

Developing a country level strategy for misoprostol for PPH

Melodie Holden, MS, MPH

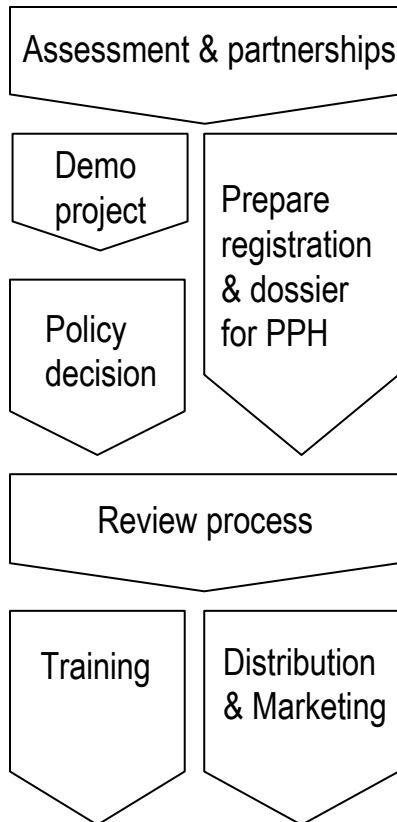
Vice President, Venture Strategies for Health & Development and
Faculty, University of California, Berkeley



Objectives of this session

- » Understand steps to making misoprostol **approved** for use and **registered** for use
- » Define objectives for making it **available**
- » Identify components of a misoprostol rollout strategy
- » Understand steps countries have already taken toward approval, registration, & availability
- » Integrate lessons learned in Nigeria, Ethiopia, and Tanzania?

Misoprostol Program Concept



<p>Assessment & Partnerships Objectives: Obtain knowledge of country-specific registration & regulatory process; identify local distributor(s); engage manufacturer; identify local champions; conduct policy meetings with Ministry of Health, regulatory agency, NGOs, etc.; identify collaborators and site for demonstration project (if required)</p>
<p>Demonstration Project (Optional) Objective: Provide country-specific evidence of acceptability, feasibility, and level of access of misoprostol.</p>
<p>Policy decision (Optional) Objective: Approve misoprostol for use for post-partum hemorrhage in the country, for example, by adding it to national / essential drug list.</p>
<p>Prepare for registration & submit dossier for PPH Objectives: Obtain contract or agreement between manufacturer & distributor, including agreement on pricing; develop & submit dossier in required format to regulatory agency.</p>
<p>Review process Objective: Regulatory agency approves product for registration, fast-tracked if possible. Once drug is registered, drug can be imported and distributed.</p>
<p>Training Objective: Train to competency all authorized providers on use of Active Management of Third Stage of Labor (AMTSL) & misoprostol for prevention & treatment of PPH. Often done in phased approach. A full rollout includes public and private sectors at all levels.</p>
<p>Distribution & Marketing Objective: Ensure misoprostol's availability through authorized outlets in urban & rural settings. Increase knowledge and demand for misoprostol among potential beneficiaries.</p>

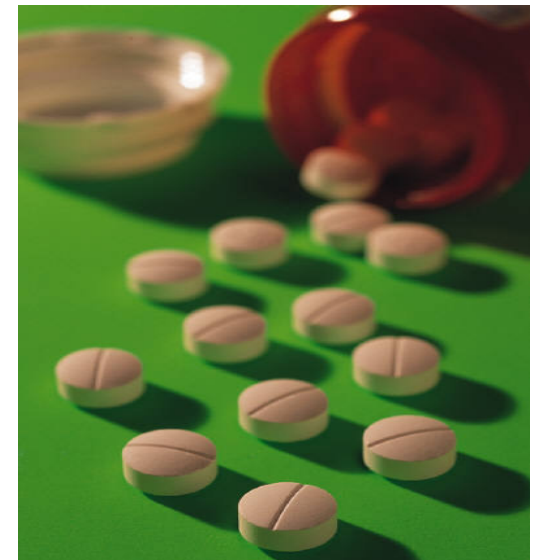
Goal: All countries with high maternal mortality will have misoprostol widely available at affordable prices along with correct information for use to control PPH.

Country action plan: 1. Add to Essential Drug list & include in guidelines

Criteria used by the WHO Expert Committee on the Selection and Use of Essential Medicines	Misoprostol
Sound and adequate evidence of efficacy and safety in a variety of settings	✓ Yes
Cost relative to efficacy	✓ Yes
Available in a form in which adequate quality, including bioavailability, can be ensured	✓ Yes
Stable under the anticipated conditions of storage and use	✓ Yes
Single compounds are preferred	✓ Yes

2. Engage a low-cost manufacturer

- » South-South trade – generics vs. brand
 - Price: Generic, high-quality from Egypt, China, & India as low as US \$ 0.135 per tablet
 - Willing to submit registration for PPH indication



3. Determine level of availability and evaluate distribution channels

» **Level of drug availability**

- Medical
- Paramedical
- Pregnant women

» *Criteria*

- ✓ *Who attends most deliveries?*

» **Level of IEC**

- During prenatal care or from community volunteers
- Women's groups
- Social marketing
- Health campaigns

» *Criteria*

- *Who reaches most women?*

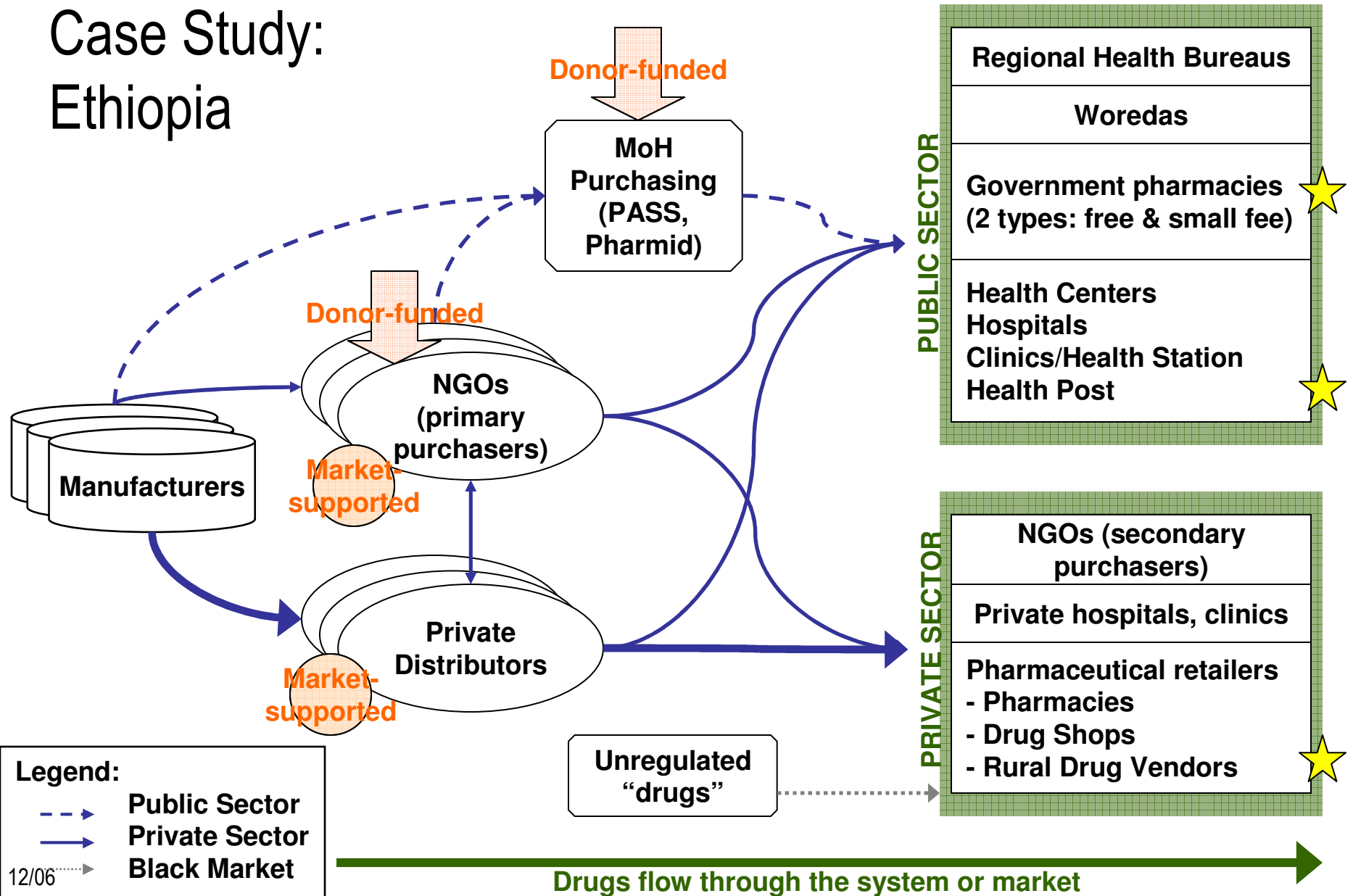
» **Level of distribution**

- Public sector
- Private & NGO sectors
- Over the counter at pharmacies & drug shops in remote communities
- *Hybrid*

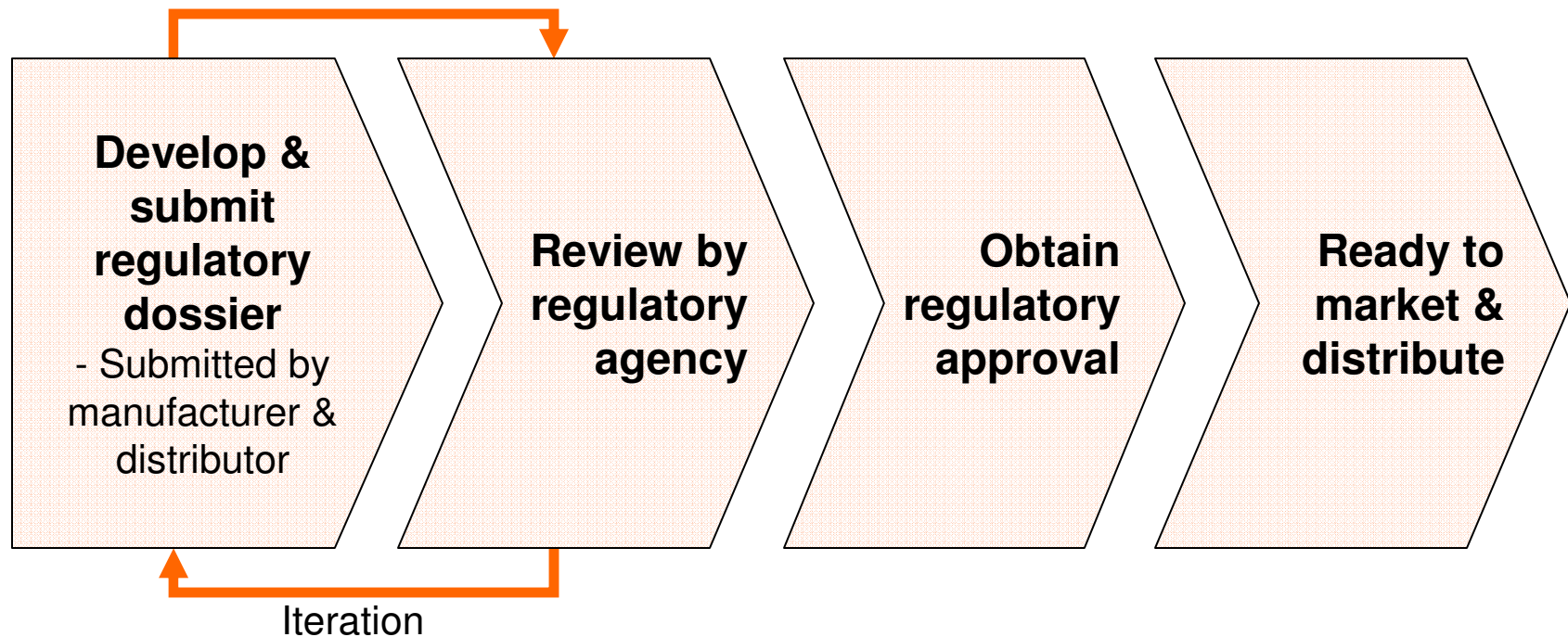
» *Criteria*

- ✓ *Where do the poor go for care?*
- ✓ *Where do deaths from PPH occur?*
- ✓ *Is there a commitment to low pricing in rural markets?*

Case Study: Ethiopia



4. Complete the regulatory process for a specific manufacturer/distributor pair



Options for registration

- » Indications
- » Packaging
- » Prescription/OTC
(or other)
- » Approved outlets
- » Approved marketing

Typical dossier components:

Manufacturer & local agent
Indications & prescription/non-prescription status
Packaging & insert
Chemical structure/Shelf life
Manufacturing process, GMP
Administration/Dosage/
Side Effects
Warnings/Contraindications/
Precautions/Overdose
Teratogenicity/Toxicology/
Bioavailability/Metabolism
Clinical Data
Registration in other countries
Motivation Letter

5. Build awareness: What tools can be used to carry the message through training, education, and communications?

- Networks of women's groups
- Professional organizations
- Simple posters & brochures designed for literate and illiterate
- Educating midwives, community health workers, TBAs
- Public awareness or marketing campaign

What is “availability?” When women have access to misoprostol at every delivery

		<i>Who assists at delivery?</i>		
		Health care providers	Paramedical providers	Pregnant women
<i>How are essential medicines acquired?</i>	Public sector purchasing for facilities & pharmacies	✓	✓	✓
	Private distributors & retailers	✓	✓	✓
	NGOs & FBOs	✓	✓	✓

What does it take to make misoprostol available? Make its use *institutionalized*.

- » Ministries of Health and regulatory agencies
 - Add misoprostol for PPH to the national/essential medicines list
 - Integrate into training and guidelines
- » Professional organizations & universities, NGOs & FBOs
 - Integrate into training and guidelines
- » Public & private sector distributors, NGOs & FBOs
 - Apply for regulatory approval with generic manufacturers
 - Import and distribute at low cost
 - Build awareness through information, education, and communication campaigns
- » Donors
 - Fund information, education, and communication campaigns, drug purchases, and training

Questions to consider when developing a country-level misoprostol rollout strategy

- » **1. Level of availability**
- » **2. Rollout plan**
- » **3. Training**
- » **4. Educational materials**
- » **5. Communications campaign**
- » **6. Funding**
- » **7. Local distribution agents**
- » **8. Regulatory process**
- » **9. End user pricing and volume projections**
- » **10. Monitoring and evaluation**
- » **11. Operations research / demonstration project**

* Please reference handout which provides additional detail on each category.

Where is misoprostol registered now?

3 categories of availability

Registered but <u>not</u> for <u>PPH</u>	Approved <u>for</u> PPH (national or essential drug list*)	Product registered <u>for</u> <u>PPH</u>
Egypt, South Africa, Ghana, China, most countries outside Africa		
Tanzania	Tanzania	Tanzania (dossier submitted & under review)
	Ethiopia	Ethiopia (dossier submitted & under review)
		Nigeria

*In many countries where misoprostol is not registered for PPH, it is legally used off-label for this indication because of the overwhelming medical evidence. In the US, misoprostol is listed for PPH in the US Pharmacopeia.

What are the lessons from Nigeria, Ethiopia, and Tanzania?

- » Support from the medical community is essential
- » Policy meetings are effective for mobilizing and building awareness at any step in the process
- » “Fast track” options available from most regulatory agencies
- » Orphan drug status can build commitment (as in Nigeria)
- » Reuse successful regulatory documents (we can provide these)
- » The order of the process may be different for each country; some will first add it to their essential medicines list while others start with a product registration

Thank you

What can be done to expedite global availability?

- » Professional organizations (OB/GYN and nurse midwife societies) provide technical consul to Ministries of Health
 - The medical community must advocate for its use at the community level to save the most lives
- » Donors can help Ministries of Health to place a priority on misoprostol
 - Fund policy reform, information, education, and communication, drug purchases, and training
- » NGOs & FBOs can have an important role
 - DKT & PSI are early adopters

Where are we on the misoprostol adoption curve?

Borrowing a concept from business strategy

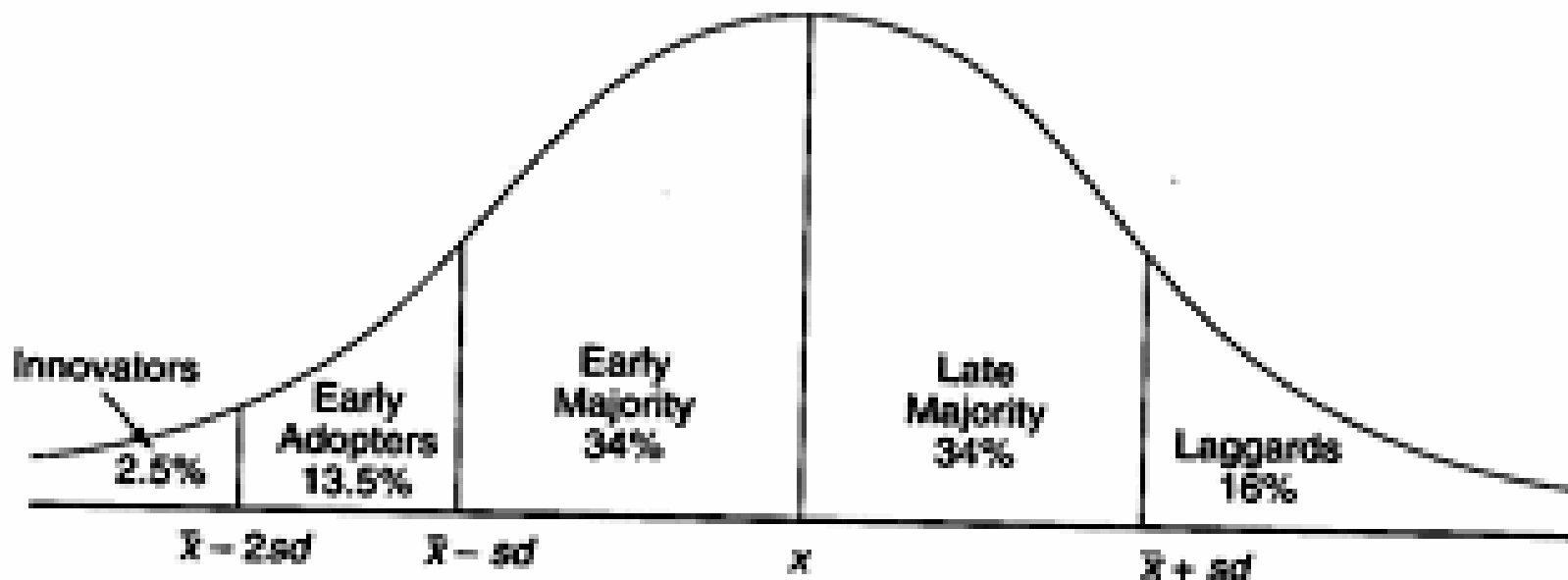


FIGURE 6.4 Relationship between types of adopters classified by innovativeness and their location on the adoption curve

source: Everett M. Rogers, *Diffusion of Innovations*, 3rd ed. (New York: Free Press, 1983), p. 247.