Dealing with Quality Defects and Rapid Alerts

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• Related procedures
  – GMP non-compliance
  – CEP suspension/revocation
Responsibilities of Manufacturing Authorisation Holders (1)

  - Must have a systems for
    - Recording and reviewing complaints
    - Recalling medicinal products in the distribution network
  - Obliged to report to their Competent Authority any defect in a medicinal product handled under their authorisation that could result in a recall or abnormal restriction in supply.
Responsibilities of Manufacturing Authorisation Holders (2)

• EU GMP Guide 8.8
  – The Competent Authority should be informed if a manufacturer is considering action following:
    • possibly faulty manufacture
    • product deterioration
    • detection of counterfeiting
    • any other serious quality problems with a product

• EU GMP Guide 6.32
  – Need to inform the competent authority of out of specification results and adverse trends from ongoing stability monitoring
Responsibilities: Wholesale Distribution Authorisation Holder

• Art 80 Directive 2001/83/EC (and Art 65 2001/82/EC) : the Wholesale Distribution Authorisation Holder :

• Must have an emergency plan to ensure effective implementation of any recall from the market ordered by the authorities, in cooperation with the manufacturer or marketing authorisation holder
Responsibilities: Member States

• Article 117 of Directive 2001/83/EC and Article 83 of Dir 2001/82/EC
  – Responsibility to take all appropriate measures to ensure that medicinal product batches are withdrawn from the market if
    • harmful under normal conditions of use
    • composition not as declared
    • the controls on the finished product or during the manufacturing process or other requirement of the manufacturing authorisation not fulfilled

• Article 2 of Directive 2003/94/EC
  – Compilation of Community Procedures
    – Handling suspected Quality Defects
    – Rapid Alerts
    – Dealing with GMP non-compliance
Procedure

• Each National Competent Authority (NCA) must have a contact point for reporting suspected quality defects
  – Many NCAs have a special format for being informed

• The NCA that receives the defect notification is responsible for dealing with it
  – May delegate it to the Supervisory Authority
  – If a centrally authorised product is involved EMEA should be informed and will coordinate the process

• NCA evaluates the information provided by the MAH
  – It may require further information

• If a recall is necessary this is agreed with the MAH
Defect notification received by EMEA

- The MAH sends the Defective Product Report Form, with information on:
  - Details on the affected product & batches (including distribution)
  - Nature of the defect
  - Preliminary investigation report
  - Risk assessment to public health
  - Actions taken/planned/proposed
  - Any previous contacts with other authorities (who may have already assessed the issue)
Classification of Quality Defects

– Class 1
  • Defects, which are potentially life-threatening or could cause serious risk to health.

– Class 2
  • Defects, which could cause illness or mistreatment but are not Class 1.

– Class 3
  • Defects which may not pose a significant hazard to health but where a recall has been initiated (perhaps not required by the competent authority) for other reasons, but are not Class 1 or 2.
Time Scales

- Class 1: immediate action with minimum delay
- Class 2: within 24 hours or less
- Class 3: within 48 hours if possible
Rapid Alert distribution list

• EMEA maintains a Rapid Alert list
  – Includes all EEA Member States, MRA partners, WHO and PIC/S participating authorities

• Class 1 and Class 2 Rapid Alerts are transmitted by the initiating authority to the whole list except for class 2 alerts where the distribution of affected batches is known.
National Competent Authority Actions on receiving a Rapid Alert

• Investigation as to whether the affected product/batch(es) are on its own market

• If so, initiate its own procedure for recall
  – The MAH activates the recall
  – Depending on national procedures the authority may also alert potential recipients of the batch

• Monitor the conduct and effectiveness of the recall
GMP non-compliance

• GMP non-compliance notification
  – Issued via EudraGMP to Rapid Alert contact list
  – Issuing authority indicates actions taken or proposed
  – Teleconference may be convened
  – Affected NCAs take coordinated action

• Potential actions
  – Full or partial suspension of MIA or MA
  – Variation of MIA or MA
  – Recall of product(s)/batch(es)
  – Suspension of QP
  – Prohibition of supply
  – Suspension of clinical trials
  – Suspension of CEP
CEP (Certificate of European Pharmacopoeia) suspension

- Notified by EDQM via its own contact list
- CEP suspension invalidates affected marketing authorisations
- NCAs and EMEA take appropriate action
  - Suspend MAs
  - Vary MAs
  - Recall of product(s)/batch(es)
- Suspension of CEP may be triggered by GMP non-compliance
Thank you for your attention!