Impurity Management Strategies in Generic APIs: A Case Study on the Dialkylated Impurity of Fesoterodine Fumarate

R. Rossi,[a] *S. Mantegazza*,[a]

[a] *Dipharma Francis S.r.l., via Bissone 5, 20021 Baranzate (MI)-Italy*

Impurity management represents one of the most critical aspects in the development and lifecycle management of generic APIs.

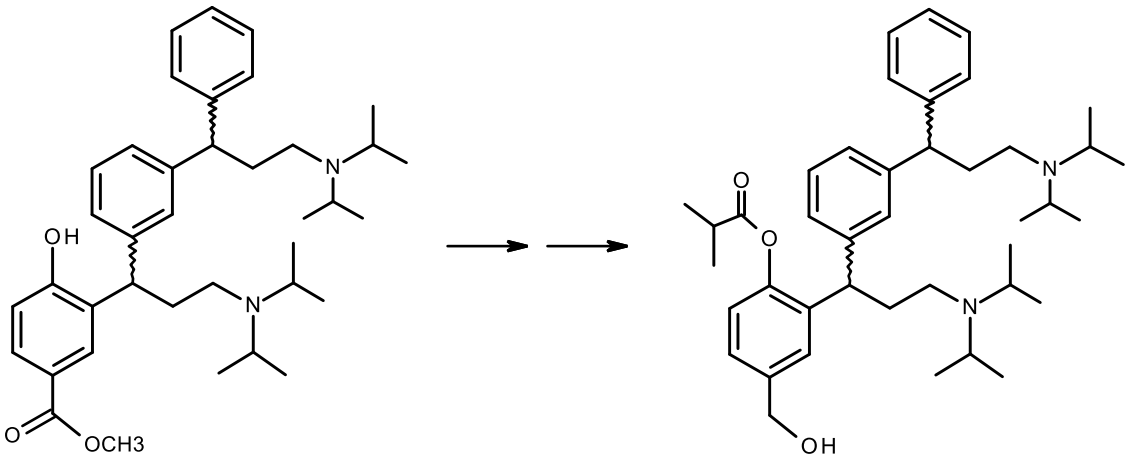
In particular, ICH guidelines impose stringent requirements for impurity identification, qualification, and control, making it necessary to carefully evaluate not only the chemical profile, but also the technical and regulatory sustainability of the strategies adopted.

This complexity becomes even more relevant for those impurities that are not covered by pharmacopoeial monographs.

Within this framework, initial assessments may be subject to revision by regulatory authorities. In particular, the classification of an impurity as "known" and the proposal of its structure, if not adequately supported by robust experimental evidence, may lead to requests for further investigation, with a significant impact on development strategies.

In this context, a case of interaction with the FDA concerning an impurity (Figure 1- dialkylated impurity) declared as known in an intermediate during the industrial production of Fesoterodine Fumarate is presented.

This case can be considered an example of the progressive tightening of regulatory expectations. Traditional approaches such as fate or purge ratio are no longer sufficient and are increasingly complemented by more robust strategies, such as spike-and-purge studies.



dialkylated impurity

Formula Weight: 572,82038
Exact Mass: 572,397793544

dialkylated impurity (derivative)

Formula Weight: 628,9267
Exact Mass: 628,4604

Figure 1

References:

[1] US patent appl. US -8530691-B2 filed on 29.10.2009