October 29, 2010

Drs. Sue Hill and Anna Ridge  
Department of Medicines Policy and Standards  
Health Technology and Pharmaceuticals  
World Health Organization  
Avenue Appia 20  
1211 Geneva 27  
Switzerland

RE: Request to add 4% chlorhexidine solution and gel formulations to the Essential Medicines List (EMLc) and withdraw the current listing of 20% chlorhexidine solution (digluconate).

Dear Drs. Hill and Ridge,

The 17th Expert Committee on the Selection and Use of Essential Medicines convened by WHO in 2009 concluded that data from a community-based, cluster-randomized trial in Nepal that showed a significant reduction in neonatal mortality after use of a 4% chlorhexidine (7.1% chlorhexidine digluconate) solution for umbilical cord care\(^1\) was sufficient to include such a product and indication for use in the EMLc. Due to the absence of a commercially available 4% chlorhexidine solution, this recommendation of the expert review committee resulted in 20% chlorhexidine digluconate solution being listed in the EMLc with the instruction to dilute for umbilical cord care.

PATH respectfully requests that you consider modifying the current listing to include both a gel and a solution containing 4% chlorhexidine (7.1% chlorhexidine digluconate) and withdraw the current listing of 20% chlorhexidine digluconate solution. The efficacy of the 4% chlorhexidine (7.1% chlorhexidine digluconate) solution is already well documented\(^1\) and recent data from Nepal shows the non-inferiority of a 4% chlorhexidine gel for umbilical cord care\(^2\). In this study, newborns (n=694) from normal deliveries at a hospital in Kathmandu were randomly assigned to cord cleansing with either gel or aqueous chlorhexidine, applied by finger. Immediately before and 24 hours after cleansing, periumbilical swabs were collected and cultured. At 24 hours post application 4.6% of cultures in the gel group and 10.7% in the aqueous group were positive. The absolute difference in rates (gel minus aqueous) was - 6.1% (95% CI: - 10.2%, - 2.1%) thereby establishing non-inferiority of the gel formulation, defined as the upper bound of the 95% confidence interval being less than +10%.


Availability of 4% chlorhexidine gel
The 4% chlorhexidine gel used in the Nepal clinical trial had the same concentration of chlorhexidine as the solution and was thickened using pharmaceutical-grade guar gum (2%). The gel chlorhexidine is currently available on a commercial basis from the manufacturer, Lomus Pharmaceuticals Pvt. Ltd., Kathmandu. Established in 1986, Lomus Pharmaceuticals is one of leading pharmaceutical manufacturers in Nepal and complies with WHO GMP standards and maintains ISO 9001 and ISO 14001 certifications (http://www.lomus.com.np/about_us.htm).

Availability of 4% chlorhexidine solution
Since the beginning of 2008, USAID, PATH, and a large, locally based pharmaceutical company have been working jointly to develop and commercialize 4% chlorhexidine solution in Bangladesh. We anticipate that 4% chlorhexidine solution will be commercially available in Bangladesh in 2011. The Bangladeshi pharmaceutical company committed to commercializing this product is already WHO cGMP-certified for their existing products and is capable of producing and exporting 4% chlorhexidine solution for large-scale use.

In addition to the current efforts in Nepal and Bangladesh, the product specifications for gel and solution containing 4% chlorhexidine (7.1% chlorhexidine digluconate) will soon be released in the public domain for transfer to interested manufacturers in other countries. We believe that this will ensure that 4% chlorhexidine gel or solution will be commercially available in other parts of the world in the near term.

We welcome your consideration of this timely and relevant information and urge you to add 4% chlorhexidine solution and gel formulations to the EMLc list and withdraw the current listing of 20% chlorhexidine solution (digluconate). Should you have any questions, we would be happy to respond.

Sincerely,

Michael Free
Vice President and
Senior Advisor for Technologies