EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Work instructions

Title: Recording, validation and production of certificates of medicinal products		
Applies to: Compliance and Inspections Sector, Parallel Distribution and Certificates Section		
Status: **PUBLIC**		Document no.: WIN/INSP/2029
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1. Changes since last revision

New WIN.

2. Records

Hard copies of requests for Certificates of Medicinal Product (CMP) and all related correspondence are stored in the Certificates office for at least three months and after that archived off site for 10 years. Also, electronic records of the CMP and its corresponding annexes are saved in the certificates database and in the appropriately labelled folders on G:drive (G:\SharedAreas\Certificate\Products).

3. Instructions

This WIN should be read in conjunction with SOP/INSP/2000 Certificates of medicinal products.
The tasks in this WIN are performed by the Certificates assistant (AST).

A CMP is intended to confirm the status of marketing authorisation and GMP compliance in EU/EEA to support regulatory processes in importing countries. The European Medicines Agency can certify a product only if a valid application for Marketing Authorisation or for the Scientific Opinion pursuant to art. 58, has been submitted to the Agency via the centralised procedure.

A CMP consists of the master certificate (M), explanatory notes and annexes. The master certificate is generated by the certificates database. The explanatory notes in all four languages (English, French, Spanish and Portuguese) are saved on the G: drive (G:\SharedAreas\Certificate\Products___templates\New logo). And the annexes are compilations of the product information, in accordance with every individual request.

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A master certificate can be created in English, French, Spanish, any combinations of these three languages or in Portuguese.

The documents needed for this WIN are available on the Agency website: Home > Regulatory > Human medicines > Post-authorisation > Certificates for products > Requesting certificates:

- Application form for European Medicines Agency certificates of medicinal products.
- European Medicines Agency certificates of medicinal products – instructions on how to fill the application form.
- Statement of quantitative composition (Q), if applicable.
- Template for letter from marketing-authorisation holder (MAH) permitting the Agency to send certificates elsewhere than to MAH address.

The rules relating to the Agency's fees are available on the Agency website: Home > Regulatory > Human medicines > Fees.

- Rules of implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures.
- Explanatory note on fees payable to the European Medicines Agency.

Step	Action
Recording requests for CMP	
1	Check the mailboxes for the **urgent** and **standard procedure** at least once a day and flag relevant e-mails as “new request”. The mailbox for the **urgent procedure** can be found in Outlook under Public Folders/ All Public Folders/ Compliance and Inspection/ PDC/ Certificate_urgent (for internal use only). The mailbox for the **standard procedure** can be found in Outlook under Public Folders/ All Public Folders/ Compliance and Inspection/ PDC/ Certificate (for internal use only). ***Note: The timeframe for the urgent procedure is 2 working days, starting on the following working day of receipt of request.*** ***The timeframe for the standard procedure is 10 working days, starting on the following working day of receipt of request.***
2	Print e-mail requesting a CMP and all attachments.
3	Is the application form attached as an .xml file? If yes, save the application form on your desktop as 1.xml, open it with the application “CertApplForm” (Forms/Manage from data/Import data/1.xml) and print it out. If application form is received as PDF file, go to step 3.1.
3.1	Contact the company and ask to re-send it as .xml file (by clicking on “Submit by E-mail” field on the form). *Note: For the purpose of this WIN, the word company refers to the certificate requesting company.*
4	Upload the application form in the certificates database: from the main menu, click on PDF Import, type the name of the file (1.xml) in the “PDF Filename”, click on “PDF Import” and then “Copy to new order”. A new record has been created in the certificates

Step	Action
	database and a five-digit number has been assigned to it. This is the request number. ***Note: The urgent requests are marked in <u>RED</u> in the certificates database.***
5	Check that the following fields have been populated: • SAP. • Billing details. • Delivery address and e-mail. • Job status: standard or urgent. • Fee (ensure it is the current fee and it corresponds to either the standard or urgent procedure or €0 if SME box is ticked). • Company reference.
6	Type in manually the following fields according to the application form: • Number of sets. • Total number of certificates. • Received on (received date of email). • Choose between H (human medicinal product) or V (veterinary medicinal product). • Product Name(s) (choose from the drop-down menu). Please fill in only the first word of the product name in this field (e.g. Product Name HCT, choose from the drop-down menu Product Name and manually type HCT in the "Note" field, in order to have the full name of the product. • Note, if applicable (in case of product name with two or more words).
7	No later than the day the procedure starts, send e-mail acknowledging receipt of request and start of the procedure and notify the requester about the applicable fee.
8	Print record for request of certificates by clicking on "Print request" and put all the documents in a plastic folder.
Print GMP status confirmation and product status report	
9	Print "Post authorisation application" report from SIAMED Human or Vet depending on the product: Reports/m. Summary of procedures/b. Post authorisation. Type in the product name. Sort by "g. Notification/Opinion" and "h. Commission", Descending. Tick "Include renewal appplications". OK.
10	Print "Product Information" report from SIAMED Human or Vet, depending on the product: Reports/c. Product Information. In the field "Product Nr." type in the name of the product. Make sure only "Presentations data" is ticked. OK. Print.
11	Put all the reports in the plastic folder together with the request.
Validation of requests for CMP	
12	Validate request for CMP. Get all the documents out of the plastic folder in order to do the checking and validation of the request.
12.1	Validation of Part A of the application form: • Check that the MAH's or Opinion Holder's name and address are correct (Section A.2. on the application form). • Check if SME field is ticked on the application form. If yes, check that a SME status confirmation letter is provided, the SME field is also ticked in the certificates database and the fee is EUR 0.00. If a valid letter is not provided, write down the issue in the certificates database in "Remarks (internal use)" field. • If the requesting company is not the MAH, check that Section A.3, Note (13) on the application form is ticked, a permission letter from MAH is provided and that names

Step	Action
	and addresses of MAH and requesting company are the right ones in the permission letter. It is preferable to use the permission letter template published on the website, but different formats can be accepted, provided that the information included is at least the same. If the permission letter is missing or it is incorrect, write down your findings in the certificates database in “Remarks (internal use)” field. • Check Section A.4 Precondition for acceptance of a request for certificates on the application form. If “restricted” is ticked, add your findings in the “Remarks (internal use)” field. • Check that customer number on the form and in certificates database is the same. • Check that the current fee is assigned to the request. • Check the form is dated and signed (Section A.6 of the application form).
12.2	Validation of Part(s) B of the application form: • Check that the product(s) and presentation(s) included in the request are either authorised via the centralised procedure or a centralised application has been submitted to EMA or an application under Article 58 of Regulation (EC) no 726/2004 has been submitted to the Agency. If one or more products or presentations requested are not centralised, reject the request, write your outcome in the certificates database in “Validation outcome” field and the reason(s) in the “Remarks (internal use)” field and inform the company about the reasons for rejection. • Check that GMP status is OK for all sites included in the request. If clarification is needed regarding the sites and/or the GMP status, write down your findings in the certificates database in “Remarks (internal use)” field. • Check that the importing countries for each set of certificates are included in the list of countries, territories and currencies edited by the European Commission (link is available on the EMA website). If not, write down the issue in the certificates database in “Remarks (internal use)” field. • Check that for each set of certificates requested, only one presentation or all the presentations in a given pharmaceutical form are requested. If not, write down the issue in “Remarks (internal use)” field in the certificates database. • If statement of quantitative compositon is requested, check that it is available on the G:drive or it has been included in the request using the template published on the certificates webpage of EMA website and that the composition stated is consistent with the one in the Agency database. If not, write down your findings in “Remarks (internal use)” field in the certificates database. • Check that the total number of certificates and the total number of sets in the application form match the total number of sets and certificates in the certificates database. If not, update the certificates database in accordance with the application form.
12.3	Check your issue(s)/findings list in “Remarks (internal use)” field in the certificates database. If there are any issues, record the outcome of the validation as on hold, fill in the date in “Co contact” field and go to step 12.4. If no issues, go to step 13.
12.4	Compile all your findings (issues) in an e-mail to the company and ask for clarification and/or updates.
12.5	If clarifications and/or documents received within 30 working days, check that you have all your issues answered, type in the date you received them in “Reply date” field, fill in the validation date and outcome as accepted and proceed with step 13. If not all issues have been answered go back to step 12.4. If no update received within 30 working days, reject the request, write the validation

Step	Action
	outcome as rejected, fill in the validation date in the certificates database, inform the company about the reason for rejection and proceed with step 28.
Master update/ creation	
13	In the certificates database, in the “Request details” form, open the list of masters by clicking on the number shown under the M column. Choose from the list of masters the one you need to update, by checking the language and the MA Number(s), in accordance with the application form. Click on “Master Number/ Edit/ Yes” to open the master for updating and go to the next step. If the master you need is not in the list, click on “New Master” and proceed with the next step.
14	In the Master Certificate form update/ fill in the following fields: • Master Number: Enter a crescent two digits number/last two digits of the current year/ (e.g. 03/11/). If it is a new master or the master is updated for the first time during the current year, put 01/last two digits of the current year/ (e.g. 01/11/). • Language(s): choose from the drop-down list in accordance with the application form. • MA number: application form against the European Public Assessment Report (EPAR). Certificates can be issued for a single presentation (e.g. EU/0/00/000/001) or for all presentations in one pharmaceutical form (e.g. EU/0/00/000/001-013). Type in “n/a” if the product has not yet been centrally authorised, but a valid application has been submitted to the Agency. For Art. 58 products, type in Art. 58. • Trade name, application form against the EPAR. In case of products not yet authorised, but for which a valid application has been submitted to the Agency, the information is available in SIAMED. • Trade name in the importing country, if applicable, as provided by the requester in the application form. • Active substances, as in the EPAR or in the case of products not yet authorised, SIAMED. • Strengths, as in the EPAR or SIAMED for not authorised products. • Presentations: refers to packaging and pack sizes, as in the EPAR or SIAMED for products not yet authorised. • MA date: the date the presentation has been authorised on the EU market or in case of a range of presentations, the date the first presentation in the range has been authorised on the EU market. Take this information from SIAMED. • MAH, as in the EPAR. • Manufacturing sites: check the information provided in the application form against the GMP status confirmation reports. • MAH status: Tick “a” if MAH is also the manufacturer of the pharmaceutical form, “b” if MAH is the packager or “c” if MAH is involved in none of the above. • SPC from Commission Decision (CD): enter the latest variation approved that has affected the annexes and the approval/completion date, according to the “Post authorisation application” report from SIAMED. Use the format: “variation type/variation number date (dd/mm/yyyy)” (e.g. IA/0059 15/02/2011). In order to establish which is the latest variation look up the most recent date under the “Commission decision date” column, make sure the status is completed or accepted and annexes affected are listed. • On market: choose from the drop-down menu, according to the appplication form. It

Step	Action
	should be yes if at least one presentation is marketed in at least one EU country. For Art. 58 products it should read: “Not applicable. Applications submitted under Article 58 of Regulation (EC) No. 726/2004 are intended exclusively for markets outside the European Union.”
	• Authorised: choose from the drop-down menu: for centrally authorised products, the options are: yes, yes under exceptional circumstance or yes conditional approval (this information is available on the EPAR and in SIAMED database). For products not yet authorised but with a valid application form choose no and for Art. 58 products it should read: “Not applicable. The product was submitted under Article 58 of Regulation No. 726/2004 and received a positive Scientific Opinion from the Committee for Medical Products for Human Use (CHMP) thereby confirming that a full scientific review of Quality, Safety and Efficacy data has been undertaken (see also section 2.4).”
	• SPC official: choose from the drop-down menu: “yes” for authorised products including Art. 58 products and “no”, for products not yet authorised but with a valid application form.
	• GMP OK?: choose from the drop-down menu, according to the GMP status confirmation reports. For Art. 58 products it should read “Not applicable (see also section 2.4)”.
	• If not auth. reason: leave the field empty for centrally authorised products. For products that have not yet been authorised, but for which a valid application has been submitted, write “under evaluation”. For Art. 58 products, write “Not required”.
	• Master ready date: by clicking on this field it will update to the current date.
	• Request ID: number of the request.
	• Sent for comment date, if applicable: the date the master has been sent for comments to the requesting company.
	• Comments received date, if applicable: the date the comments are received from the company.
	• Remarks: free text. For Art. 58 products it should read “Application submitted under Article 58 of Regulation (EC) No. 726/2004 and pursuant to Article 6 of Regulation (EC) No 726/2004 of 31 March 2004, in the context of cooperation with the World Health Organization, for the evaluation of certain medical products for human use intended exclusively for markets outside the European Union a Positive Scientific Opinion from the Committee for Medicinal Products for Human Use (CHMP) confirms that a full scientific review of the quality, safety and efficacy data has been undertaken. As the product is not intended for markets within the European Union, the administrative steps required for marketing authorisation to be granted by the European Commission are not undertaken. Manufacturing sites located outside of the European Union are not subject to periodic routine inspections under the Article 58 procedure.” Make sure the “Print remark” box is ticked for the Art. 58 products.
	Once all the above-mentioned fields have been checked and filled in, click on “CLOSE”. The master has been completed and assigned to the request. Close also the list of masters and go back to the request details.
Recording the sets of CMP	
15	In the “Request details” form, click on “Assigned” in order to display the list of all masters assigned to the request.
16	Click on “Master number/Certificate” in order to create a set of Certificates based on the

Step	Action
	master. Repeat this step to create as many sets as requested in the application form and then close this window.
17	In the “Request details” form, click on “List Certificates” to display all these newly assigned certificates and fill in the empty fields according to the application form: Importing country, EPAR, Signed by, Annex and No of C(opies).
18	Then, click on “Sig. Page/Print” in order to print the form “Certificates of Medicinal Products for Signature”, which is the checklist for the rest of the process. Sign and date it and put it in the folder together with all the related correspondence and documentation.
Creating annexes	
19	Create a folder for the latest variation under the product folder on the G: drive. Name it following the pattern: Variation Type-Variation Number (e.g. R-0007, IA-0114, WS-0170 or OD for Original Decision etc.). Save the product information under this folder in English, French, Spanish and Portuguese, following the pattern: Product name-Variation Type-Variation Number-language code (e.g. Product name-II-0110-G-EN).
20	In case of products **not yet authorised**, but for which a valid application form has been submitted to the Agency, the annex is only composed by the statement of quantitative composition (refered to as Q) that is provided by the company following the Agency’s template published on the website. Check the Q against our records (SIAMED), and once validated, stamp it and save it on the G: drive (G:/SharedAreas/Certificate/Products), under the product folder, following the pattern: Q-Product Name-000-lc.PDF, where “000” represents the last three digits of the presentation number and lc the language code. The language code (lc) is: EN for English, ES for Spanish, FR for French and PT for Portuguese (e.g. Q-Product name-001-FR.PDF or Q-Product Name-001-017-EN, in case of a range of presentations or Q-Product Name-001+005+007-EN for random presentations). For **authorised products**, the annex always contains the Summary of Product Characteristics (SPC) and then the requester has the option to add any or all of the following: Statement of Quantitative Composition (Q), Annex II (AII), Labelling (L), Package Leaflet (P) and /or European Public Assessment Report (EPAR). The sequence of the EPAR’s modules are as follows: 1. Summary for the public 2. All authorised presentations 3. Scientific Discussion/ Public assessement report 4. Procedural steps taken before authorisation 5. Procedural steps taken and scientific information after authorisation. Save the EPAR on the G: drive (G:/SharedAreas/Certificate/Products), in the appropiate product folder and follow the pattern: EPAR-Product Name-RevX.PDF (e.g. EPAR-Product Name-Rev19.PDF). In case of a safety warning, the press release, EPAR and SPC are compulsory annexes in addition to the annexes that the company may request, i.e. Q, L, P and/or AII. The sequence of documents is as follows: 1. Press Release 2. Statement of Quantitative Composition 3. EPAR 4. SPC 5. Annex II 6. Labelling 7. Package leaflet 8. Annex IV (if applicable). Add electronically the Agency logo watermark on your newly created annex and save it on the G: drive, under the relevant variation folder following the pattern: Product-Variation Type-Variation Number-lc-000-Annexes. PDF (e.g.: Product name-IA-0081-G-EN-001-PressRelease+QLP+AII+AIV+EPAR Rev19.PDF).

Step	Action
	In case of a certificate for all the presentations of one pharmaceutical form, the annex will only include one presentation, as a relevant example, and this should be the presentation for the highest strength. The settings for the watermark are: Rotation: None, Opacity: 65%, Scale relative to target page: 102% and Location: Appear behind page.
Printing master certificates and annexes	
21	Print the master certificates from Filemaker in accordance with your checklist "Certificates of Medicinal Products for Signature". Open the request and click on "List Certificates". If multiple copies in one set need to be printed open request, go to "Scripts/ Print certificates multiple", type in the number of copies, then click "OK/Short". If only one copy of each set needs to be printed, go to "Scripts/ Print certificate multiple one copy/Yes".
22	Print the annexes from the G: drive (G:/SharedAreas/Certificate/Products) in accordance with your form "Certificates of Medicinal Products for Signature".
Binding the master certificates and annexes together	
23	The sequence of documents is: 1. Master certificate 2. Explanatory Notes (in the same language as the master certificate) 3. Annexes (same language as the master certificate). Checklist when binding: • Certificate number and request are the same on all pages of the master certificate. • Language(s) of the master certificate, explanatory notes and annexes is/are the same. • The name of the product, pharmaceutical form and marketing authorisation number are the same in the master certificate and annexes.
Sending, filing and archiving the Certificates	
24	From certificates database print cover letter and a summary of the certificates requested. Go to "Requests/Open req.". Then open the request you need to dispatch by clicking on the request number and then go to "Processing list". This will bring up a list of all pending requests. Go to the request you need to dispatch, click on "Process stops on (Letter date)/Yes" and the system will automatically fill in the current date. Fill in "Days to issue": count the days from the next working day the request has been received until the date the process stops. Do not count bank holidays, weekends and the days in between "Contact with company" and "Reply received". Then click on "Print letter", choose 2 copies and OK.
25	For the **urgent procedure** only, click on "Fast Track e-mail", confirm if the application has been processed in time and send an e-mail to the company informing them about the outcome of the procedure. If certificates are not dispatched within the set time frame (2 working days), confirm the fee change in the database and check that the job status has changed to "LATE" and the correct fee for the standard procedure applies.
26	Perform quality review of the certificates. Check the Certificates hard copies against your checklist "Certificates of Medicinal Products for Signature". • Total number of certificates. • Certificate and request number. • Importing country. • Name of product.

Step	Action
	• MA number. • Language throught the Certificate. • Annexes. • Addressee's name and address on the cover letter.
27	Sign both copies: one copy of the cover letter and summary of the requested certificates go in the plastic folder together with all the other supporting documents and the second copy of the cover letter, the summary of the certificates requested and a copy of the "Samples of Authorised Sigantures" letter go with the certificates.
28	File request and all supporting documents in the relevant company folder. After three months forward request for archiving. Ask the Archiving team for boxes and fill in the excel spreadsheet saved on the G: drive (G:\SharedAreas\Certificate\Products___templates\Archiving).