

**AD HOC WORKING GROUP ON  
VALIDATION ISSUES/NATIONAL REQUIREMENTS  
COMMON GROUNDS SEEN FOR DELAYING DAY 0  
RENEWALS**

*July 2008*

Although there is only an automatic validation phase for Renewals, Day 0 is often delayed.

The common grounds seen for delaying Day 0 are<sup>1</sup>:

- The application form is either incorrect and / or incomplete:  
For example: an original signature is absent, the name of the medicinal product is not that approved, the MA number(s) is incorrect, the list of variations is not in accordance with those previously submitted, the manufacturers are not in accordance with those previously approved, the product composition is not in accordance with that approved.  
The form is only partially completed, with necessary information missing.
- The documentation package is incomplete:
  - Details of contact persons responsible for pharmacovigilance, products defects/recalls and/or the scientific service in charge of information about the medicinal product are missing or incomplete.
  - Statements or certificates of GMP compliance are missing.
  - Declaration(s) are missing from the Qualified Person of the manufacturing authorisation holder responsible for batch release and from the Qualified Person of each of the manufacturing authorisation holders (i.e. located in EEA) using the active substance(s) as a starting material that the active substance(s) is/are manufactured in compliance with the detailed guidelines on good manufacturing practice for starting materials. A declaration may also be signed by one Qualified Person on behalf of all Qualified Persons involved (provided this is clearly indicated)
  - Approved SmPC, package leaflet and labelling in English are missing.
  - Proposed SmPC, package leaflet and labelling in English are missing (where applicable).
  - Quality and/or clinical expert statements, incl. CVs, are missing
- The renewal application is submitted outside of 60 days of the last DLP without the necessary Line Listing/Addendum Report.
- Two or more PSURs are submitted without the necessary Summary Bridging Report.

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<sup>1</sup> General administrative grounds for Delaying validation e.g. Fees, number of copies etc - Please refer to the NtA and CMD(h) guidance paper on Common Grounds for Invalidation/Delaying validation: <http://www.hma.eu/91.html>

Applicants (Marketing Authorisation Holders) should also note that the submitted PSURs are often incomplete, causing inefficiencies in the regulatory procedure because additional, but avoidable, questions need to be raised by MSs:

For example:

- The scope of the PSUR is too narrow because it does not address the “World-wide marketing authorisation status” of the product(s).
- The “Update of Regulatory Authority or MAH Actions taken for Safety Reasons” is deficient with many applicants forgetting e.g. Referrals.
- Differences in the PSUR reference document, CCSI and SmPC are not highlighted in the Cover Letter.
- The currently approved SmPC is missing.
- The proposed changes in the SmPC section 4.3-4.9 are not discussed.
- The “Information on Patient Exposure” is inconsistent or incorrect, e.g. the application form states that the product is marketed in several countries, but the PSUR states “no patient exposure”.
- The “Presentation of Individual Case Histories” is incomplete.
- The “Line listings” is missing.
- The “Summary Tabulations” is missing.
- The “Section on Published Studies” is incomplete.
- The “Overall Safety Evaluation” is too brief.

The CMD(h) would also like to make the applicants (Marketing Authorisation Holders) aware of the PSUR synchronisation and the possibility for an early renewal to achieve that the submission of a PSUR coincides with the renewal application for the product concerned (<http://www.hma.eu/80.html>)

- Finally, the applicants are reminded also to consider compliance with any national requirements (e.g. national QP for pharmacovigilance).