Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Post inspection consideration of regulatory action – Active Substance manufacturer

Potentially critical GMP / GDP deficiencies are independently reviewed by a senior or expert inspector prior to the final classification being confirmed in writing. The active substance manufacturer / distributor will have 7 days from the date of receipt to respond with their proposals for corrective action.

Critical and/or multiple major deficiencies may provide grounds for the Licensing Authority to require the issuance of an EU Statement of Serious Non-Compliance with GMP / GDP. This will prevent batch certification and release to market of medicinal products in the EU containing the affected active substance(s) from the date of publication, unless otherwise indicated. Any previous GMP / GDP certificates will be withdrawn. The Statement of Serious Non-compliance with GMP / GDP will also be publicly visible on the EudraGMDP website (http://eudragmdp.ema.europa.eu/) and international regulatory partners will be informed. Any active substance batches manufactured between the date of publication of the document and any subsequent return to GMP compliance (confirmed following re-inspection) will not be considered suitable for use in dosage forms manufactured for the EU market.

It is normal practice for the active substance manufacturer / distributor to be given the opportunity to respond to the reported GMP / GDP deficiencies prior to taking regulatory action, unless it is considered necessary to do so with immediate effect in the interests of safety.

Regulatory action may also lead to recommendations to the MHRA Licensing Division to consider action against relevant marketing authorisations (MA) or clinical trial authorisations, or applications for such authorisations currently under assessment. No new MA applications naming the site will be approved. The European Directorate for Quality of Medicines (EDQM) may also be notified in cases where the compliance failures impact current CEPs or applications.

There are opportunities for the active substance manufacturer / distributor to submit representations in response to a notice of proposed regulatory action, which will be outlined in correspondence from the Licensing Authority if such action is proposed. This is in addition to the post inspection responses to address the identified deficiencies.

The above actions are not a permanent barrier to manufacturing or distribution activity, and regulatory restrictions will be lifted if the manufacturer / distributor is able to demonstrate (usually upon re-inspection) the effective implementation of corrective actions which address the identified GMP / GDP deficiencies.

Any action taken will consider the potential impact to supply chain for products considered medically critical (products for which there is no available therapeutic alternative, as agreed by the national competent authority). Any restricted regulatory actions taken in the interests of maintaining the supply of medically critical products will be notified by the Licensing Authority as subsequent correspondence.

The regulatory action process is administered on behalf of the Licensing Authority by the Inspection Action Group (IAG). This multidisciplinary group meets regularly, usually fortnightly, to deal with ongoing business and to consider new referrals. Ad hoc meetings may be called by the Chairman for urgent cases. The active substance manufacturer / distributor may wish to provide an interim response to the IAG for discussion at their next meeting, prior to submitting their formal response to the written inspection deficiency notice. The date of the next meeting can be obtained from the site inspector.

It is very important for the company to maintain open communication channels with the IAG throughout the process, and notify any significant changes in GMP compliance (positive or negative), including delays in implementing corrective action commitments, in a timely manner. Contact details will be provided in the initial correspondence from IAG to the company.

October 2017