Quality Defects – Recent Trends

GMP & Market Compliance Information Day 2012

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Content & Objective

- Highlight significant trends in Quality Defect area
  - Part I – All 2011 Quality Defects
  - Part II – 2011 Quality Defects & Irish Manufacturers

- Why?
  - These are reaching the market → patient/animals/HCP
  - Key areas to focus on for prevention
# Part I - Quality Defects over the Years

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor</td>
<td>105</td>
<td>147</td>
<td>241</td>
<td>314</td>
</tr>
<tr>
<td>Major</td>
<td>299</td>
<td>345</td>
<td>332</td>
<td>364</td>
</tr>
<tr>
<td>Critical</td>
<td>127</td>
<td>105</td>
<td>173</td>
<td>231</td>
</tr>
<tr>
<td>Not Justified</td>
<td>23</td>
<td>17</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>555</td>
<td>614</td>
<td>751</td>
<td>917</td>
</tr>
</tbody>
</table>
Q: Most Common Category of Defect in 2011?

1. Stability Issues
2. Packaging Component Defects
3. Printed Text Artwork Errors
4. Product Mix – Up
5. Contamination
6. MA Non-Compliances
1. Contamination – 11.2%

2. Printed Text Artwork Error – 10.8%

3. Packaging Component Defect – 10.6%
1. Contamination

- 103 products in total
- 66 (64%) affected Ireland
- 24 recall actions in Ireland

![Pie chart showing the distribution of contamination types: Microbial (44%), Particulate (40%), Biological (11%), Chemical (5%).]
2. Printed Text Artwork Errors

- Errors in SPC, carton, leaflet, blister foil, label text
- Failure to implement /delay updates to text

  - 98 products - 91 affecting Ireland (93%)
  - 17 recall actions in Ireland

MAH inspections (Kevin O’Donnell’s Presentation)
3. Packaging Components

- Packaging defects not related to text
  - Container closure defects
  - Use of immediate packaging of incorrect composition
  - Ampoules shattering upon opening
  - Syringe nozzle breakages

- 97 Products - 79 affecting Ireland (81%)
- 5 recalled in Ireland
Reminder: Contamination

- 103 products in total
- 66 (64%) affected Ireland
- 24 recall actions in Ireland

- Microbial: 44%
- Particulate: 11%
- Biological: 40%
- Chemical: 5%
Contamination & Packaging Components

• Microbial
  • Alcohol swabs contained in packs
  • Infusion bag stoppers

• Chemical
  • Empty plastic bottles contaminated during storage
  • Incorrect composition of vial stoppers
    chemical contamination of finished product
Contamination & Packaging components

- Particulate
  - Coring of Bung
  - Plastic from Infusion bags
  - Glass delamination in vials
  - Metallic particles embedded in glass vial/amp
The **sampling plan** for packaging materials should take account of at least the following:

- the *quantity* received,
- the *quality* required,
- the *nature* of the material (e.g. Primary packaging materials and/or printed packaging materials),
- the *production methods*, and
- what is known of the *Quality Assurance system of the packaging materials manufacturer* based on audits. The number of samples taken should be determined statistically and specified in a sampling plan.

- Inspection only – Is this enough to prevent?
• Should these be applied to packaging components?

• nature and status of the manufacturer/supplier and their understanding of the GMP requirements of the Pharmaceutical Industry

• Quality Assurance system of the manufacturer of the starting material

• the manufacturing conditions under which the starting material is produced and controlled

• the nature of the starting material and the medicinal products in which it will be used
917 Quality Defects - Human & Veterinary Products

QUESTION:
What percentage of the 917 correlate to products manufactured at Irish manufacturing sites?
Fingers on your Buzzers!

1: 10%
2: 25%
3: 33%
4: 50%
5: 77%
6: 95%
## Seriousness of Defects - 2011

<table>
<thead>
<tr>
<th>Human &amp; Vet Products</th>
<th>Critical</th>
<th>Major</th>
<th>Minor/NJ</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>QDRs (Irish sites)</td>
<td>21</td>
<td>146</td>
<td>136</td>
<td>303</td>
</tr>
<tr>
<td>% of all QDRs (classification)</td>
<td>10%</td>
<td>40%</td>
<td>42%</td>
<td>33%</td>
</tr>
</tbody>
</table>

27th September 2012
Minor & Non-Justified Defects

- 136 related to Irish manufactured products
- 121 reported by MAH/Manufacturer (89%)
- Potentially non-reportable

Guidance Note on Reporting Quality Defects
(Presentation Rob Smyth – updates to guide)
12 Defects

- Stability OOS: 59%
- MA Non-Compliance: 8%
- SPC/Printed Artwork Text: 8%
- Packaging Component: 8%
- Cold Chain issue: 17%
Veterinary Product Overview

• No recalls

• No Critical defects

• 2 Major & 10 Minor

• All reported by manufacturer

• Stability OOS results
Human Products

291 Defects

- Packaging Component: 18%
- Printed Packaging/SPC: 13%
- Contamination: 13%
- MA non-compliance: 13%
- Non-compliance with Spec: 13%
- Stability: 13%
- Other: 13%

27th September 2012
• 59 recalls on Irish Market
  • 20% of 291 reported
  • 25% of all recalls on Irish Market
• 27 additional recalls outside of Ireland
Conclusions & Recommendations

• No. contamination cases is high, and often high risk, resulting in increased need for market action

• Packaging components account for a large portion of defects and can also play a significant role in the introduction of contaminants (or are the contaminants themselves)

• Recommend review of potential risks presented by packaging components and introduce measures to reduce
  - Use of guidance for starting materials
  - Annex 8
Conclusions & Recommendations

- No one stand out defect category related to Irish manufacturers – in line with what is seen overall

- Number of minor defects reported by Irish manuf/MAH is high – Review reporting guidance note

- Reporting from Veterinary Manufacturers is low – review reporting procedures to ensure compliance with guidance
Recommendations to potentially reduce contamination:

- More risk-based validation of manufacturing processes
- More risk-based validation of visual inspection processes
- More risk-based qualification of visual inspection equipment
Conclusions & Recommendations

Packaging Components – possible ways to reduce defects

• Better qualification of suppliers

• Improved validation of handling, cleaning and packaging processes
Questions?