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Post-authorisation Evaluation of Medicines for Human Use

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COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

STATUS REPORT

ON THE IMPLEMENTATION OF THE PROVISIONS OF CHAPTER 2a OF DIRECTIVE 2001/83/EC AS AMENDED BY DIRECTIVE 2004/24/EC AS REGARDS TRADITIONAL HERBAL MEDICINAL PRODUCTS

OCTOBER 2006

FINAL

On the request of the European Commission, the Committee on Herbal Medicinal Products (HMPC) has during the 3rd and 4th quarters of 2006 discussed the progress on, and the current status of, the implementation of the provisions of Chapter 2a of Directive 2001/83/EC as amended by Directive 2004/24/EC as regards traditional herbal medicinal products.
These discussions are materialised in this document, which is a status report on the progress made in relation to the implementation of the Directive since its entry into force. Its contents are based on the Committee's experience with the Directive with a main focus related to Chapter 2a of the Directive.

This status report was sent to the European Commission in October 2006 as a contribution to their draft communication to the Council and the European Parliament "Report on the experience acquired as a result of the application of the provisions of Chapter 2a of Directive 2001/83/EC (introduced by Directive 2004/24/EC) on specific provisions applicable to traditional herbal medicinal products" which was published on the Commission website on 30 May 2007.

The information presented in *Table 1: Overview of applications under the simplified registration procedure* and in the *Annexes* to this status report has been updated and they are published on the EMEA website as separated documents.

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List of abbreviations

CHMP	Committee for Medicinal Products for Human Use
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EFSA	European Food Safety Authority
EFTA	European Free Trade Association
EMEA	European Medicines Agency
GMP	Good Manufacturing Practice
HMPC	Committee on Herbal Medicinal Products
HMPWP	Herbal Medicinal Products Working Party
IRCH	WHO International Regulatory Cooperation on Herbal Medicines
MLWP	HMPC Working Party on Community Monographs and Community List
MS	EU Member State
NCA	National Competent Authority
NTA	Notice to Applicants
ORGAM Group	HMPC temporary Organisation Matters Drafting Group
PCWP	EMEA Human Scientific Committees Working Party with Patients and Consumers Organisations
PEG	CHMP Paediatric Working Party
PhVWP	CHMP Pharmacovigilance Working Party
Quality Group	HMPC temporary Quality Drafting Group
S&E Group	HMPC temporary Safety and Efficacy Drafting Group
SWP	CHMP Safety Working Party

I. INTRODUCTION

The Committee on Herbal Medicinal Products (HMPC) was established in September 2004 and replaced the Working Party on Herbal Medicinal Products (HMPWP), a subgroup under the Committee for Medicinal Products for Human Use (CHMP).

The establishment of the HMPC has its legal basis in Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use and in Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004.

Directive 2004/24/EC introduces a new pathway for marketing traditional herbal medicinal products, the "simplified registration". It lays down specific provisions applicable to traditional herbal medicinal products. These are introduced as Chapter 2a in Title III of Directive 2001/83/EC[1] as amended by Directive 2004/24/EC.

This document is a status report on the progress made in relation to the implementation of the Directive since its entry into force, and its contents are based on the Committee's experience with the Directive. The main focus is related to Chapter 2a of the Directive, which lays down the new procedure for registration of herbal medicinal products with traditional-use. There is a secondary focus on key issues related to herbal medicinal products with well-established use, but the status report does not attempt to fully address all issues surrounding these products.

The remaining part of this document falls in three sections:

- Section II provides a status on how the specific provisions applicable to traditional herbal medicinal products have been implemented at the level of the EMEA and HMPC. This part of the document mirrors Chapter 2a, i.e. with headings corresponding to the individual provisions laid down in the Directive. Each section provides a summary on how the individual provisions have been/are currently being implemented at the level of the EMEA and HMPC as well as summary describing the experience of the HMPC and its members gained from working with the Directive.

- Section III concerns other, more general, tasks of the HMPC, most of which stem from Regulation (EC) No 726/2004. As above, each section provides a summary on how the individual provisions have been/are currently being implemented at the level of the EMEA and HMPC as well as summary describing the experience gained by the HMPC and its members.

- Section IV presents the HMPC's general conclusions based on the Committee's experience with the application of the individual provisions laid down in Chapter 2a of Directive 2001/83/EC as amended.

The document has been drafted in the 3rd and 4th quarters of 2006. The contents are updated until 31 October 2006, thereby covering the first two years of the HMPC's experience with Directive 2004/24/EC and one year after the directive had to be implemented by the Member States. It should be noted that only limited experience with the new registration scheme could be collected during the relatively short time since the deadline for the implementation of Directive 2004/24/EC.

[1] In the following referred to as "Directive 2001/83/EC as amended" or as the "Directive"

II. PROVISIONS APPLICABLE TO TRADITIONAL HERBAL MEDICINAL PRODUCTS

II.1 ESTABLISHMENT OF THE HMPC

Article 16h of Directive 2001/83/EC as amended establishes the Committee on Herbal Medicinal Products (HMPC) and outlines its competence. The HMPC conducted its inaugural meeting on 23-24 September 2004. The members elected Dr Konstantin Keller as Chairman and Dr Heribert Pittner as Vice Chairman for the HMPC for a term of three years.

In accordance with Article 59 of Regulation 726/2004, the HMPC adopted in November 2004 its own Rules of Procedure (EMEA/HMPC/139800/2004), which are established with a view to the application of the provisions laid down in Chapter 2a of the Directive.

During 2004 and 2005 the HMPC directed significant efforts towards identification of the need for subgroups (temporary drafting groups and/or permanent working parties under the Committee) as well as the appointment of co-opted members with expertise in fields relevant for the Committee's tasks. In addition, the Committee initiated the work relating to establishment of Community herbal monographs and a 'list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products'[2].

The Committee held 2 meetings in 2004, 6 meetings in 2005 and 6 meetings in 2006. In 2004 and 2005 the meetings were of 2 days duration, rising to 3 days in 2006 in an effort to increase throughput of priority documents e.g. Community herbal monographs and entries to the Community list, which are considered to be primary tasks of the Committee. These meeting days have been divided in 2006 into 1.5 days for the HMPC plenary meeting and 1.5 days for its Working Party on Community monographs and Community list (MLWP) to further facilitate the development and adoption of monographs and list entries[3].

II.1.1 HMPC members/alternates

In accordance with Article 16h(2) of the Directive, each Member State shall appoint, for a three-year term, which may be renewed, one member and one alternate to the Committee for Herbal Medicinal Products. Article 16h(2) furthermore states that the members and alternates shall be chosen for their role and experience in the evaluation of herbal medicinal products and shall represent the competent national authorities.

At the inaugural meeting in September 2004, 24 members and 21 alternates had been nominated by EU Member States and 2 members and 1 alternate nominated by EEA-EFTA States.

In October 2006, the Committee had a Member State representation of 25 members and 22 alternates nominated by EU Member States and 2 members and 2 alternates nominated by EEA-EFTA States (Norway and Iceland). 4 co-opted members have been elected on basis of their scientific expertise (cf. section II.1.2)

In addition to those 31 members, the HMPC has observers from Bulgaria, Romania, Croatia, Turkey and the European Directorate for the Quality of Medicines (EDQM).

This brings the actual number of members to 31, including the members from Norway and Iceland. The 25 members from the EU and the 4 co-opted members have full rights to vote, whereas members from EEA may present a separate vote. The minimum number of members who must be present at a meeting to conduct a vote (quorum) is 20/29, the minimum number of positive votes to adopt a given measure is 16/29. An overview of the composition of the HMPC can be found in Annex 1.

[2] In the following referred to as the "Community list".
[3] For the purpose of this report the terms "list entries", "Community list entries" and "entries to the Community list" are interchangeable.

Appointments are submitted in writing to the EMEA who includes new members in the EMEA Experts Database. Experts in specific scientific or technical fields, who are also included in the EMEA Experts Database, may accompany members to HMPC meetings. Experts have mainly been used in relation to discussions of draft monographs/list entries in the HMPC (a task which has been with the MLWP since March 2006).

The EMEA 'Policy on the handling of conflicts of interests for EMEA Scientific Committees' members and experts' (EMEA/31653/03) also applies to members and experts of the HMPC.

II.1.2 Co-opted members

Article 16h(2) of the Directive provides a possibility for the HMPC to co-opt a maximum of five additional members chosen on the basis of their specific scientific competence. These members shall be appointed for a term of three years, which may be renewed, and shall not have alternates.

The HMPC has on basis of Article 16h(2) and the HMPC Rules of Procedure developed a 'Procedure for the nomination and appointment of co-opted members of the Committee on Herbal Medicinal Products' (EMEA/HMPC/147281/2004). In accordance with this, the HMPC had within three meetings after the constitution of the Committee decided to complement its expertise with co-opted members specialised in the fields of:

- Clinical pharmacology
- Toxicology
- Pre-clinical pharmacology
- Paediatric medicine
- Traditional herbal medicine (such as Anthroposophic medicine, Ayurvedic medicine or traditional Chinese medicine)

Candidates for co-opted membership of the HMPC are nominated by HMPC members. Elections are carried out in accordance with the rules laid down by the HMPC in the HMPC Rules of Procedure and the 'Procedure for the nomination and appointment of co-opted members of the Committee on Herbal Medicinal Products' (EMEA/HMPC/147281/2004). An absolute majority of the HMPC members eligible to vote must vote in favour of a given candidate for this person to be elected as co-opted member of the Committee.

Experts in toxicology and clinical pharmacology were elected in July 2005. An expert in pre-clinical pharmacology was elected in November 2005 and an expert in paediatric medicine was elected in January 2006. The 5th co-opted member was not elected, cf. section II.1.4.

II.1.3 HMPC subgroups

To accomplish the duties arising from Chapter 2a of the Directive, and in accordance with Article 56 of Regulation (EC) No 726/2004, the HMPC has established a number of temporary and permanent working parties. In September 2004, the following three temporary drafting groups were established, each with a specific objective of assisting the HMPC with implementation of Directive 2004/24/EC as well as drafting the main guidance documents considered necessary for the tasks arising from the Directive:

- HMPC Organisational Matters Drafting Group (ORGAM Group)
- HMPC Quality Drafting Group (Quality Group)
- HMPC Safety and Efficacy Drafting Group (S&E Group)

The ORGAM Group and the Quality Group are still in operation. The Quality Group has produced a number of guidance documents relating to quality aspects of herbal medicinal products and has also been involved in ensuring coordination of guidelines for human medicines at the Agency level, with particular emphasis on coordination with the Joint CHMP/CVMP Quality Working Party (cf. list of HMPC quality guidance documents in Annex 3). It is expected that the Quality Group will have fulfilled the objective of preparing key guidance documents in the area of quality of herbal medicinal products during 2007. The HMPC is at that time expected to discuss how to best handle quality related

issues in the future based on an assessment of the need for developing further specific guidance in the area of quality.

The ORGAM Group has prepared a number of templates and guidance documents aiming at facilitating implementation of tasks laid down in the Directive (cf. list of HMPC organisational matters guidance documents in Annex 3). The ORGAM Group's work is expected to continue throughout 2007.

The S&E Group has developed a number of guidance documents relating to safety and efficacy of herbal medicinal products and has also prepared a number of draft Community herbal monographs and Community list entries. In March 2006 the S&E Group was replaced by a permanent "Working Party on Community monographs and Community list" (MLWP), which is chaired by Dr Heribert Pittner.

The core task of the MLWP is to carry out assessments underpinning draft monographs and list entries as well as to prepare these documents. In addition, the MLWP continues the work on guidance documents related to safety and efficacy, i.e. the tasks previously undertaken by the S&E Group (cf. list of Safety and Efficacy guidance documents as well as monographs and list entries in the Annex 3).

The mandate of HMPC drafting groups is laid down in the HMPC Rules of Procedure. The MLWP has established a separate mandate and Rules of Procedures. An overview of the composition of HMPC subgroups can be found in Annex 1.

II.1.4 Experiences of the HMPC

Co-opted members

In relation to identification of candidates for co-opted membership in traditional herbal medicine, HMPC members identified only one candidate who did not obtain a majority support from the Committee. The HMPC therefore requested the EMEA to make a call for nominations of such experts among the interested parties to the HMPC (non-industry organisations only). This resulted in a short-list of proposed candidates who submitted to an appointment procedure in May 2006. No candidate received an absolute majority of votes and the HMPC decided to not pursue appointment of a 5th co-opted member at this point in time.

Not all co-opted members are associated with a national regulatory agency. Some are working at university or research institutes and the candidates identified above for co-optation in the area of traditional medicine came from medical practice. This may explain why some NCAs find it difficult to deliver support to these members, e.g. in terms of library service, literature searches and preparation of assessment reports. Whereas members from national authorities contribute to the HMPC work as part of their main professional work, co-opted members may have to dedicate time to their HMPC related tasks by interrupting their professional work e.g. cancelling medical appointments etc. The EMEA has no specific resources to deliver support to co-opted members or to compensate their potential financial losses. This situation may in the future limit the availability of clinical and preclinical experts that could be co-opted to the Committee.

The HMPC has together with the EMEA sought to put some initiatives in place that may help improve this situation, e.g. encouraging a broader support from interested parties by making public calls for submission of bibliographic material/scientific data. In addition, the EMEA library can assist HMPC members and Rapporteurs with literature searches.

II.2 SIMPLIFIED REGISTRATION PROCEDURE

The legal basis for the simplified registration procedure is laid down in Article 16a of Directive 2001/83/EC as amended. Only traditionally used herbal medicinal products [4] are eligible for this procedure and only if certain criteria are fulfilled.

[4] Traditional herbal medicinal product: herbal medicinal product which fulfil all the criteria laid down in Article 16a(1) of the Directive, including the period of traditional use as laid down in Article 16c(1)(c).

In order to obtain traditional-use registration, the applicant shall submit an application to the competent authority of the Member State concerned. The registration is a national procedure and there are no provisions for a centralised registration procedure. However, mutual recognition and decentralised procedures for traditional-use registration will be applicable as long as a Community herbal monograph or Community list entry has been established.

The Member State, where the application for traditional-use registration has been submitted, can request the HMPC to draw up an opinion on the adequacy of the evidence of the long-standing use of the product, or of the corresponding product. For further information on this and other referral procedures involving the HMPC, cf. section II.7.

II.2.1 Level of utilisation by Member States and industry (incl. economic impact)

The EMEA does not maintain a register of products granted simplified registration. However, as per October 2006 a small but growing number of applications for simplified registration are being processed in the EU Member States. Table 1 provides an overview of the applications received in the different Member States as reported by HMPC members.

Table 1: Overview of applications under the simplified registration procedure (status October 2006)

Member State	Applications	Under assessment	Finalised	
			Positive	Negative
Austria (AT)	None	-	-	-
Belgium (BE)	None	-	-	-
Cyprus (CY)	None	-	-	-
Czech Republic (CZ)	None	-	-	-
Denmark (DK)	None	-	-	-
Germany (DE)	16	15	1	-
Estonia (EE)	None	-	-	-
Spain (ES)	Dir not implemented	X	X	X
Finland (FI)	1	1	-	-
France (FR)	Dir not implemented	X	X	X
Greece (GR)	12	12	-	-
Hungary (HU)	None	-	-	-
Ireland (IE)	Dir not implemented	X	X	X
Iceland (IS)	Dir not implemented	X	X	X
Italy (IT)	None	-	-	-
Lithuania (LT)	None	-	-	-
Luxembourg (LU)	None	-	-	-
Latvia (LV)	1	1	-	-
Malta (MT)	None	-	-	-
Netherlands (NL)	2	2	-	-
Norway (NO)	None	-	-	-
Poland (PL)	Dir not implemented	X	X	X
Portugal (PT)	None	-	-	-
Sweden (SE)	5	5	-	-
Slovenia (SI)	2	2	-	-
Slovakia (SK)	None	-	-	-
United Kingdom (UK)	13	13	-	-
Croatia (HR)*	Dir not implemented	X	X	X
Romania (RO)*	Dir not implemented	X	X	X
Bulgaria (BG)*	Dir not implemented	X	X	X

* Candidate Member State
Dir: Directive 2004/24/EC

II.2.2 Consultation of HMPC (requests from Member States)

As per October 2006, the HMPC has not received any requests from Member States for drawing up an opinion on the adequacy of the evidence of the long-standing use of a product, or of the corresponding product, for which an application for simplified registration has been submitted. No referral from Member States for a product that has less than 15 years of traditional use within the EU has been submitted.

II.2.3 Experiences of the HMPC

Simplified registration procedure

Several NCAs report a growing interest in utilisation of the registration procedure for traditional herbal medicinal products. As indicated in Table 1, more than 10 applications are in different stages of assessment in some countries, e.g. Germany, Greece and United Kingdom. In other Member States few, if any, applications have been submitted.

It should be recognised that the date for implementation of the Directive (31 October 2005) has only recently past and that national procedures for processing such applications may only just be coming into practical effect. A further reason could be the absence of Community herbal monographs and entries to the Community list, the first of which are only now emerging. Without these documents in place, the industry may be hesitant to apply via the new registration route. The Directive foresees a seven year transition period applying to all products already on the market at the time of entry into force, which allows industry to continue supplying such products until more definitive procedures and guidance emerge, both at national and European level.

II.3 HMPC PRIORITIES FOR ASSESSMENT WORK

With consideration to the provisions of Chapter 2a of Directive 2001/83/EC as amended, the HMPC has defined the establishment of Community herbal monographs and entries to the Community list as being among the Committee's core duties. In addition, it is one of the main indicators on which external stakeholders consider the outcome of the HMPC as a new scientific Committee on the European level. Both types of documents are established on the background of an assessment report, which is prepared by the assigned Rapporteur and peer reviewed by the Committee.

The Committee has therefore from the early phases of its work made prioritisations with regard to which herbal substances should be first assessed. To ensure consistency with work previously carried out in the former Working Party on Herbal Medicinal Products (HMPWP), and with a view to make the best use of bibliography that was already available to the HMPC, it was decided to elaborate on assessment work undertaken by the HMPWP – primarily in relation to the so-called 'Core Data', which had many characteristics in common with development of monographs.

In an effort to establish priorities for assessment work in the medium to long term, the HMPC has obtained feedback from interested parties regarding their view on the issue and compiled a priority list taking into account the priorities given by stakeholders balanced against availability of data with which to conduct the review.

The HMPC has published a list of assessment tasks for which Rapporteurs have been allocated and with planned initiation of assessment during 2006-2007 (cf. list of HMPC documents in Annex 3). The ORGAM Group is during 4Q 2006 discussing a procedure for the submission of proposals for inclusion of new plants to the priority list and for revising the existing priorities.

In addition an overview of distribution of assessment work related to establishment of Community herbal monographs and/or Community list entries between the HMPC members, as well as the distribution of other types of assessment work, is presented in Annex 2.

The interested parties to the HMPC are on a regular basis requested to support the HMPC with submission of scientific data/literature for all ongoing assessments (cf. section II.7.4).

II.4 ESTABLISHMENT OF A 'LIST OF HERBAL SUBSTANCES, PREPARATIONS AND COMBINATIONS THEREOF FOR USE IN TRADITIONAL HERBAL MEDICINAL PRODUCTS'

As laid down in Article 16f(1) of Directive 2001/83/EC as amended, a 'list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products' shall be established in accordance with the procedure referred to in Article 121(2) of Directive 2001/83/EC as amended – the so-called 'comitology' procedure.

The HMPC has chosen to structure its work of establishing this list (or "entries" to the list) in close connection to the work of establishing Community herbal monographs (cf. section II.5). As a general

principle for work initiated by the HMPC itself, an assessment report of a given herbal substance is carried out before agreeing on basis of the Rapporteur's recommendation whether the substance has a traditional-use indication[5] or a well-established use indication[6]. The assessment report thus contains the HMPC's view on whether the substance fulfils the criteria for an entry to the Community list.

II.4.1 Overview of regulatory guidance

The following guidance documents and templates have been prepared by the ORGAM Group and adopted by the HMPC (status 31 October 2006):

- Procedure for the appointment by the HMPC of a Rapporteur responsible in the simplified procedure for the evaluation of a proposal for inclusion in the list of herbal substances, preparations and combinations thereof and for the development of Community herbal monographs (EMEA/HMPC/108877/2005)

- Structure of the list of herbal substances, preparations and combinations thereof (EMEA/HMPC/100824/2005)

- Guideline on the documentation to be submitted for inclusion in the List of herbal substances, preparations and combinations thereof (EMEA/HMPC/107399/2005)

- draft Assessment report template for the development of community monographs and for inclusion of herbal substance(s), preparation(s) or combinations thereof in the list (EMEA/HMPC/418902/2005)

II.4.2 List of published documents

The following draft entries to the Community list have been adopted by the HMPC for release for public consultation (status 31 October 2006):

- Lini semen (linseed)
- Valerianae radix (valerian root)
- Foeniculi amari fructus (bitter fennel fruit)
- Foeniculi dulcis fructus (sweet fennel fruit)

The consultation period is 3 months for all the above-mentioned draft entries to the Community list. Once the Committee has adopted an opinion on an entry to the Community list, it is translated into all official EU languages and transmitted to the European Commission.

II.4.3 Experiences of the HMPC

To draft an entry to the Community list requires significant resources from the Member States and the EMEA. The general problems are identical to the drafting of Community Monographs (cf. section II.5.3). As the inclusion of an herbal substance/preparation into the Community list is legally binding in Member States in so far that no additional data on safety and traditional use can be requested from applicants, a harmonised position within the Committee is often difficult to obtain, especially if information on safety is not complete. Some galenical forms, such as preparations for topical use that contain complex excipients, e.g. ointments, cannot be fully covered by a Community list entry, because additional data on clinical safety/local tolerance that are product-specific would be necessary. In such a situation, a monograph describing the traditional use might be established.

In developing the very first series of list entries the HMPC identified major issues concerning availability and quality of genotoxicity data for these herbal substances, which are likely to be encountered with other herbal substances. The HMPC is of the view that if relevant questions related to safety remain unanswered, the adoption of a positive opinion on a Community list entry is not

[5] Article 16a(1) of Directive 2001/83/EC as amended lays down the criteria for an application for simplified registration based on traditional use.

[6] Article 10a of Directive 2001/83/EC as amended lays down the criteria for an application for marketing authorisation based on well-established use. Well-establish use should be demonstrated according to rules laid down in the Annex to Directive 2001/83/EC as amended.

possible as such entries formally substitute for the provision of data identified in Article 16c(1)(b)(c) and (d) and effectively prevent NCAs from requesting additional data from applicants.

Although the HMPC has developed guidance to applicants in the area of genotoxicity testing requirements[7] it is not known to what extent the industry will conduct such testing, within which timeframes or whether the results will be made generally available in order resolve this difficulty. Until the genotoxicity testing issue is satisfactorily resolved, the HMPC will be unlikely to develop and adopt opinions on the high numbers of entries to the Community list that had been anticipated (for 2006, 30 entries had been anticipated). This is expected to have a consequent negative effect on the rate of uptake and utilisation of the traditional-use registration, which may be considered to be the primary objective of the legislation on traditional herbal medicinal products. However, the establishment of Community herbal monographs may help to provide a solution to this issue.

II.5 ESTABLISHMENT OF COMMUNITY HERBAL MONOGRAPHS

As laid down in Article 16h(3) of Directive 2001/83/EC as amended, the HMPC shall establish Community herbal monographs for herbal medicinal products with regard to the application of Article 10a of the Directive (well-established use) as well as traditional herbal medicinal products.

II.5.1 Overview of regulatory guidance

The following guidance documents and templates have been prepared by the ORGAM Group and adopted by the HMPC (status 31 October 2006):

- Timetable for the finalisation of a Community herbal monograph (EMEA/HMPC/126542/2005)
- Procedure for the preparation of Community monographs for traditional herbal medicinal products (EMEA/HMPC/182320/2005 Rev.1)
- Procedure for the preparation of Community monographs for herbal medicinal products with well-established medicinal use (EMEA/HMPC/182352/2005 Rev.1)
- Template for a Community herbal monograph (EMEA/HMPC/107436/2005)
- Draft Assessment report template for the development of Community monographs and for inclusion of herbal substance(s), preparation(s) or combinations thereof in the list (EMEA/HMPC/418902/2005)

II.5.2 List of published documents

The following Community herbal monographs have been adopted by the HMPC (status 31 October 2006):

- Aloe barbadensis (barbados aloes) and aloe capensis (cape aloes)
- Frangulae cortex (frangula bark)
- Lini semen (linseed)
- Plantaginis ovatae seminis tegumentum (ispaghula husk)
- Plantaginis ovatae semen (ispaghula seed)
- Psyllii semen (psyllium seed)
- Sennae fructus (senna pods)
- Sennae folium (senna leaf)
- Valerianae radix (valerian root)

In addition, the following draft Community herbal monographs have been adopted by the HMPC for release for public consultation:

- Anisi fructus (Aniseed)

[7] HMPC 'Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in applications for simplified registration' (EMEA/HMPC/32116/2005)

- Anisi aetheroleum (Anise oil)
- Foeniculi amari fructus (bitter-fennel fruit)
- Foeniculi amari aetheroleum (bitter-fennel oil)
- Foeniculi dulcis fructus (sweet-fennel fruit)

The consultation period has been 3 months for all the above-mentioned draft monographs.

All Community herbal monographs adopted by the HMPC are published on the EMEA website.

II.5.3 Experiences of the HMPC

Community monographs represent a valuable tool to improve harmonisation within the Community and to facilitate access to the EU market. They offer sufficient flexibility to reflect critical deficiencies in the data, e.g. insufficient information on genotoxicity, while achieving a broad consensus on the remaining areas of safety and efficacy. They are however only to be "taken into account" by Member States when examining an application as opposed to the more binding nature of a list entry backed up by a Commission Decision addressed to all Member States.

The establishment of a Community herbal monograph requires significant resources, including financial resources. Whereas there is, in principle, consensus that the assessment work will be mainly performed by the members of the HMPC and MLWP, there is no agreement between Member States and the EMEA on who will supply the resources that are necessary for performing literature searches, collecting and compiling comprehensive literature and editing published texts. Even the preparation of assessments will pose a challenge for those agencies that depend on fees, because this type of work is not covered by a fee.

Moreover, the monographs adopted by the HMPC need to be periodically updated through an *ad hoc* procedure to be put in place for retrieving and evaluating new data from the literature. The systematic revision and updating processes are essential in order to prevent HMPC monographs from becoming outdated as well as to avoid misleading Member States.

This stands in contrast to the centralised procedure for marketing authorisation applications whereby the applicant supplies both the data to be reviewed in the application file and the fee to fund the scientific review and ancillary support activities. In the case of the work of the HMPC the applicant is absent and his/her place is taken up by interested parties e.g. AESGP, ESCOP and others. Such interested parties have on several occasions confirmed preparedness to deliver bibliographic and other scientific data to support the work of the HMPC. Major support has been provided, in particular by ESCOP and AESGP, for preparation of the first examples of monographs and list entries. However, ESCOP declared recently that this support would be temporarily suspended as a consequence of EU legislation on intellectual property, specifically copyright protection, and the significant financial burden resulting from the need to produce bibliographic compilations for supply to the HMPC. Only if ESCOP can resolve these issues satisfactorily will the direct support to the HMPC in terms bibliographic and other scientific data be resumed.

In the area of indications related to the well-established use, consensus is sometimes difficult to reach as the practices differ significantly between Member States. This has lead to the adoption of some Community herbal monographs by majority vote rather than by consensus opinion, which, although foreseen in the Rules of Procedure of the HMPC, may lead to subsequent difficulties when applicants attempt to rely on these monographs in some Member States whose nominated member to the HMPC has expressed a divergent position. Specific guidance prepared by the HMPC and new guidance from the Commission on the definition of serious risk to public health may facilitate future discussions in this area.

II.6 S&E GUIDANCE RELATING TO MONOGRAPHS AND LIST ENTRIES

The MLWP (before March 2006 the S&E Group) has prepared a number of guidance documents covering aspects of safety and efficacy in relation to applications for well-established and traditional use herbal medicinal products. These have subsequently been discussed and adopted in the HMPC and include: (status 31 October 2006):

- Guideline on the clinical assessment of fixed combinations of herbal substances/herbal preparations (EMEA/HMPC/166326/2005)

- Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in applications for simplified registration (EMEA/HMPC/32116/2005)

- Guideline on the assessment of clinical safety and efficacy in the preparation of Community herbal monographs for well-established and of Community herbal monographs /lists for traditional herbal medicinal products/substances/preparations (EMEA/HMPC/104613/2005)

- Draft Concept paper on the development of a guideline on the assessment of genotoxic constituents in herbal substances/preparations (EMEA/HMPC/413271/2006)

II.7 REFERRALS TO THE HMPC

Directive 2004/24/EC introduced several provisions for referrals that shall be dealt with by the HMPC, including:

- An optional referral of products for which there is no established Community herbal monograph and that are not included in the Community list or for which the HMPC has not prepared a monograph and which are subject to long-standing use [Article 16c(1)(c)].

- A mandatory referral of products for which there is no established Community herbal monograph and that are not included in the Community list or for which the HMPC has not prepared a monograph and which has been used in the Community for less than 15 years [Article 16c(4)].

The Directive moreover has provisions for registrations granted in accordance with Article 16a where Chapter 4 of Directive 2001/83/EC as amended applies by analogy [Article 16d(1)]:

- Referrals of products registered for traditional use for which a Community herbal monograph exists or where the herbal substance, preparation or combination thereof has been included in the Community list [Article 16h(c)].

This implies that the Articles in Chapter 4 will apply in full to herbal medicinal products and that the regulatory procedures applicable to those referral procedures will apply to herbal medicinal products with an existing Community herbal monograph or where the herbal substance, preparation or combination thereof has been included in the Community list.

In addition to this, Article 16 h(1)(d) states that the HMPC shall give an opinion, where appropriate, where other medicinal products containing herbal substances are referred to the Agency under Chapter 4 of Title III. In practice this means that the CHMP would refer to the HMPC a part of the dossier for an opinion.

The HMPC is currently developing guidance on referrals. However, no referrals have been made to the HMPC as of October 2006. Moreover, no fees are applied to referrals and no other form of compensation is foreseen in relation to this work to be carried out by the HMPC.

II.7.1 Overview of regulatory guidance

The following guidance documents have been adopted by the HMPC (status 31 October 2006):

- Guidance on document to be provided by Member States and Applicants/MAHs in support of a Simplified Registration Referral under Articles 16c(1)(c) and 16c(4) (EMEA/HMPC/431129/2005)

- HMPC ORGAM proposal for inclusion of simplified registration referrals for traditional herbal medicinal products into Chapter 3 of the NTA (EMEA/HMPC/98723/2006) *(The document has been submitted to the NTA group as draft. Publication is expected 4Q 2006)*

II.7.2 Experiences of the HMPC

With regard to developing procedures on referrals the Committee is aware that the Directive does not provide the HMPC with a more detailed procedure to follow in any of the provisions introduced through Article 16c. The Article lacks a reference to Article 32 of Directive 2001/83/EC as amended, and as a consequence the HMPC opinion adopted under the above-mentioned provisions will not be formalised through a Commission Decision and hence can only be considered advisory to the Member States. In addition to this, the legislation does not deliver a time frame for handling the referrals. In order to fill this legislative gap the HMPC has proposed that the procedure and timelines established in Article 32 will as far as possible be applied to these Article 16c referrals by analogy. However, the timing for triggering the referrals during the evaluation of the simplified registration procedure is still under discussion and difficulties are foreseen in the application of Article 16c(4) when HMPC may consider establishing a Community herbal monograph, which shall be taken into account by the Member State when taking its final decision.

III. OTHER TASKS OF THE HMPC

Further to its core duties as outlined above, the HMPC carries out a number of additional tasks, in particular relating to pharmacovigilance of herbal medicinal products and provision of scientific services.

III.1 PHARMACOVIGILANCE

The HMPC regularly discusses and assesses issues relating to clinical safety and pharmacovigilance of herbal medicinal products. This work is coordinated with the CHMP Pharmacovigilance Working Party (PhVWP) on matters where this is relevant. Public statements/reflection papers relating to pharmacovigilance are usually coordinated with the PhVWP (examples can be found in the list in Annex 3).

III.1.1 Overview of scientific guidance

The HMPC has issued a number of public statements and reflection papers with recommendations for patients and health care professionals. A list of these can be found in Annex 3 under 'pharmacovigilance'.

III.1.2 Experiences of the HMPC

Herbal medicinal products are not well reflected in current pharmacovigilance databases. A harmonised thesaurus on herbal substances and herbal preparations would be essential to improve their status. The EMEA's Post Authorisation and Safety Evaluation Sector has embarked on a co-operation with HMPC and external partners (Kew Royal Botanic Gardens) to create a "herbal thesaurus" to address reports on herbal medicinal products in an adequate way. The presence of traditional herbal medicinal products in distribution channels distinct from pharmacies may require a more active investigation of possible adverse events. During the transition period for implementation of the new legislation, a significant number of traditional herbal medicinal products will not be fully captured by existing pharmacovigilance systems, e.g. because the product had been considered to be a food supplement, and therefore a significant under-reporting might be expected. The fact that the legislation does not require a responsible person for pharmacovigilance for holders of traditional use registrations may add to the difficulties.

The HMPC has also contributed to the European Commission's assessment of the current pharmacovigilance system during a consultation period in the first part of 2006.

III.2 SCIENTIFIC SUPPORT AND ADVICE PROVIDED BY THE HMPC

In accordance with the EMEA rules in the area[8], fees for scientific support and advice by the HMPC to applicants in the field of traditional herbal medicinal products have been introduced. These fees comprise EUR 17 400 for request for scientific support and advice by the HMPC on multiple areas related to traditional herbal medicinal products and EUR 11 600 for requests for scientific support and advice by the HMPC on single areas, e.g. quality or safety or long-standing use, related to traditional herbal medicinal products. The fees may be significantly reduced under the SME provisions implemented at the EMEA.

A template for requesting advice has been adopted by the HMPC and is available on the EMEA website. As of October 2006 no requests for assistance relating to scientific support have been made to the HMPC.

The Committee continuously receives requests for regulatory and scientific advice from Member States. Such requests are normally processed in coordination with the European Commission, the EMEA and/or the relevant HMPC subgroup.

[8] 'Rules for the implementation of Regulation (EC) No 297/95 as amended on fees payable to the European Medicines Agency and other measures' (EMEA/MB/356866/2005)

As a result of this support and advice a Q&A document has been published on the EMEA website[9]. The document also contains information derived from handling of external parties' request and is updated on a regular basis. It is expected that the European Commission will publish a parallel questions and answers document concerning legal/regulatory issues.

III.3 COORDINATION TASKS

In accordance with Article 16h(1) of Directive 2001/83/EC as amended, the HMPC shall ensure the appropriate coordination with the Committee for Human Medicinal Products (CHMP) by a procedure to be determined by the Executive Director of the Agency in accordance with Article 57(2) of Regulation (EEC) No 2309/93 [Article 64(d)(2) of Regulation (EC) No 726/2004].

III.3.1 Coordination with other EMEA Scientific Committees

The HMPC undertakes its coordination with other EMEA Scientific Committees in accordance with the EMEA 'Policy on appropriate coordination between the scientific committees of the Agency' (EMEA/314447/2005). The Committee has taken a number of measures to ensure and improve coordination with other scientific Committees of the EMEA involved in the evaluation of human medicines, including:

- EMEA Human Scientific Committees Working Party with Patients and Consumers Organisations (PCWP)
- CHMP/CVMP Quality Working Party (QWP)
- CHMP Safety Working Party (SWP)
- CHMP Paediatric Working Group (PEG)
- Pharmacovigilance Working Party (PhVWP)
- GMP Inspection Services Group

The HMPC endeavours to ensure early internal coordination of documents, which are likely to have relevance for coordination/consultation with other Committees. Likewise, coordination/consultation with the HMPC has been sought from the CHMP on a number of CHMP documents. To facilitate the discussion of HMPC documents in other Committees, the HMPC has developed a practice of sending Rapporteurs to the relevant CHMP sub-group meetings on an ad-hoc basis.

Successful co-operation has been established with several CHMP working parties (QWP, SWP, PhVWP) and the GMP Inspection Services Group. Delegates from HMPC participate as observers in the SWP, PEG and the PCWP.

On the request from the Committee on Orphan Medicinal Products (COMP) the HMPC has delivered comments (regarding quality aspects) on two orphan medicinal product designation applications.
In accordance with the EMEA policy on coordination, the EMEA Secretariat also has a general responsibility to ensure that relevant issues are identified and information exchanged between the Committees so that coordination is continuous and consistent.

III.3.2 Coordination with other EU bodies

The HMPC is committed to the EMEA's work on ensuring appropriate coordination with other EU bodies in accordance with Article 59 of Regulation (EC) No 726/2004. The Committee has been consulted on the 'EMEA Reflection paper on the cooperation with other bodies in the European Union for identification and management of potential conflict over scientific opinions' (EMEA/17013/2005) and agreed to its contents.

In addition, the HMPC has identified a need for a more systematic way of exchanging information between Member States on the regulatory status of individual herbal medicinal products marketed in the Member States. The ORGAM Group is currently developing a draft procedure for this and it is expected that coordination with the Coordination Group for Mutual Recognition and Decentralised Procedures – Human CMD(h) would form part of this procedure.

[9] 'Overview of questions and answers relating to technical/scientific issues' (EMEA/HMPC/151144/06)

The HMPC exchanges information with the European Food Safety Authority (EFSA) on an ad-hoc basis. In addition, the Italian HMPC member, V. Silano, is also Chairman of EFSA's Scientific Committee, and thus in a position to facilitate the identification of relevant coordination issues.

A contact has been established between the HMPC and DG SANCO's Scientific Committee for Cosmetic Products (SCCP) through which information and requests for assistance can be exchanged for mutually relevant topics.

The HMPC has a close collaboration with the European Directorate for the Quality of Medicines (EDQM) with one observer attending HMPC meetings on a permanent basis and the HMPC Chairman being member of the EDQM Scientific Steering Committee for Certification. The HMPC Chairman also presents herbal substances/preparations related topics during the meeting organised at the beginning of each year as a forum for discussions between EMEA and its scientific committees and the European Pharmacopoeia.

The EMEA/HMPC have provided technical support to the EC in relation to the 'EU-India Strategic Partnership'. The Chairpersons of the HMPC and HMPC subgroups attended a meeting of the Working Group on Pharmaceuticals and Biotechnology held in May 2006 with a view to discussing with an Indian delegation the application of the EU legal framework of herbal medicinal products to Ayurvedic medicines and the authorisation routes available for such products. A constructive dialogue was established as a basis for further discussions.

III.3.3 Coordination / meetings with non-EU / international organisations

In accordance with Article 77 of Regulation (EC) No 726/2004 the Commission may, in agreement with the Management Board and the Committee, invite representatives of international organisations as observers.

Romania and Bulgaria have been observers as of 1 September 2005 following a EU grant under the PHARE programme. Croatia and Turkey are invited as observers as of September 2006 under the same programme.

In terms of general collaboration with non-EU Regulatory Authorities, the HMPC heard in 2005 presentations from Health Canada and the Australian Therapeutic Goods Administration on the regulatory schemes applicable to medicinal products of herbal origin, particularly on the provisions related to herbal products defined as traditional. In addition, the Swissmedic Authorities have approached the EMEA on the possibilities of sending an observer to the HMPC.

The EMEA/HMPC is participating in the WHO International Regulatory Cooperation on Herbal Medicines (IRCH), with the HMPC Chairman/HMPC secretariat as the formal contact point.

III.3.4 Interaction with interested parties

In accordance with the HMPC Rules of Procedure Article 21, an interface for regular contact between the HMPC/MLWP and relevant stakeholders has been established.

Based on a public call for interest, the Committee had by the end of 2005 established a 'list of interested parties to the HMPC' (enclosed as Annex 4). The organisations included in this list are considered by the HMPC to have a relevant focus in relation to the work of the HMPC and have documented their representation on the level of the European Union. The list is updated regularly on basis of new applications for acknowledgement as interested party to the HMPC or organisations wishing to be deleted from the list.

The HMPC and the MLWP seek to maintain a proactive and transparent relationship with the organisations included on the list. In November 2005 these were invited to attend a hearing with the HMPC to discuss the work and priorities of the Committee and the expectations for the future interaction. It is expected that such general hearings/info-days will be held on a regular basis. In addition, the MLWP has held ad-hoc meetings with selected organisations providing specific support to the working party, e.g. by assisting with identification and submission of data for assessments.

On a broader level, the HMPC strives to ensure a high degree of transparency towards the public. One of the key initiatives in this respect is the relatively detailed meeting report that is published on the EMEA website following each HMPC meeting. In addition, draft Community herbal monographs, draft entries to the Community list and most draft guidance documents are subject to a phase of public consultation before finalisation.

Furthermore, the HMPC has together with the MLWP established a priority list from which assessments underpinning Community herbal monographs/entries to the Community list are undertaken. In relation to this, public calls are made for submission to the MLWP of assessment data (cf. section II.3), and contributions are generally received from a number of the acknowledged interested parties.

III.4 EXPERIENCES OF THE HMPC

Scientific support

The fees for scientific advice are still very high. Most of the producers of traditional herbal medicinal products are very small companies who may not have sufficient resources. Such companies may be not aware of the SME provisions in place, because they are not organised in EU interest groups and English language might be a barrier. The HMPC is of the view that information on possibilities to make best use of information resources at the EMEA should be expanded and focused on that type of producers. On the other hand, it presently seems doubtful that the EMEA would gain significant revenues in the short-term from such a kind of service to be provided for by the HMPC.

Coordination with other EU bodies

The HMPC has identified a need to further improve exchange of information and scientific co-operation with EFSA in the area of herbal preparations. The HMPC has in September 2006 highlighted this need in a letter to EFSA and proposed a workshop between the HMPC and EFSA's Scientific Committee to be held in 2007.

The HMPC is of the opinion that cooperation with the EDQM should be improved. The HMPC might e.g. define for which herbal substances/preparations a standardisation or quantification is necessary with regard to the current scientific knowledge.

Coordination / meetings with non-EU / international organisations

In view of the significant workload of the HMPC relating to implementation of the EU legislation an extension of external contacts and activities will be difficult.

IV. GENERAL CONCLUSIONS

Directive 2004/24/EC represents a significant improvement in the situation of herbal medicinal products and it offers a suitable framework for those products. Significant progress in the regulatory implementation has already been achieved by the HMPC. Progress in the implementation at the level of Member States is expected to follow guidance and criteria prepared at the European level. The main challenge is the availability of human and financial resources for preparing and regularly updating Community herbal monographs and Community list entries as well as availability of adequate sources of key safety information e.g. genotoxicity studies to allow comprehensive list entries/monographs to be prepared.

The current legislation does not specifically address how resources for the scientific work of the HMPC should be provided. Until now data sources have been largely provided voluntarily by some interested parties and indeed there are threats to the continuation of this supply due to financial resource limitations and copyright issues. Apart from this support, HMPC assessments/evaluations are currently entirely based on the input from HMPC members, most of who are working within NCAs. However, for many of the NCAs concerned it is increasingly difficult to provide the resources necessary to support the scientific work. Some NCAs have declared that they will not prepare assessment reports or make other major contributions due to different priorities and allocation of resources.

A partial progress has been achieved by the HMPC through optimising the process of preparation and discussion of monographs in the MLWP and by suitable guidance on the assessment procedures and criteria. However, a fair distribution of the burden of work between HMPC members supported by their NCAs is far from being reached. A clear allocation of responsibilities and of resources for delivering the bibliographical or other scientific basis for assessment needs to be established. An overview of the current distribution of assessment work related to establishment of Community herbal monographs and/or Community list entries between the HMPC members, as well as the distribution of other types of assessment work, is found in Annex 2.

The efforts of the HMPC to improve patients' and consumer safety may be reduced if the difficult situation in the area of borderline products such as food, cosmetics and medical devices is not further addressed[10]. Even after implementation of the new EU legislation on health claims for foods, it is still possible that products, which cannot be registered as traditional herbal medicinal products, because an appropriate quality cannot be proven or because the safety cannot be assured, will still be available on the market as non-pharmaceutical products outside the medicinal product regulatory framework.
The HMPC is committed to ensure appropriate coordination with other EU bodies, in accordance with Article 59 of Regulation (EC) No 726/2004, in an effort to minimise these difficulties.

[10] See also "Summary of discussion" from Eur. Com. Workshop on 'Borderline Products with Pharmaceuticals' 28 October 2004.

Annex 1

Composition of the HMPC and HMPC subgroups, (status October 2006)

Member (state)	**HMPC**		**MLWP**	**DG Q**	**ORGAM**
	Member	Alternate			
Konstantin Keller (DE)	C		X		
Heribert Pittner (AT)	VC		C		
Wolfgang Kubelka (AT)		X		X	
Arnold J Vlietinck (BE)	X		X		
Heidi Neef (BE)		X		X	
Panayiotis Triantafyllis (CY)	X				
Maria Stavrou (CY)		X			
Marie Heroutova(CZ)	X		X		
Steffen Bager (DK)	X				X
Kristine Hvolby (DK)		X		X	
Marje Zernant (EE)	X				
Ain Raal (EE)		X	X		
Anneli Törrönen (FI)	X		X		
Sari Koski (FI)		X		X	
Antoine Sawaya (FR)	X				
Jacqueline Viguet Poupelloz (FR)		X	X		X
Werner Knöss (DE)	X				
Christine Werner (DE)		X	X		
Ioanna Chinou (GR)	X		VC		
Eleni Skaltsa (GR)		X			
Zsuzsanna Biró-Sándor (HU)	X		X		
Thorbjörg Kjartandsdóttir (IS)	X				
Sesselja Ómarsdóttir (IS)		X			
Dairíne Dempsey (IE)	X		X	C	
Cora Nestor (IE)		X			
Vittorio Silano (IT)	X				
Marisa Delbó (IT)		X	X	X	
Dailonis Pakalns (LV)	X		X		
Dace Kalke (LV)		X			
Artūras Kažemekaitis (LT)	X				
Mariette Backes-Lies (LU)	X				
Jacqueline Genoux-Hames (LU)		X			
Christian Cuschieri (MT)	X				X
Caroline Attard (MT)		X			
Emiel Van Galen (NL)	X				C
Burt H Kroes (NL)		X	X	X	
Steinar Madsen (NO)	X				
Gro Fossum (NO)		X	X		
Wojciech Dymowski (PL)	X				X
Elzbieta Wojtasik (PL)		X			
Ana Paula Martins (PT)	X				X
Maria Helena Pinto Ferreira (PT)		X	X		

Member (state)	**HMPC**		**MLWP**	**DG Q**	**ORGAM**
	Member	Alternate			
Dáša Salugová (SK)	X				
Pavel Mucaji (SK)		X			
Samo Kreft (SI)	X		X		
Barbara Razinger (SI)		X			X
Gloria García Lorente (ES)	X		X		X
Adela Velázquez (ES)		X			
Per Claeson (SE)	X		X		
Ubonwan Claeson (SE)		X			X
Linda Anderson (UK)	X		X	X	
Sue Harris (UK)		X			
Gert Laekeman (BE)	# Pre-clinical pharmacology		#		
Olavi Pelkonen (FI)	# Toxicology		#		
Kurt Widhalm (AT)	# Paediatric medicine		#		
Ulrike Wissinger-Gräfenhahn (DE)	# Clinical pharmacology		#		
Ewa Widy Tyszkiewicz (PL)			X		
Isabelle Fouraste (FR)				X	
Klaus Reh (DE)				X	X
	Observer	***Alternate***			
Stefan Nikolov (BG)	O				
Gerassim Kitanov (BG)		O			
Maria Niculescu (RO)	O				
Laurentia Ruscan (RO)		O			
Josipa Cvek (HR)	O				
Meral Gündoğan (TR)	O				
Ellen Pel (Pharmacopoeia Commission)	O				
Michael Wierer (Pharmacopoeia Commission)		O			

C = Chairperson
VC = Vice Chairperson
X = Member / Alternate member
# = Co-opted member
O = Observer / Alternate observer

Annex 2

Overview of distribution of HMPC assessment work, (status October 2006)

Table 1: Distribution of HMPC assessment work related to Community herbal monographs / entries to the Community list

MEMBER STATES	2005		2006		Total R and [Co-R]
	R	[Co-R]	R	[Co-R]	
Austria (AT)	3		2		5
Belgium (BE)	3		1		4
Cyprus (CY)					0
Czech Republic (CZ)			1		1
Denmark (DK)	1				1
Estonia (EE)	1				1
Finland (FI)					0
France (FR)	1		1		2
Germany (DE)	12		2		14
Greece (EL)			1		1
Hungary (HU)	3				3
Ireland (IE)	2				2
Italy (IT)	2				2
Latvia (LV)	1				1
Lithuania (LT)					0
Luxembourg (LU)					0
Malta (MT)					0
The Netherlands (NL)	2				2
Poland (PL)	1				1
Portugal (PT)	3				3
Slovakia (SK)					0
Slovenia (SI)	1		3		4
Spain (ES)	3				3
Sweden (SE)	2		1		3
United Kingdom (UK)	2				2
Iceland (IS)	1				1
Norway (NO)					0
G. Laekeman*					0
O. Pelkonen*		1			[1]
K. Widhalm*					0
U. Wissinger-Gräfenhahn*	1			1	1 [1]
Total R and [Co-R]	**45**	**1**	**12**	**1**	**57 [2]**

R = Rapporteur
Co-R = Co-Rapporteur

* = co-opted member

Table 2: Distribution of HMPC assessment work related to development of guidance in the areas of quality, safety & efficacy, pharmacovigilance and organisational matters.

Member States	**Quality**		**Safety & Efficacy**		**Pharmaco-vigilance**		**ORGAM**		**TOTAL R and [Co-R]**
	R	**[Co-R]**	**R**	**[Co-R]**	**R**	**[Co-R]**	**R**	**[Co-R]**	
HMPC Chairman			3						**3**
Austria (AT)	2					2			**2 [2]**
Belgium (BE)	4				2				**6**
Cyprus (CY)									
Czech Republic (CZ)									
Denmark (DK)	1	2							**1 [2]**
Estonia (EE)									
Finland (FI)	1								**1**
France (FR)					1		2	1	**3 [1]**
Germany (DE)	5				8		3		**16**
Greece (EL)									
Hungary (HU)									
Ireland (IE)	1				1			1	**2 [1]**
Italy (IT)	2								**2**
Latvia (LV)									
Lithuania (LT)									
Luxembourg (LU)									
Malta (MT)								2	**[2]**
The Netherlands (NL)	1	2					2		**3 [2]**
Poland (PL)									
Portugal (PT)							1	2	**1 [2]**
Slovakia (SK)									
Slovenia (SI)									
Spain (ES)	1	2					1	5	**2 [7]**
Sweden (SE)				1	1		5		**6 [1]**
United Kingdom (UK)	4								**4**
Iceland (IS)									
Norway (NO)									
G. Laekeman*									
O. Pelkonen*			1	1	1		`		2 [1]
K. Widhalm*									
U. Wissinger-Gräfenhahn*									
Total R and [Co-R]	**22**	**[6]**	**4**	**[2]**	**14**	**[2]**	**14**	**[11]**	**54 [21]**

R = Rapporteur
Co-R = Co-Rapporteur

* = co-opted member

Annex 3

Overview of HMPC activities

Status of documents / publication on EMEA website, (status October 2006)

ORGANISATIONAL MATTERS		
Title	**Reference**	**Status**
Guideline on the documentation to be submitted for inclusion in the 'List of herbal substances, preparations and combinations thereof'	EMEA/HMPC/107399/2005	Adopted September 2005
Procedure for the appointment by the HMPC of Rapporteur responsible in the simplified procedure for the evaluation of a proposal for inclusion in the list of herbal substances, preparations and combinations thereof and for the development of a Community herbal monograph	EMEA/HMPC/108877/2005	Adopted September 2005
Structure of the list of herbal substances, preparations and combinations thereof	EMEA/HMPC/100824/2005 Rev.1	Adopted September 2005
Template for a Community herbal monograph	EMEA/HMPC/107436/2005 Rev.2	Adopted September 2005
Template for a submission of a request for expert advice on herbal medicinal products	EMEA/HMPC/119889/2005	Adopted September 2005
Timetable for the finalisation of a Community herbal monograph [not resulting from any referral procedure]	EMEA/HMPC/126542/2005	Adopted September 2005
Procedure for the preparation of Community monographs for herbal medicinal products with well-established medicinal use	EMEA/HMPC/182352/2005 Rev.1	Adopted March 2006
Procedure for the preparation of Community monographs for traditional herbal medicinal products	EMEA/HMPC/182320/2005 Rev.1	Adopted March 2006
Concept paper on CTD for traditional herbal medicinal products	EMEA/HMPC/261344/2005	Adopted March 2006
Public statement on the interpretation of the term 'external use' for use in the field of traditional herbal medicinal products	EMEA/HMPC/31897/2006	Adopted May 2006
Assessment report template for the development of Community monographs and for inclusion of herbal substance(s), preparation(s) or combinations thereof in the list	EMEA/HMPC/418902/2005	Adopted for release for consultation May 2006
Procedure for calls for scientific data for use in HMPC assessment work	EMEA/HMPC/1004/2006	Adopted October 2006
Guidance on documentation to be provided by Member States and applicants/MAHs in support of a simplified registration referral under Articles 16c(1)(c) and 16c(4)	EMEA/HMPC/431129/2005	Adopted September 2006

QUALITY		
Title	**Reference**	**Status**
Concept paper on the declaration of herbal substances/herbal preparations in finished herbal medicinal products	EMEA/HMPC/241953/2005	Adopted for release for consultation July 2005
Guideline on quality of herbal medicinal products/traditional herbal medicinal products	CPMP/QWP/2819/00 Rev.1 and EMEA/CVMP/814/00 Rev.1	Adopted March 2006
Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products	CPMP/QWP/2820/00 Rev.1 and EMEA/CVMP/815/00 Rev.1	Adopted March 2006
Guideline on good agricultural and collection practice (GACP) for starting materials of herbal origin	EMEA/HMPC/246816/2005	Adopted January 2006
Concept paper on combination herbal medicinal products/traditional herbal medicinal products	EMEA/HMPC/58222/2006	Adopted for release for consultation June 2006
Guideline on the declaration of herbal substances and herbal preparations in herbal medicinal products/traditional herbal medicinal products in the SPC	EMEA/HMPC/CHMP/CVMP/287539/2005	Adopted for release for consultation June 2006
Reflection Paper on the use of Fumigants	EMEA/HMPC/125562/06	Adopted October 2006

SAFETY & EFFICACY		
Title	**Reference**	**Status**
Public Statement on "CPMP List of Herbal Drugs with serious risks, dated 1992"	EMEA/HMPC/246736/2005	Adopted November 2005
Guideline on the clinical assessment of fixed combinations of herbal substances/herbal preparations	EMEA/HMPC/166326/2005	Adopted January 2006
Overview of comments received on 'Guideline on the clinical assessment of fixed combinations of herbal substances/herbal preparations' (EMEA/HMPC/166326/2005)	EMEA/HMPC/419395/2005	January 2006
Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in applications for simplified registration	EMEA/HMPC/32116/2005	Adopted July 2006
Overview of comments received on 'Guideline on non-clinical documentation for herbal medicinal products in applications for marketing authorisation (bibliographical and mixed applications) and in applications for simplified registration' (EMEA/HMPC/32116/2005)	EMEA/HMPC/132154/2006	July 2006
Guideline on the assessment of clinical safety and efficacy in the preparation of Community herbal monographs for well-established and of Community herbal monographs/entries to the Community list for traditional herbal medicinal products/substances/preparations	EMEA/HMPC/104613/2005	Adopted September 2006

Overview of comments received on 'Guideline on the assessment of clinical safety and efficacy in the preparation of Community herbal monographs for well-established and of Community herbal monographs / entries to the Community list for traditional herbal medicinal products / substances / preparations'(EMEA/HMPC/104613/2005)	EMEA/HMPC/314947/2006	September 2006
Concept paper on the development of a guideline on the assessment of genotoxic constituents in herbal substances/preparations	EMEA/HMPC/413271/2006	Adopted for release for consultation October 2006

COMMUNITY HERBAL MONOGRAPHS / COMMUNITY LIST		
Title	**Reference**	**Status**
Overview of status of HMPC assessment work (continuously updated)	EMEA/HMPC/278067/2006	Adopted September 2006
Community herbal monograph for Lini semen	EMEA/HMPC/340849/2005	Adopted July 2006
Entry to the Community list for Lini semen	EMEA/HMPC/340854/2005	Adopted for release for consultation October 2005
HMPC assessment report for Lini semen	EMEA/HMPC/167395/2006	Adopted September 2006
Community herbal monograph for Valerianae radix	EMEA/HMPC/340719/2005	Adopted July 2006
Entry to the Community list for Valerianae radix	EMEA/HMPC/340779/2005	Adopted for release for consultation October 2005
HMPC assessment report for Valerianae radix	EMEA/HMPC/167391/2006	Adopted September 2006
Community herbal monograph for Plantaginis ovatae semen	EMEA/HMPC/340861/2005	Adopted July 2006
HMPC assessment report for Plantaginis ovatae semen	EMEA/HMPC/166377/2006	Adopted September 2006
Community herbal monograph for Plantaginis ovatae seminis tegumentum	EMEA/HMPC/340857/2005	Adopted July 2006
HMPC assessment report for Plantaginis ovatae seminis tegumentum	EMEA/HMPC/165838/2006	Adopted September 2006
Community herbal monograph for Psyllii semen	EMEA/HMPC/340865/2005	Adopted July 2006
HMPC assessment report for Psyllii semen	EMEA/HMPC/167338/2006	Adopted September 2006
Community herbal monograph for Aloe	EMEA/HMPC/76310/2006	Adopted September 2006
HMPC assessment report for Aloe	EMEA/HMPC/76313/2006	Adopted September 2006
Community herbal monograph for Frangulae cortex	EMEA/HMPC/76307/2006	Adopted September 2006
HMPC assessment report for Frangulae cortex	EMEA/HMPC/76306/2006	Adopted September 2006
Community herbal monograph for Sennae fructus	EMEA/HMPC/51871/2006	Adopted September 2006
HMPC assessment report for Sennae fructus	EMEA/HMPC/51870/2006	Adopted September 2006

Community herbal monograph for Sennae folium	EMEA/HMPC/51869/2006	Adopted September 2006
HMPC assessment report for Sennae folium	EMEA/HMPC/51868/2006	Adopted September 2006
Community herbal monograph for Anisi fructus	EMEA/HMPC/137423/2006	Adopted for release for consultation October 2006
Community herbal monograph for Anisi aetheroleum	EMEA/HMPC/263273/2006	Adopted for release for consultation October 2006
Community herbal monograph for Foeniculi amari fructus	EMEA/HMPC/137428/2006	Adopted for release for consultation October 2006
Entry to the Community list Foeniculi amari fructus	EMEA/HMPC/428817/2006	Adopted for release for consultation October 2006
Community herbal monograph Foeniculi amari aetheroleum	EMEA/HMPC/263292/2006	Adopted for release for consultation October 2006
Community herbal monograph for Foeniculi dulcis fructus	EMEA/HMPC/263293/2006	Adopted for release for consultation October 2006
Entry to the Community list Foeniculi dulcis fructus	EMEA/HMPC/428963/2006	Adopted for release for consultation October 2006

PHARMACOVIGILANCE		
Title	**Reference**	**Status**
Public statement on the risks associated with the use of herbal products containing Aristolochia species	EMEA/HMPC/138381/2005	Adopted November 2005
Public statement on the use of herbal medicinal products containing asarone	EMEA/HMPC/139215/2005	Adopted November 2005
Public statement on Capsicum/capsaicin containing herbal medicinal products	EMEA/HMPC/138379/2005	Adopted November 2005
Public statement on the use of herbal medicinal products containing estragole	EMEA/HMPC/137212/2005	Adopted November 2005
Public statement on the use of herbal medicinal products containing methyleugenol	EMEA/HMPC/138363/2005	Adopted November 2005
Overview of comments received on 'Public statement on the use of herbal medicinal products containing estragole' and on 'Public statement on the use of herbal medicinal products containing methyleugenol'	EMEA/HMPC/381090/2005	November 2005
Public statement on the use of herbal medicinal products containing pulegone and menthofuran	EMEA/HMPC/138386/2005	Adopted November 2005
Public statement on the allergenic potency of herbal medicinal products containing soya or peanut protein	EMEA/HMPC/138139/2005	Adopted January 2006
Overview of comments received on 'Public statement on the allergenic potency of herbal medicinal products containing soya or peanut protein'	EMEA/HMPC/381405/2005	January 2006

Public statement on Chamomilla containing herbal medicinal products	EMEA/HMPC/138309/2005	Adopted March 2006
Overview of comments received on 'Public statement on Chamomilla containing herbal medicinal products'	EMEA/HMPC/379986/2005	March 2006
Public statement on herbal medicinal products containing Cimicifugae Racemosae Rhizoma (Black Cohosh, Root)	EMEA/269259/2006	Adopted July 2006
Assessment of case reports connected to herbal medicinal products containing Cimicifugae Racemosae Rhizoma (Black Cohosh, Root)	EMEA/HMPC/269258/2006	Adopted July 2006

GENERAL DOCUMENTS		
Title	**Reference**	**Status**
Committee on Herbal Medicinal Products: Rules of Procedure	EMEA/HMPC/139800/2004	Adopted November 2006
Mandate, Objectives and Rules of Procedure for the HMPC Working Party on Community Monographs and Community List (MLWP)	EMEA/HMPC/379153/2005	Adopted March 2006
Overview of Questions and Answers relating to technical/scientific issues	EMEA/HMPC/151144/06	Adopted May 2006

Annex 4

List of interested parties to the HMPC, (status October 2006)

Industry Associations	
AEFMUTA **European Association of Manufacturers of Medicines for Anthroposophic Therapy**	9, rue E. Jung 68330 Huningue France
AESGP **The Association of the European Self-Medication Industry** Website: http://www.aesgp.be	7, avenue de Tervuren 1040 Brussels Belgium
EFPIA **European Federation of Pharmaceutical Industries and Associations** Website: http://www.efpia.org	108 Rue du Trône, Bte 1 1050 Brussels Belgium
EGA **European Generic Medicines Association** Website: http://www.egagenerics.com	PO Box 193 1040 Brussels Belgium
EHGA-EUROPAM **European Herb Growers Association** Website: http://www.europam.net	Clakenweg 132 8081 LZ Elburg The Netherlands
EHPM **European Federation of Associations of Health Product Manufacturers** Website: http://www.ehpm.org	Rue de l'Association, 50 1000 Brussels Belgium
Scientific Societies	
ESCOP **European Scientific Cooperative on Phytotherapy** Website: http://www.escop.com/	ESCOP Secretariat Argyle House Gandy Street Exeter Devon EX4 3LS United Kingdom
GA **Society for Medicinal Plant Research** Website: http://www.ga-online.org	Institute of Pharmaceutical Sciences Dept. of Pharmacognosy Karl-Franzens-Universitaet Graz Universitaetsplatz 4/I 8010 Graz Austria

PSE **The Phytochemical Society of Europe** Website: http://www.phytochemicalsociety.org/about.htm	University of London, The School of Pharmacy Centre for Pharmacognosy and Phytotherapy 29-39 Brunswick Square London WC1N 1AX United Kingdom
Healthcare professionals and Consumers & Patients Organisations	
BEUC **Bureau Européen des Unions de Consommateurs** Website: http://www.beuc.org	Avenue de Tervuren 36 Bte 4 1040 Brussels Belgium
CPME **Standing Committee of European Doctors** Website: http://www.cpme.be	Rue de la Science 41 1040 Bruxelles Belgium
EFCAM **European Forum for Complementary and Alternative Medicine** Website: http://cam.epha.org/	39-41 Rue d'Arlon 1000 Brussels Belgium
EFNMU **European Federation of Natural Medicine Users** Website: http://www.efnmu.de	Gerhard-Kienle-Weg 18 58313 Herdecke Germany
EHPA **European Herbal Practitioners Association** Website: http://www.ehpa.eu/index.html	8 Lion Yard Tremadoc Road London SW4 7NQ United Kingdom
IVAA **International Federation of Anthroposophical Medical Associations** Website: http://www.ivaa.info/	Rüttiweg, 4143 Dornach Switzerland **Operational site:** **(to be used for correspondence)** Via Vincenzo Monti 79/4 20145 Milano Italy
PGEU **Pharmaceutical Group to the European Union** Website: www.pgeu.org	Rue du Luxembourg 19-21 Box 6 1000 Brussels Belgium