BIOSIMILARS: DRUG SUBSTANCE QUALITY ISSUES AND THEIR IMPACT ON THE SAFETY PROFILE OF BIOLOGICS

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INTRODUCTION

Patent expiry of biologics heralded a new category of medicinal products known as biosimilars, approved on the basis of similarity to their reference products. However, concerns exist among healthcare professionals about the quality and safety of biosimilars compared to their reference products.[1]

AIMS

- To identify and analyse quality issues encountered during development and manufacture of biosimilars' drug substance
- To determine whether the advent of biosimilars in the EU changed the safety landscape of biologics

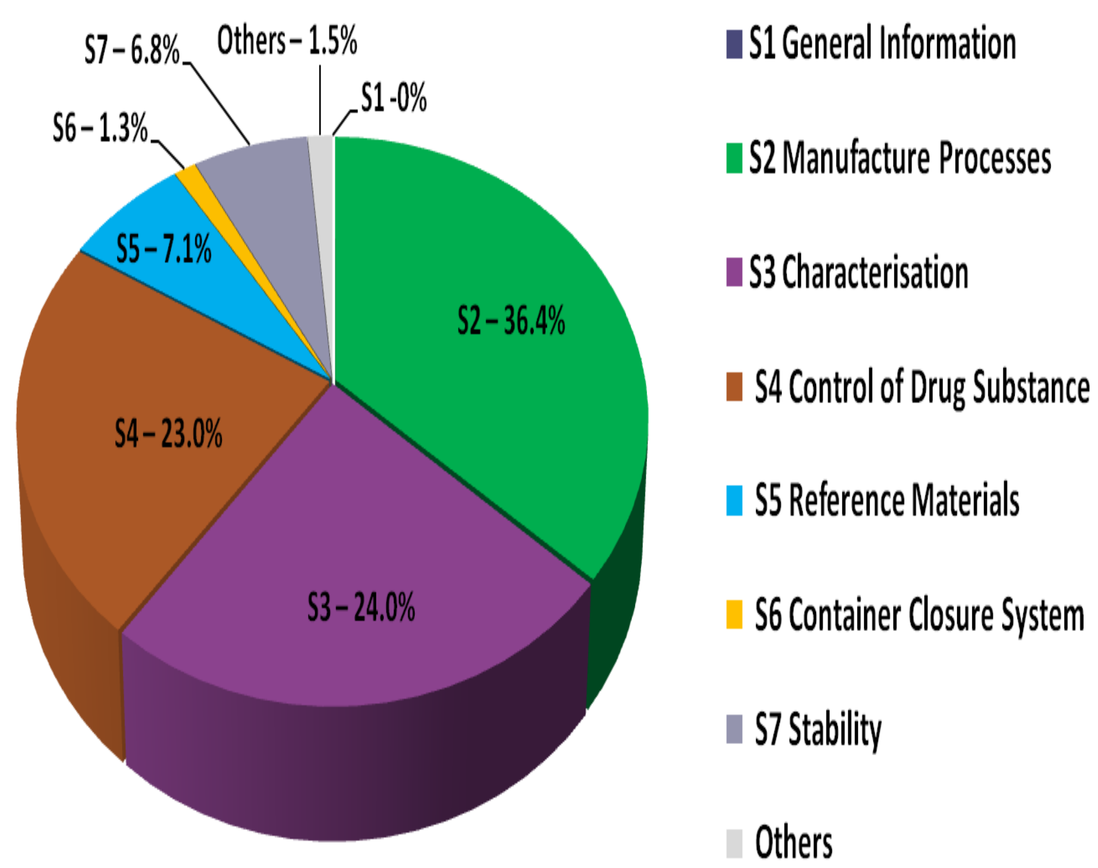
METHOD

- Questions on the drug substance quality module adopted during the European Union (EU) centralised procedure for 22 biosimilars' marketing authorisation applications (MAAs) were analysed. Questions raised, describing pharmaceutical issues, are termed as 'Major Objections' or 'Other Concerns', collectively referred to as deficiencies.
- Identified deficiencies were classified according to the Common Technical Document format for the drug substance quality module and frequencies calculated to determine the most common pharmaceutical issues encountered during development and manufacture of biosimilars' drug substance. Summarised descriptions of identified pharmaceutical issues were included.
- Changes in the safety profile of biologics with the advent of biosimilars were explored via a data mining exercise of adverse events reported in Eudravigilance, the EU pharmacovigilance database, using its inbuilt Eudravigilance Data Analysis System for signal detection.
- Any safety signals detected which emerged only after the advent of biosimilars on the EU market, were assessed for causality using the French Imputability method.[2]

RESULTS

- Analysis of questions raised for drug substance of the 22 biosimilar MAAs identified 15 'Major Objections' (mean 0.7/application, range 0-6) and 547 'Other Concerns' (mean 25/application, range 13-63) as deficiencies.
- The 3 main areas of deficiencies identified were related to the manufacturing processes (36.4%), such as inadequately identified critical steps, and issues related to drug substance characterisation (24.0%) and control (23.0%) (Figure 1).
- The data mining exercise of adverse events associated with biosimilars and their reference products did not result in any confirmed signal showing a changing safety landscape of biologics.

Figure 1: Percentage frequency of identified pharmaceutical issues (Other Concerns) for drug substance (N= 547)



CONCLUSION

This study contributes towards an in-depth understanding of quality issues related to biosimilars' drug substance development and manufacture, and indicates that to-date the advent of biosimilars on the EU market did not impact the safety profile of biologics.

References

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