The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

7 June 2001
CPMP/1577/01 Corr

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
29 to 31 MAY 2001 PLENARY MEETING

TECHNICAL REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 71th plenary meeting from 29 to 31 May 2001.

Product related issues

Centralised procedures

The CPMP noted the withdrawal of three Marketing Authorisation Applications for initial applications, corresponding to two active substances (two part B).

An appeal procedure under article 9 of Council Regulation (EEC) No 2309/93 was initiated following the negative opinion adopted by CPMP at its April 2001 CPMP plenary meeting for EVOXAC (see April 2001 CPMP Technical Report (CPMP/1252/01)). A new Rapporteur and Co-Rapporteur were appointed for this appeal procedure.

An overview of centralised procedures since 1995 is given in **Annex 1**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the last CPMP plenary meeting in April 2001 is provided in **Annex 2**. Finally, the post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

Scientific Advice procedures

The CPMP was informed of the outcome of the discussions of the Scientific Advice Review Group (SciARG) meeting, which was held on Monday 28 May 2001. For further details, please see **Annex 4**.

Other product related issues

The CPMP is closely following the manufacturing and supply problems with **Kogenate Bayer/Helixate NexGen – octocog alfa (Recombinant Factor VIII)** (indicated for the treatment and prophylaxis of bleeding in patients with haemophilia A) experienced by the Marketing Authorisation Holder, Bayer AG. A number of technical deficiencies at its Bayer Berkeley (USA) production site have led to a reduced production capacity with consequent product shortages. An EU inspection of this facility was requested by CPMP and took place at the end of April 2001. The results of the inspection were reported to the May meeting of the CPMP. The conclusions from the inspection are that Bayer is taking appropriate remedial action and that there is no cause for concern with respect to product on the market. Release of new batches is proceeding according to Bayer's enhanced release protocol and testing procedures.

According to Bayer's current projections, release of batches for the remainder of the year and the first quarter of 2002 will be significantly less than normal as a consequence of these technical issues. Bayer will provide the CPMP with monthly updates on the supply situation until normal stocks are re-established.

In addition, Bayer has organised a series of meetings in May and June in order to inform patients and health professionals of the reduced supply of recombinant Factor VIII, and will keep the CPMP updated on such communications.

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Non-product related issues

CPMP Working Parties and Ad-Hoc Groups

Dr. Manfred Haase was appointed Chairman of the already existing multi-disciplinary group on Thiomersal.

Dr. Eric Abadie, Vice-Chairman of the CPMP, was appointed Chairman of the Ad-Hoc Expert Group on terminology in pharmacogenetics and a first meeting to address the requirements and approaches currently undertaken in various Member States on proposed pharmacogenetics terminology is expected to take place in July 2001.

Dr. Barbara van Zwieten-Boot reported from the meeting of the Ad-Hoc Expert Group on clinical efficacy of beta-interferons in Multiple Sclerosis treatment held on 28th May 2001. The experts discussed issues related to the design of clinical trials, primary variables for efficacy and feasibility of placebo controlled clinical trials, in view of the ongoing revision of the "Note for guidance on clinical investigation of medicinal products for the treatment of multiple sclerosis" (CPMP/EWP/561/98).

Dr. Markku Toivonen reported from the second meeting of the Ad-Hoc Expert Group on comparability of biotechnology products – preclinical and clinical issues held on 2d May 2001. An addendum to the Note for Guidance on Comparability of Medicinal Products Containing Biotechnology-Derived Proteins as Active Substance (CPMP/BWP/3207/00) could be envisaged. The next meeting is scheduled for the 5th September 2001.

Following the report from Dr. Pekka Kurki on the meeting on Xenogenic Cell Therapy held on 23 April 2001, the CPMP agreed to develop a CPMP Points to Consider which will be restricted to principles underpinning the development and the assessment of cell therapy medicinal products only. This document will be developed on a modular format with input from CPMP Working Parties (BWP, SWP, EWP and PhVWP) and from CVMP experts.

The CPMP adopted the mandate, composition and functioning of the Ad-Hoc Expert Group on Paediatrics, chaired by Dr. Daniel Brasseur, and the first meeting is expected to take place in July 2001. The Paediatric Ad-Hoc Expert Group will co-ordinate the necessary actions and advise the EMEA and its scientific committees, the CPMP and COMP, as well as the MRFG, on all questions relating to the development and use of medicinal products in children. This will be done in concertation with the existing Working Parties and Ad-Hoc Experts Working Groups according to the topic, and in co-operation with National Competent Authorities.

An overview of guidance documents adopted during the meeting or released for consultation to Interested Parties is attached as **Annex 5**.

Organisational Matters

The Committee was informed of the outcome of the Regulators, Steering Committee and various Expert Groups meetings which took place in the framework of the ICH meeting held in Tokyo on 21-24 May 2001 (for further details, please see the following ICH website: http://www.ifpma.org/ich7.html).

The fourth CPMP Ad-Hoc Group on Organisational Matters (ORGAM) was held on 28 May 2001. During the meeting the following topics were discussed: proposals on formalisation of the Scientific Advice Review Group (SciARG) as a permanent CPMP Working Party, the accelerated review process, review of the use of clock-stops in the Centralised Procedure and an update to the guideline on processing of renewals in the Centralised Procedure (see **Annex.5**). The group also discussed the general issue of compliance with post-authorisation commitments and agreed on the general principles of an EMEA policy on this particular aspect.

EMEA TRANSPARENCY POLICY UPDATE

As a follow-up to the first EMEA "day 0" publication of Summary of Opinions for initial Marketing Authorisation Applications which was made after the April 2001 CPMP plenary meeting, please find annexed to this document (see **Annex 6**), the description of the procedure followed in relation to publication of these CPMP Summaries of Opinion.

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 28 May 2001, which is circulated together with this May 2001 CPMP Technical Report (see **Annex 7**), including the status of the activities of the sub-group on harmonisation of Summary of Product Characteristics.

Next meetings

The CPMP was informed of the following meetings/conferences:

- CTD safety training meeting to be held at the EMEA on 7 June 2001;
- European Pre-clinical Assessors meeting to be held in Uppsala, Sweden on 17 – 19 June 2001;
- CTD Efficacy training meeting to be held at the EMEA on 20 June 2001;
- CTD Quality training meeting to be held at the EMEA on 19 July 2001;
- Conference on Antibiotic Use in Europe which to be held on 15 – 17 November 2001 in Brussels, under the Belgian EU Presidency;
- The next Informal CPMP meeting under the Belgian EU Presidency will be held in Bruges on 29 – 30 October 2001.

The 72nd plenary meeting of the CPMP will be held from 26 to 28 June 2001.

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This Press Release and other documents are available on the Internet at the following address:

http://www.emea.eu.int

EMEA CENTRALISED PROCEDURES

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	74	122	196	7	24*	24	220
Follow-up to scientific advice	15	11	26	3**	2	5	31

* Including two Protocol Assistance requests.
** Including one Protocol Assistance request.

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	97	182	279	13	14	27	306
Withdrawals	12	37	49	0	7	7	56
Positive CPMP opinions	64	112	176	9	7	16	192[1]
Negative CPMP opinions[2]	1	3	4	0	2	2	6[3]
Marketing authorisations granted by the Commission	56	95	151	7	20	27	178[4]

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	265	551	816	82	112	194	1010
Positive opinions, variations type II	159	224	383	38	69	107	490
Negative opinions, variations type II	0	2	2	0	1	1	3
Extensions (Annex II applications)	34	20	54	0	2	2	56

[1] 192 positive opinions corresponding to 150 substances
[2] In case of appeal the opinion will not be counted twice
[3] 6 negative opinions corresponding to 4 substances
[4] 178 Marketing Authorisations corresponding to 136 substances

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE APRIL 2001 PRESS RELEASE

Brand name	Osteogenic Protein 1 Howmedia International S. de R.L.
INN	Osteogenic Protein-1 BMP-7
Marketing Authorisation Holder	Howmedia International S. de R.L.
ATC code	M09AX
Indication	Treatment of non-union of tibia of at least 9 month duration
CPMP Opinion date	14/12/2000
Date of Commission Decision	17/05/2001

Brand name	Apomorphine hydrochloride Abbott
INN	apomorphine
Marketing Authorisation Holder	Abbott Laboratories
ATC code	G04BE
Indication	Treatment of erectile dysfunction
CPMP Opinion date	25/01/2001
Date of Commission Decision	28/05/2001

Brand name	Uprima
INN	apomorphine
Marketing Authorisation Holder	Abbott Laboratories
ATC code	G04BE
Indication	Treatment of erectile dysfunction
CPMP Opinion date	25/01/2001
Date of Commission Decision	28/05/2001

Brand name	Ixense
INN	apomorphine
Marketing Authorisation Holder	Takeda Europe R&D Centre Ltd. UK
ATC code	G04BE
Indication	Treatment of erectile dysfunction
CPMP Opinion date	25/01/2001
Date of Commission Decision	28/05/2001

OUTCOME OF THE MAY 2001 CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
11 (SPC/PL update)	Positive by consensus
2 (Pharmaceutical Aspects)	Positive by consensus

Opinions for Annual Re-Assessment		
Name of Medicinal Product	**Outcome**	**Comments**
Renagel	Positive by consensus	Marketing Authorisation to remain under exceptional circumstances

Opinions for Renewal applications		
Name of Medicinal Product	**Outcome**	**Comments**
Caelyx	Positive by consensus	----

OUTCOME OF THE MAY 2001 CPMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Substance	Intended indication(s)	Topic				
		Type of Request		Pharma-ceutical	Pre-Clinical	Clinical
		New	Follow-up			
Biological	Treatment of hormone refractory prostate cancer.	**X**				**X**
Biological	Treatment of severe congenital protein C deficiency.	**X**		**X**		
Chemical	Management of Chronic pain.		**X**			**X**
Chemical	Treatment of invasive fungal infections.	**X**				**X**
Chemical	Treatment of resistant depression.		**X**			**X**
Biological	Treatment of menopausal symptoms related to oestrogen deficiency; prevention of postmenopausal osteoporosis.	**X**				**X**
Chemical	Treatment of metastatic carcinoma of the ovary.	**X**				**X**

In addition to the adoption of the above final Scientific Advice letters, the Committee accepted six new requests from companies for Scientific Advice, of which two are follow-up Scientific Advice requests.

DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD-HOC GROUPS ADOPTED DURING THE MAY 2001 CPMP MEETING

QUALITY WORKING PARTY

Reference number	Document	Status
CPMP/QWP/72/96	Note for guidance on Start of shelf life of the finished dosage form (Annex to Note for guidance on Manufacture of finished dosage form)	Adopted in May 2001

BIOTECHNOLOGY WORKING PARTY

Reference number	Document	Status
CPMP/BWP/41450/98	Points to consider on the Manufacture and quality control of human somatic cell therapy medicinal products	Adopted in May 2001
CPMP/BWP/1129/01	Joint CPMP/CVMP Note for guidance on Minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products: explanatory note and footnote (dated 24 April 2001) for guideline	Adopted in May 2001

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/1045/01	Concept paper on the Revision of the CPMP/BWP Note for guidance on Harmonisation of requirements for influenza vaccines (CPMP/BWP/214/96)	Adopted in May 2001
CPMP/EWP/967/01	Concept paper on the Development of a CPMP Note for guidance on the Evaluation of medicinal products indicated for thrombolysis in acute myocardial infarction (AMI)	Adopted in May 2001
CPMP/EWP/512/01	Concept paper on the Development of a CPMP Note for guidance on the Evaluation of medicinal products for the treatment of dyslipoproteinaemia	Adopted in May 2001

EFFICACY WORKING PARTY (Cont'd)

Reference number	Document	Status
CPMP/EWP/788/01	Concept paper on the Development of a CPMP Note for guidance on the Evaluation of medicinal products for treatment of migraine	Adopted in May 2001
CPMP/EWP/2330/99 draft 8	Points to consider on Application with 1. Meta-analyses; 2 one pivotal study	Adopted in May 2001
CPMP/EWP/205/95 rev. 1	CPMP Note for guidance on Evaluation of anticancer medicinal products in man	Adopted in May 2001

AD-HOC WORKING GROUP ON ANTI-HIV MEDICINAL PRODUCTS

Reference number	Document	Status
CPMP/602/95 rev. 3	Points to consider on the Assessment of anti-HIV medicinal products (CPMP/602/95 rev. 3)*	Released for 3 months' consultation in May 2001

* The scope of the revision of the Points to Consider is the addition of an appendix III on clinical development of dual or boosted Protease Inhibitors.

ORGANISATIONAL MATTERS

Reference number	Document	Status
CPMP/2990/00 rev.2	CPMP Guideline on the processing of Renewals in the Centralised Procedure.	Adopted in May 2001

ANNEX 6 to CPMP May 2001
London, 29 May 2001
EMEA/H/12984/01

EMEA PUBLICATION POLICY OF CPMP SUMMARIES OF OPINION

1. Introduction

In February 2000, following the outcome of the public consultation on the EMEA transparency initiatives with Interested Parties and the EMEA's Management Board's decision, Summaries of Opinion were published after the adoption of the Opinion by the CPMP, once the 15 day period for notification of appeal had elapsed and the Opinion had therefore become final. It was also agreed that applicants should not communicate before "day 15". This initiative started in June last year and its implementation was monitored in collaboration with EFPIA.

Thereafter following the Transparency Workshop of November 2000, the EMEA Management Board, at its February 2001 meeting, gave a mandate to the Executive Director to implement the recommendations made by the Workshop with effect from 1 April 2001. These recommendations include the publication on the day of adoption of CPMP opinions for initial applications.

In April 2001, the EMEA published for the first time Summaries of Opinion at "day 0" corresponding to the date of adoption of the CPMP opinion (see EMEA Website). Such Summaries of Opinion will continue to be published following the conclusion of each plenary CPMP meeting. The procedure for the publication of Summaries of Opinion is outlined below.

2. Procedure

The process **only applies to CPMP Opinions on initial applications for Marketing Authorisation.** The EMEA will publish Summaries of Opinion after adoption of the CPMP Opinion, at "day 0", which corresponds to the day of the adoption of the CPMP Opinion. Such information will be mentioned in the CPMP Press Release published together with these Summaries of Opinion. **Both positive and negative CPMP opinions will be published**[1]. After the adoption of the CPMP opinion following an appeal procedure or further to a request from the European Commission in the framework of the Standing Committee procedure, the same procedure publication applies (see Templates I and II describing the content of such Summaries of Opinion).

Steps	Task description
Step 1	▪ The week prior to the CPMP week (at the latest the Monday of the CPMP week) the applicant will receive a copy of the draft Summary of Opinion (e-mail or fax) from the EMEA Product Team Leader **for comments** (24 hours).
Step 2	▪ Following the adoption of the CPMP Opinion[2], the Summary of Opinion is sent (e-mail or fax) to the applicant during the last day of the CPMP plenary meeting **for information** prior to its publication on the EMEA Website and at the latest the Friday of the CPMP week.
Step 3	▪ Once the Commission Decision is issued, the Summary of Opinion will be deleted from the EMEA Website and replaced by the EPAR.

3. References

- Twenty-ninth meeting of the Management Board Press Release (EMEA/MB/011/01).
- Outcome of public consultation on new EMEA Transparency initiatives (EMEA/D/16906/00).

[1] This does not apply to any withdrawn applications prior to adoption of CPMP opinion.
[2] Applicants may appeal any CPMP opinion, provided they notify the EMEA in writing of their intention to appeal within 15 days of receipt of the opinion adopted by CPMP.

TEMPLATE I

London, <date>
CPMP/<no.>/01

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS SUMMARY OF OPINION[*] for <NAME OF THE PRODUCT>

International Nonproprietary Name (INN): ***<name of the active substance>***

On *<date of the adoption of the opinion (last day of the CPMP meeting)>* the Committee for Proprietary Medicinal Products (CPMP) adopted a *<positive/negative>* opinion,[**] recommending *<not>* to grant a marketing authorisation for the medicinal product *<name of the product, strengths, pharmaceutical form>* intended for *<treatment of /prophylaxis against/diagnosis of> <disease>*. *<Name of product was designated as an orphan medicinal product on <date>>*. The applicant for this medicinal product is *<name of the company>*.

The active substance of *<name of the product>* is *<INN>*, an *<therapeutic class>* medicinal product *<(ATC Code) and brief description of mode of action>*.

(For a positive opinion)

The benefits with *<name of product>* are its *<brief statement on the character of the main clinical benefits in terms of the approved indication(s)>*. The most common side effects are *<brief statement on the character of the main safety concerns>*.

The approved indication is: "*<the indication as worded in the CPMP approved SPC>*". *<It is proposed that <name of the product> is prescribed by physicians experienced in the treatment of <disease>* ***the wording of this particular sentence should be in line with section 4.2 SPC***>. Detailed conditions for the use of this product will be described in the Summary of Product Characteristics (SPC) which will be published in the European Public Assessment Report (EPAR) and will be available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CPMP, on the basis of quality, safety and efficacy data submitted, considers that there is a favourable benefit to risk balance for *<name of the product>* and therefore recommends the granting of the marketing authorisation *<under exceptional circumstances>*.[***]

(For a negative opinion)

The grounds for the negative opinion relate to the following points*:*

<Brief statements on the major grounds for refusal of the marketing authorisation)>.

The CPMP, on the basis of quality, safety and efficacy data submitted, considers that there is an unfavourable benefit to risk balance for *<name of the product>* and therefore cannot recommend the granting of the marketing authorisation.

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[*] Summaries of opinion are published without prejudice to the Commission Decision, which will normally be issued within 90 days from adoption of the Opinion.

[**] Applicants may appeal any CPMP opinion, provided they notify the EMEA in writing of their intention to appeal within 15 days of receipt of the opinion.

[***] Marketing Authorisation under exceptional circumstances refers to the fact that in exceptional circumstances an authorisation may be granted subject to certain specific obligations, to be reviewed annually.

TEMPLATE II

London, < date >
CPMP/<no.>/01

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS SUMMARY OF OPINION[*] for <NAME OF THE PRODUCT>

further to new information[**] or to a request from the European Commission in the framework of the Standing Committee procedure

International Nonproprietary Name (INN): ***<name of the active substance>***

On <*date of the adoption of the opinion (last day of the CPMP meeting)*> the Committee for Proprietary Medicinal Products (CPMP), having considered new information, adopted a <*positive/negative*> opinion,[***] recommending <*not*> to grant a marketing authorisation for the medicinal product <*name of the product, strength(s), pharmaceutical form*> intended for <*treatment of /prophylaxis against/diagnosis of*> <*disease*>. <*Brief statement on the background with dates*>. <*Name of product was designated as an orphan medicinal product on <date>*>. The Applicant for this medicinal product is<*name of the company*>.

The active substance of <*name of the product*> is <*INN*>, an <*therapeutic class*> medicinal product *(ATC Code) and brief description of mode of action*>.

(For a positive opinion)

The benefits with <*name of product*> are its <*brief statement on the character of the main clinical benefits in terms of the recommended indication(s)*>. The most common side effects are <*brief statement on the character of the main safety concerns*>.

The approved indication is: "<*the indication as worded in the CPMP approved SPC*>". <*It is proposed that <name of the product> is prescribed by physicians experienced in the treatment of <disease>* ***the wording of this particular sentence should be in line with section 4.2 SPC*** >. Detailed conditions for the use of this product will be described in the Summary of Product Characteristics (SPC) which will be published in the European Public Assessment Report (EPAR) and will be available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CPMP, on the basis of quality, safety and efficacy data submitted, considers that there is a favourable benefit to risk balance for <*name of the product*> and therefore recommends the granting of the marketing authorisation <*under exceptional circumstances*>.[****]

(For a negative opinion)

The grounds for the negative opinion relate to the following points*:*

<*Brief statements on the major grounds for refusal of the marketing authorisation: (indicate as per category in the annex of the List of Questions template)*>. The CPMP, on the basis of quality, safety and efficacy data submitted, considers that there is an unfavourable benefit to risk balance for <*name of the product*> and therefore cannot recommend the granting of the marketing authorisation.

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[*] Summaries of opinion are published without prejudice to the Commission Decision, which will normally be issued within 90 days from adoption of the Opinion.

[**] See *Conduct of Pharmacovigilance for Centrally Authorised Products*, CPMP/183/97, page 7

[***] Applicants may appeal any CPMP opinion, provided they notify the EMEA in writing of their intention to appeal within 15 days of receipt of the opinion.

[****] Marketing authorisation under exceptional circumstances refers to the fact that in exceptional circumstances an authorisation may be granted subject to certain specific obligations, to be reviewed annually.

Report from the meeting held on 28 May 2001

General issues

Sub-group meeting on harmonisation of SPC's

The fifth Sub-group meeting on harmonisation of SPC's was held on 28 May 2001. The MS's responsible for co-ordinating the information concerning products selected for possible harmonisation, have fulfilled their task and presented their reports to the MRFG. The MRFG will forward a list of products in priority order to the Heads of Agencies meeting to be held on 12-13 June 2001. Since it is the Heads of Agencies who will decide on the future of the harmonisation exercise, the MAH's are advised not to contact the MS's regarding the future of the project.

Possibilities for a medicinal product authorised through a national procedure to transfer to the Mutual Recognition Procedure

The MRFG discussed the issue related to a medicinal product with a strictly national marketing authorisation and its possibilities to enter Mutual Recognition Procedure. The MRFG agreed that the Repeat Use MR–procedure (not the renewal procedure) is the proper tool for transferring a medicinal product authorised through a national procedure to the Mutual Recognition Procedure. This approach is also applicable to old "ex-concertation" medicinal products.

MR-SPC for influenza vaccines

The MRFG adopted the revised MR-SPC for influenza vaccines, which will be published on the Heads of Agencies Website.

TSE and Mutual Recognition Procedure

The MRFG agreed on the following positions in connection to TSE related questions:

- *Does the MAH have to apply for a variation if the information given when demonstrating compliance with the TSE Directive is changed (change of material and/or supplier)? If so, by which procedure?*

Regarding "Change in raw materials, covered by the scope of the TSE guideline, used as excipient or raw or source materials or reagents used in production" a Type I variation procedure should be followed for changes such as:

- Change from a vegetable or an animal derived raw material to another animal derived raw material covered by a Ph.Eur. TSE Certificate of Suitability.
- Change from an animal derived raw material to a vegetable derived raw material.
- Addition of an alternative supplier of an animal derived raw material covered by a Ph.Eur. TSE Certificate of Suitability.
- Addition of an alternative supplier of a vegetable derived raw material if the supplier of that specific material is stated in the dossier.

A type I variation procedure should be applied for only if the change complies with the requirements as stated for variation 4, 12 or 15, as relevant, of the Guideline on dossier requirements for Type I variations.

If the change to an equivalent raw material might affect the quality of the product in such way that a new quality, safety or clinical assessment would be needed (e.g. on viral safety), a type II variation should be applied for.

For a change to or an addition of an animal derived raw material covered by the scope of the TSE Guideline EMEA/410/01, for which there is no Ph.Eur. TSE Certificate of Suitability, a type II variation procedure should be followed for " Change in raw materials covered by the scope of the TSE guideline used as excipient or raw or source materials or reagents used in production".

- *If a TSE Certificate of Suitability (CoS) is revised, does the MAH have to submit a copy of the revised CoS to the National Authorities? If so, by which procedure?*

A copy of the revised CoS should be submitted as a notification.

- *What should actually be submitted regarding TSE in a Renewal application?*

In the application form for Renewals it is written that a TSE statement and TSE certificates should be submitted with the application. Our proposal is to exclude this claim.

Since all MAHs have submitted documentation for all their products regarding the TSE risk status in accordance with the TSE Directive by 1 March 2001, it should not be necessary to repeat this during the renewal procedure.

Changes in the TSE risk status should rather be notified to the authorities on an on-going basis. This should be carried out through variation procedures (see examples on variations above).

Furthermore, please observe that TSE certificates (i.e. Ph.Eur. TSE certificates of Suitability) do not exist for all ruminant materials included in the medicinal products, since some risk materials have been approved through type II variations (full documentation provided to Rapporteur/MS).

Hence, submission of TSE certificates (where one or more exists) during the renewal procedure is not a routine requirement for all member states. However, this remains a national requirement for some member states as detailed in Chapter 7, section 3.2. of the Notice to Applicants.

Procedure for the granting of a marketing authorisation by CADREAC Drug Regulatory Authorities for Human Medicinal Products already authorised in EU Member States following the Decentralised Procedure

The MRFG acknowledged the final document adopted by the CADREAC Annual meeting on 2 April 2001. The document has been published on 3 May 2001 on the provisional CADREAC website http://www.sukl.cz/CADREAC.htm (under “documents” section).

Point of time for applications for variations after granting of a marketing authorisation for a medicinal product applied through a Mutual Recognition Procedure

The MRFG agreed that in a case where all CMS’s have granted the marketing authorisation, the MAH may submit variations regardless of the number of days after day 90. The applicant should confirm to the RMS the dates of granting the marketing authorisation in all CMS’s. This may be done by notification on the automatic validation document sent by the applicant to the RMS when submitting the variation by inserting a statement such as *“The above Marketing Authorisation have been granted in all Concerned Member States”*.

Whereas, in situations where not all CMS’s have granted a marketing authorisation within 30 day Best Practice Guide agreement, MAH could submit a variation after having delivered adequate translated SPC, labelling and PIL reflecting the Day 90 MR agreement to all CMS’s. (MAHs are reminded that they should submit final translated SPC, labelling and PIL within 10 working days after Day 90).

Mutual Recognition Procedure – extension of the trial period regarding change in the timetable

In December 2000 the MRFG agreed that in order to have more time for discussion between Member States within the Mutual Recognition Procedure, CMS (s) should send their comments to the RMS within 50 days (instead of 55 days).

During the May 2001 MRFG meeting it was decided to extend the trial period by another six months until 31 December 2001. Therefore for MR-procedures starting before 1 January 2002 the CMS(s) should send their comments at Day 50. The MRFG repeated the request that applicants should send the Response Report within another 10 days (at Day 60).

Meeting schedule

The next MRFG meeting will be held on 25 June 2001.

Mutual Recognition Monitoring

The MRFG noted that 20 new mutual recognition procedures were finalised during the month of April 2001, as well as 149 type I and 49 type II variations.

The status as of 30 April 2001 of procedures under mutual recognition is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures from Type I variations finalised	Procedures from Type I variations pending	Procedures from Type II variations finalised	Procedures from Type II variations pending	Arbitrations referred to CPMP
2001	89	130	431	73	136	209	--

53 new procedures (regarding 118 products) started in April 2001. The categories of these procedures are as follows:

3 new active substances (first authorisation in the European Community after RMS approval) including **1** repeat use.

9 known active substances (already authorised in at least one member state), including **2** multiple applications.

38 abridged applications including **4** repeat use and **8** multiple applications.

3 line extension applications.

The new procedures started this month relate to 10 full dossiers, 25 generics, 2 fixed combination applications and 16 for different use, route or dose.

The procedures consisted of 52 chemical substances and 1 biological-blood product[1].

51 of these procedures were prescription-only medicinal products in the reference Member State and 2 were Non-prescription (including OTC) medicinal products[2].

1. As considered by RMS.
2. In this category products are classified as prescription-only or Non-prescription (OTC) products when the RMS has approved them accordingly, although the legal status is not part of the Mutual Recognition Procedure.

Number of countries involved in the new applications procedures started in April 2001

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (3)	5
BE (1)	6
BE (1)	6
DE (4)	3
DK (2)	2
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	1
DK (4)	3
DK (4)	1
DK (4)	1

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (4)	1
DK (4)	1
DK (4)	1
DK (4)	1
FI (1)	3
FR (1)	12
FR (1)	3
FR (1)	6
FR (1)	2
IT (2)	1
NL (5)	1
NL (2)	15
NL (2)	8
NL (2)	11
NL (2)	12
NL (2)	1
NL (2)	6
NL (2)	4
NL (2)	14
NL (2)	2
NL (2)	3
NL (2)	2
NL (1)	1
NL (2)	1
NL (2)	1
NL (3)	10
NL (3)	6
SE (2)	16
SE (3)	4
SE (3)	1
SE (2)	5
SE (2)	5
SE (2)	15
SE (2)	9
SE (2)	9
SE (1)	14
SE (1)	2
SE (1)	2
SE (3)	1
SE (1)	1
SE (1)	1

All documents mentioned in this press release can be found at the MRFG website at the European Medicines Authorities Windows under the heading SOP.

Information on the above mentioned issues can be obtained by the presiding chair of the MRFG:

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Alternatively, you could visit the **MRFG web site** at the EUROPEAN NATIONAL MEDICINES AUTHORITIES WINDOW:

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