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Beginning of end to Indian CROs?

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Given the countries clinical trial woes already, the fresh new controversy seems to have given yet another major blow to India in the international clinical trials scene. The country is also tasting the bitter pill of witnessing the dwindling number of CROs.

Four European Union (EU) countries including Belgium, France, German, and Luxembourg banned marketing authorizations of 25 generic drugs whose clinical tests were conducted by GVK Bio at its Hyderabad site.

On December 5, 2014, the European Medicines Agency (EMA), the EU drug regulator, said on its website, "Some member states have decided to suspend the marketing authorizations of medicines that have been authorized on the basis of studies conducted at the GVK Biosciences site in Hyderabad. EMA is currently reviewing findings of non-compliance with good clinical practice at this site, and determining their impact on medicines authorized on the basis of studies performed."

The suspensions taken at national level are precautionary measures until the review is finalized, EMA said. The regulatory body now believes that GVK Bio has been 'systematically manipulating' its clinical studies.

Data reliability

EMA pointed that it started the review back in September 2014 post the inspection carried out by the Agence Nationale de SÃ©curitÃ© du MÃ©dicament et des Produits de SantÃ© (ANSM), the French medicines agency, at the GVK Biosciences site, raising issues related on the reliability of studies conducted between 2008 to 2014.

ANSM conducted the inspections between May 19 to 23, 2014, at GVK Biosciences Hyderabad site.

Rippling impact?

Though there is no visibility on the revenue impact on GVK Bio following this announcement, Mr Joshua Owide, director, healthcare industry dynamics, GlobalData, said, ""The collateral damage to those companies implicated in the decision to suspend sales of GVK-associated products could be fairly significant, not only in terms of their revenue, but also their credibility as a whole."

The banned products belonged to major drug-makers including US-based Abbott, Mylan, Teva and Zydus.

Mr Owide believes that the most direct impact on GVK will be to its CRO business.

"India represents a key hub for clinical trials not only for domestic players, but also for multinationals, and there are already high levels of scrutiny surrounding the correct following of clinical trial regulations. This is exemplified by the announcement of new trial regulations enforced by Central Drugs Standard Control Organization (CDSCO), although it appears to be too-little-too-late in this case," he added.

The Federal Institute for Drugs and Medical Devices (Bundesinstitut fÃ¼r Arzneimittel und Medizinprodukte, BfArM), Germany, noted that 'it has ordered drug manufacturers, wholesale dealers, medical stores and other outlets not to sell or use these medicines any longer.'

The dispute

In its official statement, GVK Bio disputed, "....We believe that the conclusions of the ANSM and the subsequent actions by the EMA are highly disproportionate to the actual risk posed to human health. At the same time, we respect and honor the conclusion made by the European regulators, and are working with our clinical development customers to provide new data that meets all regulatory requirements."

When approached by *BioSpectrum*, GVK Bio refused to comment further. However, Mr Manni Kantipudi, CEO GVK Bio, told Reuters, "We have agreed to redo the studies. I'm fine with that, but don't say that there was gross manipulation of the ECGs." He also revealed that the company had received approval from its board to spend US $5.7 to 6.5 million for conducting fresh new studies on the same.

India's image hurt?

Ms Suneela Thatte, president, Indian Society for Clinical Research (ISCR), expressed, "It is important to stress that there are several hundreds of clinical trials taking place in the country in compliance with international and local guidelines. There have been over 40 USFDA clinical trial audits done in India with no critical findings reported. There have also been several European regulatory audits of Indian clinical trial sites, again with no critical findings. Global studies have also shown that there is no difference in quality of data across geographies, including India."

She feels that it is not as much about the ban as the imbalance between positive and negative news which is hurting the image of India in the clinical research world.

"It is important that we use facts, statistics and data provided by leading organizations such as Association of Contract Research Organizations (ACRO) to build trust and confidence about the high quality and caliber of research being done in India," she stressed.

Further recommendations

Now the EMA's Committee for Medicinal Products for Human Use (CHMP), a committee said to be responsible for preparing opinions on questions concerning medicines for human use, is expected to review GVK Bio's clinical data in question and then suitably suggest whether the suspended marketing authorizations will be maintained, varied or withdrawn across the EU territory.

The recommendation is expected in January 2015, pointed EMA on its website.

In a notification by the European Commission to the CHMP, the following findings were reported:

- Falsifications of electrocardiograms in each and every one of the 9 trials inspected by the ANSM
- Number of members of staff involved show lack of GCP training, awareness and understanding of members of GVK Bio staff, a lack of understanding by them of the importance of data integrity, and of the possible consequences of their acts, as well as a lack of overview of clinical trial activities by the investigators.

The deputy spokeswoman at the Federal Institute for Drugs and Medical Devices told *BioSpectrum*, "The review is still ongoing. The CHMP opinion will be forwarded to the European Commission, which will adopt a legally binding decision."

The experts also believe that depending on the gravity of the data review, CHMP might extend its inspection to studies conducted at GVK Bio prior to 2008.

Future of Indian CROs?

Mr Owide said that when there is doubt over regulatory proceedings being correctly followed, overseas players remain judicial in their approach towards doing business with affected companies, regardless of the end product.

"While India's healthcare sector has typically found success over other developing markets in terms of cost and qualification, it falls short, like many of these markets, in terms of regulatory standards being upheld. While there may be an element of protectionism by the relevant governing bodies in the EU, it ultimately serves as a warning sign for companies in India to retain the high standards that helped them to flourish and become major players in a global context," Mr Owide remarked.

"We do not believe foreign regulators have any vested interest in singling out a particular country," Ms Suneela pointed. "In a global study where trials take place across markets and sites, any query over data at a particular site or in a particular country could put the entire study submission at high risk, and no regulator would want to risk that."

Despite this, Mr Owide held, "India will remain a major hub for outsourcing, collaboration and partnership, provided it can learn from this lesson and follow new regulatory guidelines more closely to ensure the integrity of its life science sector."