Integrating Transparency into a University Quality Management System

Patricia Henley
Quality & Governance Manager
Head, Research Governance & Integrity Office (RGIO)
patricia.henley@lshtm.ac.uk

LSHTM

About LSHTM

- LSHTM is a leading centre for research and postgraduate education in public and global health
- School has over 4000 students, 1200 staff and 20000 alumni working in 180 countries worldwide
- Income from research grants £110 million in 2015-2016, including:
  - £36.7 million from charities
  - £33.9 million from UK government, research councils and other
  - £23.2 million from EU

Research Numbers

LSHTM is legal sponsor for 88 trials:

Clinical Trial of a public health intervention (eg health management, training)	48
Clinical Trial of an Investigational Medicinal Product (IMP) (eg drug)	26
Clinical Trial - Device	8
Clinical Trial - other	4
Clinical Trial of a non-IMP (vitamins etc)	2

Where in the world?

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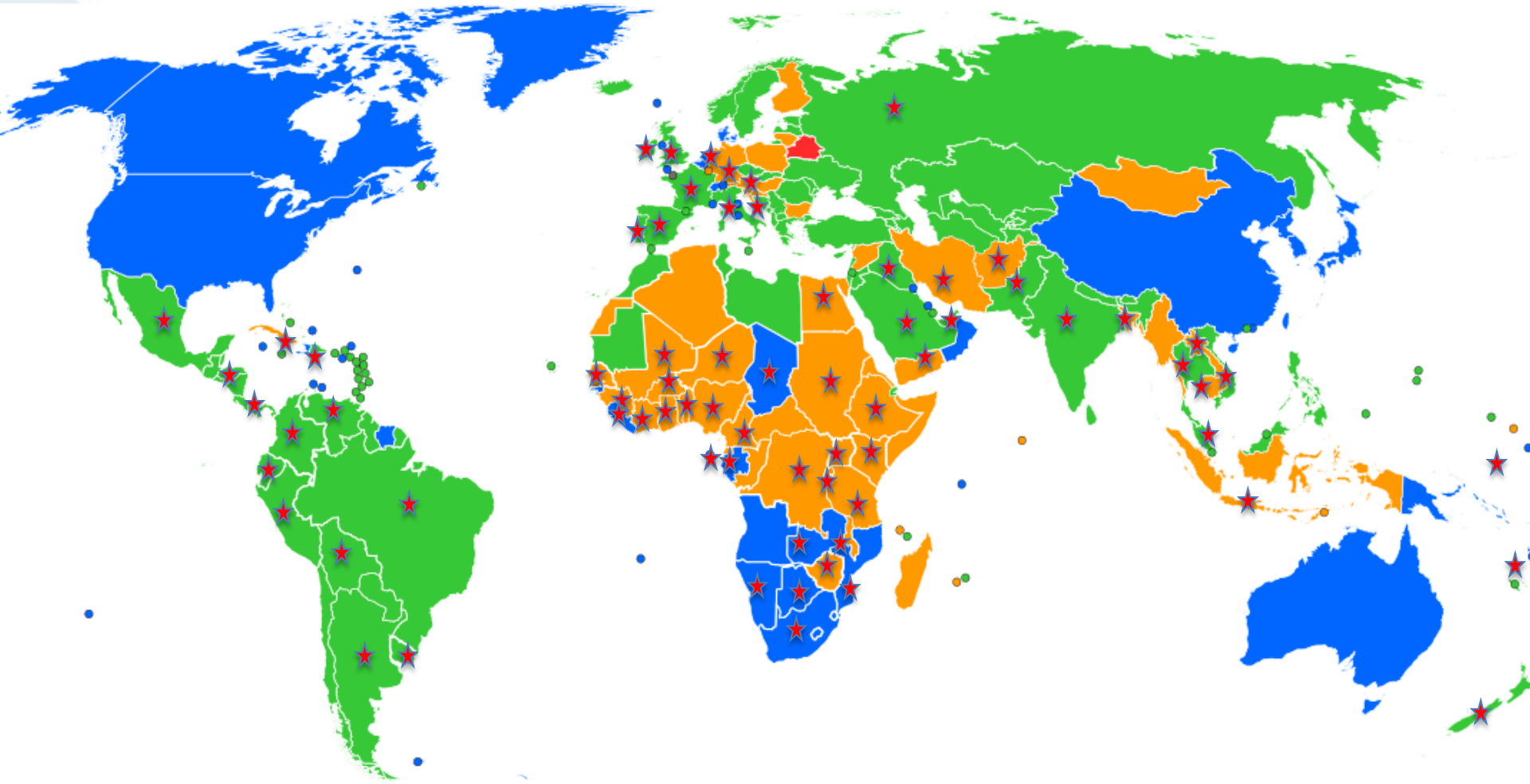
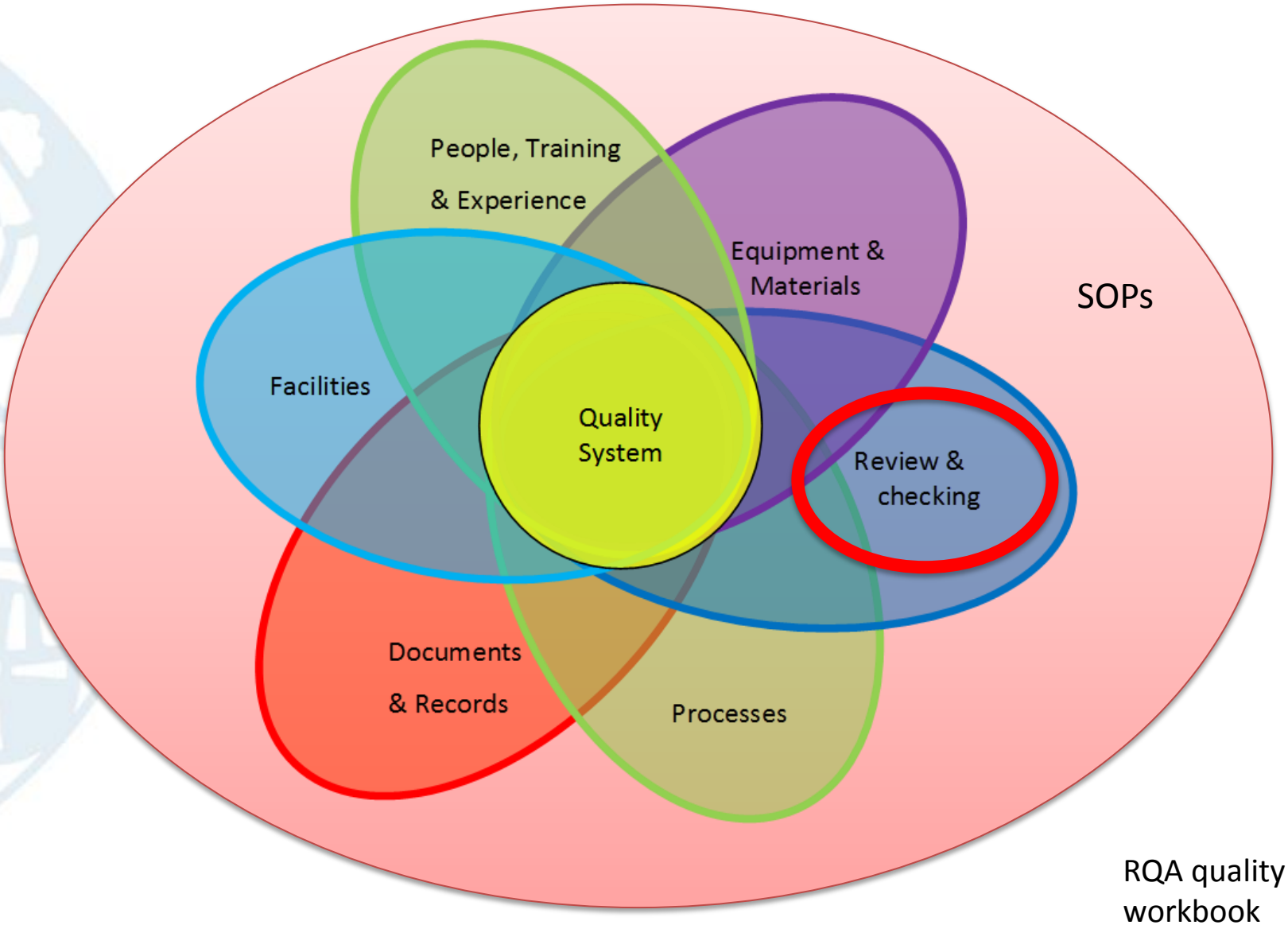


Components of a QMS



RQA quality systems workbook

LSHTM audit programme

- Risk-based approach
  - Risk assessment conducted at sponsor review
  - Consider training, finances, adverse reaction likelihood, project management, care for participants
- Higher risk studies added to audit programme
  - reviewed quarterly
- Aim to conduct 8-10 audits per year
- Tissue holdings: 2 audits/year
- Also conduct for-cause audits

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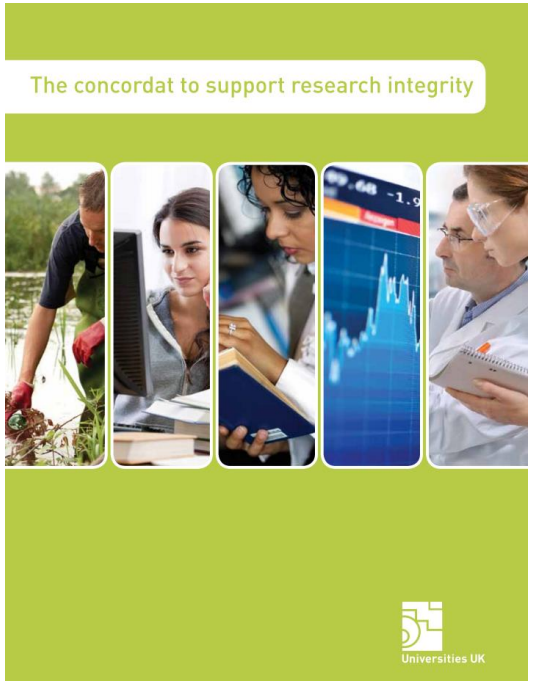
Instilling transparency in the QMS in academia

Concordat to Support Research Integrity

- Provides assurances that the UK research community works to the highest standards of rigour and integrity
- Assures that procedures are in place place for dealing with allegations of misconduct.
  - Including public statement on website



Gap Analysis

- Reviewed Concordat against current practices, policies and procedures
- Highlighted areas of improvement
  - Particularly with regards to transparency of misconduct investigations
- Felt that audit results, as a key component of the School's QMS, should be made more transparent
  - Falls within the spirit of the Concordat

Why transparency?

- To help ensure that all staff can learn from common discrepancies in trial conduct
- Allows the RGIO to
  - target training
  - clarify SOPs and templates
  - share knowledge across LSHTM
  - benchmark findings
- Promotes good practice and integrity in research

Building an audit database

- Over five years' worth of audits (2012-present) have been added to the database
- Findings aggregated into excel spreadsheet from audit reports in word format
- Used DIA TMF reference model as starting point for generating categories and sub-categories
- To assure anonymity, audits are given a number
  - Identifiable details (PI, title etc) are not on the findings database

Audit findings database

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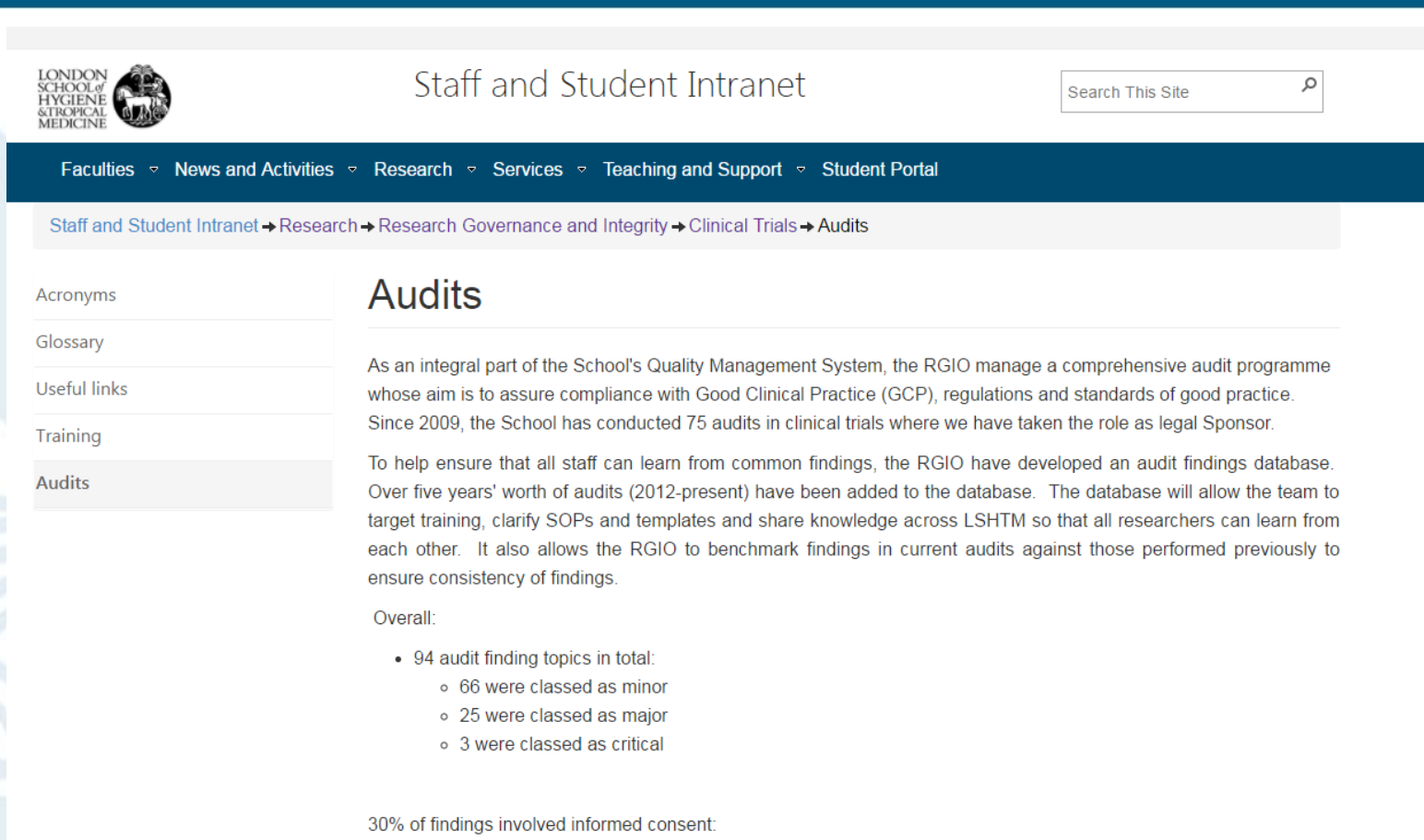
	A	B	C	D	E	F
1	Audit reference	Grade of finding	Finding Category	Finding sub-category	Core or recommende	ICH-GCP reference
2	16-007	Minor	Data Management	Audit trail planning and testing	Core	5.5.3a, 5.5.3c, 5.5.3d
3	13-012	Minor	Data Management	Data Management Plan	Recommended	5.1, 5.5
4	13-013	Minor	Data Management	Data Management Plan	Recommended	5.1, 5.5
5	16-007	Minor	Data Management	Documentation of Corrections to Entered Data	Core	4.9.3, 5.5.3a, 5.5.3c, 5.5.3d, 8.3.15
6	17-001	Minor	Data Management	Documentation of Corrections to Entered Data	Core	4.9.3, 5.5.3c, 8.3.15
7	16-007	Minor	Data Management	System Account Management, eg each to have own log-in suitable to role	Core	5.5.3a, 5.5.3c, 5.5.3d
8	13-013	Minor	Database	Data Entry Procedures	Core	5.1, 5.5
9	16-007	Minor	Database	Validation Documents	Core	5.5.1, 5.5.3
10	13-012	Minor	Essential documents	any document detailed in section 8	core	8.1-8.4
11	13-013	Minor	Essential documents	any document detailed in section 8	core	8.1-8.4
12	13-014	Minor	Essential documents	any document detailed in section 8	core	8.1-8.4
13	16-007	Minor	Essential documents	Various missing	core	2.8, 8.1-8.4, 8.2.3, 8.2.12
14	17-004	Minor	Ethics Committee	Amendments submitted and approved prior to implemntation	core	1.4.5, 8.2.2, 8.3.2
15	13-010	Minor	IMP	IMP Accountability Documentation	Core	4.6.2, 5.14.4, 8.3.23, 8.4.1
16	13-013	Major	IMP	IMP Accountability Documentation	Core	4.6.2, 5.14.4, 8.3.23, 8.4.1
17	15-004	Minor	IMP	IMP Accountability Documentation	Core	4.6.2, 5.14.4, 8.3.23, 8.4.1
18	17-001	Minor	IMP	IMP Instructions for Handling not followed or not accurate	Core	5.13.2, 5.14.3, 8.2.14
19	17-001	Minor	IMP	IMP Unblinding Plan	Core	5.13.4, 8.2.17, 8.4.6
20	13-006	Major	Informed consent	Consent not done per SOPs and GCP (general findings)	core	4.8.1, 4.8.8, 4.8.9
21	13-012	Minor	Informed consent	Consent not done per SOPs and GCP (general findings)	core	4.8.1
22	16-005	Minor	Informed consent	correct completion of informed consent forms	Core	2.9
23	15-007	Major	Informed consent	Inclusion of participant without capacity to consent	Core	4.8.5, 4.8.12
24	13-005	Minor	Informed consent	Incorrect completion of informed consent forms	Core	4.8.8

Critical | Major | Minor | Summary of headings | consent | cat of finding | **Summary of sub-headings** | audit fi

Informing staff - intranet page



Staff and Student Intranet

Search This Site

Faculties | News and Activities | Research | Services | Teaching and Support | Student Portal

Staff and Student Intranet → Research → Research Governance and Integrity → Clinical Trials → Audits

- Acronyms
- Glossary
- Useful links
- Training
- Audits

Audits

As an integral part of the School's Quality Management System, the RGIO manage a comprehensive audit programme whose aim is to assure compliance with Good Clinical Practice (GCP), regulations and standards of good practice. Since 2009, the School has conducted 75 audits in clinical trials where we have taken the role as legal Sponsor.

To help ensure that all staff can learn from common findings, the RGIO have developed an audit findings database. Over five years' worth of audits (2012-present) have been added to the database. The database will allow the team to target training, clarify SOPs and templates and share knowledge across LSHTM so that all researchers can learn from each other. It also allows the RGIO to benchmark findings in current audits against those performed previously to ensure consistency of findings.

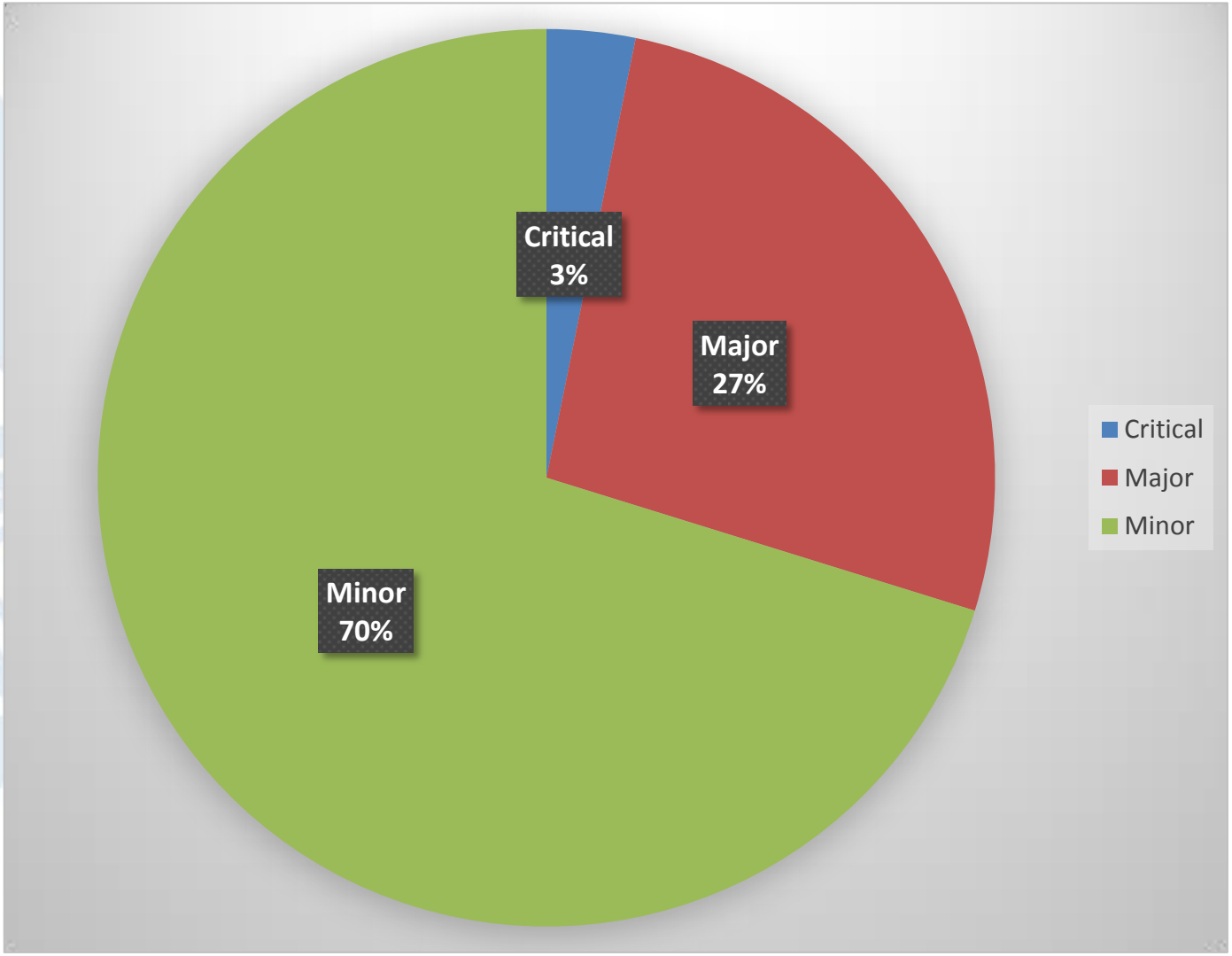
Overall:

- 94 audit finding topics in total:
  - 66 were classed as minor
  - 25 were classed as major
  - 3 were classed as critical

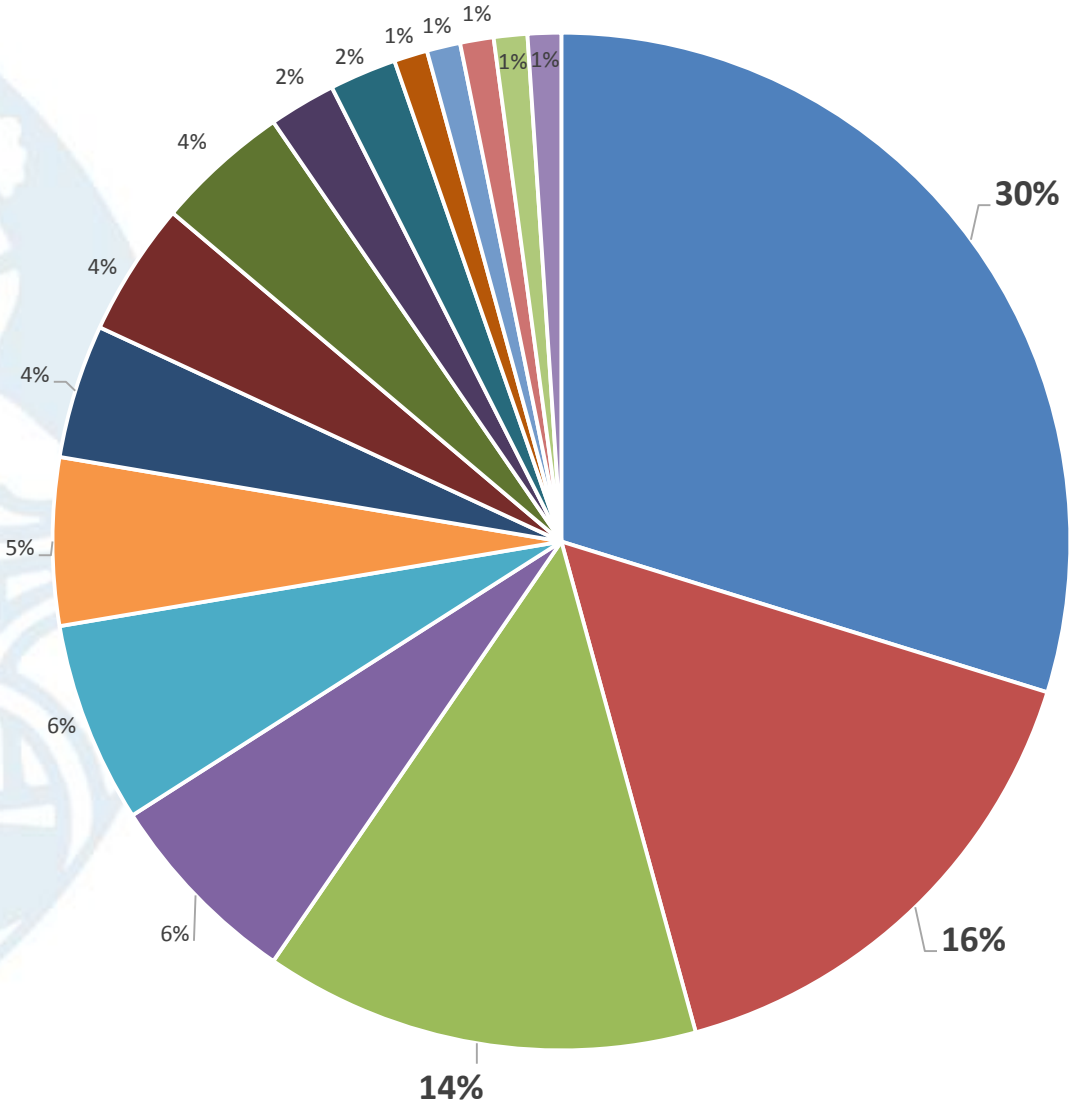
30% of findings involved informed consent:

- Re-consent not done appropriately following waiver/PrLR (35%)
- Informed Consent Form not written per SOP with all required elements (35%)
- Incorrect completion of informed consent forms (18%)
- Incorrect use of impartial witness (7%)
- Inclusion of participant without capacity to consent (4%)

Category of Finding



GCP Categories

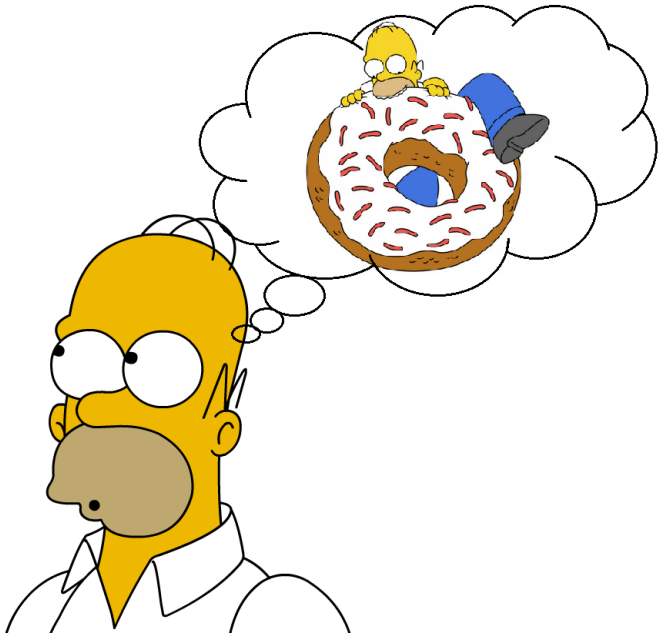


- **Informed consent**
- **Site Management**
- **Laboratory**
- Safety Documentation
- Data Management
- IMP
- Essential documents
- Protocol
- Monitoring / QC
- Protocol Management
- Database
- Ethics Committee
- QA / QMS
- Trial Management Team
- QA/QMS
- Regulatory Authority Approval

Drilling down: consent

Informed consent	n
Re-consent not done appropriately following waiver/PrLR	10
Informed Consent Form not per SOP with all required elements	10
Incorrect completion of informed consent forms	5
Incorrect use of impartial witness	2
Inclusion of participant without capacity to consent	1
Total	**28**

Next steps



What next?

- Add further years to the findings database
- Move from excel to a relational database
  - To be queriable by PIs
- Incorporate into GCP teaching, newsletters
- Trial CAPA plans to be amalgamated to ensure robustness of PI's response

Concluding thoughts

- Undertaking this exercise was beneficial:
  - PIs can see common findings
  - Targeted messages to PIs on key areas of improvement
  - Allows benchmarking of audit findings to ensure consistency
- Continuous review of the audit programme by all staff
- Greater awareness of issues in research integrity and conduct

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References & Further Reading

- UKRIO
  - www.UKRIO.org
- Office for Research Integrity
  - http://ori.hhs.gov/
- Research Integrity Concordat
  - www.universitiesuk.ac.uk/highereducation/Documents/2012/TheConcordatToSupportResearchIntegrity.pdf
- European Code of Conduct for Research Integrity
  - www.esf.org/fileadmin/Public_documents/Publications/Code_Conduct_ResearchIntegrity.pdf
- Concordat to support the career development of researchers
  - www.vitae.ac.uk/policy/concordat-to-support-the-career-development-of-researchers
- DIA Global TMF model v3
  - www.diaglobal.org/en/resources/tools-and-downloads#Trial-Master-File