NATIONAL CENTRE FOR THE CONTROL
AND EVALUATION OF MEDICINES
(CNCF)

OFFICIAL CONTROL AUTHORITY BATCH RELEASE PROCEDURE

Blood Products and Vaccines

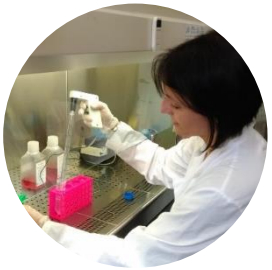
INTRODUCTION

In Italy, the National Centre for the Control and Evaluation of Medicines (CNCF) of the Istituto Superiore di Sanità (ISS) is the Italian Official Medicines Control Laboratory (OMCL-IT_ISS-H) within the European Official Medicine Control Laboratories (OMCLs) Network (Decree of the Ministry of Health of 2 March 2016).

The Biologicals and Biotechnologicals Unit of the CNCF carries out the control of Blood Products and Vaccines by means of its four sections as indicated below:

- Blood Products 1:
  - ✓ Human Immunoglobulin preparations
    (This section carries out also the plasma pool testing, see Point 6 below)

- Blood Products 2:
  - ✓ Human Albumin
  - ✓ Clotting factor concentrates (FVIII, FIX, PCC)
  - ✓ Antithrombin III concentrates
  - ✓ Fibrin Sealant Kit
  - ✓ Human plasma (pooled and treated for virus inactivation)



- Bacterial Vaccines:
  - ✓ Diphtheria
  - ✓ Tetanus
  - ✓ Glycoconjugates (Men ACWY and Hib)
  - ✓ Menigoccocal serogroup B

- Viral Vaccines:
  - ✓ Influenza
  - ✓ Measle, Mumps and Rubella
  - ✓ Varicella
  - ✓ HPV
  - ✓ Hepatitis A and B
  - ✓ Rotavirus
  - ✓ OPV (only MAPREC test)

1. HOW TO SUBMIT A REQUEST FOR AN EU-OCABR CERTIFICATE

(Article 114 of Council Directive 2001/83/EC)

For Blood Products/ Vaccines batches to be tested by the CNCF, a formal *Request Form For Batch Release* should be submitted in accordance with the Administrative Procedure for Official Control Authority Batch Release (OCABR, https://www.edqm.eu/en/batch-release-human-biologicals-vaccines-blood-and-plasma-derivatives).

To trigger the process, the respective *Request Form For Batch Release* (see Attachments 1 and 2), duly signed by the Marketing Authorisation Holder (MAH), should be sent to the ISS along with the samples (see Point 3 below for details about shipment).

The *Request Form For Batch Release* should also be sent in advance by email to the CNCF Technical Secretariat along with all documents (in PDF format) related to the batch, e.g. the Summary Protocol or any additional document.

The emails of the CNCF secretariat are:

- ✓ ocabr-blood.cncf@iss.it for Blood Products
- ✓ ocabr-vaccine.cncf@iss.it for Vaccines

The following contacts should be copied in the email:

- Dr. Carlo Pini (Head of the National Centre for the Control and Evaluation of Medicines) carlo.pini@iss.it
- Dr. Giulio Pisani (Head of the Biologicals and Biotechnologicals Unit) giulio.pisani@iss.it

2. PARALLEL TESTING PROCEDURE

If requested by the MAH, Blood Products/Vaccines batches can be tested by the *Parallel Testing Procedure*, i.e. before the Quality Control of the manufacturer has completed the analytical testing. In this case, the approach to be followed differs from the one described above (see Paragraph 1) in that the *Request Form* sent to the ISS indicates *Parallel Testing Procedure* and the documents related to the batches are sent at the completion of the tests by the Quality Control of the manufacturer.

The CNCF issues an *EU-OCABR Certificate* after testing the samples and reviewing the Summary Protocol.

If during the *Parallel Testing Procedure*, the batch is withdrawn by the MAH because of non-compliance with the specifications during the analytical testing or other aspects, including GMP issues, the CNCF stops the procedure and, in compliance with the EC Administrative Procedure for Official Control Authority Batch Release, informs the members of the EU/EEA OCABR network of the withdrawal.

3. HOW TO SUBMIT SAMPLES

The samples to be submitted should be collected in a manner that they are truly representative of the relevant batch.

Each dosage container should be labelled with the final labelling, unless there are valid reasons for not doing so. In case of the *Parallel Testing Procedure* (see Paragraph 2), the containers should be labelled with the name of the product, batch number, dosage and name of the MAH.

Samples from starting materials or in process steps (i.e. plasma pools or bulks) should be labelled to clearly indicate the step of the manufacturing process, the date on which the samples were taken, the name of the final product, the batch number (or other appropriate identification) and the name of the MAH.

Samples should be shipped to:

Istituto Superiore di Sanità

Ufficio Campioni

Via Castro Laurenziano 25,

00161 Rome (ITALY)

The courier should be informed that the office is open from 8:00 to 16:00, Mondays through Fridays. In case it is not possible to guarantee delivery during the opening hours, the CNCF should be contacted to arrange the delivery (see contacts below at the end of the document).

Please note that the ISS is closed on the following National or local holidays:

1st and 6th of January
Easter Monday
25th of April
1st of May
2nd of June
29th of June
15th of August
1st of November
8th of December
25th and 26th of December

4. SAMPLE PACKAGING AND TRANSPORT DOCUMENTS

It falls under the responsibility of the MAH to ensure that all samples sent to the CNCF are accompanied by a suitable documentation for transport and custom clearance (if required). It is important to assure that samples reach the CNCF in proper conditions. The following points should be taken into consideration:

- Samples that require storage at +2°C/+8°C must be delivered in appropriate temperature-controlled containers that ensure maintenance of cold chain. The external box used for shipping at +2°C/+8°C must be clearly labelled as such.

- Samples that require storage at temperatures below -20°C (plasma pools samples, virus-inactivated plasma) must be shipped with dry ice or any other appropriate freezing system that ensures appropriate maintenance of the sample's temperature. The external box used for shipping frozen material must be clearly labelled as such.

5. OTHER CERTIFICATIONS

In addition to the *EU-OCABR Certificate*, the CNCF can issue Certificates for non-EU countries (e.g. *WHO certificate*) or other Testing Certificates/Reports as per the MAH request.

Testing Certificates/Reports are issued only after an Agreement between the interested parties has been formalized. The Agreement specifies the type of tests to be carried out for each batch, the type and number of samples to be submitted, the documentation related to the product to be submitted as well as the type of Certificate requested by the MAH.

6. PLASMA POOL TESTING CERTIFICATE

The CNCF also carries out Plasma Pool Testing and issues an *EU/EEA Certificate of Approval for Plasma Pool* within the framework of the OCABR of medicinal products derived from human blood and plasma.

The tests carried out by the CNCF on plasma pools are:

- Hepatitis B surface Antigen (HBsAg) by serological assay
- Human Immunodeficiency Viruses types 1 and 2 (HIV 1 and 2) by serological assay
- Hepatitis C Virus (HCV) RNA by NAT
- Hepatitis A Virus (HAV) RNA by NAT
- Hepatitis E Virus (HEV) RNA by NAT
- Parvovirus B19 (PVB19) DNA by NAT

To trigger the process, the respective *Request Form For Plasma Pool Testing* (see Attachment 3), duly signed by the MAH, should be sent to the ISS along with the samples (see Point 3 below for details about shipment).

The *Request Form For Plasma Pool Testing* should also be sent in advance by email to the CNCF Technical Secretariat along with all documents (in PDF format) related to the batch, e.g. the Summary Protocol or any additional document, using the email contacts reported under Point 1.

7. NUMBER OF TEST SAMPLES

For the *EU-OCABR Certificate* of Blood Products, the required number of samples is reported in the table below:

Blood Products	No. of samples
Intravenous Immunoglobulin preparations	2
Intramuscolar Immunoglobulin preparations	5
Albumin	3
Clotting Factors	3
Virus-inactivated Plasma	3
Antithrombin III concentrates	3
Fibrin Sealant Kit	3
Plasma pools	5 aliquots, 1.5 mL each

For the *EU-OCABR Certificate* of Vaccines, the type and number of samples to be supplied is indicated in the specific vaccine guideline published on the EDQM website (https://www.edqm.eu/en/human-ocabr-guidelines).

For other types of Certificate, the number of test samples may vary.