Conditions to the marketing authorisation

The National Competent Authorities coordinated by the Reference Member State, shall ensure that the following conditions are fulfilled by the MAH.

The below conditions should be fulfilled **before batches are being released on the market**:

QUALITY

1. A variation to the terms of the marketing authorisations concerning the changes to the manufacturing process as identified during the assessment should be submitted by the MAH.

CLINICAL

2. Results of additional immunogenicity tests should be submitted before batches are being released on the market.

   The required additional immunogenicity tests should show that the clinical immunogenicity profile after implementation of the additional steps in the manufacturing process is still comparable to the immunogenicity profile shown in the clinical trials for the initial MAA; safety data for the product manufactured with the updated process should also be provided.

   Submission of a revised risk management plan once results of the immunogenicity testing become available should be considered and agreed with the National Competent Authorities accordingly.

3. In addition, the Committee requires the MAH(s) to provide National Competent Authorities with interim results of the above-mentioned non-interventional PASS after release of the batches on the market.

PHARMACOVIGILANCE

4. a protocol and milestones for a non-interventional PASS to further collect safety data following the improvement of the manufacturing process, with a specific focus also on all hypersensitivity reactions (including anaphylactic reactions) should be provided by 2Q2013; this needs to be reflected in the updated risk management plan

5. The MAH is requested to submit a revised RMP to the NCAs. The RMP should be amended, in particular to include the following:
   a. a close monitoring of ADR reporting rates focusing on reports of hypersensitivity reactions;
   b. monthly ADR reporting rates focusing in particular on the incidence of all hypersensitivity reactions ;
   c. a comparison of monthly reporting rates vs. 2011/12;
   d. a separate evaluation of hypersensitivity ADRs (including anaphylactic reactions) in PSURs.

The below conditions should be fulfilled **following the release of batches produced according to the revised manufacturing process:**

PHARMACOVIGILANCE

6. Results/interim results of the non-interventional PASS in order to achieve further evidence on the safety of the product should be submitted in accordance with the agreed milestones (see condition 4).

7. The RMP should be updated to reflect the results of the non-interventional study.