Global Regulatory Landscape of Complex Generics

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Study Summary

Regulatory agencies worldwide have established guidelines and requirements for generic manufacturers of small-molecule immediate release oral solid dosage forms and aqueous injections, to ensure therapeutic equivalence and minimize the need for extensive clinical trials, but the development and approval of generic versions of complex products necessitate additional studies beyond the scope of general guidelines for simpler generics. Complex products, which have been classified in five categories by U.S. Food and Drug Administration (FDA)[1], are referred here as non-biological complex products (NBCPs)[2]; a term that includes innovators and the corresponding complex generics (CGx).[3,4]

To understand the international regulatory landscape of NBCPs, a USP study was conducted in ten countries across Africa, Asia, Europe, and Latin America. A focused analysis in seven of these countries was also conducted for twelve selected active pharmaceutical ingredients (APIs). The findings revealed the following:

- Most countries have NBCPs in all U.S. FDA-defined categories, with quality information available for specific NBCPs and general bioequivalence guidelines for certain product types within those categories.
- Complex APIs have the least information on quality and bioequivalence.
- From the selected APIs, Benzoyl Peroxide and Fluticasone Furoate were identified in all countries only as CGx, while other APIs primarily consist of non-complex products.
- From the selected APIs, complex formulations and dosage forms were identified in all countries except China; and complex route of delivery products were identified in all countries except South Korea and Turkey.
- National pharmacopeias from four of the seven countries lack compendial standards for most of the selected APIs.
- Four out of the seven pharmacopeias do not have monographs for drug products containing the selected APIs.
- China, India, and Turkey (European Pharmacopeia) have the most monographs for the selected APIs.
- India and Turkey have the highest number of registered products containing the selected APIs.

None of the assessed countries have a specific definition or specific guidelines for NBCPs or CGx.

The lack of regulatory information and quality standards for assessing CGx poses potential risks to their quality, safety, and efficacy. Advocating for convergence among regulatory agencies worldwide and establishing inter-agencies collaborations, like U.S. FDA and EMA[5], is essential to facilitate the registration and ensure access to high-quality, effective, and safe generic medicines for patients.

For more information, scan the QR code.

References

1. U.S. Food and Drug Administration. 2022. MAPP 5240.10. https://www.fda.gov/media/157675/download?utm_medium=email&utmsource=govdelivery (accessed on June 12, 2023)

2. The term NBCP is used instead of non-biological complex drugs (NBCDs) because the latter has been applied to complex APIs and to the various types of complex finished products included in U.S. FDA categories.

3. United States Government Accountability Office. https://www.gao.gov/assets/gao-18-80.pdf (accessed on June 20, 2023).

4. Complex Generics News: https://www.fda.gov/drugs/generic-drugs/complex-generics-news (accessed on June 20, 2023).

5. U.S. Food and Drug Administration. 2022. FDA-EMA Parallel Scientific Advice Pilot Program for Complex Generic/Hybrid Products. https://www.fda.gov/drugs/generic-drugs/fda-ema-parallel-scientific-advice-pilot-program-complex-generichybrid-products (accessed on June 22, 2023)