Impact of 2013 US FDA Actions on Indian Pharma
Material Top-line Erosion Unlikely, Compliance Key to Capitalise on Investments

Special Report

No Material Revenue Impact, Urgent Correction Indicated: India Ratings & Research (Ind-Ra) expects the 2013 US Food and Drug Administration (US FDA) import alerts to not have a material impact on the existing US exports revenue of Indian pharmaceutical manufacturers. Ind-Ra believes that the potential for the Indian pharmaceutical industry to grow at a 20% CAGR over the next five years is intact, which primarily depends on US exports growth. This is considering the rapid increase in product approvals by US FDA along with the increasing number of manufacturing facilities registered with it, strong trend of growth in drug exports coupled with considerable opportunities in the US and the correctable nature of regulatory actions.

We also believe that the Indian pharmaceutical industry will be able to establish quality assurance processes as well as a compliance culture to reduce import alerts.

Regulatory Actions May Continue: Ind-Ra believes that Indian pharmaceuticals manufacturers will face increased US FDA inspections. This is considering the US’ increasing dependence on Indian pharmaceuticals manufacturers and the bad press earned by Indian pharmaceuticals on account of the recent spate of import alerts. India also has the highest number of US FDA approved facilities outside the US and Indian manufacturers have been registering increasing number of products every year. India also accounted for 40% by volume of US generic drug imports in 2013 and Indian exports to US have also been growing steadily.

USFDA issued import alerts against 21 Indian manufacturing facilities during 2013, including pharmaceutical majors Ranbaxy Laboratories Limited and Wockhardt Limited.

US Holds Largest Growth Opportunity: India is the largest supplier of generic drugs to the US in terms of volume. The likely increase in the use of generics in the US as a consequence of the implementation of the Patient Protection and Affordable Care Act (commonly called ACA/Obamacare) provides an opportunity to Indian pharmaceuticals to expand exports. The US has become the single-largest destination for Indian pharmaceutical exports, a position Ind-Ra expects to continue in view of the high CAGR of exports of 27% over 2008-2013 (Source: Centre for Monitoring Indian Economy (CMIE)). In 2013, 26% of Indian pharmaceutical exports were to the US (2012: 25.7%).

Ball in Indian Industry’s Court: To grasp the opportunity, Indian pharmaceuticals manufacturers have registered the largest number of manufacturing facilities with US FDA in the world (outside the US) and also accounted for 39% of the total generic drug approvals during 2013. However, to effectively capitalise on the investment and effort, the continuance of good manufacturing practices and high quality standards including a strict compliance and record keeping regime will have to be put in place urgently.

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Highest Number of Import Alerts in a Year

US FDA issued import alerts against 21 Indian manufacturing facilities during 2013 including those of Ranbaxy Laboratories Limited and Wockhardt Limited. In 2014 so far, the FDA has issued import alerts against two Indian facilities including an active pharmaceutical ingredients (API) manufacturing facility of Sun Pharmaceutical Industries Limited (Sun Pharma). A total of seven Indian facilities were under import alert in 2011, nine in 2012 and 32 in March 2014, the highest ever.

An import alert effectively bans all exports of pharmaceutical products from the subject plants into the US and renders all the stocks of the impacted production batches unsalable in the US market. Import alerts issued against Indian plants in 2013 accounted for 49% of the total 43 such imports alerts issued by US FDA worldwide.

Indian pharmaceutical manufacturers continuously and steadily increase their product approval pipeline. Products typically receive approval along with identified manufacturing facilities. The new products, once approved by US FDA, would boost US exports in the coming years. As the import alerts have effectively embargoed all products manufactured from subject facilities, all molecules approved to be manufactured in these facilities cannot be introduced in the US market. This has dented the prospective revenue streams of banned Indian manufacturers.

Similarly, the R&D effort that went into the development of new molecules, for which approvals were planned to be obtained for manufacture in the banned facilities, cannot be commercialised/monetised for the duration of the import alert.

Limited Revenue Impact, So Far

Although an important and urgent matter for the Indian pharmaceutical exporters, Ind-Ra believes that the higher number of import alerts from the FDA is ‘business as usual’ for the industry. The import alerts have so far not reduced the Indian pharmaceutical exports to the US by a substantial amount, which grew 14.2% yoy in 2013 to INR225bn. Ind-Ra expects the impact on the existing exports revenue to be around 7%-8% of the total exports to the US and around 2% of the overall 2013 pharmaceutical exports from India.

Most of the manufacturing sites which came under the FDA import alert in 2013 and 1Q14 were small API manufacturers. Sun Pharma’s Gujarat-based API unit that came under FDA import alert in March 2014 accounts for below 1% of the company’s revenue.

A substantial revenue impact is likely for Wockhardt (above 25% top-line erosion likely) and Smruthi Organics Limited (above 50%). Ranbaxy Laboratories and RPG Life Sciences Limited also will not see any significant revenue erosion. However, they may face a substantial opportunity loss on account of postponed product introductions and expenditure on corrective actions along with the time and effort required to regain FDA approval (usually one to two years).

USFDA Inspections – the ‘Gold Standard’

US FDA’s drug approval and review process is recognised worldwide as a preeminent certification standard for Good Manufacturing Practices (GMP) for drugs. To regulate the quality of drug delivery in the world’s largest pharmaceutical market, US FDA maintains (and regularly updates) the high standards for drug and manufacturing process review and approval. The FDA’s machinery for overseeing and regulating this quality process includes the Centre for Drug Evaluation and Research, the Office of New Drugs and Office for Drug safety. These ‘offices’ are responsible for approval of new drugs, maintaining quality of the drugs approved and ensuring safety of patients and overseeing the complete process of drug delivery for the US citizens and millions of residents of poor countries where the US government and philanthropic organizations provide healthcare.

Figure 1
Import Alerts Issued in 2013

<table>
<thead>
<tr>
<th>Company</th>
<th>Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amsal Chem Pvt Ltd</td>
<td>1</td>
</tr>
<tr>
<td>Global Calcium Private Limited</td>
<td>5</td>
</tr>
<tr>
<td>Kamud Drugs Pvt Ltd</td>
<td>1</td>
</tr>
<tr>
<td>Kondukar Laboratories Pvt Ltd</td>
<td>1</td>
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<tr>
<td>Micro Labs Limited</td>
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<tr>
<td>Nivedita Chemicals P Ltd</td>
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<tr>
<td>Promed Exports Private Limited</td>
<td>1</td>
</tr>
<tr>
<td>Ranbaxy Laboratories Limited</td>
<td>2</td>
</tr>
<tr>
<td>RPG Life Sciences Limited</td>
<td>2</td>
</tr>
<tr>
<td>Smruthi Organics Limited</td>
<td>1</td>
</tr>
<tr>
<td>Unique Chemicals</td>
<td>1</td>
</tr>
<tr>
<td>Vignesh Life Science Pvt Ltd</td>
<td>2</td>
</tr>
<tr>
<td>Wockhardt Limited</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
</tr>
</tbody>
</table>

Source: US FDA
India – Cost-effective and Reliable Source of Generics to the US

Indian exports of generics to the US account for 40% of the world’s largest pharmaceutical market’s generic drugs share in volume terms. Understandably, the FDA’s interest and focus on vigilance in India is more than in other countries. India has always undergone the most number of facility inspections for any foreign country on account of the large number of facilities.

The increasing number of inspections should be seen in the context of the increasing number of manufacturing facilities registered with USFDA. 523 Indian facilities were registered with USFDA as on March 31, 2014, which is the highest number for any country outside the US. The share of US imports from India (2008: 2.5%; 2013: 6.1%) has also increased steadily in the US drug import pie.

US’ pharmaceuticals imports grew at a low CAGR of 1.26% between 2008 and 2013, and so did the country’s imports from its major pharmaceuticals suppliers. Indian pharmaceuticals exports to the US more than doubled during this period on the back of an annual growth rate of above 20%.

The numbers in Figure 3 should be seen in the context of Ireland being a tax haven from where most US companies prefer to import. Most of the actual process of drug manufacture is done in facilities outside Ireland. The drugs are brought into Ireland and re-exported with some minor value additions. Switzerland, the UK and Germany are home to large pharmaceuticals companies such as Bayer AG, Novartis AG and AstraZeneca Plc which primarily market patented and costly drugs in the world’s largest pharmaceuticals market. Israel, home of Teva Pharmaceutical Industries Ltd, also manufactures generics pharmaceuticals, while almost all Indian exports to the US are inexpensive generics.

At a time when demand for generics is poised to increase in the US, the Indian pharmaceutical industry is leading the effort to meet the demand by registering the largest number of generic products as well as manufacturing facilities with US FDA.
Importance Likely to Increase
The total number of US-based fixed dosage formulations (FDF) facilities listed on the FDA's the Generic Drug User Fee Amendments of 2012 (GDUFA) page was 315 at end-January 2014 and that of foreign FDF was 433. API facilities were 128 and 775, respectively. The total number of US FDA registered facilities in India was 523 on 19 February 2014. This is about 17.4% of the total 2,997 such facilities in the world outside the US. The number of manufacturing facilities approved by US FDA (both FDF and API) increased to around 325 as of 30 September 2013 from below 100 in 2008. The latest number is highest in any country outside of the US.

The number of product approvals has also been large. Indian companies accounted for 39% of all Abbreviated New Drug Application (ANDA) approvals in 2013. This tremendous increase in activity provides context to assess the impact of regulatory actions.

Figure 4
Increasing Share of Product Approvals

Inspections to Continue
Ind-Ra believes that the continuously increasing number of approved manufacturing facilities and products increases the potential for Indian imports into the US. Moreover, the negative press that the Indian pharmaceutical manufacturers have been facing since early 2013 has increased the sensitivity of the US public towards drugs imported from India. Consequently, the frequency and quantum of FDA inspections are bound to increase. The FDA is increasing the number of its American inspection staff stationed in India to 19 from 12 earlier.

Regulatory Oversight to Intensify, While Actions May Subside
The amount of effort, time and funds required to obtain US FDA’s nod (manufacturing plant as well as products) is substantial. Moreover, Indian manufacturers can ill-afford to be on the wrong side of the regulation in view of the tremendous opportunity for growth that Obamacare presents. The cost of approvals has also gone up due to recent fee revisions. Ind-Ra believes the examples of Ranbaxy Laboratories and Wockhardt (among others) will establish the pre-eminence of regulatory compliance among Indian manufacturers. Given sizeable opportunities, the agency believes large pharmaceutical companies will spend more effort and resources to improve compliance resulting in a lower number of regulatory actions.

Medium to large Indian manufacturers are proactively engaging third party consultants to ensure compliance to the FDA’s current GMP.
US Not Discouraging Indian Pharmaceuticals

There is an increasing concern about the large number of sanctions against the Indian pharmaceutical manufacturers by the FDA and whether India is being targeted due to its policy on compulsory licensing.

A closer scrutiny of the warning letters issued since 2013 reveals that most Indian manufacturers struggle with maintaining proper records and thereby an audit trail. Considering the life-saving nature of the products in question (drugs), it is imperative that proper records and audit trail are maintained. Ind-Ra believes that Indian pharmaceutical manufacturers will have to meet such genuine requirements or risk losing the lucrative business.

We believe that the US will not discourage the largest source of generic drugs, given its focus on reducing the cost of healthcare delivery and the consequent increase in usage of cost-effective generics. However, at the same time it will actively enforce its quality standards.
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