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Sampling and Testing of Centrally Authorised Products – Procedure for Ad Hoc API Programme

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SAMPLING AND TESTING OF CENTRALLY AUTHORISED PRODUCTS

PROCEDURE FOR AD HOC API PROGRAMME

Introduction

This paper describes the Ad Hoc API Programme operational procedure for post-authorisation sampling and testing of API linked to centrally authorised products (CAPs), on an ad hoc basis, upon request by a member state or EMA whenever samples are available from a manufacturing site where there is suspicion of GMP non-compliance. It should be read in conjunction with the General procedure PA/PH/CAP (05) 49 in its current version.

This procedure does not cover testing of APIs linked to CAPs initiated by national authorities without a CHMP or CVMP decision. Nevertheless, in this situation the national authority should inform EMA and EDQM that testing will be initiated, the reason for testing, the work to be carried out and the results. EMA may request the inclusion of additional samples or analyses.

Step 1: **Adoption of the Programme**

The list of APIs for which ad hoc testing is requested for one or several parameters are adopted by the EMA Scientific Committees (CHMP, CVMP).

EMA will inform EDQM once a decision for ad hoc API testing has been taken and request the product to be included in the current annual programme and initiate the testing with the necessary degree of urgency as defined in the request.

EMA informs simultaneously:

a) EDQM that an ad hoc API testing is needed specifying the product and parameter(s) to be tested and potentially proposal from the EMA Scientific committees for possible testing OMCL(s). Not more than 3 requests per year shall be made by EMA with respect to this ad hoc API testing programme.

b) The API Manufacturer and/or Marketing Authorisation Holders (MAHs) of related CAPs that an ad hoc testing will be performed on the API; the API Manufacturer and/or MAHs concerned will be requested to provide to the EDQM specific documentation. The API Manufacturer and/or MAH(s) concerned is/are informed that a request for samples of the API, reference materials and key reagents (where applicable) might be issued by the EDQM, and if so, will have to be provided with the necessary degree of urgency.

Step 2: **Sampling**

EDQM will coordinate the sampling of material with the support of the EMA.

The EMA informs the EDQM about the sampling strategy. Their GMP inspectors' network might be involved in collecting the samples. The EDQM might liaise with the API manufacturer or alternatively the MAH of the related CAP in order to obtain suitable reference materials, standards or any other key reagent(s) needed and (if appropriate) test samples. The API manufacturer / MAH must provide the materials within the specified timeframe, preferably directly to the testing OMCL.

The EDQM might provide technical assistance for the transfer of refrigerated samples.

Step 3: **Testing and Reporting**

EDQM prepares the testing protocol according to the recommendations received from the EMA and prepared by the Rapporteurs/Co-Rapporteurs and/or GMP Inspectors. The methods to be used for the testing can be Ph. Eur., MAH and/or in-house methods specifically developed.

As a standard rule, testing for a given API is performed by a single OMCL. If required, additional OMCLs can be involved. Potential testing OMCL(s) might be proposed by the EMA Scientific Committees. If not, the EDQM will contact (a) potential OMCL(s) based on previous experience, expertise and equipment available (the list is not exhaustive). The product testing agreement is prepared and the relevant parts of the dossier as well as any relevant information are provided to the selected OMCL. After the receipt of the documentation from EDQM, the OMCL checks whether or not it has the possibility to carry out the requested tests in the timeframe indicated and inform the EDQM as quickly as possible. The OMCL signs the product testing agreement and sends it back to EDQM.

The OMCL performs the tests and the testing results are provided to the EDQM in agreement with reporting principles for CAP APIs and within the time frame agreed between the testing OMCL(s), the EDQM and the EMA. EDQM will prepare the testing report (compilation of the OMCL testing results with all relevant information on sampling and management of the project) and provide it to EMA with the necessary degree of urgency. The testing report will be circulated to the relevant samplers, EMA and all OMCLs.

In case an out-of-specification result is detected, the procedure PA/PH/CAP (16) 103 in its current revision shall be followed.

Step 4: **Follow-up actions**

Any follow-up action is the responsibility of EMA in co-operation with the relevant Scientific Committees and with the Competent Authorities of the Member States.

In case of discussion at the European level further to the results of the controls, the EDQM and the OMCL(s) might be invited to provide further assistance.

Step 5: **Annual status report at Annual Meeting**

The EDQM reports about the Ad Hoc API Programme during the CAP Annual Meeting.

Last year of the co-operation agreement

Step 6: **Final report to EMA/OMCLs**

An overall CAP testing report covering the 5 year sampling and testing programmes performed on Centrally Authorised Products is set up by EDQM and distributed to the EMA and the OMCLs by 1st November in the last year of the co-operation agreement. The Rapporteur and Co-Rapporteur receive the document for information on the overall outcome of the testing exercise.