocates fiercely for improvements and changes to drug research and development, production, and pricing to better meet the medical needs of the people we serve. By excluding donations from the pharmaceutical industries, MSF avoids conflicts of interest. Forgoing donations from these industries



ABOVE FROM TOP: A family in Ethiopia’s Lietchuor refugee camp after receiving vaccines in a 2015 MSF campaign. © Aurelie Baumel/MSF

MSF logisticsicians unload vaccines during a measles vaccination campaign in Yida refugee camp, South Sudan. © Karin Ekholm/MSF



allows us to continue advocating independently for the best possible drugs, tools, and equipment for patients.

Donations In-Kind: Principles and Exceptions

For many reasons, donations of drugs, vaccines, and other medical products are not sustainable, and therefore are not MSF's preferred solution for meeting medical operational needs. Corporate donation programs rely on the will of companies whose priorities will always be paying customers; donations therefore typically come with constraints, risks, and uncertainties that hinder MSF's ability to respond to medical emergencies. Instead, as a professional organization, MSF prefers to negotiate directly with companies for the sustainable, affordable purchase of medical products. The WHO and many other global health entities also have policies and recommendations against relying on product donations.

Sometimes, however, MSF is forced to rely upon donations in order to access the medical products we need. For example, when MSF decided to use the pneumococcal conjugate vaccine (PCV) in our op-

erations, we negotiated with the vaccine's manufacturers, Pfizer and GlaxoSmithKline, for approximately five years in an attempt to access a fair and sustainable price. Our efforts failed, but the medical needs persist, so MSF had no choice but to accept product donations from both companies.

While MSF is thankful for the donations of vaccines, the agreements are a notable and extraordinary exception to our policy, and are only an interim—and limited—solution. MSF continues to negotiate and strongly advocate for vaccine price reductions.

Ways to Give

While MSF cannot accept donations from the pharmaceutical, extraction, arms, tobacco, or alcohol industries, we encourage their employees to consider giving personally—and act politically. Employees of pharmaceutical companies in particular are in a unique position to challenge—and change—corporate policies to promote innovation for neglected patients and affordable access to medical technologies. There are many ways you can get involved to help MSF deliver independent, impartial medical humanitarian aid worldwide. To learn more, visit doctorswithoutborders.org/support-us. For questions, email the Corporate Relations team at corporate.donations@newyork.msf.org

INCREASE YOUR IMPACT

Does your employer have a matching gift program? Many companies have matching gift programs that will double or even triple the impact of your gift. Companies will sometimes also match donations made by spouses, retirees, and board members. Because conditions and criteria for gift matching vary by employer, please check with your company's human resources department for details. MSF-USA is happy to confirm your gift or to satisfy any other requirements your company may have.

If you or your company are interested in learning more or have questions about our matching gift program, please call **(212) 763-5745** or email corporate.donations@newyork.msf.org.

JOIN OUR LEGACY SOCIETY

Naming MSF-USA as a beneficiary on a retirement or other account is a simple way to leave a legacy without writing or re-writing your will or living trust. Please ask your IRA administrator or institution for the appropriate form.

If you have already named MSF-USA as a beneficiary of your estate, please tell us so we can welcome you to our Legacy Society.

To learn more about beneficiary designations to MSF or other legacy giving opportunities, please contact Beth Golden, planned giving officer, at **(212) 655-3771** or beth.golden@newyork.msf.org.

STRENGTHEN YOUR COMMITMENT

MSF-USA would like to thank all of our donors who have made commitments towards the Multiyear Initiative. With annual commitments of \$5,000 or more, these generous supporters help provide MSF with a predictable revenue stream that better serves our ability to respond rapidly to emergencies and ensure the continued operation of our programs. To date, we have received commitments totaling more than \$33 million towards the initiative.

To find out how you can participate, please contact Mary Sexton, director of major gifts, at **(212) 655-3781** or mary.sexton@newyork.msf.org, or visit doctorswithoutborders.org/support-us/other-ways-to-give/multiyear-initiative.

STOCK DONATIONS

Did you know you can donate gifts of securities to MSF-USA? Making a stock gift is simple and offers a number of valuable financial benefits. You can donate appreciated stocks, bonds, or mutual funds, and the total value of the stock upon transfer is tax-deductible. Also, there is no obligation to pay any capital gains taxes on the appreciation.

MSF-USA currently maintains an account with Morgan Stanley Smith Barney to offer donors an easy way to transfer securities hassle-free. For more information on how to make a security donation, please visit doctorswithoutborders.org/support-us/other-ways-give. You can also call **(212) 679-6800** and ask to speak to our Donor Services Department.

UPCOMING EVENTS

Join us for a special October webcast featuring MSF experts discussing the high cost of medicines and the ways in which intellectual property rights, international trade agreements, and the current R&D system limit and endanger access to affordable medicines.

The exact date for the October webcast will be announced soon. Please check doctorswithoutborders.org/upcoming-events for announcements concerning this and other events.



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Médecins Sans Frontières
(MSF) works in nearly
70 countries providing
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in need regardless of their
race, religion, or political
affiliation.



TOP: Amoxicillin antibiotic pills at Ahmed Shah Baba Hospital in Kabul, Afghanistan.
© Doris Burtcher/MSF

BOTTOM: MSF used MenAfriVac, a vaccine for meningitis A, in a 2010 vaccination
campaign in Mali. © Julie Damond

