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TESTIMONY FROM DOCTORS WITHOUT BORDERS/MÉDECINS SANS FRONTIÈRES (MSF) FOR THE SENATE FOREIGN RELATIONS COMMITTEE SUBCOMMITTEE ON AFRICAN AFFAIRS HEARING ON "FIGHTING HIV/AIDS IN AFRICA: A PROGRESS REPORT"

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Ladies and gentlemen,

My name is Dr. Lulu Oguda, and I would like to share with you my perspective as an African physician that has been working to provide treatment for people with HIV/AIDS in sub-Saharan Africa, with a particular emphasis on my experience as a volunteer for Doctors Without Borders/Médecins Sans Frontières (MSF) in Malawi.

Malawi is a country of 11 million people, bordered by Mozambique and Tanzania to the north and Zambia to the west, with an HIV prevalence of 15%. It is one of the poorest countries in the world. HIV/AIDS is the leading cause of death in Malawi among people adults 20-49 years of age. In the program that I worked in as a field doctor for one year, in Chiradzulu district in the south, over 20% of women in antenatal clinics test positive for HIV. Twenty-five thousand people—one fifth of the population—are estimated to be living with HIV/AIDS, and 5,000 of them are estimated to clinically require antiretroviral (ARV) treatment now or else they will die.

It is difficult for me to paint a picture of what Chiradzulu was like before ARV treatment arrived without making it sound like a caricature. There was a mixture between despair and anticipation. People with HIV/AIDS had no hope; they just thought they would die, but they were beginning to hear that ARVs would soon be available at the hospital. One patient of ours named Fred Minandi said:

> *"When I was sick then, I knew I had HIV, but I would never admit it or speak about it. Speaking about it would have not changed anything for me except making me depressed. My neighbors were seeing me becoming weaker and weaker every day. Of course, they all knew what I had, but nobody asked me. They just gradually started to not come see me. Most of the people are like that in Malawi: they don't speak because they don't want to know. It is why my country is dying in silence."*

Health workers, many of whom were HIV positive themselves, were desperate, looking at the wards full of people they could do nothing for and not wanting to get their hopes up that

ARVs would really come. Sometimes the wards in the hospital we worked in were so crowded you would have two or three people for each bed. It is an 80-bed hospital with an average daily occupancy of 200 patients. If you have not seen such a scene yourself, you simply cannot imagine it.

Then, in 2001, all this changed with the arrival of ARVs in our program in Malawi. Although it was not easy getting started, the benefits to our patients were amazing to witness. After approximately one year on treatment, Fred said:

> *"I had 107 CD4 cells [medical indicator from a blood test for the body's natural resistance capacity to infections] when I started the treatment and today I have got 356 CD4 and I am very proud. Today, I am back in my field, back in my church. I can feed my family. I used to harvest only about two bags of maize for the past years because I was too weak. Now I am talking of harvesting 10 bags of maize just this year alone. I feel have a future. My neighbours started coming to see me again like before."*

At first, our first-line treatment protocol was AZT/3TC/nevirapine or AZT/3TC/efavirenz. Patients would take six to eight pills each day, not including additional pills they may have needed to take for the treatment or prophylaxis of opportunistic infections. The program has always provided treatment for free.

We also had to draw up eligibility criteria for enrolment in the program, because there were so many more people that needed treatment than we could accommodate at the time. First, we enrolled patients with advanced HIV disease (World Health Organization stage 3 or 4) and CD4 counts of less than 200/ml of blood. In addition to the medical/clinical criteria, patients had to be within two hours' walking distance from the hospital, so that they could make it in for appointments. But this was too stringent—people were coming from hours away to get treatment and we knew it—so we made it six hours. Imagine: a person with HIV co-infected with tuberculosis and an immune system so weakened getting out of bed was a struggle, having to walk six hours to get to the hospital.

Although there were only expatriate doctors working in the hospital at the time and we could not possibly see all the patients who needed to start ARVs, only physicians could prescribe and monitor ARV therapy. We were enrolling an average of 20 patients per month.

Today, MSF is able to provide treatment for more than 2,500 people in Chiradzulu, and we are enrolling 250 new patients in the program every month. In 2003 alone, the number of patients on ARV treatment increased by 420%. There are several factors that have enabled us to rapidly scale up access to ARV treatment in this district. Beginning in August 2002, we simplified, adapted, and decentralized our approach.

We simplified treatment protocols by minimizing pill burden; adapted our clinical approach to suit the prevailing conditions in the district, meaning that we reduced the complexity of the inclusion process and started relying less on sophisticated laboratory tests; and decentralized the point of care from the hospital to health posts in rural areas while taking better advantage of the skills and resources of existing health care professionals such as clinical officers and nurses.

We have set up mobile treatment clinics at each of 10 primary care health centers in the district, facilitating greater access to treatment in remote, rural communities. In effect, rather

than asking patients to walk six hours to get their treatment, we are bringing it to them at the community level. Services at the health centers include voluntary testing and counseling with on-site rapid HIV tests, management of opportunistic infections, and treatment with ARVs including adherence counseling.

Basic patient care and follow-up is delegated to nurses and health workers for medical monitoring and community counselors, including people living with HIV/AIDS, for education, adherence support and treatment literacy. The project follows uniform guidelines for treatment and minimizes use of laboratory tests, which facilitates access to care and treatment even for the most vulnerable people in this remote area where there are few doctors and even fewer laboratories. In many cases, treatment begins after a positive HIV test and clinical assessment by trained staff. We measure CD4 count at baseline and every 12 months, and have reduced reliance on biological follow-up tests, performing Hemoglobin and liver function tests, for example, on clinical indication only. Viral loads are not performed on an individual basis. Difficult cases are referred to the district hospital.

Clinical results from Malawi are encouraging. The probability of survival at 12 months is 88%. Average CD4 increase among our patients is 192 cells/ml at 12 months, and the median weight gain is 4 kg at 12 months. The adherence rate of our patients is high, averaging approximately 90%.

Our fundamental tool in simplifying, adapting, and decentralizing the program has been triple fixed-dose combinations (FDCs) of ARVs – three different ARV drugs taken in the form of one pill, twice a day. Approximately 70% of patients in the Chiradzulu program are taking the World Health Organization (WHO)-recommended fixed-dose combination of d4T/3TC/nevirapine for their first-line regimen.

The availability of these FDCs has made the lives of our patients easier—taking just two pills a day facilitates adherence, which encourages better clinical outcomes and reduces the risk of resistance. It has also enabled nurses and clinical officers to administer standardized ARV treatment at the community health post level, and made training of on-ground personnel easier. It is easier to project program needs and procure FDCs compared with single agents with different transportation and cold-chain requirements, which lowers the risk of stock-outs. And, of course, the price of these triple FDCs, available only from generic manufacturers because of patent barriers, is the lowest of any ARV cocktail in the world. In Malawi, we currently pay approximately $240 per person per year, compared with a minimum of $562 if we were to purchase the same agents from originator companies. This is no small thing. It means we are able to treat two to three people rather than one with every $500-600 we allocate for the program.

This certainly does not mean that the FDCs we use are the answer to all of our problems. For example, for any of you who has ever tried to decide the paediatric dose of a drug that is available in capsule form, or had to watch the face of a child take horrible tasting ARV syrups, or try to divide up an unscored tablet, you will agree that paediatric treatment is a literal nightmare. Clinicians and care-givers, who are usually elderly grandmothers because children's' mothers and fathers have already died of AIDS, need to be able to have fixed-dose liquid formulations for infants and low-dosage or breakable FDC tablets for children. Likewise, we need a first-line FDC that can be used in both people co-infected with HIV/TB and women of child-bearing age. We need affordable and simplified second-line drugs and simplified diagnostic tools to help monitor efficacy, detect treatment failure, and diagnose

opportunistic infections, particularly TB in patients with HIV/AIDS. In order to face the next generation of operational challenges, we need these new tools and strategies.

But when you consider that a safe, effective, and affordable first-line treatment, which is easy-to-use could be prolonging millions of lives – not just thousands – it is a medical ethical imperative to make it more widely available to humans in peril as urgently as possible. And this is not a job that MSF has the capacity or mandate to do; that responsibility rests with governments.

That is why I am truly bewildered by the debate I have been hearing over the past few weeks about FDCs.

I have heard US government officials claim that the generic AIDS medicines, including FDCs, which are being used by MSF and others are not the same as "generic drugs" sold in the US and are sub-standard. But the World Health Organization (WHO) has certified that numerous medicines from both generic and brand-name companies, including generic FDCs, meet stringent international standards for quality, safety, and efficacy through a prequalification system that borrows drug regulatory experts from North America and Europe to inspect manufacturing sites and establish bioequivalence and is utilized and respected by all key actors, including the World Bank, UNICEF, and the Global Fund to Fight AIDS, TB and Malaria. In fact, these medicines are manufactured by the same pharmaceutical labs that produce hundreds of generic medicines used by Americans every day.

I have heard US government officials say that there are no agreed upon principles for evaluating FDCs, and that without the approval of the US Food and Drug Administration (FDA) or a similarly stringent regulatory authority they cannot be proven safe or effective. But in 2000, the FDA approved a brand-name triple combination therapy, GlaxoSmithKline's Trizivir, on the basis of bioequivalence data, the very same data WHO has reviewed to certify the generic FDCs we use. There were no clinical trials conducted to compare the individual compounds with the fixed-dose combination.

I have heard US government officials assert that use of these drugs could create resistance, which would be a disaster for the continent of Africa. Unfortunately, drug resistance is inevitable and, indeed, disastrous. It is something we are deeply concerned about as well. But this has nothing to do with the question of FDCs. In fact, it seems to me that if the US is concerned about resistance, it should be doing everything possible to ensure that FDCs are used – since they promote adherence, the key to delaying the onset of resistance – that communities are mobilized to carry out treatment education and adherence support, and that future FDCs are developed urgently so that when resistance does emerge, patients have viable treatment options.

Finally, I have heard US government officials say that they will not tolerate a different standard for Africans. As an African doctor who has personally treated hundreds of people with HIV/AIDS using these medicines and witnessed my patients' spectacular return from death's door, I find this particularly appalling. It is simply untrue that generic FDCs are substandard. These sorts of baseless assertions will only result in depriving Africans of affordable, easy-to-use treatment; setting up disruptive and parallel systems, which will waste precious resources, confuse patients, and undermine confidence in existing programs; undermining national policies and protocols in African countries; and wasting money on

“brand name” medicines, despite the fact that the difference in price will mean prolonging and improving the life of one person instead of four.

That is intolerable.

Millions of lives are at stake.

APPENDIX:

GENERAL BACKGROUND INFORMATION

In the developing world today, over 40 million people are living with HIV/AIDS. Of the more than six million people in urgent clinical need of ARV treatment, only 400,000 have access to it, and one-third of them live in one country, Brazil. An estimated 8,000 people die each day of AIDS-related complications. These are premature, avoidable deaths.

Currently, MSF is providing ARV treatment as part of a comprehensive continuum of care for over 11,000 people living with HIV/AIDS in more than 20 countries in Africa, Asia, Latin America, and Eastern Europe. MSF is an international medical humanitarian organization with field operations in nearly 80 countries and the recipient of the 1999 Nobel Peace Prize.

We have learned important lessons about both the benefits and challenges of providing ARV treatment in resource-limited settings and are in the process of adapting our approach to AIDS treatment to better fit the real-life conditions faced in developing countries. Our projects are using treatments with fewer pills, relying less on sophisticated laboratory tests, taking better advantage of the skills and resources of existing health care professionals such as clinical officers and nurses, and decentralizing the point of care to district hospitals and health posts.

In addition, we have produced several reports, some of which are joint publications with the World Health Organizations (WHO), UNAIDS, and UNICEF, to help other providers of ARV treatment—including governments, non-governmental organizations (NGOs), and community-based organizations—identify sources, prices, and patent status of needed medicines and assist with strategies for efficient procurement of medicines. We have also participated actively in the development of the WHO initiative to scale up treatment to at least three million people by 2005 ("3x5").

While our ARV treatment programs have had a significant impact on the individuals and communities with whom we work and have demonstrated the feasibility of providing ARV treatment in resource-limited settings, they are relatively small-scale, and we have neither the capacity nor the mandate to provide the wide-scale access to treatment that is so urgently needed. That responsibility rests with national governments.

We do, however, feel a responsibility to share our experience and impart the lessons we have learned in order to inform efforts to scale up access to treatment, including the United States President's Emergency Plan for AIDS Relief (PEPFAR). This is why we would like to highlight the following critical issues, which in our experience must be considered as utmost priorities as the U.S. government begins to implement its PEPFAR:

- Simplifying treatment protocols, particularly by minimizing patients' pill burden;
- Decentralizing and adapting clinical approaches to treatment and monitoring;
- Decreasing the prices of medicines, ensuring efficient procurement of medicines, and making treatment available for free;
- Involving communities, including people living with HIV/AIDS, in treatment programs; and
- Promoting research and development for desperately needed new tools.

MSF'S AIDS TREATMENT EXPERIENCE

MSF has been caring for people living with HIV/AIDS in developing countries since the early 1990s. In 2000, MSF started to provide ARV therapy in addition to other services. Approximately 11,000 people living with HIV/AIDS, including nearly 500 children, are currently on ARVs in more than 20 countries worldwide. These countries include Burkina Faso, Burundi, Cambodia, Cameroon, China, Democratic Republic of Congo, Guatemala, Honduras, Indonesia, Kenya, Laos, Malawi, Mozambique, Myanmar, Rwanda, South Africa, Thailand, Uganda, and Ukraine.

MSF provides ARV treatment in both urban and rural settings, and in almost every project works within public sector health facilities—including primary care clinics/community health posts, district hospitals, and provincial hospitals—in collaboration with national, provincial, or district departments of health. Clinical eligibility criteria are, for the most part, uniform throughout MSF projects (< 200 CD4 cells or 15% for children), though some projects are increasingly initiating treatment in very advanced patients on clinical grounds. In MSF projects, treatment is provided free of charge.[1]

Clinical outcomes in our projects are encouraging, and parallel those found in the US: patients' CD4 counts are increasing, they are gaining weight, and they are suffering from fewer opportunistic infections. Adherence rates are excellent, exceeding 90% in many projects. People are returning to work and again becoming productive members of their communities. In short, treatment is transforming the face of AIDS.

MSF does not offer ARV treatment in a vacuum, so we aim to integrate treatment into a continuum of care that includes prevention efforts (e.g. health education, condom distribution, and prevention of mother-to-child transmission programs), voluntary counseling and testing, treatment and prevention of opportunistic infections, nutritional and psychosocial support, and palliative care.

MSF expects the total number of patients treated in its projects to reach 25,000 in 25 countries by the end of 2004.

LESSONS LEARNED FROM MSF'S ARV EXPERIENCE

Although there are no simple formulas or models for providing ARV treatment, MSF has learned several clear lessons by delivering ARV in diverse settings, which could be helpful in designing and implementing initiatives aimed at scaling up access to ARV therapy, including PEPFAR. Below is a summary of some of the key lessons we have learned.

- **Simplify treatment**

One of the most important tools in simplifying and adapting treatment is fixed-dose combinations (FDCs) of ARVs. Today, 50% of patients in MSF projects, and 70% of those newly enrolled, are taking triple FDCs as their first-line treatment. That is, patients are taking the three different ARV drugs they need in the form of one pill, twice a day. Taking a smaller number of pills per day facilitates adherence, which encourages better clinical results

[1] Except in Cameroon, due to government policy requiring entrance fee.

and also lessens the risk of drug resistance, as it is impossible to take partial doses. The FDCs MSF uses, which have been pre-qualified by the World Health Organization (WHO), are also the most affordable combinations available worldwide and have significant distribution advantages (procurement and stock management).

- **Decentralize and adapt**

Treatment and monitoring protocols must be designed in a way that facilitates access even for the poorest and most vulnerable people in remote settings where there are few hospitals, few doctors and even fewer laboratories. In several MSF projects in Africa, including those in Malawi, Kenya, Mozambique, and South Africa, basic patient care and follow-up is being delegated to nurses and health workers (for medical monitoring) and community counselors (for education, adherence support and treatment literacy). MSF follows uniform guidelines for treatment minimizing use of laboratory tests; in many projects, treatment begins after a positive HIV test and clinical assessment by trained staff. More difficult cases are referred to district hospitals. In Chiradzulu, Malawi, this approach has allowed the number of patients under treatment in the district to rise quickly, to a rate of 250 new patients each month.

- **Decrease the price of medicines and ensure availability even for the poorest**

The lower the price of medicines, the more patients can be treated and the more sustainable treatment is in the long term. Globally, the prices of AIDS drugs have dropped by over 98% in less than three years (see graph on page 10). Under certain circumstances, WHO pre-qualified FDCs cost less than $140[2] per person per year. These FDCs are available only from generic manufacturers due to patent barriers. In MSF's experience, crucial factors in bringing about lower prices for ARVs include government commitment to centralized procurement, overcoming patent barriers when necessary, and fostering generic competition. Come 2005, when most World Trade Organization (WTO) member states will have to become compliant with the WTO Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS), generic production of patented medicines will rely upon compulsory licensing; therefore, flexible conditions for granting compulsory licenses must be in place. The right of countries to use this and other TRIPS-compliant public health safeguards is currently under threat, particularly in regional and bilateral trade negotiations launched by the US with a number of countries and regions heavily affected by HIV/AIDS. On a related note, the cost of treatment for the patient should never be a barrier, and that means treatment will have to be free for the majority of patients. The cost of drugs is frequently cited as a reason for treatment interruptions.

- **Involve the community**

The knowledge and meaningful participation of people living with HIV/AIDS is key to the success of treatment. At its HIV clinics in Khayelitsha, South Africa, MSF and grassroots treatment advocates have fostered community-based education programs. Through carefully designed patient-centered adherence programs (not directly observed therapy), people on ARVs in MSF programs have the support of their peers and of trained counselors. Community mobilization, in partnership with medical services, has had a powerful effect on the community, decreasing stigma and discrimination, and supporting prevention efforts. In Khayelitsha, there have been significant increases in the distribution and use of condoms, the

[2] Due to negotiations with generic manufacturers brokered by the Clinton Foundation.

number of sites providing voluntary counseling and testing, and the uptake rate of testing. According to a study conducted by the Center for AIDS Development, Research and Evaluation (CADRE) and the South African Department of Health, the self-reported condom use at last sexual intercourse, willingness to use a female condom, and consent to an HIV test in the Khayelitsha community is the highest in South Africa.

- **Urgently promote research and development of new tools**

It will not be possible to solely base scaling-up efforts on existing tools. New tools and strategies for treatment will have to be developed urgently. For example, at present, ARVs are not well-suited for use by children, so fixed-dose liquid formulations for infants and low-dosage or breakable FDC tablets for children are needed. The pharmaceutical industry is not going to spontaneously fill existing and future gaps such as easy-to-use first-line treatments for children, simplified second-line treatments and simplified diagnostic tools (e.g. semi-quantitative tools to measure CD4 and viral load). The public sector, with leadership from WHO, should therefore seek to define and lead the work on this research agenda. This needs to be a part of the overall U.S. global AIDS strategy. There is also an urgent need for operational research, for example on pediatric treatment, management of HIV/TB co-infection, ideal second-line regimens, and structured treatment interruptions. Furthermore, we will not be able to face the next generation of operational challenges without new tools and strategies: these challenges include the inevitable development of resistance to first-line drugs; the need for new strategies for monitoring efficacy and detecting treatment failure, particularly as we reduce reliance on lab monitoring; the price and practicality of second-line drugs; the management of side effects; and the role of prevention of mother-to-child-transmission (pMTCT) using monotherapy in the era of ARVs.

Graph 1

The Effects of Generic Competition:
A first-line antiretroviral (ARV) triple-combination: stavudine (d4T) + lamivudine (3TC) + nevirapine (NVP).
Lowest world prices per patient per year (in US$).