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BMJ Paediatrics Open

Increasing access to essential medicines through partnership: experience in developing and delivering chlorhexidine gel for newborn cord care

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March 2022

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Increasing access to essential medicines through partnership: experience in developing and delivering chlorhexidine gel for newborn cord care

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CHX Review article

March 2022

ABSTRACT (149/300)

Sustainable access to essential medicines in low- and middle-income countries requires innovative cross-sectoral collaboration throughout the lifecycle of a medicine. Partnerships are essential to address the systemic challenges of global health and health inequity. Pharmaceutical companies, funders, governments, international non-governmental organisations (I-NGOs) and other key stakeholders can leverage, through effective partnership working, their unique expertise to help drive innovation and share learnings and risks. Here we reflect on one approach taken in the development and supply of chlorhexidine digluconate 7.1% w/w gel (equivalent to 4% w/w chlorhexidine) for neonatal cord care. We describe and analyse the steps taken by GlaxoSmithKline to increase access to chlorhexidine gel, including partnering with the I-NGO Save the Children in Western Kenya. Learning points gained along the journey are shared, together with subsequent steps taken to increase access, with the aim of making recommendations that may be applicable to similar enterprises in the future.

CHX Review article

March 2022

KEY MESSAGES

- Barriers to medicine access in low-resource settings are common; to address this, effective partnerships are required. Here we describe learnings from a multisectoral collaboration to develop and supply chlorhexidine gel for neonatal cord care in Western Kenya.
- Insights and learnings from service users and context-based development partners are critical throughout a product's lifecycle to optimise suitability and acceptability.
- Manufacturing processes should be simple to enable transfer to local manufacturers but may fail without proactive engagement strategies to stimulate demand and interest.
- Sustainable side-effect reporting/pharmacovigilance is essential when introducing a new medicine in resource-limited settings where side-effect-reporting mechanisms may not be robust.
- Integrating new commodities is complex. Governmental commitment and actions to improve service supply, stimulate demand and sustain community-level engagement, creates better conditions for adoption.

Keywords (1–5): Public health; Neonatal health; Health policy; Health education and promotion; Prevention strategies

INTRODUCTION

The World Health Organization (WHO) defines essential medicines as those that “satisfy the priority health care needs of the population”.^[1] As such, they are crucial for saving lives, promoting health and achieving sustainable development: they must be both available and affordable, in appropriate dosages and with assured quality.^[2] However, access to essential medicines in low- and middle-income countries (LMICs) remains a significant problem, and such countries face numerous barriers to access.

PARTNERSHIPS TO ADDRESS BARRIERS TO MEDICINES ACCESS

The scale, potential and contribution of the private sector towards the United Nations (UN) Sustainable Development Goal (SDG) 3 (Good Health and Well-Being) to achieve universal health coverage and overcome obstacles for accessing essential medicines in LMICs has been an important and recurring focus of discussion.^[3] Innovative cross-sectoral partnerships may leverage the complementary expertise of different partners to ensure sustainability of access while also helping to share risk. Here we reflect upon a partnership between GlaxoSmithKline (GSK), Save the Children (STC) and other stakeholders to increase access to chlorhexidine digluconate 7.1% (CHX) gel (included in the WHO list of essential medicines) for neonatal cord care in Western Kenya. Lessons learned from this partnership and a Managed Access Programme (MAP) are shared, with the aim of making key recommendations that may be of relevance for similar projects in the future. For the interested reader, a more detailed summary of learnings can be found here:

<https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned-document.pdf>. **Figure 1** summarises key steps in the programme.

NEWBORN CORD CARE IN LMICs

Newborns in LMICs – where births commonly occur at home without trained healthcare workers – are susceptible to infection, with the newly cut umbilical cord representing a frequent bacterial entry point.^[4] To address this need, the WHO recommends application of CHX in settings with high

CHX Review article

March 2022

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3 neonatal mortality rates (>30 deaths/1,000 live births) or to replace harmful traditional cord care
4 substances.[5] This followed successful development, field-trialling and scale-up of CHX gel in South
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7 Asia, most notably in Nepal.[6] The UN estimated that if high-quality affordable CHX was supplied to
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10 50 resource-limited countries, 422,000 neonatal lives could be saved over a 5-year period.[7]

11 12 13 **ENHANCING ACCESS TO CHX FOR NEWBORN CORD CARE IN KENYA THROUGH A PUBLIC-** 14 15 **PRIVATE PARTNERSHIP**

16
17
18 In 2012, in response to these needs, GSK set out to develop a not-for-profit, quality assured gel
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20
21 formulation of 7.1% CHX (equivalent to 4% w/w CHX) suitable for use in resource-limited countries
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23 that could pass stringent regulatory review. With access in mind, the formulation was kept as simple
24
25 as possible to enable local manufacturers to produce an identical product to both increase global
26
27 CHX supply and enable a sustainable supply. In 2016, following an accelerated review, GSK's CHX gel
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29 was granted a positive opinion by the European Medicines Agency (EMA) which supported national
30
31 registrations (**Figure 1**).

32
33
34 In Kenya, neonatal mortality contributes to over 40% of child deaths,[8] with infection a leading
35
36 cause.[9] Although the national neonatal mortality rate in Kenya is below the WHO threshold for
37
38 recommending CHX, wide regional disparities exist with high levels of home deliveries and harmful
39
40 traditional cord-care practices in some regions. Following a request from the Kenyan Ministry of
41
42 Health (MoH) for early access to CHX gel in preparation for national scale-up, GSK worked closely
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44 with STC, who partnered with the Bungoma County Department of Health to implement a MAP and
45
46 facilitated collection of insights on user experiences and practices. The MAP provided opportunities
47
48 to understand acceptability of CHX gel among healthcare providers and mothers, examine factors
49
50 influencing provision and uptake, and determine acceptability of information, education and
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52 communication materials.[10, 11] In parallel, the Kenyan MoH led development and dissemination
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54 of national guidelines and updated the Kenya essential medicines list to include CHX.
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CHX Review article

March 2022

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3 STC, Amref Health Africa and the Kenyan MoH (Division of Neonatal and Child Health), with
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5 engagement from the County First Ladies Association[12], subsequently partnered to perform
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7 advocacy and sensitisation work. This led to the development of national guidelines, healthcare
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9 worker training, development of educational materials and job aides, and the inclusion of CHX in the
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11 *Mother and Child Health Handbook*, a parent-held record of vaccination, growth and advice, offered
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13 in Kenya to all new parents.[13] Crucially, STC and the other partners fostered sustained community
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15 engagement, which was key to building trust and overcoming deep-rooted cultural practices about
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17 cord care among families and healthcare workers.
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21
22 At a county level, local advocacy led Bungoma and another county, Busia, to incorporate CHX for
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24 cord care into their county-specific guidelines and ensured funds were secured to support routine
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26 procurement of locally manufactured CHX through the national supply chain system, thereby
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28 encouraging sustainability. Additionally, a pharmacovigilance training model, jointly disseminated by
29
30 GSK and STC, successfully generated short-term safety information for CHX gel during the MAP,
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32 which complemented the well-established safety profile of CHX products.
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34

35
36 In order to facilitate the transfer of technical and quality know-how to multiple local manufacturers,
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38 an agreement with United States Pharmacopeia (USP) through the Promoting the Quality of
39
40 Medicines programme funded by the United States Agency for International Development
41
42 (USAID)[14], was established. This aimed to transfer the technical know-how to a team of experts
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44 dedicated to helping LMICs strengthen the quality, manufacturing and regulatory systems that are
45
46 required to ensure the quality and increase the supply of essential medicines.
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50 **LESSONS LEARNED**

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52
53 Innovation and partnership working have characterised the development and distribution of CHX gel
54
55 in LMICs from the outset. Established in 2014, the CHX Working Group (CWG) – comprising
56
57 manufacturers, international non-governmental organisations (I-NGOs), universities and
58
59 governments – was convened by the non-profit organisation PATH to advance the use of CHX
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CHX Review article

March 2022

1
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3 through advocacy and technical assistance. Insights from CWG members contributed to the decision
4
5 to package CHX gel in single-dose sachets to facilitate ease of use and optimal dose application to
6
7 avoid retention of excess gel for alternative uses, and inclusion of pictorial instructions to reinforce
8
9 appropriate use in low literacy settings.
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13 Generating these insights as early as possible is recommended; however, it is also important to
14
15 continue to gather information throughout the lifecycle of the medicine during and after the
16
17 development pathway and adapt accordingly. For example, reports of other chlorhexidine solutions
18
19 and gel products being mistaken for eye treatments and causing irreversible eye-injury, including
20
21 blindness, reinforced the importance of suitable packaging, labelling and appropriate warnings.[15]
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23

24
25 The formulation and manufacturing process for CHX gel was developed to be as simple as possible
26
27 while adhering to high quality standards, with control strategies in place to minimise formation of
28
29 impurities, in particular the potential human carcinogen 4-chloroaniline.[16] It was essential the
30
31 manufacturing process was easily transferable to local manufacturers without compromising quality.
32
33 Working with an organisation like United States Pharmacopoeia can greatly facilitate the transfer of
34
35 technical and quality know-how to multiple local manufacturers, allowing efficient resource use and
36
37 enhancing sustainability, while complying with quality standards. However, even with technical
38
39 transfer details freely available[17], a simple manufacturing process may not be sufficient, and thus
40
41 additional proactive strategies may be required to engage with local manufacturers to stimulate
42
43 demand and interest in new products.
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48 The regulatory environment is also highly complex and can be challenging. Although a fast-track
49
50 positive opinion of CHX gel was achieved under the EMA's Article 58 process[18], in some instances
51
52 national registrations took in excess of 2 years. Humanitarian organisations are often the primary
53
54 procurers of essential medicines in LMICs, adhering to strict quality standards for the medicines they
55
56 procure. Generally, this requires a product to be approved by a stringent regulatory authority or
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CHX Review article

March 2022

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3 adherence to the WHO prequalification process. Thus, greater alignment between the EMA and
4
5 WHO may hasten access to other essential medicines in LMICs.
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8 As more medicines are developed in response to diseases common to resource-limited settings,
9
10 sustainable pharmacovigilance is a concern. A low-intervention pharmacovigilance training model
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12 was jointly and successfully disseminated by GSK and STC in Kenya; however, further improvements
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14 in underlying healthcare systems and new multi-stakeholder initiatives, such as the WHO Project 3-
15
16 S[19], may enable local stakeholders to play a greater role in long-term safety monitoring in the
17
18 future.
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21
22 Despite high user acceptability, a relatively supportive policy environment and availability of locally
23
24 manufactured product in Kenya, CHX products still fail to reach some newborns who would benefit
25
26 most, as a consequence of policies that inadvertently prevent CHX from easily reaching babies born
27
28 at home where impact on infection might be greatest. This highlights the importance of ensuring
29
30 that healthcare policies are not in conflict but promote equitable approaches to context-based
31
32 public health procurement and access to interventions that strengthen the effectiveness and reach
33
34 of maternal and neonatal care.
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38
39 Two randomised controlled trials of chlorhexidine in sub-Saharan Africa (Tanzania and Zambia)[20,
40
41 21] failed to show efficacy of CHX in reducing neonatal mortality, although one study did
42
43 demonstrate significantly reduced rates of omphalitis (cord infection) following CHX use. However,
44
45 in both studies, all participants were encouraged to keep umbilical cords clean and dry. These
46
47 improved cord-care practices are likely to have led to lower mortality in both the CHX and control
48
49 groups, emphasising that decisions on targeted CHX roll-out should be considered in the context of
50
51 other educational and healthcare provision practices in that region.
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55 Evidence of efficacy and safety is crucial to maintain confidence in any product. The aforementioned
56
57 WHO safety alert relating to errors in administration reinforced the need for education and training
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59 on appropriate use and the importance of differential packaging of the product and patient
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CHX Review article

March 2022

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3 information. However, the safety alert, taken together with data from the two previously described
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5 clinical trials in sub-Saharan Africa[20, 21], is likely to have contributed to hesitancy among some
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7 governments to implement CHX more widely despite the successful introduction and long-term use
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9 in some South Asian countries.

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12 The integration of a new commodity in a low-resource setting with traditional customs, as is the case
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14 for umbilical cord care, is a complex process. A top-down approach from government may be
15
16 insufficient for a product to be adopted and accepted. Trusted field partners can work effectively
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18 with the spectrum of stakeholder groups to ensure the context and perspectives of community users
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20 and other actors are represented and accounted for. Changing knowledge, attitudes and practices is
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22 required at all levels. A combined approach to improve service supply and demand (e.g. provision of
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24 training for healthcare workers and local campaigns to raise awareness among mothers) and
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26 sustained community-level engagement, creates better conditions for a product to be successfully
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28 adopted and accepted.
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32
33 The uptake of CHX products for cord care has been slow in high-need countries due to many factors,
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35 including lack of awareness and demand from end users, competing county demands and
36
37 inadequate resources. Limited funding for essential medicines, a challenge in many LMICs, has
38
39 delayed the national scale-up of CHX in Kenya and many other countries, sometimes necessitating
40
41 difficult procurement choices to be made, even between medicines that are deemed essential.
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43 Locally manufactured CHX has helped to increase access in Kenya but there remains a need for
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45 continuous, sustained long-term effort to ensure uptake of essential medicines such as CHX.
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50 **CONCLUSIONS**

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52 Innovative partnerships are required throughout the lifecycle of a new intervention to ensure
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54 sustainable access to essential medicines in LMICs. Pharmaceutical companies, funders,
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56 governments, I-NGOs and other key stakeholders need to integrate their unique expertise to inform
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58 the design and implementation stages. For example, market awareness and community sensitization
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CHX Review article

March 2022

initiated in parallel to product development and regulatory harmonization would accelerate availability and uptake. Ongoing partnerships with in-country stakeholders would enable continued learnings and optimization. Through this, realisation of the UN's SDG of achieving universal health coverage, and a world where all people have equitable access to quality, essential healthcare without risk of financial hardship by 2030, can be greatly enhanced.

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COMPETING INTERESTS

EDA, RG are employees of GSK. EDA, RG and PW hold stocks/shares in GSK. AC and KK are employed by Save the Children, UK.

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March 2022

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REFERENCES

1. World Health Organization. The selection and use of essential medicines : report of the WHO Expert Committee, 2002 : (including the 12th model list of essential medicines), 2003. Available: <https://apps.who.int/iris/handle/10665/42620> [Accessed 26 January 2022].
2. Ozawa S, Shankar R, Leopold C, *et al.* Access to medicines through health systems in low- and middle-income countries. *Health Policy Plan* 2019;34(Supplement_3):iii1-iii3.
3. United Nations. Sustainable development goals; goal 3 targets, 2019. Available: <https://www.un.org/sustainabledevelopment/health/> [Accessed 27 August 2019].
4. Coffey PS, Brown SC. Umbilical cord-care practices in low- and middle-income countries: a systematic review. *BMC Pregnancy Childbirth* 2017;17(1):68. <https://10.1186/s12884-017-1250-7>.
5. World Health Organization. WHO recommendations on newborn health, 2017. Available: <https://apps.who.int/iris/bitstream/handle/10665/259269/WHO-MCA-17-07-eng.pdf;jsessionid=D842C772FDA84BBD83CF9A4142D2433F?sequence=1> [Accessed 22 November 2019].
6. Tuladhar S. Chlorhexidine in Nepal: A Public-Private Partnership Case Study., 2013. Available: https://www.healthynewbornnetwork.org/hnn-content/uploads/PPP_for_CHX_program_in_Nepal_v6-SHLK_edits_07242013_1-2.pdf [Accessed November 2021].
7. United Nations. UN commission on life-saving commodities for women and children: commissioners' report, 2012. Available: https://www.unfpa.org/sites/default/files/pub-pdf/Final%20UN%20Commission%20Report_14sept2012.pdf [Accessed 27 August 2019].
8. United Nations Children's Fund and World Health Organization. Tracking progress towards universal coverage for reproductive, newborn and child health: The 2017 report, 2017. Available: <https://www.countdown2030.org/pdf/Countdown-2030-complete-with-profiles.pdf> [Accessed 14 July 2021].
9. Murphy GAV, Waters D, Ouma PO, *et al.* Estimating the need for inpatient neonatal services: an iterative approach employing evidence and expert consensus to guide local policy in Kenya. *BMJ Glob Health* 2017;2(4):e000472. <https://10.1136/bmjgh-2017-000472>.
10. Obare F, Abuya T, Musika S, *et al.* Kenya signature programme endline evaluation report: Bungoma, Busia and Wajir counties. Nairobi: population council and save the children.; 2018.
11. Muriuki A, Obare F, Ayieko B, *et al.* Health care providers' perspectives regarding the use of chlorhexidine gel for cord care in neonates in rural Kenya: implications for scale-up. *BMC Health Serv Res* 2017;17(1):305. <https://10.1186/s12913-017-2262-8>.
12. County First Ladies Association, CFLA, Available: <https://cfla.or.ke/> [Accessed 8 September 2021].
13. Kenya Ministry of Health. Mother and child health handbook, 2020. Available: <https://www.kenyaepidemiology.org/ecd/wp-content/plugins/pdfjs-viewer-shortcode/pdfjs/web/viewer.php?file=/ecd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true> [Accessed 13 January 2021].
14. United States Pharmacopeia. The United States Pharmacopeia., 2019. Available: <https://www.usp.org/> [Accessed 19 September 2019].
15. World Health Organisation. Chlorhexidine 7,1% digluconate (CHX) aqueous solution or gel (10ml): Reports of serious eye injury due to errors in administration, 2020. Available: [https://www.who.int/news/item/28-08-2020-chlorhexidine-7-1-digluconate-\(chx\)-aqueous-solution-or-gel-\(10ml\)-reports-of-serious-eye-injury-due-to-errors-in-administration](https://www.who.int/news/item/28-08-2020-chlorhexidine-7-1-digluconate-(chx)-aqueous-solution-or-gel-(10ml)-reports-of-serious-eye-injury-due-to-errors-in-administration) [Accessed 20 January 2022].
16. World Health Organization. Concise international chemical assessment document 48. 4-chloroaniline, 2003. Available: <https://www.who.int/ipcs/publications/cicad/en/cicad48.pdf> [Accessed 27 August 2019].

CHX Review article

March 2022

17. PQM. GSK Chlorhexidine Digluconate (7.1%) Gel Technology Transfer Report. Rockville, MD; 2018.
18. European Medicines Agency. Medicines for use outside the EU - EU-M4all., 2020. Available: https://www.ema.europa.eu/en/documents/leaflet/infographic-medicines-use-outside-eu-eu-m4all_en.pdf [Accessed 15 December 2021].
19. World Health Organization. Safety of medicines. Priming resource-limited countries for pharmacovigilance, 2017. Available: https://www.who.int/medicines/publications/druginformation/issues/WHO_DI_31-4_Safety-Medicines.pdf [Accessed 28 August 2019].
20. Sazawal S, Dhingra U, Ali Said M, *et al.* Efficacy of chlorhexidine application to umbilical cord on neonatal mortality in Pemba, Tanzania: a community-based randomised controlled trial. *Lancet Glob Health* 2016;4(11):e827-e44. [https://10.1016/S2214-109X\(16\)30223-6](https://10.1016/S2214-109X(16)30223-6).
21. Semrau KEA, Julie Herlihy, Caroline Grogan, *et al.* Effectiveness of 4% chlorhexidine umbilical cord care on neonatal mortality in Southern Province, Zambia (ZamCAT): a cluster-randomised controlled trial. *Lancet Glob Health* 2016;4(11):e766-e8.

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Figure 1. Increasing access to essential medicines through partnership: the journey of chlorhexidine.

Confidential: For Review Only



Increasing access to essential medicines through partnership



Newborns in resource-limited countries, where births frequently occur at home without trained healthcare workers, are particularly susceptible to infection through the newly cut umbilical cord. Use of chlorhexidine digluconate (CHX) for umbilical cord care can help to prevent infection



2011

WHO list CHX as a priority medicine

CHX listed by the WHO as a priority medicine for children's health, requiring further R&D

2012

UN call to action

UN Commission identified CHX as a life-saving commodity for women's and children's health

UN called for additional manufacturers to supply high-quality, affordable CHX for newborn cord care that, with widened access across 50 resource-limited countries, could save 422,000 lives over 5 years

GSK began to reformulate their existing CHX product into a gel suitable for use in resource-limited settings

2013

A partnership with a mission

Partnership established between GSK and Save the Children (STC) to find new ways to reduce childhood mortality from preventable and treatable diseases

2014

Partnerships in action

The Chlorhexidine Working Group began coordinating approaches to advancing use of CHX for umbilical cord care via a collaboration with manufacturers, international NGOs, governments and universities
STC and others worked with the Kenyan Ministry of Health to develop national guidelines on the use of CHX for cord cleansing

2016

Managed Access Programme (MAP) established in Kenya

GSK and STC partnered to implement a MAP in Kenya, which ran to 2018. Insights from healthcare worker interviews, user focus groups and informal local feedback informed the CHX gel formulation, packaging and patient information materials developed by GSK

Acceptability of CHX gel was very high (99%) from both service providers (n=39) and mothers (n=479) and 92% of mothers (n=479) stated they would recommend the product to other mothers

Positive opinion by the EMA

Following accelerated review, GSK's CHX gel was granted a positive opinion by the EMA, facilitating approval in 19 countries, including Kenya (in 2017)



2018

Learnings shared

Learnings from the Kenyan MAP successfully applied to a 2-year CHX implementation research project in Papua New Guinea. Agreement with USP/USAID established with aim to transfer CHX technical know-how to LMICs

2021

CHX supplied locally and widely used

GSK stopped manufacturing CHX gel because generic manufacturers are now supplying affordable product in sufficient volumes to meet local demand

Locally-manufactured CHX is now available in all counties in Kenya and all newborns receive the protection provided by CHX

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Increasing access to essential medicines through partnership: experience in developing and delivering chlorhexidine gel for newborn cord care

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1 **Increasing access to essential medicines through partnership: experience in**
2 **developing and delivering chlorhexidine gel for newborn cord care**

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2
3 16 **ABSTRACT (149/300)**
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6 17 Sustainable access to essential medicines in low- and middle-income countries requires innovative
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8 18 cross-sectoral collaboration throughout the lifecycle of a medicine. Partnerships are essential to
9
10 19 address the systemic challenges of global health and health inequity. Pharmaceutical companies,
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12 20 funders, governments, international non-governmental organisations (I-NGOs) and other key
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14 21 stakeholders can leverage, through effective partnership working, their unique expertise to help
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16 22 drive innovation and share learnings and risks. Here we reflect on one approach taken in the
17
18 23 development and supply of chlorhexidine digluconate 7.1% w/w gel (equivalent to 4% w/w
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20 24 chlorhexidine) for neonatal cord care. We describe and analyse the steps taken by GSK to increase
21
22 25 access to chlorhexidine gel, including partnering with the I-NGO Save the Children in Western Kenya.
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24 26 Learning points gained along the journey are shared, together with subsequent steps taken to
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26 27 increase access, with the aim of making recommendations that may be applicable to similar
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28 28 enterprises in the future.
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3 30 **KEY MESSAGES**
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- 6 31 • Barriers to medicine access in low-resource settings are common; to address this, effective
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8 32 partnerships are required. Here we describe learnings from a multisectoral collaboration to
9
10 33 develop and supply chlorhexidine gel for neonatal cord care in Western Kenya.
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12
13 34 • Insights and learnings from service users and context-based development partners are
14
15 35 critical throughout a product's lifecycle to optimise suitability and acceptability.
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17 36 • Manufacturing processes should be simple to enable transfer to local manufacturers but
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19 37 may fail without proactive engagement strategies to stimulate demand and interest.
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22 38 • Sustainable side-effect reporting/pharmacovigilance is essential when introducing a new
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24 39 medicine in resource-limited settings where side-effect-reporting mechanisms may not be
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26 40 robust.
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29 41 • Integrating new commodities is complex. Governmental commitment and actions to
30
31 42 improve service supply, stimulate demand and sustain community-level engagement,
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33 43 creates better conditions for adoption.
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37 45 **Keywords (1–5):** Public health; Neonatal health; Health policy; Health education and promotion;
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40 46 Prevention strategies
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48 INTRODUCTION

49 The World Health Organization (WHO) defines essential medicines as those that “satisfy the priority
50 health care needs of the population”. [1] As such, they are crucial for saving lives, promoting health
51 and achieving sustainable development: they must be both available and affordable, in appropriate
52 dosages and with assured quality. [2] However, access to essential medicines in low- and middle-
53 income countries (LMICs) remains a significant problem, and such countries face numerous barriers
54 to access.

55 PARTNERSHIPS TO ADDRESS BARRIERS TO MEDICINES ACCESS

56 The scale, potential and contribution of the private sector towards the United Nations (UN)
57 Sustainable Development Goal (SDG) 3 (Good Health and Well-Being) to achieve universal health
58 coverage and overcome obstacles for accessing essential medicines in LMICs has been an important
59 and recurring focus of discussion. [3] Innovative cross-sectoral partnerships may leverage the
60 complementary expertise of different partners to ensure sustainability of access while also helping
61 to share risk. Here we reflect upon a partnership between GSK, Save the Children (STC) and other
62 stakeholders to increase access to chlorhexidine digluconate 7.1% (CHX) gel (included in the WHO
63 list of essential medicines) for neonatal cord care in Western Kenya. Lessons learned from this
64 partnership and a Managed Access Programme (MAP) are shared, with the aim of making key
65 recommendations that may be of relevance for similar projects in the future. For the interested
66 reader, a more detailed summary of learnings can be found here:

67 [https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned-](https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned-document.pdf)
68 [document.pdf](https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned-document.pdf). **Figure 1** summarises key steps in the programme. [4]

69 NEWBORN CORD CARE IN LMICs

70 In 2018, an estimated 15% of all neonatal deaths globally were due to sepsis, with the overall
71 highest incidence in low-income countries. [5] Newborns in LMICs – where births commonly occur at
72 home without trained healthcare workers – are susceptible to infection, with the newly cut umbilical

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3 73 cord representing a frequent bacterial entry point.[6] The efficacy of CHX 7.1% solution for the
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5 74 prevention of umbilical cord infection was demonstrated by three community-based randomised
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7 75 controlled trials in South Asia.[7,8,9] WHO recommends the use of CHX in settings with high
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9 76 neonatal mortality rates (>30 deaths/1,000 live births) or to replace harmful traditional cord care
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11 77 substances.[10] This followed successful development, field-trialling and scale-up of CHX gel in South
12
13 78 Asia, most notably in Nepal.[11] The UN estimated that if high-quality affordable CHX was supplied
14
15 79 to 50 resource-limited countries, 422,000 neonatal lives could be saved over a 5-year period.[12]
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20 80 **ENHANCING ACCESS TO CHX FOR NEWBORN CORD CARE IN KENYA THROUGH A PUBLIC-** 21 22 81 **PRIVATE PARTNERSHIP**

23
24 82 In 2012, in response to these needs, GSK set out to develop a not-for-profit, quality assured gel
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26 83 formulation of chlorhexidine digluconate 7.1% w/w gel (equivalent to 4% w/w chlorhexidine) -
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28 84 referred to as CHX suitable for use in resource-limited countries that could pass stringent regulatory
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30 85 review. Insights gathered during development suggested that a gel rather than a liquid formulation
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32 86 would increase ease of use. With access in mind, the formulation was kept as simple as possible to
33
34 87 enable local manufacturers to produce an identical product to both increase global CHX supply and
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36 88 enable a sustainable supply. In 2016, following an accelerated review, GSK's CHX gel was granted a
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38 89 positive opinion by the European Medicines Agency (EMA) which supported national registrations
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40 90 **(Figure 1).**[4]
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45 91 In Kenya, neonatal mortality contributes to over 40% of child deaths,[13] with infection a leading
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47 92 cause.[14] Although the national neonatal mortality rate in Kenya is below the WHO threshold for
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49 93 recommending CHX, wide regional disparities exist with high levels of home deliveries and harmful
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51 94 traditional cord-care practices in some regions. Following a request from the Kenyan Ministry of
52
53 95 Health (MoH) for early access to CHX gel in preparation for national scale-up, GSK worked closely
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55 96 with STC, who partnered with the Bungoma County Department of Health to implement a MAP and
56
57 97 facilitated collection of insights on user experiences and practices. The MAP provided opportunities
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3 98 to understand acceptability of CHX gel among healthcare providers and mothers, examine factors
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5 99 influencing provision and uptake, and determine acceptability of information, education and
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7 100 communication materials.[15, 16] In parallel, the Kenyan MoH led development and dissemination
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9 101 of national guidelines and updated the Kenya essential medicines list to include CHX.
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12 102 STC, Amref Health Africa and the Kenyan MoH (Division of Neonatal and Child Health), with
13
14 103 engagement from the County First Ladies Association,[17] subsequently partnered to perform
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16 104 advocacy and sensitisation work. This led to the development of national guidelines, healthcare
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18 105 worker training, development of educational materials and job aides, and the inclusion of CHX in the
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20 106 *Mother and Child Health Handbook*, a parent-held record of vaccination, growth and advice, offered
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22 107 in Kenya to all new parents.[18] Crucially, STC and the other partners fostered sustained community
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24 108 engagement, which was key to building trust and overcoming deep-rooted cultural practices about
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26 109 cord care among families and healthcare workers.
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31 110 At a county level, local advocacy led Bungoma and another county, Busia, to incorporate CHX for
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33 111 cord care into their county-specific guidelines and ensured funds were secured to support routine
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35 112 procurement of locally manufactured CHX through the national supply chain system, thereby
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37 113 encouraging sustainability. Additionally, a pharmacovigilance training model, jointly disseminated by
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39 114 GSK and STC, successfully generated short-term safety information for CHX gel during the MAP,
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41 115 which complemented the well-established safety profile of CHX products.
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45 116 In order to facilitate the transfer of technical and quality know-how to multiple local manufacturers,
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47 117 an agreement with United States Pharmacopeia (USP) through the Promoting the Quality of
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49 118 Medicines programme funded by the United States Agency for International Development,[19] was
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51 119 established. This aimed to transfer the technical know-how to a team of experts dedicated to
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53 120 helping LMICs strengthen the quality, manufacturing and regulatory systems that are required to
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55 121 ensure the quality and increase the supply of essential medicines.
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122 LESSONS LEARNED

123 Innovation and partnership working have characterised the development and distribution of CHX gel
124 in LMICs from the outset. Established in 2014, the CHX Working Group (CWG) – comprising
125 manufacturers, international non-governmental organisations (I-NGOs), universities and
126 governments – was convened by the non-profit organisation PATH to advance the use of CHX
127 through advocacy and technical assistance. Insights from CWG members contributed to the decision
128 to package CHX gel in single-dose sachets to facilitate ease of use and optimal dose application to
129 avoid retention of excess gel for alternative uses, and inclusion of pictorial instructions to reinforce
130 appropriate use in low literacy settings.

131 Generating these insights as early as possible is recommended; however, it is also important to
132 continue to gather information throughout the lifecycle of the medicine during and after the
133 development pathway and adapt accordingly. For example, reports of other chlorhexidine solutions
134 and gel products being mistaken for eye treatments and causing irreversible eye-injury, including
135 blindness, reinforced the importance of suitable packaging, labelling and appropriate warnings, as
136 detailed in the 2015 WHO Alert.[20]

137 The formulation and manufacturing process for CHX gel was developed to be as simple as possible
138 while adhering to high quality standards, with control strategies in place to minimise formation of
139 impurities, in particular the potential human carcinogen 4-chloroaniline.[21] It was essential the
140 manufacturing process was easily transferable to local manufacturers without compromising quality.
141 Working with an organisation like USP can greatly facilitate the transfer of technical and quality
142 know-how to multiple local manufacturers, allowing efficient resource use and enhancing
143 sustainability, while complying with quality standards. However, even with technical transfer details
144 freely available,[22] a simple manufacturing process may not be sufficient, and thus additional
145 proactive strategies may be required to engage with local manufacturers to stimulate demand and
146 interest in new products.

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3 147 The regulatory environment is also highly complex and can be challenging. Although a fast-track
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5 148 positive opinion of CHX gel was achieved under the EMA's Article 58 process,[23] in some instances
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7 149 national registrations took in excess of 2 years. Humanitarian organisations are often the primary
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10 150 procurers of essential medicines in LMICs, adhering to strict quality standards for the medicines they
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12 151 procure. Generally, this requires a product to be approved by a stringent regulatory authority or
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14 152 adherence to the WHO prequalification process. Thus, greater alignment between the EMA and
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16 153 WHO may hasten access to other essential medicines in LMICs.

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20 154 As more medicines are developed in response to diseases common to resource-limited settings,
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22 155 sustainable pharmacovigilance is a concern. A low-intervention pharmacovigilance training model
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24 156 was jointly and successfully disseminated by GSK and STC in Kenya; however, further improvements
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26 157 in underlying healthcare systems and new multi-stakeholder initiatives, such as the WHO Project 3-
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28 158 S,[24] may enable local stakeholders to play a greater role in long-term safety monitoring in the
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31 159 future.

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34 160 Despite high user acceptability, a relatively supportive policy environment and availability of locally
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36 161 manufactured product in Kenya, CHX products still fail to reach some newborns who would benefit
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38 162 most, as a consequence of policies that inadvertently prevent CHX from easily reaching babies born
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40 163 at home where impact on infection might be greatest. This highlights the importance of ensuring
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42 164 that healthcare policies are not in conflict but promote equitable approaches to context-based
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44 165 public health procurement and access to interventions that strengthen the effectiveness and reach
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46 166 of maternal and neonatal care.

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50 167 Two randomised controlled trials of chlorhexidine in sub-Saharan Africa (Tanzania and Zambia)[25,
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52 168 26] failed to show efficacy of CHX in reducing neonatal mortality, although one study did
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54 169 demonstrate significantly reduced rates of omphalitis (cord infection) following CHX use. Participants
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56 170 in both studies were encouraged to keep umbilical cords clean and dry which is likely to have led to
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59 171 lower mortality in both the CHX and control groups. Aligned to the recently updated WHO
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3 172 Guidelines,[27] decisions on targeted CHX roll-out should be considered in the context of other
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5 173 educational and healthcare provision practices in that region, and prevalence of harmful substance
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7 174 application on cords.
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10 175 Evidence of efficacy and safety is crucial to maintain confidence in any product. The aforementioned
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12 176 WHO safety alert relating to errors in administration reinforced the need for education and training
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14 177 on appropriate use and the importance of differential packaging of the product and patient
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16 178 information. However, the safety alert, taken together with data from the two previously described
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18 179 clinical trials in sub-Saharan Africa,[25, 26] is likely to have contributed to hesitancy among some
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20 180 governments to implement CHX more widely despite the successful introduction and long-term use
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22 181 in some South Asian countries.
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27 182 The integration of a new commodity in a low-resource setting with traditional customs, as is the case
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29 183 for umbilical cord care, is a complex process. A top-down approach from government may be
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31 184 insufficient for a product to be adopted and accepted. Trusted field partners can work effectively
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33 185 with the spectrum of stakeholder groups to ensure the context and perspectives of community users
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35 186 and other actors are represented and accounted for. Changing knowledge, attitudes and practices is
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37 187 required at all levels. A combined approach to improve service supply and demand (e.g. provision of
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39 188 training for healthcare workers and local campaigns to raise awareness among mothers) and
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41 189 sustained community-level engagement, creates better conditions for a product to be successfully
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43 190 adopted and accepted.
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48 191 The uptake of CHX products for cord care has been slow in high-need countries due to many factors,
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50 192 including lack of awareness and demand from end users, competing county demands and
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52 193 inadequate resources. Limited funding for essential medicines, a challenge in many LMICs, has
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54 194 delayed the national scale-up of CHX in Kenya and many other countries, sometimes necessitating
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56 195 difficult procurement choices to be made, even between medicines that are deemed essential.
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3 196 Locally manufactured CHX has helped to increase access in Kenya but there remains a need for
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5 197 continuous, sustained long-term effort to ensure uptake of essential medicines such as CHX.
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8 198 **CONCLUSIONS**

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11 199 Innovative partnerships are required throughout the lifecycle of a new intervention to ensure
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13 200 sustainable access to essential medicines in LMICs. Pharmaceutical companies, funders,
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15 201 governments, I-NGOs and other key stakeholders need to integrate their unique expertise to inform
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17 202 the design and implementation stages. For example, market awareness and community sensitization
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19 203 initiated in parallel to product development and regulatory harmonization would accelerate
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21 204 availability and uptake. Ongoing partnerships with in-country stakeholders would enable continued
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23 205 learnings and optimization. Through this, realisation of the UN's SDG of achieving universal health
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25 206 coverage, and a world where all people have equitable access to quality, essential healthcare
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27 207 without risk of financial hardship by 2030, can be greatly enhanced.
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251 **REFERENCES**

- 252 1. World Health Organization. The selection and use of essential medicines : report of the WHO
253 Expert Committee, 2002 : (including the 12th model list of essential medicines), 2003. Available:
254 <https://apps.who.int/iris/handle/10665/42620> [Accessed 26 January 2022].
- 255 2. Ozawa S, Shankar R, Leopold C, *et al.* Access to medicines through health systems in low-
256 and middle-income countries. *Health Policy Plan* 2019;34(Supplement_3):iii1-iii3.
257 <https://doi.org/10.1093/heapol/czz119>.
- 258 3. United Nations. Sustainable development goals; Goal 3: Ensure healthy lives and promote
259 well-being for all at all ages, 2019. Available: <https://www.un.org/sustainabledevelopment/health/>
260 [Accessed 27 August 2019].
- 261 4. Save the Children. Increasing access to essential medicines through partnership: experience
262 in developing and delivering chlorhexidine for newborn cord care, 2021. Available:
263 [https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned-](https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned-document.pdf)
264 [document.pdf](https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned-document.pdf) [Accessed 11 May 2022].
- 265 5. World Health Organization. Global report on the epidemiology and burden of sepsis: current
266 evidence, identifying gaps and future directions, 2020. Available:
267 <https://apps.who.int/iris/rest/bitstreams/1302383/retrieve> [Accessed 28 April 2022].
- 268 6. Coffey PS, Brown SC. Umbilical cord-care practices in low- and middle-income countries: a
269 systematic review. *BMC Pregnancy Childbirth* 2017;17(1):68. <https://10.1186/s12884-017-1250-7>.
- 270 7. Arifeen SE, Mullany LC, Shah R, *et al.* The effect of cord cleansing with chlorhexidine on
271 neonatal mortality in rural Bangladesh: a community-based, cluster-randomised trial. *Lancet*
272 2012;379(9820):1022-8. [https://doi.org/10.1016/s0140-6736\(11\)61848-5](https://doi.org/10.1016/s0140-6736(11)61848-5).
- 273 8. Soofi S, Cousens S, Imdad A, *et al.* Topical application of chlorhexidine to neonatal umbilical
274 cords for prevention of omphalitis and neonatal mortality in a rural district of Pakistan: a
275 community-based, cluster-randomised trial. *Lancet* 2012;379(9820):1029-36.
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- 1
2
3 277 9. Mullany LC, Darmstadt GL, Khatri SK, *et al.* Topical applications of chlorhexidine to the
4
5 278 umbilical cord for prevention of omphalitis and neonatal mortality in southern Nepal: a community-
6
7 279 based, cluster-randomised trial. *Lancet* 2006;367(9514):910-8. <https://dx.doi.org/10.1016%2FS0140->
8
9 280 6736(06)68381-5.
- 11
12 281 10. World Health Organization. WHO recommendations on newborn health; guidelines
13
14 282 approved by the WHO guidelines review committee 2017. Available:
15
16 283 <https://apps.who.int/iris/bitstream/handle/10665/259269/WHO-MCA-17.07->
17
18 284 [eng.pdf;jsessionid=D842C772FDA84BBD83CF9A4142D2433F?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/259269/WHO-MCA-17.07-eng.pdf;jsessionid=D842C772FDA84BBD83CF9A4142D2433F?sequence=1) [Accessed 22 November
19
20 285 2019].
- 23 286 11. Tuladhar S. Chlorhexidine in Nepal: A Public-Private Partnership Case Study, 2013. Available:
24
25 287 [https://www.healthynewbornnetwork.org/hnn-content/uploads/PPP_for_CHX_program_in_Nepal_-](https://www.healthynewbornnetwork.org/hnn-content/uploads/PPP_for_CHX_program_in_Nepal_-_v6-_SHLK_edits_07242013_1-2.pdf)
26
27 288 [v6- SHLK edits 07242013 1-2.pdf](https://www.healthynewbornnetwork.org/hnn-content/uploads/PPP_for_CHX_program_in_Nepal_-_v6-_SHLK_edits_07242013_1-2.pdf) [Accessed November 2021].
- 29
30 289 12. United Nations. UN commission on life-saving commodities for women and children:
31
32 290 commissioners' report, 2012. Available: <https://www.unfpa.org/sites/default/files/pub->
33
34 291 [pdf/Final%20UN%20Commission%20Report_14sept2012.pdf](https://www.unfpa.org/sites/default/files/pub-pdf/Final%20UN%20Commission%20Report_14sept2012.pdf) [Accessed 27 August 2019].
- 36
37 292 13. United Nations Children's Fund and the World Health Organization. Tracking progress
38
39 293 towards universal coverage for reproductive, newborn and child health, 2017. Available:
40
41 294 <https://www.countdown2030.org/pdf/Countdown-2030-complete-with-profiles.pdf> [Accessed 14
42
43 295 July 2021].
- 45
46 296 14. Murphy GAV, Waters D, Ouma PO, *et al.* Estimating the need for inpatient neonatal services:
47
48 297 an iterative approach employing evidence and expert consensus to guide local policy in Kenya. *BMJ*
49
50 298 *Glob Health* 2017;2(4):e000472. <https://10.1136/bmjgh-2017-000472>.
- 52
53 299 15. Obare F, Abuya T, Musika S, *et al.* Kenya signature programme endline evaluation report:
54
55 300 Bungoma, Busia and Wajir counties. Nairobi: population council and Save the Children, 2018.

- 1
2
3 301 16. Muriuki A, Obare F, Ayieko B, *et al.* Health care providers' perspectives regarding the use of
4
5 302 chlorhexidine gel for cord care in neonates in rural Kenya: implications for scale-up. *BMC Health Serv*
6
7 303 *Res* 2017;17(1):305. <https://10.1186/s12913-017-2262-8>.
8
9
10 304 17. County First Ladies Association, CFLA, Available: <https://cfla.or.ke/> [Accessed 8 September
11
12 305 2021].
13
14 306 18. Republic of Kenya Ministry of Health. Mother and child health handbook, 2020. Available:
15
16 307 [https://www.kenyapaediatric.org/e.cd/wp-content/plugins/pdfjs-viewer-](https://www.kenyapaediatric.org/e.cd/wp-content/plugins/pdfjs-viewer-shortcode/pdfjs/web/viewer.php?file=/ecd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true)
17
18 308 [shortcode/pdfjs/web/viewer.php?file=/ecd/wp-content/uploads/2021/04/Mother-Child-Health-](https://www.kenyapaediatric.org/e.cd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true)
19
20 309 [Handbook-MOH-NEW-LAYOUT-10th-Sep-](https://www.kenyapaediatric.org/e.cd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true)
21
22 310 [2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true](https://www.kenyapaediatric.org/e.cd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true) [Accessed 13 January 2021].
23
24 311 19. United States Pharmacopeia. The United States Pharmacopeia, 2019. Available:
25
26 312 <https://www.usp.org/> [Accessed 19 September 2019].
27
28 313 20. World Health Organisation. Chlorhexidine 7,1% digluconate (CHX) aqueous solution or gel
29
30 314 (10ml): Reports of serious eye injury due to errors in administration, 2020. Available:
31
32 315 [https://www.who.int/news/item/28-08-2020-chlorhexidine-7-1-digluconate-\(chx\)-aqueous-solution-](https://www.who.int/news/item/28-08-2020-chlorhexidine-7-1-digluconate-(chx)-aqueous-solution-or-gel-(10ml)-reports-of-serious-eye-injury-due-to-errors-in-administration)
33
34 316 [or-gel-\(10ml\)-reports-of-serious-eye-injury-due-to-errors-in-administration](https://www.who.int/news/item/28-08-2020-chlorhexidine-7-1-digluconate-(chx)-aqueous-solution-or-gel-(10ml)-reports-of-serious-eye-injury-due-to-errors-in-administration) [Accessed 20 January
35
36 317 2022].
37
38 318 21. World Health Organization. Concise international chemical assessment document 48; 4-
39
40 319 chloroaniline, 2003. Available: <https://apps.who.int/iris/handle/10665/42605> [Accessed 27 August
41
42 320 2019].
43
44 321 22. PQM. GSK Chlorhexidine Digluconate (7.1%) Gel Technology Transfer Report. Rockville, MD;
45
46 322 2018.
47
48 323 23. European Medicines Agency. Medicines for use outside the EU - EU-M4all, 2020. Available:
49
50 324 [https://www.ema.europa.eu/en/documents/leaflet/infographic-medicines-use-outside-eu-eu-](https://www.ema.europa.eu/en/documents/leaflet/infographic-medicines-use-outside-eu-eu-m4all_en.pdf)
51
52 325 [m4all_en.pdf](https://www.ema.europa.eu/en/documents/leaflet/infographic-medicines-use-outside-eu-eu-m4all_en.pdf) [Accessed 15 December 2021].
53
54
55
56
57
58
59
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2
3 326 24. World Health Organization. Safety of medicines. Priming resource-limited countries for
4
5 327 pharmacovigilance, 2017. Available: <https://apps.who.int/iris/handle/10665/330944> [Accessed 28
6
7 328 August 2019].
- 9
10 329 25. Sazawal S, Dhingra U, Ali Said M, *et al.* Efficacy of chlorhexidine application to umbilical cord
11
12 330 on neonatal mortality in Pemba, Tanzania: a community-based randomised controlled trial. *Lancet*
13
14 331 *Glob Health* 2016;4(11):e837-44. [https://10.1016/S2214-109X\(16\)30223-6](https://10.1016/S2214-109X(16)30223-6).
- 16 332 26. Semrau KEA, Julie Herlihy, Caroline Grogan, *et al.* Effectiveness of 4% chlorhexidine umbilical
17
18 333 cord care on neonatal mortality in Southern Province, Zambia (ZamCAT): a cluster-randomised
19
20 334 controlled trial. *Lancet Glob Health* 2016;4(11):e827-36. <https://doi.org/10.1016/s2214->
21
22 335 109x(16)30215-7.
- 25 336 27. World Health Organization. WHO recommendations on maternal and newborn care for a
26
27 337 positive postnatal experience, 2022. Available:
28
29 338 <https://www.who.int/publications/i/item/9789240045989> [Accessed 9 May 2022].
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3 **Figure 1.** Increasing access to essential medicines through partnership: the journey of
4 chlorhexidine.[4]
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Confidential: For Review Only



Increasing access to essential medicines through partnership

The journey of chlorhexidine



Save the Children

HELPING TO SAVE ONE MILLION CHILDREN'S LIVES

Newborns in resource-limited countries, where births frequently occur at home without trained healthcare workers, are particularly susceptible to infection through the newly cut umbilical cord. Use of chlorhexidine digluconate (CHX) for umbilical cord care can help to prevent infection.



2011

WHO list CHX as a priority medicine

CHX listed by the WHO as a priority medicine for children's health, requiring further R&D

2012

UN call to action

UN Commission identified CHX as a life-saving commodity for women's and children's health

UN called for additional manufacturers to supply high-quality, affordable CHX for newborn cord care that, with widened access across 50 resource-limited countries, could save 422,000 lives over 5 years

GSK began to reformulate their existing CHX product into a gel suitable for use in resource-limited settings

2013

A partnership with a mission

Partnership established between GSK and Save the Children (STC) to find new ways to reduce childhood mortality from preventable and treatable diseases

2014

Partnerships in action

The Chlorhexidine Working Group began coordinating approaches to advancing use of CHX for umbilical cord care via a collaboration with manufacturers, international NGOs, governments and universities
STC and others worked with the Kenyan Ministry of Health to develop national guidelines on the use of CHX for cord cleansing

2016

Managed Access Programme (MAP) established in Kenya

GSK and STC partnered to implement a MAP in Kenya, which ran to 2018. Insights from healthcare worker interviews, user focus groups and informal local feedback informed the CHX gel formulation, packaging and patient information materials developed by GSK

Acceptability of CHX gel was very high (99%) from both service providers (n=39) and mothers (n=479) and 92% of mothers (n=479) stated they would recommend the product to other mothers

Positive opinion by the EMA

Following accelerated review, GSK's CHX gel was granted a positive opinion by the EMA, facilitating approval in 19 countries, including Kenya (in 2017)



2018

Learnings shared

Learnings from the Kenyan MAP successfully applied to a 2-year CHX implementation research project in Papua New Guinea. Agreement with USP/USAID established with aim to transfer CHX technical know-how to LMICs

2021

CHX supplied locally and widely used

GSK stopped manufacturing CHX gel because generic manufacturers are now supplying affordable product in sufficient volumes to meet local demand

Locally-manufactured CHX is now available in all counties in Kenya and all newborns receive the protection provided by CHX

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4 1 **Increasing access to essential medicines through partnership: experience in**
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6 2 **developing and delivering chlorhexidine gel for newborn cord care**
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16 **ABSTRACT (149/300)**

17 Sustainable access to essential medicines in low- and middle-income countries requires innovative
18 cross-sectoral collaboration throughout the lifecycle of a medicine. Partnerships are essential to
19 address the systemic challenges of global health and health inequity. Pharmaceutical companies,
20 funders, governments, international non-governmental organisations (I-NGOs) and other key
21 stakeholders can leverage, through effective partnership working, their unique expertise to help
22 drive innovation and share learnings and risks. Here we reflect on one approach taken in the
23 development and supply of chlorhexidine digluconate 7.1% w/w gel (equivalent to 4% w/w
24 chlorhexidine) for neonatal cord care. We describe and analyse the steps taken by
25 [GlaxoSmithKlineGSK](#) to increase access to chlorhexidine gel, including partnering with the I-NGO
26 Save the Children in Western Kenya. Learning points gained along the journey are shared, together
27 with subsequent steps taken to increase access, with the aim of making recommendations that may
28 be applicable to similar enterprises in the future.

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3 30 **KEY MESSAGES**
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- 6 31 • Barriers to medicine access in low-resource settings are common; to address this, effective
7
8 32 partnerships are required. Here we describe learnings from a multisectoral collaboration to
9
10 33 develop and supply chlorhexidine gel for neonatal cord care in Western Kenya.
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13 34 • Insights and learnings from service users and context-based development partners are
14
15 35 critical throughout a product's lifecycle to optimise suitability and acceptability.
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17 36 • Manufacturing processes should be simple to enable transfer to local manufacturers but
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19 37 may fail without proactive engagement strategies to stimulate demand and interest.
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22 38 • Sustainable side-effect reporting/pharmacovigilance is essential when introducing a new
23
24 39 medicine in resource-limited settings where side-effect-reporting mechanisms may not be
25
26 40 robust.
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29 41 • Integrating new commodities is complex. Governmental commitment and actions to
30
31 42 improve service supply, stimulate demand and sustain community-level engagement,
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33 43 creates better conditions for adoption.
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36 44

37 45 **Keywords (1–5):** Public health; Neonatal health; Health policy; Health education and promotion;
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40 46 Prevention strategies
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48 INTRODUCTION

49 The World Health Organization (WHO) defines essential medicines as those that “satisfy the priority
50 health care needs of the population”.^[1] As such, they are crucial for saving lives, promoting health
51 and achieving sustainable development: they must be both available and affordable, in appropriate
52 dosages and with assured quality.^[2] However, access to essential medicines in low- and middle-
53 income countries (LMICs) remains a significant problem, and such countries face numerous barriers
54 to access.

55 PARTNERSHIPS TO ADDRESS BARRIERS TO MEDICINES ACCESS

56 The scale, potential and contribution of the private sector towards the United Nations (UN)
57 Sustainable Development Goal (SDG) 3 (Good Health and Well-Being) to achieve universal health
58 coverage and overcome obstacles for accessing essential medicines in LMICs has been an important
59 and recurring focus of discussion.^[3] Innovative cross-sectoral partnerships may leverage the
60 complementary expertise of different partners to ensure sustainability of access while also helping
61 to share risk. Here we reflect upon a partnership between ~~GlaxoSmithKline (GSK)~~^{7z}, Save the Children
62 (STC) and other stakeholders to increase access to chlorhexidine digluconate 7.1% (CHX) gel
63 (included in the WHO list of essential medicines) for neonatal cord care in Western Kenya. Lessons
64 learned from this partnership and a Managed Access Programme (MAP) are shared, with the aim of
65 making key recommendations that may be of relevance for similar projects in the future. For the
66 interested reader, a more detailed summary of learnings can be found here:
67 <https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned->
68 [document.pdf](https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned-document.pdf). **Figure 1** summarises key steps in the programme.^[4]

69 NEWBORN CORD CARE IN LMICs

70 In 2018, an estimated 15% of all neonatal deaths globally were due to sepsis, with the overall
71 highest incidence in low-income countries.^[5] Newborns in LMICs – where births commonly occur at
72 home without trained healthcare workers – are susceptible to infection, with the newly cut umbilical

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3 73 cord representing a frequent bacterial entry point.[4] ~~To address this need, the WHO recommends~~
4 ~~application~~6] The efficacy of CHX 7.1% solution for the prevention of umbilical cord infection was
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6 demonstrated by three community-based randomised controlled trials in South Asia.[7,8,9] WHO
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8 recommends the use of CHX in settings with high neonatal mortality rates (>30 deaths/1,000 live
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12 76 births) or to replace harmful traditional cord care substances.[510] This followed successful
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14 77 development, field-trialling and scale-up of CHX gel in South Asia, most notably in Nepal.[611] The
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16 78 UN estimated that if high-quality affordable CHX was supplied to 50 resource-limited countries,
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18 79 UN estimated that if high-quality affordable CHX was supplied to 50 resource-limited countries,
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20 80 422,000 neonatal lives could be saved over a 5-year period.[712]

81 **ENHANCING ACCESS TO CHX FOR NEWBORN CORD CARE IN KENYA THROUGH A PUBLIC-** 82 **PRIVATE PARTNERSHIP**

83 In 2012, in response to these needs, GSK set out to develop a not-for-profit, quality assured gel
84 formulation of chlorhexidine digluconate 7.1% CHXw/w gel (equivalent to 4% w/w
85 ~~CHX~~chlorhexidine) - referred to as CHX suitable for use in resource-limited countries that could pass
86 stringent regulatory review. Insights gathered during development suggested that a gel rather than a
87 liquid formulation would increase ease of use. With access in mind, the formulation was kept as
88 simple as possible to enable local manufacturers to produce an identical product to both increase
89 global CHX supply and enable a sustainable supply. In 2016, following an accelerated review, GSK's
90 CHX gel was granted a positive opinion by the European Medicines Agency (EMA) which supported
91 national registrations **(Figure 1)**.[4]

92 In Kenya, neonatal mortality contributes to over 40% of child deaths,[813] with infection a leading
93 cause.[914] Although the national neonatal mortality rate in Kenya is below the WHO threshold for
94 recommending CHX, wide regional disparities exist with high levels of home deliveries and harmful
95 traditional cord-care practices in some regions. Following a request from the Kenyan Ministry of
96 Health (MoH) for early access to CHX gel in preparation for national scale-up, GSK worked closely
97 with STC, who partnered with the Bungoma County Department of Health to implement a MAP and

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3 98 facilitated collection of insights on user experiences and practices. The MAP provided opportunities
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5 99 to understand acceptability of CHX gel among healthcare providers and mothers, examine factors
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8 100 influencing provision and uptake, and determine acceptability of information, education and
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10 101 communication materials.^[10, 11, 15, 16] In parallel, the Kenyan MoH led development and
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12 102 dissemination of national guidelines and updated the Kenya essential medicines list to include CHX.
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15 103 STC, Amref Health Africa and the Kenyan MoH (Division of Neonatal and Child Health), with
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17 104 engagement from the County First Ladies Association,^[127]; subsequently partnered to perform
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19 105 advocacy and sensitisation work. This led to the development of national guidelines, healthcare
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21 106 worker training, development of educational materials and job aides, and the inclusion of CHX in the
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23 107 *Mother and Child Health Handbook*, a parent-held record of vaccination, growth and advice, offered
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25 108 in Kenya to all new parents.^[1318] Crucially, STC and the other partners fostered sustained
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27 109 community engagement, which was key to building trust and overcoming deep-rooted cultural
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29 110 practices about cord care among families and healthcare workers.
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34 111 At a county level, local advocacy led Bungoma and another county, Busia, to incorporate CHX for
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36 112 cord care into their county-specific guidelines and ensured funds were secured to support routine
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38 113 procurement of locally manufactured CHX through the national supply chain system, thereby
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40 114 encouraging sustainability. Additionally, a pharmacovigilance training model, jointly disseminated by
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42 115 GSK and STC, successfully generated short-term safety information for CHX gel during the MAP,
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44 116 which complemented the well-established safety profile of CHX products.
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48 117 In order to facilitate the transfer of technical and quality know-how to multiple local manufacturers,
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50 118 an agreement with United States Pharmacopeia (USP) through the Promoting the Quality of
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52 119 Medicines programme funded by the United States Agency for International Development
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54 120 (USAID)^{[14], [19]} was established. - This aimed to transfer the technical know-how to a team of
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56 121 experts dedicated to helping LMICs strengthen the quality, manufacturing and regulatory systems
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58 122 that are required to ensure the quality and increase the supply of essential medicines.
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123 LESSONS LEARNED

124 Innovation and partnership working have characterised the development and distribution of CHX gel
125 in LMICs from the outset. Established in 2014, the CHX Working Group (CWG) – comprising
126 manufacturers, international non-governmental organisations (I-NGOs), universities and
127 governments – was convened by the non-profit organisation PATH to advance the use of CHX
128 through advocacy and technical assistance. Insights from CWG members contributed to the decision
129 to package CHX gel in single-dose sachets to facilitate ease of use and optimal dose application to
130 avoid retention of excess gel for alternative uses, and inclusion of pictorial instructions to reinforce
131 appropriate use in low literacy settings.

132 Generating these insights as early as possible is recommended; however, it is also important to
133 continue to gather information throughout the lifecycle of the medicine during and after the
134 development pathway and adapt accordingly. For example, reports of other chlorhexidine solutions
135 and gel products being mistaken for eye treatments and causing irreversible eye-injury, including
136 blindness, reinforced the importance of suitable packaging, labelling and appropriate warnings.^{[15,}
137 [as detailed in the 2015 WHO Alert.](#)^[20]

138 The formulation and manufacturing process for CHX gel was developed to be as simple as possible
139 while adhering to high quality standards, with control strategies in place to minimise formation of
140 impurities, in particular the potential human carcinogen 4-chloroaniline.^[16,21] It was essential the
141 manufacturing process was easily transferable to local manufacturers without compromising quality.

142 Working with an organisation like [United States Pharmacopoeia USP](#) can greatly facilitate the
143 transfer of technical and quality know-how to multiple local manufacturers, allowing efficient
144 resource use and enhancing sustainability, while complying with quality standards. However, even
145 with technical transfer details freely available^{[17],[22]} a simple manufacturing process may not be
146 sufficient, and thus additional proactive strategies may be required to engage with local
147 manufacturers to stimulate demand and interest in new products.

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3 148 The regulatory environment is also highly complex and can be challenging. Although a fast-track
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5 149 positive opinion of CHX gel was achieved under the EMA's Article 58 process^{[18],[23]} in some
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8 150 instances national registrations took in excess of 2 years. Humanitarian organisations are often the
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10 151 primary procurers of essential medicines in LMICs, adhering to strict quality standards for the
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12 152 medicines they procure. Generally, this requires a product to be approved by a stringent regulatory
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14 153 authority or adherence to the WHO prequalification process. Thus, greater alignment between the
15
16 154 EMA and WHO may hasten access to other essential medicines in LMICs.

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19 155 As more medicines are developed in response to diseases common to resource-limited settings,
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21 156 sustainable pharmacovigilance is a concern. A low-intervention pharmacovigilance training model
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23 157 was jointly and successfully disseminated by GSK and STC in Kenya; however, further improvements
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25 158 in underlying healthcare systems and new multi-stakeholder initiatives, such as the WHO Project 3-
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27 159 S^{[19],[24]} may enable local stakeholders to play a greater role in long-term safety monitoring in the
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30 160 future.

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33 161 Despite high user acceptability, a relatively supportive policy environment and availability of locally
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35 162 manufactured product in Kenya, CHX products still fail to reach some newborns who would benefit
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37 163 most, as a consequence of policies that inadvertently prevent CHX from easily reaching babies born
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39 164 at home where impact on infection might be greatest. This highlights the importance of ensuring
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41 165 that healthcare policies are not in conflict but promote equitable approaches to context-based
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43 166 public health procurement and access to interventions that strengthen the effectiveness and reach
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45 167 of maternal and neonatal care.

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50 168 Two randomised controlled trials of chlorhexidine in sub-Saharan Africa (Tanzania and Zambia)^{[20,}
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52 169 ^{21,25, 26]} failed to show efficacy of CHX in reducing neonatal mortality, although one study did
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54 170 demonstrate significantly reduced rates of omphalitis (cord infection) following CHX use.
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57 171 ~~However, Participants~~ in both studies, ~~all participants~~ were encouraged to keep umbilical cords clean
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59 172 and dry. ~~These improved cord care practices are~~ which is likely to have led to lower mortality in both
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3 173 the CHX and control groups, ~~emphasising that.~~ Aligned to the recently updated WHO Guidelines,[27]

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5 174 decisions on targeted CHX roll-out should be considered in the context of other educational and

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7 175 healthcare provision practices in that region, and prevalence of harmful substance application on

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9 176 CORDS.

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13 177 Evidence of efficacy and safety is crucial to maintain confidence in any product. The aforementioned

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15 178 WHO safety alert relating to errors in administration reinforced the need for education and training

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17 179 on appropriate use and the importance of differential packaging of the product and patient

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19 180 information. However, the safety alert, taken together with data from the two previously described

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21 181 clinical trials in sub-Saharan Africa [20, 21], [25, 26] is likely to have contributed to hesitancy among

22
23 182 some governments to implement CHX more widely despite the successful introduction and long-

24
25 183 term use in some South Asian countries.

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29 184 The integration of a new commodity in a low-resource setting with traditional customs, as is the case

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31 185 for umbilical cord care, is a complex process. A top-down approach from government may be

32
33 186 insufficient for a product to be adopted and accepted. Trusted field partners can work effectively

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35 187 with the spectrum of stakeholder groups to ensure the context and perspectives of community users

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37 188 and other actors are represented and accounted for. Changing knowledge, attitudes and practices is

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39 189 required at all levels. A combined approach to improve service supply and demand (e.g. provision of

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41 190 training for healthcare workers and local campaigns to raise awareness among mothers) and

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43 191 sustained community-level engagement, creates better conditions for a product to be successfully

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45 192 adopted and accepted.

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49 193 The uptake of CHX products for cord care has been slow in high-need countries due to many factors,

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51 194 including lack of awareness and demand from end users, competing county demands and

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53 195 inadequate resources. Limited funding for essential medicines, a challenge in many LMICs, has

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55 196 delayed the national scale-up of CHX in Kenya and many other countries, sometimes necessitating

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57 197 difficult procurement choices to be made, even between medicines that are deemed essential.

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3 198 Locally manufactured CHX has helped to increase access in Kenya but there remains a need for
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5 199 continuous, sustained long-term effort to ensure uptake of essential medicines such as CHX.
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8 200 **CONCLUSIONS**

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11 201 Innovative partnerships are required throughout the lifecycle of a new intervention to ensure
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13 202 sustainable access to essential medicines in LMICs. Pharmaceutical companies, funders,
14
15 203 governments, I-NGOs and other key stakeholders need to integrate their unique expertise to inform
16
17 204 the design and implementation stages. For example, market awareness and community sensitization
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19 205 initiated in parallel to product development and regulatory harmonization would accelerate
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21 206 availability and uptake. Ongoing partnerships with in-country stakeholders would enable continued
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23 207 learnings and optimization. Through this, realisation of the UN's SDG of achieving universal health
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25 208 coverage, and a world where all people have equitable access to quality, essential healthcare
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27 209 without risk of financial hardship by 2030, can be greatly enhanced.
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58
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255 **REFERENCES**

- 256 1. World Health Organization. The selection and use of essential medicines : report of the WHO
257 Expert Committee, 2002 : (including the 12th model list of essential medicines), 2003. Available:
258 <https://apps.who.int/iris/handle/10665/42620> [Accessed 26 January 2022].
- 259 2. Ozawa S, Shankar R, Leopold C, *et al.* Access to medicines through health systems in low-
260 and middle-income countries. *Health Policy Plan* 2019;34(Supplement_3):iii1-iii3.
261 <https://doi.org/10.1093/heapol/czz119>.
- 262 3. United Nations. Sustainable development goals; ~~g~~Goal 3 ~~targets, 2019~~: [Ensure healthy lives](#)
263 [and promote well-being for all at all ages, 2019](#). Available:
264 <https://www.un.org/sustainabledevelopment/health/> [Accessed 27 August 2019].
- 265 4. [Save the Children. Increasing access to essential medicines through partnership: experience](#)
266 [in developing and delivering chlorhexidine for newborn cord care, 2021](#). Available:
267 <https://www.savethechildren.org.uk/content/dam/gb/reports/umbipro-lessons-learned->
268 [document.pdf](#) [Accessed 11 May 2022].
- 269 5. [World Health Organization. Global report on the epidemiology and burden of sepsis: current](#)
270 [evidence, identifying gaps and future directions, 2020](#). Available:
271 <https://apps.who.int/iris/rest/bitstreams/1302383/retrieve> [Accessed 28 April 2022].
- 272 6. Coffey PS, Brown SC. Umbilical cord-care practices in low- and middle-income countries: a
273 systematic review. *BMC Pregnancy Childbirth* 2017;17(1):68. <https://10.1186/s12884-017-1250-7>.
- 274 57. [Arifeen SE, Mullany LC, Shah R, et al. The effect of cord cleansing with chlorhexidine on](#)
275 [neonatal mortality in rural Bangladesh: a community-based, cluster-randomised trial. *Lancet*](#)
276 [2012;379\(9820\):1022-8](#). [https://doi.org/10.1016/s0140-6736\(11\)61848-5](https://doi.org/10.1016/s0140-6736(11)61848-5).
- 277 8. [Soofi S, Cousens S, Imdad A, et al. Topical application of chlorhexidine to neonatal umbilical](#)
278 [cords for prevention of omphalitis and neonatal mortality in a rural district of Pakistan: a](#)
279 [community-based, cluster-randomised trial. *Lancet* 2012;379\(9820\):1029-36](#).
280 [https://doi.org/10.1016/s0140-6736\(11\)61877-1](https://doi.org/10.1016/s0140-6736(11)61877-1).

- 1
2
3 281 [9.](#) Mullany LC, Darmstadt GL, Khatri SK, *et al.* Topical applications of chlorhexidine to the
4
5 282 umbilical cord for prevention of omphalitis and neonatal mortality in southern Nepal: a community-
6
7 283 based, cluster-randomised trial. *Lancet* 2006;367(9514):910-8. <https://dx.doi.org/10.1016%2FS0140->
8
9 284 [6736\(06\)68381-5.](#)
- 10
11
12 285 [10.](#) World Health Organization. WHO recommendations on newborn health; [guidelines](#)
13
14 286 [approved by the WHO guidelines review committee](#) 2017. Available:
15
16 287 <https://apps.who.int/iris/bitstream/handle/10665/259269/WHO-MCA-17.07->
17
18 288 [eng.pdf;jsessionid=D842C772FDA84BBD83CF9A4142D2433F?sequence=1](#) [Accessed 22 November
19
20 289 2019].
- 21
22
23 290 [611.](#) Tuladhar S. Chlorhexidine in Nepal: A Public-Private Partnership Case Study; [2013.](#)
24
25 291 Available: <https://www.healthynewbornnetwork.org/hnn->
26
27 292 [content/uploads/PPP_for_CHX_program_in_Nepal_-v6_-SHLK_edits_07242013_1-2.pdf](#) [Accessed
28
29 293 November 2021].
- 30
31
32 294 [712.](#) United Nations. UN commission on life-saving commodities for women and children:
33
34 295 commissioners' report, 2012. Available: <https://www.unfpa.org/sites/default/files/pub->
35
36 296 [pdf/Final%20UN%20Commission%20Report_14sept2012.pdf](#) [Accessed 27 August 2019].
- 37
38
39 297 [813.](#) United Nations Children's Fund and [the](#) World Health Organization. Tracking progress
40
41 298 towards universal coverage for reproductive, newborn and child health: [The 2017 report](#), 2017.
42
43 299 Available: <https://www.countdown2030.org/pdf/Countdown-2030-complete-with-profiles.pdf>
44
45 300 [Accessed 14 July 2021].
- 46
47
48 301 [914.](#) Murphy GAV, Waters D, Ouma PO, *et al.* Estimating the need for inpatient neonatal services:
49
50 302 an iterative approach employing evidence and expert consensus to guide local policy in Kenya. *BMJ*
51
52 303 *Glob Health* 2017;2(4):e000472. [https://10.1136/bmjgh-2017-000472.](https://10.1136/bmjgh-2017-000472)
- 53
54
55 304 [1015.](#) Obare F, Abuya T, Musika S, *et al.* Kenya signature programme endline evaluation report:
56
57 305 Bungoma, Busia and Wajir counties. Nairobi: population council and [sSave the eChildren](#); [2018.](#)
- 58
59
60

- 1
2
3 306 ~~1416~~. Muriuki A, Obare F, Ayieko B, *et al*. Health care providers' perspectives regarding the use of
4
5 307 chlorhexidine gel for cord care in neonates in rural Kenya: implications for scale-up. *BMC Health Serv*
6
7 308 *Res* 2017;17(1):305. <https://10.1186/s12913-017-2262-8>.
9
10 309 ~~1217~~. County First Ladies Association, CFLA, Available: <https://cfla.or.ke/> [Accessed 8 September
11
12 310 2021].
13
14 311 ~~13~~.—~~18~~. Republic of Kenya Ministry of Health. Mother and child health handbook, 2020.
15
16 312 Available: [https://www.kenyapaediatric.org/ecd/wp-content/plugins/pdfjs-viewer-](https://www.kenyapaediatric.org/ecd/wp-content/plugins/pdfjs-viewer-shortcode/pdfjs/web/viewer.php?file=/ecd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true)
17
18 313 [shortcode/pdfjs/web/viewer.php?file=/ecd/wp-content/uploads/2021/04/Mother-Child-Health-](https://www.kenyapaediatric.org/ecd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true)
19
20 314 [Handbook-MOH-NEW-LAYOUT-10th-Sep-](https://www.kenyapaediatric.org/ecd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true)
21
22 315 [2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true](https://www.kenyapaediatric.org/ecd/wp-content/uploads/2021/04/Mother-Child-Health-Handbook-MOH-NEW-LAYOUT-10th-Sep-2020.pdf&dButton=true&pButton=true&oButton=false&sButton=true) [Accessed 13 January 2021].
23
24 316 ~~1419~~. United States Pharmacopeia. The United States Pharmacopeia~~72~~ 2019. Available:
25
26 317 <https://www.usp.org/> [Accessed 19 September 2019].
27
28 318 ~~1520~~. World Health Organisation. Chlorhexidine 7,1% digluconate (CHX) aqueous solution or gel
29
30 319 (10ml): Reports of serious eye injury due to errors in administration, 2020. Available:
31
32 320 [https://www.who.int/news/item/28-08-2020-chlorhexidine-7-1-digluconate-\(chx\)-aqueous-solution-](https://www.who.int/news/item/28-08-2020-chlorhexidine-7-1-digluconate-(chx)-aqueous-solution-or-gel-(10ml)-reports-of-serious-eye-injury-due-to-errors-in-administration)
33
34 321 [or-gel-\(10ml\)-reports-of-serious-eye-injury-due-to-errors-in-administration](https://www.who.int/news/item/28-08-2020-chlorhexidine-7-1-digluconate-(chx)-aqueous-solution-or-gel-(10ml)-reports-of-serious-eye-injury-due-to-errors-in-administration) [Accessed 20 January
35
36 322 2022].
37
38 323 ~~1621~~. World Health Organization. Concise international chemical assessment document 48~~2~~; 4-
39
40 324 chloroaniline, 2003. Available:
41
42 325 [https://wwwapps.who.int/ipcs/publications/cicad/en/cicad48.pdf](https://wwwapps.who.int/ipcs/publications/cicad/en/cicad48.pdf?ipcs/publications/cicad/en/cicad48.pdf/firis/handle/10665/42605)
43
44 326 [Accessed 27 August 2019].
45
46 327 ~~1722~~. PQM. GSK Chlorhexidine Digluconate (7.1%) Gel Technology Transfer Report. Rockville, MD;
47
48 328 2018.
49
50 329 ~~1823~~. European Medicines Agency. Medicines for use outside the EU - EU-M4all~~72~~ 2020. Available:
51
52 330 [https://www.ema.europa.eu/en/documents/leaflet/infographic-medicines-use-outside-eu-eu-](https://www.ema.europa.eu/en/documents/leaflet/infographic-medicines-use-outside-eu-eu-m4all_en.pdf)
53
54 331 [m4all_en.pdf](https://www.ema.europa.eu/en/documents/leaflet/infographic-medicines-use-outside-eu-eu-m4all_en.pdf) [Accessed 15 December 2021].
55
56
57
58
59
60

- 1
2
3 332 ~~1924~~. World Health Organization. Safety of medicines. Priming resource-limited countries for
4
5 333 pharmacovigilance, 2017. Available:
6
7 334 [https://wwwapps.who.int/medicines/publications/druginformation/issues/WHO_DI_31-4_Safety-](https://wwwapps.who.int/medicines/publications/druginformation/issues/WHO_DI_31-4_Safety-Medicines.pdf)
8
9 [Medicines.pdf](https://wwwapps.who.int/medicines/publications/druginformation/issues/WHO_DI_31-4_Safety-Medicines.pdf)[iris/handle/10665/330944](https://wwwapps.who.int/medicines/publications/druginformation/issues/WHO_DI_31-4_Safety-Medicines.pdf) [Accessed 28 August 2019].
10
11
12 336 ~~2025~~. Sazawal S, Dhingra U, Ali Said M, *et al*. Efficacy of chlorhexidine application to umbilical cord
13
14 337 on neonatal mortality in Pemba, Tanzania: a community-based randomised controlled trial. *Lancet*
15
16 338 *Glob Health* 2016;4(11):~~e827-e44~~[e837-44](https://doi.org/10.1016/S2214-109X(16)30223-6). [https://10.1016/S2214-109X\(16\)30223-6](https://doi.org/10.1016/S2214-109X(16)30223-6).
17
18
19 339 ~~2126~~. Semrau KEA, Julie Herlihy, Caroline Grogan, *et al*. Effectiveness of 4% chlorhexidine umbilical
20
21 340 cord care on neonatal mortality in Southern Province, Zambia (ZamCAT): a cluster-randomised
22
23 341 controlled trial. *Lancet Glob Health* 2016;4(11):~~e766-e8~~[e827-36](https://doi.org/10.1016/s2214-109x(16)30215-7). [https://doi.org/10.1016/s2214-](https://doi.org/10.1016/s2214-109x(16)30215-7)
24
25 [109x\(16\)30215-7](https://doi.org/10.1016/s2214-109x(16)30215-7).
26
27
28 343 ~~27~~. World Health Organization. WHO recommendations on maternal and newborn care for a
29
30 344 positive postnatal experience, 2022. Available:
31
32 345 <https://www.who.int/publications/i/item/9789240045989> [Accessed 9 May 2022].
33
34
35
36
37
38
39
40
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3 **Figure 1.** Increasing access to essential medicines through partnership: the journey of chlorhexidine-
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