Worksharing variations for veterinary medicinal products

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Abstract
On 1 January 2010 the revised Variations Regulation 1234/2008/EC came into force. Within the Regulation, the concept of optional coordinated assessment of a (group of) variation(s) on the terms of marketing authorisations issued under the centralised, decentralised and mutual recognition procedures (CP/DCP/MRP) was introduced. This is known as variation worksharing. The amendment to this Regulation (712/2012/EC) which came into force on 2nd November 2012 extended the scope of worksharing variations to include marketing authorisations issued on a national only basis.

The CMDv would like to encourage greater use of the workshare facility for variations, and as such this article will outline the legislation, promote the benefits of worksharing and offer guidance regarding submission of applications.

Article 20 of Regulation 1234/2008/EC, as amended by Regulation 712/2012/EC introduces variation worksharing. This is optional for marketing authorisation holders (MAHs) and applies to products authorised under the centralised procedure (CP), decentralised procedure (DCP), mutual recognition procedure (MRP) and also those products authorised on a national-only basis. A workshare request can include a combination of products authorised under these routes. Should a workshare request involve at least one centrally authorised product then the European Medicines Agency (EMA) will automatically take the lead assessment role.1

The workshare application should only contain Type IB variations or Type II variations or a combination of these. It is not possible to include extension applications, nor is it possible to include Type IA notifications unless these are consequential changes to the Type IB/Type II changes. Within the application it is possible to include several changes to one product which is authorised to the same holder in several EU member states, or the same change(s) to a range of products if held by the same holder as defined within European Commission Communication 98/C229/03. The important aspect to note is that the same data package must apply to all the authorisations included within the application and that the end position for the change(s) must be the same for all included marketing authorisations. It is not necessary for the “current” position to be identical at the start of the procedure for all products included within the workshare application. It is not possible to submit a workshare application where only some of the data apply to some of the authorisations.

Variation worksharing brings benefits to both the MAHs and to national competent authorities (NCAs). The largest benefit is that there is a single assessment, following an agreed and predictable timetable, leading to a single outcome. The same data package would be prepared and submitted to those NCAs involved within the workshare application and/or the EMA if applicable. The EMA or one of those NCAs would be the Reference Authority taking the lead, and would conduct the primary assessment under a Type II variation European timetable. There would be no need to submit national applications, no need to wait for separate national decisions running on different national timeframes. Also, once approved then the change(s) may help in other aspects, for example benefits in manufacturing processes resulting from greater harmonisation in Part II of the respective dossiers, or uniform withdrawal periods approved across product ranges.

Should there be any divergent opinions between the member states involved in the workshare procedure, then harmonisation under the established mechanisms of the CMDv 60-day referral procedure,2 with a subsequent referral to the CVMP, if necessary, would be automatic. Again, the result would be a harmonised outcome.

Where changes to the summary of product characteristics (SmPC) are made within the context of a workshare application, then any subsequent changes to that section must be submitted to all the member states involved in the original workshare application in order to maintain the achieved harmonisation.

Before submitting your workshare application, please first liaise with your preferred reference authority to seek agreement. They can also advise on timings and the proposed classifications. Once you have discussed your workshare application with your preferred reference authority, you are ready to submit the workshare variation request to the CMDv Secretariat. There is guidance on worksharing and a letter of intent template available on the CMDv webpages of the Heads of Medicines Agencies (HMA) website.3

The CMDv will then consider your workshare request. Although the CMDv does not undertake any formal validation, it will consider four main aspects:

- To endorse the preferred reference authority; the CMDv has the final say
- To endorse the proposed variation classifications
- To review the proposal to see if any possible products or member states are not included within the request that are not specifically included within the covering letter

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Check that the authorisation holders are linked as defined within the Commission Communication 98/C229/03.

Where a workshare application has a combination of authorisations issued under MRP, DCP and on a national only basis, the reference authority will automatically be the reference member state (RMS) of the MRP/DCP product(s) included. Where there may be more than one RMS, or where the workshare application is a mixture of national marketing authorisations, the CMDv will consider the reference authority but usually the MAH preference is endorsed by the CMDv.

It is also highly recommended that, in cases where a particular product or member state is deliberately excluded from a workshare request, the explanation for this is included within the letter of intent. If this is not included then there is a good chance that this member state will query this decision at the CMDv meeting where the request is being considered, resulting in a delay to the process.

Once the CMDv has considered the request, the endorsed reference authority will write to the applicant, to confirm acceptance (or refusal) and to provide a procedure number. The CMDv may also request further information or clarification. This letter will be copied to the CMDv and member states. A copy of this letter should be attached to the application at the time of submission.

When preparing your worksharing request, please carefully consider the timings of submitting the letter of intent and your proposed variation submission date. The CMDv needs to review these requests and therefore the letter of intent must be included within the meeting papers which are circulated to CMDv members two weeks in advance of the meeting. The CMDv meeting dates can be found on the CMDv pages of the HMA website. Submission of the request to the CMDv Secretariat should be made at least 15 days before the CMDv meeting, ideally four weeks beforehand. Unfortunately, the CMDv has had examples where requests have been received one week prior to the CMDv meeting with a proposed submission date shortly after the CMDv meeting. In such cases it is not possible to meet these timeframes, with a consequential delay to the MAH’s planned submission date. The CMDv has also received requests too far in advance – these were endorsed by the CMDv and because of the passage of time to submission the MAH’s plans have changed and the previously endorsed workshare request has been amended. The amended request then has to be returned to the CMDv for endorsement, resulting in a duplication of effort.

Over the years, variation worksharing has become more popular, but the CMDv feels that much more could be made of this opportunity. (Figure 1 indicates the number of workshare requests received between 2012 and 2016.) Relatively few MAHs seem to take advantage of worksharing, but with so many products authorised on a national-only basis, the CMDv feels that there could be scope for an even greater uptake. The benefits and the process have been outlined and the CMDv would strongly encourage MAHs to consider variation worksharing.

References