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'Biosimilar guidelines: a regulatory perspective'

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'Biosimilar guidelines: a regulatory perspective'



Central Drugs Standard Control Organization and Department of Biotechnology mutually formed and implemented national regulatory guidelines on "Similar Biologics: Requirements for Marketing Authorization in India" from September 15, 2012 onwards. These guidelines were much needed as many of the highly expensive innovator biotherapeutics came close to their patent expiry and Indian biopharmaceuticals manufacturers needed clear uniform set regulatory process for the development of biosimilars in India.

The guidelines were created with the rationale of creating access to affordable drugs at reasonable prices while maintaining the quality and thus safety and the efficacy. In markets like India, only a sliver of the population could perhaps pay for the biotherapeutics at the innovator's exorbitant prices. The guidelines want Indian innovation to complement the low cost manufacturing capabilities possible in India and thus attract international investors. Indian guidelines have been based on the European Medicines Agency (EMA) guidelines and this has raised the bar for approval process for our country.

Indian developers understand that the regulators want to give them a shot at clearing the standards of the regulated countries and realize the significant export opportunity in these markets helped by India's low manufacturing capabilities. This will help us overcome the myth of "Made in India" biologics-unlike the Indian generic counterparts where such stringency in regulatory pathway is not required to make a name and there is consequent widespread acceptance.

More than 20 biosimilars have been approved in India through a standalone approach before the Indian similar biologics guidelines were released. Â These "biosimilars" are yet to gain an approval from the regulatory markets like European Union, Australia, Canada, US and Japan. This raises a question on the lack of comparability process required for the approval of these biosimilars at that time.

The new generation of Indian similar biologics guidelines being developed on the basis of the stringent comparability requirements of similar biologics would have to overcome a "Made in India" bias with respect to quality and approvability for the regulated markets. This has been a factor for Indian biosimilar developers looking to collaborate with international players.

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While keeping the foreign export potential in mind with high quality biosimilars, the developer must have some incentive to develop biosimilars. This cost of development goes up as head-to-head comparability studies with the innovator's product are required starting from the first-Chemistry, Manufacturing and Control (CMC) section.
Thus a balancing act is required to maintain low development cost to make the final biosimilar retain its quality, safety and efficacy.

By getting the approval process through a variety of approval committees, the process has got thorough but is quite long winding and time to market has significantly got affected in the process.

Thus the process should be stringent while streamlining the committees and hence the review period. Every delay is costing the developers a significant amount of resources and consequently affecting their approval process in other countries either emerging or regulated. Biosimilars are getting highly competitive and time is a key factor to watch
out for.

The foreign manufacturers' who wanted to register their product earlier in India had to go directly to the Drug Controller General of India (DCGI) office for approval but after the introduction of new biosimilar guidelines, even their review has come under the purview of Review Committee on Genetic Manipulation (RCGM), Department of Biotechnology (DBT). But despite this, the applicant finds it difficult to figure out who is actually going to review their dossier because of lack of clarity of the roles of the different regulatory bodies among themselves.

The provisions for exporting biosimilar drug substance and drug product have not been addressed in the Indian similar biologics guidelines. Moreover the biosimilars manufactured in India which do not yet not possess a Marketing Authorization; do not face the same scrutiny by the RCGM, DBT with respect to data requirements for CMC, animal and human studies. Switching and interchangeability of biosimilars have not been addressed in the guidelines along with packaging and labeling of the biosimilars also having ambiguity going forward.

The biosimilar candidate, gaining Indian approval may be allowed to use the non-proprietary name of the innovator biotherapeutic reducing the branding of an individual/standalone biotherapeutic with a similar target to the innovator's biotherapeutic, reducing the marketing costs. This again would have to be determined by how similar does the biosimilar

candidate have to be to the innovator and the ambiguous "high degree of confidence" mentioned in the guidelines. As Indian developers gain hands on experience with biotherapeutics, the regulators must give them the adequate support by in depth discussions and making case by case expectations clear.

These guidelines are definitely a step in the right direction, but some kinks have to be smoothened out to derive maximum utility for the patients and developers.