EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

GMP Inspections MAA submission preparedness

12th Industry Stakeholder Platform meeting on the Centralised Procedure

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Agenda

1. GMP Inspections during Marketing Authorisation Applications

2. Type of GMP pre-approval Inspections

3. GMP information at pre-submission, MAA submission (validation) and during the procedure

4. Conclusions

GMP Inspections during MA Applications

GMP compliance of manufacturers is checked at submission of applications for marketing authorisation

Issues noted with GMP compliance information and **GMP inspections during validation and procedures**, especially after the Covid-19 pandemic

**** Delays to MAA validation or MAA procedure***

Applicants can help by providing **accurate information on GMP compliance** at validation on all the proposed sites in the supply chain.

**** avoid delays to validation and allows for pre-approval GMP inspections to be planned as early as possible***

Supply chain information at **pre-submission stage** can support early identification of GMP inspection **and is encouraged.**

Questions on MRA batch testing arrangements can be addressed in this setting.

Inspection readiness of the proposed manufacturers is very important to avoid non-compliances or delays due to the procedure

EMA Pre-authorisation guidance, updated March 2024, **to underline and further explain** points concerning GMP inspections, track changes available

What type of GMP pre-approval Inspections?

What

verify ***compliance with GMP***

cover ***product or process related issues*** from the assessment of the dossier

***not to be confused with routine GMP re-inspections, which do not impact on the procedure timelines.**

How

Adopted by CXMP and announced to the applicant

- **scope** of the inspection
- **target** date for carrying out the inspection
- **inspection team**

When

can take place as early as **D80** and usually take place during the **"clock stop"** period

needs to be finalized before the opinion

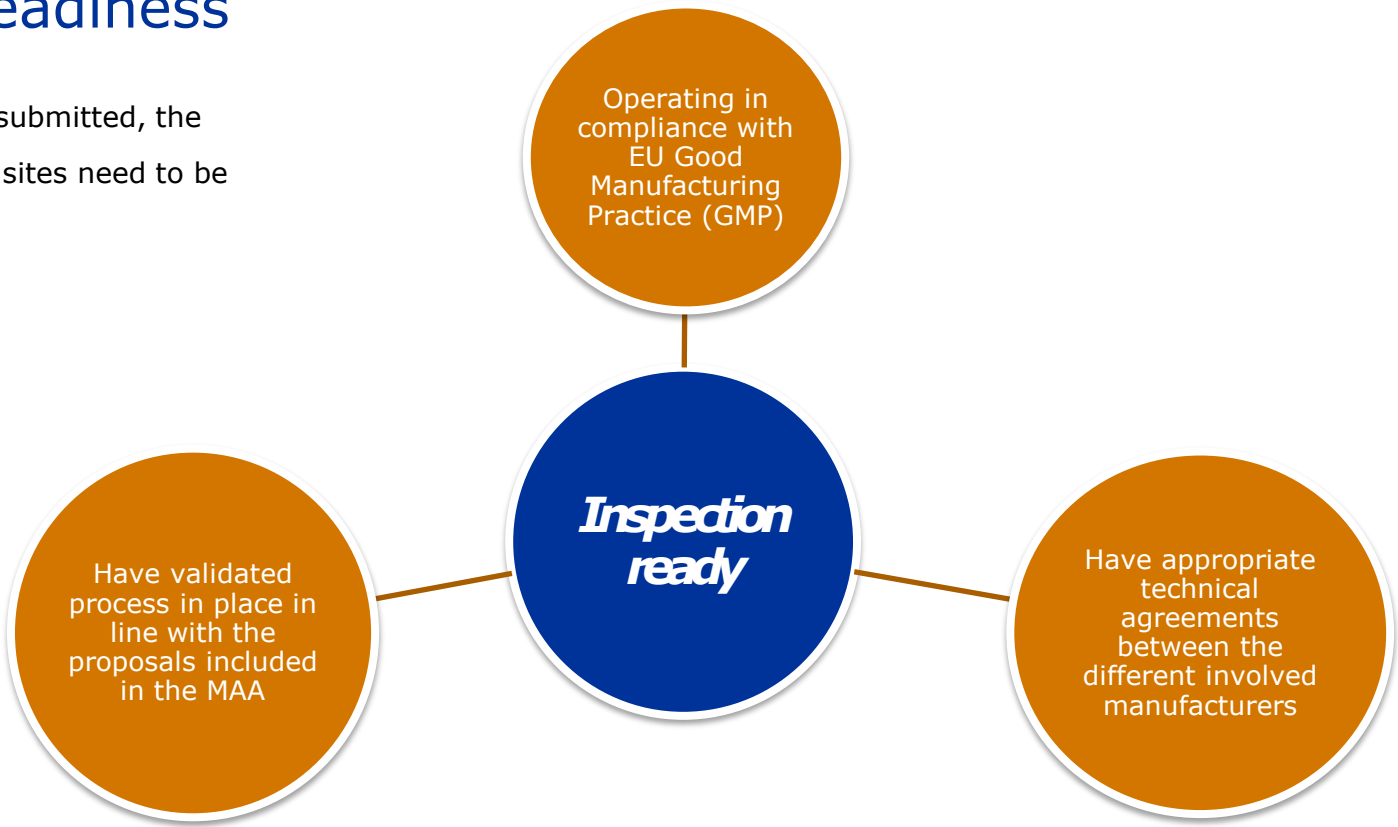
Who

conducted by inspectors of the EEA NCAs (i.e. the Supervisory Authority) and **coordinated** by EMA

*** The Supervisory Authority is the authority of the site where batch release takes place***

Inspection readiness

Once the MAA has been submitted, the proposed manufacturing sites need to be *inspection ready*



Pre-submission

Manufacturing site information and inspection history **encouraged to be provided at pre-submission.**

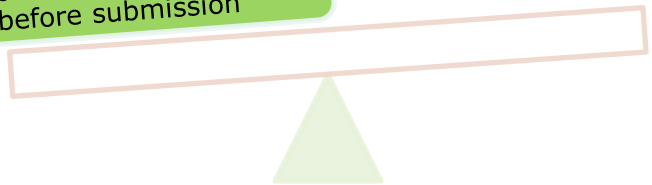
Allows early inspection identification and planning

Identifies potential validation issues

Final manufacturing, testing and release arrangements, including MRA batch testing arrangements

Any changes to be notified as soon as possible before submission

Potential blocking issues at validation or delays to any pre-approval inspections during the evaluation procedure



For accelerated assessments this information is **required** and should be provided in line with the published templates and timelines
Any late changes to the manufacturing, testing and release arrangements can lead to delays in the assessment procedure

Validation

Information concerning GMP in MAA application form:

Annex 5.6 (**Manufacturing authorisations**)

Annex 5.9 (**GMP certificates**)

Manufacturing authorisation are also required for sites located in **3rd countries** as a legal requirement (Article 8.3.(k) of Directive 2001/83/EC)

"manufacturing authorisations or equivalent document showing that the manufacturers are authorised in the country of origin to produce medicinal products"

Absence of the manufacturing authorisation can be a blocking issue for the validation of the application

Not to be confused with the lack of a valid GMP Certificate issues by an EEA authority, which does not satisfy the requirement

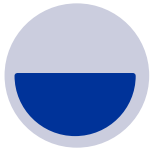
Once the application is validated, it is **normally not permitted to change manufacturing sites during the procedure**, any change should be submitted as a variation

During the procedure

If, during the scientific assessment, updated information regarding **ongoing/planned inspections** of the manufacturing sites by other international authorities (e.g. **MRA Authorities**) become available, this **should be communicated to EMA**

This can help with **sharing of inspection outcomes and collaboration** on inspections

Conclusions



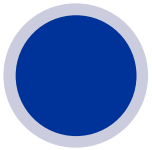
Accurate and timely information on GMP compliance inspections for MAAs are important to support mature applications

Points of note from March 2024 update of EMA pre-submission guidance

At pre-submission, sharing supply chain information is encouraged for all products (not just Accelerated Assessments procedures) to support early inspection planning

At validation, manufacturing authorisations are also required for 3rd country sites and can constitute a blocking issue

During the MAA, ongoing/planned inspections by other authorities should be communicated to facilitate reliance, where possible



Inspection readiness of manufacturers important to avoid non-compliances

Any questions?

Further information

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