



# How can we improve the quality of oxytocin?

## **Challenge: Oxytocin saves lives, but its quality is often compromised**

In low- and middle-income countries, the leading cause of maternal mortality, postpartum hemorrhage (PPH), is largely preventable and treatable by an effective and affordable drug. This drug, oxytocin, requires stable cold-chain infrastructure to maintain its quality. However cold-chain storage is often interrupted in these settings, routinely compromising drug potency and stability. When quality concerns keep a normally effective drug from saving lives, what can be done to improve drug quality?

Accelovate is a five-year, United States Agency for International Development (USAID)-funded program charged to increase availability of and access to lifesaving technologies and commodities in low-resource settings. In keeping with its mission, Accelovate addressed the challenge of improving oxytocin quality for the prevention and treatment of PPH.

## **Challenge Background: Oxytocin quality is challenged by production and infrastructure**

PPH refers to excessive bleeding after childbirth. Left untreated, it can lead to anemia, shock, and also death. It affects more than 8 million women and claims the lives of an estimated 69,000 women worldwide each year,<sup>1</sup> making it the leading cause of maternal mortality in low- and middle-income countries. Proper screening, prevention, and treatment for PPH can reduce global burden of maternal mortality.

Oxytocin, a uterotonic drug, is the first-line treatment for PPH and is recognized by the World Health Organization (WHO) as the safest and most effective medicine for preventing and treating PPH. Global policies recommend its use, and oxytocin is listed on WHO's Essential Medicines List as well as the 13 priority commodities as defined by the UN Commission on Life-Saving Commodities for Women and Children.<sup>2,3</sup> Also included on these lists is another uterotonic drug, misoprostol. Since oxytocin must be administered in a health facility but many women deliver

When poor quality diminishes a drug's ability to save lives, what can be done?

Oxytocin is effective but underused in many low- and middle-income countries, where about 99% of PPH deaths occur.



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outside of a facility, misoprostol is the recommended second-line drug for home deliveries.

Despite strong evidence and usage recommendations, **oxytocin is not universally used** in many low- and middle-income countries where about 99% of PPH deaths occur.<sup>4</sup> This is despite its low cost—about 20 cents for a prevention dose, and one dollar (US) for a treatment dose.<sup>5</sup>

However, **the true challenge with oxytocin is its quality**. Recent studies in Ghana and Indonesia demonstrated that a large percentage of oxytocin did not meet quality standards. In Ghana, 65.5% of tested samples did not meet quality standards, and in Indonesia, 11.5% of refrigerated samples failed assays for Active Pharmaceutical Ingredient (API). In addition, 15.8% of unrefrigerated samples failed these assays.<sup>6</sup>

In recent studies, a large percentage of oxytocin did not meet quality standards.

Solution Area	<ul style="list-style-type: none"> <li>Oxytocin quality</li> </ul>
Identified Solution Gap	<ul style="list-style-type: none"> <li>Unknown oxytocin quality in low-resource settings as defined by % API, and point of degradation in the supply chain</li> </ul>
Accelerate Product/Solution	<ul style="list-style-type: none"> <li>Solution Landscape on Oxytocin Quality Solutions (2012)</li> <li>Oxytocin Quality Audits (2015)</li> <li>Oxytocin Solution Value Proposition and Business Cases (2015)</li> <li>Convening a focused Oxytocin Quality Stakeholder group (2015)</li> </ul>
Result Achieved	<ul style="list-style-type: none"> <li>Potential solutions for oxytocin quality (36 solutions across 7 categories) identified</li> <li>Point of degradation in the supply chain identified</li> <li>Oxytocin Quality Solution value chain mapped out</li> </ul>
Hand-off Strategy	<ul style="list-style-type: none"> <li>Inform future product development – publish document for product developers and innovators as evidence of continued solution development</li> <li>Provide recommendations to program implementers/ device procurers on appropriate device selection</li> <li>Quantify market</li> </ul>
Strategic Partner(s)	<ul style="list-style-type: none"> <li>Implementing partners, e.g., Maternal and Child Survival Program (MCSP)</li> <li>International procurement agencies</li> <li>UN (United Nations)</li> </ul>

Several challenges in health sector infrastructure and health service delivery can create barriers to oxytocin quality:

- Oxytocin must be manufactured in a sterile facility and the manufacturer must test the finished pharmaceutical product for drug content and bioavailability, or the rate and extent to which the active substance is absorbed from the pharmaceutical form, which can be challenging for manufacturers.<sup>7</sup>
- Additionally, oxytocin must be included in the cold chain (storage and transport equipment that enables medicines to be

kept refrigerated from the point of manufacture to the point of use). The storage requirements for oxytocin are confusing, as some labels state storage requirements of 2° to 8° Celsius while others list “controlled room temperature,” which can be between 20° and 25° Celsius.<sup>8</sup> Furthermore, many health workers are unaware that oxytocin requires cold chain storage.<sup>9</sup>

- Because oxytocin is administered through intravenous or intramuscular injection, most countries require that trained health care workers administer the drug. Administration requires specialized skills, sterilized equipment, and proper disposal of medical waste.<sup>10</sup> This means that women delivering at home or with a traditional birth attendant probably will not have access to oxytocin.
- Because there are so many manufacturers of the drug, and there are no prequalified products, it can be difficult for procurement agencies to identify high-quality products.<sup>11</sup> To ensure quality, many international tenders require market authorization from a Stringent Regulatory Authority<sup>12</sup> or prequalification by the WHO, through a program that assesses medicines, active pharmaceutical ingredients, vaccines, diagnostics, injection devices, and quality control laboratories. As of September 2014, no oxytocin products are prequalified, although one is currently going through the prequalification process, and one is going through the Expert Review Panel process.

### **Accelovate’s Solution: Promoting a priority formulation of magnesium sulfate**

Through this work, Accelovate identified two critical bottlenecks to compromised oxytocin quality: manufacturing the drug and knowing its potency.

Prequalifying manufacturers of oxytocin and clarifying labeling and storage requirements would reduce procurer confusion and ensure quality supplies of the drug. Accelovate’s work on PPH treatment focuses on overcoming barriers to ensuring the quality of oxytocin as well as exploring solutions that can both boost and ensure the quality of oxytocin throughout the supply chain up to the point of care.

### **Results Achieved**

With low global access to high-quality oxytocin, advocates need data to demonstrate the utility and impact of ensuring drug quality and to urge production by prequalified manufacturers. The Accelovate team, with funding from the Reproductive Health Supplies Coalition, has built a business case to demonstrate the value of investing in the manufacture and distribution of high-quality oxytocin. “[Business Case: Investing in Production of High-Quality Oxytocin for Low-Resource Settings](#)” demonstrates that market sizes are sufficiently large to incentivize manufacturers to produce this

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product. The business case approximates market sizes for the drug, and characterizes market dynamics. The case is a resource for country-level manufacturers, ministries of health, national policymakers, and donors wanting to demonstrate the economic and business value of investing in high-quality oxytocin, as well as advocates attempting to encourage the prequalification of oxytocin.

Accelovate has also developed an interactive resource entitled [“Maternal Health Drug Business Assessments: Excel Tool and User's Guide”](#) that contains global market data pertaining to three maternal health products, including oxytocin. This tool allows users to manipulate assumptions to generate tailored market projections. National health organizations, donors, and manufacturers wanting to explore the impact of investing in oxytocin, and advocates attempting to assess the business case for the drug in their countries, may use this tool to explore scenarios to support their decision-making.

In addition to increasing access to existing commodities, Accelovate partners with innovators to develop new solutions in critical areas. Bringing innovative solutions to low-resource settings is expected to translate into improvements in quality assurance of oxytocin throughout the supply chain and at the time of use. In 2015, Accelovate will continue its work documenting the solution landscape in order to aid donors, program implementers, host country governments, communities, and regulatory agencies in prioritizing areas of highest need and greatest impact. Accelovate has also assessed efforts to drive new, existing, or emerging innovations in PPH management.

Accelovate recommends improving clinic-level quality of oxytocin; creating visible markers of potency; developing portable, off-grid cold storage solutions; controlling drug distribution systems; establishing systematic and electronic tracking of quality and demand; and experimenting with new formulations and presentations of the drug. Accelovate also recommends creating tools and tests for quality assessment at the point of care and training providers to test quality. The continuation of this work is a priority for Accelovate in 2015; it is hoped that findings will become advocacy tools for donors, ministries of health, national policymakers, and clinical care providers.

### **Next Steps: Building on Accelovate's achievements**

Accelovate continues to work with strategic partners to promote high-quality oxytocin. These partners include but are not limited to: the UN Commission on Life-Saving Commodities for Women and Children, the Reproductive Health Supplies Coalition, WHO, various ministries of health, procurement agencies, commodity manufacturers, product developers, researchers, and implementing partners.

A commercial opportunity exists to manufacture high-quality oxytocin in low-resource settings.

Accelovate's work builds on the excellent tools produced by partners and advocates in the field. Family Care International, with funding from the Reproductive Health Supplies Coalition, has produced briefs on [Essential Medicines for Maternal Health](#), including oxytocin. The brief outlines the barriers to use of oxytocin, strategies to ensure potency and quality with anecdotal evidence from the field, and examples of innovations in oxytocin delivery, as well as priority actions for ensuring quality and potency of oxytocin.

<sup>1</sup> Jhpiego. 2014. *Business Case: Investing in Production of High-Quality Oxytocin for Low-Resource Settings*. Publication prepared by C. Schocken through the Reproductive Health Supplies Coalition. Available at <http://reprolineplus.org/oxytocin-case>. Accessed 2 January 2015.

<sup>2</sup> Life-Saving Commodities. UN Commission on Life-Saving Commodities. 2013. Available at <http://www.lifesavingcommodities.org/about/lifesaving-commodities/>. Accessed 25 November 2014.

<sup>3</sup> World Health Organization. 2013. WHO Model Lists of Essential Medicines. Available at [http://apps.who.int/iris/bitstream/10665/93142/1/EML\\_18\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/93142/1/EML_18_eng.pdf?ua=1). Accessed 25 November 2014.

<sup>4</sup> Haeri S and Dildy GA. 2012. Maternal mortality from hemorrhage. *Seminars in Perinatology* 36(1):48–55

<sup>5</sup> Jhpiego. *Business Case: Investing in Production of High-Quality Oxytocin for Low-Resource Settings*.

<sup>6</sup> *Ibid.*

<sup>7</sup> *Ibid.*

<sup>8</sup> Jhpiego. *Business Case: Investing in Production of High-Quality Oxytocin for Low-Resource Settings*.

<sup>9</sup> Jhpiego. *Business Case: Investing in Production of High-Quality Oxytocin for Low-Resource Settings*.

<sup>10</sup> Family Care International, "Oxytocin." Essential Medicines for Public Health. Reproductive Health Supplies Coalition: 2014. Available at [http://www.rhsupplies.org/fileadmin/user\\_upload/Maternal\\_Health\\_Supplies/Essential\\_Medicines/Essential\\_Medicines\\_Maternal\\_Health.pdf](http://www.rhsupplies.org/fileadmin/user_upload/Maternal_Health_Supplies/Essential_Medicines/Essential_Medicines_Maternal_Health.pdf). Accessed 2 January 2015.

<sup>11</sup> Jhpiego. *Business Case: Investing in Production of High-Quality Oxytocin for Low-Resource Settings*.

<sup>12</sup> A Stringent Regulatory Authority is a regulatory authority that is a member of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) or an ICH Observer and associated with an ICH member.

## Accelovate—a Partnership in Accelerated Global Health Innovation

Accelovate is a global program dedicated to increasing the availability and use of lifesaving innovations for low-resource settings. Led by Jhpiego, the Accelovate program began in 2011 as a five-year, United States Agency for International Development (USAID)-funded program under the Technologies for Health (T4H) grant.

### Also available from Accelovate:



Postpartum  
Hemorrhage



Rehabilitative  
Medicine



Pre-eclampsia  
& Eclampsia



Male  
Circumcision

**Design Challenges** promote the development of innovative solutions where appropriate technology is lacking

**Solution Landscapes** assess what solutions exist

**Value Propositions** assess the benefits and drawbacks of an array of solutions for our context

**Business Cases** assess manufacturability and commercial potential

**Market Readiness Assessments** evaluate a selected technology/solution for market-level readiness factors

**Briefs** describe technology access and utilization challenges in a topical area and outline Accelovate's approach

**Excel Tools** present raw data that implementers may develop for programming and advocacy purposes

**Literature Reviews** review secondary data, usually to understand a bottleneck

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Accelovate invites innovators, advocates, funders, and programmers addressing the procurement and use of maternal health drugs and technologies in low-resource settings to share our tools and join our efforts to ensure a market of standardized, high-quality oxytocin.