



Making Medicines Affordable

## **EGA Questions**

### **MRP procedure after Enlargement**

*February 2004*

EGA welcomes the MRFG initiative to clarify regulatory practice linked to functioning of the MRP procedure after accession.

We fully understand that application of MRP rules is part of the *acquis*, which should be applicable to 25 Members. It could be also a great opportunity to reduce the workload of Agencies, especially those of Accession Countries. However, we are afraid that the environment is not completely ready for smooth implementation of MRP rules and consequences for producers, particularly from New Member States, could be very negative. This is particularly pertinent to pending applications which will not be finalised by 1 May 2004.

We would like to draw your attention to some practical aspects of the MRP at the time of Enlargement and the real impact on activity of producers and Authorities during this period.

#### **Repeat use MRP – administrative procedure**

**Situation 1.** Products that have been authorised in the acceding countries through the simplified CADREAC procedure i.e. which have dossiers and SPCs harmonised with those in the RMS, will benefit from an administrative 30-day repeat-use procedure. However, the dossier may not be exactly identical in terms of product name, pack sizes, assembly site and batch release site.

Questions: How will these differences be handled? Can they be incorporated into the administrative 30-day procedure or will separate variations need to be submitted after completion of the repeat-use procedure. If variations need to be submitted can the product still be marketed in the interim?



Suggestion of Solution: As all of these differences fall under Type IA or IB variations, our proposal is to incorporate these changes into the administrative procedure.

**Situation 2.** Products with national authorisations in the acceding countries (not via CADREAC simplified procedure), when the dossiers and SmPCs in CMSs are harmonised with the RMS.

Questions

Can these products benefit from a shortened 30-day repeat-use procedure to switch all national MAs to MRP?

If differences are Type IA or IB variations (as described above), is it possible to incorporate these variations into the procedure in parallel?

**Situation 3.** Products not yet authorised in the acceding countries (pending applications), but already authorised in EU-15.

Question – Is it possible to consider making special arrangements (if not finalised before accession) and to allow a shorter 30-day administrative procedure for simplified CADREAC procedures still pending on 1 May 2004? To carry out the normal repeat-use procedure for these applications adds no particular value/benefit. The acceding country already has a copy of the RMS assessment report referred to in Article 18 of Directive 2001/83/EC.

Suggestion of Solution: Our proposal is to allow a 30-day administrative procedure for these products.

**Situation 4.** Declaration from the MAH on meeting the needs of the new Member States.

Question – Will there be a template to follow?

## **2. MRP in Acceding Countries (including countries with a Transitional Period - PL, SLO, LITH, CY, MLT)**

According to the Accession Treaty, products on the transitional lists cannot benefit from MRP until renewal (deadline for renewal defined in the Treaty) or till the end of the transitional period (whichever is earlier). For example, in Poland this list was created based on MAs granted or Applications pending at the moment of preparation of this list, without assessment of whether dossiers were in line with *acquis* or not. In practice, products with dossiers conforming with EU requirements are now also included in this list.

**Situation 1.** MA already granted in one AC (e.g. Poland), applications submitted in some ACs (Cz, Hu) and current EU Members (e.g. UK, F via “daughter” company as companies from Acceding Countries could not be MAH at that time because of necessity for MAH to be established in the EU). The product registered in Poland has an EU dossier however is on the list of products covered by transitional period till 2008. Due to the huge workload in the Polish Agency, organisation of the



renewal process (in practice – official confirmation that the dossier is in line with *acquis*) will usually be determined only by the deadline defined in the Treaty.

If it is necessary to use repeat-use MRP, the producer from Poland will be obliged to wait, e.g. until 2006, for an Assessment Report which can be recognised in, e.g., the Czech Republic and Hungary as CMSs.

Question:

Instead of asking for an Assessment Report and waiting till 2006, would it be possible to continue the registration processes in other Countries (Cz, Hu, UK, F) as national applications or at least to select one of the new Countries with a pending application as RMS?

**Situation 2. Request of Assessment Report.**

Product X was registered in one of the Acceding Countries (e.g. Latvia) 5 years ago, when the EU standard Assessment Report was not required. The Latvian company now wants to register this product X in Lithuania, after 1 May 2004. The Latvian Company has to ask the Latvian Authorities for an Assessment Report to start MRP.

We are aware that the Acceding Country authorities have to prepare, in fact, retrospective assessment reports from scratch, as the EU standard report was not binding at that time. This will definitely take more than 90 days as a lot of companies will be asking for assessment reports at the same time.

CEE companies operating in particular on Acceding Country markets (being their traditional export markets), will be blocked due to a lack of assessment reports and their export activities will be sorely reduced. At the same time, a competitor from the EU-15 which already has an assessment report in the EU format (or can have one updated in 90 days), MRP repeat use procedure will clearly be easier. This obviously has an implication on competition.

Question: Could you confirm that the deadline for preparing/updating of the Assessment Report is 90 days from the moment of official request made by the Applicant? What can the Applicant do if deadlines are not respected and the delay is much longer than 90 days?

**3. Obligatory suspension of assessment after 1 May 2004 by the Authorities (art. 17, 18)**

Authorities may suspend assessment of pending Applications and wait for the assessment report from the first country. Companies are recommended to withdraw pending applications and to start repeat-use MRP procedures after 1 May 2004 based on the first MA granted.

- **Different approach for WEU and other applications**

**Situation 1:** For WEU pending applications: there is a possibility to continue via national applications (even if the product is “the same” according to the Commission definition - the same qualitative and quantitative composition of active



principle, the same pharmaceutical form); however other pending applications (e.g. generics) must follow art. 17 and 18.

Question: Why is this interpretation of possibility to continue via national application only mentioned in the context of some types of applications (WEU, line extension) but is not allowed in the others (e.g. generics)?

Suggestion of Solution: Possibility to extend this possibility to continue as national applications on other types of applications if there are a lot of obstacles to applying MRP rules (transitional period, not harmonised products, huge delay with retrospective reports etc.).

Comments: The UE-15 example shows how difficult a practical implementation of the MRP rules despite of 3 years' optional period was. Acceding countries Authorities and industry will not have this privilege to learn smoothly the MRP rules. Considerable number of problems will definitely arise after the 1 of May. Lack of understanding and lack of certain flexibility will have a very negative impact on New Member States.

- **Withdrawal of application**

**Situation:** Recommendation to select one RMS, to withdraw pending Applications, and reapply in other countries after receiving first MA in RMS.

**Comments:** We consider this process as very time and resource consuming for both authorities and applicants, without any added value. Specially dedicated people will be involved in recollection of the files already redistributed internally between experts in Agencies, giving back files to companies.... In Poland alone, almost 3000 products are currently in the assessment process. We wonder if these time and recourses could not be better used.

Additionally, some work has already been done (including the analysis of the samples), fees have already been paid. Usually there is a difference between fees paid in the case of RMS and CMS.

Question: How is it intended to regulate this financial contribution?

- **Choice of potential RMS**

**Situation:** There is no full transparency of the registration progress in all Agencies and possible estimation of registration time still necessary for granting final MA. Due to this fact choice of future RMS becomes very difficult. There is no clear picture of how many procedures the Competent Authorities (especially small Agencies with quite limited resources) are able to manage per year.

Question: It is highly probable than distribution of applications between ACs will not be proportional. If a majority of Applications should be assessed by 3-4 authorities acting as RMSs, are they ready to deal with such situations within a timeline of 210 days?

- **Harmonisation through variation process**

**Situation:** Compulsory MRP for products already submitted or MA granted nationally will force a necessary harmonisation process through variation

procedures before final recognition through MRP. This will result in huge delays of MAs because of the time necessary for approval of all variations (often official approval and annex to MA Certificate is required from a legal point of view in ACs and the “tell and do” approach has not yet been introduced into legislation).

### 3. SmPC Harmonisation and Referrals

**Situation:** According to the Commission’s interpretation, as acceding countries and/or companies have not been addressees of referrals’ decisions, the outcomes of referrals are not legally binding on them.

Question: Does it cover all Referrals (i.e., art. 29, 30, 31)?

**Situation:** For Acceding countries it is recommended to apply the outcome of those referrals on a voluntary basis (for both reference product and generics). For example, the indication or contraindication has been introduced or deleted from SmPC in the EU 15 after referrals.

Question: How should this voluntary implementation of referrals be managed in practice?

Which procedure should be used? Variation type I (for example Type IB point 46), type II Variation? Which data should be presented (especially in the case of generics if the outcome comes from originator studies)?

Question: If differences already exist between the SmPCs of the reference product and generics (especially in the area of indication, contraindication), but there is no link to the outcome of referrals (e.g. SmPC of Reference product has been changed during an update or renewal process), which type of variation should be used by the generic producer to bring them in line with the reference product and which data should be provided? Variation type I (for example Type IB point 46), Type II?

Suggestion of Solution : To facilitate the harmonisation process, it would be very useful to put officially approved SmPCs on Agencies website (as it is in case of EMEA and some national Agency as well).

**Comments:** Due to the disharmony of the SmPCs of originators between the EU and ACs, satisfactory MRP for generic producers will be almost impossible. As the originators’ SmPCs are still under revision in ACs, generic applications could be postponed until after clarification of the situation concerning reference products. Moreover, as there is no legal basis for compulsory harmonisation in the EU legislation as well as in the majority of ACs, some serious problems are to be expected during this process (especially in the case of more indications than in an already-harmonised SmPC in the EU).

Additionally, in some ACs this SmPC revision process will be postponed because of transitional periods.

How should the applicant combine into one MRP application a country with a transitional period and one without a transitional period? How should the applicant combine into one MRP application a country with approved SmPCs and one where the SmPC has not yet been revised?



We are very much in favour of harmonisation, however, only once as the Reference Product SmPC is harmonised. If not harmonised in parallel with the Reference Product, it will result in a disadvantageous SmPC for generics (from a marketing point of view) with less indications and more contraindications in an AC and it will cause confusion for patients and health professionals.

#### **4. Switch to one MRP after Accession**

**Situation:** Reference Product X exists in 3 strengths: 10, 20 and 40 mg. All 3 strengths are registered in FR, NL, DK (as MRP applications); two strengths are registered in PL, HU, CZ (as national applications). A generic producer has registered product G in the same countries (the same distribution of strengths by country as the Reference Product). After 1 May the generic producer wants to convert its independent national MAs product into one MRP MA.

##### Questions:

Is it possible to convert the generic product into one MRP Marketing Authorisation if in some countries one strength is missing?

Is it possible to include a Polish marketing authorisation if a product is still on the list covered by the transitional period (and hence cannot benefit from MRP)?