Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

MHRA GMP Symposium

Novotel London West, London
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#GMDPevents

Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Inspection trends and common deficiencies

Presented by: Vivian Rowland, GMDP Inspector

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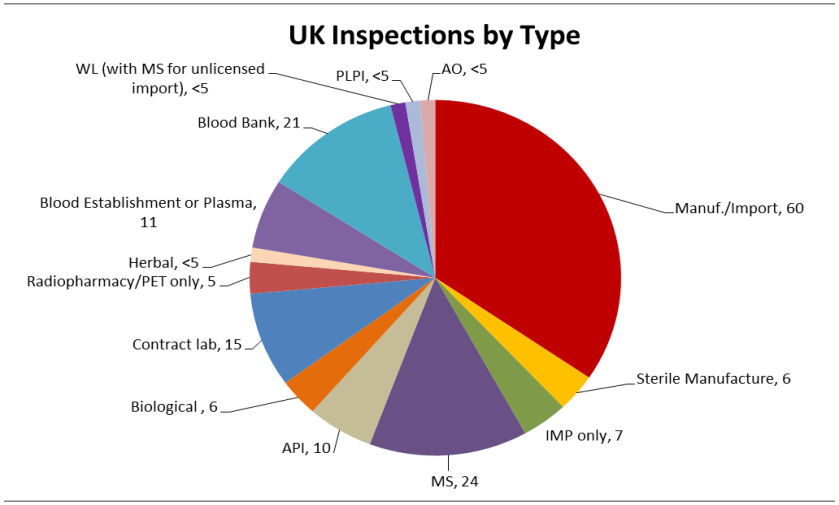
Presentation Outline

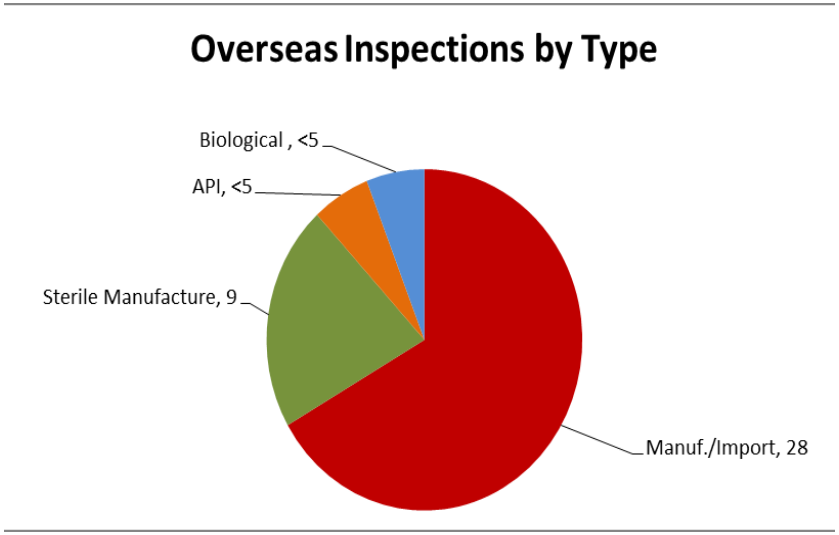
- Improvement in deficiency data trending
- The New Look Data Trend
- 2015 ‘High impact’ inspection findings
- Summary

Question Time

Improvement in deficiency data trending

Data Trending 2013





1. Quality Management 262	3. Materials Management 102	7. Validation 65
Batch release procedures	Supplier and contractor audit	Validation master plan and documentation
Complaints and Product recall	Compliance with TSE guidelines	Analytical Validation
Quality management	Warehousing and distribution activities – General Issues	Cleaning validation
Quality management – change control	Warehousing and distribution activities - Transportation Temp Control and Monitoring	Equipment validation
Quality management – product quality review	Warehousing and distribution activities - General Storage Temp Control and Monitoring	Computerised systems – validation
Quality management – risk management	Warehousing and distribution activities - Lack of inventory control and segregation	Computerised systems – documentation and control
Self inspection	Warehousing and distribution activities - Records – receipt and distribution	Process validation
Investigation of anomalies	Warehousing and distribution activities - Returns Management	Process validation - rework/reprocessing
Investigation of anomalies – CAPA	Starting material – API compliance with GMP	8. Regulatory Compliance 41
Investigation of anomalies – OOS	Supplier and contractor technical agreements	Regulatory issues – non compliance with MIA
Documentation - procedures/PSF/TAs	4. Premises and Equipment 86	Regulatory issues – non-compliance with MA/CTA
2. Production 127	Design and maintenance of equipment	Regulatory issues – unauthorized activity
Sterility Assurance - Aseptic Practices	Design and maintenance of premises	Regulatory issues – non compliance with DMF
Sterility Assurance - Sterilisation	Environmental control	Failure to respond to previous inspection findings
Sterility Assurance - Process Design	Calibration of measuring and test equipment	10. Personnel 38
Sterility Assurance - Media Fill	5. Quality Control 68	Personnel issues – training
Sterility Assurance - Sterility Investigations	Sampling procedures and facilities	Personnel issues – duties of key personnel
Contamination, chemical/physical – potential for	Sampling procedures &facilities – retention & retain samples	Personnel issues – hygiene and clothing
Documentation – manufacturing	Documentation – specifications and testing	
Line clearance, segregation and potential for mix-up	Starting material and packaging component testing	
Housekeeping – cleanliness and tidiness	Computerised systems – data manipulation	
Contamination, microbial – potential for	Finished product testing - chemical	
Status labelling – work in progress, facilities, equipment	Finished product testing - microbiological	
Environmental monitoring	Finished product testing – on-going stability monitoring	
In-process control and monitoring of production operations	Intermediate and bulk product testing	
Handling and control of packaging components	Calibration of reference materials and reagents	
Production planning and scheduling		

Changes following stakeholders discussions

Data changes:

- High impact vs high frequency issues
- All classifications (C, M, O)
- Example deficiencies, with context
- ‘Big data’ opportunities

Reporting and analysis:

- Sub-chapters of EU GMP Guide
- Low frequency-high impact and high frequency low impact issues
- CMT/ IAG/ Regulatory action
- Sector, geography, size

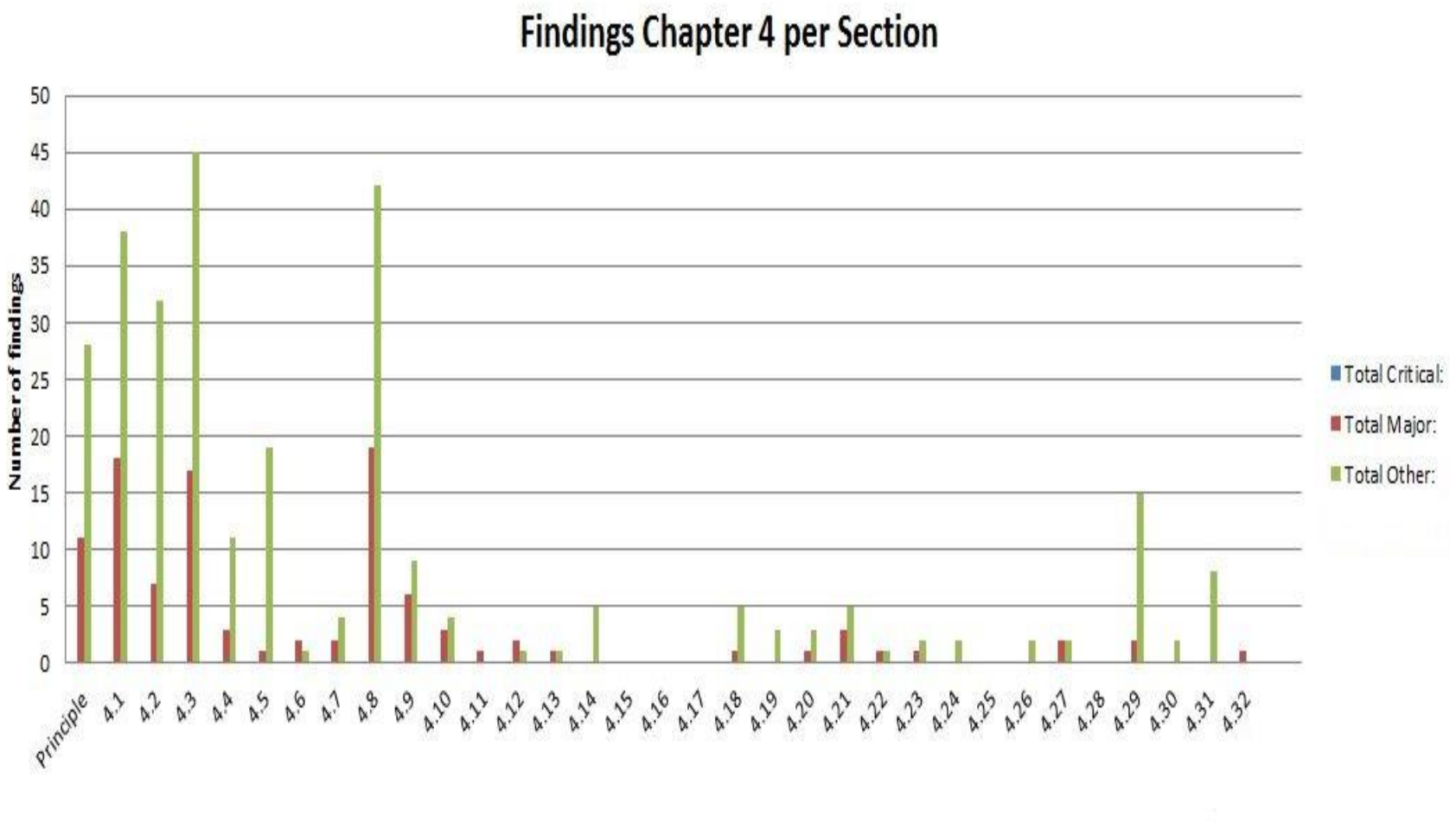
Benefits for Industries

Industries use:

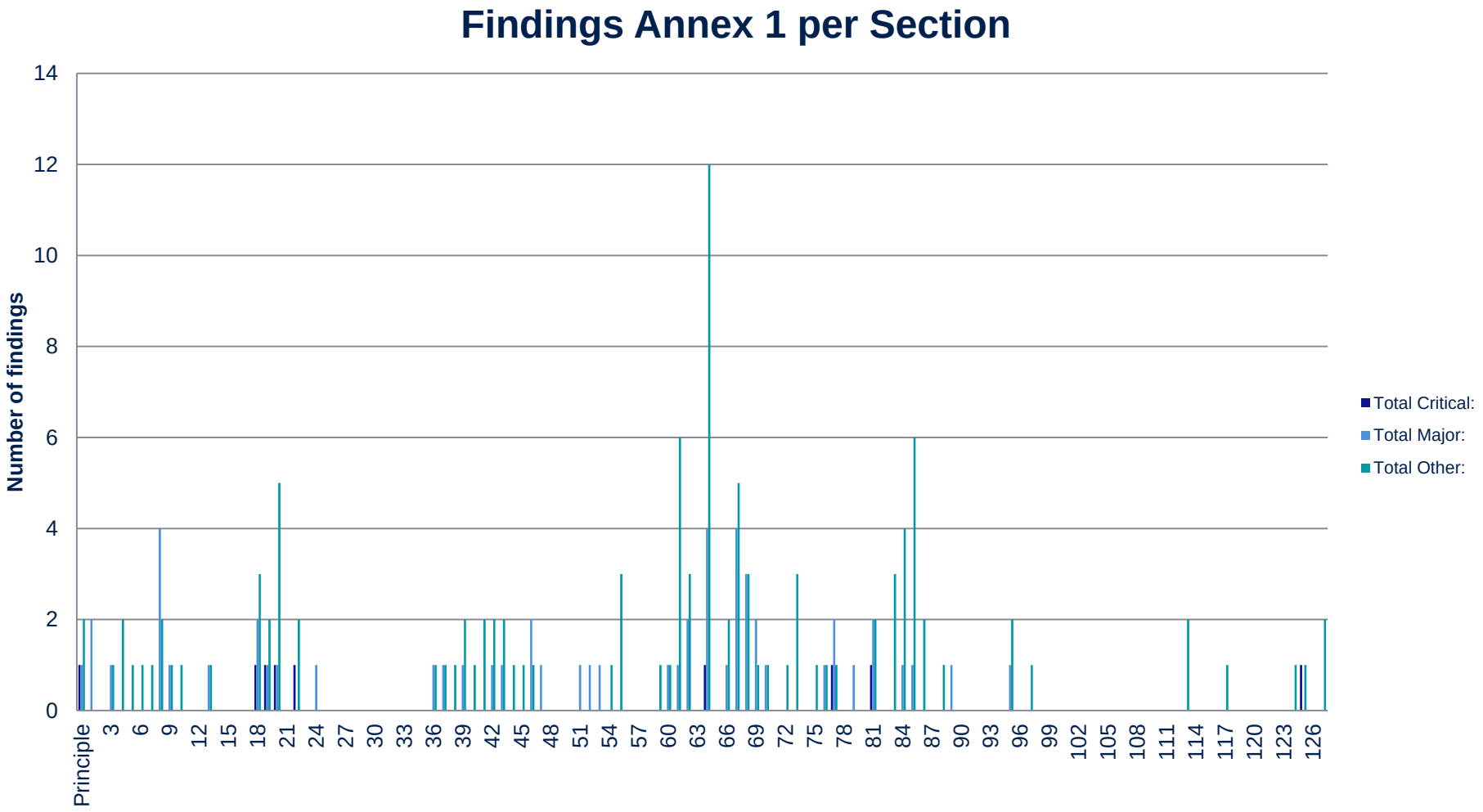
- Organisational learning, self inspection, risk based resource allocation

The New Look Data Trend

New trending tool: example 1



New trending tool: example 1



2015 ‘High impact’ inspection findings

Deficiencies resulted in CMT Referrals

	C1	C2	C3	C4	C5	C6	C7	C8	C9
C					2				
M	25	8	4	12	8	1	3	3	2
O	22	2	5	16	10	18	2	6	3
T	47	10	9	28	20	19	5	9	5

Chapter 1 Principle, 1.1, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8 ,1.10

Chapter 2 Principle, 2.1, 2.2, 2.4, 2.10, 2.11

Chapter 4 Principle, 4.1, 4.2, 4.3, 4.6, 4.8, 4.12, 4.29

Chapter 5 Principle, 5.2, 5.8, 5.12, 5.13, 5.14, 5.15, 5.21

2015 ‘High impact’ inspection findings

Failing PQS

Risk based investigations and actions

Personnel knowledge / experience

Documentation issues

Deficiencies resulted in IAG Referrals

	C1	C2	C3	C4	C5	C6	C7	C8	C9
C	15					1		5	
M	40	13	10	19	19	6			
O	46	11	30	24	20	5	11		3
T	101	24	40	43	39	12	11	5	3

Chapter 1 Principle,1.4, 1.5, 1.8 , 1.9, 1.10, 1.11, 1.12

Chapter 6: 6.27

Chapter 8 Principle, 8.9, 8.13, 8.15, 8.16

2015 ‘High impact’ inspection findings

Failing PQS

Mgmt oversight and resourcing – ICH Q10

Quality defect investigations and actions

Operational cross contamination controls

Failing PQS

Risk based investigations and actions

Personnel knowledge / experience

Documentation issues

Common themes; increasing severity

Deficiencies resulted in IAG with SONC

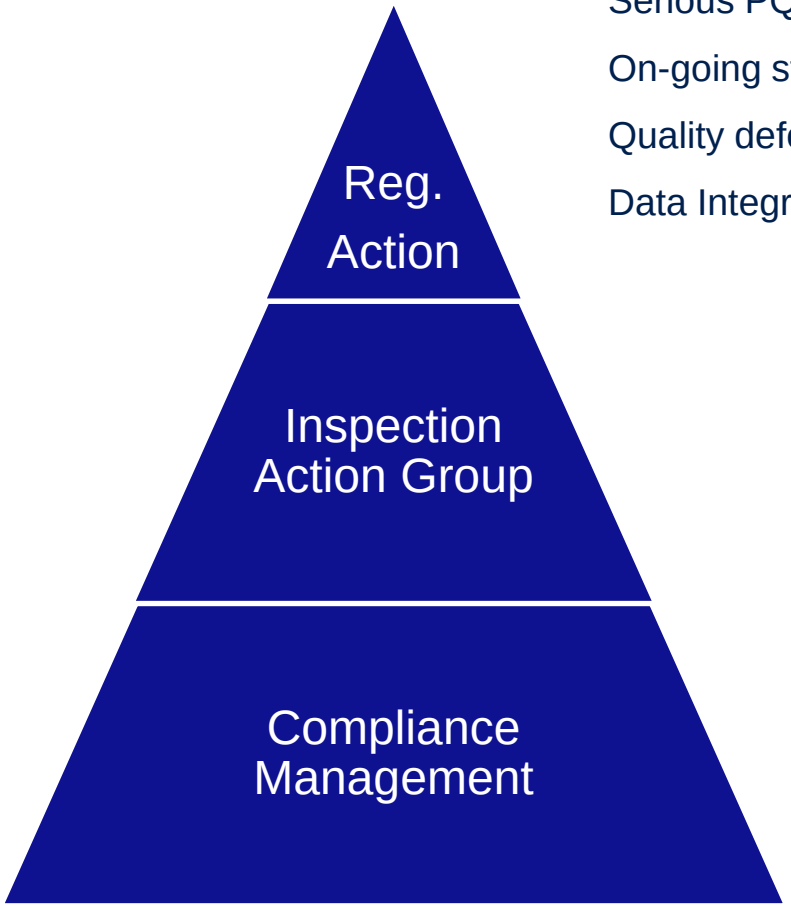
	C1	C2	C3	C4	C5	C6	C7	C8	C9
C	4					1		5	
M	12	1		4				1	
O	3	3		2	2		2		1
T	19	4		6	2	1	2	6	1

Chapter 1: 1.1, 1.4, 1.8 ,

Chapter 6: 6.27

Chapter 8 Principle, 8.9, 8.13, 8.15, 8.16

2015 ‘High impact’ inspection findings



Serious PQS failure

On-going stability programme

Quality defects with public health impact

Data Integrity (basic ALCOA)

Failing PQS

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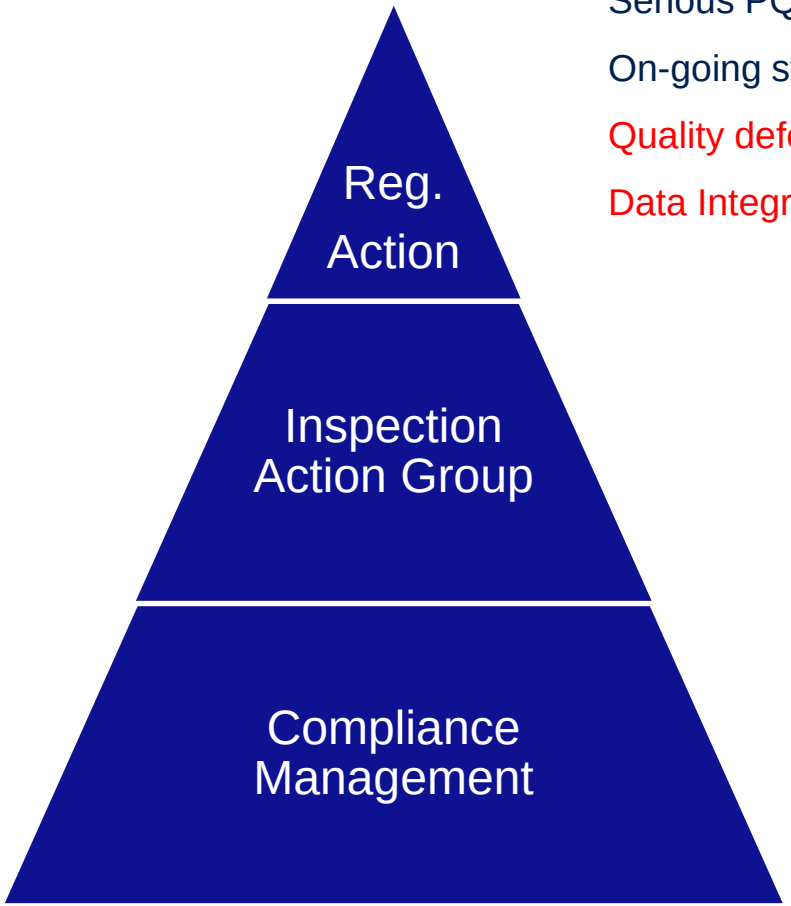

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Important notes

- Deficiencies not from the latest update in Chapters or Annexes, they are failures to be in compliance with basic GMP requirements, e.g.
  - Deficiencies related to DI from Chapter 4
  - Deficiencies related to Chapter 3 & 5 are due to lack of operational controls
  - Lots of IAG/CMT cases were due to the lack of management oversight from Chapter 1

Summary – What we have done

- Trending of all deficiency classifications including “Other” category
- Improved deficiency trending by breaking down into specific sub-chapter of the EU GMP Guide
- Reporting of low frequency-high impact and high frequency low impact issues rather than just frequency
- Set the framework to include data from other regulators to provide a ‘big data’ view in the future

Summary - How we hope this data will be used

- 2015 Trending data will be published in early 2016
- Look out for the Blog with links to GOV.UK to obtain the trend data
- Conduct analysis against the relevant chapters / annexes that are applicable to the organisation / site

New….but Exciting

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