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

BioBridge Strategies, LLC
Louis J. Riceberg, Ph.D. and Harald Rinde, MD, MBA

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 Interviewed

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

China
- Nanjing Baijingyu 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]
## Interview Mix

<table>
<thead>
<tr>
<th>Executive Management</th>
<th>Senior Business Management</th>
<th>Quality Managers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chairman &amp; CEO</td>
<td>Vice President, Int'l Marketing</td>
<td>Director of Quality</td>
</tr>
<tr>
<td>Deputy General Manager (4)</td>
<td>Vice Director, Int'l Affairs</td>
<td>Vice Director of Quality</td>
</tr>
<tr>
<td>Founder &amp; CEO</td>
<td>Vice President</td>
<td>Manager Quality Assurance</td>
</tr>
<tr>
<td>Vice Chairman</td>
<td>Director, Export Sales</td>
<td></td>
</tr>
<tr>
<td>General Manager (2)</td>
<td>Director, Foreign Trade and Economic Office</td>
<td>QA Manager</td>
</tr>
<tr>
<td>Vice General Manager (2)</td>
<td>Head of Medical Service</td>
<td></td>
</tr>
<tr>
<td>Assistant General Manager</td>
<td>Business Manager (2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>International Business Supervisor</td>
<td></td>
</tr>
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</table>

N= 13

N=15

N=6
### Types of Companies

<table>
<thead>
<tr>
<th>Experience with RH PQP</th>
<th>Non-RH Medicines Approved by PQP (No RH Experience)</th>
<th>No Medicines Approved by PQP</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0</td>
<td>5</td>
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</table>
Focus of Our Study

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
Key Stakeholders - Donors

- 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

<table>
<thead>
<tr>
<th>Product Category</th>
<th>TOTALS</th>
</tr>
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<tbody>
<tr>
<td>Subdermal Implants</td>
<td>76.85</td>
</tr>
<tr>
<td>Injectable Contraceptives</td>
<td>68.54</td>
</tr>
<tr>
<td>Combined Low Dose OC Pills</td>
<td>40.83</td>
</tr>
<tr>
<td>Progestagen only Pills</td>
<td>5.27</td>
</tr>
<tr>
<td>Emergency Contraceptives</td>
<td>0.98</td>
</tr>
<tr>
<td>Grand Total US$</td>
<td>192.47</td>
</tr>
</tbody>
</table>

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

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

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

**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

<table>
<thead>
<tr>
<th>Region</th>
<th>2012</th>
<th>2018</th>
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<tbody>
<tr>
<td>USA</td>
<td>$4,375</td>
<td>$5,868</td>
</tr>
<tr>
<td>CANADA</td>
<td>444</td>
<td>564</td>
</tr>
<tr>
<td>JAPAN</td>
<td>371</td>
<td>525</td>
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<tr>
<td>EUROPE</td>
<td>2,568</td>
<td>3,547</td>
</tr>
<tr>
<td>ASIA-PACIFIC</td>
<td>1,059</td>
<td>2,205</td>
</tr>
<tr>
<td>LATIN AMERICA</td>
<td>1,424</td>
<td>2,061</td>
</tr>
<tr>
<td>ROW</td>
<td>358</td>
<td>426</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>$10,602</strong></td>
<td><strong>$15,200</strong></td>
</tr>
</tbody>
</table>

Reproductive Health Supplies Coalition, RHInterchange, database accessed July 2012
Guttmacher 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
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

From: IMS Health®, March 2013
Avoidable Maternal Deaths

Pregnancies in sub-Saharan Africa: 70 million

Unwanted preventable pregnancies: 28 million (40%)

Maternal unwanted pregnancy related deaths: 100,000

Deaths due to unsafe abortions: 50,000

Sources:
Impact of Providing Contraceptives

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
- 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.
Market Challenges

- 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

*Italics = different from HIV, TB and malaria*
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
Business Strategies

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
Company Types

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
Reasons for Applying for RH PQP (1 of 2)

- 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*

*Italics = different from HIV, TB and malaria*
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*
What Business Case Related Information Is Needed To Decide To Apply for PQP

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

<table>
<thead>
<tr>
<th></th>
<th>&quot;ARV&quot; Product Perspective</th>
<th>&quot;RH&quot; Product Perspective</th>
<th>Percent</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Net Sales</strong></td>
<td>100.0%</td>
<td>100.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>COGS</strong></td>
<td>85.0%</td>
<td>75.0%</td>
<td></td>
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<tr>
<td><strong>Gross Profits</strong></td>
<td>15.0%</td>
<td>25.0%</td>
<td></td>
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</tr>
<tr>
<td><strong>Expenses</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R&amp;D</td>
<td>2.0%</td>
<td>2.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sales and Marketing</td>
<td>2.0%</td>
<td>2.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General and Admin.</td>
<td>3.0%</td>
<td>3.0%</td>
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<tr>
<td><strong>Total Expenses</strong></td>
<td>7.0%</td>
<td>7.0%</td>
<td></td>
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<tr>
<td><strong>Operating Profit (Pretax)</strong></td>
<td>8.0%</td>
<td>18.0%</td>
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## Balance Sheet Assumptions

<p>| | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Receivables (DSO)</strong></td>
<td>90 days</td>
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<tr>
<td><strong>Inventory Turns</strong></td>
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<tr>
<td><strong>Accounts Payable</strong></td>
<td>30</td>
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<tr>
<td><strong>Accrued Expenses</strong></td>
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<tr>
<td><strong>Depreciation</strong></td>
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</tr>
<tr>
<td>Equipment</td>
<td>3 years</td>
</tr>
<tr>
<td>Facilities</td>
<td>20 years</td>
</tr>
<tr>
<td><strong>Discount Rate</strong></td>
<td>15%</td>
</tr>
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</table>
## Annual Revenue for a Favorable Return

<table>
<thead>
<tr>
<th>Expenses</th>
<th>Year 1</th>
<th>Year 2</th>
<th>ARV</th>
<th>RH</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D (Bioequivalence)</td>
<td>$945,750</td>
<td>$315,250</td>
<td>$59,355,144</td>
<td>$3,101,291</td>
</tr>
<tr>
<td>Sales and Marketing (Local)</td>
<td>$31,250</td>
<td>$93,750</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General and Administration</td>
<td>$0</td>
<td>$0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Expenses</strong>:</td>
<td><strong>$1,386,000</strong></td>
<td></td>
<td><strong>$59,355,144</strong></td>
<td><strong>$3,101,291</strong></td>
</tr>
</tbody>
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### Capital Investments

<table>
<thead>
<tr>
<th>Expenses</th>
<th>Year 1</th>
<th>Year 2</th>
<th>ARV</th>
<th>RH</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D Equipment</td>
<td>$0</td>
<td>$0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manufacturing Equipment</td>
<td>$0</td>
<td>$0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plant and Facilities</td>
<td>$0</td>
<td>$0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Capital</strong>:</td>
<td><strong>$0</strong></td>
<td></td>
<td></td>
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</table>

### Expenses

<table>
<thead>
<tr>
<th>Expenses</th>
<th>Year 1</th>
<th>Year 2</th>
<th>ARV</th>
<th>RH</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D (Bioequivalence)</td>
<td>$383,250</td>
<td>$127,750</td>
<td>$128,813,763</td>
<td>$6,730,486</td>
</tr>
<tr>
<td>Sales and Marketing (Local)</td>
<td>$31,250</td>
<td>$93,750</td>
<td></td>
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<tr>
<td>General and Administration</td>
<td>$0</td>
<td>$0</td>
<td></td>
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<td><strong>Total Expenses</strong>:</td>
<td><strong>$636,000</strong></td>
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### Capital Investments

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<th>Year 2</th>
<th>ARV</th>
<th>RH</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D Equipment</td>
<td>$37,500</td>
<td>$12,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manufacturing Equipment</td>
<td>$1,012,500</td>
<td>$1,012,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plant and Facilities</td>
<td>$247,500</td>
<td>$82,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Capital</strong>:</td>
<td><strong>$2,405,000</strong></td>
<td></td>
<td><strong>$128,813,763</strong></td>
<td><strong>$6,730,486</strong></td>
</tr>
</tbody>
</table>

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 …

Manufacturers

Procurers

Regulators

Governments

Donors

NGO’s

Supply Chain

Quality RH Supplies

…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.