European Medicines Agency
Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CHMP/CVMP)

CONCEPT PAPER ON REVISION OF THE NOTE FOR GUIDANCE ON THE USE OF NEAR INFRARED SPECTROSCOPY BY THE PHARMACEUTICAL INDUSTRY AND THE DATA REQUIREMENTS FOR NEW SUBMISSIONS AND VARIATIONS

AGREED BY QUALITY WORKING PARY	May 2006
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	1 June 2006
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	22 June 2006
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 September 2006

The revised Guideline will replace the Note for Guidance on the use of near infrared spectroscopy by the pharmaceutical industry and the data requirements for new submissions and variations CPMP/QWP/3309/01 and EMEA/CVMP/961/01.

Comments should be provided to qwp@emea.eu.int

KEYWORDS	NIR, NIRS, PAT, Near Infra Red,

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1. INTRODUCTION

This concept paper addresses the need to update the CPMP/CVMP 'Note for Guidance on the use of Near infrared spectroscopy by the pharmaceutical industry and the data requirements for new submissions and variations' (1). The update is necessary in the light of recent developments in this area, regulatory experience and feedback from pharmaceutical industry (2,3,4).

2. PROBLEM STATEMENT

Since the publication of the current Guideline, more experience has been gained with NIRs. This additional knowledge together with the coming into force of Q8 and ongoing discussions on PAT, make it opportune to revise this Guideline.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

The current Guideline was developed in 2001-2002 and came into force in August 2003. At that time Near Infrared was a known and commonly used method in the food, chemical, agrochemical and petrochemical industry and some of the larger innovative pharmaceutical companies used the method for additional quality control. Near Infrared was still a relatively unknown method to the other pharmaceutical companies and assessors. Until 2000, no applications for the use of Near Infrared were received by EU regulatory competent authorities.

The current Guideline was developed such that it provided detailed guidance to industry and assessors. It was the opinion of the Quality Working Party that such detailed guidance was necessary to reduce the risk of misuse of the method by inexperienced pharmaceutical companies and also of inappropriate assessments. In view of the wording of the text (highly preferred etc) and the fact that deviations from every Guideline are acceptable if justified, the Quality Working Party meant that the detailed information would not block other approaches to Near Infrared.

Since 2001 the application of Near Infrared by the pharmaceutical industry has matured and the method is no longer unknown to assessors. The technical abilities and transferability of the method has significantly improved and competent authorities have gained experience with the assessment of the method. Moreover the description of the general method for Near Infrared spectroscopy in the European Pharmacopoeia became more detailed. The need for detailed guidance does therefore no longer exist.

4. RECOMMENDATION

Based on the above mentioned discussion, it is recommended to revise the current Guideline

The revised Guideline should take account of technical progress and novel equipment abilities. It should clarify to industry which data shall be considered part of GMP and which data need to be submitted to the regulatory competent authorities for variations and new submissions. The revised Guideline should be less prescriptive. The requirements should however enable regulators and inspectors to distinguish the good from the less or even insufficiently developed and validated methods.

A drafting group consisting of 4-6 experts will be established. The Rapporteur will be appointed by the QWP. Experts will be nominated by QWP and the ad-hoc GMP inspectors group. 1 drafting group meeting is planned for 2006 and a further one for 2007, if considered necessary. Other discussions will be held in written or by teleconference.

Where specific questions during development arise, those could be discussed with external experts.

5. TIMETABLE

- Meeting of Drafting Group and discussion in QWP QIII-IV 2006.
- Release for consultation QI 2007
- Discussion of received comments in Drafting Group Q IV 2007
- Discussion in QWP QI 2008.
- If necessary meeting with interested parties Q II 2008
- Rediscussion in QWP Q III 2008
- Expected date of publication of final guideline Q IV 2008, coming into effect Q II 2009.

6. RESOURCE REQUIREMENTS FOR PREPARATION

The EMEA will provide secretarial support. It will also enable the drafting group to have discussions per mail and telephone. Subject to resource considerations, the drafting group will meet two times at the EMEA. Where possible, the meetings will take place just before or after the meeting of either the Quality Working Party or the GMP inspector's ad-hoc meeting.

7. IMPACT ASSESSMENT (ANTICIPATED)

The revised Guideline will have impact on

- *Public and Animal health*

The use of Near Infrared, especially as a tool for Process Analytical Technologies will enable the European pharmaceutical industry to implement the 6 sigma approach. The key characteristic of this approach is an increased knowledge of the manufacture of a product, leading to process optimization and fewer costs. The approach has advantages for human and animal patients, as it increases the guarantees for the sufficient and consistent quality of the medicinal product, whereas it reduces the risk that the product will become (temporarily) unavailable. The cost reduction for the pharmaceutical industry may also lead to lower prices.

- *Environment*

The use of Near Infrared as a tool for the quality control of medicinal products in the light of Good Manufacturing Practices and Regulatory compliance reduces the need for wet chemical testing. A lot of solvents and reagents used in wet chemical testing can be considered harmful. Consequently, increased application of Near Infrared by the pharmaceutical industry will contribute to a better environment.

- *Pharmaceutical industry*

The use of Near Infrared, especially as a tool for Process Analytical Technologies, will lead to a better return on investment in the end. This goal will be reached by several means, i.e. reduction of production costs, fewer out of specification results etc.

- *European Union*

The use of Near Infrared will lead to a better return on investment and fewer costs for the pharmaceutical industry. It is also expected to reduce the costs of regular medicines. This will have a positive impact on the European health status.

- *Regulatory competent authorities and Inspection Services*

The new Guideline will avoid conflicting policy with the European Pharmacopoeia. It will probably lead to increase applications of Near Infrared in routine Quality Control, as the current Guideline is felt too restrictive by pharmaceutical industry.

- *Official Medicines Control Laboratories*

Medicinal products may be released to the European market by quality control tests using Near Infrared. Retrospective quality control of such medicinal products by OMCLs using the same Near Infrared methodology is currently not possible and/or feasible. The current requirement that

pharmaceutical companies need to keep an alternative analytical method in place will therefore be maintained. This would suggest that Near Infrared doesn't have a positive impact on OMCLs. However, Near Infrared is recognized as an efficient and fast tool for Counterfeiting of medicinal products. The Guideline will guide OMCLs in such application of the method.

8. INTERESTED PARTIES

The following interested parties are regarded stakeholders in the revision process of the Guideline:

QWP interested parties, EDQM (Expert Working group on NIR), OMCLs. Where particularly controversial comments have been received during public consultation or where input of industry is considered otherwise beneficial, a meeting with Interested parties after public consultation will be considered.

9. REFERENCES TO LITERATURE, GUIDELINES ETC

1. CPMP/QWP/3309/01 and EMEA/CVMP/961/ 01 Note for Guidance on the use of Near infrared spectroscopy by the pharmaceutical industry and the data requirements for new submissions and variations, EMEA, London, 2003.

2. EMEA/CHMP/CVMP/QWP/186773/2005 Joint CHMP/CVMP Quality Working Party Work programme 2006, EMEA, London, 2005.

3. Letter EFPIA with request for update of the Guideline.

4. European Directorate for the Quality of Medicines, European Pharmacopoeia