Recalls of Medicinal Products – Key Requirements and Pitfalls

Wholesale Distribution Conference

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Overview

• Recalls – background and figures for 2015
• Key requirements and pitfalls relating to
  – Customer listings
  – Quarantine actions
  – Communication
  – Recall procedure effectiveness
  – Roles and responsibilities
Legal basis and guidelines

• S.I. No. 538/2007 - Medicinal Products (Control of Wholesale Distribution) Regulations 2007-2013, as amended
• Directive 2001/83/EC Articles 84 and 85b(3)
• EC Guidelines on Good Distribution Practice of Medicinal Products for Human Use (2013/C 343/01)
• HPRA Guide to Good Distribution Practice of Medicinal Products for Human Use
• HPRA Guide for Recall of Medicinal Products for Human and Veterinary Use
Recalls
Recalls

• A recall is the retrieval of a batch or batches of a medicinal product from the marketplace due to a quality defect, MA non-compliance or safety/efficacy issue

• Recalls are risk-mitigating actions that take place to protect the patient, animal or other user

• Most recalls involve wholesalers at some level

• 2013/C 343/01: “Recall operations should be capable of being initiated promptly and at any time”
Recalls: - Wholesaler roles and responsibilities

• Two scenarios affecting wholesalers
  – Where the MAH / manufacturer is responsible for the recall, the recall notification will be issued by the MAH / manufacturer to wholesalers and other customers which it has supplied
  – If the quality defect occurs when the medicinal product is under wholesaler control, the wholesaler will have responsibility for reporting that quality defect to the HPRA. Responsibility for co-ordination of the recall is decided by the wholesaler and the MAH.

Primary wholesalers: MAH / manufacturer can delegate responsibility for co-ordinating a recall to the primary wholesaler

• All recalls on the Irish market must be agreed in advance with the HPRA
Recalls on the Irish market 2015

• 110 recalls of human medicines
  • 35 % to wholesale level
  • 17 % to pharmacy/retail level
  • 45 % to patient/user level
• 13 recalls (12 %) in 2015 due to defects occurring in products when under wholesaler control
  – 8 Cold-chain / temperature excursions
  – 2 Unlicensed medicine on the market issues
  – 2 Erroneous distribution issues
  – 1 Unapproved over-labelling issue
Defects occurring under wholesaler control 2014 - 2016

• Distribution of batches where quarantine of those defective batches had been confirmed to the HPRA as complete (failed quarantine)
• Distribution of batches where those defective batches had previously been subject to a recall (failed quarantine of recalled stock)
• Recalling from the marketplace without informing the HPRA of the defect issue or that a recall was being proposed
• Distribution of expired stock
• These issues, once identified and investigated, resulted in recalls by the concerned wholesaler (in agreement with the HPRA) of the affected stock. Such issues can, and do, lead to patient-level recalls, on a risk basis
Key Requirements
Key requirements

1. Timely generation of accurate, complete customer listing
2. Perform required actions without delay and in full, e.g. effective quarantine
3. Communication to customers and stakeholders, as required
4. Effective recall SOP and evaluation of its effectiveness
5. Roles and responsibilities
Why are these important factors?

• Recalls are risk-mitigating actions that take place to protect the patient, animal or other user

• 51 recalls (46 %) in 2015 were for critical defect issues, i.e. defects which were potentially life-threatening or could cause serious risk to health

• Failure to
  – produce verified, accurate, complete customer listings in a timely manner
  – perform quarantine actions without delay and in full
  – communicate the correct message to the right parties

prolongs unnecessary exposure to defective product
1. **Customer listings**

- GDP Guide: “There should be an efficient and effective method for identifying customers supplied with a product subject to a recall” (Section 5.24)

- Accurate, timely, complete customer listings
  - Required for **targeted recalls** to ensure that all customers within scope are identified. The recall letter will be targeted at those customers
  - Required for **blanket recalls** where the recall letter is sent to:
    - all retail pharmacy businesses (RPBs) registered with the Pharmaceutical Society of Ireland (PSI)
    - any other customer which is not a registered RPB. These customers will not be on the PSI listing. They must be identified through customer listings
Customer listings

• Identify all customers and customer type within the scope of the recall without delay
  – For recalls past primary wholesale level, the process of identifying wholesalers needs to cascade until no further wholesaler is identified in the supply chain
  – For recalls past secondary wholesale level, all wholesalers need to identify their customers including customer type
Timely generation of accurate customer listings

• Accuracy of data in the Inventory Management System (IMS)
  – Customer set-up
  – Batch details
  – How is your information uploaded and is the data verified?
• Batch tracking to pharmacy / retail level offers exact listing
• Robust recall SOP
• Mock recalls
• Trained and experienced staff
2. Quarantine actions

- 2013/C 343/01: “Any falsified medicinal products, expired products, recalled products and rejected products found in the supply chain should be immediately physically segregated and stored in a dedicated area away from all other medicinal products. The appropriate degree of security should be applied in these areas to ensure that such items remain separate from saleable stock. These areas should be clearly identified.”
2. Quarantine actions cont’d

• The quarantine action should be performed without delay upon receipt of a recall communication

• Consideration must be given to all possible locations (e.g. picking, dispatch) where stock may be held

• Recalled stock should be visibly identified as such (e.g. labels)

• The ability to overwrite a quarantine / recall status in the Inventory Management System must be adequately controlled and, for recalled stock, preferably unavailable
Ineffective quarantine

- Lack of effective, timely quarantine creates the potential for defective stock to be supplied after a recall.
- Once identified, an ineffective quarantine of recalled stock usually warrants a reiterated recall to at least the same level as the original recall. Responsibility for coordination of the recall is decided by the wholesaler and the MAH.
- The issue usually poses a higher risk than the risk posed by the original defect, as it is compounded by the time lapse and other factors introduced by the GDP non-compliance.
- A recall report including details of the investigation into the defect, root cause analysis and CAPAs will be required of the wholesaler at which facility the defect occurred.
- The HPRA should be contacted without delay should such an issue be identified.
Quarantine – things to get right

Effective quarantine

- Identify all stock in all potential areas, e.g. picking, dispatch
- For recalls, apply a physical quarantine in a secure area
- Visibly identify recalled stock, e.g. labels
- Block stock electronically, controlling or eliminating access to unblocking
- Quarantine SOP - is it effective?
- Communication within the facility to include all possible stock locations
3. Communication

• Effective communication is key for effective recalls

• Who needs to receive the communication? – accurate customer listings

• What key messages do they need to receive? – importance of clear, concise, approved, recall letter

• How is the email communicated?
  – Recall letters (approved by the HPRA) should always be issued
  – Phone-calls and e-mail may also be employed, where agreed with the HPRA, to communicate a recall action in a timely manner
What is the importance of effective communication?

• If the recall is not effectively communicated, it cannot be expected that the recall will be effective

• Proper planning aids effective communication and is a key element of recall execution

• For receiving wholesalers, the recall SOP should outline how a recall notification, once received, should be communicated both to relevant personnel within the facility and other stakeholders as specified in the recall letter
4. Recall effectiveness

• How does your company evaluate the effectiveness of its Recall SOP?
  – Evaluation of marketplace recalls?
  – Mock recalls?

 2013/C 343/01: “The effectiveness of the arrangements for product recall should be evaluated regularly (at least annually).”

• A once-yearly challenge is a minimum expectation
Mock recalls

• GDP Guide: “A mock recall need not be carried out where the company has participated in an actual recall during the previous year which has utilised the same traceability.”

• Where this justification is provided, it is important that
  – the effectiveness of the actual recall is demonstrated
  – where gaps are identified, appropriate CAPAs are raised; the SOP revised appropriately and the effectiveness of the revised SOP is challenged by way of mock or actual recall

• The actual / mock recall should reflect the complexity of the supply chain within which the company operates in addition to the higher-risk products within the portfolio
Recalls – risk review

Risk Review

Plan

Act

Check

Do
5. Roles and responsibilities

• 2013/C 343/01: The responsibilities of the responsible person include: coordinating and promptly performing any recall operations for medicinal products

• GDP Guide: The recall procedure should include, at a minimum, the following:
  – the role of the RP
  – nominated responsibilities for coordination of the recall action

• Become familiar with your role and responsibility in recalls affecting your facility. Use risk-based mock recalls, challenge the system and address gaps
Summary

• Recalls are often high-risk activities which are carried out to mitigate against a risk posed by a defective medicine to patients, animals and other users.

• Ineffective quarantine and recall actions prevent effective recalls, prolong exposure to the defective medicine and can compound or increase the risk to patients.

• Effective recalls require the ability to identify all affected customers within the scope of the recall; timely completion of actions, effective communication with the right stakeholders, robust procedures and proper oversight.
HPRA contacts for Quality Defects and Recalls

- **Breda Gleeson** (Market Compliance Inspector)
- **Rob Smyth** (Market Compliance Scientific Officer)
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- Note: Out-of-hours contact numbers are listed on [www.hpра.ie](http://www.hpра.ie) as well as on our telephone voice message (+353-1-6764971) when rung out-of-ours.
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