PROCEDURE FOR BATCH RELEASE OF BLOOD PRODUCTS ONTO THE MARKET FOR BATCHES OF A BLOOD PRODUCTS TO BE MARKETED IN SPAIN

USER'S MANUAL

MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

SUBJECT INDEX

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1. INTRODUCTION

1.1 Subject

The purpose of this document is to produce a user´s manual for the electronic procedure for Batch Release of Blood Products onto the market.

The procedure of implementation in market of blood products and vaccines, with the implementation of the Law 10-2013, that modifies Royal Decree 1345/2007, introduces the rate 1.15 for that procedure.

1.15	Tasa por liberación de lotes de hemoderivados y vacunas de acuerdo con los artículos 41.4 y 43.3 del Real Decreto 1345/2007, de 11 de octubre:
	(a) cada solicitud individualizada
	(b) entre 6 y 10 solicitudes/año (por año)
	(c) entre 11 y 40 solicitudes/año (por año)
	(d) entre 41 y 160 solicitudes/año (por año)
	(e) por más de 161 solicitudes/año (por año)

https://www.boe.es/diario_boe/txt.php?id=BOE-A-2013-8083

Payment is made once a year to the best option according to number of annual applications. The access is made through the following link:

https://sede.aemps.gob.es/pagoTelemaTasas/pago-telematico-tasas.html

Instructions for completing the form for Market Release of Blood Products for Human Use

1st Instruction

Batches of blood-derived products for human use shall not be placed on the market without authorization, according to the following procedure.

2nd Instruction

This provision does not extend to plasma-derived products used as excipients or reagents in the production of other medicines or health products.

Neither does apply to foreign medicines, or products undergoing clinical trials.

3rd Instruction

Prior to the placing on the market of the product in question a request for Market Batch Release shall be sent to the Division of Biological Products, Advanced Therapies and Biotechnology (DPB) of the Spanish Agency for Medicines and Health Products (AEMPS).

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For this purpose it is available an electronic system set by the Spanish Agency for Medicines for submitting applications. Accessed through the website of the AEMPS: https://www.aemps.gob.es

The address to be connected to is the following: (It is important to type in the S after http as if not done, the connection is not made).

https://sinaem4.aemps.es/hemoderivados/inicial.do?metodo=detalleInicial

Instruction 4th

The application shall be accompanied by the following documentation:

* Annexes to document "EC Administrative Procedure for Official Control Authority Batch Release" (OMCL, Batch Release - Human Biologicals) https://www.edqm.eu/documents/52006/293199/01_adproc_131219.doc/43cc946d-99a8-8667-5429-c03b7d-31f8a5?t=1642415580325)

- ANNEX IIB - EU official control authority batch release certificate for medicinal products derived from human blood or plasma
- ANNEX IID - EU official control authority batch release certificate of approval for plasma pool
- ANNEX IV - Marketing information form, model for manufacturers
- Statement of compliance of Note 1/98 of the general Directorate of Pharmacy (Circular 1/98 de la Dirección general de Farmacia), or failing that, a document stating the country of origin of the plasma.

Instruction 5th

After a period of 5 working days from sending the last valid documentation without a negative pronouncement, and taking into account the special need for these products, the lot is deemed approved for marketing.

The electronic system allows the laboratory making the request to have proof that the request has been made, and the AEMPS to be aware that the communication has been sent.

In the event that there is a computer system crash the applicant will proceed through fax (91.822.78.92), email (hemoderivados@aemps.es), or an alternative procedure.

Instruction 6th

In the case that the batch of the blood-derived product in question does not have a batch release certificate of the of the European Union, prior to the placing on the market of the medicinal product, a request for release onto the market, including the statement that the batch has not been sent to another Official Medicines Control Laboratory (OMCL) for its release shall be sent to the DPB. In addition, it shall be accompanied by the following documentation:

- ANNEX IV - Marketing information form, model for manufacturers.

- The following samples will be sent:
    - An image/mockup of the packaging material of the finished product of the lot in question, which allows complete viewing, as well as an image of the label attached to the immediate packaging of that batch.
    - 4 containers of 1.5 ml of the plasma pool which the product derives that must be sent in accordance with the relevant procedures, or failing an OMCL Certificate e of approval for plasma pool corresponding to the medicine in question (in this case the fee shall not be paid and in addition, the period of administrative silence for the placing on the market will be 5 days).

If within the period of 60 days after shipping there is no communication notifying of the existence of problems in the documentation or samples sent, the release of the lots onto the market can proceed.

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2. PROCEDURE

2.1 Application access

To access the application open a web page with the address:

https://sinaem4.aemps.es/hemoderivados/inicial.do?metodo=detalleInicial

The initial screen opens with the forms for Market Release and Request for Clarification, for both vaccines and blood-derived products.

In this initial screen appears the AENOR logo and our certificate number, which indicates that the process is certified by this entity.

Figure 1 - Initial Screen

Solicitud de Puesta en Mercado de Hemoderivados: to submmit a first application

Aclaraciones a la Puesta en Mercado de Hemoderivados: sending the information requested and need of increase previously requested batches

Imprimir justificante: search and print an application

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2.2 Blood-derived products marketing form

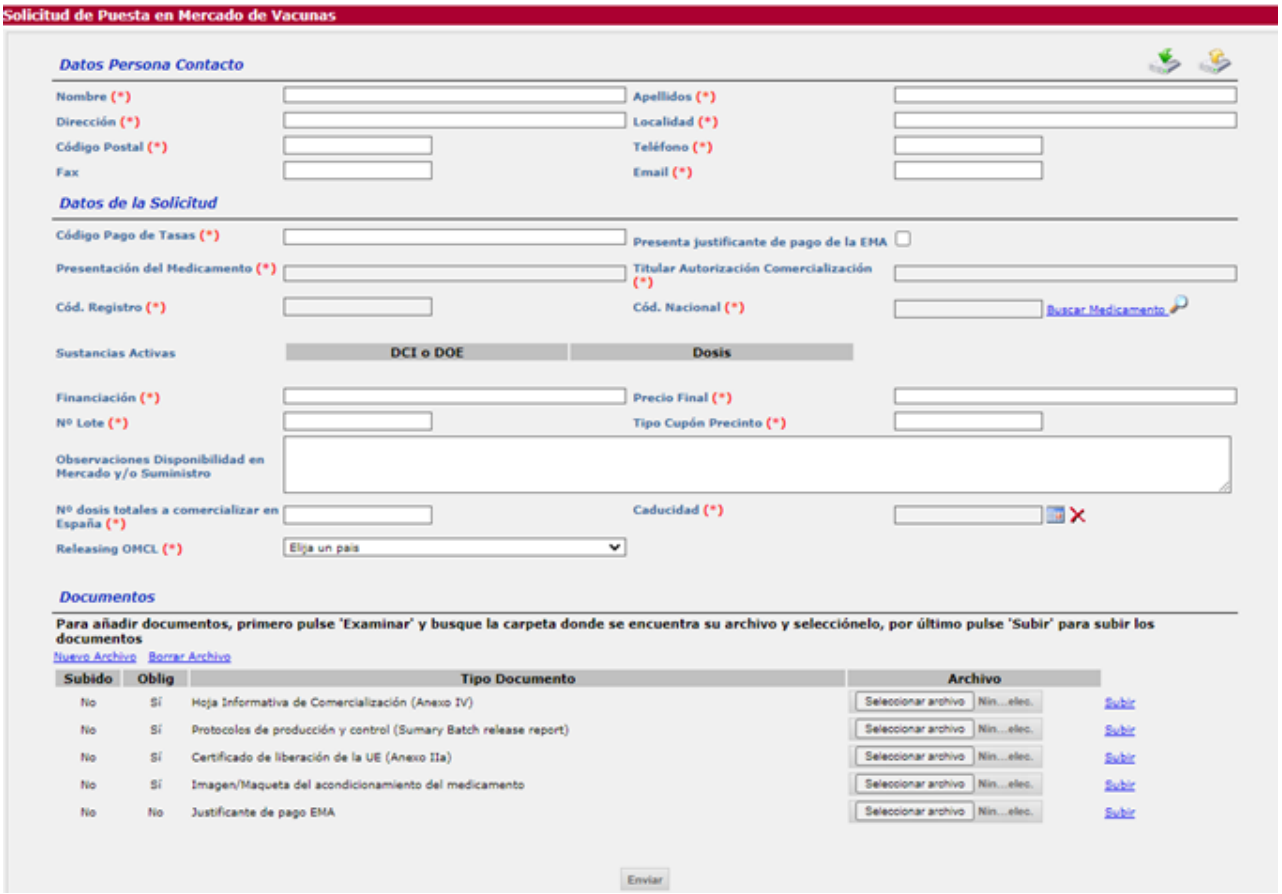

Figure 2 - Blood products Marketing Form

Required fields are marked with a red asterisk.

- Contact person details:

  The applicant company must fill in the contact details of the person responsible for the application for placing on market of blood products. These data can be stored in the form of XML file, for in subsequent requests, you can load automatically without having to re-enter the information.

  For this purpose, be typed data marked with red asterisk and are saved in XML format by pressing the green arrow at the top right of the screen icon.

  In successive requests, data is loaded without typing them, by pressing the yellow arrow (beside the green arrow) and with the option to 'Examinar', seeks the saved XML file, and the data is loaded.

- Application data details

  In the Application Data section you are asked to fill in the following fields:

  Payment of Taxes Code will indicate the generated number , according to the law 10-2013, that modifies Law 29/2006, introduces the 1.15 rate for this procedure

  There is another electronic application for payment of fees from which you can make any kind of payments to the AEMPS. This application is available at:

  https://sede.aemps.gob.es/pagoTelemaTasas/pago-telematico-tasas.htm

  An additional field is available for Parallel Distribution applications, "**Presenta justificante de pago de la EMA**". In this cases It´s not necessary to submit a payment of national Taxes.

  - Search "Medicamento": a sub-form opens to locate the correct product.

Figure 3 - Product Search Form

The search can be performed by pharmaceutical product name and / or Registration Code. Once the product is loaded, the following sections have to be filled in:

- Batch N°
- Comments
- Number of vials
- Number of doses
- Expiry date
- Releasing OMCL (OMCL performing batch release).

The attached documents must be uploaded and there is the possibility of uploading the pools that make up the medicine, through the option of automatically uploading an Excel file.

As stated in Section 4, after 5 working days from the dispatch of the last valid documentation without negative decision (positive silence procedure), and taking into account the special needs of these products, the lot shall be deemed marketed.

In the event of faults in the documentation either because it is considered wrong or incomplete, the applicant company will receive via email a “request for clarification” document formatted according to Figure 4.

COMUNICACIÓN DE DOCUMENTACIÓN INCOMPLETA O ERRONEA

Examinada la documentación aportada según *SOLICITUD Nº REFERENCIA* les notificamos la falta de documentación o algún error en la misma. Se deberá enviar la documentación señalada en la siguiente tabla con una cruz o algún comentario:

NOMBRE DEL MEDICAMENTO	
LOTE	
PRINCIPIO ACTIVO	
SOLICITUD Nº REF / FECHA ENTRADA	
TITULAR	
DOCUMENTACIÓN A COMPLETAR o SUBSANAR ERROR	
Hoja informativa de comercialización (Anexo IV*)	
Certificado de liberación de la Unión Europea de la mezcla de plasma correspondiente (Anexo IId*)	
Certificado de liberación de lote de la Unión Europea (Anexo IIb *)	
Documento acreditativo de cumplimiento de la Circular 1/98 de la Dirección General de Farmacia	
Declaración de que el lote no se ha enviado a otro Laboratorio Oficial de Control de Medicamentos (OMCL) para su liberación (si aplica)	
Documento acreditativo del pago de la tasa 1.13 (si es de aplicación)	
Envío de Muestras o Certificado de liberación de lote por OMCL (si aplica)	
Imagen del Acondicionamiento del medicamento (si aplica)	
Otras causas	

Como consecuencia de ello y hasta que se subsane el defecto correspondiente, no se podrá poner en el mercado el producto, y una vez subsanado el mismo, tras el envío de la documentación solicitada, se deberá esperar el tiempo establecido (5 días naturales) siempre que no haya nueva información de defectos a subsanar

Figure 4 - Request for Clarification Form

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As a result and until the corresponding defect is remedied, the product cannot be placed on the market. Once the problem is fixed, after sending the required documentation, the set time (5 working days) should be awaited, provided that there is no new information with defects to correct.

2.3 Request for Clarification form:

Need of increase previously requested batches

In the same way as the initial application, but selecting the link “Clarifications for Batch Release of Blood Products” (“Aclaraciones a la puesta en mercado de hemoderivados”) rather than “New application”.

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This will load the following screen:

Figure 5 - Clarification Form for the Batch Release of Blood Products

To submit the clarifications the applicant company has to provide the code of the application to which the clarifications are associated with and to load from the XML data file information such as contact details of the person making the marketing application and the clarification data itself. Likewise it allows to attach new documentation if needed.

- In the case of documentation to remedy by mistake in the initial request, will select the option “New file” and is displayed on the tab that the document appears.
- In the case of need of increase previously requested batches, the “New file” option is selected, a new document “Marketing Information Form” is required”(annex IV) specifying the additional number of units of the lot.

From this point the procedure is the same again: after the 5 working days period from sending the last valid documentation without negative decision issued (positive silence procedure), and taking into account the special need for these products, the lot shall be deemed marketed.

2.4 Authorization without 5 days waiting period

Taking into account the potential situations of the special needs of these products, may be the case that the Company make a request not to wait the five working days that the procedure requires. This special situation should be communicated by sending a mail to hemoderivados@aemps.es and uploading a document that justifies the special need.

After reviewing the documentation, if it is correct and if applicable, the DPB will send to the Company (positive pronouncement) a document authorizing the placing onto the market of the batch product concerned, without having to wait the 5 day period specified in the procedure.

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SOLICITUD DE PUESTA EN MERCADO SIN ESPERAR 5 DÍAS

Examinada la documentación aportada según *SOLICITUD* ***Nº*** _____ les notificamos que, ante las razones de urgencia expuestas por su compañía, y teniendo en cuenta la conformidad de la documentación aportada en la solicitud, se les autoriza a poner en mercado:

NOMBRE DEL MEDICAMENTO:
LOTE:
PRINCIPIO ACTIVO:
SOLICITUD Nº REF / FECHA ENTRADA:
TITULAR:
UNIDADES:
FECHA:

Puesta en Mercado de Hemoderivados y Vacunas

Agencia Española de Medicamentos y Productos Sanitarios
División de Productos Biológicos, Terapias Avanzadas y Biotecnología
Parque Empresarial Las Mercedes,Edif. 8, c/Campezo, 1
28022 Madrid
Tlf.00 34 91 822 58 18
Fax 00 34 91 822 58 92
e-mail: hemoderivados@aemps.es

Figure 6 - Authorization form without 5 days waiting period

3. PROCEDURE FOR PARALLEL DISTRIBUTION APPLICATIONS

The Procedure starts when the parallel distributor (pharmaceutical company independent of the marketing-authorisation holder) wants to market a centrally authorised medicinal product from one Member State to Spain.

Before placing a product on the national market the Parallel Distributor should send a request to DPB by mail (hemoderivados@aemps.es) indicating the trade name and batch number of the blood product to be distributed, as well as the country of origin. The DPB will contact with the OMCL of this country of origin asking for a copy of the ANNEX IIB EU official control authority batch release certificate for medicinal products derived from human blood or plasma. Once received, the parallel distributor will be informed that an application should be submitted and the OMCL who signs the European Certificated. In this case it is not necessary the payment of national taxes and, as is stated in pag 8, by clicking the "**Presenta justificante de pago de la EMA**" box.

The documents required are:

- Marketing Information Form, adapted for this purpose (Figure 7):
- Accreditation form issued by the AEMPS, that allows the parallel distributor carry out these activities, and/or Accreditation form issued by the AEMPS Department of Inspeccion y Control
- Accreditation fee paid to the Agency (EMA) for checking that the conditions laid down in Union legislation on medicinal products
- An image (photo or mock-up) of packaging material of the finished product from the batch in question. I should be visible the name and the Company address, the Código Nacional with the IP mention, which indicate on the packaging that the medicinal product is being marketed by parallel distribution

The rest of the procedure is carried out in the same way as the rest of the requests, with five days of positive silence and the option of clarification where appropriate.

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Marketing Information Form

Notificación de intención de comercializar un lote de un medicamento inmunológico o derivados de sangre o plasma humano, que posee autorización de comercialización, en España, procedente de _____

Dirigido a	*Agustín Portela* División de Productos Biológicos y Biotecnología Departamento de Medicamentos de Uso Humano

Nombre Comercial	
Nº lote que aparece en el cartonaje	
Otros nº de lote asociados a este lote	
Nº de envases que se van a comercializar	
Nº Autorización de comercialización	
Nombre y Dirección del Titular de Autorización de comercialización	
Compañía responsable de la Comercialización Paralela	
Fecha de inicio del periodo de validez	
Fecha de Caducidad en el Estado miembro donde va a ser comercializado	
OMCL que emite el Certificados de Liberación de lote	
Fecha prevista de comercialización :	
Nombre y firma de la persona responsible de esta comercialización	
Fecha	

Figure 7: Marketing Information Form adapted ot Parallel Distribution

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