ISPE/FDA Conference Baltimore June 2014

Securing Reliable Supply From India

David Smith
Executive Vice President, Global Operations
AstraZeneca

Connecting a World of Pharmaceutical Knowledge

Pharmaceutical exports from India $15 B in 2013

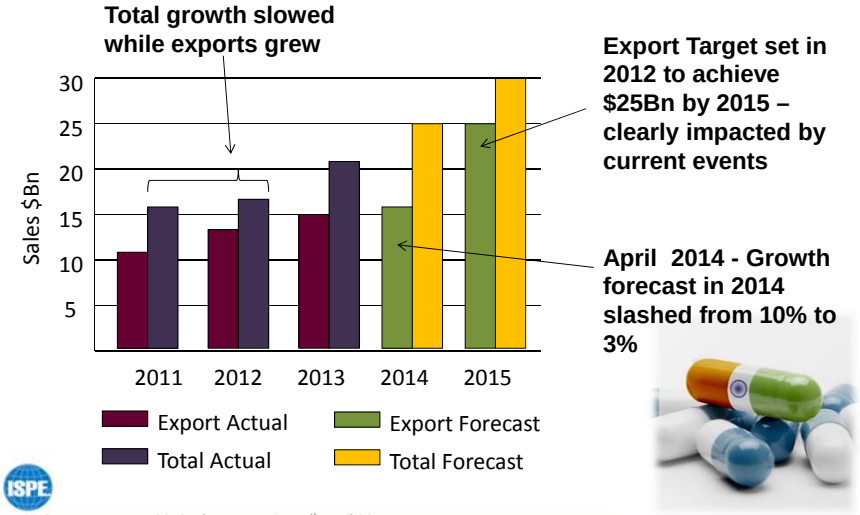
India's Pharma market is growing rapidly and is a major source of generic medicines to the US

- **25% US market, 18% for EU 17% Africa**
- **API sales significant**
- **370 US FDA approved manufacturing facilities in India**
- **US imports in 2013 $4.23Bn – 40% of generic and OTC medicines in the US**

Source The Economist 17th April 2014

Set area descriptor | Sub level 1 2

India's Pharma market is volatile in growth and forecasts are aggressive

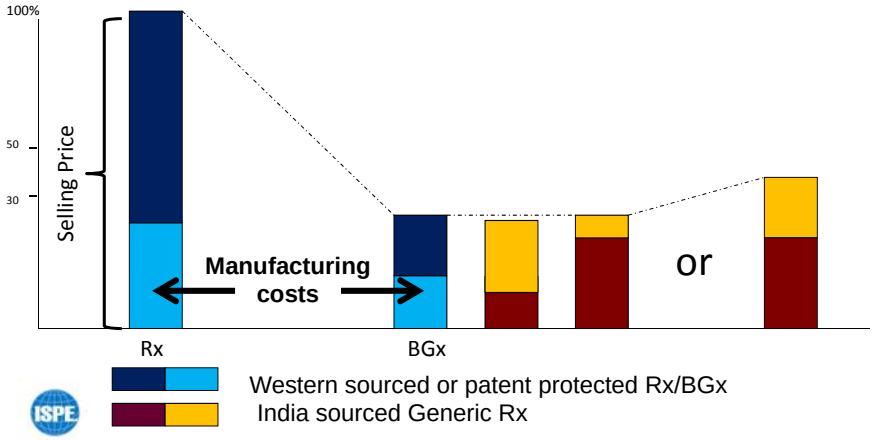


Source DIPP Dec 2013, The Economist 17th April 2014

The Economic Rationale

The cost basis of patented drugs is different to generics

..and as standards rise, costs and margins will be under pressure



Views from the market are clear about the fundamental issues

From what I have seen and experienced, there is a fundamental difference in operating philosophy, US/Western health agencies are process-oriented and ask for evidence of 'building in quality' to comply with regulations - build robust and flexible processes to ensure that the final product is of appropriate and reliable quality

Emerging markets are still maturing in their approach to quality, and continue to rely on 'testing in quality' – meaning to rely on testing efforts/inspections as a quality assurance failsafe; because of this together with the way plant personnel are incentivised you have a situation whereby in the event of failure, you get repeated testing performed until a "success" result is obtained and a huge effort to erase any record of the previous "fail" results (fraud)

5

The level of warning letters issued in India has increased and the recurring issues are based on system failures rather than facilities

Warning letters issued in India have increased 300% since 2008-12

- **85% observations in quality systems, laboratory control systems and production systems**
  - inadequate incident investigation, root cause analysis
  - inadequate SOP inadequate batch records
- **Data integrity is a recurring issue**
  - unsubstantiated retesting, unofficial records, fraud, poor data security

6

Reaction from Regulators and other stakeholders

External Regulators	**FDA** **•Established local offices in India and China** **•Attends sites with little notice for inspections** **•Conducting sessions to explain expectations on quality;** **•Focus is on risk based audits** **•Focus on supply of critical medicines** **Other regulators – less obvious, different actions - (studying FDA actions)** **EMA planning surprise inspections in 2014**
Internal Regulators (DGCI)	**Indian regulators trying to move to global approaches and standards** **Further reaction is unclear** **Plans to increase number of inspectors threefold in 3-5 years**
India Industry bodies	**Discussions on setting up industry wide movements on quality such as setting up centres of excellence**
Local Companies	**Leading companies are embarking on organization wide quality transformations** **Building plans for Quality Transformation in various ways** **Potential for cost increases in line with greater compliance**

Impact to India market has been substantial

2014 forecast growth slashed from 10% to 3%

Economic impact in India

- Some companies impacted 10-20% of their top line, Wockhardt 30%
- FDA has issued import bans on multiple manufacturing facilities of Indian and foreign companies
- Some evidence of loss by one local company typically taken up by another local company
- Competition for 'quality capacity' will be high
- Cost pressures as a result of greater compliance

Pharmaceutical landscape

- Some local companies will accelerate the journey for quality improvement
- Others may take alternative paths and look for markets/sectors with less regulatory challenge

Source The Economist 17th April 2014

What can be done ?

Supplier selection and ongoing management are key to securing reliable supply from India?

1. **Select the right partners through rigorous audit of systems prior to selection**
   - Look at past performance and develop risk based assessment tools – primarily based on 'system performance and robustness'
   - Consider the whole supply chain – materials and suppliers
2. **Develop stronger ongoing audit processes**
   - Learn from non-Pharma examples such as Apple and Nike
3. **Continuous Supplier Engagement**
   - Change the paradigm of managing suppliers
   - Use of leading metrics focused on key risk areas
   - Dedicated people who 'know' the site
   - Ongoing fact based risk assessment and mitigation

9

Key Messages for Manufacturing/QA Professionals

- Remember, the patient comes first

- Protect Corporate Reputation

- Take a Risk-based, cautious approach

- Invest in the future

Author | 00 Month Year Set area descriptor | Sub level 1 10

Questions,Comments ?