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CHLORHEXIDINE *for* UMBILICAL CORD CARE:

A VALUE CHAIN ANALYSIS *in* Bangladesh

Duke
CENTER on GLOBALIZATION, GOVERNANCE & COMPETITIVENESS
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ACRONYMS

BRAC	formerly Bangladesh Rehabilitation Assistance Committee and later Bangladesh Rural Advancement Committee, now acronym only
CWG	Chlorhexidine Working Group organized and operated by PATH
CXH	chlorhexidine
CXHUCC	chlorhexidine for umbilical cord care
DGFP	Directorate General of Family Planning, Bangladesh Ministry of Health
DGSP	Directorate General of Health Services, Bangladesh Ministry of Health
NGO	non-governmental organization
PATH	formerly Program for Appropriate Technology in Health, a Seattle-based NGO now acronym only
SMC	Social Marketing Company Bangladesh
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
VCA	Value Chain Analysis

EXECUTIVE SUMMARY

In many regions of the world, including South Central Asia, infection is a leading cause of neonatal mortality. 7.1% chlorhexidine digluconate (gel or solution) is a lifesaving commodity which, when properly applied to newborn umbilical cords, can significantly reduce neonatal mortality. Chlorhexidine (CHX) for umbilical cord care was introduced in Bangladesh after a decade of clinical trials, implementation studies and revisions to the essential newborn care guidelines (2014 to include a single application of 7.1% chlorhexidine digluconate solution in the first 24 hours after birth.) A team of students, faculty and staff from Duke University applied a value chain analysis to the CHX launch in Bangladesh. Primary source material gained from fieldwork in Dhaka during March and May 2015 built upon a review of existing literature conducted during the Fall 2014. The student engagement was supported through a grant from Duke's Bass Connections. USAID's Health Education Solutions Network, of which Duke University is also a participating member, also provided support for the effort.

The value chain analysis (VCA) methodology examines the labor, policy, capabilities, inputs, technologies, standards, regulations and markets that are involved in the production, distribution and consumption of commodities, thus providing a holistic view of the CHX introduction in Bangladesh. Along the value chain, various points—called leverage points—are identified where suppliers and recipients can "upgrade" their scale or scope of operations, increase efficiencies and improve livelihoods. In addition to the learning experience for students, the Duke work is intended to identify opportunities to create greater synergies, reduce supply interruption risks and increase the adoption of CHX in the medium or long term to CHX technical working groups in countries. Global CHX coordinators can also extract transferable insights from the Bangladesh experience to other existing or potential CHX markets.

The report identifies seven leverage points with a discussion of the options available to optimize the opportunity at this juncture in the value chain.

- **Research and Development** – Bangladesh chose a solution formulation which had been tested in clinical trials in neighboring Nepal. Although some evidence exists, more information is needed comparing differing packaging for the solution formulation.

- **Packaging** – Recent safety concerns in Nigeria relating to solution "dropper" bottle packaging (can be confused as an ophthalmic preparation) suggest a packaging redesign should be considered among other options to ensure safe use. There is also a cost reduction motivation given the current dropper packaging represents ~75% of the cost of goods. Bangladesh has made specific packaging provisions to reduce the risk of packaging-related improper use incidents as were observed in Nigeria.

- **Regional supply and market expansion** – Currently there is only one CHX supplier, ACI, in Bangladesh. The single supplier strategy creates a vulnerability in the chain if the single supplier exits the market or has a shortage of supply. A South Asia CHX market exists with the introductions of CHX in Nepal, Pakistan, Bangladesh. India is initiating pilot tests which could create a significant regional market. Aggregating

demand across a geographic region can create larger markets which are more attractive to manufacturers who can meet export quality and supply requirements. Competition for the larger markets could reduce prices while maintaining or improving quality; multiple global suppliers can also reduce the risk of supply interruption.

• **Safe Delivery Kits (SDKs)** – Inclusion of chlorhexidine into SDKs can help increase access for mothers who give birth at home. However, higher bundled costs and increased regulatory burdens associated with adding CHX to the kits could reduce uptake due to price sensitivity. CHX + SDK seeks to emulate the anti-diarrheal programs where oral re-hydration salts were combined with zinc; both products increased their uptake.

• **Distribution** – Three distribution channels exist in Bangladesh (public, private and NGO). Currently the NGO channel is not distributing chlorhexidine, limiting its adoption in-country.

• **Global Coordination** – A global coordinator, Chlorhexidine Working Group[1], transfers best practices across CHX markets. A global value chain approach may be useful to the global coordinator to expand its remit with particular attention to regional supply strategies, underwriting package redesign efforts and assisting markets in aggregating the demand for CHX product.

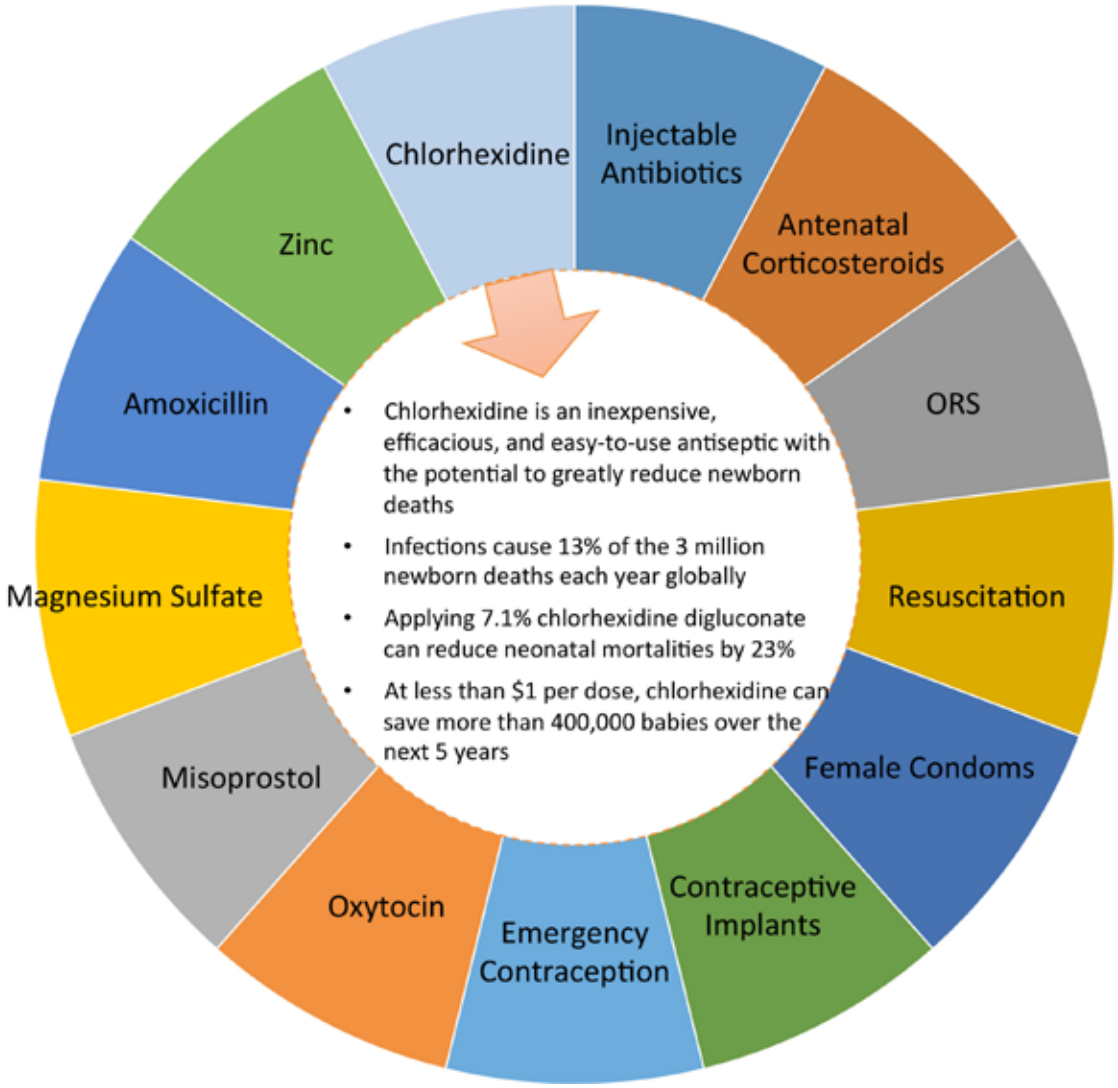
• **Monitoring and Performance Metrics** – Development of a dashboard with accepted metrics and indicators along the value chain will allow all actors to monitor the system and anticipate problems before they arise. It also allows for a quantifiable measure of the success of the program and transparency of information along the chain.

National markets are unique and the identified Bangladesh CHX leverage points are locally contextualized. However, it is reasonable to expect recurring and similar challenges wherever CHX becomes an addition to essential newborn care. South Central Asia has evolved into a regional CHX market with introductions in Nepal, Pakistan and Bangladesh, with India initiating pilot tests. The report discussion suggests that a regional approach to CHX supply may face barriers in the form of tariffs and cumbersome export/import approval processes. It is unknown whether these countries have the capabilities to aggregate public and private demand for CHX and participate in a regional tendering approach. The opportunity to reduce costs, maintain or increase quality, and reduce supply interruption threats could be mitigated or eliminated by these trade and capacity barriers. The report acknowledges local manufacture will continue as the preferred approach while advocating for an assessment of the “readiness” for a regional supply approach.

[1] “The Chlorhexidine Working Group (CWG) is an international collaboration of organizations committed to advancing the use of 7.1% chlorhexidine digluconate (delivering 4% chlorhexidine) for umbilical cord care through advocacy and technical assistance” (from HNN website).

CHLORHEXIDINE FOR UMBILICAL CORD CARE (CHXUCC): 1 OF 13 LIFESAVING COMMODITIES

The UN Commission on Life-Saving Commodities for Women and Children advocates "the potential benefits of investing in these 13 commodities over a five-year period are extraordinary. It would save an estimated 6 million lives…. an extra 1.8 million child deaths a year"[2] in addition to saving maternal lives.



[2] UN Commission on Lifesaving Commodities for Women and Children, September 2012, pg 5.

Chlorhexidine for umbilical cord care (CHXUCC) is one such commodity medication. CHX markets are being created through the intervention of international public and private collaborators organized as individual market introductions (e.g. Pakistan, Nepal, Bangladesh, Nigeria). Countries where the neonatal mortality rate is high due to infection have been identified as targets for the introduction of CHX. The specific steps in market preparation differ from country to country but generally require identifying local advocates, understanding current birthing practices, identifying local resources and starting a process that can result in the formation of formal/informal linkages among public and private in-country actors to become the implementing partners. Such a process occurred in Bangladesh and in the other countries (Nepal, Pakistan, Nigeria[4]) where CHX has been introduced. The introduction of CHX also raises an awareness of the current global status of birthing practices, particularly the roles of birth attendants, and the government health organizational structures that support maternal and child health.

The "Every Mother Every Child" and "Saving Lives at Birth" initiatives reflect three global contextual realities: preference for skilled v. traditional birth attendants, improving care for mothers segregated from improving care for newborns, and a growing number of clinic v. home births. Stephen Hudgins has argued:

> *"….both the SBA [skilled birth attendant] and Postnatal Home Visit strategies have focused mainly on contact, either with a health worker of a certain occupational category at the time of delivery or with a community health worker during a postnatal home visit. In both cases, we have prescriptive strategies that all are enjoined to adopt, focusing on how services are provided (that is, that there be a contact of a certain kind). This is quite different from providing guidance on what specific technical content should be delivered."*[3]

Hudgins argues that the assumed training level of attendants (traditional v. skilled birth attendant) has diverted global efforts from a more important consideration: a prescriptive emphasis on the "what" of care, specific care standards, emphasizing new essential birthing practices that can include CHX application. He describes a historical context where newborn care advancements have been segregated from changes in standards of care for mothers at birth. Hudgins suggests the mother/newborn care advancement separation "defies biology" since mothers and in utero babies are inseparable before birth and this close companionship continues as newborns are born and mothers care for them and themselves. Chlorhexidine, launched as a lifesaving commodity, enters into this global context of mother care segregated from newborn care with an emphasis on the type of caregiver v. the specifics of essential newborn and mother care. This segregation is demonstrated at the health system level where differing agencies have responsibilities for newborns v. mothers. For example, in Bangladesh the DGHS and DGSP share responsibility for the launch of CHX. Each department has differing leadership, program approaches and distribution systems that are described in the report.

Many countries, including Bangladesh, report significant increase in clinic births over the past decade. The 2014 Bangladesh Demographic and Health Survey reports:

> *Although still low, the proportion of births delivered at health facilities has been increasing rapidly from 12% in 2004 to 17% in 2007, 29% in 2011, and to the current level of 37%.*

[3] Hudgins, S. "Achieving better maternal and newborn outcomes: coherent strategy and pragmatic, tailored implementation" Global Health: Science and Practice, August 1, 2013, vol. 1, #2, p. 149

[4] CHXUCC introductions were underway in Bangladesh, DRC, Ethiopia, Liberia, Kenya, Madagascar,Malawi, Mozambique, Nepal, Nigeria, and Pakistan at the time of this writing although additional countries are anticipated to introduce CHX.

> *Bangladesh has been making progress in reducing the gap between the poorest and the richest women in the use of facilities for delivery. In the 2014 BDHS, 15 percent of births in the past three years to women in the lowest wealth quintile were delivered in a health facility compared with 70 percent of births in the highest wealth quintile. This translates to a ratio of about 1 to 5. In the effort to achieve equity in delivery in a health facility, the HPNSDP sets a ratio of less than 1 to 4 between women in the lowest and the highest quintiles (MOHFW, 2011). The corresponding ratios in the 2007 BDHS and 2011 BDHS among births in the three years before the survey are 1 to 8 and 1 to 6, respectively.*[5]

Yet in spite of this progress, greater than 50% of births occur at home. Therefore CHX is launched in a context that demands proper use techniques be communicated to mothers through traditional and skilled birth attendants who are organized into many non-governmental and government-sponsored outreach programs. Governments, including Bangladesh, have been reluctant to invest in the training of traditional birth attendants as they emphasize more clinic births.[6] Yet the adoption of CHX must engage all types of attendants to accomplish the goal of all 3.2 million annual births in Bangladesh receiving chlorhexidine application in the first 24 hours after birth in the home or clinic. A pragmatic assessment suggests that traditional birth attendants are an important actor in the supply chain who must understand and adopt this practice. It seems shortsighted to suggest the continuing effort to increase clinic births is an argument against greater investment in traditional birth attendants relating to CHX. The "perfect"—all births occur in a high-skill, controlled clinic environment—becomes the enemy of the "good"—CHX is adopted by all actors, at home or in clinic, as one part of essential newborn care. Given the poverty level and geographical challenges in Bangladesh, it appears most realistic to assume there will be, for the foreseeable future, a meaningful fraction of home births.

The events that led to the Bangladesh launch of chlorhexidine in July 2015 are noteworthy. Dry cord care has been the standard of newborn care for many years. It has taken a decade of clinical trial activity and close consultation with physicians, ministry officials and the complex network of NGOs involved with child and maternal health to arrive at the CHX launch. A Bangladesh trial[7] compared dry cord care with single dose chlorhexidine on the day of birth and a seven-day chlorhexidine application. Single chlorhexidine application reduced newborn deaths by 20%, and moderately reduced severe cord infection ("omphalitis"), and cord bacterial colonization. Seven-day chlorhexidine application reduced severe cord infection by 65% and reduced bacterial colonization; but neonatal mortality was only 6% lower in this group than among controls (not statistically significant). The investigators concluded that the relative lack of mortality effect in the 7-day chlorhexidine application group had occurred as a result of chance and further trials are needed to establish the best frequency of chlorhexidine application. A non-inferiority trial in Nepal[8] compared solution with gel and found the outcomes of both formulations were similar although gel "reduced bacterial colonization to a greater degree". The study findings also demonstrated no significant differences in compliance between the two formulations although gel was preferred. Global funders have supported these trials, and Bangladesh becomes the "use case" for single-application solution in a low-resource, high-population country context. It is a tribute to the medical community, ministry of health, and local and global non-governmental organizations that Bangladesh has reached this portentous launch moment. And global advocates for CHX express hope that the market preparation steps leading to CHX launch (e.g. identifying local advocates, understanding current birthing practices, identifying local resources, conducting local clinical trials) can be achieved more quickly in future launches. While acknowledging that each country has its own requirements for evidence and local adaptation, the avoidable deaths due to neonatal infection will continue until new essential newborn practices, including CHX, are introduced.

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[5] Singh S, Drroch JE, Ashford, LS "Adding It Up: The Need for and Cost of Maternal and Newborn Care – estimates for 2012" May 2013 Guttmacher Institute. P. 25

[6] #AddingItUp Guttmacher Institute, oral communication to authors, September 2015

[7] Shams El Arifeen, Luke C Mullany, Rasheduzzaman Shah, Ishtiaq Mannan, Syed M Rahman, M Radwanur R Talukder, Nazma Begum, Ahmed Al-Kabir, Gary L Darmstadt, Mathuram Santosham, Robert E Black, Abdullah H Baqui "The effect of cord cleansing with chlorhexidine on neonatal mortality in rural Bangladesh: a community-based, cluster-randomised trial" Lancet, 2012; 379: 1022–28

[8] Hodgins, S., K. Thapa, L. Khanal, S. Aryal, K. Bal Suvedi, U. Baidya, and L. Mulling. Chlorhexidine Gel Versus Aqueous for Preventive Use on Umbilical Stump: A Randomized Non-inferiority Trial. Pediatric Infectious Disease Journal. Pp 999-1003. November 2010.

Emerging best practices in countries where CHX has been launched include other countries where a local manufacturer has been used; others where the product was imported . The table below identifies manufacturers, CHX products, prices and expected timing. *(Note the table below is subject to change and may not reflect current in-country manufacturers, current prices or all countries where CHX has been introduced; the table data are from September 2015. The most current information is available at http://www.healthynewbornnetwork.org/resource).*

Country	Formulation	Product	Price	Manufacturer
Bangladesh (2015)	Single-Day Liquid, 10 mL	Hexicord	$0.39	ACI Limited
Ethiopia	Multi-Day Gel, 20g	Misrach		Addis Pharmaceutical Factory
Kenya	Multi-Day TBD			TBD
Malawi	Single-Day Gel*			Imported*
Mozambique	Multi-Day Gel**			Imported*
Pakistan	Multi-Day Gel			Mediserch Pharma ZAFA Pharmaceutical
Liberia	Multi-Day Gel*			Imported*
DR Congo	Multi-Day Liquid & Gel*			Imported*
Madagascar (2013)	Single-Day Gel*			Imported (Lomus, UNICEF)*
Nepal (2011)	Single-Day Gel, 3g	Kawach	$0.37	Lomus Pharmaceuticals
Nigeria (2013)	Multi-Day Gel, 25g†	Chlorxy-G	$0.58	Drugfield Pharmaceuticals Tuvil Pharmaceutical Industries

* Initially imported single-day liquid (10 mL) from UNICEF supply division catalog ($0.36/unit).
** Mozambique received CWG donation of Drugfield multi-day gel, but will likely import from UNICEF supply division catalog in future.
† Nigeria focused only on single-day use during pilot, but will switch to multi-day use for national scale-up.

ACI, a pharmaceutical manufacturer in Bangladesh, began production of CHX for the local market in spring 2015. By entering the market, ACI is creating a supply chain. From a supply chain perspective, ACI is sourcing and procuring active pharmaceutical ingredients, manufacturing chemicals and reagents, and packaging and distributing to various outlets. Yet the full scope of forces that will influence demand for CHX, all the processes and actors beyond distribution, may not be fully revealed in a simple supply chain analysis. Procurement and sourcing activities, before production, take the manufacturer outside of the local domestic market into global dynamics. A broader analytical approach, "value chain analysis" was applied to the introduction of CHXUCC in Bangladesh in spring/summer 2015. A team of students, faculty and staff from Duke University, supported through the Bass Connections program at Duke University, applied value chain analysis to the CHX launch. The team of students and faculty from a variety of disciplines (nursing, business, biomedical engineering, global health) visited Dhaka in March and May 2015. They interviewed more than 40 local implementing partners during those visits, creating primary source material. In preparation for the trips, several months of analysis went into a review of secondary sources regarding CHX and its implementation in other markets. Students also received training in the value chain analysis methodology by a researcher at the Duke Center on Globalization, Governance, and Competitiveness. The faculty engagement in the project was supported through USAID's Health Education Solutions Network (HESN). Duke University is a member of the HESN.

VALUE CHAIN ANALYSIS (VCA)

VCA describes the full range of activities that bring CHX from development to production, production to distribution, distribution to adoption. VCA examines the labor, policy, capabilities inputs, technologies, standards, regulations, products, processes and markets that go into the life cycle of various goods and services, thus providing a holistic view of industries both from the top down and the bottom up.[9] In the case of CHXUCC, international collaborators require a manufacturer who will provide product at low cost, yet high quality in an uninterrupted supply. The demand for CHX is created by the behavior and policies of governments, private clinics, dispensary shops, care providers (informal and formal) and mothers. Determining how demand is created and how supply will meet that demand requires a thorough understanding of how the CHXUCC market works.

Value chain analysis is a useful methodology to trace the shifting patterns of production and demand creation, link geographically dispersed activities and actors of a single initiative, and determine the roles they play. The value chain framework creates an understanding of the policies, behavior and public and private actors' interaction and organization; in essence the structure and dynamics of the various actors involved in the CHX introduction in Bangladesh.

The relationship among the various actors in the CHX Bangladesh value chain is referred to as the "governance structure" of the chain. Value chains are generally dynamic as firms enter into, or move between, different stages of the chain in order to gain higher returns on their participation. Currently only one manufacturer of the commodity product, CHX, is in Bangladesh to apply the governance concept. ACI manufactures other strengths of chlorhexidine for different uses (e.g. hand cleaning) and has the capability to manufacture other formulations for CHXUCC (e.g. digluconate 7.1% gel) and presentations (e.g. 3g, 10g tubes).

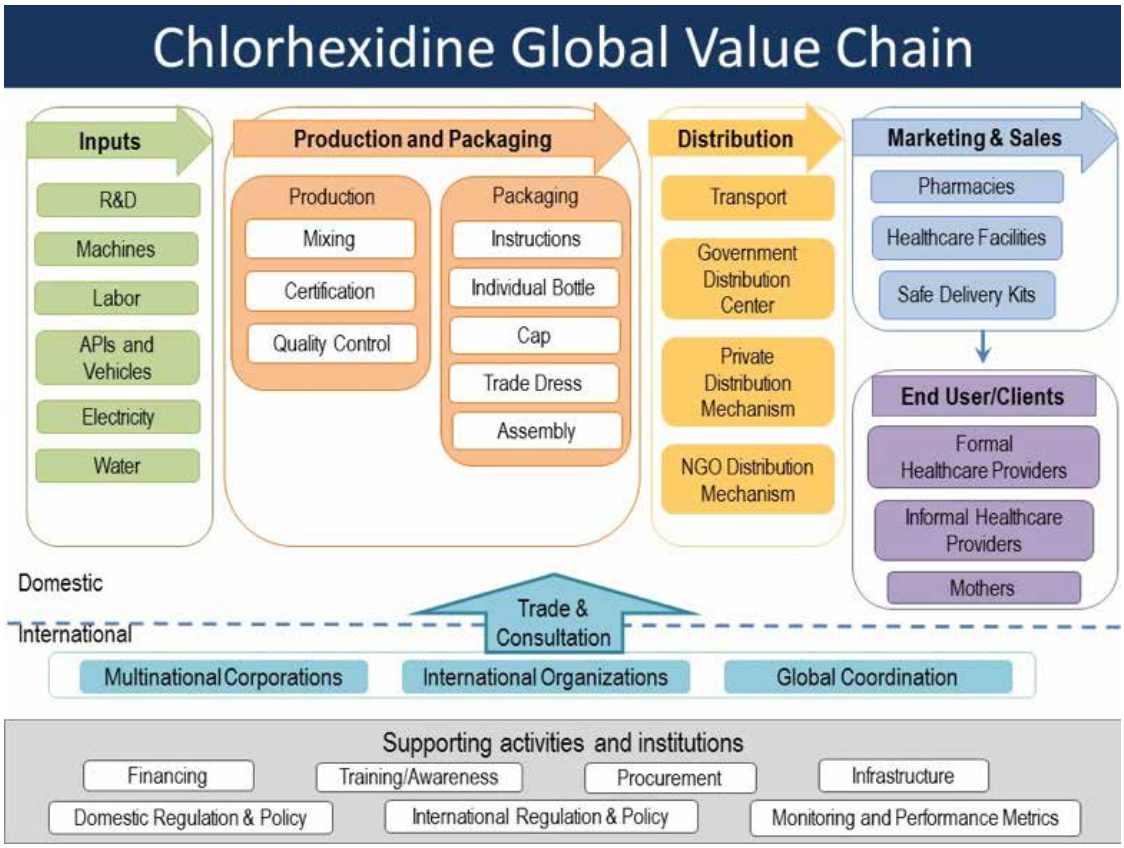
Strategies, such as those undertaken by ACI, seek to enhance the competitiveness of firms and increase revenue, a process known as "upgrading." Although originally conceptualized as economic activity geared toward increased efficiencies and profit, upgrading has increasingly incorporated social and environmental upgrading into their analysis. Building on the International Labor Organization's recent framework, social upgrading looks at both worker well-being and enabling rights.[10] Environmental upgrading looks into the sustainability of development programs and the ability of economic development to occur without environmental degradation.[11] Finally, a growing body of research is using VCA to look at new development challenges including food security[12], inequality and health[13]. This report provides another application of VCA to studies of global health by highlighting the various roles actors play, the governance structures that guide activities and for crucial leverage points, which influence the success of health initiatives like CHXUCC.

[9] Gereffi, G. and K. Fernandez-Stark. "Global Value Chain Analysis: A Preimer." Duke Center on Globalization, Governance, and Competitiveness. May 2011.
[10] Barrientos, S.; G. Gereffi; and A. Rossi. "Economic and Social Upgrading in Global Production Networks: Developing a Framework for Analysis. Capturing the Gains Working Paper 2010/03. July 2010.
[11] Khattak, A.; C. Stringer; M. Benson-Rea; and N.Haworth. "Environmental upgrading of apparel firms in global value chains: Evidence from Sri Lanka." Competition and Change. May 2015.
[12] Ahmed, G.; D. Hamrick; A. Guinn; A. Abdulsamad; G. Gereffi. "Wheat value chains and food security in the Middle East and North Africa region." Duke Center on Globalization, Governance, and Competitiveness. August 2013.
[13] Christian, M. and G. Gereffi. "The marketing and distribution of fast food." Pediatric Obesity. Pp 439-450. January 2010.

THE CHLORHEXIDINE VALUE CHAIN IN BANGLADESH

The chlorhexidine value chain (see figure 3) is marked by six key segments: Inputs; Production and Packaging; Trade and Consultation; Distribution; Marketing and Sales; and End User/ Clients. It also has several supporting institutions and activities important for its success. In this section each of the components is described to provide an overview of the CHX Bangladesh context.

Figure 3: The Chlorhexidine Value Chain



Inputs: Production of CHX requires inputs including machines, water, electricity, labor, active pharmaceutical ingredients (APIs) and vehicles. APIs are imported from Indian firms and are sourced primarily from one supplier[14]. Additionally, a phase of research and design is required to assure the manufacturing process results in a solution that delivers the expected pharmacokinetics and pharmacodynamics of the product as used in the clinical trials (which established the evidence in support of CHXUCC). Informing the choice of solution formulation for Bangladesh was a Nepalese non-inferiority trial which compared chlorhexidine 7.1% digluconate solution with gel and as discussed previously showed no meaningful differences.

Production and Packaging: In the second stage, APIs are combined with vehicles and water to reach the desired solution and after quality control checks and certification, packaged into individual bottles and prepared for distribution. At the processing stage, it is beneficial for firms to have Good Manufacturing Practices (GMP) certification. The main producer in Bangladesh for CHXUCC met GMP certification standards in late May 2015. In Bangladesh, stability studies demonstrated the solution could be packaged in a dropper typically used for ophthalmic solutions with 24 months of "dating" (expiry occurs 24 months after packaging, which is printed on each manufactured presentation). The risk of improper use due to mis-applying CHX to the eye was considered. The stakeholders agreed to bottle CHXUCC using purple caps to distinguish it from other products in a 10 ml dropper with Bangla language use information and pictures showing appropriate use on the packaging. While this approach attempts to address the risk of AEs, the cost of the dropper packaging is discussed below (see Leverage Point #2: Production and Packaging).

Trade and Consultation: As an addition or substitution to local production, countries may procure supplies from UNICEF, which has distributed CHX products produced by Galentic (Note: tenders are issued from time to time and Galentic may or may not be the manufacturer of choice in future), or from emerging regional pharmaceutical companies, such as Nepal's Lomus. The suppliers of CHX may also increase as a multi-national corporation GlaxoSmith-Kline submitted a regulatory application for CHX gel to the EMA under Article 58 and was granted an accelerated assessment in recognition of the public health need addressed by CHX gel.[15] Best practices have emerged where in many CHX launch countries local manufacturers provide product where there is local manufacturing capability, government regulatory capability exists and market conditions support this approach. Where those conditions do not exist importing product is required. In addition to supplies, a host of international organizations offer a wide range of support from financial funding, quality certifications, and consultation and technical assistance. These organizations work in collaboration with other governments, such as USAID; multilateral organizations, such as UNICEF, and international NGOS such as PATH.

Distribution: After packaging, CHX reaches retailers and marketers through three separate channels: private, public and NGO distributors. Within Bangladesh, each of these channels is well-developed, and CHX will follow the same distribution flows of other medical commodities. The private channel for CHXUCC distribution will utilize ACI's existing infrastructure including 80 motorized vehicles and local transport companies that have existing relationships with ACI. It takes an average of four hours to distribute from ACI's central warehouse locations to any part of the nation. The NGO distribution channel is similarly well-established and reaches across Bangladesh. Officials in BRAC, the largest global NGO founded and headquartered in

[14] Field interviews. May 2015.
[15] Personal communication to the authors from Kevin LaWall, Global Marketing Director, Maternal & Neonatal Health, GlaxoSmithKline.

Dhaka, estimate that they can have CHX distributed throughout the country; however, due to concerns about pricing and supply the NGO is not currently distributing the product. The Social Marketing Company (SMC), a USAID-funded NGO, also has plans for distributing CHX in its pharmacies and kiosks. Public distribution will occur through both the Directorate General for Family Planning (DGFP) and the Directorate General for Health Services (DGHS). DGHS launched its CHXUCC program in 2015, and DGFP plans to distribute CHX starting in 2016. Detailed below, the complex distribution system in which CHX is embedded will pose a significant leverage point for Bangladesh.

Marketing: Marketing, or methods of procurement for delivery to users, is primarily done through three distinct mechanisms: pharmacies, healthcare facilities and safe delivery kits. Distribution channels use all three marketers to various degrees to reach end users. In Bangladesh, ACI uses pharmacies across the country to directly sell products, including CHXUCC to customers. Additionally, SMC runs a special set of pharmacies, known as Blue Star pharmacies. Blue Star pharmacies differ from traditional pharmacies in their focus on essential and antenatal care services, including HIV testing. Currently, there are 6,000 Blue Star pharmacies in Bangladesh. Additionally, community clinics throughout the country serve community clinics throughout the country sell CHX to medical professionals or expected mothers. These clinics are run by the government, private sector and NGOs. Some clinics are mobile, traveling to remote rural villages. While clinics are numerous, the majority of births are still conducted at home. Safe delivery kits are used in home deliveries but the percentage of home births with and without SDK's was not available.[16] Kits consist of several inexpensive, yet vital sanitary items for birth and are distributed to mothers and traditional birth attendants. Kits are currently used in 14% of home births[17] and are accessible from several NGOs. Despite their utility, SDKs are not typically sold in pharmacies due to their low profit margin, with the exception being Blue Star pharmacies. The kits represent an attractive option for the delivery of CHXUCC given the timing of CHX application and the ability to promote use to mothers who are giving birth at home. However, the addition of CHX to the kit introduces new regulatory requirements (e.g. registration with the drug authority) and may increase the price for poor, price-sensitive mothers.

End Users/Clients: CHX adoption ultimately occurs at this stage where it is used by mothers or given to babies at birth by formal and informal healthcare workers. In the case of Bangladesh, the majority of births occur at home and are overseen by informal healthcare workers. In this climate, it is crucial that CHXUCC promotions and proper training reach both the informal healthcare workers and mothers to ensure that proper application occurs at the optimal time.

Supporting Activities and Institutions: Finally, the CHXUCC chain has a vast array of supporting activities that are essential for success. Financing must be secured from domestic and international sources. In the case of Bangladesh, both international partners, such as USAID, and the government of Bangladesh are investing in CHXUCC. Infrastructure from other commodities is being leveraged for the program. The regulatory and policy environment, both national and International, comes from intense study and planning. In the case of Bangladesh, domestic policy differs from suggestions set by the WHO

[16] Kits are interchangeably referred to as safe birthing kits, safe birth kits or safe delivery kits. We use "safe delivery kits" (SDK) in the report.
[17] National Institute of Population Research and Training (NIPORT), Mitra and Associates, and ICF International. 2013. *Bangladesh Demographic and Health Survey 2011*. Dhaka, Bangladesh and Calverton, Maryland, USA: NIPORT, Mitra and Associates, and ICF International.

in terms of using a single-application gel in the country. This is based on the initial research into the best approach for the country. As the country proceeds with the CHXUCC launch, it is crucial that the correct training and awareness as well as a system of monitoring and evaluation are implemented to mitigate the chances of improper use as well as to help ensure a stable supply at all stages of the value chain.

Actors in the CHXUCC Bangladesh value chain have a variety of motivations and influences. Governance is among them. One can argue that private actors are primarily driven by profit or market opportunities associated with CHXUCC adoption. But non-market factors such as reputation and interactions with government health decision-makers are also at play. For NGOs and government health ministry actors, we draw upon a political economy (PE) model to understand actions and motivations. It is beyond the scope of this paper to perform a complete political economic analysis of the adoption of CHX. But we draw on the legacy of PE to suggest there is a calculus for each actor in the CHX value chain that follows from the economic condition of the country, the interplay among various civil institutions and the political self-interest of governmental actors that will determine their CHX-related actions. We assume that saving Bangladeshi children's lives at birth by avoiding infection and sepsis through the use of CHX, while a worthy goal, competes with other high valence health interventions for the investment of attention, time and effort. It is not that actors wish to deny neonates CHX, but they give their time and attention to other goals based on a political calculus that is often unconscious and unrecognized. Non-profit actors will consider their own political fortunes as they determine how much effort and how sustained that effort will be over time in support of CHXUCC in Bangladesh. We make this PE claim not to denigrate health officials anywhere and certainly not in Bangladesh (our interactions were with dedicated, hardworking and highly intelligent actors fixed on the successful adoption of CHX), but simply to acknowledge that health interventions everywhere are political in nature and they compete with other worthy campaigns for resources including political capital. While we cannot conduct a complete PE on CHXUCC in Bangladesh, we can offer below an analysis for selected leverage points.

CHLORHEXIDINE APPLICATION ADDED TO "ESSENTIAL NEWBORN CARE"

CHX use, as part of the recommended standard of care for newborns, can be inferred (in future demographic health surveys it can be separately evaluated) using the Bangladesh Demographic and Health Survey annual assessment of key indicators. Chlorhexidine has been added as a component of the "essential newborn care" guidelines, which include a clean delivery kit, clean or "boiled" blade, dry cord or chlorhexidine application, newborn drying/ toweling within five minutes, delayed bathing (72 hours) and breastfeeding. The 2014 report of key indicators demonstrates that adherence to the essential newborn care elements is low, less than 15%, across many factors: mother's age; income and educational level; infant birth order; birth settings; and geographical regions.[18]

Table 20 Essential newborn care

Percentage of non-institutional most recent live births in the three years preceding the survey by essential newborn care practice, according to background characteristics, Bangladesh 2014

Background characteristic	Used safe delivery kit or boiled blade during delivery	Nothing applied to the umbilical cord or applied chloroxidine after it was cut and tied	Dried within 0-4 minutes after birth	Delayed bathing (72+ hours after delivery)	Immediate breastfeeding (within 1 hour after birth)	All the essential newborn care practices[1]	Number of non-institutional births
Mother's age at birth							
<20	82.4	46.9	66.1	36.6	59.2	6.3	920
20-34	90.2	49.2	67.5	34.1	56.1	6.1	1,793
35+	90.4	47.5	65.5	22.0	58.0	4.4	123
Birth order							
1	82.7	45.4	67.1	35.5	58.2	5.4	955
2-3	89.8	50.4	66.0	36.6	57.5	6.7	1,352
4-5	91.3	49.1	71.3	28.1	54.0	5.8	388
6+	91.0	48.2	63.1	22.6	55.8	5.8	141
Residence							
Urban	89.6	41.1	68.1	30.0	54.7	5.5	501
Rural	87.3	50.0	66.7	35.3	57.7	6.3	2,335
Division							
Barisal	85.5	30.7	56.2	33.2	56.4	2.6	186
Chittagong	88.3	47.8	65.6	28.2	50.1	3.6	648
Dhaka	86.4	53.2	63.7	33.8	58.1	5.2	941
Khulna	91.5	38.8	71.7	31.1	52.2	6.8	166
Rajshahi	76.2	47.4	74.6	35.9	63.0	6.8	278
Rangpur	93.2	53.3	73.9	50.7	64.3	13.3	292
Sylhet	94.1	47.3	70.3	34.6	60.3	8.6	326
Education							
No education	85.8	51.9	65.0	23.2	58.1	4.2	549
Primary incomplete	84.8	47.5	67.3	29.4	57.6	5.7	570
Primary complete[2]	89.3	48.7	69.4	38.6	55.9	6.1	376
Secondary incomplete	88.0	48.6	66.4	38.8	56.1	6.3	1,100
Secondary complete or higher[3]	94.5	40.9	69.5	44.6	61.0	10.6	241
Wealth index quintile							
Lowest	84.8	53.5	66.5	28.8	62.4	6.1	812
Second	87.6	50.7	65.1	35.1	51.7	6.6	649
Middle	88.0	48.6	62.6	38.9	55.7	5.8	548
Fourth	90.3	46.1	69.1	37.5	56.8	5.5	521
Highest	90.3	33.4	76.3	34.2	58.5	6.7	306
Total	87.7	48.4	67.0	34.4	57.2	6.1	2,836

[1] All essential newborn care includes used clean delivery kit or boiled blade, nothing applied to cord or applied chloroxidine, dried within 5 minutes after birth, delayed bathing 72 hours or over, and immediate breast feeding.
[2] Primary complete is defined as completing grade 5.
[3] Secondary complete is defined as completing grade 10.

[18] 2014 Bangladesh Demographic and Health Survey, National Institute of Population Research and Training, Ministry of Health and Family Welfare, Dhaka, Bangladesh, Mitra and Associates, The DHS Program, ICF International, Rockville, Maryland, USA.

As chlorhexidine use is introduced as part of revised essential newborn care guidelines, and is separately assessed in the health survey audit of mothers, it is forecast that chlorhexidine use will increase with the launch of Hexacord® and the accompanying national guidelines. Generally, chlorhexidine modelers assume that CHX uptake will be higher in hospital and clinic settings v. home births. These same models do not include sensitivities to price (lower income mothers may be more price sensitive) or variation by geographical region.

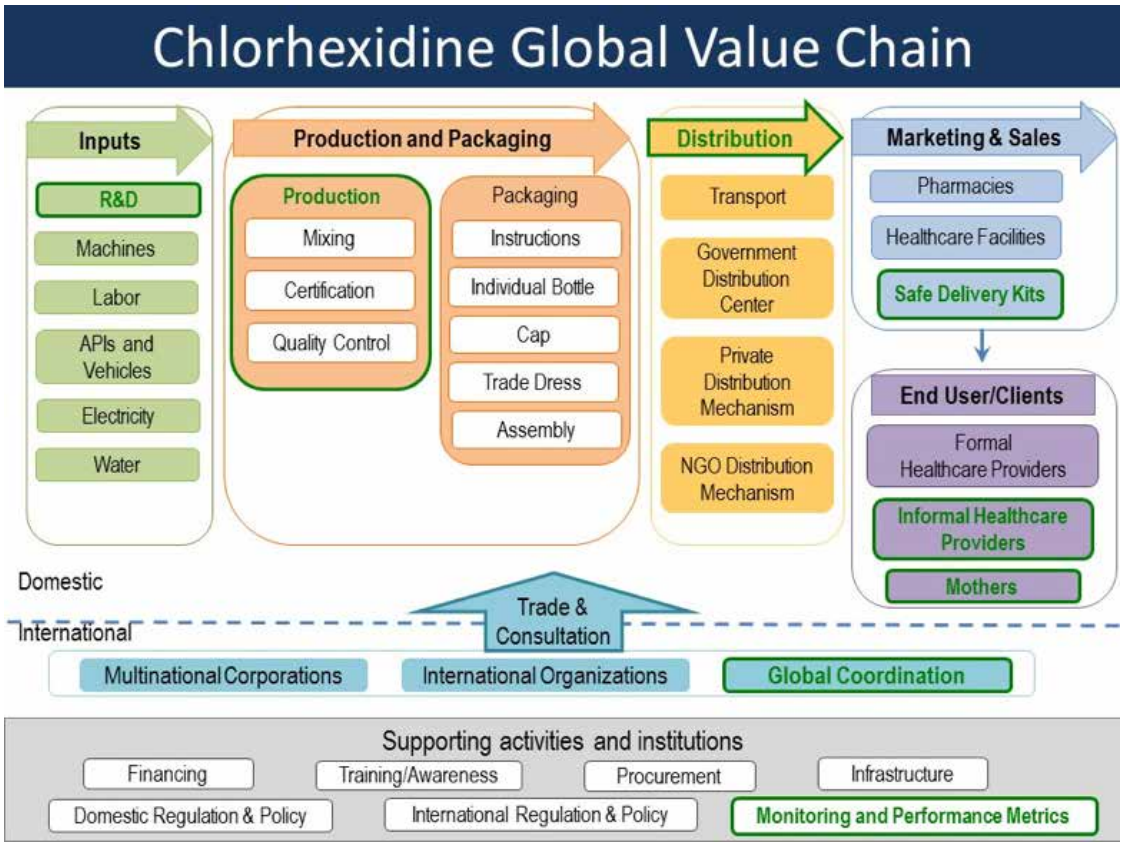
LEVERAGE POINTS

When a value chain is mapped, various junctures, interactions or exchanges (J/I/E) are identified: opportunities for suppliers and recipients in the chain (NOTE: every actor on a VCA map is a supplier or recipient to every other actor) to upgrade, improve efficiencies (for profit-makers this could be improve margins), reduce costs (actual and transactional) or increase volumes.

Leverage points (see figure #4) offer opportunities where J/I/E can be analyzed to determine how they influence the manufacture, movement, demand and consumption of CHX throughout the entire chain. J/I/E can be examined for "bottle necks": stoppages or reductions in movement. Based on our experience in Bangladesh we choose to call these J/I/E "leverage points." We use "leverage" to suggest an opportunity where the market creators, the broad coalition of advocates for the adoption of CHX, can use analysis to anticipate where short term optimization of the J/I/E or leverage point may sub-optimize the sustained viability of the entire value chain. Bottlenecks are but one outcome that should be avoided. Examining leverage points should connote analysis and making informed choices that create the conditions for a sustainable value chain.

Actors in the CHXUCC Bangladesh, who hope to create a sustainable CHX value chain, can examine a leverage point considering interventions that enhance the attractiveness of medium- and long-term sustainability over short-term gains. A value chain that has key junctures that are vulnerable to short-term v. long-term optimization trade-offs can become compromised with low demand, supply gaps or exit of key actors. The analysis below examines each of the selected leverage points and suggests options for discussion and consideration.

Figure 5: Major Leverage Points in the CHX Value Chain (in bold green outline)



Our analysis has revealed several critical leverage points in the Bangladesh CHXUCC value chain. In this section we analyze the following seven points:

1. Research and Development
2. Packaging
3. Regional Supply and Market Expansion
4. Safe Birthing Kits
5. Distribution
6. Global Coordination
7. Monitoring and Performance Metrics

Leverage Point #1: RESEARCH AND DEVELOPMENT

Pharmaceutical products with adequate margins and sales often receive additional post-marketing investments in research and development. These investments may be responses to competition, new scientific and technologic breakthroughs suggesting new indications or uses of the product, opportunities to expand into new markets, responses to safety concerns for the existing product. As described below, Hexacord®, ACI brand of CHX for umbilical cord care (or other locally manufactured CHX products) may not have adequate sales or margins to justify post-marketing investments. Despite the lack of justification to a local manufacturer, there are considerations that suggest the product—specifically the product packaging—should receive additional investment.

We note several key facts regarding chlorhexidine for umbilical cord care:

• There are two formulations in use for 7.1% chlorhexidine digluconate for umbilical cord care: solution and gel. Single dose solution within the first 24 hours after birth[19] is the national guideline for Bangladesh. There is clinical trial evidence which has informed the development of national guidelines for multi-day applications beginning within 24 hours after birth. One disadvantage of topical antiseptics is that its application re-hydrates the cord and can delay average time to cord detachment.[20] This delay can cause mothers concern or confusion.

• Hexacord® is packaged in a 10ml dropper bottle with purple cap that is obtained from Cadila, an Indian pharmaceutical firm. (NOTE: The purple cap is required by the Bangladesh government to ensure that Hexacord® will not be confused with ophthalmic medications; it also has an irreversible seal with "teeth" to protect against multi-use and counterfeiting). This packaging accounts for ~75% of the cost of goods for the product (see leverage point #2, "Packaging," below).

• In most markets CHXUCC has been introduced as a topical gel with aluminum "squeeze" tube packaging in both 3 gram and 10 gram presentations.

The evidence base for the CHX solution formulation has not compared differing packaging designs although in launch preparation some end users and service providers commented on packaging choices.[21]

[19] The effect of cord cleansing with chlorhexidine on neonatal mortality in rural Bangladesh: a community-based, cluster-randomised trial. Arifeen, Shams El et al. The Lancet , Volume 379 , Issue 9820 , 1022 - 1028

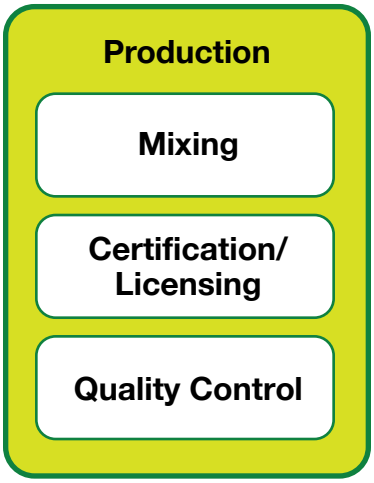
[20] Topical applications of chlorhexidine to the umbilical cord for prevention of omphalitis and neonatal mortality in southern Nepal: a community-based, cluster-randomised trial Mullany, Luke C et al., The Lancet , Volume 367 , Issue 9514 , 910 - 918

[21] Personal communication to the authors from the Chlorhexidine Working Group

Leverage Point #1
CONSIDERATIONS AND DISCUSSION

Can global research and development investments be reduced by acceptance of studies conducted in one jurisdiction by another regulatory authority? Can CWG play a role as global evidence coordinator to ensure cumulative evidence is expanding and focused at high need research questions?

It is costly to invest in clinical trials in each market to prepare for CHX introduction. Continuing harmonization and cross-market acceptance of clinical studies is a work stream of the CWG. As CWG pursues this goal to speed introduction in more local markets and reduce the global investment in CHX clinical trials it can also perform another role: advocating for research designs that extend our knowledge of CHX. For example, global coordinators such as Medicines for Malaria Venture (MMV) play the role of ensuring that the cumulative body of research extends the scientific knowledge of malaria diagnosis and treatment as well as supporting local introductions of safe and effective medicines. CWG can advocate for clinical trial designs and research that generate needed evidence on formulations and packaging as well as increasing the acceptance of clinical evidence across national jurisdictional boundaries. See discussions below in Packaging, Regional Supply and Market Expansion, and Global Coordination for further discussion.



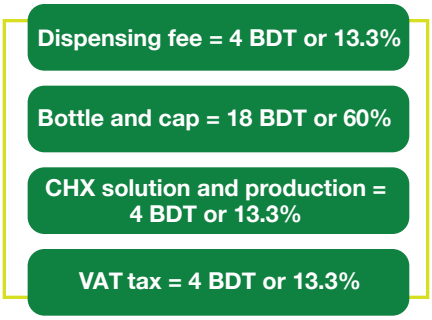
Leverage Point #2:
SOLUTION PACKAGING

Galentic makes CHX solution that was involved in a 2015 incident in Nigeria where CHX was improperly used. The solution packaging (coupled with the lack of package insert or packaging written in local language) was confused as an ophthalmic solution for eye care. This incident demonstrated that inappropriate use can pose a blinding risk for newborns. (NOTE: The factors which led to the improper use should be reviewed carefully by the reader and additional evidence and mitigation strategies are being developed to ensure safety.) The solution packaging also constitutes a significant proportion of cost of goods. The leverage point discussion considers the opportunity to redesign solution packaging.

Several key facts regarding ACI's production of Hexacord® are noted at the leverage point.

- ACI and Galentic are currently the only manufacturers of 7.1% chlorhexidine digluconate solution.

- The unit price for Hexacord® is ~ 30 BDT (Bangladeshi Taka currency), 40 U.S. cents.



- 10ml dropper bottle with purple cap is also obtained from Cadila. (NOTE: The purple cap is required by government to ensure that Hexacord® will not be confused with eye drops; it also has an irreversible seal with "teeth" to protect against multi-use and counterfeiting. (See "Research and Design" Leverage point #1 discussion above.)

- Dropper packaging safety risk: *"There are five known cases of irreversible blindness associated with the use of these drops [CHX produced by Galentic] already, three reported in Yobe State and two in Adamawa State. The three children in Yobe are 3 weeks, 4 weeks and two years old."*[22]

Leverage Point #2
CONSIDERATIONS AND DISCUSSION

Do packaging costs and recent adverse events in Nigeria suggest solution package redesign? Who should bear the cost of redesign?

The recent safety issue in Nigeria raises concerns regarding the dropper packaging and potential confusion as an eye preparation. While Bangladesh has changed the color of the dropper top (purple) and has product use and safety information that is both pictorial and in Bangla, the safety risk remains. Coupling this with the fact that the dropper packaging represents a high proportion of cost of goods suggests package redesign for solution formulation should be made a priority. Given the low margins and low volumes it may be unrealistic to expect ACI or any other local solution manufacturer to invest in such a package redesign. Global advocates and underwriters for lifesaving commodities, and specifically for chlorhexidine for umbilical cord care, should consider whether full or partial subsidies could be provided to resource a package redesign. The results of the redesign work would become a global public good by making the technical knowledge available to existing and future manufacturers.

[22] http://nigeriahealthwatch.com/what-you-need-to-know-about-the-yobe-eye-drops-story/ The reader should carefully consider information at the HNN website that fully reveal the circumstances of this incident which include an unapproved product and formulation entering the country, inadequate warnings in a non-local language (English) on the packaging and other circumstances. There is no evidence from the "Yobe eye drops" incident to suggest CHX is unsafe when appropriately used following the guidelines for essential new born care in Nigeria.

The evidence base for the CHX solution formulation has not compared differing packaging designs. While costly, research comparing package designs could examine a variety of factors beyond efficacy and safety including ease of use, mother/caregiver preferences and costs. Upgrading or revising the existing solution packaging appears to be an immediate need since the packaging is an all-white dropper bottle/cap, with English and French language use and safety instructions on the bottle. The incidences of improper use in Nigeria will lead to safety information that can have broader application to other markets where CHX solution is used.

API solution and bottle/cap represent ~75% of the total cost of Hexacord® and are imported from India. Does this create an opportunity for package redesign?

A rational manufacturer of a low margin commodity product will look for savings, not only from increased volumes (reducing variable costs) but cost reductions in the product components. The bottle/cap in Hexacord® is an obvious target with its high proportion of total product costs. The current bottle/cap configuration has many advantages: accurate dropper, ease of use with wet hands, protections against multi-use/counterfeiting and safety against misuse (confused as eye drops). But alternative packaging for a solution is available. Sachets or a modified dropper that is less costly should be considered. Informal reports have suggested that 30 BHD may be the ceiling for price sensitive mothers who are using Hexacord® for home births.[23] When discussions were conducted regarding the addition of CHX to safe delivery kits, the combined unit price was flagged as a barrier; SDK + CHX may be too high. Reducing the unit cost of CHX is of interest to the manufacturer and to advocates for CHX where the savings can be passed on to purchasers.

ACI has suggested that sourcing bottle/cap components domestically is among its strategic goals once it can better estimate the size of the Hexacord® market in Bangladesh. The low margins of the product likely will not justify such an investment by ACI to explore alternative packaging designs. It is advantageous for the entire value chain to explore alternative packaging designs. We suggest the international collaborators consider commissioning such design work; perhaps CHX packaging redesign can be linked to a “grand challenge” context.

[23] Personal communication to the authors during May 2015 site visit to Dhaka, Bangladesh.

Leverage Point #3: REGIONAL SUPPLY AND MARKET EXPANSION

In Bangladesh the local producer is Advanced Chemical Industries (ACI), which is manufacturing Hexicord® for the local market. As noted above, ACI has significantly greater capacity (full manufacturing capacity five times greater than 3.2 million annual Bangladesh births) and has aspirations to enter the global CHXUCC market. As a key step in the supply of CHX and as the only local supplier, it represents a potential bottle- neck (supply interruption). This circumstance is also true in Nepal where local manufacturer Lomus Pharmaceuticals Pvt. Ltd. makes a gel formulation of CHX under the branded name Kawach®. Chlorxy-G® Gel is available from Drugfield Pharmaceuticals Ltd. for the Nigeria market. Drugfield is seeking approvals to export to Niger and Ghana. Drugfield is not exporting outside Nigeria but have received approval to export to Ghana and Niger and is providing product for clinical and pilot studies in other countries. CHX is also available from Galentic, a UNICEF-approved generic supplier of the solution. Lomus and ACI branded products, and UNICEF generic, are manufactured in three adjacent countries (India, Nepal and Bangladesh) where producers have significant excess capacity. The safety issues created by the Yobe eye drops incident, packaging and the cost of goods relating to the branded products manufactured in Nepal and Bangladesh suggest a leverage point opportunity. What opportunities are there for new approaches to regional supply, package redesign and global branding that are not being pursued in the current local market manufacturing approaches?

We note several key facts regarding CHX branded, regional production.

- CHX is available in single-dose 7.1% chlorhexidine digluconate solution (Hexacord®) and as multi-dose 7.1% chlorhexidine digluconate gel manufactured in Nepal. Lomus has a proprietary brand name Kawach®; ACI uses the proprietary brand name Hexacord®; Drugfield uses Chloryx-G®[24] [25]. Generic CHX solution is manufactured by Galentic PvT in India and available for purchase through UNICEF; "Universal Corporation, LTD (Kenya) also manufactures CHX." (NOTE: New manufacturers of CHX may appear as additional CHXUCC markets are opened. An up-to-date list of manufacturers and the countries where their product is in use is available at CWG's Healthy Newborn Network site http://www.healthynewbornnetwork.org.)
- ACI, Lomus and Drugfield have met WHO pre-qualification standards to manufacture supply levels to meet the estimated demand for a combined Nepal, Pakistan, Bangladesh regional market.[25]
- Drugfield, Lomus, ACI and Galentic source the Active Pharmaceutical Ingredient (chlorhexidine salt) from Cadila Pharmaceuticals, an Indian manufacturer.
- 10ml dropper bottle with purple cap that is obtained from an Indian manufacturer.[26]

[24] CHX has not been introduced in India although a pilot trial is in discussion for the Bihar state.
[25] NOTE: The purple cap is required by government to reduce the risk that Hexicord® will be confused with eye drops; cap seal with "teeth" to protect against multi-use and counterfeiting.)
[26] NOTE: Personal communication to authors has suggested that Drugfield has aspirations to be the CHX supplier for Anglophone and Francophone West Africa.

Leverage Point #3
CONSIDERATIONS AND DISCUSSION

How will ACI exercise its single source power in the Bangladesh CHX market? Are the CHX implementing partners vulnerable to an ACI market exit if the CHX introduction does not result in sufficient demand?

The reputational risks for ACI to exit the CHX market in the near term are considerable. But over time the commitment to Hexacord® could wane if demand is too low. ACI has committed resources to the product that, if they lie idle, are vulnerable to re-allocation by the firm. ACI's exit or reduction in supply could be justified on the grounds it was prepared to supply the market, but the collective efforts of the CHX initiative were insufficient to justify continuing commitment of ACI resources.

Will ACI's commitment to Hexacord® as a corporate social responsibility be realized as uninterrupted supply over multiple years? What if demand is far less than expectations?

Experience suggests that over time corporate social responsibility commitments are not as durable as contracts with negotiated terms. An "advance market commitment" (AMC) is an attractive instrument for both the CHX implementing partners and ACI. The commitment guarantees ACI a contracted number of units at a negotiated price. An AMC could include penalty clauses for shortages or supply gaps, but that seems to be a smaller risk given the ACI Hexacord® supply capacity.

Can/will ACI make other formulations of CHX in addition to solution to serve other markets (gel is the approved formulation in Nepal, Pakistan and Nigeria)? What support, if any, should international CHX collaborators provide to CHX manufacturers who aspire to expanded CHXUCC markets?

API and Lomus have excess capacity to produce their brands of CHX. Galentic may also have excess capacity since CHX gel and solution have low capital investment and operating costs to manufacture the products. Assuming the three manufacturers will continue to make the necessary investments to meet export quality standards, the risk for any to exit the market relates to low local market demand and lack of access to other CHX markets.

A regional cluster of CHXUCC introductions has occurred in Nepal, Pakistan and Bangladesh. Bangladesh has a significant pharmaceutical manufacturing sector and its neighbor, India, has the world's largest export generic manufacturing capability (China has a larger generic manufacturing capability but it is primarily used for domestic supply). Experience with value chain analysis suggests that local manufacturers will upgrade and seek greater volumes for low-capital, low-margin product. Increased volumes are an opportunity for the manufacturer. With increased volumes, at scale variable manufacturing costs could be reduced, and other costs reductions associated with packaging, could lower the CHX cost to purchasers: government, NGO's and mothers. It remains to be seen the degree to which governments in these low-income countries have challenging budgets for health care programs including CHX.

To the degree that upgrading and increasing volumes reduces marginal costs, which can be accomplished through regional approaches to supply, these are worthy goals for a commodity like CHX.

A logical extension of the market-making activities of international CHX collaborators would be to evaluate the feasibility of a regional market to procure and tender for CHX. NOTE: The Chlorhexidine Working Group has a "market sizing tool" at its website which can be useful to assess feasibility. To pursue such a strategy requires 1) an assessment of the regional market potential including any negative impact on local demand if market is supplied by a non-local manufacturer, 2) a careful review of any import/export tariffs and possible changes to those policies, 3) an assessment of the tendering capabilities of local entities (governments, FP and NFP procurers) participating in the regional tendering, and 4) a proposed set of actions and time-line to arrive at a point where regional tendering could be accomplished without interruption of local CHX supply. A global coordinator may also be required, which is described below (Leverage Point #6, "Global Coordinator"). One approach would be to assess #1-#3 in a technical report and estimate CHX cost reductions realized in a regional tendering approach. A second technical report, assuming favorable responses to the first report, would describe the timing and steps (#4) to realize the regional tendering opportunity.

Can aggregating demand across local markets create an attractive market for high-volume manufacturers? Does the opportunity to reduce costs by having one manufacturer tender for volumes created by aggregating multiple markets outweigh the advantages of local manufacturing?

Kawach®, Hexicord®, Chlorxy-G® Gel, Universal Corporation, LTD (Kenya) and Galentic's generic presentations of CHX are available now. Additional local manufacturers will introduce CHX products. Yet many of the local manufacturers will aspire to larger export markets as CHX is a low-margin product. Registration in individual countries is eased when a local manufacturer is involved. This may be one of the considerations that led to the WHO local manufacturing recommendation.

Since the publication of Segre et al's study, GlaxoSmithKline is pursuing Article 58 registration of chlorhexidine 7.1% digluconate gel for umbilical cord care. GSK will brand its presentation of CHX gel upon registration, resulting in as many as five different offerings (by amount of gel) of the CHX product.[27] Although GSK is seeking the EMEA registration, individual country approvals are also required.

CWG works with select countries to establish production capabilities. CWG should continue to assess the viability of local production with the potential advantages (both near and longer term) of a regional or global tender to supply CHX to multiple countries by a single manufacturer. That assessment must include the local registration requirements for a non-local manufacturer, the capability of local markets to participate in an international tendering process as well as the country capability to import product while ensuring the quality and security of imported drug products.

[27] Segre J., Coffey P., Metzler M., Villadiego A, Brandes N., Hodgins S., Mullany L, Morris S. ""Case Study: Chlorhexidine for Umbilical Cord Care" February 2012, p. 6

Leverage Point #4: BUNDLING CHX WITH SAFE DELIVERY KITS (SDK)

In 2013 Michael Foley, national director, Save the Children Bangladesh, cautioned, "Essential Newborn Care (ENC)… simple practices that can keep newborns healthy, including drying and wrapping, delayed bathing, cutting the cord with a sterile blade, immediate breast feeding (within one hour) and exclusive breast feeding for six months" is needed since 71% of births occur at home and Bangladesh has a high rate of newborn mortality due to infection, asphyxia and premature birth.[28] The addition of chlorhexidine application to ENC can reduce infections and the resulting newborn deaths. What then, is the most effective means of adding CHX to ENC for the vast majority of births occurring at home while still prioritizing the Directorates of Family Planning (DGFP) and Directorate of Health Services (DGHS) to have more births in a clinical setting with skilled care?

A scaled approach that simultaneously acknowledges the long-term need for increased clinic births attended by skilled providers while also prioritizing the safety and immediate needs of mothers currently delivering at home strikes an important balance. In-country experience demonstrates that increasing clinic births with skilled attendants requires the time needed for substantial structural and human resource capacity building. For example, the MaMoni Integrated Safe Motherhood, Newborn Care and Family Planning Project (2009-2014) demonstrated gains in delivering improved care to newborns and mothers in two Bangladesh health districts, Sylhet and Habiganj. Yet after a five-year effort the number of home births declined only slightly with a concomitant small increase in clinic births (see Fig #5 below).[29] Greater gains were made in providing an attendant at the birth, either a skilled birthing attendant (SBA) or traditional birth attendant (TBA). Making home births safer for mothers and children is a primary objective at the launch of CHXUCC.

Figure 5: MaMoni Achievements by District

Indicator	Sylhet		Habiganj	
	Oct. 2010	May 2012	Oct. 2010	May 2012
% women who received four ANC visits	13.7%	8.2%	10.2%	8.7%
% of pregnant women who received two doses of tetanus toxoid	88.3%	89.5%	92%	93.5%
% of women who received iron folate during pregnancy	48.2%	48.2%	36.1%	41.8%
% of women who used new blade	13.6%	70%	92.6%	87.5%
% of women delivering in facilities	19.1%	23%	12.6%	17.6%
% of women delivering at home	80.9%	77%	87.4%	82.3%
% of women delivering with an SBA	21.0%	25.8%	15%	19.4%
% of women delivering with a trained TBA	39.5%	43.7%	13.3%	30%

[28] Foley, Michael "1 Newborn dies every 7 minutes in Bangladesh" Save the Children, Tuesday 7 May 2013, https://www.savethechildren.net/article/1-newborn-dies-every-7-minutes-bangladesh

[29] "USAID/Bangladesh: Final Evaluation of the MaMoni Integrated Safe Motherhood, Newborn Care and Family Planning Project", http://pdf.usaid.gov/pdf_docs/pdacy101.pdf

The Every Newborn Action Plan (ENAP) and the Ending Preventable Maternal Mortality (EPMM) plans recommend "Skilled birth attendance… Where skilled care is not available, consider clean birth practices."[30] Clean birth practices include kits, interchangeably called "Safe Birthing Kits", "Safe Delivery Kits" and "Clean Birthing Kits," for mothers and attendants when the birth is at home [hereafter referred to as safe delivery kits (SDK)]. SDKs generally include soap for hand washing, a plastic or absorbent pad to serve as a clean delivery surface, clean string for tying the umbilical cord, a new blade for cutting the umbilical cord and pictorial instructions illustrating the sequence of delivery events and hand washing. The kits are available from a variety of not-for-profit and for-profit entities, such as JANMA, SMC and BRAC; the cost can vary from ~$.50 to $5 depending on the vendor and supplies included.

Section 7.6 of the 2014 "Supply Chain Management" National Guideline for Bangladesh calls for the inclusion of CHX in the safe delivery kit, yet the details for implementing this guideline, such as whether CHX (Hexacord®) will be physically inserted into safe delivery kits, are unclear.

Will Hexacord® be physically inserted into the kit as a component of the SDK?

Adding Hexicord as a component in SDKs has two primary advantages: 1) convenience (one assembled kit v. kit plus Hexicord®), and 2) increases likelihood of CHX use at birth; and two disadvantages: 1) cost (kit plus Hexicord®) and, 2) registration requirements and expiry (Hexacord®'s stability dating spills over to other kit components). Hexicord® has a product expiry date of 24 months after manufacture. BRAC-assembled SDKs examined in March and May 2015 did not have expiry dates on the kit components (e.g. soap, plastic sheet, clean string and blade) although BRAC representatives commented that the soap out dates after ~24 months. By inserting Hexicord® into a SDK it creates an implied expiry for the entire kit (if a kit doesn't have other components, like soap, with its own expiry dating) and new regulatory requirements. SDK PLUS Hexicord® kits would have to be monitored for Hexicord® outdating as well as other components; and registration.

SDKs and Hexacord® are available to mothers via their SBA or TBA who attends the birth. SBAs/TBAs purchase SDKs and Hexacord at their own expense, add a small mark-up, and receive payment for these disposable products by the mothers. Unattended births require mothers to prepare in advance by purchasing SDK and Hexacord® through retail channels. Some NGO representatives have suggested, extrapolating from a "willingness to pay study" for 7.1% chlorhexidine, that the cumulative 90 BHD (~$1) for an SDK PLUS Hexacord® may create a difficult choice for a mother living in poverty.[31]

The bundling issue suggests a useful performance monitoring metric of NGO practices (kit-inserted Hexacord or bundled together as separate products) during the post-launch period, July-December 2015. Monitoring would include purchases together and separately for Hexacord and SDK. It will be an important consideration to determine if price-sensitive mothers choose Hexacord or SDK rather than purchase both.

In reviewing this leverage point we draw from the experience with oral re hydration salts (ORS) as an anti-diarrheal and the later introduction of zinc as adjunctive, combination therapy with ORS.[32] In the 1970s ORS became the standard of care for childhood diarrhea treatment and prevention in Bangladesh. By 2004, the WHO had sufficient evidence to call for the addition of zinc with traditional ORS care. ORS and zinc are provided through informal providers at the community level. ORS and zinc also utilized private sector distribution channels quite similar to the CHX introduction. The optimistic finding is that both zinc and ORS utilization increased in combination. Zinc pricing (~$.25) is less than Hexacord®, yet the ORS/zinc bundled price is similar to current estimates of SDK PLUS Hexacord®.

[30] EWEC Technical Content Workstream working Group on ending preventable maternal and newborn mortality and stillbirths (23/03/2015) http://www.everywomaneverychild.org/images/07__Ending_Preventable_Maternal_andNewborn_Mortality_and_Stillbirths.pdf
[31] Coffey, PS; Metzler, M., Islam Z., Koehlmoos, T.P. "Willingness to pay for 4% chlorhexidine (7.1% digluconate) product for umbilical cord care in rural Bangladesh: a contingency valuation study" BMC International Health and Human Rights, 13 (October 18, 2013)
[32] Larson, et al. (2011). Scaling up zinc treatment of childhood diarrhea in Bangladesh: theoretical and practical considerations guiding the SUZY Project. Health Policy & Planning 27:102 – 114. Rahman, AS, et al. (2014). Impact of NGO training and support interventions on diarrhea management practices in a rural community of Bangladesh: An uncontrolled, single-arm trial. PLoS ONE 9(11): e112308

Leverage Point #5: DISTRIBUTION

Despite the growing rate of urbanization in Bangladesh, many births continue to occur in rural areas with less access to medical facilities. In this context, the distribution channels in-country become an important factor in the successful adaptation of CHX among new mothers. This section explores the various distribution channels in-country that can help reach mothers. We focus on three sets of distribution channels: public, private and NGO.

Public

Primary healthcare ranges from small community clinics to the slightly larger upazila health centers at the sub-district level. The Ministry of Local Government, Rural Development and Cooperatives oversees both type of facilities in rural regions. Secondary and tertiary healthcare, which deliver more complex and advanced treatments, occur mainly in district hospitals and tertiary hospitals spread across the eight divisions in Bangladesh.[33] There are two main distribution channels that filter through from the division level to the ward level: the Directorate General of Health Services (DGHS) and Directorate General of Family Planning (DGFP). DGHS and DGFP are two divisions within the Ministry of Health and Family Welfare (MOHFW). Chlorhexidine produced from ACI is distributed through these two government branches.

[33] The country of Bangladesh contains eight major areas, called divisions. These are similar to states or provinces. These are further divided into 64 smaller units, known as districts, which are broken down into 493 sub-district areas, known as upazilas. Upazilas are further divided into communities or wards, but these units have little or no representative power.

DGFP

Figure 6: DGFP Capacity[34]

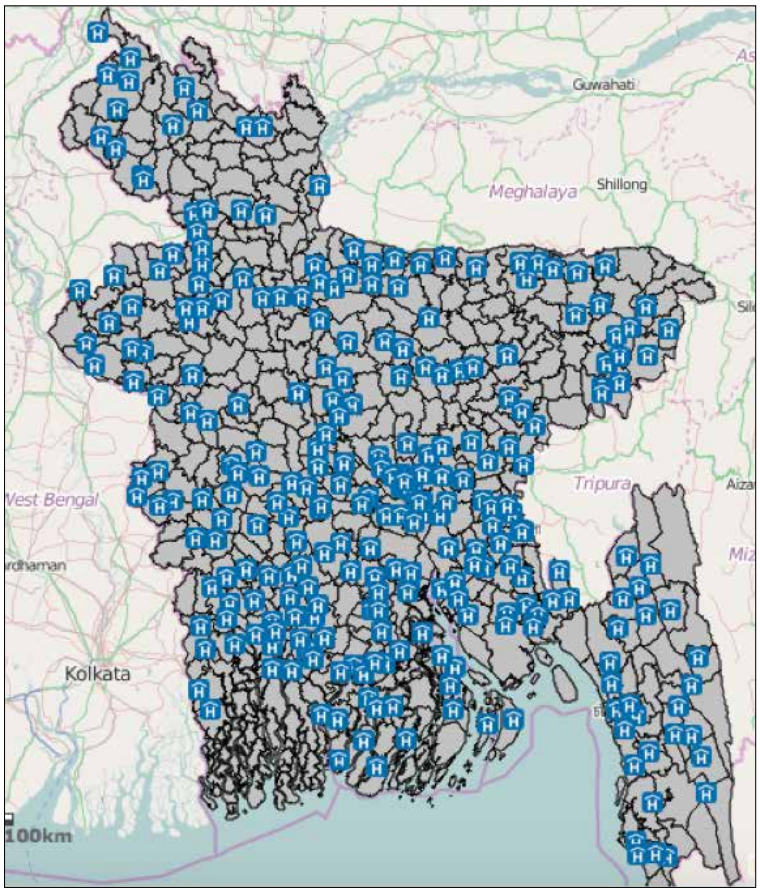
DGFP has a supply chain system to deliver commodities, including Hexacord, from one central warehouse in Dhaka to 20 regional warehouses, 488 Upazila Family Planning Stores and about 30,000 Service Delivery Points. Delivery points are places and people who have direct contact with mothers and newborns and include: Upazila Health Complexes, Maternal and Child Welfare Centers, Family Welfare Assistants, and Health and Family Welfare Clinics. The DGFP has 20 regional warehouses: three large regional warehouses in Chittagong, Khulna and Bogra, and 17 newly upgraded regional warehouses from the formerly District Reserve Stores. The Central Warehouse, Chittagong Regional Warehouse and Khulna Regional Warehouse act as suppliers for the lower region of Bangladesh while all the other warehouses distribute Hexacord for their respective areas.[35]

[34] Ministry of Health and Family Welfare. MOHFW Supply Chain Management Portal. Accessed May 11, 2015. http://dgfplmis.org/index.php/dgfp-supply-chain-system
[35] NHSDP Surjer Hashi Clinics. Accessed May 11, 2015. http://www.arcgis.com/home/webmap/viewer.html?webmap=98a5cde0040a4f4b8d6a0a63643fa8cf

DGHS

There are 297 government facilities in the DGHS supply chain network as of March 2015.[36]

Figure 7: DGHS Health Facilities



Community clinics, which are present in many villages, do not buy Hexacord directly from ACI, but procurement occurs through a set budget every month from the government's central distribution warehouse.

Upazila health complexes, which also distribute CHX for the DGHS, pass Hexacord on to both the Union level and the Community Skilled Birth Attendants (CSBA), and people at the Upazila level decide the proportion of Hexacord that is distributed. CSBAs receive Hexacord for free and are able to provide it to mothers at no cost.

Private

ACI, the sole private actor involved in CHXUCC, owns sales centers in 20+ different locations across the country (Dinajpur, Faridpur, Jossore, Rangpur, Bogra, Rajshahi, Maymensingh, Tangail, Gazipur, Chittagong, Bandarban, Maijdi, Cox's Bazar, Dhaka, Narayangang, Comilla, Kustia, Khulna, Sreemangal, Sylhet, Chandpur). ACI has a developed distribution system consisting of around 300 skilled and training manpower, as well as 22 distribution centers and more than 80 vehicles.

[36] NHSDP Surjer Hashi Clinics. Accessed May 11, 2015. http://www.arcgis.com/home/webmap/viewer.html?webmap=98a5cde0040a4f4b8d6a0a63643fa8cf

Figure 7: ACI distribution centers in Bangladesh

The distribution system is fully equipped to handle a diverse range of products, including chlorhexidine, and ACI is able to distribute products to any part of the country within four hours.[37] ACI plans to work with 50,000 of the 75,000 private pharmacies in its network to sell CHX. The supply of chlorhexidine is based on a pull effect, as the amount of the solution distributed to each district is based on the demand of that particular area. Although ACI does work with a large number of pharmacies, there are four main chain pharmacies (Lazz Pharma-Dhaka, Lavender Pharma-Dhaka, Almost-Dhaka and QP- Chittagong) that account for a large share percentage of ACI's distribution network. ACI expects to sell 0.1- 0.2 million units for the first month of Hexacord's launch. They anticipate a peak production level of 2 million units per year, with 200,000 units per month to private pharmacies.

NGOs Distribution

Non-governmental organizations serve as a middle-man between the producer of Hexacord (ACI) and end users through their ability to market the product and facilitate the distribution and training for CHX usage. Our research identified the top individual NGOs and a network of NGOs that are involved with the distribution of CHX: BRAC; Social Marketing Company and Smiling Sun; a network of NGOs in Bangladesh.

[37] Field interviews

BRAC

BRAC, founded in Bangladesh, is the largest NGO in the world based on the number of people helped (138 million) and the number of employees (100,000; nearly 70% are women). It is present in all districts in Bangladesh and maintains offices in 13 other countries, including Pakistan, Haiti, Philippines and Liberia. BRAC is involved in many different areas, including education, food security and child health. Its primary role is to mobilize the population and not to provide care. For example, BRAC will provide and develop infrastructure to provide care on a temporary basis and withdraw once the government fills the gap.[38] It is currently unclear whether BRAC will be involved in the distribution of Hexacord® because BRAC supports traditional birth attendants and the traditional way of dry cord care. Hence, the introduction of Hexacord® will promote the eradication of this type of method.

If BRAC were to adopt the distribution of Hexacord®, the solution will most likely be included in the safe delivery kits (SDKs) and follow that same distribution channel.[39] The SDKs are sold to traditional birth attendants, called Shasthya Shebikas, who are trained by BRAC staff and report back to them. BRAC currently trains 110,994 TBAs. Shasthya Shebikas act as entrepreneurs, buying SDKs from BRAC at factory price and selling them to patients at a small profit; they also receive financial compensation for completing BRAC's training. Currently, 232 women working in five production centers across the country[40] assemble SDKs for BRAC. These kits have been very popular in the rural areas, and have also been commercially retailed in many hard-to-reach regions including Tekmaf Tetulia and the Chittagong Hill Tracts.[41]

SOCIAL MARKETING COMPANY (SMC)

Social Marketing Company (SMC), a local-based NGO funded by USAID, offers education and products for family planning, maternal and child health, and the prevention of sexually transmitted diseases. It also plays a role in creating demand for products through advertising and covers more than 240,000 outlets each year directly through its sales network.[42]

To obtain its products, SMC either produces them, sources them from donated goods, purchases them from local suppliers, or imports from other countries. The products are then stored either in SMC's central warehouse in Bhaluka, Mymensingh or in rented warehouses in Chittagong and Ultara. If needed, such as for the safe delivery kits, products are packaged in the SMC packing unit in Bhaluka. SMC is structured with 12 sales area offices and 150 sales officers distributed around eight areas in Bangladesh. It has 3 distribution channels: private pharmacies, including USAID sponsored Blue Star Pharmacies, institutions and groceries/ kiosks. These products are transported via trucks, both SMC owned and hired trucks, as well as delivery vans. Its supply is based on a bottom-up system, and the company require cash on delivery for purchases.[43] Figure 8, on the next page, shows the distribution of SMC sales offices, factories and distribution centers.

[38] BRAC Homepage. 2015. BRAC. Accessed May 11, 2015. http://www.brac.net/content/brac-bangladesh
[39] Field interviews
[40] Production centers are located in the Manikganj, Baniachang, Nilfamari, Ramdia and Kurigram districts of Bangladesh
[41] BRAC. 2013. BRAC Sanitary Napkins and Delivery Kits. Accessed May 11, 2015. http://enterprises.brac.net/brac-sanitary-napkins-and-delivery-kits
[42] Social Marketing Company. 2014. About SMC. Accessed May 11, 2015. http://www.smc-bd.org/index.php/common_modules/index/23
[43] Assignment Point. Institutional Background of SMC. Accessed May 11, 2015. http://www.assignmentpoint.com/business/organizational-behavior/institutional-background-smc.html

Figure 8: SMC in Bangladesh[44]

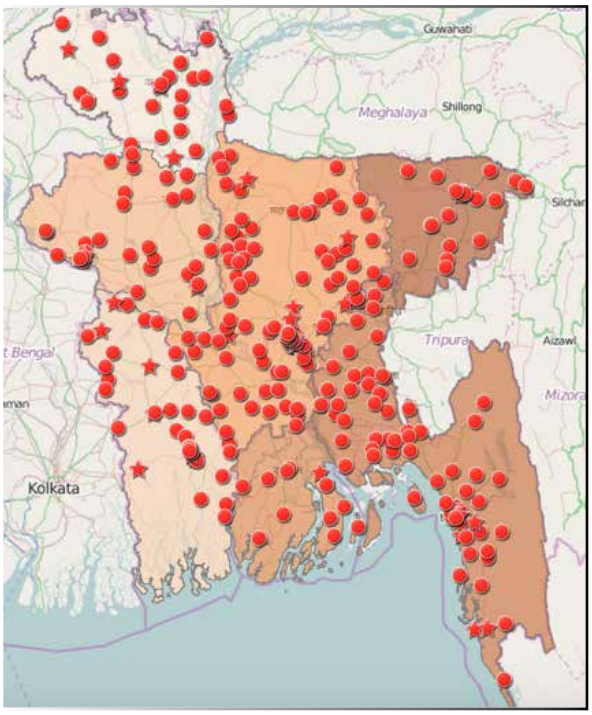
Blue Star Pharmacies, a major retail outlet for SMC, is a specialized channel and network of mostly non-formal private sector health providers who are trained by SMC. There are 6,000 Blue Star pharmacies in Bangladesh. They differ from most pharmacies because they provide essential and antenatal care services (e.g. HIV testing), as well as family planning and nutrition related services.[45] Additionally, they promote safe delivery kits (SDKs), which, other pharmacies often don't due to low profit margins. SDKs are bought from SMC and are subsidized, which covers the cost. SMC regulates about eight of the 30 products and services provided at Blue Star Pharmacies, setting a maximum price and product line specifications. Although they do promote SDKs, only 10-20% of their products are sold via the kits. It is currently unknown whether SMC will adopt the distribution of Hexacord.

[44] Social Marketing Company. 2014. SMC at a Glance. Accessed May 11, 2015. http://www.smc-bd.org/index.php/map
[45] Social Marketing Company. 2014. About SMC. Accessed May 11, 2015. http://www.smc-bd.org/index.php/common_modules/index/23

SMILING SUN - SMILING SUN WEBSITE AND PDF AND INTERVIEW OF SMC FROM APRIL

Smiling Sun is the largest NGO healthcare network in Bangladesh. It is funded by USAID and consists of 27 national NGOs. Smiling Sun serves more than 20 million customers annually and has 27 pre-existing NGO health clinics, 9,133 satellite clinics, 323 static clinics, and 6,327 community service promoters (CSPs) across all 64 districts of Bangladesh. The areas of health Smiling Sun covers include family planning, maternal health and STD prevention. Smiling Sun clinics target low-income populations, migrant/refugees, women and youth in providing a variety of primary care. Figure 9 shows the distribution of Smiling Sun clinics around Bangladesh, with the red circles showing the "Vital" clinics, which offer basic care services, and the red stars showing the "Ultra" clinics, which in addition to basic care also offer emergency obstetric care. The "Vital" clinics have 12 staff members on average, and the "Ultra" clinics have 30 staff members on average.[46]

Figure 9: Smiling Sun Vital and Ultra Clinics[47] [48]



CONSIDERATIONS FOR THE DISTRIBUTION LEVERAGE POINT

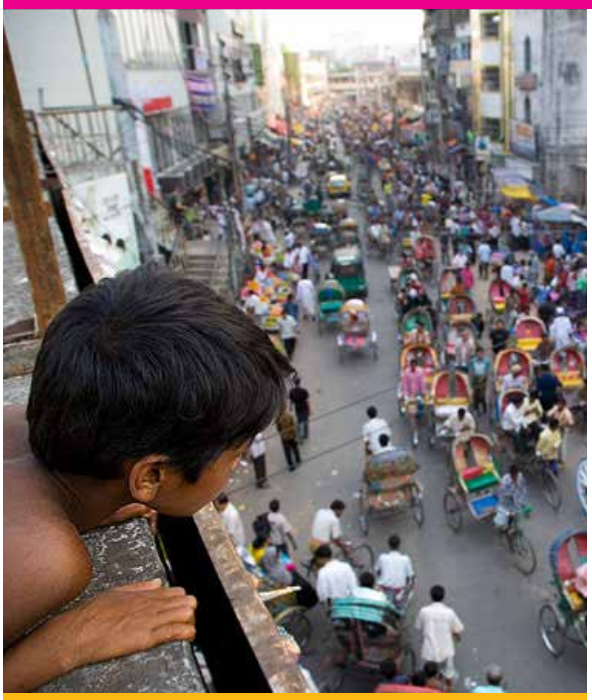
The distribution system is highly complex and varies significantly between public and private; pharmacy sales v. NGO sales by a birth attendant to a mother; and the fact that two different departments within the Ministry of Health have responsibility for distributing Hexacord.

Perhaps more than other leverage points, distribution is "mission critical" to the success of the launch and serves as a bellwether of its success. If there are problems in creating demand from the various users, or there are interruptions in supply from the manufacturer, they will be observed quickly in the distribution system. Training birth attendants who provide the product to mothers or advise them to purchase it themselves will help create demand in the non-governmental channel. The efficiency of the various distribution channels will vary. It is critical that the implementing team develops a performance monitoring system (see Leverage Point #7 below) that allows them to closely observe the flow of Hexacord. As a leading indicator, it allows the implementing partners to identify any problems in distribution and resolve them.

[46] Smiling Sun Franchise Program. 2015. Health Market Innovations. Accessed May 11, 2015. http://healthmarketinnovations.org/program/smiling-sun-franchise-program-ssfp

[47] Shading shows the percentage of newborns receiving antenatal care. Darker brown corresponds to a higher percentage of births receiving no antenatal care.

[48] NHSDP Surjer Hashi Clinics. Accessed May 11, 2015. http://www.arcgis.com/home/webmap/viewer.html?webmap=98a5cde0040a4f4b8d6a0a63643fa8cf



Leverage Point #6: GLOBAL COORDINATION

Global non-governmental organizations (NGOs) can play useful roles to coordinate R&D; facilitate local market treatments and diagnostics availability and accessibility; shape markets and encourage price competition. Global coordinators operate on the supply side when they invest or co-ordinate efficient research and development activities, and operate on the demand side when they help negotiate prices and/or facilitate purchases of treatments and diagnostics. Well-known global coordinators include Medicines for Malaria Venture, Clinton Health Access Initiative, GAVI and FHI360. To date CWG has to date primarily played a supply side and informal coordination role encouraging the introduction of CHX into a growing number of local markets. Expanding CWG's role on the demand side, emulating larger global coordinators, is needed as the number of countries with CHX expands and donors require greater efficiencies to maximize the returns on their CHX investments. The role FHI360 has played with Sino-implants may be an illustrative case. Massive increases in resources are needed for the CWG to be able to obtain the same level of coordination as FHI360 in Sino-implants.

A Sino-implant is made of two thin, flexible, silicone rods, each containing 75 mg of levonorgestrel, a synthetic progesterone for implant under a woman's arm. It can provide up to four years of continuous effective and safe contraception. Sino-implants are manufactured by Shanghai Dahua Pharmaceuticals Co., Ltd. FHI360 has served as a global coordinator providing technical assistance to the manufacturer to meet WHO Good Manufacturing Practices and pre-qualification. Of particular interest as the "use case" for CHX is the role FHI360 has played in securing local distributors. FHI360 has identified distributors in 20 markets and worked with the local operator to secure country registration, negotiated public sector price-ceiling agreements and organized clinical trials. Its work has been supported by the Bill & Melinda Gates Foundation as well as USAID. FHI360 works closely with local governments, international NGOs, distributors and service delivery groups. The effect of FHI360's work with Dahua has been to create price competition with Merck and Bayer who also provide implantable contraceptives. These multi-national manufacturers have met Dahua's lower price, and as a result, donor contributions and subsidies will provide more contraceptives for the same level of investment.

What would be the activities of an expanded global coordinator?

The Chlorhexidine Working Group (CWG) is an effective point of communication and coordination. The number of CHX introductions to date has created the opportunity for CWG (or another organization if CWG did not want such a role) to play an expanded global coordination role. All or some of the considerations described in leverage points 1-6 could become amended terms of reference for a CHX global coordinator.

- Clinical trial results coordinated as a global activity v. local market
- Advocacy for the recognition of clinical trial results adoption across markets
- Advocating for and securing product or package redesign funding
- Best practices captured and shared with manufacturers
- Assessing the regional or global tendering capabilities of local CHX markets
- Identifying manufacturers to participate in regional or global tendering

Monitoring and Performance Metrics

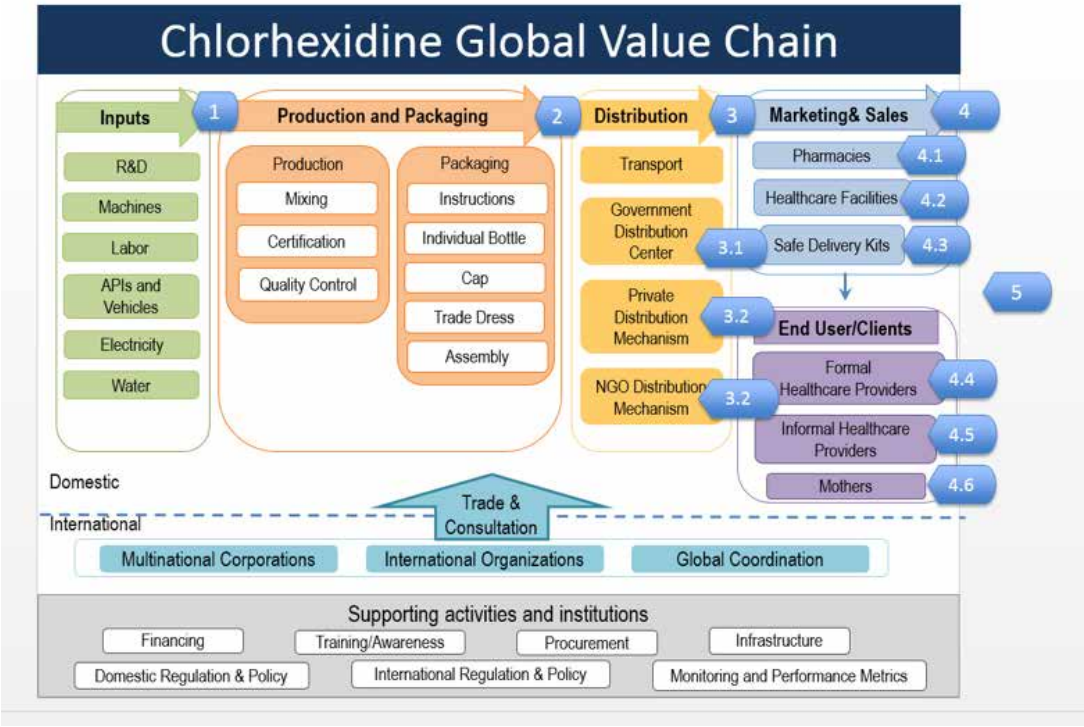
Leverage Point #7: MONITORING AND PERFORMANCE METRICS

The successful implementation of CHX in Bangladesh will be complex and challenging. The value chain that leads from the importation of chlorhexidine salt and bottle/cap assembly to a mother applying Hexacord® to a newborn's umbilical cord within 24 hours of birth has many points where gaps or bottlenecks can occur. Monitoring the launch and being able to diagnose and remedy gaps in performance of the CHX launch requires an effective performance monitoring system. The monitoring and performance management system will be of particular value to the technical working groups in Bangladesh organized around the CHX launch. Both the "monitoring and evaluation" and "operations research" disciplines have approaches to establishing performance metrics. In reviewing the leverage point we suggest a blended approach to develop a CHX performance monitoring system. Our discussion is for illustrative purposes only. A system is in development and will be refined as the launch progresses.

The blended approach to monitoring and performance suggests the following criteria for selecting or creating performance indicators.

1. Causal Linkages: Make explicit assumed causal linkages from one activity to another (if the causal assumptions are correct the relationships between indicators will reflect the linkage; if the causal assumptions are incorrect, refining the causal linkages will help support a continuous quality improvement approach to the launch)
2. Indicator Utility: Use existing indicators (e.g. budget, capacity, output) and invest in the development of new indicators where the increase in utility justifies the cost
3. Indicator Variety: Use measures that are qualitative and quantitative, one-time and repeated, self-reported and more objective, etc.

We use the value chain map to suggest possible placements of performance indicators. The implementing partners in Bangladesh will know the best locations that balance causal linkage, utility and variety considerations.



#1 "Inputs" – indicators to include ACI re-orders of CHX salt and bottle/cap components

#2 "Production and Packaging" – indicators to include ACI manufacturing plant ex-factory Hexacord® shipments (including purchaser, destinations, order and delivery dates)

#3 "Distribution" – indicators to include current inventory and incoming/outgoing shipment history at "government distribution center" (3.1), "private distribution mechanism" (3.2) and "NGO distribution mechanism" (3.3):

#3.1 DGFP (Directorate General for Family Planning) - 20 regional warehouses (3 large regional warehouses in Chittagong, Khulna and Bogra – (17 regional warehouses); DGHS (Directorate General for Health System) use Central Warehouse Data

#3.2 Current inventory and incoming/outgoing shipment history at ACI's 22 national distribution centers

#3.3 Current inventory and incoming/outgoing shipments of Hexacord® (see Leverage Point #5 above for more detail on NGO distribution systems)

#4 "Marketing & Sales" – indicators include sales/use data by NGOs, government clinics, pharmacies; formal and informal delivery attendants and mothers:

#4.1 Hexacord® inventories and sales from Lazz Pharma, Lavender Pharma, ALMsot, QP and Blue Star pharmacies; sample from the five leading pharmacy chains to estimate Hexacord® inventories and sales at the ~75,000 pharmacies in Bangladesh

#4.2 "service provision assessment" conducted in clinics and hospitals regarding CHX use and availability

#4.3 Safe Delivery Kits bundled with Hexacord® at SMC warehouses in Bahluka, Mymensingh, Chittagong and Ultara; BRAC warehouses in Manikganj, Baniachang, Nilfamari, Ramdia and Kurigram; sample of 323 clinics in the Smiling Sun NGO network (excluding SMC or BRAC)

#4.4 sample of inventory (on-hand stock for the attendant) and re-purchase by Community Skilled Birth Attendants

#4.5 sample of inventory (on-hand stock for the attendant) and re-purchase by Traditional Birth Attendants

#4.6 annual "demographic health survey audits" regarding essential newborn care components including the use of CHX

#5 "Overall Index of Performance" – an aggregate index drawn from #1-#4 to provide a snapshot or dashboard of performance

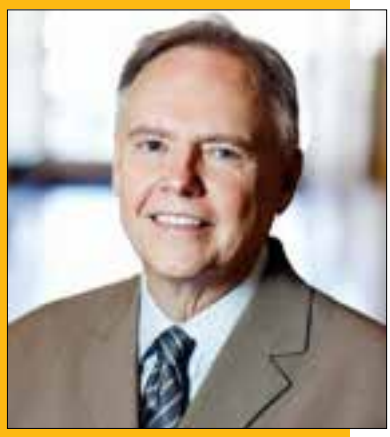
A monitoring and performance system needs to provide timely information to implementing partners and lay the foundation for moving from evidence to evaluation. Indicators need to be both leading and lagging to give the implementing partners timely and objective information. The indicators can also be viewed as establishing initial evidence to guide interventions to ensure there are no interruptions in supply, all distribution channels have demand and that mothers, birthing attendants and hospital staff use chlorhexidine safely. As performance is monitored can begin the evidence development for a more elaborate and costly evaluation of the program in future years. NOTE: CWG has developed drafted key indicators for "monitoring and evaluation" of CHX implementation available at the HNN website.

CONCLUSION

The launch of CHXUCC in Bangladesh is the result of a decade of research, planning and coordination. Technical working teams will be focused on near-term execution so that birth attendants, clinicians and mothers at home apply CHX to their newborns as one part of essential newborn care standards. Yet, the launch also creates an opportunity to look beyond the immediate execution of the launch plan to anticipate medium-term issues and to transfer best practices to other existing or potential CHX markets. The VCA approach is a holistic, system-based view of the CHX introduction and has suggested several leverage points discussed in the report. Bangladesh technical working groups can use these leverage points for deeper analysis and to make decisions now that can create future efficiencies and increase the chances for adoption of CHX. Global CHX coordinators can apply the VCA approach to existing markets where similar leverage points exist along the value chain. Markets are unique and so too are the contexts of CHX leverage points. But it is reasonable to expect recurring and similar challenges wherever CHX is under consideration as an addition to essential newborn care. The Bangladesh leverage points and associated choices can become useful, transferable insights.

Value chain analysis suggests the global CHX market is changing as the number of CHX in-use countries increases. The advantages of local CHX manufacture, which have informed best practices to date, must now consider the reality of a nascent global CHX market. While the analysis has not been done, experience suggests that barriers exist between jurisdictions in the form of tariffs or cumbersome export/import approval processes. The promise of reduced costs, while maintaining quality, could be mitigated or eliminated by these barriers. And there's the in-country matter of each jurisdiction's capability to aggregate its public and private demand for CHX and participate in a global or regional tender. We can assume some countries where CHX has been introduced have yet to develop the skills, knowledge and capacities to effectively participate in a regional or global approach to CHX supply. Therefore local manufacture will continue as the best approach for some time, but where the readiness exists the steps should be taken to assess feasibility and prepare for a regional approach. Bangladesh is in such a region with neighboring Nepal and Pakistan as CHX in-use countries and India taking the first steps to consider CHX Introduction.

BIOGRAPHICAL SKETCHES OF AUTHORS



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BASS Connections Team

The BASS team in Dhaka in March.
Top L to R:
Courtney Caiola, Jeffrey Moe
Bottom L to R:
Dayne Hamrick, Chelsea Dulcille, Ben Hu

BASS Connections Team

The BASS team in Dhaka in May.
L to R: Dayne Hamrick, Kimberly Chew, Henry Yuen, Peter Hogue and Elizabeth Ziser-Misenheimer
(Not Shown: Jeffrey Moe and Nimmi Ramanujam)