4 August 2016
EMA/395730/2012 Rev 2* - Track-change version following public consultation

Guideline on good pharmacovigilance practices (GVP)

Module VIII Addendum I – Requirements and recommendations for the ~~transmission~~ submission of information on non-interventional post-authorisation safety studies (Rev 2)

Date for coming into effect of first version	2 July 2012
Date for coming into effect of Revision 1*	25 April 2013
Draft Revision 2 finalised by the Agency in collaboration with Member States	23 June 2015
Draft Revision 2 agreed by the European Risk Management Facilitation Group (ERMS FG)	16 July 2015
Draft Revision 2 adopted by Executive Director	3 August 2015
Release for public consultation	11 August 2015
End of consultation (deadline for comments)	9 October 2015
Revised draft Revision 2 finalised by the Agency in collaboration with Member States	14 April 2016
Revised draft Revision 2 agreed by ERMS FG	15 July 2016
Revised draft Revision 2 adopted by Executive Director as final	4 August 2016
Date for coming into effect of Revision 2*	9 August 2016

This track-change version identifies the majority of changes introduced to the public consultation version of this document as the Agency's response to the comments received from the public consultation. This track-change version is published for transparency purposes and must not be taken or quoted as the final version.

* For this reason, the timetable above, and in particular the date of coming into effect, apply only the clean version published as final.

See websites for contact details

European Medicines Agency www.ema.europa.eu
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*Note: Revision 2 contains the following:

- ~~Inclusion of notification requirements to the Agency and amendment accordingly of the title of the Addendum~~Change of the title;

- ~~Revision~~ Deletion of Tables XIII~~.~~ Add I.1. and XIII~~.~~ Add I.2. and simplification of presentation of submission requirements and recommendations based on legislation related to non-interventional post-authorisation safety studies;

- Update of submission requirements for study protocols and progress reports according to Art 107m(5) ~~based~~based on updated information provided by Member States;

- Addition of ~~a statement that the statistical analytical plan (SAP) should follow the same requirements as for PASS protocols if it is not included in the protocol.~~information regarding study registration in the EU PAS Register.

Note on the public consultation:

The public consultation was restricted to the yellow highlighted revised texts (i.e. replaced by new texts with deletions and additions) or deleted texts (i.e. not replaced). However, if revisions or deletions impacted or contradicted other existing text, comments on such non-highlighted texts were processed too and taken into account for the finalisation process.

VIII.Add.I.1. Introduction

This Addendum ~~specifies requirements~~provides additional information on legal requirements (identifiable by the modal verb "shall") and recommendations (identifiable by the modal verb "should") for the ~~transmission~~ submission of study protocols, ~~, updated protocols following substantial amendments, final study reports and~~ progress reports and final study reports ~~if requested on~~ of non-interventional post-authorisation safety studies (PASS) to national competent authorities and the Agency. It also provides additional information as regards the registration of non-interventional PASS in the EU PAS Register. It~~post-authorisation safety studies initiated, managed or financed by marketing authorisation holders voluntarily or pursuant to an obligation. Where the full statistical analytical plan is not included in the protocol, it should be reported following the same requirements as for the study protocol.~~

~~These requirements are based on Directive 2001/83/EC Art 107 m-q and the GVP Module VIII. They do not cover the situation of studies conducted in only one Member State that requests the study according to Article 22a of Directive 2001/83/EC, in which case the marketing authorisation holders shall submit the draft protocol and the other study information to the national competent authority of the Member State in which the study is conducted.~~

~~These Tables cover the requirements for transmission of information to competent (i.e. regulatory) authorities, not to ethics committees, national review boards or other bodies in place according to national legislation~~ does not provide recommendations for the transmission of information to ethics committees, national review boards or other bodies in place according to national legislation.

VIII.Add.I.2. Study registration

According to IR Annex III.3 *(Format of the final study report),* the date of study registration in the electronic study register shall be included as a milestone in the final study report for non-interventional post-authorisation safety studies (PASS) imposed as an obligation. VIII.B.2. also states that marketing authorisation holders should register all non-interventional PASS conducted voluntarily in the EU or included in the risk management plan agreed in the EU. Non-interventional PASS should be registered before the study commences or at the earliest possible date, and the study protocol (and its updates), the progress reports and the study reports should be uploaded in the register.

The EU PAS Register is a register of post-authorisation studies publicly available through the EU PAS Register webpage [1] that serves as the electronic study register mentioned in IR Annex III. The information requested at the time of study registration in the EU PAS Register includes administrative details, targets of the study and methododological aspects. The study protocol, the study report and other documents can be uploaded. Administrative information includes whether the study has been requested by a regulatory authority, information about the percentage of funding from different sources and the country(-ies) where the study will be conducted. In case the record for a new registered study indicates that the study has been requested by a regulatory authority, is funded even partially by a pharmaceutical company and is conducted in at least one EU country, the Agency sends a notification message with the full study title, the name of the funder(s), the name of the country(-ies) where the study will be conducted and a link to the current study record to all national competent authorities of the EU Member States. This notification aims to systematically inform Member States of the public registration of a post-authorisation study requested by a regulatory authority, funded by a marketing authorisation holder and conducted on their territory.

[1] http://www.encepp.eu/encepp_studies/indexRegister.shtml

Uploading of the study protocol, the progress report(s) and the final study report in the EU PAS Register is not a legal obligation. Therefore, registration of a non-interventional PASS in the EU PAS Register cannot be the only channel for the submission of these documents to national competent authorities and the Agency.

VIII.Add.I.3. Requirements and recommendations for non-interventional PASS ~~imposed as a legal~~conducted pursuant to an obligation imposed by an EU competent authority

These studies include non-interventional PASS of categories 1 and 2 of studies of GVP Module V.

The draft protocol, the updated study protocol following substantial amendment and the final study report shall be submitted according to the normal procedure to the Pharmacovigilance Risk Assessment Committee (PRAC) and the Agency, or to the national competent authority of the Member State that requested the study if the study is conducted in only one Member State [DIR Art 107n to 107p]. The final study report shall be submitted within 12 months after the end of data collection [DIR Art 107p(1)].

According to DIR Art 107m(5), the marketing authorisation holder may be required by the national competent authority to submit the progress reports to the competent authorities of the Member States in which the study is conducted. The national competent authority of all Member States in which the study is conducted, except Denmark, stated they require submission of the progress reports. The progress reports should also be submitted to the Agency for centrally-authorised products.

VIII.Add.I.4. Requirements and recommendations for non-interventional PASS conducted voluntarily

These studies include non-interventional PASS of category 3 of the GVP Module V and other non-interventional PASS voluntary conducted by marketing authorisation holders.

According to DIR Art 107m(6), the final study report shall be submitted according to national procedures to the competent authorities of the Member States where the study was conducted within 12 months of the end of data collection.

According to DIR Art 107m(5), the marketing authorisation holder may be required by the national competent authority to submit the study protocol and the progress reports to the competent authorities of the Member States in which the study is conducted. The national competent authority of the following Member States in which the study is conducted stated they require submission of the study protocol and progress reports through national procedures:

> Austria, Bulgaria, Croatia, Czech Republic, France, Germany, Italy, Lithuania, The Netherlands, Portugal, Romania, Slovakia, Slovenia, Spain.

For studies of category 3, the progress reports should also be submitted to the Agency for centrally-authorised products.

For studies of category 3, study protocols should also be submitted with the risk management plan according to the recommendations of GVP Module V.

~~For centrally-authorised products and nationally-authorised products, study protocols and reports should be reported to Member States according to Table VIII Add I.1. or Table VIII Add I.2., depending on the regulatory status of the study. For centrally-authorised products, study protocols and reports should always also be sent to the Agency.~~

Table VIII Add I.1. Studies imposed as an obligation by a competent authority

	Study protocols, updated study protocols following substantial amendments, final study reports [1]		Progress reports if requested [1]
	Direct transmission by MAH to MS [2]	*Transmission by MAH to MS via PRAC* [3]	*Direct transmission by MAH to MS* [2]
Member States where the study is conducted	All except DK		All except DK
Member States acting as Rapporteur or RMS for the medicinal product *		All	All except DK
Member States where the medicinal product is authorised, but not acting as Rapporteur of RMS for the medicinal product *		All	DE

[1] *Study information should also be entered and maintained in the EU PAS Register.*

[2] *Final study protocols, substantial amendments to study protocol, any progress reports, abstracts of final study report and final study reports to be transmitted by marketing authorisation holders to Member States according to national procedures.*

[3] *Information to be transmitted by marketing authorisation holders to the Agency and all PRAC members in the context of the oversight of post-authorisation safety studies by the PRAC as described in Directive 2001/83/EC Art 107 n p.*

** even if study not conducted in the Member State*

Table VIII Add I.2. Studies initiated, managed or financed voluntarily by marketing authorisation holders

	Study protocols, updated study protocols following substantial amendments, progress reports if requested and final study reports	
	Transmission by MAH via registration in the EU PAS Register [4]	*Additional transmission by MAH to the MS* [5]
Member States where the study is conducted	All	AT, BG, CZ, DE, ES, IT, NL, PT, RO, SI, HR, LT, SK, FR
Member States acting as Rapporteur or RMS for the medicinal product **	All	DE, DK, NL, PT, RO, CZ, SK, FR
Member States where the medicinal product is authorised but not acting as Rapporteur or RMS for the medicinal product **	All	DE, RO

[4] *After the study has been registered, a notification message is sent by the Agency to all EU Member States with a link to the study record.*

[5] *Information to be transmitted by marketing authorisation holders to Member States according to national procedures.*

*** even if study not conducted in the Member State*