EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal products (HMPC)

Concept paper on the development of a Reflection Paper on new analytical methods/technologies in the quality control of herbal medicinal products[2]

Agreed by HMPC Quality Drafting Group	April 2017
Adopted by HMPC for release for consultation	19 September 2017
Start of public consultation	31 October 2017
End of consultation (deadline for comments)	30 November 2018

Comments should be provided using this template. The completed comments form should be sent to hmpc.secretariat@ema.europa.eu

Keywords	Herbal Medicinal Product, quality control, DNA-based technologies, NMR, UV/MIR/NIR spectroscopy, chemometric methods, biosensors

[1] Extension of deadline for comments from 30 April 2018 to 30 November 2018
[2] Includes Traditional Herbal Medicinal Products as well as herbal substances/herbal preparations and combinations thereof.

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1. Introduction

Quality control is a prerequisite to assure safe and effective use of (traditional) herbal medicinal products, which are complex mixtures of numerous phytochemical constituents. For the majority of herbal substances, herbal preparations and (traditional) herbal medicinal products the active constituents are not known or are only partly understood. Requirements on quality control are based on Directive 2001/82/EC and Directive 2001/83/EC and specified in detail in Annex I (Directive 2003/63/EC) and relevant guidelines published by EMA (see references). Binding quality standards are also described in the relevant monographs of the European Pharmacopeia.

There is an established set of methods (such as HPLC, TLC, GC, etc.) which is currently used in quality control of (traditional) herbal medicinal products (HMPs). In total, the system established cannot exactly measure all features or constituents in parallel, but is an appropriate and generally applied convention. When considering introduction of new methodology, this will usually be complementary to the existing methodology. Although some new techniques offer the option to create a type of “holistic” fingerprint, it is necessary to consider if such approaches offer added value in terms of quality control.

2. Problem statement

A range of new analytical methods/technologies, as set out below, are being developed and applied which may have an impact on the quality control of herbal substances, herbal preparations and (traditional) herbal medicinal products.

To date, these new analytical technologies have not been used widely in development or quality documentation in applications for marketing authorisations. Such methods are sometimes used to complement the findings which are generated using established methods. It is known that some applicants are using new analytical methods to collect information in addition to the official batch records for applications and GMP documentation. However, the place of such new analytical methods/technologies needs to be considered for its potential value in the overall quality control system when applied to HMPs. The new analytical methods/technologies include:

- DNA-based technologies (e.g. DNA-fingerprinting and DNA-sequencing)
- Nuclear magnetic resonance spectroscopy (NMR)
- Ultraviolet (UV), mid-infra-red (MIR) and near infra-red (NIR) spectroscopy combined with computational analysis
- Hyphenated techniques (HPLC-MS, LC-NMR, etc.)
- Chemometric approaches (including Multivariate analysis (MVA) and Principal component analysis (PCA)
- Biosensors

3. Discussion (on the problem statement)

It is considered of primary importance that interested parties provide examples and comments covering the range of new analytical methods/technologies they apply to herbal substances, herbal preparations and HMPs in their current manufacturing practice. Examples used for qualitative and quantitative evaluation of herbal ingredients and potential contaminants are of particular interest. This will provide a platform for discussion for use in the development of a reflection paper on this subject. The key issue is to discuss the opportunities and challenges in the application of these new analytical

methods to HMPs and the expectations when they are included in the marketing authorisation/registration dossier.

4. Recommendation

In view of scientific/technological developments and emerging trends the aim is to raise the topic with interested parties and seek their cooperation in providing examples and comments of methods/technologies used in quality control of herbal substances/preparations. Based on the information provided by interested parties, the Quality Drafting Group of the HMPC will develop first a reflection paper to stimulate and further foster the discussion and dialogue on the subject. Thereafter, more specific guidance can be developed, where appropriate.

5. Proposed timetable

It is anticipated that the drafting of the reflection paper will start after the public consultation of the concept paper and take approximately 9-12 months before release for consulation.

6. Resource requirements for preparation

Several co-rapporteurs will be involved in drafting of the reflection paper. The draft is expected to be discussed at future meetings of the HMPC Quality Drafting Group. External experts may be involved, if necessary.

7. Impact assessment (anticipated)

The reflection paper should support industry in the development and application of new analytical methods.

Some guidelines may later need to be amended or updated as a result of the reflection paper. The considerations may also contribute to the discussion on appropriate concepts for quality control of HMP's in close coordination with Ph. Eur. expert groups.

8. Interested parties

The interested parties include regulators, pharmaceutical industry, academic groups, and Pharmacopoeia expert groups.

9. References to literature, guidelines, etc.

Guideline on quality of herbal medicinal products/traditional herbal medicinal products (EMA/CPMP/QWP/2819/00, EMA/CVMP/814/00, EMA/HMPC/201116/2005)

Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products (EMA/CPMP/QWP/2820/00, EMA/CVMP/815/00, EMA/HMPC/162241/2005)

Guideline on Quality of Combination Herbal Medicinal Products/ Traditional Herbal Medicinal Products (EMEA/HMPC/214869/2006)

Reflection Paper on Markers used for Quantitative and Qualitative Analysis of Herbal Medicinal Products and Traditional Herbal Medicinal Products (EMEA/HMPC/253629/2007)

European Pharmacopoeia General Chapter 2 “Methods of analysis”

European Pharmacopoeia monograph 5.21. “Chemometric methods applied to analytical data”