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History, results, and benefits of testing MRP/DCP products

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History, results, and benefits of the post-marketing surveillance scheme for the testing of mutual recognition/decentralised procedure products

Introduction

The end of year 2000 saw the start of a new testing scheme for post-marketing surveillance (PMS) of Mutual Recognition Procedure (MRP) products. This scheme was initiated on a voluntary basis by members of the General European OMCL (Official Medicines Control Laboratory) Network (GEON) from EU/EEA Member States and the EDQM, the Network's secretariat. After a 4-year trial period, it was clear that the scheme was of great value in achieving a more co-ordinated surveillance approach for medicines within EU/EEA and a decision was made to continue with and further develop the scheme on a regular basis.

Value of the scheme

The value of this surveillance scheme is demonstrated by the number of OMCLs and Member States that have regularly participated in it year on year; since 2014 approximately 25-30 OMCLs from 20-25 Member States participate in the scheme every year. It has also been subjected to on-going development and improvement work. For example, following the implementation of a new community marketing authorisation procedure in October 2005, the Decentralised Procedure (DCP), the scope of the surveillance scheme was extended to include products authorised under that procedure. This added value to the surveillance scheme, given the fact that more and more medicinal products were authorised via the DCP route during the following years, with a corresponding reduction in the number of MRP applications that were being submitted.

This surveillance scheme is of value to competent authorities and OMCLs, because it is designed around the principles of work-sharing, which involves making best use of available laboratory resources and capacity across the OMCL Network, and on the sharing of test results. The scheme provides a practical approach for avoiding superfluous duplicate testing of the same product and/or the same product batches in different Member States. It has the added benefit of providing a ready-made tool that facilitates the sampling of medicinal products in several markets at the same time.

The scheme represents a coordinated and cost-effective approach to PMS activities. The cost-effectiveness of the scheme is emphasised by the better use of resources that are associated with the co-ordination of such surveillance activities for MRP and DCP products. When planning their testing programmes, OMCLs can check if the MRP/DCP product has recently already been tested by another OMCL. If it is the case and when results are satisfactory, the OMCL can decide to focus on other MRP/DCP products not recently tested.

IT support and data distribution

To further develop the scheme and to facilitate effective communication among participating OMCLs and concerned authorities, the EDQM has developed and installed an IT share point database to support the scheme. This is known as the MRP/DCP Product Testing Database. Launched in July 2007, it provides a work- and data-sharing approach that allows for the co-ordination of the planning, sampling and reporting activities with

respect to the surveillance of MRP and DCP products. The database also serves as a platform for information exchange on the follow-up actions that have been taken on the basis of the test results that were obtained on such products.

The development of the database for the MRP/DCP surveillance programme added additional value, in terms of data security and confidentiality. Access to the database is restricted to OMCLs actively involved in the scheme. Importantly however, read-only access to the surveillance data is granted to users of the Communication and Tracking System (CTS), as well as to staff members of drug regulatory departments and pharmacovigilance units in National Competent Authorities (NCAs), and also to GMP/GDP inspectors.

Statistical evaluation of the scheme

The following are some statistics on the scheme from 2002 to 2019 that show its extent of usage, as well as results and benefits:

By cut-off date 14/10/2019, a total of 12029 surveillance projects have been recorded in the MRP/DCP Product Testing Database, and each year the number grows typically with around 1000 new ones being added. A project is equivalent to the testing of one MRP or DCP product. It can represent the testing of more than one batch of a product, and this often occurs when samples are exchanged between OMCLs. More than one OMCL might be involved in the testing of one product or a product group, e.g. in case where test parameters are shared (physico-chemical and microbiological tests). Some project have to be cancelled sometimes when samples are not available in one country. This information can also be of used for other OMCL.

The number of new MRP projects is decreasing while the number of DCP projects is increasing, and this reflects well the number of products on the European market that have been authorised through these two procedures.

A vast majority of MRP/DCP products are chemical products for human use, and the MRP/DCP surveillance scheme reflects this. This is seen when one assesses the distribution of products that have been selected for testing: 9% veterinary vs. 91% human medicinal products, containing chemical active ingredients in 98.5% and biological active ingredients in 1.5% of cases.

Once product testing has been completed, the scheme allows for the speedy and wide availability of important market surveillance data to all members of the OMCL Network. This provides useful information to health authorities on the quality of medicinal products on their territories and across the EU.

For example, the scheme demonstrates the effectiveness of the present procedures for the granting of marketing authorisations, for the inspection of manufacturers and related laboratories, and the official laboratory control of products on the market. It shows that out-of-specification parameters in MRP/DCP products that were subjected to the surveillance programme are found in 2.3% of the products. This indicates a high level of quality is present in the medicines that are in use within the EU.

In addition, the scheme shows that it can facilitate continual improvements in the control of medicines across the EU. For example, this surveillance programme is capable of identifying issues that may need to be addressed in the authorised analytical methods that are used by the quality control laboratories of manufacturers. As it is not always possible

to identify such issues during assessment of the marketing authorisations, the MRP/DCP scheme adds value in this area. While such issues arise only in about 2.4% of cases, the scheme allows for them to be addressed and corrected by the concerned MAHs in a timely manner. This adds to the protection of public and animal health, because it assures that well evaluated and suitable test methods are in use when companies are testing the medicines that they produce.

It is important to note that the MRP/DCP surveillance scheme has demonstrated that the frequency of quality problems in such products, including generic products, is no larger than what is typical for other types of medicinal products on the market.

When the total numbers of tested products marketed in participating Member States are compared to the numbers of products tested between 2002 and 2019 in each participating Member State, it has been calculated that there is at an average a 9-fold gain for the EU/EEA countries. This means that an average participating Member State, by testing one product, benefits from the scheme by receiving the testing results for 9 marketed products. Considering individually the values of recent calendar years, this figure has meanwhile moved towards 11. In addition to the benefits realised nationally, the results of the scheme provide a significant amount of information on the quality of medicines within the EU/EEA.

Outlook

While a lot has been achieved to date in this surveillance scheme, there remain opportunities for improvement. For example, one of the main goals of this testing scheme is to facilitate the exchange and testing of samples in targeted campaigns by individual OMCLs on behalf of the Network. Sample exchange is very beneficial for the participating member states, because analysing a series of samples from other countries together with samples from one's own national market is both cost effective and work-reducing for all of the concerned OMCLs; but this feature of the scheme has been under-utilised to date. In recent years only about 5% of the products tested have originated outside the Member State of the testing OMCL, and so most samples have come from the market of the OMCL performing the testing.

There is merit in increasing efforts to promote more participation in the sample exchange aspect of this surveillance programme. In a well-balanced sample exchange system, there is the opportunity for OMCLs to send increasing numbers of samples to other OMCLs for analysis.

Another opportunity is to increase sharing of follow-up actions related to OMCL findings. The reporting of activities in particular taken by regulators or inspectors on basis of analytical results illustrates the immediate impact that OMCLs have on the quality of medicines in Europe.

In 2020, new information related to the risk of products as well as testing recommendations from quality assessors have become available via the MRP/DCP Product Testing Database which contribute to a risk-based selection of products for PMS testing and strengthen the dialogue in particular between assessors and OMCLs.

The testing scheme is described in more details in the document Co-operation in post-marketing surveillance of Mutual Recognition / Decentralised Procedure Products (PA/PH/OMCL (06) 116 in its current version and is available on the EDQM website under <http://www.edqm.eu/en/Postmarketing-surveillance-scheme-686.html>.

Note: This document represents a snapshot of the situation in October 2019. The figures given in the document are based on the statistics of that time and change from one year to another.