Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Post inspection consideration of regulatory action – UK MIA, MIA(IMP) and third country manufacturers

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

The deficiencies may provide grounds for the Licensing Authority to require the issuance of a Statement of Serious Non-Compliance with GMP.

For sites located in the UK there may also be grounds for refusal to grant a manufacturing or import authorisation application, or to take formal action against an existing manufacturing or import authorisation.

It is normal practice for a manufacturer to be given the opportunity to respond to the reported GMP / GDP deficiencies prior to taking regulatory action against licences, unless it is considered necessary to suspend licences with immediate effect in the interests of safety. The implications of regulatory action are as follows:

- **The issuance of a Statement of Serious Non-compliance with GMP** will prevent batch certification and release to market of medicinal products from the date of publication, unless otherwise indicated. Any previous GMP certificates will be withdrawn. The Statement of Serious Non-compliance with GMP will also be publicly visible on the EudraGMDP website (http://eudragmdp.ema.europa.eu/). Any 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 batch certification or release.
- **For sites located in the UK: Action against manufacturing licences or authorisations** (either suspension in full or variation to remove specified activities, facilities or sites) will be preceded by a notice period of at least 28 days, unless the Licensing Authority considers that immediate action is required to protect public health. It is a criminal offence under regulation 34(1) of the Human Medicines Regulations to manufacture or distribute medicinal products without the required licence.
- **For sites located in the UK: Action to remove named persons from manufacturing licences or authorisations** (e.g. Qualified Persons). A Qualified Person removed from a manufacturing licence would not be permitted to certify medicinal products manufactured under that licence. Furthermore, unless there are other persons already named on the manufacturing licence as responsible for the relevant role, the holder will also have to submit a variation to propose a replacement in order to maintain a valid licence.

Regulatory action may also lead to recommendations to the Licensing Division to consider action against relevant marketing authorisations (MA) or clinical trial applications (CTA). No new applications (MA or CTA) naming the site will be approved.

There are opportunities for the manufacturer 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 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 manufacturer 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 manufacturer 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.

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