

## EUROPEAN AGENCY FOR THE EVALUATION OF MEDICINAL PRODUCTS (EMEA)

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Chairman, ladies and gentlemen,  
I am honoured on this 10th anniversary of ESCOP to have been invited to represent the position on Phytomedicines and Consumer Protection of the European Agency for the Evaluation of Medicinal Products (EMEA). Our Executive Director Mr. Ferdinand Sauer also sends his best wishes for the success of this 5th ESCOP Symposium.

### EMEA and Herbal Medicinal Products

This presentation follows immediately one given by Dr. Manfredi on the position of the European Commission DG XXIV. The separation of powers there also applies to the EMEA. We do not have legislative or decisive power. These rest and remain with the European Commission. As the table shows the EMEA has a number of formal tasks in particular, and generally is responsible for adopting European scientific opinions. To this end we use two Scientific Committees, the Committee for Proprietary Medicinal Products (CPMP), currently chaired by Professor Jean-Michel Alexandre and the Committee for Veterinary Medicinal Products (CVMP) currently chaired by Professor Reinhard Kroker.

I should now like to describe the tasks in which the EMEA is involved and how they relate to and encompass herbal medicinal products.

#### EMEA Tasks

- Evaluation Centralised Procedures
- Co-ordination Member States' Pharmacovigilance Activities
- Arbitration Decentralised Procedures
- Co-ordination member States' Inspections (GMPs, GCPs, GLPs)
- Scientific Advice to Companies

### Centralised procedure

As set out in Council Regulation (EEC) No 2309/93 the centralised procedure constitutes the main task for the EMEA and has turned out to be the major step forward towards achieving a single market for innovative medicinal products. Herbal medicines with their longstanding tradition of use would only rarely be expected to fit the criteria set out in the legislation that allows access to this procedure.

Scientific advice is made available via the CPMP. Any important question concerning herbal medicinal products - irrespective of future centralised or mutual recognition matters - would be given the necessary scientific attention there (the CPMP is currently amending the Scientific advice procedure).

Since early 1995 when the EMEA became operative the centralised procedure has been used successfully for

Part A biotech products and, increasingly  
Part B new chemical substances/  
innovative products

#### Summary Statistics Centralised Procedures

September 1998

New Applications, Opinions given by CPMP:	91
New applications, Marketing Authorisation granted by Commission:	77
New applications pending:	58
New applications withdrawn:	19
Total number of applications submitted since 1.1.95	168

As we all know new or innovative herbal medicinal products have not yet been presented for review through the centralised procedure.

### Pharmacovigilance

The involvement of EMEA in pharmacovigilance is manifold. This can be easily understood when looking at the immense activities undertaken by the Member States. The EMEA is available as a platform for discussion or to co-ordinate referral procedures on a case-by-case basis for Member States regulators. The EMEA provides secretarial support to the CPMP Pharmacovigilance Working Party and also interacts with international partners (WHO, ICH...).

#### Involvement of the EMEA in the Field of Pharmacovigilance

- Centrally Authorised Products
  - Single case reporting of ADRs
  - Monitoring and control of authorisations
  - Proceedings in case of safety concerns
- Non Centrally Authorised Products
  - Article 12 referral (Council Directive 75/319/EEC)
  - Article 15 a referral (Council Directive 75/319/EEC)
- Secretariat of the CPMP PhV Working Party
- External Communication

### Arbitration Procedure

Although arbitration has not been triggered for herbal medicinal products, and is generally seldom used so far, it may provide an opportunity to reach a single market for single products.

#### Arbitration Procedure

Referral to the EMEA for arbitration  
(Article 10 of Council Directive 75/319/EEC)

Agreement note reached between RMS and CMS  
by Day 90 of the Mutual Recognition phase

A joint report is prepared  
indicating the reasons for disagreement\*

The precise questions of Arbitration are referred to the CPMP

Starting of the timetable

\*where there is a risk to public health

This procedure uses the scientific power of the CPMP if the mutual recognition does not succeed, within the very tight time frame allowed for.

#### Non Centrally Authorised Products Referral to the EMEA/CPMP

- Discussion at CPMP level in accordance with legal time frame, resulting in a CPMP Opinion
- CPMP Opinion transformed by European Commission in a binding Decision
- Outcome: withdrawal, suspension or variation (i.e. restriction, amendment) of existing Marketing Authorisation - or confirmation of the position/MA issued by the RMS

### CPMP Guidelines

The EMEA is also involved in the preparation of guidelines adopted by the CPMP. Guidelines are not binding but they do interpret legal requirements and attempt to be of practical use for everyone involved.

They are based on the best scientific arguments and prepared following a transparent and open procedure involving interested parties and learned societies.

#### CPMP Guidelines

##### For the benefit of medicinal products to be authorised via the Centralised and Mutual Recognition Procedures

The making of a guideline

- Concept Paper
- Concept Paper disseminated
- Working party activity
- CPMP agreement for dissemination to Interested Parties
- Comments
- Finalisation by Working Party
- CPMP agreement
- Implementation/publication by EMEA/European Commission

Normally the CPMP is the scientific body responsible for the guidelines to be published by the European Commission. As the ad hoc Working Group on Herbal Medicinal Products is not covered by the CPMP, guidelines concerning herbal medicinal products specifically need attention by the Member States (and the EMEA).

### Herbal medicinal products

We can now turn from general EMEA matters to more specific areas addressing herbal medicinal products. Terminology is always important and one of the early achievements of the ad hoc Working Group was to agree the term “herbal medicinal products”. These products thus clearly fall within the scope of Directive 65/65/EEC giving them the benefits, rights and burdens that all medicinal products have. This includes access to the European single market via the available procedures, centralised or mutual recognition.

#### Herbal Medicinal Products

- Finished herbal medicinal products fall within the scope of Council Directive 65/65/EEC.
- Access to European Market through the Centralised Procedure, e.g. new Ayurvedic products, Chinese medicines.
- Access to the European Market through the Mutual Recognition Procedure. Main route to bring herbal medicinal products to European patients.

As the access to the centralised procedure is legally limited one expects that Mutual Recognition of Reference Member State’s Marketing Authorisation by other Concerned Member States will form the main route to bring -on equal terms- herbal medicinal products to European patients.

The current experience of this procedure for herbal medicinal products is limited. Three products have been authorised via Mutual Recognition. The small number of CMS and the withdrawal (for one procedure) may be seen as an indication that the conditions for herbal medicinal products to become mutually recognised are not perfect yet and can be improved.

There are a number of obvious reasons for such difficulties.

- There are still major differences in the under-

standing and acceptance of herbal medicinal products and the requirements to be fulfilled in all three important areas regulated by European Council Directives: Quality, Safety, and Efficacy.

- It is also clear that complex preparations like those contained in herbal medicinal products create their own difficulties.
- The positive interpretation of bibliographic data is a central issue for herbal medicinal products.

You will probably agree with my conclusion that applicants and National Competent Authorities need better guidance so that Mutual Recognition for herbal medicinal products can function more often, with high efficiency and success.

If and once the need for better guidance is agreed - how do we achieve it?

### Ad hoc Working Group on Herbal Medicinal Products

The EMEA Executive Director, Dr. Ferdinand Sauer, together with the European Commission and EMEA management agreed to set up an ad hoc Working Party under the chairmanship of Dr. Keller.

#### Ad Hoc Working Group on Herbal Medicinal Products

- Created in May 1997 on the initiative of European Commission and the EMEA Executive Director and with the support of the EMEA Management Board
- Chairman Dr. K. Keller (BfArM, Berlin)
- Supported by the EMEA Secretariat
- Three meetings in 1997 (June, September and November)
- Two meetings in 1998 (March and July)
- Two/three meetings planned for 1999

**Mutual Recognition Procedures for  
Herbal Medicinal Products**

Product	Reference MS	Concerned MS	Withdrawal	Status
Sesame Oil	SE	DK, FI	-	Finalised
Ispagula husk	DK	LU, AT	BE, PT, DE, SE, FI	Finalised
Valerian root	UK	AT, EL, PT, IT	-	Finalised

Such ad hoc groups can be set up to tackle specific problems if there is financial support available. Within the EMEA budget this can only be drawn from the Community contribution. You will be aware of the budgetary problems encountered at the EMEA this year.

The EMEA Management Board made it clear that under such financial restrictions a contingency plan would have to be set up and operated. This contingency plan has affected many meetings and in particular the last meeting of Dr. Keller's ad hoc Working Group is rescheduled for early 1999, pending availability of budgetary support. Dr. Keller and his group are obviously eager to continue their good work which up to now was also very closely monitored by the European Parliament delegates to the EMEA Management Board, Professors Benzi and Henschler.

The group has indeed achieved a lot so far.

### **Activities of the Ad Hoc Working Group on Herbal Medicinal Products**

Besides clarification concerning terminology the group has addressed:

**Notice to Applicants/Expert Report** The recommendations concerning the Notice to Applicants will be incorporated by the European Commission.

**Quality/GMP** The group's output concerning quality is agreed with and supported by Professor J.C. Robert, Chairman of the Quality Working Party.

**Safety and Efficacy.** I can also tell you that the papers prepared by the working group were presented to the CPMP who, although not being responsible, noted and acknowledged the progress made. I shall

leave any detail concerning these proposals for Dr. Keller's presentation.

A first set of proposals was released by the EMEA in January 1998 (EMEA/adhoc HMPWG/114/98) for three months consultation. They are now finalised. A second set of proposals was released by the EMEA in September 1998 (EMEA/adhoc HMPWG/33279/98) also for three months consultation.

We consider it good practice to make available and disseminate widely the EMEA papers. The EMEA homepage contains all opinions/decisions taken in eleven languages, all guidelines, and all committees etc. You will find all documents concerning Herbal Medicines on the EMEA Website:

Herbal Medicines Products.

<http://www.eudra.org/gendocs/general/hmpwg.htm>

### **Conclusions**

Although the EMEA does not expect centralised applications for herbal medicinal products in large numbers, it took up its responsibilities to support Member States and to facilitate their handling of Mutual Recognition procedures to avoid arbitration.

The EMEA Scientific Committee for Proprietary Medicinal Products acknowledged the proposals from the Ad Hoc Working Group on Herbal Medicinal Products.

The most difficult area remains to set and fulfil the required level of efficacy for herbal medicinal products.

EMEA is aiming to continue in the future to support the work started in 1997 by the ad hoc Working Group.

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