Dealing with Quality Defects and Rapid Alerts

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Responsibilities of Manufacturing Authorisation Holders (1)

- Article 13 of Directive 2003/94/EEC (and 91/412/EEC)
  - 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  - Responsibility to take all appropriate measures to ensure that medicinal product batches are withdrawn from the market if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!

http://www.emea.europa.eu/Inspections/Defects.html