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

28 January 1999
EMEA/HMPWP/16/99

AD HOC WORKING GROUP ON HERBAL MEDICINAL PRODUCTS

Final Comments for Revision of the Notice to Applicants Volume 2B Part IC1 'Tabular Formats Specific to Herbal Medicinal Products'

RELEASE FOR CONSULTATION BY THE EMEA	September 1998
DEADLINE FOR COMMENTS	December 1998
RELEASE OF FINAL PROPOSALS	January 1999

The ad hoc Working Group on Herbal Medicinal Products suggests the following tabular formats specific to herbal medicinal products to be used in Part I C 1

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Pharmaceutical Expert Report
Format 2B101A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use Only)**
PART II A : COMPOSITION		
Product Description : Volume Page(s)		**(For National Authority Use Only) COMMENTS**
Complete Composition : Volume Page(s)		
Unit and/or Percentage Formula **Active substance(s)** **Excipient(s)**		
Container (brief description) : Volume Page(s)		
Clinical trial formula(e) : Volume Page(s) **or formulae used in bibliographical application**		
Unit and/or Percentage Formula **Active substance(s)** **Excipient(s)**		

Pharmaceutical Expert Report

Format 2B102A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II A: DOSAGE FORM - DEVELOPMENT PHARMACEUTICS		
Product Development Studies Summary[1] : Volume Page(s)		**(For National Authority Use Only) COMMENTS**
Explanation of choice of the composition : Volume Page(s)		
Explanation of optimisation of concentrations of the additives in the composition : Volume Page(s)		
Summary of studies on compatibility data with other products (if necessary) : Volume Page(s)		

[1] The phytochemical overview is included in Format 2B110A and 2B111A

Pharmaceutical Expert Report

Format 2B103A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II A : DOSAGE FORM - DEVELOPMENT PHARMACEUTICS		
Summary of studies on compatibility with the container/ closure : **Volume Page(s)**		**(For National Authority Use only) COMMENTS**
Summary of in vivo bioavailability/bioequivalence studies : **Volume Page(s)**		
In vitro dissolution data on products used in the in vivo bioavailability studies : **Volume Page(s)**		

Pharmaceutical Expert Report

Format 2B104A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II B : METHOD OF PREPARATION		
Manufacturing formula : Volume Page(s)		**(For National Authority Use only) COMMENTS**
Batch size : **Formula :**		
Manufacturing process (including in process control and assembly) : Volume Page(s)		

Pharmaceutical Expert Report

Format 2B105A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II B : METHOD OF PREPARATION - PROCESS VALIDATION		
Summary of experimental studies : Volume Page(s)		**(For National Authority Use only) COMMENTS**

Pharmaceutical Expert Report

Format 2B106Ai/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S) : HERBAL DRUG PREPARATION[2]	
Specifications and routine tests : Volume Page(s)	**(For National Authority Use only) COMMENTS**
Summary of specifications and Routine Tests - Characteristics : Volume Page(s)	
Identification tests : Volume Page(s)	
Purity tests : Volume Page(s)	
Potential contamination: Loss on drying/Dry residue: Residual solvents: Relative density:	
Other tests : Volume Page(s)	
Assay/Other evaluation of potency : Volume Page(s)	
Constituents with known therapeutic activity: or Markers: or other justified determination: Compliance with Pharmacopoeia[1]:..... ☐	

[1] Reference to the Pharmacopoeia used should be given; see CD 75/318 Annex Part 2 C.1.1

[2] If no monograph for the herbal drug exists, neither in the European Pharmacopoeia nor in the pharmacopoeia of a Member State, a comprehensive specification of the herbal drug has to be presented (see Format 2B106Aii).

Pharmaceutical Expert Report

Format 2B106Aii/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S) : HERBAL DRUG	
Specifications and routine tests : Volume Page(s)	**(For National Authority Use only) COMMENTS**
Summary of specifications and Routine Tests - Characteristics : Volume Page(s)	
Identification tests : Volume Page(s)	
Purity tests : Volume Page(s)	
Foreign matter: Pharmacopoeia[1].....☐ Loss on drying/Water: Pharmacopoeia[1].....☐ Total ash/Ash insoluble in hydrochloric acid: Pharmacopoeia[1].....☐ Microbial contamination: Pharmacopoeia[1].....☐ Other potential contamination:	
Other tests : Volume Page(s)	
Assay/Other evaluation of potency : Volume Page(s)	
Constituents with known therapeutic activity: or Markers: or other justified determination: Compliance with Pharmacopoeia[1]:..... ☐	

[1] Reference to the Pharmacopoeia used should be given; see CD 75/318 Annex Part 2 C.1.1

Pharmaceutical Expert Report

Format 2B107A/HERBAL

<table>
<tr><td colspan="2">Name of Company :

Name of Finished Herbal Medicinal Product :

Name of Active substance(s) :</td><td>Tabular format Referring to Part of the Dossier</td><td>(For National Authority Use only)</td></tr>
<tr><td colspan="4">PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S): HERBAL DRUG/HERBAL DRUG PREPARATION - SCIENTIFIC DATA</td></tr>
<tr><td colspan="3">1. Nomenclature : Volume Page(s)</td><td>(For National Authority Use only) COMMENTS</td></tr>
<tr><td colspan="3">Scientific name of the plant, with the name of the authority, variety and chemotype (where applicable):

Parts of the plant :

Definition of herbal drug/herbal drug preparation :

Ratio of the herbal drug to the herbal drug preparation :

Extraction solvent(s) :

Other name :

Laboratory code :</td><td rowspan="5"></td></tr>
<tr><td colspan="3">2. Description : Volume Page(s)</td></tr>
<tr><td colspan="3">Physical form :</td></tr>
<tr><td>Constituents with known therapeutic activity:</td><td colspan="2">Justification of the appropriateness of the choice of markers:</td></tr>
<tr><td colspan="3">Other substance(s):</td></tr>
</table>

Pharmaceutical Expert Report

Format 2B108A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use Only)**
PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S): HERBAL DRUG/HERBAL DRUG PREPARATION - SCIENTIFIC DATA		
3. Manufacture : **Volume** **Page(s)**		**(For National Authority Use Only) COMMENTS**
Definition of a production batch : **Volume** **Page(s)**		
(a) Herbal drug: (b) Herbal drug preparation(s):		
Plant Production / Plant Collection: **Volume** **Page(s)**		
Geographical source : Name(s) and address(es) of the grower(s) and/or the supplier(s) of the drug : Cultivation/Collection from wild sources : Pre-harvest chemical treatment : Harvest : Drying : Cutting and milling : Other processes :		
Name(s) and address(es) of the manufacturer of the preparation : **Volume** **Page(s)**		
Manufacturing route : **Volume** **Page(s)**		

Pharmaceutical Expert Report

Format 2B109A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S) : HERBAL DRUG/HERBAL DRUG PREPARATION - SCIENTIFIC DATA	
Description of process : Volume Page(s)	**(For National Authority Use Only) COMMENTS**
Extraction solvents, reagents : Volume Page(s)	
Purification stages : Volume Page(s)	
Standardisation (adjusted to a defined content of constituents with known therapeutic activity): Volume Page(s)	
Range of the inert material or herbal drug preparation added:.....-.....%	
4. Quality control during manufacture : Volume Page(s)	
Starting materials : Volume Page(s)	
Control tests on intermediate products : Volume Page(s)	

Pharmaceutical Expert Report

Format 2B110A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S) : (DEVELOPMENT) HERBAL DRUG - SCIENTIFIC DATA	
Description of the herbal drug: Volume Page(s)	**(For National Authority Use Only) COMMENTS**
Macroscopic description: Pharmacopoeia[1].....☐ Microscopic description: Pharmacopoeia[1].....☐ Additional tests: Pharmacopoeia[1].....☐ (e.g. thin-layer chromatography):	
Composition and analytical research for constituents and physical characteristics: Volume Page(s)	
Tests for adulterants and for known toxic constituents: Volume Page(s)	
Summary of Analytical Development and Validation Studies: Volume Page(s)	

[1] Reference to the Pharmacopoeia used should be given; see CD 75/318 Annex Part 2 C.1.1

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Format 2B111A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S) : (DEVELOPMENT) HERBAL DRUG PREPARATION - SCIENTIFIC DATA		
Herbal drug preparations such as extracts		**(For National Authority Use Only) COMMENTS**
Analytical chemical profile: Volume Page(s)		
Detection of known toxic constituents/adulterants: Volume Page(s)		
Summary of Analytical Development and Validation Studies: Volume Page(s)		

Pharmaceutical Expert Report

Format 2B112A/HERBAL

Name of Company : **Name of Finished Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S) : (IMPURITIES) HERBAL DRUG/HERBAL DRUG PREPARATION - SCIENTIFIC DATA	
Potential impurities originating from cultivation harvesting/collection, storage: Page(s) :	**Test procedures and their limits of detection or limits of quantitation :**
Microbial contamination:	Pharmacopoeia[1].....☐
Pesticide residues:	Pharmacopoeia[1].....☐
Heavy metals/other toxic elements:	Pharmacopoeia[1].....☐
Mycotoxins:	Pharmacopoeia[1].....☐
Fumigation agents:	
Radioactivity:	
Potential impurities arising during the production and purification : Page(s) :	**Test procedures and their limits of detection or limits of quantitation :**
Residual solvents:	Pharmacopoeia[1].....☐
Other substance(s):	
Potential impurities/contaminants in herbal drug preparations :	**Test procedures and their limits of detection or limits of quantitation :**
Microbiological quality :	Pharmacopoeia[1].....☐
Other Substance(s) :	
Potential substitution and adulterants:	**Test procedures and their limits of detection or limits of quantitation :**

COMMENTS : (For National Authorities Use Only)

[1] Reference to the Pharmacopoeia used should be given; see CD 75/318 Annex Part 2 C.1.1

Pharmaceutical Expert Report

Format 2B113Ai/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S) : (BATCH ANALYSIS) - HERBAL DRUG PREPARATION[1]		
Batches tested :	**Volume Page(s)**	**(For National Authority Use Only) COMMENTS**
Date(s) of manufacture : Place(s) of manufacture : Batch size : Batch (Lot) number : Use of batches (incl.: preclinical & clinical testing) :		
Results of tests :	**Volume Page(s)**	
Batch Nos :		
Characteristics : Identification tests : Purity tests : Potential contaminants : Other tests : Assay(s) / potency :		
Reference standard (analytical results) :	**Volume Page(s)**	
Origin/supplier Characteristics : Identification tests : Purity tests : Potential contaminants : Other tests : Assay(s) / potency :		

[1] The batch analysis of the herbal drug has to be presented (see Format 2B113Aii)

Pharmaceutical Expert Report

Format 2B113Aii/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II C : CONTROL OF STARTING MATERIALS - ACTIVE SUBSTANCE(S): (BATCH ANALYSIS) - HERBAL DRUG			
Batches tested :		**Volume Page(s)**	**(For National Authority Use Only) COMMENTS**
Date(s) of manufacture : Place(s) of manufacture : Batch size : Batch (Lot) number : Use of batches (incl. : preclinical & clinical testing)			
Results of tests :		**Volume Page(s)**	
Batch Nos :			
Characteristics : Identification tests : Purity tests : Potential contaminants : Other tests : Assay(s) / potency :			
Reference standard (analytical results) :		**Volume Page(s)**	
Origin/supplier : Characteristics : Identification tests : Purity tests : Potential contaminants : Other tests : Assay(s) / potency :			

Pharmaceutical Expert Report

Format 2B114A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II C : CONTROL OF STARTING MATERIALS - EXCIPIENT(S) : SPECIFICATIONS AND ROUTINE TESTS		
1. Excipient(s) described in a pharmacopoeia[1]: **Volume Page(s)**		**(For National Authority Use Only) COMMENTS**
2. Excipient(s) not described in a pharmacopoeia : **Volume Page(s)**		
Characteristics : Identification tests : Purity tests : - Physical - Chemical - Biological / Immunological Other tests : Assay(s) and/or evaluations:		

[1] Reference to the Pharmacopoeia used should be given; see CD 75/318 Annex Part 2 C.1.1

Pharmaceutical Expert Report

Format 2B115A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II C : CONTROL OF STARTING MATERIALS - EXCIPIENT(S) : SCIENTIFIC DATA		
Summary of studies : Volume Page(s)		**(For National Authority Use Only) COMMENTS**

Pharmaceutical Expert Report

Format 2B116A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II C : CONTROL OF STARTING MATERIALS - PACKAGING MATERIAL (IMMEDIATE PACKAGING)		
Specifications and routine tests : Volume Page(s)		**(For National Authority Use Only) COMMENTS**
Type of material : Construction : Quality specifications (routine tests and summary of control methods) :		
Scientific data : Volume Page(s)		
Summary of development studies on packaging materials : Batch analysis (analytical results) :		

Pharmaceutical Expert Report

Format 2B117A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II D : CONTROL TESTS ON INTERMEDIATE PRODUCTS **Volume Page(s)**		**(For National Authority Use Only) COMMENTS**
PART II E : CONTROL TESTS ON THE FINISHED PRODUCT : **Volume Page(s)**		
Product specifications and tests for release at time of manufacture :		
General product characteristics : Identification tests : Quantitative determination of herbal drug/herbal drug preparations : - in case of constituents with known therapeutic activity - in case of markers Or other justified determination : Purity tests : Pharmaceutical tests :		
Identification and determination of excipient(s) : Volume Page(s)		
Approved colouring materials : Determination of preservative agents (e.g. antimicrobial or chemical preservatives) : Other additives :		

Pharmaceutical Expert Report

Format 2B118A/HERBAL

<table>
<tr><td>Name of Company :

Name of Finished Herbal Medicinal Product :

Name of Active substance(s) :</td><td>Tabular format Referring to Part of the Dossier</td><td>(For National Authority Use only)</td></tr>
<tr><td colspan="3">PART II E : CONTROL TESTS ON THE FINISHED PRODUCT - SCIENTIFIC DATA</td></tr>
<tr><td colspan="2">Summary of analytical development and validation studies :
Volume Page(s)</td><td>(For National Authority Use Only) COMMENTS</td></tr>
<tr><td colspan="2"></td><td rowspan="8"></td></tr>
<tr><td colspan="2">Batch Analysis: Volume Page(s)</td></tr>
<tr><td colspan="2">Batches tested :
Batch (Lot) number :
Date(s) of manufacture :
Place(s) of manufacture :
Batch size :
Use of batches :</td></tr>
<tr><td colspan="2">Results of Batch Analysis : Volume Page(s)</td></tr>
<tr><td>Batch Nos :</td><td rowspan="2"></td></tr>
<tr><td>Tests :</td></tr>
<tr><td colspan="2">Reference standard : Volume Page(s)</td></tr>
<tr><td colspan="2"></td></tr>
</table>

Pharmaceutical Expert Report

Format 2B119A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II F : STABILITY - STABILITY TESTS ON ACTIVE SUBSTANCE(S)
Batches tested : **Volume** **Page(s)**
Batch Nos :
General test methodology : **Volume** **Page(s)**
Accelerated test conditions (temperature ° C, % RH, light) : Normal test conditions (temperature ° C, % RH, light) :
Analytical test procedures : **Volume** **Page(s)**
Assay techniques : Determination of degradation products/chromatographic profile :
Validation of all test procedures including limits of detection (including initial results): **Volume** **Page(s)**
Results of tests : **Volume** **Page(s)**
Proposed storage conditions and Duration of Storage to be permitted before re-testing : **Volume** **Page(s)**
COMMENTS (For National Authorities Use Only)

Pharmaceutical Expert Report

Format 2B120A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**

PART II F : STABILITY - STABILITY TESTS ON THE FINISHED PRODUCT

Batches tested and packaging used :	**Volume**	**Page(s)**
Stability study methods :	**Volume**	**Page(s)**
Real time studies (temperature °C, % RH, light) : Studies under other conditions :		
Characteristics studied :	**Volume**	**Page(s)**
Physical characteristics : Microbiological characteristics : Chemical characteristics : Chromatographic characteristics : Packaging characteristics :		
Evaluation methods and validation :	**Volume**	**Page(s)**
Results of tests :	**Volume**	**Page(s)**
Interpretation of results :	**Volume**	**Page(s)**
Proposed shelf-life and storage conditions (incl. after reconstitution or after first opening if appropriate) :	**Volume**	**Page(s)**
Ongoing stability studies :	**Volume**	**Page(s)**
COMMENTS : (For National Authorities Use Only)		

Pharmaceutical Expert Report

Format 2B121A/HERBAL

Name of Company : **Name of Finished Herbal Medicinal Product :** **Name of Active substance(s) :**	**Tabular format Referring to Part of the Dossier**	**(For National Authority Use only)**
PART II G : BIOAVAILABILITY/BIOEQUIVALENCE Volume Page(s)		
Give reference to relevant sections in Part IV.		
PART II Q : OTHER INFORMATION		
Summary of analytical test procedures used in metabolism and bioavailability studies, and validation studies : Volume Page(s)		
Summary of synthesis of radiolabelled active substance(s) used in metabolic and/or pharmacokinetic studies : Volume Page(s)		
COMMENTS (For National Authority Use Only)		