

Secretary of the 17th Expert Committee on the Selection and Use of Essential Medicines
Medicine Access and Rational Use
Department of Essential Medicines and Pharmaceutical Policies
World Health Organization
20 Avenue Appia
CH-1211 Geneva 27
Switzerland

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Dear Committee Members:

This letter is to offer my support of the application to include misoprostol for the prevention of postpartum hemorrhage (PPH) on the World Health Organization's (WHO) Model List of Essential Medicines (EML).

Despite numerous safe motherhood initiatives, women continue to die in childbirth throughout the developing world. The maternal mortality ratio in sub-Saharan Africa has decreased by a mere 2% over the past 15 years. Due to population growth over the same period, 50,000 more women lost their lives due to maternal causes in sub-Saharan Africa in 2005 than in 1990 (WHO 2005). PPH is the leading cause of maternal mortality and contributes disproportionately to women's deaths in the developing world.

Our nonprofit organization, Venture Strategies for Health and Development, works across 14 countries in our Misoprostol Program, by invitation and expressly with the support of ministries of health and/or leading obstetricians/ gynecologists, with the goal of saving mother's lives in childbirth. Specifically we facilitate registration of high quality, generic misoprostol tablets for the control of postpartum hemorrhage and assist local partners in integration of misoprostol into national safe motherhood initiatives. Additionally we assist public and private sector partners to develop distribution channels to effectively reach poor, underserved women with misoprostol tablets for PPH by persons legally permitted and trained to distribute the registered tablets. We have facilitated the regulatory approval of misoprostol for PPH in eight of the current

ten countries where it has been registered for this indication.¹ Additionally, we have negotiated some of the lowest export prices of high quality generic misoprostol tablets within our network of manufacturers (as low as \$0.10 per tablet). We continue to work to ensure lower prices for end-users by negotiating price caps with local distributors in countries where we work and stimulating price competition when possible. Venture Strategies receives no financial benefit from the sale of misoprostol. In the countries where we have launched community-based misoprostol operations research, we have done so with the direct involvement or express support of the country's ministry of health and having met the highest ethical standards of both the local internal review board and that of the University of California, Berkeley.

We strongly support the inclusion of misoprostol into the WHO's Model List of Essential Medicines for PPH prevention as it is directly in line with our work to save women's lives. Our policy work brings us directly in contact with leaders within ministries of health, presidents of national obstetrics and gynecology societies, national safe motherhood coordinators and program planners at large nongovernmental organizations. We witness daily the groundswell of support for misoprostol in the countries where we work and the significance the Expert Committee's support of misoprostol for this indication would have for successful public sector integration and implementation of misoprostol programs.

The published literature repeatedly cites the important role misoprostol has in preventing PPH in resource-poor settings (Prata et al, 2008; Darney 2001, Ng et al; 2001). Because of its low cost, ease of use, heat stability and long shelf life, misoprostol provides a desperately needed alternative over conventional uterotonics which require

¹ Misoprostol was first registered on January 30, 2006 in **Nigeria** (Zhi Zhu Pharmaceuticals, China) and subsequently in **India** (Misoprost®, Cipla Pharmaceuticals and Zitotec®, Sun Pharma, India), **Tanzania** (Misotac®, Sigma Pharmaceutical Industries, Egypt), **Nepal** (Zitotec®, Sun Pharma, India and Isovent®, Square Pharmaceuticals, Bangladesh), **Bangladesh** (Isovent®, Square Pharmaceuticals Ltd., G-Misoprostol®, Gonoshasthaya Pharmaceuticals, Ltd., and Cytomis®, Incepta Pharmaceuticals, Bangladesh), **Zambia** (Misotac®, Sigma Pharmaceutical Industries, Egypt), **Uganda** (Misotac®, Sigma Pharmaceutical Industries, Egypt), **Sudan** (Misotac®, Sigma Pharmaceutical Industries, Egypt), **Kenya** (Isovent®, Square Pharmaceuticals Ltd., Bangladesh) and **Ghana** (Misotac®, Sigma Pharmaceutical Industries, Egypt). In response to requests, Venture Strategies provided technical assistance and we continue to receive similar requests from ministries of health to register the drug for PPH.

both refrigeration and parenteral administration by skilled attendants who are not normally available where most births take place. Indeed it is precisely its proven safety and efficacy in resource poor settings—where oxytocin is not an option—that makes misoprostol so promising (Walraven *et al.* 2005; Hoj *et al.* 2005; Derman *et al.* 2006).

Moreover, the literature supports the view that misoprostol is an evidenced-based approach to PPH prevention and should be included in the Model List of Essential Medicines for this indication. Misoprostol is a safe and extremely effective drug that has been shown to reduce postpartum bleeding after delivery (Derman *et al.* 2006; Lagenbach, 2006; Alfirevic *et al.* 2007). Misoprostol is also widely used to save women's lives in western obstetric hospitals (Goldberg *et al.* 2001). Furthermore, the WHO's Department of Making Pregnancy Safer published recommendations that misoprostol be used for PPH prevention in the absence of active management of the third stage of labor by a provider trained in its use (WHO 2007). Misoprostol is already included in the 14th and 15th editions of the *WHO's Model List of Essential Medicines (22.1 Oxytocics)* because of its proven safety and efficacy for labor induction and medication abortion.

In addition to the ten countries that have registered misoprostol for the prevention of PPH, several African ministries of health that have added misoprostol for the prevention of PPH to their national essential medicines lists: Ethiopia (2006), Tanzania (2007), Zanzibar (2008) and Zambia (2008). In a number of countries, ministries of health are already amending clinical guidelines to include instructions for using misoprostol for PPH prevention.

However, many countries' ministries of health adhere strictly to the WHO's Model List of Essential Medicines. Many ministries of health are simply unable to provide misoprostol for prevention of PPH via standard drug registries because the product is not listed on the EML for this important women's health indication. Likewise, United Nations agencies and organizations in conflict or emergency situations often cannot offer misoprostol because of its absence from the list. Consequently the most vulnerable populations—poor, underserved women in refugee camps—lack access to a safe drug to prevent a prevalent cause of maternal mortality. Adding misoprostol to the model list will remove a significant obstacle to wide-scale use of these tablets and facilitate access to safe and effective PPH prophylaxis where it is urgently needed. Governments are looking to the WHO and the published Model List of Essential Medicines to guide

their policies. The addition—or omission—of misoprostol for PPH has far-reaching implications for successful integration of misoprostol into safe motherhood initiatives.

For women around the globe, death from excessive bleeding after childbirth remains a pervasive concern and an all too common reality. I strongly urge the Expert Committee to prioritize mothers' lives and add this crucially important medication to the WHO Model List of Essential Medicines for the prevention of postpartum hemorrhage.

Sincerely,



Martha M. Campbell, PhD
President/ CEO

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Global Misoprostol Registration by Indication

