

**REPRODUCTIVE HEALTH SUPPLIES COALITION
14TH GENERAL MEMBERSHIP MEETING**

Quality-Assured Reproductive Health Medicines:
Is There A Business Case?

BioBridge Strategies, LLC
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7 – 11 October 2013

New Delhi, India

**Prequalification of Medicines
Programme**

*Lembit Rago
Jacqueline Sawyer*



Technical Assessment

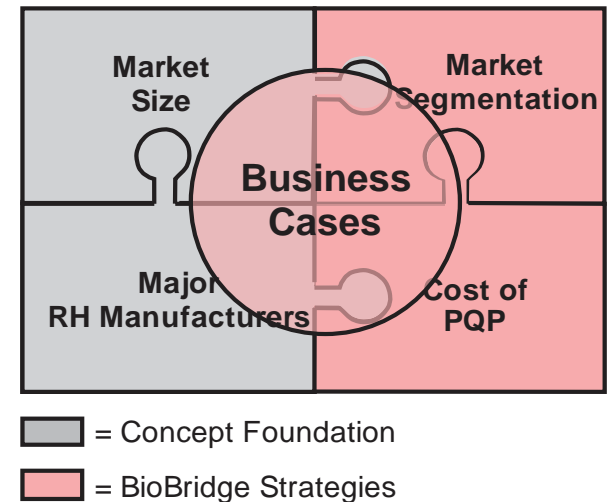


Capacity Building

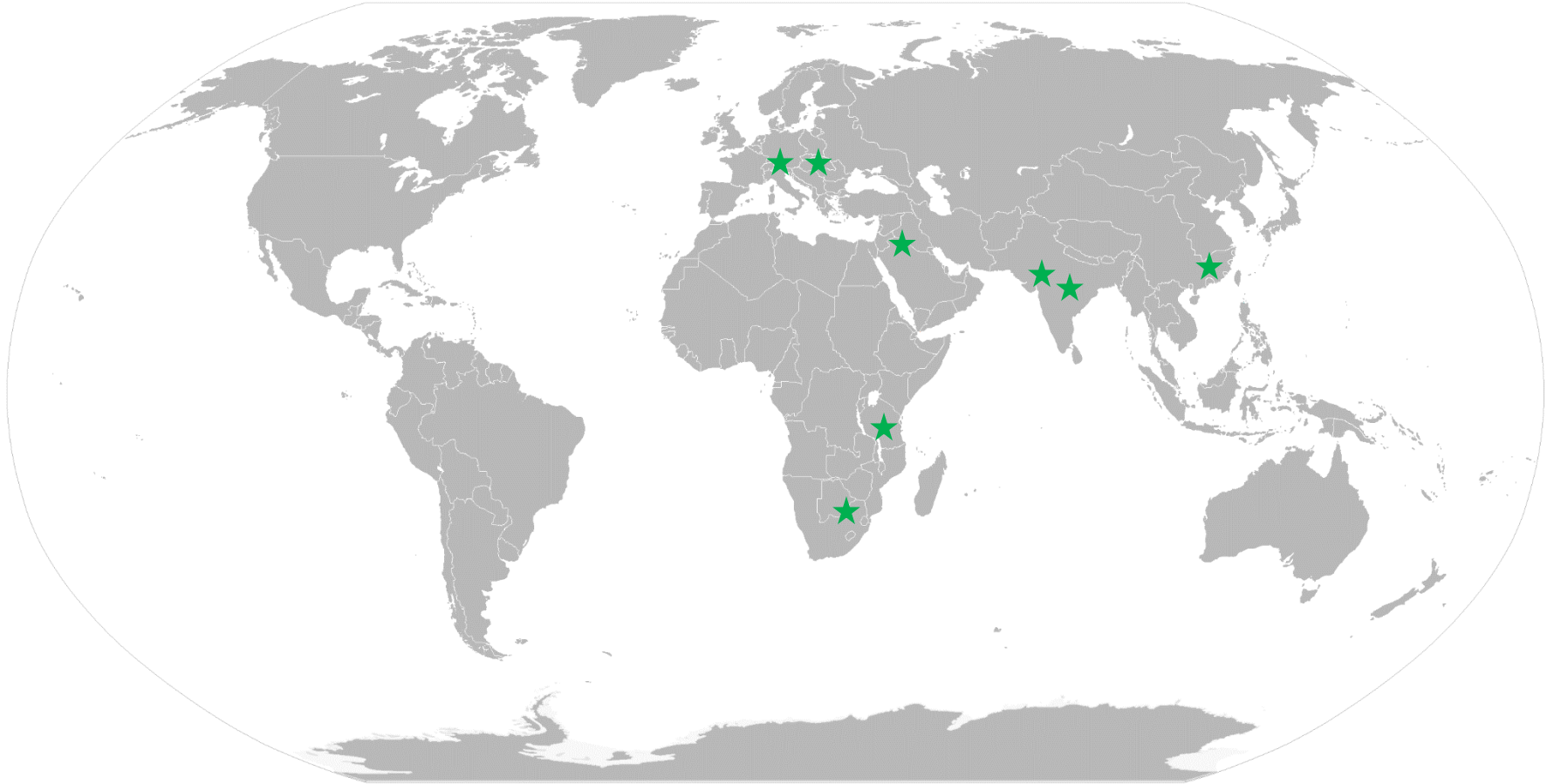


Manufacturers' Perspective

- Develop the business case(s) for manufacturers of reproductive health products.
 - Compare and contrast these with the business cases already developed for HIV, malaria and TB manufacturers.
- Create a market segmentation scenario for RH manufacturers.
- Assess the impact of being prequalified on ...
 - Revenue potential for pharmaceutical companies manufacturing reproductive health medicines.
 - Improved market access (institutional/donor and non-institutional markets).



Where were the companies that we visited?



Companies were select through inputs by WHO-PQP, Concept Foundation, McKinsey Reports and BioBridge Strategies country analyses . . .

China

- Nanjing Baijingu Pharmaceutical Co., Ltd
- Beijing Xinhui-Goldway Pharmaceutical Co., Ltd.
- Beijing Zizhu Pharmaceutical Co., Ltd
- Shanghai New Hualian Pharmaceutical Co.,LTD
- Shanghai Sine-tianping
- Dahua Pharmaceutical Co., Ltd.

India

- Cipla
- Famy Care
- Lupin
- Naari

Global Companies/Europe

- Merck / NV Organon
- Gedeon Richter Plc.
- Teva

Eastern Mediterranean countries

- European Egyptian Pharmaceutical Industries - EEPI [Egypt]
- Hikma Pharmaceuticals [Jordan]

Executive Management	Senior Business Management	Quality Managers
Chairman & CEO Deputy General Manager (4) Founder & CEO Vice Chairman General Manager (2) Vice General Manager (2) Assistant General Manager	Vice President, Int'l Marketing Vice Director, Int'l Affairs Vice President Director, Export Sales Director, Foreign Trade and Economic Office Head of Medical Service Business Manager (2) International Business Supervisor	Director of Quality Vice Director of Quality Manager Quality Assurance QA Manager
N= 13	N=15	N=6

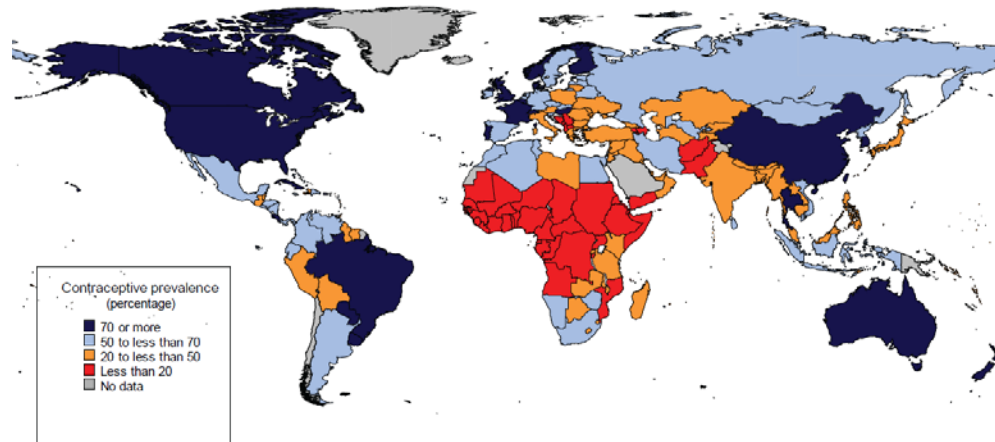
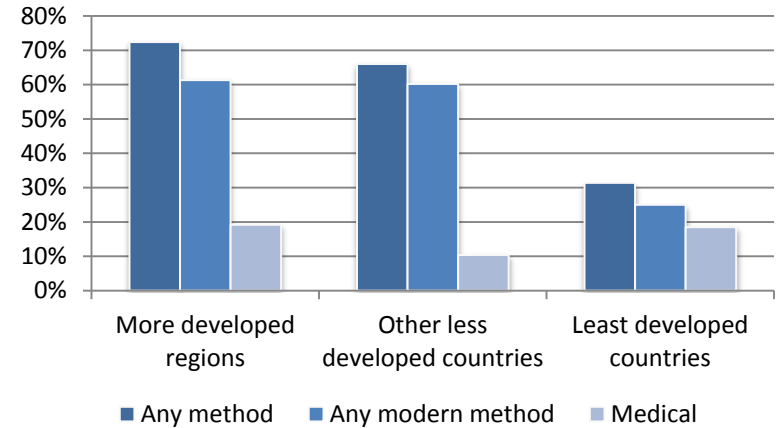
Types of Companies

Experience with RH PQP	Non-RH Medicines Approved by PQP (No RH Experience)	No Medicines Approved by PQP
10	0	5

The Contraceptive market is comprised of

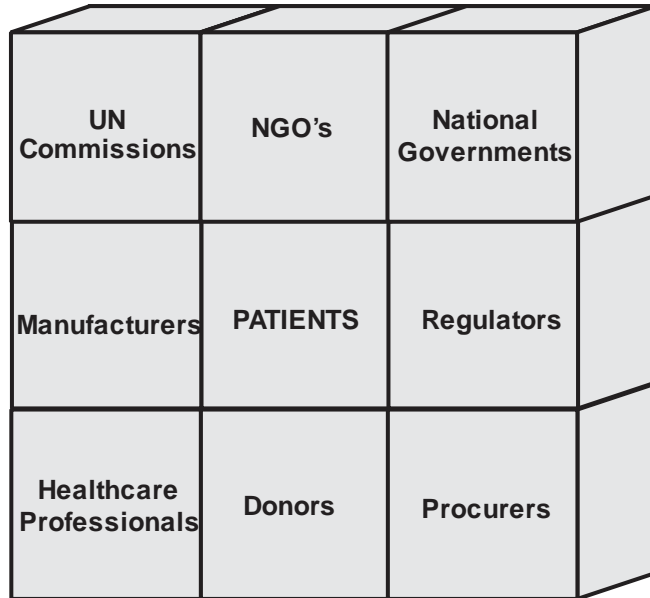
- **Medicines**
 - Oral contraceptives
 - Injectables
 - Implants
- Condoms
- Devices

Use of Contraceptives (women)



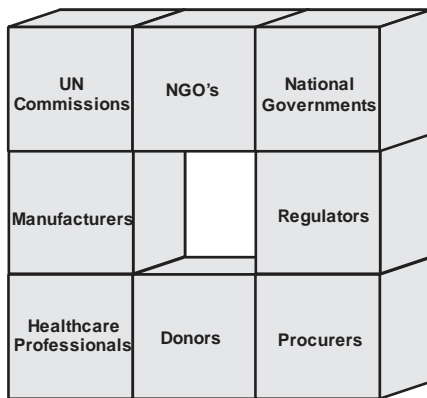
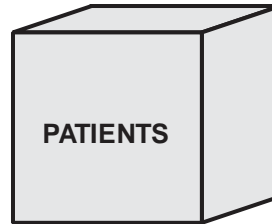
Data is based on “married women or in unions between men and a women regularly cohabiting in a marriage-like relationship.”
Data source: World Contraceptive Use 2011 Report, Department of Economic and Social Affairs, Population Division, United Nations

Many Stakeholders Involved in Supplying RH Medicines



- Variety of stakeholders
- Diverse, and sometimes conflicting, interests
- Important in the purchasing decisions
- Guiding standards
- Ensuring quality of medicines
- Patient centric
- Cost + value

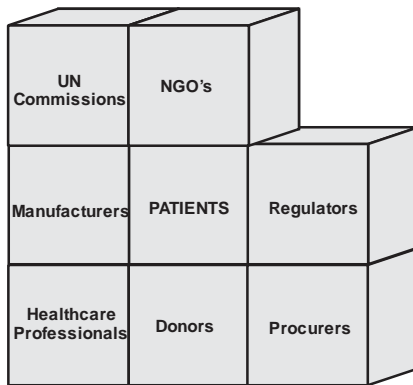
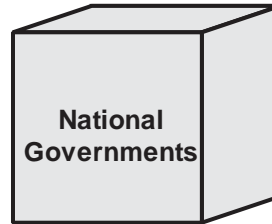
Key Stakeholders - Patients



- Females / males married or in a union*
- 15 – 49 years old
- Price sensitive
- Effective treatments
- Quality

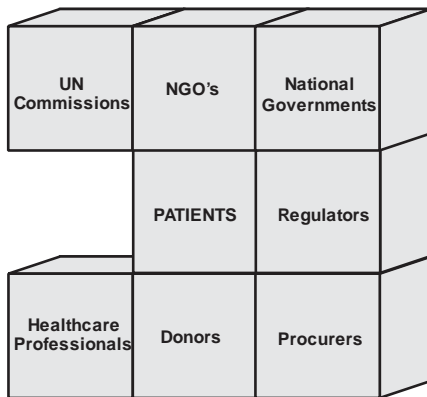
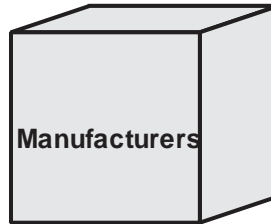
* A union involves a man and a woman regularly cohabiting in a marriage-like relationship.

Key Stakeholders – National Governments



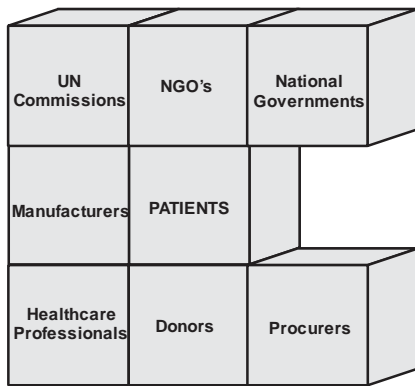
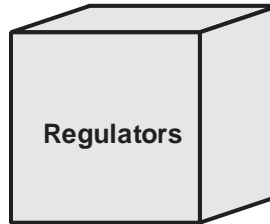
- Local policies
- Politically sensitive
- Bureaucratic by definition
- Local influencers
- Purchasing decision for local tenders
- Influenced by diverse “factors”
- Cost with a sensitivity to quality
- Often prefer local manufacturers

Key Stakeholders - Manufacturers



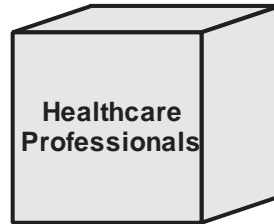
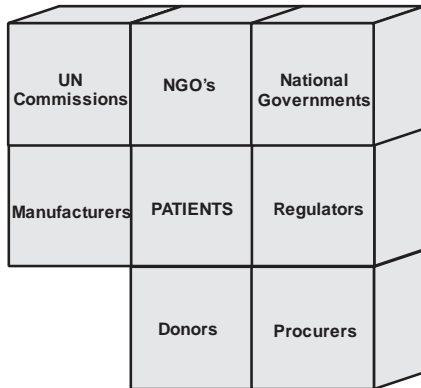
- International, national and local
- Spectrum of quality capabilities
- Highly competitive in some products
- Searching for innovation
- Efficiency driven
- Branded, branded generic, contract and generic
- Range of portfolios

Key Stakeholders - Regulators

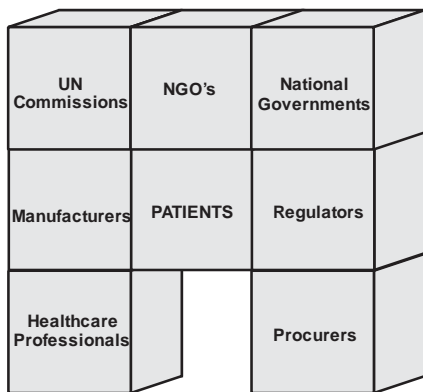
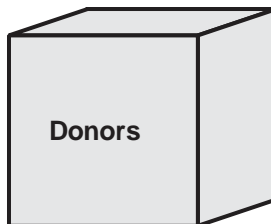


- Public safety
- Quality assured medicines
- Consistent manufacturing
- Process oriented, often intransigent
- Normally reactive rather than proactive

Key Stakeholders – Healthcare Professionals

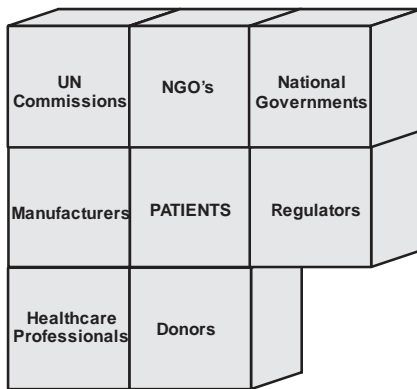
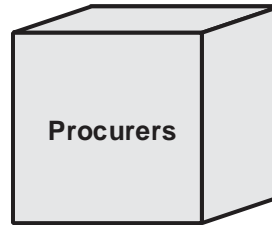


- Variety of professionals
 - Doctors
 - Nurses
 - Pharmacists
 - Local providers
- Overburdened, especially in the public sector
- Care about patient outcome
- Quality oriented but unaware or unmeasured
- Influenced by RH product representatives
- Influence patients' decisions



- Want as much medicines for their donations
- Sensitive to quality
- Focus on access and impact
- Influential

Key Stakeholders - Procurers



- Want as much medicines within their budgets
- Cost and efficiency driven
- Actively manage prices
- Managers of the supply chain
- Facilitators – manufacturers to distribution centers and patients

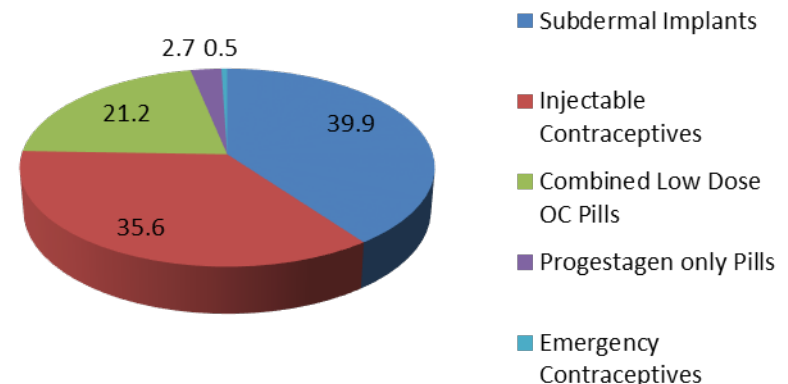
Donor Medical Contraceptives Market, Historical

- The existing donor medical contraceptive market has been steadily growing
- The donor medical contraceptives market reached in 2011:
 - Couple Years of Protection (CYP): 25 mill
 - Revenue: \$145 - 190 mill
- Approximate market sizes for comparison
 - ARVs: \$1 bill
 - Antimalarials: \$300 mill
 - Anti TB: \$400 mill

Donor RH market

Product Category	TOTALS
Subdermal Implants	76.85
Injectable Contraceptives	68.54
Combined Low Dose OC Pills	40.83
Progestagen only Pills	5.27
Emergency Contraceptives	0.98
Grand Total US\$	192.47

International procurement, breakdown of purchasing by hormonal method - percentage of value



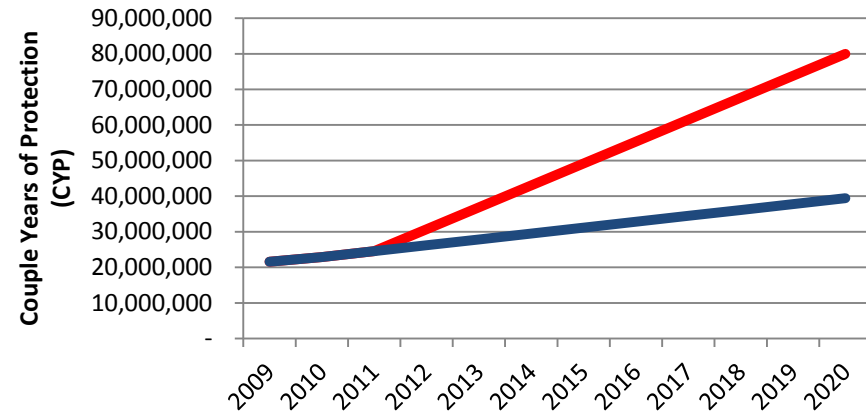
Sources:
 BioBridge Strategies
 Concept Foundation
 Reproductive Health Supplies Coalition, RHInterchange

Donor Medical Contraceptives Market, Projected

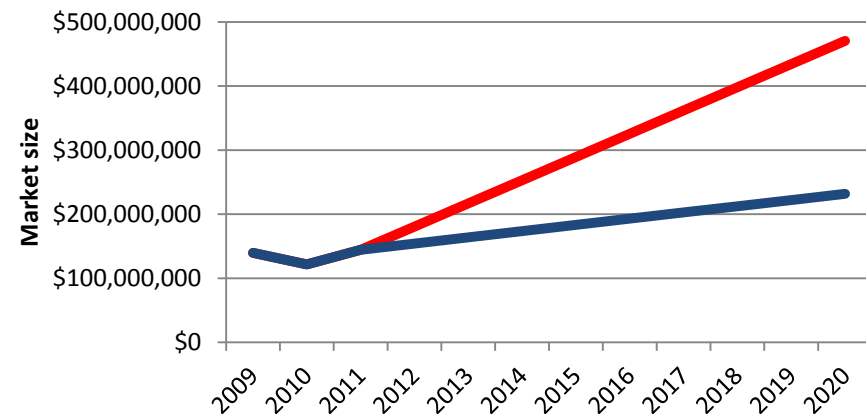
■ The projected donor medical contraceptives market:

- 2011
 - ◆ High (red): \$145 mill / 25 mill CYPs (Couple Years of Protection)
 - ◆ Low (blue): \$145 mill / 25 mill CYPs
- 2015
 - ◆ High: \$290 mill / 50 mill CYPs
 - ◆ Low: \$180 mill / 30 mill CYPs
- 2020
 - ◆ High: \$470 mill / 80 mill CYPs
 - ◆ Low: \$230 mill / 40 mill CYPs

Projected donor medical contraceptives, Couple Years of Protection (CYP)



Projected donor medical contraceptives, US\$



■ The projected donor medical contraceptive market calculations:

- High (red):
 - ◆ Based on the estimated 120 million additional couples using contraceptives in 2020 [from the July 2012 London Summit¹]
 - ◆ 57 mill CYPs from any modern contraceptive in 2011
 - ◆ 43% of couples use medical contraceptives (2011)
- Low (blue):
 - ◆ Based on a constant CYP growth equivalent to the growth from 2010 to 2011

Sources:

¹ London Summit [July 11, 2012] on Family Planning, Fact Sheet

BioBridge Strategies

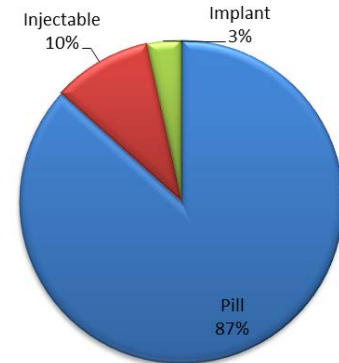
Reproductive Health Supplies Coalition, RHInterchange

Other SRA Medical Contraceptive Market Size Estimates

■ USA

- About 70 mill women aged 15 – 49
- About 18% using any form of medical contraceptives (about 12 mill women)
- About 87% of these use oral contraceptives
- Value of the US medical contraceptive market is around \$4 -5 billion

US medical contraceptive use (women)



■ Europe

- About 200 mill women aged 15 – 49
- About 21% using any form of medical contraceptives (about 40 mill women)
- About 98% of these use oral contraceptives
- Value of the European medical contraceptive market is around \$3 billion

Region	2012	2018
USA	\$4,375	\$5,868
CANADA	444	564
JAPAN	371	525
EUROPE	2,568	3,547
ASIA-PACIFIC	1,059	2,205
LATIN AMERICA	1,424	2,061
ROW	358	426
Totals	\$10,602	\$15,200

Reproductive Health Supplies Coalition, RHInterchange, database accessed July 2012

Gutmacher Institute June 2010 Facts on Contraceptive Use in the United States

<http://www.plannedparenthood.org/health-topics/birth-control/birth-control-pill-4228.htm>

Concept Foundation

Market Size for RH Medicines and Formulations Currently on the EOI List in Other SRA Markets (From IMS)

- The total IMS market for RH medicine formulations currently on the WHO PQP EOI list (2012 revenue): \$400 mill
 - By RH medicine type (Figure 1.)
 - ◆ Implantables: \$150 mill
 - ◆ Injectables: \$120 mill
 - ◆ Orals: \$47 mill
 - ◆ Oxytocin: \$70 mill
 - ◆ Magnesium: \$10 mill

- By region (Figure 2.)
 - ◆ North America: \$300 mill
 - ◆ Europe: \$47 mill
 - ◆ Asia/Australasia: \$44 mill
 - ◆ South Africa: \$7 mill

Figure 1. 2012 revenue by medicine type

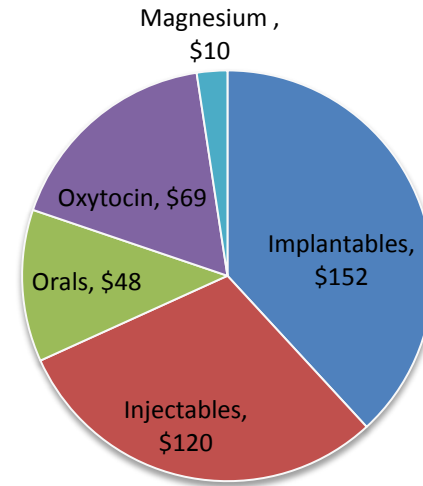
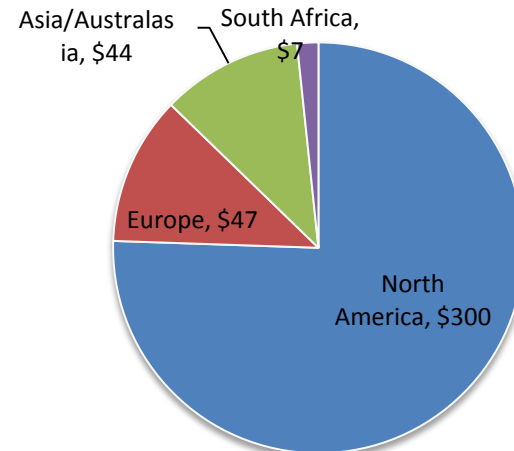


Figure 2. 2012 revenue by region



From: IMS Health®, March 2013

Pregnancies in sub-Saharan Africa: 70 million ¹



Unwanted preventable pregnancies: 28 million (40%) ^{1,4}



Maternal unwanted pregnancy related deaths: 100,000 ^{2,3,4}



Deaths due to unsafe abortions: 50,000 ⁴

Sources:

¹Dirk Van Braeckel, Marleen Temmerman, Kristien Roelens, Olivier Degomme. Slowing population growth for wellbeing and development. *Lancet Family Planning*, Published July 10, 2012

²Hogan MC, Foreman KJ, Naghavi M, et al. Maternal mortality for 181 countries, 1980–2008: a systematic analysis of progress towards Millennium Development Goal 5. *Lancet* 2010; 375: 1609–23.

³Lozano R, Wang H, Foreman KJ, et al. Progress towards Millennium Development Goals 4 and 5 on maternal and child mortality: an updated systematic analysis. *Lancet* 2011; 378: 1139–65.

⁴Singh S, Darroch J, Ashford L, Vlassoff M. Adding it up: the costs and benefits of investing in family planning and maternal and newborn health. New York: Guttmacher Institute and United Nations Population Fund, 2009.

From: London Summit [July 11, 2012] on Family Planning, Fact Sheet

If, by 2020, an additional 120 million women who want contraceptives could get them, the cumulative result would include:

- More than 110 million fewer unintended pregnancies
- 200,000 fewer women and girls dying in pregnancy and childbirth
- Over 50 million fewer abortions
- Nearly 3 million fewer babies dying in their first year of life
- Simply giving women the means to space the births of their children by three years would decrease deaths of children under five by 25 percent

Sources:

Family Planning Summit Technical Note: data sources and methodology for developing the 2012 baseline, 2020 objective and costings. May 2012, FPS Metrics Group

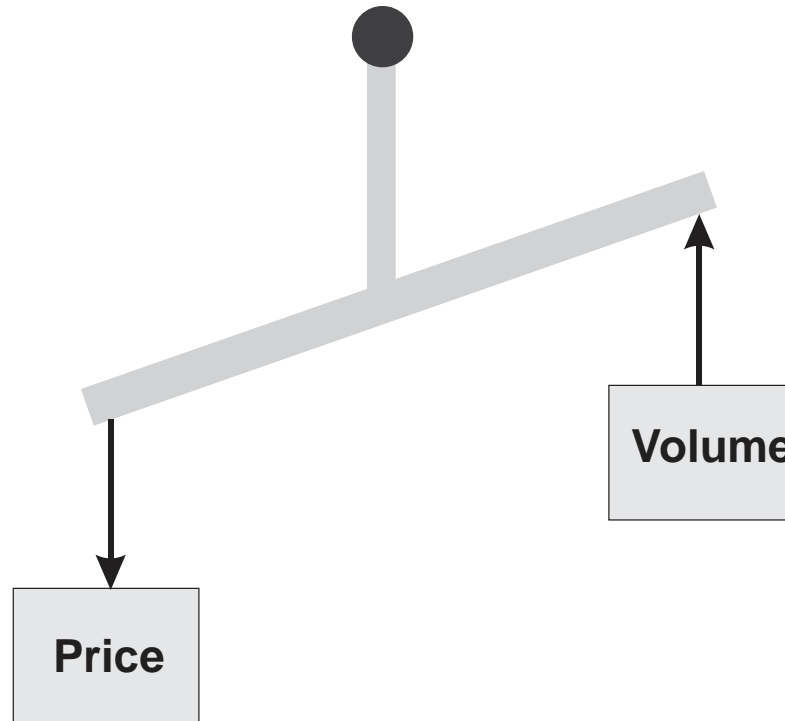
Back to Basics: The Rationale for Increased Funds for International Family Planning. Guttmacher Policy Review volume 11, no. 3, 2008

- *RH market perceived as less competitive than e.g. ARV or anti TB markets*
- *Consumer focused – brand awareness*
 - *Often the tenders request a branded product, especially at the MoH level*
 - *NGO's can be loyal customers, often create their own brands*
 - *Some manufacturers create new brands for the institutional / donor market*
- *Some manufacturers are focused on RH alone*
- *Planning by government or agencies is usually poor and a “family planning mindset” is needed*
- *Ramifications of poor quality are not directly life or death and governments and local procurers often do not fully appreciate the benefits of quality*

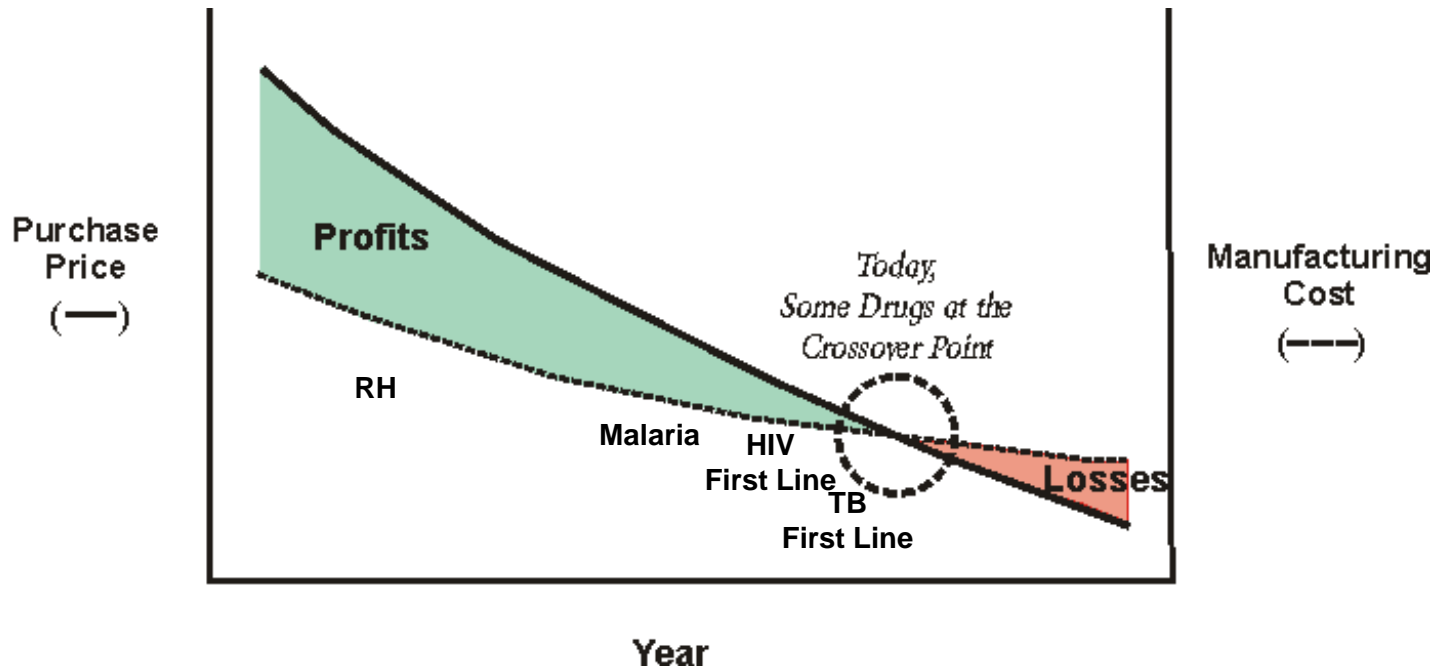
- *Donor markets are more injectable and implant focused than US/Europe, which are focused on oral contraceptives*
- *Local private markets (which are larger than institutional markets) are also more oral contraceptive focused*
- *RH medicines have higher margins than first line ARV's, TB and malaria*

- Demand forecasting is a problem
- The process of procurement is complicated and sometimes takes a long time
- Supply chain is riddled with issues (e.g., cold chain, storage, local stocks)
- *It gets more complicated because the user has a choice which can vary from year to year. Condoms, orals, implants, injectables, IUD's, etc.*
- Governments often prioritize products produced in their own countries
- Erosion of profit margin over time

Balance of Increased Coverage Versus Price Reduction



The Business Challenge – Manage Overall Profitability



Evolution of products in institutional / donor markets

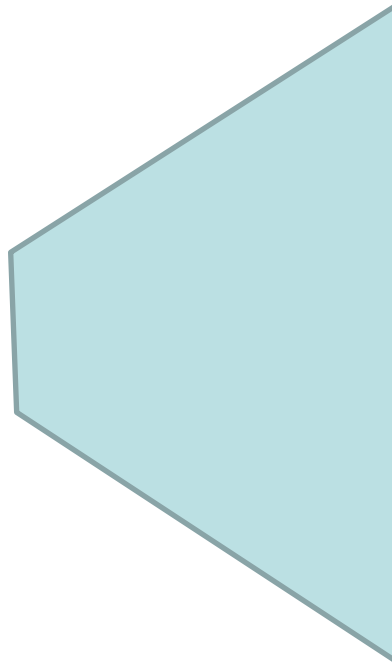
Opportunistic



Business Interest

- Established, international companies
- SRA approval for RH medicines
- Completed bioequivalence studies consistent with PQP requirements
- Minimal incremental investment
- Adequate returns due to attractive margins

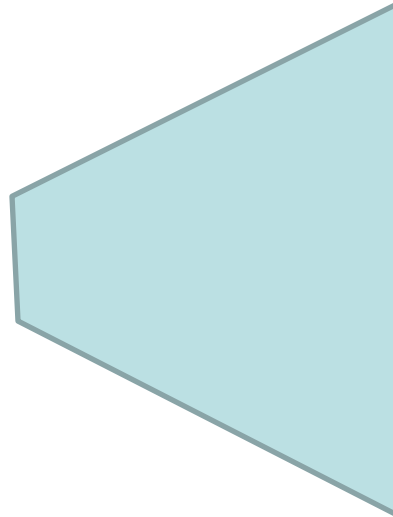
Niche



Business Interest

- Small companies (<\$20 million annual revenue)
- Single product focus
- Need to be prequalified to gain broader market access
- Need external funding
- Defensive posturing; if don't invest, they will lose market share
- Market is too small in and of itself

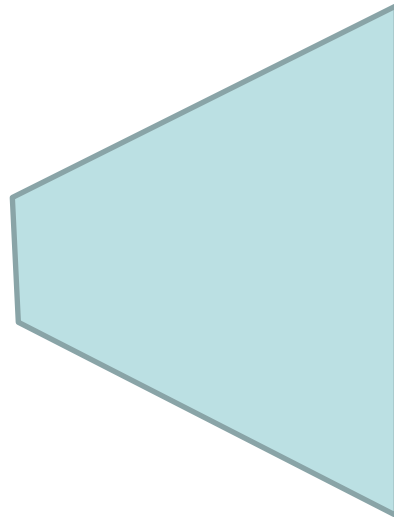
RH Focused



Business Interest

- Established in the RH market
- Broad market presence
- Sufficiently high margins
- Social responsibility
 - Global population growth
 - Understand the negative health impact of unwanted pregnancies

Fledgling



Business Interest

- RH focused
- Young, small, hungry companies that are investing in SRA/PQ in general
- Want to be recognized as a quality manufacturer in all its markets
- Do not necessarily need to make a high operating profit percent but want to grow the business profitably
- See an opportunity for innovation in RH and, perhaps, other indications

- Access to institutional and non-institutional markets
- “Stamp of approval”
- Part of a geographic and portfolio strategies (provide the same products globally)
- WHO-PQP capacity building
- *Opportunism*
 - *Already have SRA approval and/or GMP facilities so incremental investment is marginal*
 - *Already providing medicines to the private market*

- *Be well positioned for additional 120 million women using contraceptives by 2020 (London Summit 2012)*
- *Social responsibility*
 - *Reducing maternal mortality and improving maternal health*
 - *Believes in the rights of women to be informed about their healthcare choices and have medicines be accessible to all*
 - *Believe the need for population control will be a market driver*

Direct and Indirect Benefits for Being Prequalified (1/2)

- Building SRA capabilities within the company
 - *Access to international RH markets*
 - Access to donor markets
- Simplifying and expediting registration in African markets
 - PQP pilot program
- Approval from WHO PQP used to promote a “quality” image
 - *Quality product positioning within the local country (e.g., private market)*
- Ability to apply quality manufacturing approach to other product lines

Italics = different from HIV, TB and malaria

Direct and Indirect Benefits for Being Prequalified (2/2)

- *Margins for RH medicines are still good*
- Creates entry barriers for non-PQ'd competition
- Utilization of existing manufacturing plants (which often run at below 100% capacity) thus improving profitability of the entire business
- Perceived as social entrepreneurs
- *Impact on share price*

Italics = different from HIV, TB and malaria

Disadvantages of Being Prequalified (1/2)

- Requirement for incremental skills and extra staff for generating required information
- Cost and effort to prepare a dossier and GMP infrastructure
- Length of time for approval
 - Sometimes no immediate additional sales after being prequalified, need to take a long term view
- Difficult to forecast revenues and profits

Italics = different from HIV, TB and malaria analysis but could be the same.

Disadvantages of Being Prequalified (2/2)

- *Cost of producing quality products is 5 - 10% greater than non-quality products*
- *Donor markets in and of themselves can be too small (depends on company and market expectations)*
- Application has to be in English and translation is an issue

Italics = different from HIV, TB and malaria

Information that is required for executive decision ...

- Strategic coherence
 - Target markets
 - Product portfolio
 - Fit to company skills

- Financial info
 - Market size and future demand
 - Revenue potential
 - Cost of applying for PQP
 - Schedule
 - Profit potential

Financial Perspective – Companies ARV vs RH

Business P&L An Example		
	"ARV" Product Perspective	"RH" Product Perspective
	<i>Percent</i>	<i>Percent</i>
Net Sales	100.0%	100.0%
COGS	85.0%	75.0%
Gross Profits	15.0%	25.0%
Expenses		
R&D	2.0%	2.0%
Sales and Marketing	2.0%	2.0%
General and Administration	3.0%	3.0%
Total Expenses:	7.0%	7.0%
Operating Profit (Pretax)	8.0%	18.0%

Balance Sheet Assumptions	
Receivables (DSO)	90 days
Inventory Turns	4
Accounts Payable	30
Accrued Expenses	30
Depreciation	
Equipment	3 years
Facilities	20 years
Discount Rate	15%

Annual Revenue for a Favorable Return

	Year 1	Year 2	Revenue to Positive NPV	
			ARV	RH
Expenses				
R&D (Bioequivalence)	\$945,750	\$315,250		
Sales and Marketing (Local)	\$31,250	\$93,750		
General and Administration	\$0	\$0		
Total Expenses:	\$1,386,000			
			\$59,355,144	\$3,101,291
Capital Investments				
R&D Equipment	\$0	\$0		
Manufacturing Equipment	\$0	\$0		
Plant and Facilities	\$0	\$0		
Total Capital:	\$0			
Expenses				
R&D (Bioequivalence)	\$945,750	\$315,250		
Sales and Marketing (Local)	\$31,250	\$93,750		
General and Administration	\$0	\$0		
Total Expenses:	\$1,386,000			
			\$161,128,825	\$8,418,940
Capital Investments				
R&D Equipment	\$37,500	\$12,500		
Manufacturing Equipment	\$1,012,500	\$1,012,500		
Plant and Facilities	\$247,500	\$82,500		
Total Capital:	\$2,405,000			
Expenses				
R&D (Bioequivalence)	\$383,250	\$127,750		
Sales and Marketing (Local)	\$31,250	\$93,750		
General and Administration	\$0	\$0		
Total Expenses:	\$636,000			
			\$128,813,763	\$6,730,486
Capital Investments				
R&D Equipment	\$37,500	\$12,500		
Manufacturing Equipment	\$1,012,500	\$1,012,500		
Plant and Facilities	\$247,500	\$82,500		
Total Capital:	\$2,405,000			

NPV ~ a calculation of financial return

A company rarely will invest unless the NPV is positive

Everyone believes that

Poor quality RH medicines are a major health problem.

There is analytical evidence that ...

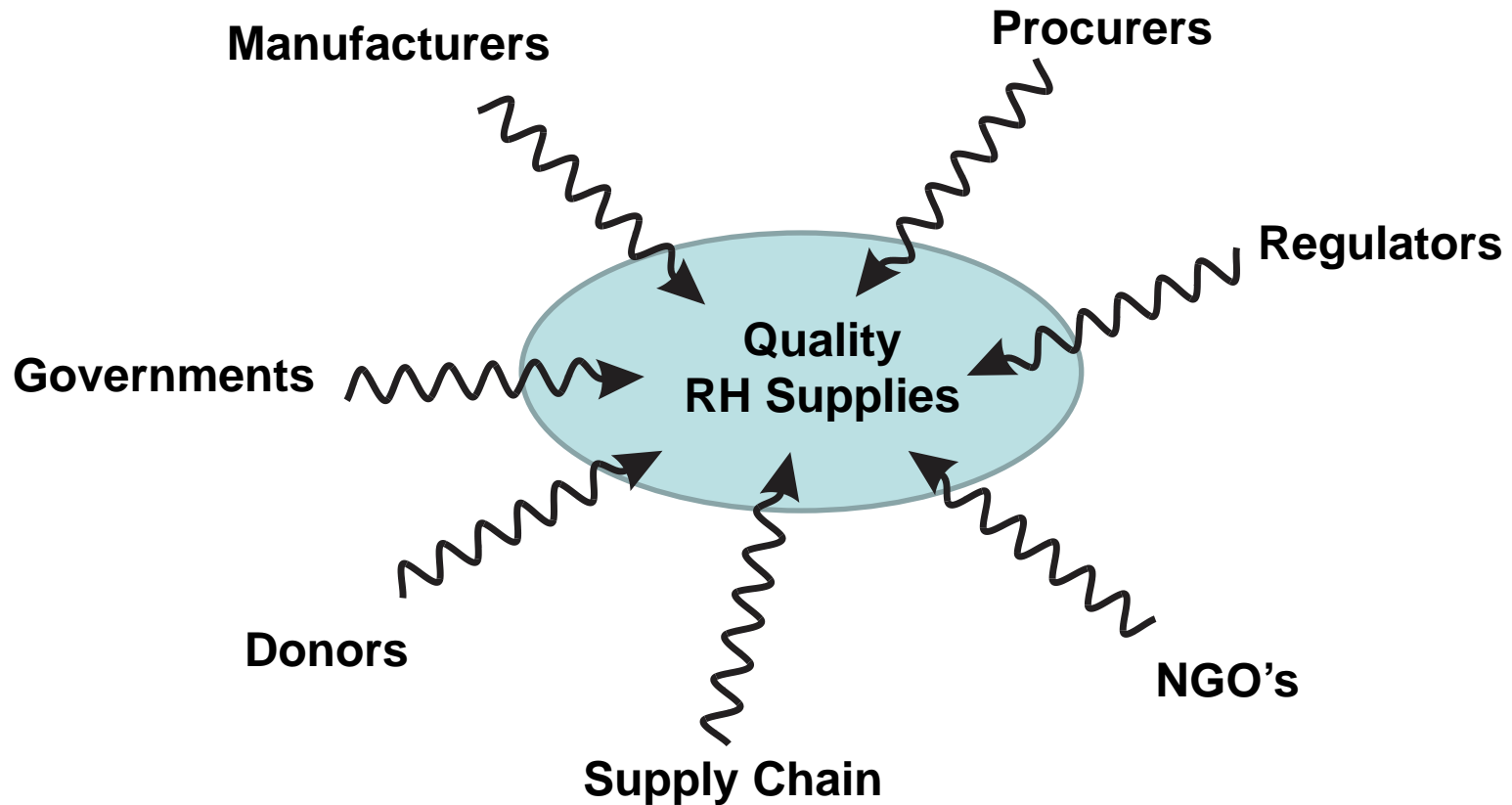
Poor quality RH medicines are being sold to the public.

BUT ...

There are no outcome studies to show the clinical and economic impact of poor quality drugs.

How Do We Integrate Quality in Comprehensive RH Program

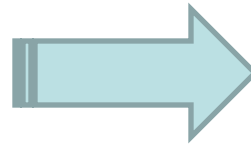
We are in transition and it will take a combined effort of ...



... but ...

Quality will prevail

1957 Toyota



2013 Toyota Camry



Top-Rated Midsize Car (J. D. Power)

What are the differences between RH and HIV, TB, Malaria?

- *For a new participant, the RH donor market in and of itself is not sufficiently attractive to justify the investment in PQP. In contrast, HIV, TB and malaria donor markets are sufficient to justify an investment.*
- *The RH market has higher profit margins.*
- *The RH/contraceptive market is more consumer focused with branding as a key marketing strategy.*
- *Several manufacturers in the RH market are exclusively focused on RH products (which often include products like condoms or pregnancy tests).*

Is there a business case for RH?

YES – SEVERAL POTENTIAL BUSINESS CASES

- There is definitely a business case for RH but it's different from those of HIV, TB and Malaria (studied previously).*
- A favorable case can only be enacted by companies with a certain set of characteristics. As an example, a company that already focuses on the RH market.*
- There will be changes at the country level (regulatory, policy, practices, procedures, infrastructure) that will enable it.*