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Quality Defects – Recent Trends

GMP & Market Compliance Information Day 2012

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Quality Defects & Recall Manager

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

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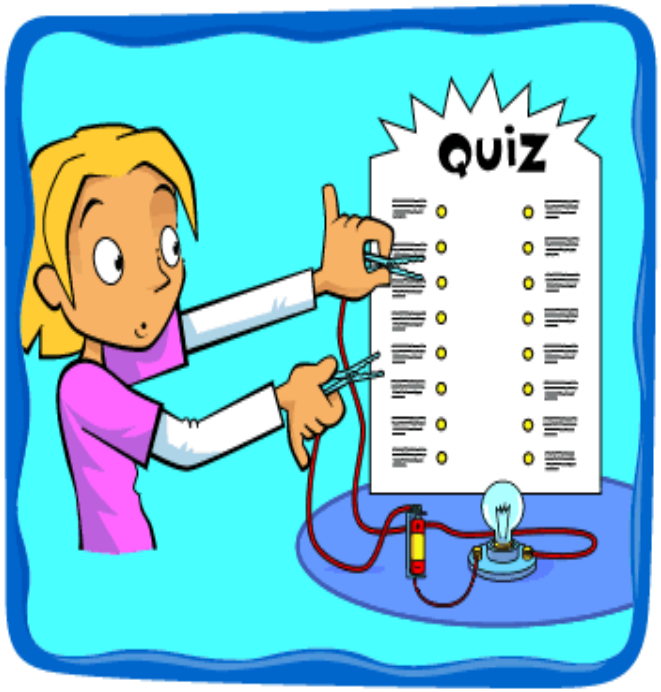
Part I - Quality Defects over the Years

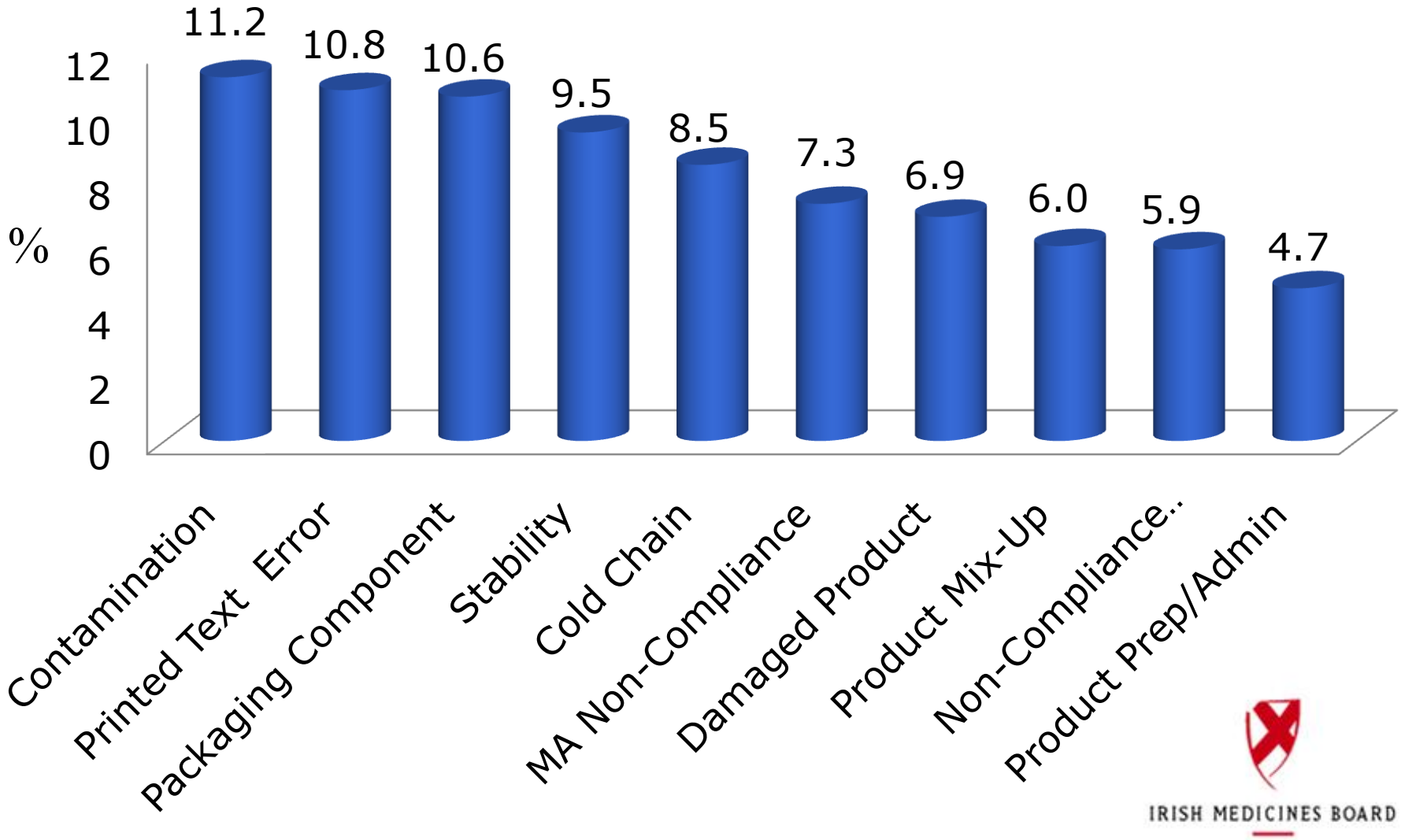
	2008	2009	2010	2011
Minor	105	147	241	**314**
Major	299	345	332	**364**
Critical	127	105	173	**231**
Not Justified	23	17	5	**8**
Total	555	614	751	**917**

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



Category of Defect 2011



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Most Frequent Quality Defect Reports

1. Contamination – 11.2%

2. Printed Text Artwork Error – 10.8 %

3. Packaging Component Defect – 10.6%

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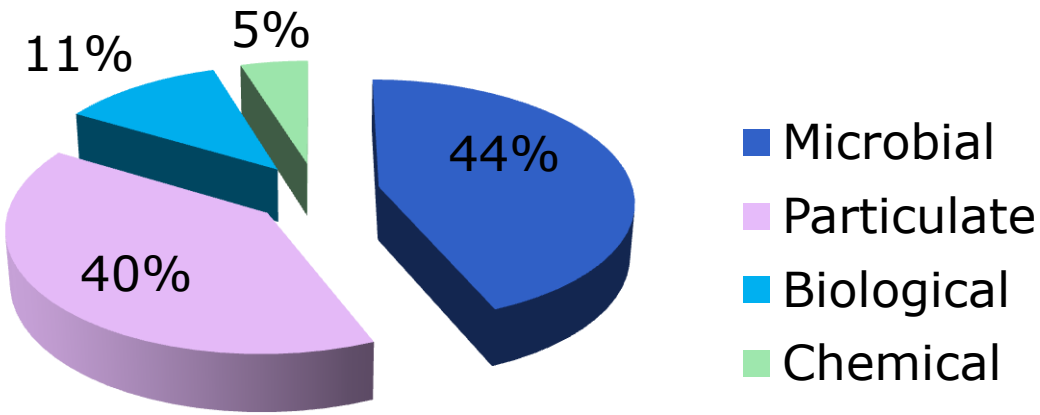
1. Contamination

- 103 products in total



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

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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)

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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

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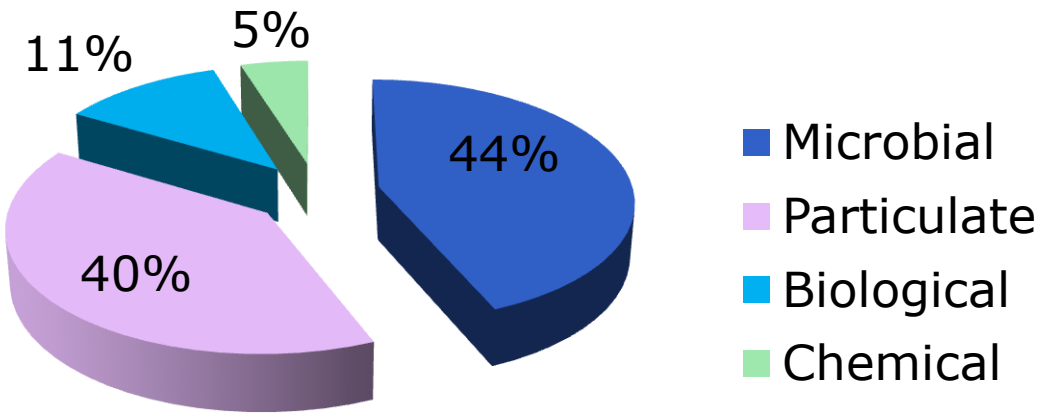
Reminder: Contamination

- 103 products in total



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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

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Contamination & Packaging components

- Particulate
  - Coring of Bung
  - Plastic from Infusion bags
  - Glass delamination in vials
  - Metallic particles embedded in glass vial/amp

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GMP Guide Annex 8

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?

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GMP Guide Annex 8 – Starting Materials

- 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*

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Part II - Quality Defects & Irish Manufacturers

- 917 Quality Defects - Human & Veterinary Products

QUESTION:

What percentage of the 917 correlate to products manufactured at Irish manufacturing sites?

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Fingers on your Buzzers!

1: 10%

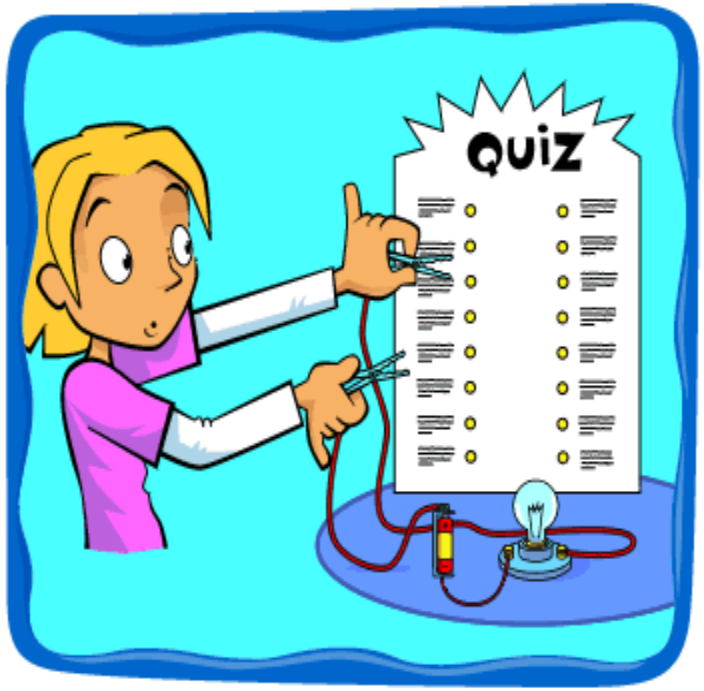
2: 25%

3: 33%

4: 50%

5: 77%

6: 95%



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Seriousness of Defects - 2011

Human & Vet Products	Critical	Major	Minor/ NJ	Total
QDRs (Irish sites)	21	146	136	303
% of all QDRs (classification)	10%	40%	42%	33%

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)

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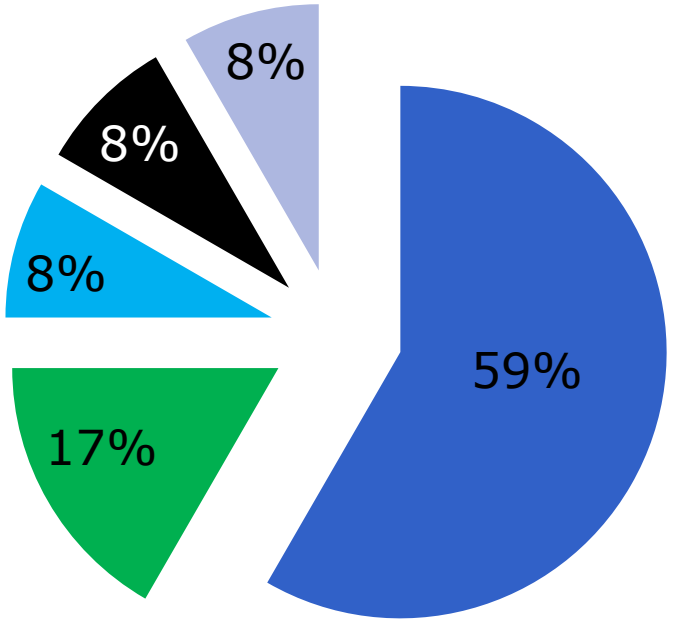
Veterinary Products

12 Defects



- Stability OOS
- MA Non-Compliance
- SPC/Printed Artwork Text
- Packaging Component
- Cold Chain issue

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Veterinary Product Overview

- No recalls
- No Critical defects
- 2 Major & 10 Minor
- All reported by manufacturer
- Stability OOS results

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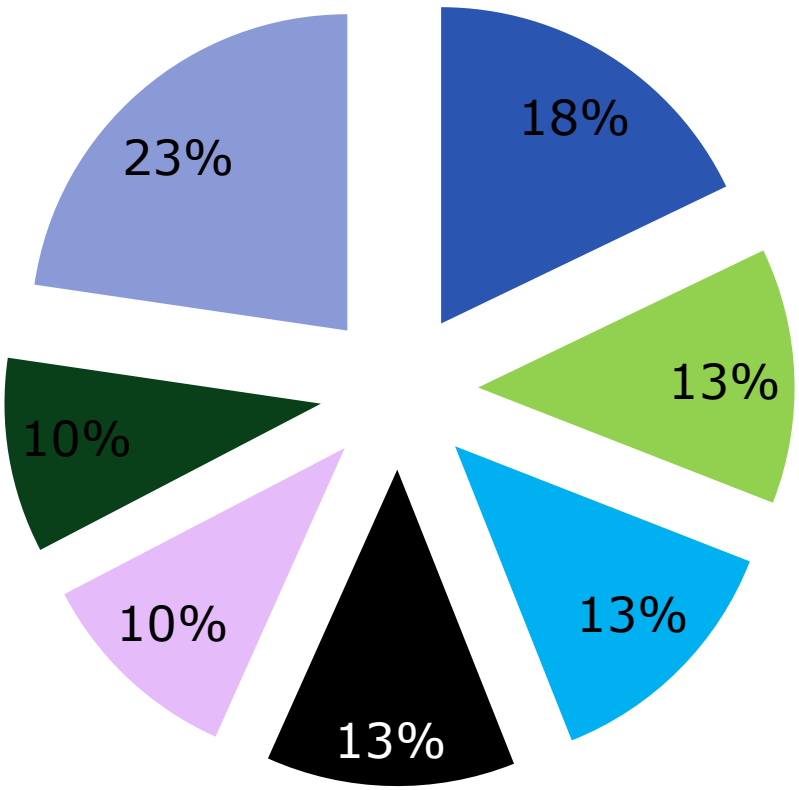
Human Products

291 Defects



- Packaging Component
- Printed Packaging/SPC
- Contamination
- MA non-compliance
- Non-compliance with Spec
- Stability
- Other

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Human Product Manufacture Overview

- 59 recalls on Irish Market
  - 20% of 291 reported
  - 25% of all recalls on Irish Market

- 27 additional recalls outside of Ireland

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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

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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

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Conclusions & Recommendations

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

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Conclusions & Recommendations

Packaging Components – possible ways to reduce defects

- Better qualification of suppliers
- Improved validation of handling, cleaning and packaging processes

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Questions?

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