Ministerial Statement on Microbicides

MINISTRY OF HEALTH

To be presented to parliament by the Hon. Minister of Health

Introduction

Mr. Speaker, thank you for this opportunity to present a Ministerial Statement on the Microbicide study. Allow me to start by stating that, the Ministry of Health fully recognizes the value of medical research in advancing the security of human health. Research generates data which in turn informs policy and the enactment of legislation for meeting the health needs of communities.

The Ministry of Health is also aware of the microbicides studies that have been conducted in Zambia. An earlier study was conducted in Lusaka by the Centre for Infectious Disease Research in Zambia (CIDRZ) and another by the Microbicide Development Programme (MDP) in Mazabuka. Both of these studies were multi-country trials, meaning that they were simultaneously conducted in Zambia and other countries. The CIDRZ trial included the Unites States, South Africa, Zimbabwe, and Malawi. Mazabuka was one of the six sites for this Microbicide research. The other sites were in South Africa, Uganda and Tanzania.

What are microbicides?

Microbicides are substances which kill the HIV virus. Thus, they have potential to protect women from acquiring HIV when applied in the vagina. Microbicides can take the form of a cream, pessary, sponge, foam or gel. The first products to be tested are gels which closely resemble the lubricants used with condoms.

Microbicides are still at a developmental stage. Although no proven effective products are currently available, there are several new agents in development that might be shown to protect women from HIV.

Why conduct microbicide research?

The HIV epidemic continues to infect and kill millions of people each year. The majority of these people are African women. Women are more susceptible to acquiring HIV than men, and this is why in Zambia more women are infected (16%) than men (12%). HIV prevention strategies that are currently available are mainly controlled by men hence the need for a method that can be controlled by women, such as a microbicide.

Why do we need clinical trials?

Clinical trials are carefully monitored medical evaluations of new drugs. Essentially every medicine currently in use in Zambia has been through clinical trials to prove its effectiveness. For instance, blood pressure medicines, antibiotics, ARVs, diabetes drugs, contraceptives, even panadol – all of these have been tested in clinical trials.

For every one effective drug that you find in the pharmacy there have been many, many others that came before it that did not work and that failed in clinical trials.

If we don't use clinical trials to evaluate a new medicine, then we are just guessing. New medicines must be very carefully evaluated before they are put into policy and used widely.

What is a microbicide trial?

A microbicide trial is a carefully monitored medical evaluation of a new microbicide product. Microbicide trials are conducted in populations of women who do not have HIV at the beginning of the study but who are at *natural risk* of acquiring it. In Zambia, since HIV is common in the community, many women are at risk of infection.

Microbicide trials follow up these populations to examine new infections but at the same time equip participants with the best ways of preventing themselves from acquiring HIV, including counseling and provision of condoms.

The Process of the Study Implementation:

The implementation of the Microbicide trial that took place in Mazabuka from 2003 to 2009 followed these steps:

Protocol registration and approval

The University of Zambia Research Ethics Committee (UNZA REC) and the Pharmaceutical Regulatory Authority (PRA) reviewed and approved the study. The Mandate of the UNZA REC is to protect the rights of people participating in research and to ensure that studies have a sound scientific basis. The study was also approved by International Regulatory Bodies.

Site Implementation

The community was prepared for the study by formation of the community advisory groups and meetings with the stakeholders and the local leadership. The trial started with a feasibility study in Mazabuka conducted between 2003 and 2005, and this was launched by the Ministry of Health. The aim of the feasibility study was to determine community understanding and acceptability of the study and possibility of recruitment, retention and follow up of women volunteers.

The next phase was a pilot study for six months where a placebo gel was used and the aim was to determine the acceptability of trial procedures. This was followed by a full

fledged safety and effectiveness trial which ran from July 2006 to June 2009. Potential participants were screened for eligibility and those who qualified were invited to participate after explaining the purpose of the study. Enrolment only commenced after determining that the participant understood and was willing to give signed consent voluntarily.
The trial recruited HIV negative sexually active women over 18 years of age. Each participant once enrolled into the trial was followed up every month for a year. During follow up visits, each participant received HIV/STI risk reduction counseling, screening and treatment for STIs and were supplied with gel and condoms. The participants were also tested for HIV and screened for pregnancy. In addition, the study team provided VCT, STI screening and treatment services to the male partners and the community in general. In Mazabuka, 1,340 women were recruited. Across the four participating countries 9,404 were recruited. As I mentioned earlier, the other countries include South Africa, Uganda and Tanzania.

The trial was a double blind placebo controlled study involving three groups. The first group was given 2% PRO 2000, the second group was given 0.5% PRO 2000 gel and the third group was given a placebo gel. "Double blind" means that neither the investigators nor the participants knew who was in which group. This was chiefly to avoid bias which could negatively affect the result. The placebo is an inert substance that is similar to the active product in all ways except for the fact that it does not have the active ingredient. This means it looks the same and feels the same. The Placebo group was used as a comparison for both the 2% and 0.5% groups.

Safety monitoring was done through reporting of adverse events in participants to the UNZA Research Ethics Committee and the Pharmaceutical Regulatory Authority. The trial also had an Independent Data Safety Monitoring Committee (IDMC) which met every six months to look at the accumulating un-blinded data to assess participant safety. For example, if data showed that PRO 2000 was causing harm, the study would have been stopped early.

Results

The trial showed that PRO 2000 was not effective against HIV but it was not harmful. These infection rates are similar to that seen in the general population meaning that none of the products used in this study increased the risk of HIV infection. The gel also did not decrease the risk since the number of HIV infections in each active group compared to the placebo group were very similar and in fact, not statistically different. The safety events were also not different across groups in that whatever event occurred in the active group, e.g. vaginal itching, also occurred in the placebo group.

The earlier smaller trial conducted by CIDRZ had shown that PRO 2000 was 30% effective in preventing HIV. However, this was not statistically significant. The MDP study being a bigger trial conclusively shows that PRO2000 is not effective in preventing HIV infection.

Funding

The funding of the MDP (Mazabuka study) was by the UK government through NHS and DFID. Microbicide research in general has been funded by non-profit making organizations such as governments and charitable organizations. These include the US National Institutes of Health, the European Commission, SIDA and Gates Foundation.

Conclusion

The government of Zambia believes that research is important because it provides data for policy making. Therefore, the Government supports research. The results of the MDP (Mazabuka trial) were disappointing but government recognizes that this large trial was done with high scientific and ethical standards. The researchers also engaged the stakeholders and community in which the trial was conducted. The results are clear Microbicides do not work, period! But we cannot stop here. Other means of protecting women will have to be found and trials will be conducted, hopefully this time the trials will be positive.

Mr. Speaker, trails in Medicine and indeed other trials are a risky undertaking and whether positive or negative, the participants are made aware of the dangers of the trials. And as Government, we are very cautious about trials in Zambia and in many instances we have rejected research on many issues. This research was important since we are one of the countries still overburdened with HIV/AIDS

I thank you.