European Medicines Agency
Inspections

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Procedure for worksharing – Quality variations

OUTLINE OF PROCEDURE and CALL FOR NOMINATIONS

Introduction
This procedure describes an approach for worksharing between the National Competent Autorities (NCAs) of individual member states in the European Union, where variations to the same nationally authorised product are submitted to the different NCAs. It has been elaborated by the Quality Working Party in the context of an agreement by the Heads of Medicine Agencies.

It is proposed that the worksharing exercise will normally preceed the formal variation. It uses applicable elements from the Notice to Applicants Volume 2A, Chapter 5 Variations, with modifications where relevant and necessary. In addition, the provisions for requesting inspections in the MR procedure apply.

It should be noted that it is of a voluntary nature and NCAs are not legally bound upon submission of the formal variation, to accept the decision which was reached during the worksharing. However, the procedure is structured in such a way that it will facilitate the decision making between the affected NCAs as well as final acceptance of a harmonised position. National Competent Authorities are therefore encouraged to expedite the procedure and recognise the assessment report which was generated during the worksharing phase.

It is proposed that for the time being the procedure is limited to variations introducing elements of Process Analytical Technology (PAT) and/or a design space as described in ICH Guideline Q8, where this includes PAT principles. The application of the procedure to this area is expected to be particularly beneficial, due to the fact that the variations will both be major and of an innovative nature. Therefore, the assessment will benefit from pooling the available expertise and streamlining the assessment.

The aim of this exercise is to ensure a harmonised assessment in this relatively new field. To facilitate the harmonisation exercise, the procedure foresees involvement of the EMEA PAT team. At the same time, national agencies are expected to benefit since the procedure introduces a resource efficient mechanism.

Pilot Phase
The worksharing exercise will be carried out initially as a pilot phase. Marketing Authorisation Holders which are developing PAT related variations to products which are authorised by national procedures are invited to request inclusion in the pilot phase. The pilot phase shall initially be limited to five applications for variations.

Criteria for selection to participate in the pilot phase will include
- number of affected member states
- similarity of dossiers
- expected submission date
- complexity of the proposed PAT application.

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A report will subsequently be generated with a view to concluding on the usefulness and workability of the procedure and its possible wider implementation.

Applicants who wish to participate in the pilot phase, are invited to apply for inclusion to the EMEA. A justification for inclusion, taken into account the above criteria, shall be accompanied by a completed variation application form (http://europa.eu.int/comm/enterprise/pharmaceuticals/eudralex/vol-2/c/mr-renewal-form_2004_06.doc - *Note: this will be used as information only*) with particular emphasis on or accompanied by

- Names of Products and Authorisation Status in all Member States
- possible differences in the pharmaceutical form and/or composition and specifications where relevant.
- Where slight differences between the formulations in the MSs exist, those shall be clearly outlined and an explanation given why this is of no relevance for the particular variation.
- Brief outline of the scope of the PAT application. Where available, extracts from the Quality Overall Summary or comparable summaries (1-2 pages).
- Expected submission date. This should be within the next 3-6 months.

Interested applicants need to be committed to provide appropriate resources to allow close collaboration with the EMEA and the NCAs.

The request for inclusion in the pilot phase will be assessed by the EMEA, in collaboration with the concerned NCAs. After acceptance of the product in the pilot phase, concerned competent authorities will be invited to volunteer to act as Rapporteurs.

Procedure

Submission:
For the worksharing exercise, a request for assessment making reference to the inclusion in the worksharing exercise will be submitted to all affected NCAs. The documentation will be assessed by two Rapporteurs. The first phase is not planned as a formal variation, however, if Rapporteurs consider it possible and national variation procedures allow for submission of a formal variation to the two Rapporteur Member States, within the worksharing procedure, this is encouraged.

All NCAs will be included in the assessment procedure for information at this stage and will later in the procedure have the opportunity to comment on the assessment report. Where national procedures or timetables for variations do not interfere with the proposed timetable for the worksharing, other NCAs and applicants are equally encouraged to consider submission of a formal variation during this stage.

The dossier requirements from the centralised procedure can be used for the submisssion to the NCAs: http://www.emea.eu.int/htms/human/presub/Dossier_requirements.pdf and http://www.emea.eu.int/htms/vet/presub/q24-1.htm for Vet products, unless Member States have expressed different requirements.

The date of the submission should be communicated to the EMEA as soon as possible, but at least three months in advance. The two Rapporteurs will be responsible for the coordination of the procedure.

Inspection
Companies need to be aware that PAT variations are normally expected to trigger an inspection and may involve participation of a member of the assessment team. The expected timing for the inspection will be during a clock stop, and after initial discussion of the Assessment report by the PAT team.

Assessment
It is proposed to involve the PAT team in the review of the assessment report and the identification of issues to be reviewed during inspection. Comments of the PAT team on the assessment report will be incorporated into the draft assessment report.

At day 60 of the procedure, a revised assessment report is provided together with a request for additional information and a request for inspection, as appropriate. After the clock stop, the PAT team will adopt the final assessment report by written procedure.

Timetable

The worksharing procedure which preceeds the formal variation, foresees a 60 day timetable, in line with the provisions for MRP variations, with the possibility of a 30 days extension. Please refer to the principles of the Notice to Applicants Volume 2A, Chapter 5 for further details, where not covered or amended by this procedure or the following timetable.

WORKSHARING

Day 0-10 (or more): Submission of the request for assessment/ variation (where possible and agreed with MS)
Variation dossier is submitted to all affected NCAs and the EMEA. Variation to be validated within 10 days.

Day 0: Start of procedure

Day 40: Assessment Report

Day 55: Comments from Member States.

Day 55: Feedback from PAT team.

Day 59: Request for supplementary information, including questions as identified during the meeting of the PAT team and request for inspection.

Request for inspection – Request by assessor to supervisory authority indicating specific issues to be addressed.

Day 60: CLOCK STOP
Inspection by supervisory authority.
Discussion of specific issues which were identified during the inspection in meeting of PAT team.

Day 61: start clock, upon availability of inspection report and/or responses to the adopted request for supplementary information

Day 75: Assessment Report on supplementary information

Day 85: Comments from Member states, agreement by written procedure where appropriate.

Day 89: Final Assessment Report

Day 90: Conclusion of procedure. Acceptance of assessment report on voluntary basis.

While the discretion to accept or reject the report lies with the NCA, it is expected that any concerns will be raised during the actual worksharing procedure.

FORMAL VARIATIONS

National procedures, language requirements and fees apply.

It is very important to understand that the finalisation of the procedure on a national level should not be delayed since this would endanger a positive conclusion on the exercise as a whole. National Competent Authorities are therefore encouraged to expedite the procedure and recognise the assessment report which was generated during the worksharing phase within six weeks at the most.