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Control Authority Batch Release of Vaccines and Blood Products

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EC ADMINISTRATIVE PROCEDURE FOR THE OFFICIAL BATCH RELEASE TO BE FOLLOWED BY THE COMPETENT AUTHORITIES FOR THE IMPLEMENTATION OF COUNCIL DIRECTIVE 89/342/EEC (ARTICLE 4.3) AND COUNCIL DIRECTIVE 89/381/EEC (ARTICLE 4.3)

Legal Framework

This guideline is a revision of the previous guidelines published by the European Commission in 1994 and 1995. For the purpose of this guideline all reference to Member States and to the EU shall be taken as the 15 EU Member States and the States which have signed the EEA agreement, namely Norway, Iceland and Liechtenstein.

Article 4.3 of Council Directive 89/342/EEC and Article 4.3 of Council Directive 89/381/EEC allow but do 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 batch release" within the meaning of the above-cited Directives and consists of analytical controls and document review which are additional to the batch release carried out by the manufacturer for a given batch.

The list of Official Medicines Control Laboratories (OMCL), in the EU, currently carrying out official batch release is available from the EDQM, Division IV, Batch Release Section, Council of Europe and it is regularly updated. Each of these laboratories corresponds to the "State laboratory" cited in Article 4.3 of Directives 89/342/EEC and 89/381/EEC.

The Directives require Member States to recognise official 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 in a Member State then that official batch release, if required, is valid for the other Member States, (while taking into account the next paragraph). The "EU authority batch release certificate" is the document used by a Member State to indicate that "official batch release" has taken place. Although the Directives specifically preclude any Member State from carrying out batch release 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.

Article 4.3 of Directive 89/342/EEC and Article 4.3 of Directive 89/381/EEC are almost identical, the only difference being the mention, in Directive 89/342/EEC 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 batch release, then the OMCL in that Member State would normally carry out official batch release of that particular batch. The Member State of manufacture may however decide to recognise official 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 is manufactured and that Member State does not require official batch release, then the OMCL in any Member State may be the testing authority for the purpose of official batch release within the EU of that particular batch.

For a batch of an immunological medicinal product or a medicinal product derived from human blood or plasma, which has already undergone official batch release in another Member State, Article 4.3 of Directive 89/342/EEC and Article 4.3 of Directive 89/381/EEC do not permit any additional or renewed material control, for example, requiring further information concerning the batch, such as the protocol.

Up until now, in some Member States, before a batch of an immunological medicinal product or a medicinal product derived from human blood or plasma, which has already undergone official batch release in another Member State, is placed on the market, the Official Medicines Control Laboratories (OMCL) in these Member States have been following a national administrative procedure whose origins precede Directives 89/342/EEC and 89/381/EEC. Such a procedure is not foreseen by Directives 89/342/EEC and 89/381/EEC. It remains to be clarified by the Member States what, if anything, such a procedure now adds to the protection of public health and this practice may therefore need to examined in the light of Article 30 of the Treaty of Rome.

Article 33 of Directive 75/319/EEC requires that whenever a Member State prohibits the supply of a medicinal product that they should bring this to the attention of the CPMP. Therefore it is in line with these legal provisions and it is, moreover, in the interest of public health that there should be a mechanism 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 89/342/EEC or 89/381/EEC and in accordance with the relevant EU guideline on official control authority batch release.

Purpose

This guideline is for use by Member States when implementing batch release at national level; given that the Directives require Member States to recognise batch release carried out by any other Member States, it therefore outlines the administrative procedure for official control authority batch release within the EU.

As additional safeguards for the protection of public health, it outlines a system for the exchange of information, amongst all the competent authorities and the marketing authorisation holder concerned, on batches which do not comply with batch release testing by an EU authority. Furthermore, it provides a format for the OMCLs annual reports on batch release testing.

This guideline is for use firstly by the OMCLs in the Member States, to facilitate them in meeting the requirements of Directives 89/342/EEC and 89/381/EEC and to recognise official control authority batch release within EU and its validity. Formats for official control authority batch release certificates are included.

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 product to be marketed in a Member State requiring official control authority batch release, there will be an official control authority batch release certificate common to all the Member States. This should show that the batch of product has been examined and tested by an OMCL within the EU in accordance with Official Control Authority Batch Release Guidelines pertaining to the product within the EU 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.

Procedure

1. Where appropriate, the Member State where the product is to be marketed informs the marketing authorisation holder if the product is to be subjected to the official control authority batch release procedure applicable within EU; the model letter presented in Annex I may be used. Such a letter would identify, for the marketing authorisation holder, the contact person in the Member State to whom the official control authority batch release certificate (see Annexes II) and the Marketing Information Form (see Annex IV) should be sent.

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

3. Official control authority batch release procedure within the EU 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 official control authority batch release consists only of Phase 1 testing. However, Phase 2 testing may be appropriate in cases as described in 6, as a transitory measure.

   c) Testing for viral markers of all plasma pools used in the production of blood products, as prescribed in product specific guidelines

   Within the EU official control authority batch release should 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 will move progressively towards the European standard EN 45001.

4. If a batch is satisfactory for release, the OMCL will prepare a batch release certificate, giving the details shown in the model certificate presented in Annexes IIa and IIb.

   For the specific case of monovalent bulk of Poliomyelitis vaccines (oral) and plasma pools, a certificate of approval will by issued according to the model presented in the relevant Annexes IIc and IId respectively.

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

   Should a batch be found not to comply with the specifications, this information should be provided to the marketing authorisation holder and, by a rapid information exchange mechanism, to specified contact persons (OMCL, licensing authorities, and EDQM, Division IV, Batch Release Section) within the EU OMCL Network. A list of contact persons is given in Annex III. A model Notice of Non-Compliance is presented in Annex IIe. Technical details of the non-compliance should be made available to other Member States on request. The same applies for manufacturer withdrawal or method deficiencies. Batches failing tests and subsequently withdrawn by the manufacturers before completion of the batch release procedure may not be formally considered as non-compliance. Information should nevertheless be circulated within the OMCL batch release network whenever this occurs in order to avoid the possibility of these batches being submitted for official batch release to another OMCL. This exchange of information is provided for in article 30 of Directive 75/319/EEC.

   Detailed documentation on all batches of the 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 EU will be issued to the marketing authorisation holder. The marketing authorisation holder of the batch of the 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 a marketing information form should 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 product is to be marketed. A model 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.

6. <u>Official control authority batch release within EU: Phase 2 testing</u>

More extensive testing may need to be performed by an OMCL. Examples of events which 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.

Through the rapid information system, the institution (OMCL, licensing and/or inspectorate) requiring Phase 2 testing must advise the OMCLs performing batch release that Phase 2 testing should be initiated for the product concerned by informing the specified contact persons (see Annex III) and indicating the specific reasons. Phase 2 testing represents a set of additional testing measures which 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.

Annual report

Each OMCL will produce an annual report summarising the batch release testing they have undertaken. A model format for the annual report is presented in Annex V. Exchange of annual reports should be dealt with on the basis of strict confidence and be only accessible to the OMCLs of the network concerned and EDQM division IV; the EMEA and the European Commission shall be informed 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 4.3 of Directive 89/342/EEC (or Article 4.3 of Directive 89/381/EEC, where appropriate)[1] 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 relevant product specific 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.

[1]Quote the relevant directive.

iv. Samples and protocols should be submitted to one of the OMCLs of the EU/EEA Member States (list of addresses available from the Council of Europe, EDQM, Division IV, Batch Release Section).

3. The marketing authorisation holder should inform this competent authority which OMCL(s) they intend to use 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 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 CERTIFICATE - Finished Product

Examined under Directive 89/342/EEC (Immunological Medicinal Products) and in accordance with the Administrative Procedure for Official Control Authority Batch Release within EU.

Trade name:	
International Non-proprietary Name / Ph. Eur. name / common name:	
Batch numbers appearing on package and other identification numbers associated with this batch[2]:	
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 EN 45001 standard. This examination is based on either[3]:

- the relevant Note for Guidance 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:

[2]Such as batch number of final bulk.

[3]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 Directives 89/381/EEC (Medicinal Products derived from Human Blood or Plasma) and in accordance with the Administrative Procedure for Official Control Authority Batch Release within EU

Trade name:	
International Non-proprietary Name / Ph. Eur. name / common name:	
Batch numbers appearing on package and other identification numbers associated with this batch [4]:	
Type of container:	
Total number of containers in this batch:	
Nominal dose per container:	
Expiry date	
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 EN 45001 standard. This examination is based on either[5]:

- the relevant Note for Guidance 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 the 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:

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

ANNEX IIc
EU/EEA OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE OF APPROVAL OF POLIOMYELITIS VACCINE (ORAL)

Name and address of the releasing authority
CERTIFICATE OF APPROVAL - Monovalent Bulk of Poliomyelitis Vaccine (Oral)

Examined under Directives 89/342/EEC (Immunological Products) and in accordance with the Administrative Procedure for Official Control Authority Batch Release within EU

Trade name of final product for which it is intended:	
Poliomyelitis virus[6]:	
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 EN 45001 standard. This examination is based on the relevant Note for Guidance 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:

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

ANNEX IIe

Administrative Procedure for the Official Control Authority Batch Release within EU:
GENERAL MODEL FOR NON-COMPLIANCE FAILURE

Name and address of the releasing authority

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

Examined under Directives 89/342/EEC (Immunological Products)[7] or 89/381/EEC (Blood Products)[8] and in accordance with the Administrative Procedure for Official Control Authority Batch Release within EU

Trade name:	
International Non-proprietary Name / EU Standard name / Ph. Eur. name / common name:	
Batch numbers appearing on package and other identification numbers associated with this batch[9]:	
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 EN 45001 standard. This examination is based on either[10]:

- the relevant Note for Guidance for this product, or, in the absence of the latter,
- 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.

Comments (briefly if relevant):

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

Notice Number:

[7]Delete as appropriate.

[8]Delete as appropriate.

[9]Such as batch number of final bulk.

[10]Delete as appropriate

ANNEX III

Contact persons for results & questions concerning EU/EEA Authority Batch Release

		VACCINES	BLOOD DERIVATIVES
AUSTRIA Bundesinstitut für Arzneimittel Possingergasse 38 A - 1160 WIEN	Tel: (43) 1 492 0070 Fax: (43) 1 492 0292	✓	✓
BELGIUM Roland Dobbelaer Scientific Institute of Public Health Louis Pasteur J. Wytsmanstr. 14 B - 1050 BRUSSELS	Tel: (32) 2 642 5050 Fax: (32) 2 642 5210	✓	
Ellen Voets Scientific Institute of Public Health Louis Pasteur J. Wytsmanstr. 14 B - 1050 BRUSSELS	Tel: (32) 2 642 5076 Fax: (32) 2 642 5210	—	✓
DENMARK Anette Bjerregaard National Board of Health Frederikssundsvej 378 DK - 2700 BRONSHOJ	Tel: (45) 44 88 911 Fax: (45) 44 88 9228	✓	—
Eva Sandberg National Board of Health Frederikssundsvej 378 DK - 2700 BRONSHOJ	Tel: (45) 44 88 911 Fax: (45) 44 88 9228	—	✓
FINLAND Rose-Marie Olander National Public Health Institute National Control Laboratory of Vaccines and Sera Mannerheimintie 166 FIN - 00300 HELSINKI	Tel: (358) 947 44 328 Fax: (358) 947 44 551	✓	—
Eva Sairio National Agency for Medicines Pharmacological Department Mannerheimintie 166, PB 55 FIN - 00301 HELSINKI	Tel: (358) 9 3967 2647 Fax: (358) 9 3967 2602	—	✓
FRANCE Florence Fuchs Agence du Médicament Direction des laboratoires et des contrôles Unité de contrôle des médicaments immunologiques 321 Avenue Jean Jaurès F - 69007 LYON	Tel: (33) 4 72 76 06 10 Fax: (33) 4 72 76 06 15	✓	—
Laurence Mouillot Agence du Médicament Direction des laboratoires et des contrôles Unité des produits sanguins 25, bd Saint Jacques F - 75681 PARIS Cedex 14	Tel: (33) 1 53 80 82 77 Fax: (33) 1 45 88 09 41	—	✓

		VACCINES	BLOOD DERIVATIVES
GERMANY Paul-Ehrlich-Institut Manfred Haase Paul-Ehrlich-Str. 51-59 D - 63225 LANGEN	Tel: (49) 6103 77 3700 Fax: (49) 6103 77 1251	✓	—
Paul-Ehrlich-Institut Rainer Seitz Paul-Ehrlich-Str. 51-59 D - 63225 LANGEN	Tel: (49) 6103 77 2600 Fax: (49) 6103 77 1250	—	✓
GREECE Elli Souli National Drug Organisation 284 Mesogeion Avenue GR - 155 62 HOLARGOS	Tel: (30) 1 654 95 94 Fax: (30) 1 654 95 94	✓	✓
IRELAND Mike Morris Irish Medicines Board EarlsFort Centre EarlsFort Terrace IRL - DUBLIN 2	Tel: (353) 1 676 49 71 Fax: (353) 1 676 7836	✓	✓
ITALY Isabella Donatelli Istituto Superiore di Sanità Virology Laboratory Viale Regina Elena, 299 I - 00161 ROMA	Tel: (39) 6 499 03243 or (39) 6 499 03257 Fax: (39) 6 499 02082	✓	—
Graziella Orefici Istituto Superiore di Sanità Bacteriology Laboratory Viale Regina Elena, 299 I - 00161 ROMA	Tel: (39) 6 499 02333 Fax: (39) 6 491723 or (39) 6 49902934	✓	—
Carlo Pini / Maria Orlando Istituto Superiore di Sanità Immunology Laboratory Viale Regina Elena, 299 I - 00161 ROMA	Tel: (39) 6 49902585 or (39) 6 4463493 Fax: (39) 6 49387115	—	✓
LUXEMBOURG Jean-Louis Robert Laboratoire National de Santé B.P. 1102 L - 1011 LUXEMBOURG	Tel: (352) 49 1191 extension 358 Fax: (352) 40 4319	✓	✓
NETHERLANDS Ingrid Hegger Rijksinstituut voor Volksgezondheid en Milieu Laboratory for Medicines and Medical Devices Department of Biologicals Antonie van Leeuwenhoeklaan 9 P.O. Box 1 NL - 3720 BA BILTHOVEN	Tel: (31) 30 274 3275 Fax: (31) 30 274 4422	✓	✓

		VACCINES	BLOOD DERIVATIVES
PORTUGAL Maria Celeste Freire Instituto Nacional da Farmacia e do Medicamento Parque de Saude de Lisboa Av. do Brasil no. 53 P - 1700 LISBOA	Tel: (351) 1 790 8557 Fax: (351) 17939425	—	✓
Margarida Menezes-Ferreira Instituto Nacional da Farmacia e do Medicamento Parque de Saude de Lisboa Av. do Brasil no. 53 P - 1700 LISBOA	Tel: (351) 1 790 8557 Fax: (351) 17939425	✓	—
SPAIN Francisco Salmerón Departamento de Productos Biologicos Centro Nacional de Farmacobiologia Instituto de Salud Carlos III Ctra de Majadahonda-Pozuelo Km 2 E - MAJADAHONDA 28220 MADRID	Tel: (34) 1 509 7958 Fax: (34) 1 509 7946	✓	✓
SWEDEN Karl-Henrik Jönsson Medical Products Agency Box 26 S - 75103 UPPSALA	Tel: (46) 18 17 4600 Fax: (46) 18 54 8566	✓	✓
UNITED KINGDOM David Wood National Institute for Biological Standards and Control Blanche Lane South Mimms, Potters Bar GB - HERTFORDSHIRE EN6 3QG	Tel: (44) 1707 654753 Fax: (44) 1707 646730	✓	✓
Lincoln Tsang Medical Control Agency Market Towers 1, Nine Elms Lane GB - LONDON SW8 5NQ	Tel: (44) 171 273 0465 Fax: (44) 171 273 0062	✓	✓
EEA MEMBER STATES			
NORWAY Randi Winsnes Norwegian Medicines Control Authority Sven Oftedalsvei 6 N - 0950 OSLO	Tel: (47) 22 89 77 00 Fax: (47) 22 89 77 99	✓	✓
ICELAND Einar Magnusson Pharmaceutical Division Ministry of Health & Social Security Laugavegur, 116 ISL - 150 REYKJAVIK	Tel: (354) 91 60 97 00 Fax: (354) 551 9165	✓	✓
EUROPEAN DEPARTMENT FOR THE QUALITY OF MEDICINES **Division IV, Batch Release Section** Jean-Marc Spieser B.P. 907 F - 67029 STRASBOURG CEDEX	Tel: (33) 3 88 41 21 84 Fax: (33) 3 88 41 27 71		

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 Member State.....

Addressee:	*'Name and address of specified contact person(s) in the Member State/EU where the batch of product is to be marketed'*
Trade Name:	'*Trade name of the product in the Member State/EU where the batch of product is to be marketed'*
Batch numbers appearing on the market package:	*'Batch number of the product as in the Member State where the batch of product is to be marketed'*
Identification number:	
Number of containers to be marketed in the Member State:	
Marketing authorisation (MA) 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 marketing:	
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:	

ANNEX V

MODEL FORMAT AND CONTENT OF ANNUAL BATCH RELEASE REPORTS

Each Official Medicines Control Laboratory (OMCL) performing batch release should produce an annual report. Its purpose is to share with other OMCLs relevant technical or product-related information and generally increase mutual confidence between laboratories. All batch release activity should be covered, irrespective of the destination of the product. The report should be as succinct as possible but it is important that only useful information be presented and, especially, the trend analysis of data generated by the manufacturer and the OMCL is useful. These annual reports are not intended for publication and remain strictly restricted to the EU OMCL Batch Release Network and its secretariat.

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Section 1

- The total number of each product released for the European market during the year with their batch numbers together with the total number of batches rejected or withdrawn and the reason for doing so.
- The destination country of batches released (this information may not be available in all Member States).
- List of batches released elsewhere and 'imported'.

Section 2

For each product, indicate which laboratory tests were performed by the OMCL (e.g. whether the test is defined in a European Pharmacopoeia monograph, in a WHO requirement or is a validated 'in-house' method).

Section 3

Summary tables of the results of the laboratory tests performed including specifications:

a. corresponding results from control laboratory and manufacturer for relevant parameters (potency estimates are particularly useful);
b. further data from the OMCL or manufacturer's protocol if relevant and important.

Analysis of tests should be presented in graphs and/or charts and, if possible, using a common software.

It is important to provide information on batches failing requirements; details of those batches not released, if any, and the reasons for non-compliance should be provided.

Section 4

Any problems with assays and technical developmental work and suggestions for improvement/amendment of relevant guidelines and European Pharmacopoeia monographs.

Section 5

Progress in developing a quality assurance system which meets the European Standard EN 45001.