EU Official Control Authority Batch Release

Human Vaccine and Blood Derived Medicinal Products

EU Administrative Procedure for Official Control Authority Batch Release

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European Commission
edqm European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé
COUNCIL OF EUROPE
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CONTENTS

EU ADMINISTRATIVE PROCEDURE FOR OFFICIAL CONTROL AUTHORITY BATCH RELEASE

Guideline for the administrative procedure to be followed by the competent OMCL authorities for the implementation of Directive 2001/83/EC Article 114 as amended by Directive 2004/27/EC.

Legal Framework

For the purposes of this guideline all reference to the European Union shall be taken as all European Union Member States and the States, which have signed the European Economic Area agreement, namely Norway, Iceland and Liechtenstein.

Article 114 of the codified Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use and the amending Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004, allows but does not require a Member State laboratory to test a batch of an immunological medicinal product or a medicinal product derived from human blood or plasma before it can be marketed. The competent authorities issue a Batch Release Certificate when the results are satisfactory. This is known as "Official Control Authority Batch Release" (OCABR) within the meaning of the above-cited Directives and consists of analytical controls and document review which are additional to the batch release that must be carried out by the manufacturer for a given batch in accordance with Article 51 of the said Directives.

The list of Official Medicines Control Laboratories (OMCLs), in the European Union, currently carrying out "Official Control Authority Batch Release" is available from the European Directorate for the Quality of Medicines and HealthCare (EDQM), Department of Biological Standardisation, OMCL Networks and HealthCare (DBO), OCABR Section of the Council of Europe and it is regularly updated (see www.edqm.eu). Each of these laboratories corresponds to the "Official Medicines Control Laboratory" cited in Article 1, paragraph 78 of Directive 2004/27/EC which amends Article 114 of Directive 2001/83/EC.

The Directives require Member States to recognise Official Control Authority Batch Release carried out in any other Member State, (while taking into account the next paragraph). This means that once a batch is released by the competent authority of one Member State, then that Official Control Authority Batch Release, if required, is valid for all other Member States, (while taking into account the next paragraph). The "European Union Official Control Authority Batch Release Certificate" delivered by a National competent authority is the document used by a Member State to indicate that "Official Control Authority Batch Release" has taken place. Although the Directive specifically precludes any Member State from carrying out OCABR testing of a batch already released by another Member State, nevertheless post marketing testing of this batch by any Member State, e.g. as part of post-marketing surveillance, is not precluded.

The wording of paragraph 1 (immunological medicinal products) and the wording of paragraph 2 (blood and plasma derivatives) of Article 114 of Directive 2001/83/EC, as amended by Directive 2004/27/EC are almost identical, the only difference being the mention, in paragraph 1 only, of the phrase: *'in the case of a batch manufactured in another Member State'*. The practical significance of this statement and the consequence for immunological medicinal products is that, when a batch of an immunological medicinal product is marketed in the Member State where it was manufactured and that Member State requires Official Control Authority Batch Release, then the OMCL in that Member State would normally carry out Official Control Authority Batch Release of that particular batch. The Member State of manufacture may, however, decide to recognise Official Control Authority Batch Release of that particular batch carried out by another Member State. Furthermore, when the batch of an immunological medicinal product is marketed in the Member State where it was manufactured and that Member State does not require Official Control Authority Batch Release, then the OMCL in any other Member State may be the testing authority for the purpose of Official Control Authority Batch Release within the European Union of that particular batch.

For a batch of either an immunological medicinal product or a medicinal product derived from human blood or plasma, which has already undergone Official Control Authority Batch Release in another Member State, Article 114 of Directive 2001/83/EC as amended by Directive 2004/27/EC does not permit any additional or renewed material control, for example, requiring further information concerning the batch, such as the protocol.

In the case of Centrally Authorised Immunological Medicinal Products or Medicinal Products Derived from Human Blood or Plasma the situation is similar. A specific Procedure for Official Control Authority Batch Release of Centrally Authorised Immunological Medicinal Products for Human Use and Medicinal Products Derived From Human Blood and Plasma agreed upon by the European Commission, the EMA, EDQM and the OMCL network is available and should be applied.

Article 123 of Directive 2001/83/EC requires that whenever a Member State takes the decision to prohibit the supply of a medicinal product this Member State must bring this decision to the attention of the EMA forthwith. It is, therefore, in line with these legal provisions and it is, moreover, in the interest of public health that a mechanism be in place for the exchange of information concerning non-compliance of a batch of an immunological medicinal product or a medicinal product derived from human blood or plasma, which has been examined as provided for in Directive 2001/83/EC and amending Directive 2004/27/EC and in accordance with this guideline on Official Control Authority Batch Release.

Purpose

Directive 2001/83/EC as amended by Directive 2004/27/EC requires Member States to recognise OCABR carried out by any other Member State. This guideline outlines the administrative procedure for Official Control Authority Batch Release within the European Economic Area including the European Union.

As additional safeguards for the protection of public health, this guideline outlines a system for the exchange of information, amongst all the competent authorities and the marketing authorisation holders concerned, on batches that do not comply with OCABR testing by a European Union Authority. Furthermore, it provides a format for the OMCLs annual reports on OCABR testing.

This guideline is for use firstly by the OMCLs in the Member States, to facilitate them in meeting the requirements of Directive 2001/83/EC as amended by Directive 2004/27/EC and to recognise Official Control Authority's Batch Release within the European Union and its validity. Formats for Official Control Authority Batch Release Certificates for the European Union Member States are included.

Secondly, it is also for use by marketing authorisation holders. Guidance is provided for the documents used for communications, concerning Official Control Authority Batch Release, between the marketing authorisation holder and the competent authorities in the Member States.

Principles

For batches of a medicinal product to be marketed in a Member State requiring Official Control Authority Batch Release, there shall be an Official Control Authority Batch Release Certificate common to all Member States. This shall show that the batch of medicinal product has been examined and tested by an OMCL within the European Union in accordance this procedure and with Official Control Authority Batch Release guidelines pertaining to the medicinal product within the European Union and is in compliance with the approved specifications laid down in the relevant monographs of the European Pharmacopoeia (Ph. Eur.) and in the relevant marketing authorisation.

In line with article 114 of Directive 2001/83/EC as amended the primary goal of OCABR is the release of products which meet the quality safety and efficacy requirements defined in the marketing authorisation. During this process OMCLs should give priority to the method/approach which best respects the 3R principles in line with EU Directive 2010/63 and the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Council of Europe) while still attaining the desired goal. This includes the appropriate application of validated 3R alternatives and reduced testing schemes as indicated in the various OCABR guidelines.

The current version of this procedure and product specific guidelines are available on the EDQM website www.edqm.eu.

Procedure

1. Where appropriate, the Member State where the product is to be marketed informs the marketing authorisation holder that the product is to be subjected to the Official Control Authority Batch Release procedure applicable within European Union; the model letter presented in Annex I shall be used. Such a letter shall identify, for the marketing authorisation holder, the contact person in the Member State to whom the European Union Official Control Authority Batch Release Certificate (see Annexes II) and the marketing information form (see Annex IV) must be sent.

If one does not already exist, an appropriate product specific guideline is elaborated by EDQM and the concerned OMCL network for OCABR and adopted by the OMCL network for OCABR according to the relevant procedures.

The Procedure for Official Control Authority Batch Release of Centrally Authorised Immunological Medicinal Products for Human Use and Medicinal Products Derived From Human Blood and Plasma as approved by the European Commission, the EMA, EDQM and the OMCL network for OCABR, replaces the paragraph above for Centrally Authorised Medicinal Products.

2. The marketing authorisation holder shall submit samples relevant to the batch to be released together with production and control protocols to an OMCL[1] within the European Union, which then acts as the testing authority for the purpose of release of that particular batch.

   The releasing OMCL should be notified by the MAH of any new approved variations that have an impact on product specifications or on data supplied in section 3 of the manufacturer's OCABR batch release protocol and relevant for the OMCL in the releasing Member State. The MAH should indicate from when the variation(s) will be applied (indicate 1st batch that is affected)[2].

3. Official Control Authority Batch Release procedure within the European Union consists of:

   a) a critical evaluation of the manufacturer's production and control protocol, and

   b) testing of samples submitted by the manufacturer as specified in the relevant guidelines, which may consist of two phases. Normally OCABR consists only of Phase 1 testing. However, Phase 2 testing may be appropriate in cases as described in 6, as a transitory measure; Information concerning phase 2 testing and other important technical issues is transmitted to the network using the model template for circulation of important information in annex VI.

   c) testing for viral markers of all plasma pools used in the production of medicinal products derived from human blood and plasma, as prescribed in product specific guidelines.

   Within the European Union, Official Control Authority Batch Release shall be completed by the OMCL within 60 days of receipt of the complete set which consists of the protocol and samples and the fees, where required.

   Furthermore it should be ensured that Official Control Authority Batch Release is performed under a quality assurance system, which undergoes regular external assessment based on the international standard ISO 17025.

[1] A given batch should be submitted to only one OMCL for the purpose of OCABR however it is recommended that the MAH make arrangements to interact regularly with more than one OMCL for OCABR of a given product in order to help ensure adequate coverage and back-up capacity where necessary.
[2] If an 'overlap' period with batches using the previously approved MA is expected the MAH should inform the OMCL at this time.

4. If a batch is satisfactory for release, the OMCL shall prepare an Official Control Authority Batch Release Certificate, giving the details shown in the model certificate presented in Annexes II a and II b.

   For the specific case of monovalent bulk of Poliomyelitis vaccines (oral), plasma pools, ancillary medicinal products derived from human blood and plasma to be used in medical devices and when special arrangements are required for pneumococcal polysaccharide bulk conjugates as determined by the network, a certificate of approval shall be issued according to the model presented in the relevant Annexes II c, II d, II f and IIg, respectively.

   The certificate may be written in the national language of the country of the OMCL and should be accompanied, if relevant, by a translation into English.

   Should a batch be found not to comply with the specifications, this information shall be provided to the marketing authorisation holder and, by a rapid, confidential, information exchange mechanism, to specified contact persons in the EU OCABR network (including OMCLs, competent authorities, EMA, the EU Commission, EDQM, DBO, Batch Release Section and any OCABR network observer approved through a specific network procedure) for use in the context of control of medicines by the relevant authorities. The list of specified contact persons is given in Annex III. A model notice of non-compliance/failure is presented in Annex II e.

   Technical details of the non-compliance shall be made available to other Member States, on request. The same applies for manufacturer withdrawal or method deficiencies after being informed using the appropriate annexes noted below.

   In the specific case where an arrangement has been made between the testing OMCL and the manufacturer to perform batch testing in parallel, any batches failing tests and subsequently withdrawn by the manufacturer before completion of the OCABR procedure may not be formally considered as non-compliance. Information of the withdrawal shall, nevertheless, be circulated within the OCABR network (Annex III contacts) whenever this occurs in order to avoid the possibility of these batches being submitted for official batch release to another OMCL. The model template for batch release procedural information in Annex VII is provided for this purpose. These exchanges of information take place in accordance with Article 122 of Directive 2001/83/EC as amended by Directive 2004/27/EC.

   For the sake of public health, detailed documentation on all batches of the medicinal product should be kept by the OMCLs for 10 years after their expiry date, to be made available for examination by the competent authorities upon request.

5. The Official Control Authority Batch Release Certificate within the European Union shall be issued to the marketing authorisation holder. The marketing authorisation holder of the batch of the medicinal product concerned must ensure that a copy of this certificate is provided to the competent authorities of the Member States where the batch will be marketed. A copy of the certificate and the corresponding "marketing information form" must be sent by the marketing authorisation holder to the competent

authority in the Member State(s) wherever the batch or any portion of the batch of the medicinal product is to be marketed. A model of "marketing information form" is presented in Annex IV. After sending these documents, the marketing authorisation holder could market the batch in the Member State where the batch is to be marketed if, within seven working days, the competent authority in that Member State has not raised any objection.

Without delaying placing a given batch on the market, further exchange of information and documentation may take place between OMCLs.

The OCABR certificate provided to the MAH for a given batch cannot be recalled once issued however if confirmed quality or safety issues arise which result in the recall of a batch from the market, the OMCL may issue a 'Nullification Notice' as presented in annex VIII to indicate that the original certificate should no longer be used for distribution of the batch.

6. Official Control Authority Batch Release within European Union: Phase 2 testing.

More extensive testing may need to be performed by an OMCL. Examples of events that might trigger Phase 2 testing include:

- a significant change in the manufacturing process;
- a change in the manufacturing site;
- adverse events;
- marked inconsistencies in the manufacturing process;
- changes in the manufacturer's test procedures;
- unexpected variability in the results of quality control tests performed by the manufacturer or the OMCL;
- a critical inspection report from the medicines inspectorate
- need to monitor, through testing, the consistency of a key quality parameter for a defined period.

Through the rapid information system (Annex VI), the institution (OMCL, competent authorities and/or inspectorate) requiring Phase 2 testing must advise the OMCLs performing OCABR that Phase 2 testing should be initiated for the product concerned, by informing the specified contact persons (in Annex III) and indicating the specific reasons. Phase 2 testing represents a set of additional testing measures that are only valid for a transitory period, unless otherwise specified and agreed; the latter case will then imply an appropriate revision of the product specific guideline concerned.

OCABR Database

A database is set up at EDQM to provide a current overview of the outcome of all batches of final products, plasma pools and bulks eligible for OCABR and submitted to the OCABR procedure. Each OMCL has the obligation and responsibility to contribute their own data in a timely manner (e.g. within 1 week). Access to the database is restricted to OMCLs and authorities recognised as part of the OCABR network and any network observer approved through a specific network procedure.

Annual report

Each OMCL shall produce an annual report summarising the OCABR testing it has undertaken. A model format for the annual report is presented in Annex V. Exchange of annual reports shall be dealt with on the basis of strict confidence and be accessible only to the CA/OMCLs of the OCABR network, the EDQM, the EMA and the European Commission and any network observer approved through a specific network procedure. The EMA and the European Commission shall be informed by EDQM of any relevant major issues.

ANNEX I

Template for a model letter from a Competent Authority to the Marketing Authorisation Holder as regards Official Control Authority Batch Release within EU

Dear Madam, Dear Sir,

PRODUCT NAME:
MARKETING AUTHORISATION NUMBER:
OFFICIAL CONTROL AUTHORITY BATCH RELEASE within EU

1. In accordance with Article 114 of Directive 2001/83/EC as amended by Directive 2004/27/EC the competent authority of ..... requires that samples from each batch of this product be submitted for examination by the Official Medicines Control Laboratory (OMCL) before release on the market. The OMCL must declare that the batch in question conforms with the approved specifications, i.e. those set out in the above marketing authorisation and in the relevant monographs of the European Pharmacopoeia.

   Consequently, samples of the same batch must not be submitted to another OMCL within the EU/EEA for the purpose of the examination for batch release.

2. Samples and summary protocols should be submitted in accordance with the administrative procedure for the Official Control Authority Batch Release and the product specific relevant guidelines.

i. The samples submitted should have been collected so as to be truly representative of the relevant batch.

ii. Each dosage container submitted should be labelled with the final labelling, unless there are valid reasons stated for not doing so, in which case a specimen of the final label should be provided and every dosage container labelled with the name of the product, batch number, dosage and the name of the marketing authorisation holder.

iii. Samples from stages other than the final lot stage should be labelled to clearly indicate the stage in the manufacturing process and the date on which the samples were secured, the name of the product, the batch number (or other appropriate identification) and the name of the marketing authorisation holder; in case of blood derivatives plasma pool samples should be submitted prior to product samples or at latest at that stage.

iv. Samples and protocols should be submitted to one of the OMCLs of the EU/EEA Member States (addresses available from the Council of Europe, EDQM, DBO, Batch Release Section www.edqm.eu - annex III list).

3. The marketing authorisation holder should inform this competent authority which OMCL(s) they intend to use within EU for the purpose of official control authority batch release. Any change in this arrangement should also be notified.

4. The marketing authorisation holder has the responsibility to ensure that the OMCL is provided with all the necessary documentation to allow the Official Control Authority Batch Release within EU to be undertaken i.e.:
   - copy of the marketing authorisation documents, providing details of in-process testing, finished product testing and specifications,
   - test methods including details of reference standards,
   - labels,
   - example of the protocol.

   In addition, the OMCL may request further information to facilitate the Official Control Authority Batch Release procedure and this should be provided.

   Changes to the above must be approved by the competent authority and these should be notified to the OMCL immediately.

5. Prior to placing the batch on the market a copy of the Official Control Authority Batch Release certificate should be provided to the Member States where the batch of the product concerned will be marketed. The copy of the certificate should be complemented by a marketing information form addressed by the marketing authorisation holder to the competent authority of the Member State(s) where the batch of the product is to be marketed. A model marketing information form is given in Annex IV of the administrative procedure for the official control authority batch release.

Yours faithfully,

ANNEX IIa

EU OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE FOR IMMUNOLOGICAL PRODUCTS

Name and address of the releasing authority

_____

EU/EEA OFFICIAL CONTROL AUTHORITY BATCH RELEASE - Finished Product

Examined under Article 114 of Directive 2001/83/EC as amended by Directive 2004/27/EC (Immunological Medicinal Products) and in accordance with the Administrative Procedure for Official Control Authority Batch Release.

Trade name:	
International non-proprietary Name / Ph. Eur. name / common name:	
Batch numbers appearing on package and other identification numbers associated with this batch[3]:	
Type of container:	
Total number of containers in this batch:	
Number of doses per container:	
Date of start of period of validity:	
Date of expiry:	
Marketing authorisation number (member state / EU) issued by :	
Name and address of manufacturer:	
Name and address of marketing authorisation holder if different:	

This batch has been examined using documented procedures which form part of a quality system which is in accordance with the ISO/IEC 17025 standard This examination is based on either[4]:

- the relevant EU OCABR guideline for this product, or, in the absence of the latter,
- the review of the manufacturer's protocol and the appropriate control laboratory tests as indicated in the marketing authorisation application

This batch is in compliance with the approved specifications laid down in the relevant European Pharmacopoeia monographs and the above marketing authorisation and is released.

Signed:	
Name and function of signatory:	
Date of issue:	

Certificate Number:

[3]Such as batch number of final bulk.
[4]Delete as appropriate.

ANNEX IIb

EU OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE FOR MEDICINAL PRODUCTS DERIVED FROM HUMAN BLOOD OR PLASMA

Name and address of the releasing authority

_____

EU/EEA OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE - Finished Product

Examined under Article 114 of Directives 2001/83/EC as amended by Directive 2004/27/EC (Medicinal Products derived from Human Blood or Plasma) and in accordance with the Administrative Procedure for Official Control Authority Batch Release.

Trade name:	
International non-proprietary name / Ph. Eur. name / common name:	
Batch numbers appearing on package and other identification numbers associated with this batch [5]**:**	
Type of container:	
Total number of containers in this batch:	
Nominal dose per container:	
Date of start of period of validity:	
Date of expiry:	
Marketing authorisation number (member state / EU) issued by :	
Name and address of manufacturer:	
Name and address of marketing authorisation holder if different:	

This batch has been examined using documented procedures which form part of a quality system which is in accordance with the ISO/IEC 17025 standard. This examination is based on either[6]:

- the relevant EU OCABR guideline for this product, or, in the absence of the latter,
- the review of the manufacturer's protocol and the appropriate control laboratory tests as indicated in the marketing authorisation application.

All the constituent plasma pools have been tested by an OMCL for virological markers.

This batch is in compliance with the approved specifications laid down in the relevant European Pharmacopoeia monographs and the above marketing authorisation and is released.

Signed:	
Name and function of signatory:	
Date of issue:	

Certificate Number:

[5]Such as batch number of final bulk
[6]Delete as appropriate

ANNEX IIc

EU OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE OF APPROVAL FOR MONOVALENT BULK OF POLIOMYELITIS VACCINE (ORAL)

Name and address of the releasing authority

_____

EU/EEA CERTIFICATE OF APPROVAL FOR - Monovalent Bulk of Poliomyelitis Vaccine (Oral)

Examined under Article 114 of Directive 2001/83/EC as amended by Directive 2004/27/EC (Immunological Products) and in accordance with the Administrative Procedure for Official Control Authority Batch Release.

Trade name of final product for which it is intended:	
Poliomyelitis virus[7]:	
Batch number (final bulk):	
Virus titre of bulk:	
Volume of bulk:	
Marketing authorisation number (member state) issued by :	
Name and address of manufacturer:	
Name and address of marketing authorisation holder if different:	

This batch has been examined using documented procedures which form part of a quality system which is in accordance with the ISO/IEC 17025 standard. This examination is based on the relevant EU OCABR guideline for this product.

This batch is in compliance with the approved specifications laid down in the relevant European Pharmacopoeia monographs and the above marketing authorisation and is approved.

Signed:	
Name and function of signatory:	
Date of issue:	

Certificate Number:

[7]Please indicate serotype of virus (Type I, II or III).

ANNEX IId

EU OFFICIAL CONTROL AUTHORITY BATCH RELEASE

CERTIFICATE OF APPROVAL FOR PLASMA POOL

Name and address of the testing authority

_____

_____

EU/EEA CERTIFICATE OF APPROVAL FOR - Plasma pool for use in the manufacture of medicinal products

Examined in the context of Official Control Authority Batch Release of medicinal products derived from human blood or plasma in application of Article 114 of Directive 2001/83/EC as amended by Directive 2004/27/EC.

Plasma Master File reference (core number):	
Code number of plasma pool:	
Date of manufacture:	
Country of origin of donations:	
Volume of pool:	
Name and address of manufacturer of plasma pool:	
Name and address of marketing authorisation holder (if applicable):	

This plasma pool has been examined using documented procedures, which form part of a quality system which is in accordance with the ISO/IEC 17025 standard.

This examination is based on the current EU OCABR guideline 'Official Control Authority Protocol for Approval of Plasma Pools': review of the plasma pool protocol and the following testing:

The samples of this plasma pool have been tested and found within the specifications for the following virological markers[8]:

- anti-HIV (1 and 2), HBsAg and
- HCV RNA, HEV RNA, HAV RNA and B19 DNA as determined by NAT.

This plasma pool is in compliance with the approved specifications laid down in the relevant European Pharmacopoeia monograph(s) and is approved.

Signed:	
Name and function of signatory:	
Date of issue:	

Certificate Number:

[8] Delete as appropriate

ANNEX IIe

EU Administrative Procedure for Official Control Authority Batch Release
GENERAL MODEL FOR NON-COMPLIANCE/FAILURE[9]

Name and address of the releasing authority

NOTICE OF **NON-COMPLIANCE** - Finished Product

Examined under Article 114 of Directive 2001/83/EC as amended by Directive 2004/27/EC and in accordance with the Administrative Procedure for Official Control Authority Batch Release.

Trade name:	
International non-proprietary name / Ph. Eur. name / common name:	
Batch numbers appearing on package and other identification numbers associated with this batch[10]:	
Type of container:	
Total number of containers in this batch:	
Number of doses per container:	
Date of expiry:	
Marketing authorisation number (member state / EU) issued by :	
Name and address of manufacturer:	
Name and address of marketing authorisation holder if different:	

This batch has been examined using documented procedures which form part of a quality system which is in accordance with the ISO/IEC 17025 standard. This examination is based on either[11]:

- the relevant EU OCABR guideline for this product, or, in the absence of the latter,
- the review of the manufacturer's protocol and the appropriate control laboratory tests as indicated in the marketing authorisation.

This batch is **NOT** in compliance with the specifications laid down in the above marketing authorisation/ the relevant European Pharmacopoeia monographs and cannot be released. Technical details of this non-compliance are available on request.

Reason for failure (specify non-compliance):

Comments (briefly if relevant):

Signed:	
Name and function of signatory:	
Date of issue:	

Notice Number:

[9] To be sent to the relevant marketing authorisation holder and circulated to annex III contacts
[10] Such as batch number of final bulk.
[11] Delete as appropriate

ANNEX IIf

EU OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE OF APPROVAL FOR ANCILLARY MEDICINAL PRODUCTS DERIVED FROM HUMAN BLOOD OR PLASMA IN A MEDICAL DEVICE

Name and address of the releasing authority

_____

EU/EEA OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE – Ancillary Medicinal Product

Examined under Article 1 of Directive 2000/70/EC (amending Directive 93/42/EEC as regards medical devices incorporating stable derivatives of human blood or human plasma) and in accordance with the Administrative Procedure for Official Control Authority Batch Release.

Ancillary medicinal product name: International non-proprietary name / Ph. Eur. name / common name:	
Name and address of manufacturer of ancillary medicinal product:	
Batch numbers appearing on package and other identification numbers associated with this batch[12]:	
Type of container:	
Total number of containers in this batch:	
Date of start of period of validity:	
Date of expiry:	
Trade name of medical device in which the above product is to be used:	
EMA Consultation procedure number:	
CE number of medical device and member state / EU issued by:	
Name and address of CE holder of medical device if different from address above:	

This batch has been examined using documented procedures which form part of a quality system which is in accordance with the ISO/IEC 17025 standard. This examination is based on the relevant EU OCABR guideline for this product[13]_____, with the exception of the following tests[14]_____

All the constituent plasma pools have been tested by the OMCL for virological markers.

This batch is in compliance with the approved specifications laid down in the relevant European Pharmacopoeia monograph(s) (_____)[15] with the exception of the following[16];_____ and is released for its intended use as indicated above.

This product is not intended to be used for injection in humans or incorporation in pharmaceutical/medicinal products

Signed:	
Name and function of signatory:	
Date of issue:	

Certificate Number:

[12] Such as batch number of final bulk

[13] please specify EU OCABR guideline used

[14] List test(s) which have not been completed OR delete this section as appropriate.

[15] insert monograph number

[16] list test(s) which have not been completed or do not comply with the monograph specifications and indicate the specification applied in practice (where applicable) OR delete this section as appropriate

ANNEX IIg

EU OFFICIAL CONTROL AUTHORITY BATCH RELEASE

CERTIFICATE OF APPROVAL
for
MONOVALENT PNEUMOCOCCAL POLYSACCHARIDE BULK CONJUGATES

Name and address of the releasing authority

_____

Examined under Article 114 of Directive 2001/83/EC as amended by Directive 2004/27/EC (Immunological Products) and in accordance with the Administrative Procedure for Official Control Authority Batch Release.

Trade name of final product for which it is intended:	
Serotype of monovalent pneumococcal polysaccharide bulk conjugate:	
Batch number monovalent pneumococcal polysaccharide bulk conjugate:	
Date of end of shelf life:	
Marketing authorisation number of final product for which the bulk conjugate is intended to be used: (member state) issued by:	
Name and address of manufacturer:	
Name and address of marketing authorisation holder if different:	

This monovalent pneumococcal polysaccharide bulk conjugate has been examined using documented procedures which form part of a quality system which is in accordance with the ISO/IEC 17025 standard. This examination is based on the relevant EU OCABR guideline Multivalent Pneumococcal Polysaccharide Conjugate Vaccine (concerning section 3.2.1, 3.2.2.1 to 3.2.2.5 as relevant for the bulk in question).

This batch of monovalent polysaccharide bulk conjugate IS COMPLIANT with the approved specifications laid down in the relevant European Pharmacopoeia monographs and the above marketing authorisation.

Signed:	
Name and function of signatory:	
Date of issue:	

Certificate Number:

ANNEX III

Contact persons for results and questions concerning EU/EEA Official Control Authority Batch Release

A current list containing all the names and contact details of the representatives of the 28 EU Member States, EEA Member States and mutually recognised partners responsible for OCABR of human blood and plasma derivatives and vaccines can be downloaded from the EDQM website:

www.edqm.eu

(https://www.edqm.eu/en/human-biologicals-ocabr-)

OCABR contact's details for EDQM, the EMA and the European Commission can also be found on the list.

The Annex III list is kept as up to date as possible with the latest contact information. Users are encouraged to check periodically to ensure they are using the most recent details.

OCABR contacts should notify EDQM as soon as possible should there be any change in their information.

ANNEX IV

Model for manufacturers of a MARKETING INFORMATION FORM

Notification of the intention to market a batch of an immunological medicinal product, which has a marketing authorisation, or medicinal product derived from human blood or plasma, which has a marketing authorisation, in the following EU/EEA member state .....

Addressee:	*'Name and address of specified contact person(s) in the member state/EU to whom the batch of product is to be submitted for marketing'*

Trade name:	'*Trade name of the product in the member state/EU where the batch of product is to be marketed'*
Batch number(s) appearing on the market package:	*'Batch number of the product as in the member state/EU where the batch of product is to be marketed '*
Other batch identification numbers associated with this batch[17]:	*' Filling bulk number, final lot number and packaging lot number'*
Number of containers to be marketed in the member state:	
Market authorisation number:	*'MA number in the member state/EU where the batch of product is to be marketed'*
Name and address of marketing authorisation holder :	'*MA holder in the member state/EU where the batch of product is to be marketed'*
Date of start of period of validity:	
Date of expiry in the member state where the batch is to be marketed:	
Intended date of marketing (dd/mm/yy(yy)):	

OMCL performing batch release:	
Official batch release certificate number:	

I hereby declare that:

- this batch is in compliance with the above marketing authorisation and the relevant European Pharmacopoeia monographs ;
- this batch is the batch referred to in the accompanying batch release certificate.

A copy of the batch release certificate is attached.

Signature of qualified person:	
Name of qualified person:	
Date of issue:	

[17] Sufficient detail should be given to allow clear traceability back to the level of the final bulk

ANNEX V

MODEL FORMAT AND CONTENT OF ANNUAL REPORTS FOR THE NETWORK FOR OCABR OF HUMAN BIOLOGICAL MEDICINAL PRODUCTS

Each Competent Authority (CA)/Official Medicines Control Laboratory (OMCL) requiring Official Control Authority Batch Release (OCABR) for any product on their market must complete an annual report.

Member States in the network choosing not to apply OCABR should complete at least Part 1 and Part 2 Section A and Section B.3.2 if possible. All Member States are also encouraged to report any relevant related activity (Market Surveillance study, spot-testing, release for other markets where relevant (e.g. WHO), limited national release etc.) in Part 2, section G.

Depending on the specific activity for the Member State the CA/OMCL should complete the relevant sections of the annual report below.

All EU OCABR activity should be covered, irrespective of the destination of the product. The report should be as succinct as possible but it is important that information required to promote transparency and confidence within the network be presented thus fostering the mutual recognition prescribed by the legislation for Article 114 of Directive 2001/83/EC as amended by 2004/27/EC. Trend analysis of data generated by manufacturer and the OMCL is particularly useful.

Reports should be provided electronically to the EDQM secretariat for OCABR at least 2 weeks in advance of the annual meeting unless a common decision is taken otherwise and the network informed. The use of hyperlinks for the electronic submissions is strongly encouraged to facilitate ease of use.

After receipt, the annual reports are placed in the human OCABR section of the EDQM restricted access extranet in the respective annual meeting folder (blood or vaccine) for consultation by relevant OCABR Network members including EDQM, the European Commission and EMA contacts.

These annual reports are not intended for publication and access is restricted to the EU/EEA OCABR network for human biological medicinal products and its secretariat and officially recognised partners.

STRUCTURE OF THE REPORT

CONTENTS

A table of contents should be included.

PART 1: GENERAL SECTION - *relevant to all CA/OMCLs regardless of framework of activity*

Introduction – Gives the name and address of the organisation(s) (if CA and OMCL are separate) and defines the reporting period covered in the report.

Section A: Organisation of the CA/OMCL

A.1 General Structure (Relation of the CA to the OMCL, organisation of each if separate)

A.2 Personnel Matters (indicating the name of responsible persons for the different relevant activities)

Section B: Quality Assurance System (systems in place, status of external audits/visits)

Progress in developing a quality assurance system, which (for OMCLs) meets the International Standard ISO 17025

PART 2: TECHNICAL SECTION – *specific to OCABR for human biological medicinal products*

Section A: Status of application of Article 114

A clear statement on whether article 114 is applied for blood and plasma derivatives and/or vaccines with the relevant national legal provisions noted.

Section B: Summary of batches tested for OCABR and batch traceability

This section should contain the total number of each product released for the European market during the reporting period together with the total number of batches rejected or withdrawn and the reason for doing so.

B.1 Summary Tables

Defined reporting period: *(e.g. 01/01/XXXX – 31/12/XXXX)*_____

a) Batches released through OCABR procedure by the Member State

Example for plasma pools

Source (manufacturer)	Number of pools tested	Number of pools tested for B19	Number of pools tested for HAV	Number of pools tested for HEV	Number of pools released
Octapharma					
Octapharma					

Total pools tested: Total pools released:

Example for blood and plasma derivatives

Product Type	Trade name	Manufacturer	Number of batches tested according to the EU OCABR procedure	Number of batches released with EU certificate	**Comments** *Please explain when the number of batches in column 4 and 5 are not equal*
Human Albumin	Albumina humana 20%	Grifols			
Human Albumin	Albumina humana 5%	Grifols			
Fibrin sealant kit	Tissucol duo S	Baxter			

Total batches tested:
Total batches released:

Example for Vaccines

Vaccine Type	Trade name	Manufacturer	Number of batches tested according to the EU OCABR procedure	Number of batches released released with EU certificate	**Comments** *Please explain when the number of batches in column 4 and 5 are not equal*
dT	Diftavax				
dT IPV	Revaxis				
dT ap IPV	Repevax				
DT aP	Infanrix				
DTaP IPV	Infanrix IPV				
DTP/Hib	Infanrix IPV Hib				
DTaP-IPV-Hib	*Pediacel*				

Total batches tested:
Total batches released:

b) Batches received with an EU certificate from another Member State

Product Type	Trade name	Manufacturer	Number of batches received with an EU certificate from another Member State	Member State(s) Please indicate number from each if more than 1	Comments

B.2 Details on rejected/withdrawn batches

Common name	Manufacturer	Trade Name	Batch number	Nominal potency (blood products) or number of doses (vaccines)	Total number of containers in the batch	Expiry date	Date of notice of non-compliance or withdrawal	Reason

Additional details as required: Example; any follow up action (may also refer to details in section D).

Section C: Technical Details of tests methods applied for OCABR

Indicate which laboratory test methods were performed by the OMCL for the tests listed in the OCABR product specific guidelines (Please note whether the test is described in a European Pharmacopoeia monograph, in the manufacturer's MA, in a WHO requirement or is a validated 'in-house' method).

Also indicate any relevant details such as the sharing of test sera from the manufacturer or data sharing with other OMCLs e.g. for bulk test results.

Example tables

E.g. Plasma pools

Viral Marker	**Test Kit**	**Other relevant details** (eg: sensitivity/specificity of test kit)	**Specification** (indicate origin e.g. Ph Eur, MA or other, please specify)
HCV RNA			
HAV RNA			
HBsAg			

E.g. Blood products

Product	**Release test(s)**	**Brief description; indicate if it is Ph Eur/WHO/MA or in house*[18]**
E.g. Albumin	Appearance	
	Distribution of molecular size	
	Pre-kallikrein activator	
Other relevant details (as necessary)	*e.g.; note reference material used, source and identity*	
Factor VIII	Solubility and appearance	
	Potency	
Other relevant details (as necessary)	*e.g.; note reference material used, source and identity*	

[1]*If more than 1 method is used (for different products/combinations) list them all

E.g. Vaccines (and vaccine components**)**

Vaccine component(s)	**Release test(s)**	**Brief description; indicate if it is Ph Eur/WHO/MA or in house***
E.g. Diphtheria containing vaccines including combinations	Potency Identity	
Other relevant details (as necessary)	*e.g.; note reference material used, source and identity*	
Hepatitis A vaccines including combinations	Potency Identity Antigen content	
Other relevant details (as necessary)	*e.g.; note reference material used, source and identity*	
Hepatitis B vaccines including combinations	Potency & identity In vitro HBsAg content Purity& identity	
Other relevant details (as necessary)	*e.g.; note reference material used, source and identity*	

Section D: Summary of test results

For each product (as listed in the table(s) in section B1), the specifications used for the OCABR tests for the particular product should be stated. It should be clearly noted if this is the MA approved specification or a validated in-house specification. Results should be given, preferably as graphs or figures demonstrating trend analysis (particularly for potency test data) with appropriate and clear indication of what is represented on the axes. It is helpful where possible to indicate the specification limits also on the graphs. Different products, or products of different strengths should be put on separate graphs. Tables of results for every test on every batch are not necessary where graphs are provided. OMCL data should be compared to manufacturer's data (preferably incorporated into the trend analysis graphs).

It should be indicated if an *in vivo* test reduction scheme is in place and how it is applied.

A brief interpretation of the data by the OMCL should be included.

It is not sufficient to indicate that testing is compliant with the MA or Ph Eur, the specification for each test should be given.

In conjunction with the summary figures on product data, data collected on reference preparations should be included, preferably in graphic form as a trend chart if appropriate and reference material should be clearly identified.

Further data from the OMCL or manufacturer's protocol should also be included where relevant.

It is important to provide information on batches failing the requirements; all failing batches should be reported in section B2. Additional details concerning the batches not released and the reasons for non-compliance and any follow up action may be provided here (a reference to any information provided in section D on failing batches should be indicated in section B2).

Example trend data:

dT – Diftavax Sanofi Pasteur

Specifications Applied (indicate origin of the applied specification ie MA, Ph Eur or validated in-house)

Final bulk	
Test	Actual Specification Applied (include also MA specification if different)
Assay Diphtheria	
Assay Tetanus	
Final lot	
Test	Actual Specification Applied (include also MA specification if different)
Appearance	
Identity Diphtheria	
Identity Tetanus	

D Potency assay

Insert graph comparing OMCL and manufacturer's results
Additional comments as necessary

T potency

Insert graph comparing OMCL and manufacturer's results
Additional comments as necessary

Appearance and identity

Summary of results
Additional comments as necessary

Data on reference preparations used

Section E: Developmental Work, Technical Difficulties

Any technical developmental work including highlights on development of 3R methods, observed problems with assays or suggestions for improvements/amendments of relevant guidelines and European Pharmacopoeia monographs.

Section F: Network Activity

Participation in EDQM collaborative studies or PTS studies or any other collaborative studies or performance measuring studies external to the network.

Declaration of any subcontracting arrangements for OCABR testing and identification of partners.

Section G: Other Related Activity

OMCLs are encouraged to report any relevant related activity (Market Surveillance study, spot-testing, release for other markets where relevant (e.g. WHO, limited national release etc.)).

e.g. table for non-EU procedure batch evaluation (e.g. WHO etc.- specify which type)

Product Type	Trade name	Manufacturer	Number of batches tested in a non-EU procedure	Number of batches released with non EU certificate or test report

A similar table with suitable columns is encouraged for reporting MSS or other relevant related activity.

ANNEX VI

MODEL LETTER
IMPORTANT INFORMATION

For Distribution of Important Information to the Contacts for the Official Control Authorities responsible for Human Vaccines*/Human Blood and Plasma Derivatives* in annex III

CONFIDENTIAL

Network of Official Medicines Control Authorities responsible for Human Vaccines*/ Human Blood and Plasma Derivatives*

IMPORTANT INFORMATION

(To be used for information on need for phase 2 testing, specific product or method related issues of interest to the network etc..: For notification of non-compliance of batches use annex IIe. For notification on batches withdrawn during parallel testing use annex VII)

Name of Company:

Trade Name of Product:

Nature of Problem:

Decision:

Batch Numbers (if appropriate): (include filling bulk number, final lot number and packaging lot number in addition to the batch number appearing on the product as in the member state /EU where the batch of product is to be marketed)

Comments:

Action Required (if any):

Notifying Member State/OMCL/OMCA:

Contact (include phone number and e-mail)**:**

Date:

Signed:

* delete as appropriate

ANNEX VII

MODEL LETTER
BATCH RELEASE PROCEDURAL INFORMATION

For Distribution to the Contacts for the Official Control Authorities responsible for Human Vaccines*/Human Blood and Plasma Derivatives* in annex III

CONFIDENTIAL; FOR INFORMATION ONLY

Network of Official Medicines Control Authorities responsible for Human Vaccines*/ Human Blood and Plasma Derivatives*

INFORMATION ON OCABR PROCEDURE INTERRUPTION DURING PARALLEL TESTING

(To be used to report batches withdrawn during parallel testing. For notification of non-compliance of batches use annex IIe. For information on need for phase 2 testing, specific product or method related issues of interest to the network etc. use annex VI)

Involved Member State/OMCL/OMCA:

Contact (include phone number and e-mail)**:**

The following batch(es) were withdrawn from the OCABR procedure by the manufacturer during parallel testing:

Name of Company:

Trade Name of Product:

Batch Numbers:(include filling bulk number, final lot number and packaging lot number)

Nature of Reason for interruption:

Comments:

THIS BULLETIN IS FOR INFORMATION ONLY
ALL APPROPRIATE FOLLOW UP HAS BEEN TAKEN
NO FURTHER ACTION IS REQUIRED
Please contact the notifying OMCL for any further information

Date:

Signed:.

*delete as appropriate

ANNEX VIII

EU OFFICIAL CONTROL AUTHORITY BATCH RELEASE NOTIFICATION OF NULLIFICATION OF CERTIFICATE

For circulation to the involved marketing authorisation holder and Annex III contacts

This is official notification that

Name and address of the releasing authority

_____

has found it necessary to consider null and void the EU Release Certificate number _____

that was issued for:

Trade name:	
International non-proprietary Name / Ph. Eur. name / common name:	
Batch numbers appearing on package and other identification numbers associated with this batch[19]:	
Type of container:	
Total number of containers in this batch:	
Number of doses per container:	
Date of start of period of validity:	
Date of expiry:	
Marketing authorisation number (member state / EU) issued by :	
Name and address of manufacturer:	
Name and address of marketing authorisation holder if different:	

For the following reason(s):
(e.g. Withdrawal of the batch from the market due to quality or safety concerns – details should be provided)

The above noted certificate is no longer valid for the purpose of releasing the batch in question on to the market.

Signed:	
Name and function of signatory:	
Date of issue:	

Notification Number:

[19]Such as batch number of final bulk.