EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Regulatory issues in the run-up to dossier submission: Inspections

Veterinary regulatory support for SMEs Workshop,
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Compliance and Inspections Department (P-CI)

Responsible for:

- GMP/Pharmacov. validation of new applications (MQC/CNC)
- Coordination of GMP inspections (MQC)
- Coordination GCP and Pharmacovigilance Inspections (CNC)
- Sampling and Testing (MQC)
- Certificates (PDC)

Full range of activities: please visit EMA website

Preparation of the application (1)

Batch release site

- needs to be located in the EEA
- where the QP performs the duties specified by art. 55 Dir. 2001/82 (Batch Release by QP)
- support document: reference to Eudra GMDP/ Manufacturing Authorisation covering Batch Certification

Preparation of the application (2)

Testing site(s) for the purpose of batch release

- EEA: manufacturing authorisation
- - different MSs have different arrangements for the accreditation of QC labs
- MRA: GMP Certificate /document equivalent to manufacturing authorisation (if available)

Preparation of the application (3)

Contact Person in the EEA for product defects and recalls

Important to have:

- Name of a person
- Email address
- Telephone number

Preparation of the application (4)

Manufacturing Sites (finished product, diluent/solvent, packaging, etc.)

- EEA → support document: reference to EudraGMDP/ Manufacturing Authorisation covering the relevant activity
- MRA→ support document: GMP Certificate /document equivalent to manufacturing authorisation (if available)
- 3rd Countries → support document: document showing that the site is authorised to manufacture in its country + GMP Certificate issued by EU/EEA authority

Preparation of the application (5)

Active substance manufacturing site

- QP Declaration (issued by QPs of finished product manufacturing sites and of Batch Release sites) – *different from Batch Release by QP*
- It is possible for one QP to take responsibility for all the QPs involved
- Template available (draft)
- A reference to an audit is expected

Flow-Chart showing sites and activities

Preparation of the application (6)

Detailed Description of the Pharmacovigilance System (DDPS)

- should be provided in **Part 1** of the Marketing Authorisation Application, in accordance with ***VOLUME 9B*** *of The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use – Link: http://ec.europa.eu/health/files/eudralex/vol-9/vol_9b_2011-10.pdf*

- Please see also Q&A - Question 34 and question 37. Link: *http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000059.jsp&mid=WC0b01ac058002d9ad*

- *Other guidance documents at EMA website, pre-authorisation/application guidance page.*

Pre-submission meeting

Request form with list of possible topics to address

- Question 11: do I have to submit samples together with my application?
- Question 29: when can I expect a pre-approval GMP inspection?
- Question 30: can I expect a pre-approval GCP inspection?

Pre-submission meeting request form Question 11: Samples

Reg 726/2004

Art 32: in order to prepare opinion the CVMP may request testing of the product/starting material/intermediate products/other consituent material

The scope: control methods employed and described are satisfactory

Rapporteur/CoRapporteur will indicate: OMCL, size samples, parameters to be tested, how many batches, etc.

Pre-submission meeting request form
Question 29: pre-approval GMP inspections (1)

Reg 726/2004

Art. 33: if necessary to complete the examination of the application the CVMP may require the applicant to undergo an inspection of the manufacturing site

Inspection to be completed by day 210

Pre-authorisation inspections in 3dr countries:

- Manufacturing site never inspected before
- Biological API manufacturing site never inspected before

Pre-submission meeting request form
Question 29: pre-approval GMP inspections (2)

Product/process related inspection:

- to address issues raised as a result of the assessment
- In 3rd countries and in EU/EEA countries

Pre-submission meeting request form Question 30: pre-approval GCP inspections

GCP inspections

- **only**, if requested by assessors (D120 LoQ)
- To be completed by day 210

Post-Authorisation activities (1)
Routine GMP Inspections

Reg 726/2004

Art. 44: initiated by the Commission or the CVMP

- Specific annual re- inspection programme
- 3rd countries sites
- Re-inspected every three years
- Possibility of a deferral (based on information received by trusted international partners)

Post-Authorisation Activities (2)
Sampling and Testing

CAPs can be selected for a post-authorisation surveillance programme (Sampling and Testing Programme)

Confirm compliance with authorised specifications

Risk-based selection of products e.g. immunologicals vs, chemicals, variations, quality defects, etc. + random selection

MAH are expected to cooperate by providing:

- documentation e.g. testing methods, SOPs,
- samples and other testing materials

Post-Authorisation Activities (3) Pharmacovigilance Inspections

- **Routine PhV inspections** of MAH with CAP(s) follow a **three year inspection cycle** in accordance with the risk-based programme described within the procedure. Link: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004942.pdf

- **Triggered PhV inspections**, requested following concerns. Please refer to section 2.5 Pharmacovigilance inspections of VOLUME 9B for the triggers and further information.

Reduced fees for SMEs

Explanatory notes on fees payable to the EMA
(ref:EMA/185964/2012, applies from 4 August 2013)

Inspections basic fee: 20,600.00 Euros

Inspection fee incentives for SMEs

- Pre-authorisation inspection: 90% reduction + deferral
- Post-authorisation inspection: 90% reduction

[Certificates: 100% fee reduction]

When preparing the invoice the system will flag up if a company is a SME