

## PSUR Work-sharing concept for veterinary medicinal products

Revised version - 01/11/07

The high-level surveys of EU pharmacovigilance resources, conducted from 2002 to 2004, resulted in identification of the need to make a more efficient use of available resources and expertise. In 2004, under the Dutch presidency, the Heads of Medicinal Agency (HMA) agreed to continue with the proposed work-sharing in the assessment of Periodic Safety Update Reports (PSURs) under the umbrella of the European Risk Management Strategy (ERMS) (Press release meeting 8-9.09.2004). The work-sharing is the concept result of collaborative working promotion in first instance applied to the area of PSUR for human medicinal products in order to increase the efficiency and quality of PSUR assessments based on the following:

- synchronisation of the PSUR submission schemes all over the European national competent authorities (NCAs) to ensure that medicinal products with the same active substance follow the same PSUR submission scheme in all NCAs.
- sharing the assessment made by one competent authority with the other NCAs.

This concept is described in Volume 9A (*Sections 1.7 and 6.2*), published in April 2007

*“New data on the benefits and risks of medicinal products will become available during the post-authorisation period and evaluation of this information should be carried out on an on-going basis by Marketing Authorisation Holders and Competent Authorities, taking account of the relevant authorisation procedures and/or any arrangements in place for work-sharing in respect of product specific/class related reviews. As a consequence of such evaluations, a marketing authorisation may be varied, suspended, revoked, withdrawn or not renewed, as necessary and according to the appropriate procedure”. (section 1.7)*

and

*“In addition, in order to put in place measures facilitating work-sharing of PSUR assessment among Competent Authorities, harmonisation of birth dates, renewal dates and/or PSUR submission schedules for medicinal products containing the same active substances may be proposed by the Marketing Authorisation Holder or the Competent Authorities. In this context, submission of a type II variation to amend the schedule is not required, if the Marketing Authorisation Holder follows the harmonised PSUR submission schedule”. (section 6.2)*

Based on the experiences concerning medicinal products for human use, the HMAvet agreed to the proposal from the European Surveillance Strategy (ESS) group on 27 April 2007 that the principle of work-sharing on PSUR assessments would be applicable also for veterinary medicinal products (see minutes 27.04.2007 top 4.b and 11.07.2007, top 4). This date should be considered as the start point of this new approach.

Both industry and authorities would profit from a situation where products, whatever the authorisation procedures used (MRP, DCP, or purely national procedure), would follow a pan-European PSUR submission scheme based on an European Harmonised Birthday (EU-HBD) and Harmonised EU Data Lock Points (EU-HDLP) for PSUR data. PSURs for all types of formulations (excipients, strength), presentations, routes, indications, and species should be provided at the same date (EU-HDLP) for one active ingredient (**Figure 1**). Using these EU-HDLPs, implementation of the major

steps to put in place this system (as shown in **Annex I**), would enable work-sharing between NCAs of the assessment of PSURs and, based on this, a harmonised regulatory action when needed and agreed upon.

To achieve successful implementation of the above system for veterinary medicinal products there are a fair number of conditions to be set, agreements to be made, decisions to be taken and actions to be executed. The experiences in the human sector show that to set up such a system requests a lot of work and the cooperation between authorities and industry is of paramount importance. Discussions between industry and regulators on a regularly basis would be necessary in order to settle the different steps of this approach and to exchange points of views on the work progress. Therefore, it is appropriate to establish a joint regulatory/industry group to coordinate this project and to share the experiences of both sides. It might be appropriate to consider whether facilitating tracking of the progress of this project is necessary or not and to select appropriate tools to follow the progress report of this work project if relevant.

It was agreed to start with a pilot phase based on a voluntary participation of NCAs and of industry.

On 2 July 2007, a meeting between ESS and industry (IFAH-Europe, AVC, EGGVP) took place in Brussels. The outcome was very positive. Industry is supporting the proposal considering that this would increase efficiency of both industry and regulatory authorities and decrease administrative burden. A full support was gained to harmonise birthdates of originator products and of generics as well. Following the discussion, HMAvet endorsed the proposed pilot phase and agreed to send a letter to IFAH for providing a proposal to set European Harmonised Birthdays (EU-HBD).

The pilot group constituted of six to seven volunteer NCAs and of volunteer industry will test the feasibility of such work-sharing: a single assessment of all PSURs related to the same active ingredient from data collected from a large number of individual PSURs after having set a EU-HBD and EU-HDLPs. At the end of the pilot phase, the experiences of the members of the pilot group will be shared in order to draw conclusions on difficulties and benefits of such work.

On 24 October 2007, a joint meeting between representatives from competent authorities and industry took place in Brussels. Several key points were addressed during this meeting and consensus was agreed on the following:

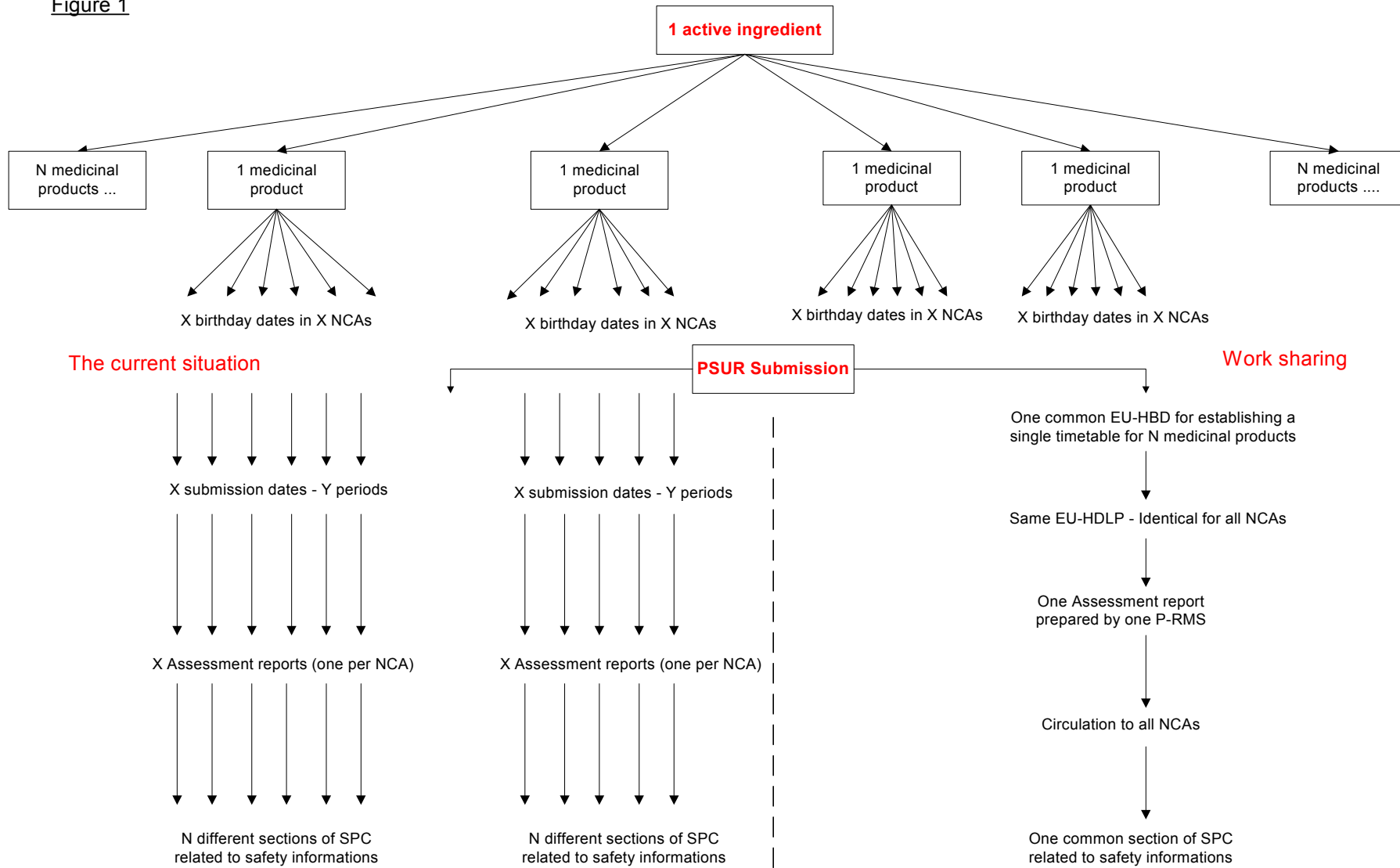
- The EU-HBD and EU-HDLP should be accepted by all NCAs having granting marketing authorisations for veterinary medicinal products containing the relevant active ingredient (including the NCAs that do not participate to the work-sharing)
- The MAHs should submit PSURs for all their products containing this active ingredient according to the agreed EU-HDLP. A PSUR may be prepared with several individual parts, each part dealing individually with a given formulation with its specific sales volume, incidence, line listing and assessment. However, in some exceptional circumstances, in case of numerous formulations, the MAH should further have the option to propose different EU-HDLPs for each formulation in order to spread the workload.
- For pharmaceutical veterinary medicinal products containing more than 1 active substance, the MAH should have the possibility to decide whether he wants to apply an existing EU-HDLP of one of the actives **OR** apply a different EU-HDLP.

- In case of a new authorisation of an existing veterinary medicinal product in a new NCA, the submission time table of the original veterinary medicinal product will systematically apply to the new authorisation, i.e. a new authorisation will directly follow the 3-yearly PSUR submission scheme if it is the current situation in other NCAs.
- For new authorisation linked to an existing medicinal product e.g. new strength, new administration route, new formulation, new indication or new species, the same principle as above will apply. However, it may be necessary to keep the legal PSUR time table till the renewal for e.g. significant new formulation, new administration route, new indication or species. This should be agreed on a case-by-case basis between the MAH and the CAs.
- For New authorisation of a generic medicinal product, the same principle as above pertains though again it may be necessary to follow the legal PSUR timetable for a generic medicinal product with e.g. a new formulation.
- Work-sharing of assessment of PSURs related to veterinary vaccines is part of this project. However, due to the differences in vaccine strains, formulations and protocols, criteria to draw up the vaccine list must be defined before starting

General agreement on these prerequisites must be obtained from all HMAvets in order to go along with this synchronisation of PSUR submission to allow work-sharing of PSUR assessments.

This note makes the point on the current reflection on PSUR work-sharing. However, it should be kept in mind that further documents should be prepared in order to define the mandates of joint regulatory/industry group and of the pilot group including the aims of such groups, their responsibilities and milestones if relevant.

Figure 1



## **Annex I: The 4 major steps of PSUR work-sharing identified from experiences in the human sector (PSUR Work-sharing based on a voluntary participation of both NCAs and Industry)**

### **Setting the harmonised EU-HBD and EU-HDLPs**

- A list of active ingredients for veterinary pharmaceutical products authorised nationally (including mutually recognised and decentralised authorised products) should be established;
- For each active ingredient, an originator should be designated, the originator being the MAH who first introduced the active ingredient on the market in Europe. The MAH who is responsible for this product will be the leader for setting the EU-HBD and EU-HDLPs in collaboration with the joint regulatory/industry group.
- Special situations requiring case-by-case consideration:
  - Several originators or no originator identified for a given active ingredient;
  - Products with numerous formulations (all with the same EU-HDLP): the MAH has the option to propose different PSUR submission dates for each formulation up to 2 months apart in order to spread the workload. It should be made sure that the submission interval between two subsequent PSURs never exceeds 3 years.
- The list of the active ingredients should be published on the HMA and all NCAs websites in order to inform the MAHs and to check that data are accurate.
- A list of vaccines (per species and/or indications) should be provided to also allow progress with harmonising submission of PSURs for veterinary vaccines.

***Benefit: harmonised submission of all PSURs for an active ingredient at a same time point, based on the originator's proposed EU HBD and EU-DLP, resulting in harmonised PSUR submission dates.***

### **Submission of PSURs**

- NCAs participating in the project should inform the concerned MAHs of the agreed EU-HBDs , EU-HDLPs and PSUR submission dates related to a specific active ingredient;
- Each MAH should prepare one identical PSUR per product that must be sent to and accepted by all the concerned NCAs. For products with several formulations, a PSUR may be prepared with several individual parts, each part dealing individually with a given formulation with its specific line listing and assessment; each formulation may alternatively have a different DLP (see above). Collaboration between different MAHs to prepare a consolidated PSUR may be of interest.
- In addition, a reference document annexed to the PSUR should be prepared by the originator in order to sum up the minimum safety information (considering not only active ingredient but also formulation) which may be subject to being addressed in all the SPCs [refers to the CCSI (Company Core Safety Information) which is part of CCDS (Company Core Data Sheet)].

***Benefit: a complete set of safety data for establishing a safety profile of each active ingredient is available within the European community at the same time.***

### **Assessment of PSURs**

In order to reduce duplication of effort and maximise the use of available resources, NCAs are encouraged to participate in the PSUR work-sharing project on assessment of PSURs by taking over the responsibility of a P-RMS.

For products authorised by MRP or DCP, the P-RMS should, preferably, be the country that acted as Reference Member State.

For purely nationally authorised products, one Member State voluntarily will act as P-RMS assessing the products authorised in his country. Other member States with authorisations of the same active ingredient will comment to the P-RMS's assessment report after checking with their national PSURs.

For veterinary medicinal products with a same active ingredient and different RMSs, the P-RMS needs to be decided on the basis of available resources at national level, on a voluntary basis.

The P-RMS is responsible for:

- Preparing a preliminary assessment report (PAR) for a specific active ingredient. All PSURs for veterinary medicinal products containing this active ingredient and authorised in the P-RMS country should be assessed at the same time;
- Distributing the preliminary assessment report (PAR) to the concerned NCAs together with a timeframe for comments;
- Collating the NCA comments and preparing a final assessment report (FAR). The NCAs should check if the assessment and conclusion are in line the safety information or the bibliography information they are aware of. If safety concerns have not been addressed by the P-RMS, NCAs should send this information as comment to the P-RMS. NCAs should check whether there are differences between P-RMS safety information in the SPC and the national safety information in the SPC of their products. In addition, NCAs may have additional information in the PSURs they have receive for other national products; this information should be sent as comments in order to contribute to an overall consolidated assessment.
- Circulating the final assessment report (FAR) to all NCAs and MAHs participating to the work-sharing related to this active ingredient.

***Benefit: at European level, the same approach will be retained for assessing PSURs of several products containing a same AI. The conclusions of the P-RMS should be endorsed by all the other NCAs. Duplication of work will be avoided.***

#### **Harmonisation of the safety information**

Based on the final assessment report, the SPC section containing safety information should be adapted where necessary; this applies to both the originator and the similar or identical generic products.

*However, it should be kept in mind that this section is related to regulatory actions and the responsibility for implementation lies with the individual NCAs participating to the work-sharing.*

***Benefit: harmonisation of the safety information contained in the SPC of all relevant products in participating Member States.***

#### List of acronyms

AI: Active Ingredient

FAR: Final Assessment Report

HBD: Harmonised Birth Date

HDLP: Harmonised Data Lock Point

MAH: Marketing Authorisation Holder

NCA: National Competent Authority

PAR: Preliminary Assessment Report

P-RMS: MS responsible for assessing the PSUR

PSUR: Periodic Safety Update Report

SPC: Summary of Products Characteristics