EU MAH GMP Guidance[1]

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Content

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Share some of the interpretations:

1. **MAH Life Cycle Responsibility**: Ultimate responsibility for the performance, safety, quality and efficacy of a pharmaceutical product. Although MAH's (some) activities may be delegated to the manufacturer (or other parties), outlined MAH's responsibilities are retained.

2. The GMP guidelines do not stipulate that where MAH and the manufacturer belong to the same group (but 2 companies with different legal entities), MAH's liability (or delegation of liability) can be reduced. In this case, the liability applicable to MAH is no different from if MAH and the manufacturer come from independent and unrelated companies.

3. **MAH and manufacturers for large groups**: Companies within the group operate (potentially) based on a shared QMS. In this case, although the work related to MAH's duties may be delegated to other companies (entities) within the group, MAH does not delegate actual duties.

4. **Domestic representative of overseas MAH**: Although MAH's GMP-related duties and activities may be delegated to the domestic representative (if any), any responsibility may not be delegated.

5. **MAH Related Responsibilities and Efforts**: MAH companies should establish systems to ensure that they are in sync with current GMP requirements and are continuously updated.

6. **CTD Module 3 Abbreviated Version**: MAH is responsible for communicating the registration to the manufacturer. During the process, MAHs sometimes prepare an abbreviated version of CTD Module 3 for use by manufacturers and QPs, which is acceptable. As long as the abbreviated version is sufficiently comprehensive and subject to formal change control and oversight activities. The provision and use of an abbreviated version of Module 3 shall be set forth in the technical agreement between the parties.

7. **Labeling and Drug Information**: Care should be taken and made to ensure that the contents and changes to the drug label (including package inserts) registered and approved in CTD Module 1/Part 1 are communicated to the manufacturer in a timely manner to ensure that all batches manufactured have correct labeling and drug information.

8. **MA Changes**: MAH should provide the manufacturer's MA change approval and target implementation date, which is another important responsibility of MAH and is a key activity. The manufacturer ensures that each future batch of the drug will comply with the changed MA.

9. **Regulatory commitments**: Managing regulatory commitments (MAHs competent authorities) are areas that have a significant impact on MAH compliance. Management regulatory commitments will become even more important in the future, with the regulatory environment moving towards greater flexibility in the area of post-approval change management (CM) as ICH Q12 approaches, depending on the effectiveness of QMS.

10. **Two-way communication systems**: MAHs establish a robust two-way communication system to facilitate compliance through national authorities, manufacturers, Qualified Persons (QPs) and any

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organization involved in monitoring post-market quality (e.g. complaint and continuous stability monitoring) to facilitate compliance and assurance:

- Manufacturers and QPs can understand the contents of the MA and the regulatory commitments of the competent authority (if have).
- **MAHs has sufficient knowledge of the process details**: the formation of impurities, and the relevant control of finished products and API process lines. This knowledge allows MAHs to ensure API and/or finished product specifications and feedback on these control strategies, if necessary.
- **MAHs are fully understand of the CM activities of the process**: help to ensure that MAHs participate in the regulatory impact assessment of the change, making any necessary notice or requesting the change to the competent authority.
- **MAHs fully inform manufacturers**: any MA changes that affect the process, such as: changing packaging instructions, changing specifications, etc.

11. **Data integrity (DI)**: another area related to MAHs; Without a robust control system to ensure MA-related DI, GMP non-compliance can (possibly) make the result. Therefore, MAHs should establish systems to ensure the integrity and reliability of the data used to perform their duties. GMP-related drug lifecycle data (including relevant MA changes) should be ensured to be reliable, complete, and accurate. MAH shall ensure the long-term security and archiving of the data on which MA depends.

12. **Non-compliance with MAH obligations**: MAH failure to comply with its obligations may (possibly) be suspended, revoked or changed by the competent authorities.

13. **MAH's GMP responsibilities and expectations**:
    - Outsourced activities (outsourcing) and technical agreements
    - Communication with manufacturers and competent authorities (e.g. MA dossier information, changes, regulatory commitments, etc.)
    - Product Quality Review / Quality Review (PQR)
    - Quality defects, complaints and recalls
    - Maintaining the supply of medicines
    - Continuous improvement activities

Reference

1. Website: https://mp.weixin.qq.com/s/_gx7XlU1oWZ9w1H47i5r_A
2. Reflection paper on GMP and MAHs. EMA/419571/2021 Human Medicines, Pharmacovigilance and Committees Division, Ver2. 10Jan2022

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