Why can the limit for total impurities in a monograph on medicinal product containing a chemically defined active substance be lower than the limit for total impurities in the corresponding active substance monograph?

Answer:

Different sets of impurities may be taken into account when setting the limit for total impurities in active substance monographs and medicinal product monographs. In medicinal product monographs, only degradation products are taken into account for the calculation of the limit for total impurities; this is in compliance with ICH Q3B. If impurities of synthesis are present at a level greater than the reporting threshold, they are disregarded after having been identified (using reference standards described in the active substance monograph or a reagent). Furthermore, any difference in reporting threshold between active substance monographs and medicinal product monographs influences the number of impurities to be taken into account for the calculation of total impurities.

Example: *Ticagrelor (3087)* and *Ticagrelor tablets (3097)*:

For the active substance *Ticagrelor,* the total impurities comprises impurities A, B, C and D as well as all other unspecified impurities present above **0.05 per cent**, whereas for *Ticagrelor tablets*, impurities A, B and D are disregarded and only impurities present above **0.1 per cent** are taken into account ("*rep orting threshold: 0.1 per cent; disregard the peaks due to impurities A, B and D.*").

For more information, please refer to the *General Notices* and the Technical Guide for the elaboration of monographs on medicinal products containing chemically defined active substances.