Dear Madam or Sir,

We would like to inform you about the following topics:

We recommend you to check the implementation within your company. If you should require support or have further questions, feel free to contact us anytime.

1. ANNOUNCEMENT REGARDING STANDARD SENCTENCES TO BE USED IN THE SUMMARY OF PRODUCT CHARACTERISTICS (SMPC) AND THE PATIENT INFORMATION LEAFLET (PIL) TO ENCOURAGE THE REPORTING OD ADVERSE DRUG EVENTS

On 7th August 2013, a "common announcement regarding standard sentences to be used in the Summary of Product Characteristics and in the Patient Information Leaflet to encourage the reporting of adverse drug events, as well as for medicinal products under additional monitoring, according to paragraph 11 (1b) and paragraph 11a (1) sentence 9 Arzneimittelgesetz (AMG)" has been published in the German Federal Gazette by the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) and the Paul-Ehrlich-Institut (PEI). Thus the deadline for the implementation of standard sentences into the product information of nationally authorized products in Germany according to paragraph 146 (2) and (3) AMG, which is 2 years after publication of the respective announcement, has been fixed with this date.

Transitional provisions for the implementation of standard texts regarding ADR reporting

The transitional periods for the implementation of the standard text regarding ADR reporting by patients are based on paragraphs 146 (2) and (3) AMG.

As illustrated by BfArM and PEI, the standard sentence regarding ADR reporting has to be implemented into the PILs of Medicinal products that have been marketed on 26th October 2012 and are subject to paragraph 11 AMG until the following time points at the latest:

- 2 years after the first renewal of marketing authorization or registration following the publication of the announcement according to paragraph 11 (1b) AMG;
- for Medicinal products that do not require a further renewal or are exempted from the obligation for marketing authorization or registration: 2 years after the publication of the announcement according to paragraph 11 (1b) AMG;

- for medicinal products registered according to paragraph 38 AMG, i. e. registered homeopathic medicines: 5 years after the publication of the announcement according to paragraph 11 (1b) AMG.

The standard sentence relevant for your medicinal products can be found on the BfArM and PEI homepages:
http://www.pei.de/SharedDocs/bekanntmachungen/2013/banz-at-07-08-2013-b10.html

As the transitional period according to paragraph 146 (2) and (3) AMG regarding the implementation of standard texts into the product information of nationally authorized products on 7th August 2013, medicinal products with a timely unlimited marketing authorization shall only be marketed by the pharmaceutical entrepreneur with a PIL including the standard sentence regarding ADR reporting by patients **from 7th August 2015**. This applies accordingly for registrations of traditional herbal medicinal products according to paragraphs 39a ff AMG, as well as for German standardized marketing authorizations (Standardzulassungen) and standard registrations (Standardregistrierungen). Medicinal products still requiring a renewal may be marketed by the pharmaceutical entrepreneur with a PIL that not yet includes the standard sentence for 2 years following renewal.
Registrations of homeopathic medicines valid for an unlimited period of time may be marketed without the standard sentence regarding ADR reporting until 6th August 2018.

The Bundesverband der Pharmazeutischen Industrie (BPI) has given the additional information that after these time points, medicinal products can be marketed further on by wholesale distributors and retailers with the old PILs. Thus supply chain remains unaffected.

2. INFORMATION REGARDING THE SUBMISSION OF VARIATIONS TO BFARM

Information regarding the submission of variations due to the “common announcement regarding standard sentences to be used in the Summary of Product Characteristics and in the Patient Information Leaflet to encourage the reporting of adverse drug events, as well as for medicinal products under additional monitoring, according to paragraph 11 (1b) and paragraph 11a (1) sentence 9 Arzneimittelgesetz (AMG)” can be found on the BfArM homepage:

1. For all maketing authorizations subject to Commission Regulation (EC) 1234/2008 (so-called “Variation Regulation”), the following applies:

- Normally, implementation of standard texts can be conducted within the context of other regulatory activities (renewal, type IB or type II variation) implying further variations of the product information (according to chapter C of the variation classification guideline) or revision according to the current QRD template. The implementation of standard texts must be highlighted accordingly and listed in the Application Form; no separate variation is required. Within this context, there are no additional costs.
- It is possible to submit the implementation of the explanatory statements on additional monitoring and ADR reporting together with Type IA or Type IA_{IN} variations. This change is classified as a Type IA_{IN} variation with the change category C.I.z. in accordance with the Article 5 recommendation. This classification is a grouping of a variation Type IA_{IN} with a variation Type IA/ IA_{IN} and the general regulations for group-

ings of national variations have to be followed (annotation: in Germany, the BfArM accepts grouping of independent type IA and IA_{IN} variation of the categories A, B and C).

- If only the implementation of the explanatory statements on additional monitoring and ADR reporting without any further changes (a single variation) is submitted, this is considered to be a Type IA_{IN} with variation a change category C.I.z. in accordance with Article 5 recommendations. In this case fees will be charged. For further information please click here for the CMDh recommendations.
  http://www.bfarm.de/SharedDocs/FAQs/EN/drugs/variations/variareg-faq/G_explanatory_statements_adr/G_variat-ba_faq9-9-2.html

To minimize workload and to speed up processing, BfArM recommends to use the PharmNet.Bund portal for the submission of variations of product information texts:
http://www.bfarm.de/DE/Arzneimittel/zul/folgeverfahren/aenderung/hinweiseEinreichung.html

3. IMPLEMANTATION OF A PHARMACOVIGILANCE SYSTEM MASTER FILE (PSMF)

From 2nd July 2012 (for centrally authorized products) and **from 21st July 2012** (for nationally authorized products, including products authorized within the context of a DCP or MRP), applicants/MAHs are required to include a summary of the applicant/MAH's pharmacovigilance system instead of a Detailed Description of the Pharmacovigilance System (DDPS) (according to Directive 2010/84/EC in order to amend Directive 2001/83/EC, as well as Regulation (EC) No. 1235/2010 in order to amend Regulation (EC) No. 726/2004):

A Summary of PSMF according to Art. 8 (3) (ia) of the named Directive shall be included in module 1.8.1. at the time of submission of an initial marketing authorization application requiring the maintenance of a PSMF. According to Art. 23 of the named Directive, competent authorities may request the PSMF at any time point and the applicant shall be able to provide the document within 7 days.

For existing marketing authorizations (MAs), according to Art. 8 of the named Directive, a summary of PSMF has to be submitted subsequently:

- **at the time of submission of the renewal application**
- **by 2nd July 2015 (for centrally authorized products) resp. 21st July 2015 (for nationally authorized products),**

whichever is the earlier.
These requirements apply to all existing MAs with or without a detailed description of the Pharmacovigilance system (DDPS) in their dossier.

With regard to the rules for the content of the PSMF and the Summary of PSMF, please refer to the Guideline on Good Pharmacovigilance Practices (GVP) Module II – Pharmacovigilance System Master File and Chapter I of the Implementation Regulation of the Comission, which can be found on the EMA website, together with the other GVP modules published so far:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac05804fcdb

4. REVISION OF PRODUCT INFORMATION TEXTS ACCORDING TO CURRENT QRD TEMPLATE

On the EMA website, templates are published by the EMA Working Group on Quality Review of Documents (QRD which should be used for the preparation of product information texts by the pharmaceutical entrepreneurs. It is within the responsibility of the pharmaceutical entrepreneurs to ensure the compliance of product information texts with these templates.

The „QRD Templates“ are available via the following link:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000134.jsp&mid=WC0b01ac0580022c59

There are implementation dates for existing product information texts. The update of product information texts should be conducted as quick as possible, however not later than 2 years after publication of the templates on the EMA website (March 2013). This applies to products with **„regulatory activity“,** i. e. variations or renewals. For these products, the new QRD template has to be implemented **by April 2015 at the latest.**

For products **without „regulatory activity“,** the changes must be implmented within 3 years, i.e. **by April 2016 at the latest.**

These time frames have also been described in a Q&A document by CMDh which can be found via the following link (section „Variations“, Question 2.11.b):
http://www.hma.eu/20.html

On the BfArM website, information regarding classification and grouping has been published in the FAQ section:
(http://www.bfarm.de/EN/Service/FAQ/_functions/drugs/variations/variareg/_node.html):

How should an adaptation of texts in line with QRD templates be submitted in the context of Type 1B or Type II variations?
If an update of the texts in line with the QRD templates (labelling, PIL and SmPC) is submitted in addition to a Type IB or Type II variation, this should be stated clearly in the cover letter and under “Precise scope and background for change” in the application form. In this constellation no fees will be charged. No further variation submission is required, nor is reference to a variation code necessary. No fees will be charged if this change is made in the context of a renewal. Further information is available on the website of the CMDh under variations, Question 3.16.

How should an update of the texts in line with the current QRD templates be submitted in the absence of any further changes to the product information?

If only the adaption of the texts in order to be in line with the current QRD template without any further changes (a single variation) is submitted, this is considered to be a Type IB variation with a change category C.I.z. for which fees will be charged.

Can an adaptation of the texts to be in line with the current QRD templates be submitted together with Type 1A or Type IA_{IN} variations?

It is possible to submit an adaption of the texts together with Type IA or Type IA_{IN} variations. This change is classified as a Type IB variation with the change category C.I.z. which is subject to fees. This classification is a grouping of a variation Type IB with a variation Type IA/ IA_{IN}. and the general regulations for groupings of national variations have to be followed. Further information can be found in the announcement Bekanntmachung vom 12. Juli 2013.

Best regards

The DiaMed Team