Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary

London, 15 May 2014

REPORT FOR RELEASE: March and April 2014

March 2014 product discussions

Three products reached day 90 of the mutual recognition procedure (MRP) and 11 products reached day 210 of the decentralised procedure (DCP). The majority were abridged applications submitted under article 13 of Directive 2001/82/EC and primarily consisted of duplicate applications for endectocides, as well as several ectoparasiticides, for companion animals. The products for use in food-producing species were antimicrobials or anti-infectives. The full applications were for minor species or repeat-use MRP to add new markets.

	MRP	DCP	Referrals
Procedures reaching D90 (MRP), 210 (DCP) or D60 (referrals)	3	15	0
Products[*]:	3	11	0

* 1 product includes all strengths and pharmaceutical forms submitted but does not include duplicate applications, which are counted separately

April 2014 product discussions

Two products reached day 90 of MRP and 16 products reached day 210 of the DCP. The MRPs were repeat-use. Approximately two thirds of the procedures involved ectoparasiticides destined for companion animal species, either submitted as a full or abridged applications. The remaining third of products destined for food-producing species were antimicrobials, hormones, antiprotozoal, endectocide and a vaccine.

	MRP	DCP	Referrals
Procedures reaching D90 (MRP), 210 (DCP) or D60 (referrals)	2	38**	0
Products[*]:	2	16	0

* 1 product includes all strengths and pharmaceutical forms submitted but does not include duplicate applications, which are counted separately

** Three procedures (duplicates of same product) ended with a negative assessment from the RMS for which there is no possibility of onward referral to the CVMP.

CMDv updates and advice to applicants

1. Worksharing

Four worksharing requests were handled in March. Three were for vaccines and involved revision of a seed lot system, additional manufacturing site for packaging/batch release and addition of the EU as a region of original for materials. One was to increase batch size and accompanying changes to manufacturing process/tests for a pharmaceutical product.

Eight worksharing requests were handled in April – all for immunologicals/biological. The changes were quality-related, including changes to shelf-life, analytical methods, manufacturing process/tests (e.g. potency) and source of active substance.

The CMDv will hold a workshop on worksharing with the CMDv's interested parties on 6 June 2014 to enable more in-depth discussion of practical considerations concerning the functioning of these procedures.

2. Variation classification C.II.8 in classification guideline C (2013) 2804 dd. 16/05/2013

The CMDv discussed the use of variation classification C.II.8 for change in the frequency and/or date of submission of periodic safety update reports (PSURs). The variations' guideline stipulates that the change in frequency and/or date of submission of the PSUR has been agreed by the competent authority. The equivalent variation classification, C.I.10, for human medicinal products clarifies that this variation only applies where the PSUR cycle is specified in the marketing authorisation *by means other than a reference to the list of Union reference dates*. An equivalent list does not formally exist on the veterinary side although there is a voluntary work-sharing initiative, under veterinary HMA and run by the European Surveillance Strategy group (ESS), for assessment and synchronisation of PSURs per active substance. Following extensive discussion (the CVMP's pharmacovigilance working party was informed, as well as the Chair of the ESS and the European Commission), the CMDv agreed that a variation should not be required if the change to the PSUR cycle results from the aforementioned PSUR work-share initiative. However if the MAH independently wishes to change the PSUR cycle then a variation should be submitted under C.II.8. It was clarified that if the MAH requests a deviation from the standard PSUR cycle then this can be discussed during the MA application but after the MA is granted it would involve a variation. It is understood that, whilst on the human side, fee waivers have been arranged for the C.I.10 variation to avoid subjecting the MAH to unnecessary administrative burden, this remains at the discretion of the competent authority.

3. Approach and timing of variations required after a Commission Decision on an EU referral procedure

It was agreed to try and harmonise the follow-up by national competent authorities (NCAs) when variations are required to the product information following a European referral procedure once the Commission Decision is published. The proposal is for the CMDv to agree on a timeframe for implementation of changes to the product information after each European referral procedure where changes are required. The standard timeframe for implementation would be six months from the date of the Commission Decision, reduced to three months in case of serious concerns regarding public/animal health or the environment or immediate effect in the most serious situations, for example, if the withdrawal period is increased and there is evidence of residue violations. The implementation of the changes to the product information would be determined by the release of new product by the Qualified Person e.g. if a three-month implementation period was agreed then the QP should not releasing product with the unchanged labelling after this point. For products authorised via MRP/DCP, the RMS will contact the MAH(s) to inform of the timeframe for the variations required. A template letter has been prepared, which may also be used by NCAs for purely-national MAs falling within the scope of a referral procedure. It was highlighted that MAs should be granted, varied or withdrawn within 30 days of the Commission Decision. MAHs should note that Germany has requested to be excluded from this initiative due to national requirements and in Finland the implementation time may vary from that agreed by the CMDv.

4. Transparent outer packaging for vaccines

In the past CMDv reviewed a letter of intent to submit a variation to change the outer carton to clear PVC packaging for a vaccine. It was discussed whether the variation (to introduce the clear PVC outer packaging) may be applied for as a Type IA_{IN} variation under category B.II.e.6.a. However, there was also a discussion on the stability of the product which might be influenced when using a transparent box. This is also reflected in the condition for this variation "The change does not concern a part of the packaging material, which affects … stability of the finished product." In case the applicant cannot confirm this condition, the variation has to be applied for as a Type IB by default under the same category.

The CMDv agreed to request advice on a scientific matter from the CVMP in relation to a growing trend for the introduction of clear plastic outer packaging for vaccines and whether this presents a need for the revision of existing guidance on stability.

Following a detailed discussion of the various aspects it was agreed that the provision of additional stability data was not seen as the appropriate approach in each case. Therefore a variation to introduce clear plastic outer packaging could be classified under B.II.e.6.a as a Type IA provided that condition 1 is fulfilled. It should be addressed in the variation application dossier that condition 1 is fulfilled, with a justification.

Although photo-stability is not considered as a mandatory test in vaccine stability studies, for those vaccines that are known to be susceptible to light, appropriate measures are necessary and it should be considered when a vaccine is intended for a market where exposure to extreme environmental factors is a real possibility.

5. Reaching agreement on the product name during the DCP

Due to practical problems that arise when finalising the invented product name during the national phase following DCP, the CMDv has agreed that the applicant would be informed within the Day 105 list of questions, if the RMS or individual CMS(s) could not accept the product name as given within the application form. The applicant will then liaise directly with these national competent authorities to agree a suitable name during the clock-stop period. When responding to the consolidated list of questions, the applicant should confirm the agreed name. It is then foreseen that no further change to the product name can be proposed, either by the applicant or the RMS/CMS(s), for the remainder of the procedure unless there is a solid justification e.g. another product with a very similar name is authorised before the end of the DCP. This initiative should result in deliberations on the product name being resolved during a period of clock-stop in order to avoid complications when the clock is running for the second phase of the DCP. Any changes to the product name after the close of the DCP should be submitted as a variation procedure. This procedure is scheduled to come into effect after from 1 September 2014. This should ensure that there is sufficient time for both industry and NCAs to accommodate this change. Further advice will be published shortly on the CMDv website.

6. Deletion of a certificate of suitability (CEP)

The CMDv confirmed that, following revocation of a CEP by the EDQM, a variation procedure is required:

- to withdraw the manufacturer from the dossier supporting the MA (A.7 - Condition: there should at least remain one site/manufacturer, as previously authorised, performing the same function as the one(s) concerned by the deletion),

  or

- to replace the current manufacturer by a new one (in case of submission of a new CEP from a new AS manufacturer: B.III.1.a.3.

7. CMDv Q&A no. 12/2006

This document has been updated, in response to a query from an applicant, clarifying the CMDv's response to the scenario described (link).

8. Election of CMDv Chair in July

In July the CMDv will hold an election for a new Chairperson. Dr Esther Werner, who has chaired the group since 2005, was recently elected as Chair of the CVMP's Immunologicals working party and has consequently taken the decision to step down from the CMDv.

9. Documents

9.1. CMDv's Best Practice Guide on Type IA variations CMDv/BPG/004

This guidance has been amended so that MAHs are asked to include national translations in the initial submission of the variation. This change follows the approach outlined in the Commission's guidelines on variations and taken by the human side. The updated document is available in clean and tracked changes on the CMDv website (link).

9.2. CMDv's Best Practice Guide on Type IB variations CMDv/BPG/005

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Information

CMDv documents are available on www.hma.eu/cmdv.html
For further information, please contact the secretariat at the European Medicines Agency, 7 Westferry Circus, Canary Wharf, London, E14 4HB, UK; cmdv@ema.europa.eu

Common abbreviations used in this document

BPG	Best practice guide (CMDv)
DDPS	Detailed description of the pharmacoviligance system)
MA	Marketing authorisation
MAA	Marketing authorisation application
MAH	Marketing authorisation holder
MS	Member State
NCA	National competent authority