



OMCL Network of the Council of Europe QUALITY ASSURANCE DOCUMENT

PA/PH/OMCL (05) 48 DEF CORR

SCOPE OF ACCREDITATION

Full document title and reference	Scope of Accreditation of Official Medicines Control Laboratories PA/PH/OMCL (05) 48 DEF CORR
Document type	Position paper
Legislative basis	The present document was also accepted by EA as recommendation document to be used in the context of Quality Management System audits of OMCLs
Date of first adoption	April 2001
Date of original entry into force	April 2001
Date of entry into force of revised document	December 2007
Previous titles/other references	This document replaces document PA/PH/OMCL (05) 48 DEF
Custodian Organisation	The present document was elaborated by the OMCL Network/EDQM of the Council of Europe
Concerned Network	GEON

Scope of Accreditation of Official Medicines Control Laboratories

Introduction

The Official Medicines Laboratories (OMCLs) act on behalf of the regulatory authorities to, independently from the manufacturers, re-test the quality of medicinal products on the national and European market. For the purpose of harmonisation and mutual recognition of national quality control tests, the European Directorate for the Quality of Medicines & HealthCare (EDQM) established the European OMCL Network in the mid-1990s.

The members of this Network decided to implement a quality system within their laboratories based on the standard EN 45001 as a common harmonised approach to build mutual confidence and foster recognition of their quality control tests.

In 1999 the OMCL Network started to implement a system of Mutual Joint Visits and Mutual Joint Audits (MJV/A) to help each other in implementing and maintaining a quality system based on EN 45001 with respect to the specific regulatory requirements for pharmaceuticals and the practical nature of the OMCL activities.

From 2003 the ISO/IEC 17025 supersedes the former standard and is the valid quality standard for calibrating and testing laboratories and includes the application of standard methods, as well as non-standard methods in combination with an adequate level of validation based on a clear validation concept of validation procedure. The OMCLs, which mainly have various activities, greatly welcome this.

The pharmaceutical field is highly regulated and the testing of medicinal products at the OMCLs must be regarded in view of this. Actors outside this field may not be aware that the confidential necessary information from the manufacturers of pharmaceutical products supplied to the authorities, including methods of analysis and validation of these methods, is available to the OMCLs and is the basis for their testing

This note gives an overview of the character of the different types of the OMCLs within Europe and their co-operation within the European Network of OMCLs. Already existing definitions of the scope of accreditation of OMCLs in different European countries and some difficulties in defining the scope are also given.

This note will explain the background of the OMCL testing and draw attention to the common point of view of the Network with respect to a definition of the scope of the different types of OMCL activities and the need for harmonisation and equal treatment in defining the scope of accreditation of OMCLs within the different countries.

Status of Official Medicines Control Laboratories (OMCLs)

Official Medicines Control Laboratories support the regulatory authorities and the national Inspection Services in controlling the quality of medicinal products on the market by independent re-testing.

This independent re-testing is based on legal requirements and includes:

- quality assessment of medicines prior to granting marketing authorisation
- official control authority batch release (for blood products and vaccines)
- post-marketing surveillance of authorised medicinal products

The area of activities also comprises analysis of medicinal products with complaints (quality and therapeutic aspects) and of illegal medicinal products.

OMCLs also perform testing activities on behalf of other governmental authorities (police, public prosecutor etc.) when medicinal products are concerned.

The products to be tested are very different in their nature (chemical-pharmaceutical, biological, biotechnological, radiopharmaceutical and different dosage forms). In relation to this, the test methods applied by OMCLs often vary as will be explained hereafter.

The character of this work requires great flexibility in order to fulfil the testing demands given by the client authorities in a timely manner.

European Network of Official Medicines Control Laboratories

In the mid-1990s a European OMCL Network was formed under the aegis of the Council of Europe in Strasbourg, France. This Network is co-ordinated by the European Directorate for the Quality of Medicines & HealthCare (EDQM) of the Council of Europe. This Network not only integrates the countries of the EU, the EEA and Switzerland, but also most of the Central and Eastern European Countries. Approximately 80 OMCLs are now involved.

The aims of the Network are:

- to facilitate the exchange of knowledge and expertise
- to co-ordinate the administrative and technical activities of common interest
- to harmonise the testing activities by use of common standards, based on legal requirements
- to organise post-marketing surveillance studies of centrally authorised products (with a centrally licensed European marketing authorisation)
- to allow mutual recognition of Control Authority batch release for blood products and vaccines in the EU and the EEA

- to coordinate different other testing activities aimed at market surveillance
- to ensure quality and comparability of the results within the Network by implementing a harmonised quality system based on ISO/IEC 17025 in the OMCLs and organising Proficiency Testing Studies on basic routine methods of analysis.
- to promote development and validation of new test methods and definition of new quality requirements.
- to perform Mutual Joint Audits

EDQM co-ordinates these MJAs, which are carried out according to a standardised procedure by auditors recruited from the OMCL Network, who are trained in the system and are familiar with the regulatory character of the activities of the OMCLs. The MJAs are carried out upon request of an OMCL on a voluntary basis.

Character of the OMCL activities

OMCL-activities can be divided into two types:

Type A: Batch release testing. The field of testing concerns Control Authority batch release testing of vaccines and blood products. These activities have a regulatory basis and a routine character. The scope is fixed: one product relates to one specific method. The relatively limited number of methods (compared to type B) in this field are used with a relatively high frequency.

Type B: All other (non-batch release) activities. The field of testing, in general, concerns chemical and biological testing of pharmaceutical and medicinal products. These activities have a regulatory basis as well, but a non-routine (flexible) character. A large number of products with a broad spectrum of methods (standard and non-standard) has to be covered on demand of the authorities. Sometimes these methods and techniques are applied with a relatively low frequency.

This means:

- the testing fields include: post market surveillance, product complaints, illegal products.
- the products and materials to be tested can vary from one single product (a pharmaceutical substance or a final product) to groups of products (e.g. dosage forms; therapeutic group).
- the methods used are pharmacopoeial (compendial) or licensed for marketing authorisation (MA). These methods have a legal character (pharmacopoeia) or are assessed (e.g. with respect to validation) and officially accepted by the regulatory authorities. When an OMCL applies these methods, which have been validated elsewhere, the '*validation of transfer*' criteria have to be met to guarantee proper performance conditions in the OMCL and to meet the requirements for producing results, which will be comparable.

- in-house methods can be used: e.g. modifications of pharmacopoeial methods or fully self-developed methods. These methods have to be validated partly (modifications) or fully by the OMCL. The level of validation depends on the modification and on the intended purpose of the method.

Analytical method validation with respect to the different types of OMCL-activities and 'validation of transfer' are described in more detail in the OMCL-guideline: 'Validation of analytical procedures', adopted by the European OMCL Network, in December 1999, and included in the current version of the Quality Assurance booklet.

OMCLs with 'type B'-activities form the great majority. OMCLs with 'type A'-activities in most cases can also have activities with a 'type B'-character (e.g. development of new methods, modifications and improvements of existing methods).

The 'type A' activities have a fixed character: in general one product relates to one method.

On the contrary the 'type B' OMCL-activities generally can be characterised as flexible with respect to the material tested, the test technique applied and the method used. The 'type B' activities can be presented schematically by:

product or group of products
related to
test method or technique
referring to
pharmacopoeial (standardised) -
and/or MA-licensed -
and/or in-house methods

Survey of existing scopes of accreditation of OMCLs

An OMCL can choose formal accreditation by a national accreditation body:

- because of internal quality policy requirements of the OMCL
- if required by their sponsors/authorities (Control Authorities, Inspectorates)
- if the flexible nature of their activities can be brought under a definition of scope which is accepted by the accreditation body and by the OMCL

Some OMCLs report that it is difficult to achieve a common understanding between the accreditation body and the laboratory about the flexible nature of the 'type B' OMCL activities. The regulatory character of the work seems to be not fully understood and seems not to be equally approached by the accreditation bodies in the different countries. This leads for some OMCLs to discussions about the definition of the scope (flexible/non-flexible, method or technique related, MA-methods included or not). However, in most cases comparable solutions were found.

When comparing the definitions of the already existing scopes of accreditation of the OMCLs in the different countries the following is observed:

- although there is a less harmonised approach in format and layout of the listed information the scope, the **contents of the scope** with respect to the testing field (pharmaceutical-chemical or control authority batch release) are comparable for parameters such as: products, test(method)/technique and reference method. Only in two reported cases additional information about the performance characteristics (e.g. measurement uncertainty; range of application, and LOD) of the tests is listed.
- in almost all cases pharmacopoeial and in-house methods are referred to (directly or indirectly) as the methods used. Methods from MA-dossiers are included in most cases.
- for the 'type A' activities (batch release testing) the scope is defined as fixed: in general one product relates to one specific method.
- for the 'type B' activities the tests are defined as 'class of products and/or method and/or technique related' and allow flexibility for application within the measurement principles covered by the scope. The degree of flexibility is clearly defined in the quality manual.
- several OMCLs report that in case of a flexible scope, technical competence must be demonstrated and appropriate validation procedures must be in place.

The ISO/IEC 17025 standard and the scope of accreditation

As the standard ISO 17025 covers both standard and non-standard methods in relation to a required level of validation, it is expected that this give more room for a flexible definition of scope towards the standard for the non-routine type of activities of OMCLs.

Definition of the scope from the OMCLs-point of view

With respect to the testing field, a definition of scope of an OMCL performing 'type B' activities should have the following characteristics:

- flexible with respect to material to be tested (product or groups of products/materials)
- flexible with respect to applied test/technique (in accordance with the measurement principles covered by the scope). Performance characteristics and additional information: only where relevant and possible.
- based on the guidelines ILAC-G4 and EA-2/05 (see ANNEX) it is not always compulsory to give this performance information in the scope. Moreover it is not relevant or even impossible in case of activities with a flexible character, because of the general formulation of the scope parameters in those cases.
- reference to pharmacopoeial, MA-licensed methods (both used in relation with 'validation of transfer' criteria) and in-house methods (non-standardised, used in relation with an appropriate and well elaborated validation procedure).

A suggestion from the OMCLs' point of view for the contents of a suitable scope for OMCL-activities contains the following information as listed in the table below.

NB. This does not concern the format but only relates to the scope parameters.

All types of OMCL-activities						
Type(s) of activity/products/materials (1)		Measurement principle (1,2)				Test method
Field of application	products/material (single/category)	properties/analysis parameter	type of tests/techniques	uncertainties	other aspects	
Quality control/testing of human and veterinary medicinal products	Product/ Dosage forms	assay	Physical-chemical tests	(2)	(2) (range, LOD, LOQ, etc)	EP-monographs
	Active ingredients and excipients.	identification	Pharmaceut./technological tests			MA-dossiers/specifications
	Intermediate products and food additives	purity	Chemical tests/techniques: e.g. HPLC, AAS, GC, etc			Validated in-house-methods
		pharmaceut./technological aspects	Radioactivity tests			
		physical aspects				
Batch release activities (1,2,3)	Vaccines, blood products	strength, etc potency	Biological tests/ Biochemical techniques			

Remarks:

- The extent of detail in the description of the scope depends on the type of activity and the property to be measured and can vary from a clear one-to-one relation (product-property-method) in a fixed scope (type A) to a more general and flexible formulation of the scope parameters (type B).
- In case of a fixed scope, listing of performance characteristics (such as LOD and uncertainty of measurement) will be more relevant and easier to express precisely than in case of a flexible description of the scope. In the latter case the performance characteristics will vary from case to case and then these characteristics better can be described in detail in clearly related underlying quality documents (SOPs) and requirements.
- When an OMCL with batch release activities (fixed scope, type A) wants to imply
 - market surveillance studies or
 - development of new methods or
 - modification (improvement) of existing methods,
 flexibility of the scope is also needed in addition.

Conclusions

In relation to the application of the ISO/IEC 17025 standard a more harmonised approach and equal treatment of the OMCLs in the 'European OMCL Network' countries with respect to the flexible OMCL-type of activities in the accreditation process is required. This will support the process of mutual recognition and mutual acceptance of results of OMCLs.

ANNEX

Reference documents for interpreting and defining the scope of accreditation

Two official guidelines on the scope of accreditation give the following information.

Nr. 1: 'Guidelines on scope of accreditation', ILAC-G4: 1994.

Point 3 of this document states: *"It is recommended that the scope contains the following elements: general field of testing, identification of test items, identification of tests, identification of methods/techniques.*

Accreditation bodies MIGHT, but must not, also include additional information like LOD, etc"

Appendix A of the guideline gives an example without uncertainty.

Point 4 of this document states (in addition to elements of point 3): *"It is recommended only for CALIBRATION LABORATORIES that the scope contains identification of the best measurement capability (expressed as uncertainty)".*

Nr. 2: 'The scope of accreditation and consideration of methods and criteria for the assessment of the scope in testing', EA-2/05 (formerly EAL-P10), edition 2, August 2001.

Point 1.3 of this document states: *"The scope of a testing laboratory is the formal and precise statement of the activities. It is a combination of information defined under 2.1".*

POINT 2.1 STATES ON SCOPE PARAMETERS:

1. *The testing field must be clearly defined*
2. *The tests must be identified in terms of quantities/properties to be measured, range of measurement, associated uncertainties (where applicable), product standards (where applicable).*
3. *The test methods, in-house methods and standardised methods.*

Point 2.2 states (about interpretation): *"Depending on the type of laboratory activity, more emphasis can be given to one or more of the scope parameters above. This will have an impact on the way the scope will be presented and assessed".*

Comments

Due to the definition and the interpretation guidelines, the OMCLs are flexible to give emphasis to the most of these points. With respect to the flexible character of the 'type B' OMCL-activities, in our opinion it is not necessary and even impossible to give precise information in the scope on the measurement uncertainty and other method or instrument parameters because of the general formulations in a flexible scope. Many of these parameters are part of the equipment specifications and shall be fixed in SOPs and checked with system suitability tests of results of OMCLs.