EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Work instructions

Title: GMP validation of initial marketing authorisation applications, line extensions and variations		
Applies to: P-CI-MQC		
Status: **PUBLIC**		Document no.: WIN/INS/2041
Lead Author	Approver	Effective Date: 29-APR-13
Name: Esther Martinez	Name: David Cockburn	Review Date: 29-APR-16
Signature: On file	Signature: On file	Supersedes: n/a
Date: 25-APR-13	Date: 29-APR-13	TrackWise record no.: 3355

1. Changes since last revision

New WIN.

2. Records

Electronic copies of the completed GMP validation checklists are saved in the appropriate folder in DREAM as follows:

Human medicinal products:

Initial marketing authorisation applications

- Cabinets/01. Evaluation of Medicine/H-C/A-Z/Product folder/02 Validation/Validation Checklist

Line extensions

- Cabinets/01. Evaluation of Medicine/H-C/A-Z/Product folder/05 Post Authorisation/Post Activities/Line extension folder/02 Validation/Validation Checklist

Veterinary medicinal products:

Initial marketing authorisation applications

- Cabinets/01. Evaluation of Medicine/V - C/2. Active applications/A-Z/Product folder/01 Pre Authorisation/02 Validation

Line extensions

- Cabinets/01. Evaluation of Medicine/V - C/2. Active applications/A-Z/Product folder/05 Post Authorisation/Post Activities/Line extension folder/02 Validation

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

3. Instructions

Definitions

- DREAM — Document records electronic archive management
- e-CTD — Electronic common technical document
- EURS — European review system
- GMP — Good manufacturing practice
- MAA — Marketing authorisation application
- MAH — Marketing authorisation holder
- PM — Project manager
- PTL — Product team leader
- PTM — Product team member
- Siamed — Sistema de Información Automatizada sobre Medicamentos, which is a model system for computer-assisted drug registration that enables the EMA to track its core processes and retrieve key registration data.

Templates

- For **new applications** and **line extensions**, the validation checklist template ("GMP validation") is located in the X drive: X:\Templates\Others\Compliance and Inspection\GMP\Inspection Coordination.
- For **variations**, there is no validation checklist template.

Related documents

This WIN interfaces with:

- SOP/H/3001 Type IA variations to centralised marketing authorisations.
- SOP/H/3002 Type IB variations to centralised marketing authorisations.
- SOP/H/3009 Validation of new applications for marketing authorisations, applications for extensions and article 58 opinions.
- SOP/H/3206 Type II variations (30-day and 60-day procedures).
- SOP/V/4004 Type II Variations.
- SOP/V/4010 Type IA variations (single and grouped) to centralised marketing authorisations (medicine for veterinary use).
- SOP/V/4011 Type IB variations to centralised marketing authorisations (medicine for veterinary use).
- SOP/V/4013 Submission of an application for the granting of a Community marketing authorisation.
- SOP/V/4015 Grouping of Type IB variation to centralised marketing authorisation (medicine for veterinary use).

This WIN describes how to perform the GMP validation of initial marketing authorisation applications, line extensions and variations for both human and veterinary medicinal products. This WIN is divided into three sections:

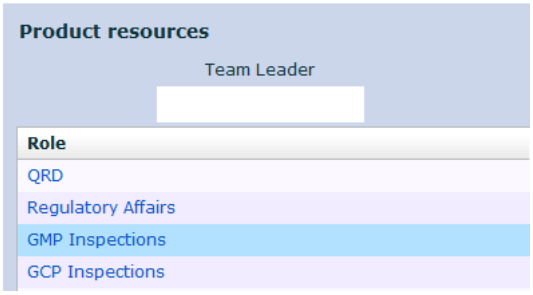
3.1 Monitoring of GxP validation mailbox.

3.2 Validation of initial marketing authorisation applications and line extensions.

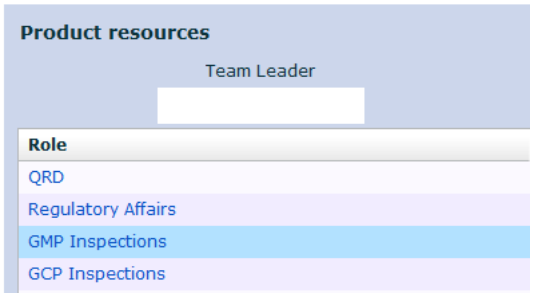
3.3 Validation of variations to marketing authorisations.

Although most of the responsibilities detailed in this WIN lie with the GMP Inspection PTMs (thereinafter referred as GMP PTM), there might be cases in which these tasks are delegated to their assistants (e.g. validation of type IA/IB variations).

3.1. Monitoring of GxP validation mailbox

Step	Action	Responsibility
1.	Check the GXP.validation mailbox at least twice a day. This mailbox can be found in Outlook under Public Folders/ All Public Folders/ Compliance & Inspection/ MQC/ GXP.validation. Receive an e-mail related to the submission of an initial MAA, line extension or variation in accordance with: • step 2 of SOP/H/3009 and step 2.2.1 of SOP/V/4013 (for initial marketing authorisation applications and line extensions); • step 3 of SOP/H/3001 and steps 8/9 of SOP/V/4010 (for type IA variations); • step 6 of SOP/H/3002, step 5 of SOP/V/4011 and step 5 of SOP/V/4015 (for type IB variations); • step 4 of SOP/H/3206 and step 1.1 of SOP/V/4004 (for type II variations).	Assistant
2.	Check in Siamed who is the GMP PTM responsible for the product and forward the e-mail to him/her so that they can start the validation of the new application, line extension or variation. 	Assistant
3.	Record the following information in the Excel spreadsheet ("Ongoing procedures") located in DREAM under Cabinets/04. Inspections/4. GMP/Planning and reporting/GMP inspections coordination: • GMP-PTM • Product name • Procedure number	Assistant

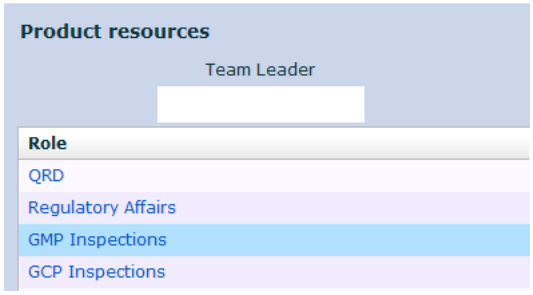
3.2. Validation of initial marketing authorisation applications and line extensions

Step	Action	Responsibility
Upon submission		
1.	Open the relevant e-CTD sequence in EURS (for human medicinal products) or O drive (for veterinary medicinal products). Perform the GMP validation[1] by using the template "GMP validation" located in the X drive (see path under *Templates* above).	GMP PTM
2.	Identify outstanding issues that need to be resolved by the applicant/MAH and set up deadlines for the response: • before the start of the procedure if there are any no-go issues (see checklist template) or • during the procedure (normally by day 10), for all the other issues. *Note: It may be necessary to discuss validation findings with the PTL/PM and/or other members of the product team.*	GMP PTM
3.	Save the GMP validation checklist as "Product name - GMP validation" in DREAM under the relevant product folder (see *Records* above) once it is complete.	GMP PTM
By the validation deadline		
4.	Send an e-mail to the PTL/PM (cc product shared mailbox) with the link to the GMP validation checklist in DREAM, highlighting the GMP issues.	GMP PTM
After the validation deadline		
5.	Receive an e-mail with the applicant/MAH's responses to the validation issues in the GXP.validation mailbox. Check in Siamed who is the GMP PTM responsible for the product and forward the e-mail to him/her so that they can review the responses.  	Assistant

[1] The documents to be checked in the dossier are:
- section 2.5 of the application form, provided in module 1.
- annexes 5.6 (manufacturing authorisations), 5.8 (flow-chart), 5.9 (GMP certificates) and 5.19 or 5.22 (QP declarations for veterinary and human medicinal products respectively), provided in module 1.
- sections 3.2.P.3.1 and 3.2.S.2.1 of module 3 (for human medicinal products only).

Step	Action	Responsibility
6.	Review applicant/MAH's responses and update the GMP validation checklist to reflect whether the issues have been resolved. • If there are outstanding issues, go to step 4. • If all issues are satisfactorily addressed, go to step 7.	GMP PTM
7.	Send an e-mail to the PTL/PM (cc product shared mailbox) informing him/her about the positive outcome of the GMP validation.	GMP PTM
8.	Record the following information in the Excel spreadsheet ("Ongoing procedures") located in DREAM under Cabinets/04. Inspections/4. GMP/Planning and reporting/GMP inspections coordination: • Validation date • Validation status • Day 70/80 AR to be available on • Inspection status	GMP PTM

3.3. Validation of variations to marketing authorisations

Step	Action	Responsibility
Upon submission		
1.	Open the relevant e-CTD sequence in EURS (for human medicinal products) or O drive (for veterinary medicinal products). Perform the GMP validation by verifying that the information provided in the variation application form and related annexes comply with the requirements of the classification guideline. This can be found on the EMA public website > Home Regulatory > Human medicines > Post-authorisation > Variations regulation.	GMP PTM
2.	Identify outstanding issues that need to be resolved by the MAH. *Note: It may be necessary to discuss validation findings with the PTL/PM and/or other members of the product team.*	GMP PTM
By the validation deadline		
3.	Send an e-mail to the PTL/PM (cc product shared mailbox) with the outcome of the validation, highlighting the GMP issues.	GMP PTM
After the validation deadline		
4.	Receive an e-mail with the MAH's responses to the validation issues in the GXP.validation mailbox. Check in Siamed who is the GMP PTM responsible for the product and forward the e-mail to him/her so that they can review the responses.  	Assistant
5.	Review MAH's responses. • If there are outstanding issues, go to step 3. • If all issues are satisfactorily addressed, go to step 6.	GMP PTM
6.	Send an e-mail to the PTL/PM (cc product shared mailbox) informing him/her about the positive outcome of the GMP validation.	GMP PTM