

Synchronisation of PSUR submission schemes for veterinary medicinal products authorised through national, mutual recognition and decentralised procedures

Questions and Answers document for Marketing Authorisation Holders

Version 5, 19th February 2010

The Head of Medicines Agencies have taken on an initiative for all veterinary medicinal products with a same active substance to follow the same PSUR submission calendar in all EU and EEA Member States. This concept is also applicable to veterinary immunological products. More detailed information on this initiative is presented in a concept paper available at: <http://www.hma.eu/236.html>.

The list of actives and vaccines for which 'virtual EU Harmonised Birth Dates (EU-HBDs) and related EU Harmonised Data Lock Points (EU-HDLPs) have been agreed on between industry and competent authorities, can be found on the HMA website, veterinary medicinal products section at: <http://www.hma.eu/236.html>. These harmonised dates shall be taken into account for the preparation and submission of synchronised PSURs. The list further provides information on the Member State nominated 'PSUR-Reference Member State' (P-RMS = Member State responsible for preparing the initial assessment report for a certain active substance or vaccine).

The list of Q&A given overleaf aims to provide guidance to industry for preparing and submitting PSURs in the framework of this 'synchronisation and work-sharing' initiative.

This is version 5 of the industry Q&A that was revised in view of the start of the consolidation phase to run from January 2010 to December 2012 and that follows the pilot phase over 2008-09. It was endorsed at the 10th meeting of the sub-group (PSSG) on 2nd February 2010. The only difference with version 4 is that questions have been re-organised and grouped by sections.

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For additional questions/queries you may have, please contact your industry association or local competent authority.

Harmonised EU-Data Lock Points

Q. 1 From what date can I start submitting S&H PSURs?

Once an EU Harmonised DLP (EU-HDLP) for an active ingredient contained in your product(s) is published on the list available from the HMA website (see: <http://www.hma.eu/236.html>), you can submit S&H PSURs based on this EU-HDLP (ensure that you take the formulations or species split into account, where applicable – see also Q. 8).

Your product may contain either one single active ingredient, a fixed combination of actives to be regarded as “one active” or other combinations, for which the originator MAH may have proposed a different EU-HDLP; thus search the list to ensure you use the correct EU-HDLP.

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Q. 2 Which date of the month shall I use for the DLP?

The agreed EU-HDLP is given in month/year. You may choose any date falling within that month as DLP, bearing in mind that some member states do prefer the last day of the month.

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Q. 3 Who is the ‘originator MAH’?

The ‘originator MAH’ is generally the first MAH to register/market an active substance (or combination of active substances) in the EU and EEA. This MAH will consequently be responsible for setting the EU-HDLP in agreement with the competent authorities (see Q. 5).

In cases where it is difficult to identify the ‘originator MAH’, any MAH that holds a MA for a product containing the given active (or combination of actives) can apply for or be asked to be the ‘originator MAH’.

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Q. 4 Can EU Harmonised DLP be changed?

No, once harmonised dates (as proposed by the originator MAH) have been agreed and published on the HMA website, these dates can no longer be changed.

Only in exceptional circumstances, i.e. serious safety concerns during assessment, may lead to a more frequent submission of PSURs.

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Q. 5 Can I add substances and EU-HDLPs to the list?

Yes, you may propose additions to the list published on the HMA website (<http://www.hma.eu/236.html>), with the exception of acids, vitamins, trace elements and minerals, which are currently excluded from the scope of the synchronisation and work-sharing. Also immunologicals are synchronised by target species and that list is deemed to be complete - see Q. 10.

When putting a substance forward, you should also propose an EU-HDLP; you will be thus regarded as the ‘originator MAH’. A proposal for an EU-HDLP must be submitted at least 6 months before the proposed harmonised date.

Your written proposal should be submitted to the contact person for national competent authorities who will bring it to the sub-group (PSUR Synchronisation Sub-Group); the current contact is Marjan van Hooft of the Medicines Evaluation Board - lj.v.hooft@cbg-meb.nl. The PSSG will then ensure that the proposed EU-HDLP does not create an unequal spread of work over the three years period, in which case a close by alternative will be suggested. In the next step, MSs will appoint a P-RMS.

Finally, the substance, the originator MAH, the agreed EU-HDLP, the P-RMS, and the EU-BD where relevant, i.e. for 'new' substances, will be added to the list.

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Content and format of S&H PSURs

Q. 6 What documents shall be prepared to accompany a S&H PSUR?

The S&H PSUR should be accompanied by the following documents:

a. **Notification/cover letter:** the MAH shall notify in its cover letter that a PSUR is submitted as part of the work-sharing initiative.

b. **Annex to the cover letter:** the MAH shall provide sufficient information to help MSs identifying PSURs of identical products between one and another country, despite different brand names. This should be presented in an annex to the cover letter in the format given below and with the following information:

< MAH Contact point >

< Active Ingredient >

< Product name for a given formulation >

Country	Brand Name in the local language	Registration Number(s)	Procedure type

This Annex should be sent to all the MSs where the products concerned are authorised and **to the P-RMS** whether the products are registered in that country or not.

c. **Core Safety Data Sheet (CSDS):** the CSDS is an **unofficial working document** prepared by all MAHs. It contains core safety information and aims to facilitate the assessment of the PSURs by the P-RMS. It must thus be prepared in **English** and should contain the following **core safety information** as extracted from the relevant SPCs:

- Contra-indications
- Special precautions and warnings: user / animal / other
- Adverse reactions (frequency and seriousness)
- Use during pregnancy, lactation or lay
- Interaction with other medicinal products and other forms of interaction
- Administration route
- Overdose (symptoms, emergency procedures, antidotes), if necessary

It is generally prepared per active but may also be done per product where several formulations and/or species are concerned, e.g. for an injectable for use in horses and chickens, a document per product would be more appropriate. It must anyhow contain all the relevant safety information of the product(s) concerned.

For immunologicals, the CSDS should be prepared per product.

The CSDS must be easily identifiable by its date (and its revision number where applicable).

Its use by the assessing CA is further explained in the Best Practice Guide for MSs available from the HMA website: <http://www.hma.eu/236.html>.

d. **Letter of attorney:** such letter should be attached in case the MAH for a same product differs amongst MSs.

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Q. 7 What information shall be contained in a S&H PSUR?

A S&H PSUR shall be prepared according to the requirements for PSURs given in Volume 9B to be published in the first half of 2010. Meanwhile, you should refer to Volume 9 of '*The rules governing veterinary medicinal products in the EU*', available at: http://ec.europa.eu/enterprise/sectors/pharmaceuticals/files/eudralex/vol-9/pdf/vol9_10-2004_en.pdf.

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Q. 8 How should the S&H PSUR of a product with different formulations be prepared?

A S&H PSUR may contain several parts, each part dealing individually with a given formulation and prepared individually according to the requirements of Volume 9B of '*The rules governing veterinary medicinal products in the EU*'. This means that each part provides its specific sales volume, incidence calculation, line listing for each single product and with its specific benefit risk assessment.

MAHs may also choose to prepare separate PSURs for each formulation, providing they are submitted at the agreed time point for that active substance.

In exceptional cases, e.g. products with numerous formulations or combinations, the originator may propose different HBDs and DLPs for each or a group of formulations/combinations in order to spread the workload in preparing and assessing PSURs.

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Q. 9 To which countries and in which format shall I send the S&H PSURs?

S&H PSURs should be submitted to all Member States where **at least 1 of the products** is authorised (as currently done). The only difference with the current practice is that the submission is done **simultaneously** to all Member States. The Annex to the letter (see Q. 6) should also be sent to the P-RMS.

Format of the PSUR: please check before submission with the respective competent authorities that should now all encourage submission in an **electronic and searchable format**. See also Annex I to the Standard Operating Procedure (SOP) on Management of Periodic Safety Update Reports on The Agency website at: <http://www.ema.europa.eu/htms/general/sop/sop.htm#Vets>.

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Vaccines

Q. 10 Can I submit S&H PSURs for vaccines?

Yes, there is a possibility to submit S&H PSURs for vaccines for use in poultry, cats, swine, dogs, cattle and horses within a 6 months window (see table below). Each MAH can define a DLP for its vaccines provided it falls within that 6 months window and that the S&H PSUR is submitted within 60 days. The S&H PSURs must be submitted to each EEA country where the concerned vaccine is registered.

			P-RMS
Rabies (monovalent) / horses (as from 2011)	1H 2008	1H 2011	PEI (rabies)
Avian vaccines	2H 2008	2H 2011	
Cat vaccines	1H 2009	1H 2012	
Swine Vaccines	2H 2009	2H 2012	
Dog Vaccines	1H 2010	1H 2013	HU
Ruminant Vaccines	2H 2010	2H 2013	BE / DE

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Miscellaneous

Q. 11 How do I switch to the EU Harmonised calendar for existing products?

The most important is that all adverse events are communicated to the authorities, i.e. gaps between the reported periods are not acceptable. In the beginning there will be overlaps, which will be accepted, since it is almost inevitable that the first harmonised PSUR will overlap with one or more PSURs submitted previously.

Thus a S&H PSUR may cover more than 3 years (addition of overlap and new report) but should not exceed 5 years. For products registered after November 2000 or which have been renewed after 20 November 2005, the time of submission shall not exceed 3 years since the last PSUR.

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Q. 12 Can I apply the EU-HDLP to a new product?

For a newly authorised product containing active(s) for which an EU-HDLP has been set, you may switch directly to the 3 yrs calendar **unless** there is a specific concern or in case the product includes a new indication or species requiring a more frequent PSUR submission.

For these products, agreement to follow the synchronised scheme should be made at the end of the registration procedure **upon request from the MAH**.

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Q. 13 Which calendar shall I follow for recently or newly authorised generic products?

When a generic is still in its 6-monthly or yearly submission cycle, a switch to the EU-HDLP can be made, **unless** there is a specific safety concern or in case the product includes a new indication or species requiring a more frequent PSUR

submission. MAHs are encouraged to consult the RMS or national CA during the assessment process to switch to the EU-HDLP.

The same applies to newly authorised generic products, for which the EU-HDLP for the relevant active may be used from the start, if agreed with the CA at the time of granting the authorisation. For this purpose, the applicant is encouraged to inform the CA that it wishes to take part in the work-sharing initiative and apply for the first PSUR submission according to the EU-HDLP, before the end of a registration procedure. The agreement will include whether an immediate start with a 3-years PSUR calendar is acceptable.

MAHs may also collaborate in the preparation of PSURs.

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Q. 14 Are the EU Harmonised BD and related EU-DLP directly linked?

For 'old products', i.e. marketed for over 5 years, the EU-HDLP is not necessarily related to the EU-HBD.

For newly to become or recently authorised products containing a new active substance, the DLP for that particular active automatically relates to the date of the product's first EU-MA, which is also the EU-HBD, unless an international birth date has already been set.

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Q. 15 What is the DLP following the originally agreed EU-HDLP?

Normally, it is the originally agreed EU-HDLP plus three years.

In exceptional cases, where specific serious safety concerns emerge, a different PSUR time schedule may be applicable; this will be notified by the national CA and indicated in the PSUR assessment report. If the frequency is different from three years, this information will also be included in the list of EU-HDLPs on the HMA website.

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Q. 16 Is the S&H PSUR submission linked to the Renewal Procedure?

In circumstances where the PSUR harmonised submission schedule is in synchrony with the renewal submission schedule and the synchronised PSUR covers the period from granting the authorisation to renewal, this PSUR may be submitted for renewal, pending agreement from the concerned CA(s).

If the period from the granting of the MA to renewal is covered by more than one PSUR, a PSUR Summary Bridging Report should be submitted.

In case the gap between the last EU-HDLP and submission of the renewal application is considered too big, a PSUR Addendum Report may be submitted in agreement with the CA.

A PSUR Addendum Report is an update of the most recently completed PSUR when a safety update is required outside the EU-HDLP PSUR schedule.

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Q. 17 Which SPC will be used to assess the S&H PSUR?

The S&H PSURs will be assessed based on the information contained in the Core Safety Data Sheet and not the SPC (see Q. 6).

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List of acronyms

AI	Active Ingredient
(H)BD	(Harmonised) Birth Date
CA	Competent Authority
CSDS	Core Safety Data Sheet
(H)DLP	(Harmonised) Data Lock Point
ESS	European Surveillance Strategy
HMA	Heads of Medicines Agencies - http://www.hma.eu/veterinary.html
MAH	Marketing Authorisation Holder
MS	Member State
P-RMS	MS responsible for assessing the PSUR
PSUR	Periodic Safety Update Report
PSSG	PSUR Synchronisation Sub-Group (composed of competent authorities and industry representatives)
S&H PSUR	Synchronised and Harmonised PSUR, i.e. prepared and submitted according to an EU-HDLP