European Directorate for the Quality of Medicines & HealthCare

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

OMCL Network of the Council of Europe
GENERAL DOCUMENT

PA/PH/OMCL (06) 116 11R

Co-operation in Post-Marketing Surveillance of MRP/DCP-Products

Full document title and reference	Co-operation in Post-marketing Surveillance of Mutual Recognition / Decentralised Procedure Products, PA/PH/OMCL (06) 116 11R
Document type	Procedure
Legislative basis	Council Directive 2001/83/EC and 2001/82/EC, as amended
Date of first adoption	May 2006
Date of original entry into force	May 2006
Date of entry into force of revised document	September 2012
Previous titles/other references	This document replaces document PA/PH/OMCL (06) 116 9R
Custodian Organisation	The present document was elaborated by the OMCL Network / EDQM of the Council of Europe
Concerned Network	EU/EEA

CO-OPERATION IN POST-MARKETING SURVEILLANCE OF MUTUAL RECOGNITION/DECENTRALISED PROCEDURE PRODUCTS

Introduction

Within the EU/EEA OMCL Network, a voluntary post-marketing surveillance scheme has been set up for medicinal products having received a marketing authorisation via the Mutual Recognition Procedure (MRP) or the Decentralised Procedure (DCP).

The marketing authorisations for the *MRP/DCP-products*[1] are granted separately by the Member States. After these products have been placed on the national market, the responsibility for the supervision of their quality rests with the individual Member States. However, in all Member States, the marketing authorisation applications for these products are based on an identical dossier, including identical specifications. This gives room for co-operation and creation of a surveillance scheme at the EU/EEA level in the field of independent official control of *MRP/DCP-products*.

The main purpose of this voluntary post-marketing surveillance scheme is to improve the surveillance of the *MRP/DCP-products* placed on the EU/EEA market through two principles:

1. Work-sharing with the aim of optimal and cost-effective use of analytical resources which is achieved:

- by reducing duplication of testing of *MRP/DCP-products* by several *participants*
- by offering testing of *MRP/DCP-products* to other *participants* and testing several batches in the same analytical run

2. Sharing of the test results, offering the individual Member States and other concerned bodies (e.g. Heads of Medicines Agencies, EMA):

- a broader and in-depth overview of the quality of *MRP/DCP-products* on the EU/EEA-market (surveillance at the EU/EEA level)
- the opportunity to focus the national surveillance activities by taking advantage of the results of testing work done in other OMCLs.

The reliability of testing results is a pre-condition for a fruitful sharing of work and results. The reliability of testing results can be better assured for *testing laboratories* with quality management systems fulfilling the requirements of ISO/IEC 17025 and having successfully undergone assessment by peers within the OMCL Network or by an internationally recognised body.

A risk based model for targeting medicinal products for market surveillance testing has been developed within the network. In 2007 *MRP-products* were the first product group selected for the evaluation of the model in a trial phase. This model is available to all members of the network beyond the MRP/DCP post-marketing surveillance group. Implementation of a risk-based approach is encouraged for the establishment of *testing plans*.

[1] Definitions of the terms *in italic* are given in the Glossary at the end of this document.

Scope

This document is a reference document describing the principles of the *MRP/DCP-product* surveillance scheme applied, in particular for

- elaboration of *Periodic Surveillance Work Programmes (PSWP)*
- sampling and testing
- reporting and sharing results
- follow-up activities

Working Principle

The Member States/OMCLs participating in the *MRP/DCP-product* surveillance scheme define their *testing plans* by entering them as proposed *projects* into the *MRP/DCP-product testing database*. If testing *overlaps* are identified, the OMCLs concerned discuss the matter bilaterally to consider whether the testing could be done by one *testing laboratory* only or if work could be shared, respectively. For *repetitions* it is verified by the OMCL if repeated testing is justifiable. The testing plans from all participants together form the MRP/DCP *periodic surveillance work programme*. Based on the *projects* in this plan, all *participants* may consider sampling of products from their own market and, upon a case-specific agreement, have the products tested by the *testing laboratories*.

The outcome of the testing is reported to all *participants* through the *MRP/DCP-product testing database* and, on request, the full results sent to interested *participants*.

Elaboration of Periodic Surveillance Work Programmes

The *participants* set up their *testing plans* by means of the *MRP/DCP-product testing database*, listing the *MRP/DCP-products* they intend to test during the forthcoming *MRP/DCP-product surveillance period*. Upon a request from the *secretariat* (about 1-2 month before beginning of the *MRP/DCP- product surveillance period)*, they enter the *testing plans* directly into the database.

The *testing plans* can be queried at any moment on-line by OMCL database users with access rights. These plans are discussed between *participants* in order to avoid unnecessary *overlaps/repetitions* and to make other organisational arrangements. When a product is on the market of the Reference Member State (RMS) or a Member State where crucial steps of production take place, testing of that product in the OMCL of one of these would facilitate follow-up activities related to the dossier or inspections, respectively. *Participants* will communicate the agreed adjustments of the *periodic surveillance work programme* to all *participants* by directly amending the relevant information in the database.

During the specified *MRP/DCP-product surveillance period* additional *projects* can be directly added while existing *projects* can be amended, cancelled or put on-hold.

Sampling and Testing

The OMCL identified as *testing laboratory* in the *periodic surveillance work programme* (or the Competent Authority of the Member State) samples the products from the national market and initiates the testing after the sampling deadline.

Before the sampling deadline, other *participants* (OMCLs or their respective Competent Authorities for sampling), interested in sending samples for testing, send a request to the *testing laboratory*. For each product the *testing laboratory* and the other *participants* will bilaterally agree on the testing. They also agree on the sample size, testing parameters, schedule for testing etc., unless this has already been fixed in advance (e.g. in the database, or in separate notifications sent out to the *participants*).

Sampling in more than one Member State is encouraged, because then the surveillance scheme will give a better view of the quality of the specific products on the EU/EEA market (improved EU/EEA level surveillance) and several *participants* can have samples taken from their own market analysed (improved national level surveillance). Furthermore, sending a sample for testing to the *testing laboratory* offers a possibility of controlling an *MRP/DCP-product* taken from the national market of an OMCL that might not have all the techniques needed for testing it. Because the sample exchange is multilateral and the *testing laboratory* receives no economic compensation for the work of analysing extra samples, it is essential for a fair co-operation that each laboratory takes care that a good balance is maintained between samples sent out and samples received for testing. Also, because no economic compensation for the testing takes place, the exchange of samples between the *testing laboratories* should not necessarily (or primarily) be considered as commercial sub-contracting.

OMCLs test the products based on approved MAH methods ("According to MAH dossier") or on other methods validated in line with OMCL Network QA principles ("Survey mode", pharmacopoeial method etc.).

Reporting and Follow-up

At the end of the control, a full test report is sent to the sample providers. This report can be a national test report, normally prepared for tested samples by the OMCL. As soon as possible after completion of the control the testing OMCL inserts results for all samples, their own and samples sent by other participants, in the MRP/DCP *product testing database* under the respective project. Several batches from different countries can be included in one project. However, the final evaluation of result is made by the sample provider.

Issues identified during testing are summarised by the *testing laboratories* in the *MRP/DCP product testing database* under item "follow-ups". The follow-up actions and decisions are completed by the sampling and/or testing OMCL. Follow-up actions can be added separately from the insertion of results after completion of the control and up-dated continuously.

In general follow-up activities lie within the responsibility of the national authorities. Thus the Competent Authority of the Member State where the product was sampled will be responsible for any follow-up activities. The *participants* are encouraged to inform each other where appropriate of such activities. In cases when an issue concerns samples from several countries, the follow-up activities should be adjusted between the National Competent Authorities (NCAs) of the involved member states.

In case of issues concerning the content of the marketing authorisation dossier (*e.g.* unclear test procedure, mistake in the mathematical formula etc.) the RMS of the medicinal product has to be informed. This could be done by using the contacts within the OMCL Network; the *testing laboratory* contacts the OMCL of the RMS that in turn informs the marketing authorisation authority about the issue. Alternatively, the representative of the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) of the member state where the *testing laboratory* is located or, where applicable, his/her veterinary colleague (CMDv), could be requested by the testing OMCL to discuss the issue with the Competent Authority of the RMS so that the RMS may follow-up on the issue with the Marketing Authorisation Holder company in order to

reach a resolution. If the sample was provided by another OMCL (a participating OMCL), that OMCL may choose to handle the communication of the issue through their CMDh or CMHv delegate. This should be agreed in advance with the testing OMCL.

If, as an outcome of a testing campaign, a pharmacopoeial issue is identified, the European Pharmacopoeia Department of EDQM (EPD) is contacted either by the Competent Authority or the *secretariat* for further action.

Participants are encouraged also to report their results for *MRP/DCP-products* not included in the *periodic surveillance work programme* (coming e.g. from ad-hoc testing). When necessary, *participants* interested are free to ask the *testing laboratory* for a detailed test report.

Meetings

The progress and development of the *MRP/DCP-product* surveillance scheme and the current *periodic surveillance work programme* is followed and discussed in one or more meetings per year. Meetings could typically be arranged as a special *MRP/DCP-product* surveillance session during the event of the annual OMCL meeting. Other meeting possibilities are teleconference or e.g. a breakout session during the CAP annual meeting.

MRP/DCP-product Testing Database

The *secretariat* is the coordinator of the *MRP/DCP-product testing database*, which contains *MRP/DCP-product* and test related information necessary to run the surveillance scheme. The product information is sourced from the common MRP/DCP database of the EU/EEA authorities, which is called *Communication and Tracking System (CTS)*.

EDQM initiates and the OMCLs maintain for their own organisation a list of the *MRP/DCP-product* surveillance contact persons, who act as *administrative*, sampling, testing contacts etc. and who at the same time are registered users (*OMCL administrator* or "conventional" user) of the *MRP/DCP-product testing database*; the complete list of OMCL users can directly be downloaded from the database.

Results of the testing according to the *periodic surveillance work programme*, are entered on an ongoing basis into the database by the *testing laboratory*. *Participants* have access to the data via a protected portal. In addition read-only access to the database is granted to quality assessors, inspectors and members of the pharmacovigilance units of NCAs of EU/EEA Member States upon request.

For the exchange of meeting documents or other general information there is for *participants* an Extranet site with controlled access in place called *MRPnet*.

Ownership of data and confidentiality

The NCA of the member state responsible for sourcing a sample is the owner of the data generated for this sample. This can either be the NCA of the testing OMCL / concerned member state for its own samples or of a participating OMCL / concerned member state for samples which were sent by this laboratory / member state to the testing laboratory.

The information generated in the programme should only be used in a shared responsibility for actions within the rules governing medicines; thus for regulatory purposes.

In the case of external use / publications, the owner(s) of the data need(s) to be contacted to obtain an agreement.

Glossary

***Administrative contact*:** Person within an OMCL, who serves as contact point for general information related to the *MRP/DCP-product* surveillance scheme.

Communication and tracking system (CTS): IT tool for licensing authorities for implementing and running the mutual recognition and decentralised procedure.

***MRPnet*:** Extranet site with restricted and controlled access (username and password required) used to exchange general information/documents amongst *participants*.

***MRP/DCP-products = Mutual Recognition Procedure or Decentralised Procedure Products*:** Medicinal products that have been authorised in more than one EU/EEA Member State using the procedures laid down in the articles 27ff of Directive 2001/83/EC as amended or article 31ff of Directive 2001/82/EC as amended.

***MRP/DCP-product surveillance period* or *testing period*:** The time between finalisation of subsequent *surveillance work programmes*. In terms of the *MRP/DCP-product testing database* it is the period (normally calendar year), which matches with the date when the corresponding official OMCL test report was signed by the responsible person. The year should also match that of the "date of release" entered in the database.

MRP/DCP-product testing database: A computer application that has been developed by the OMCL network and EDQM to serve as common data tool for running the *MRP/DCP-product* surveillance scheme.

OMCL administrator: Registered OMCL user of the *MRP/DCP-product testing database* with extended access rights allowing the inclusion of new OMCL users of the same organisation in the database and "de-freezing" of finalised projects created by the same OMCL.

Overlap: *Projects* in the responsibility of different OMCLs with identical MRP/DCP number allocated to the same *testing period*. Overlap testing does not automatically mean duplication of work. Overlaps might indicate work-sharing of test parameters between different OMCLs (chemical/pharmaceutical parameters vs. microbiological parameters) or might be caused by ad-hoc testing on national level due to an incident.

***Participant*:** OMCL participating in, contributing to or by other means being involved in the post marketing surveillance scheme of *MRP/DCP-products* described in this document. With respect to the *MRP/DCP-product testing database* the term participant comprises all registered OMCLs (active and passive participants). Active participants are OMCLs, which on a regular basis contribute or have contributed in the past or have indicated their intention to contribute in the near future to the testing scheme either as *testing laboratory* or as sample provider. The abbreviation used in this context is POMCL ("Participating OMCL"). Passive participants are OMCLs, which are registered in the *MRP/DCP-product testing database* upon request as potential future *participants* of the testing scheme but so far have not indicated their intention to contribute.

***Periodic surveillance work programme*:** Compilation of *testing plans* after possible duplication of work has been eliminated as far as possible.

Project: In context of the *MRP/DCP-product testing database* a project comprises all tests a single OMCL performs on a medicinal product with defined MRP/DCP number or on an active ingredient of an *MRP/DCP-product* with defined source.

Repetition: *Projects* with identical MRP/DCP number allocated to different *testing periods*. Subsequent testing is common practice in post-marketing surveillance schemes and might be the follow-up of observations made during the antedated testing campaign or the result of a risk-based product selection.

Secretariat**:** The secretariat of the Department Biological Standardisation, OMCL Network & HealthCare (DBO) at the EDQM.

Testing laboratory**:** OMCL that, according to the *periodic surveillance work programme*, will test an *MRP/DCP-product*. The abbreviation used in this context is TOMCL ("Testing OMCL").

Testing plan**:** OMCL plan for the surveillance of *MRP/DCP-products*.