GCP Inspection Findings for 2013

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Outline

- GCP Inspection Framework
- Objectives
- Classification of GCP Inspection Findings
- Common GCP Site Inspection Findings
- Quality Improvement Initiatives

GCP Inspection Framework

- Launched in Sep 2009
- First GCP Site Inspection done in Nov 2009
- Completed 50 GCP Site Inspections to date:
  - ► 2009-2010 : 13 (Protocol-specific)
  - ► 2011 : 15 (Protocol-specific), 1 (Systems on ICF and IP)
  - ► 2012: 10 (Protocol-specific), 1 (Systems on ICF and IP)
  - ► 2013: 10 (Protocol-specific)

Objectives of GCP Inspection

- ► To safeguard the Rights, Safety and Well-Being of trial subjects.
- ► To verify the Quality and Integrity of the clinical trial data submitted to the Regulatory Authority.
- ► To assess Compliance to protocol and applicable regulations, guidelines and standard operating procedures for clinical trials.

GCP INSPECTION CRITERIA

Classification of GCP Inspection Findings

~ adopted from EMEA SOPs on GCP Inspection.

- **Critical:** Conditions, practices or processes that adversely affect the rights, safety or well being of the subjects and/or the quality and integrity of data.
- **Major**: Conditions, practices or processes that might adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data.

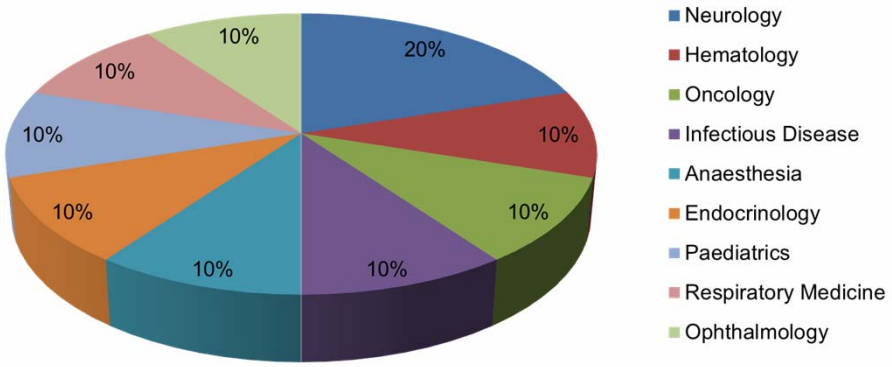
Classification of GCP Inspection Findings

~ adopted from EMEA SOPs on GCP Inspection.

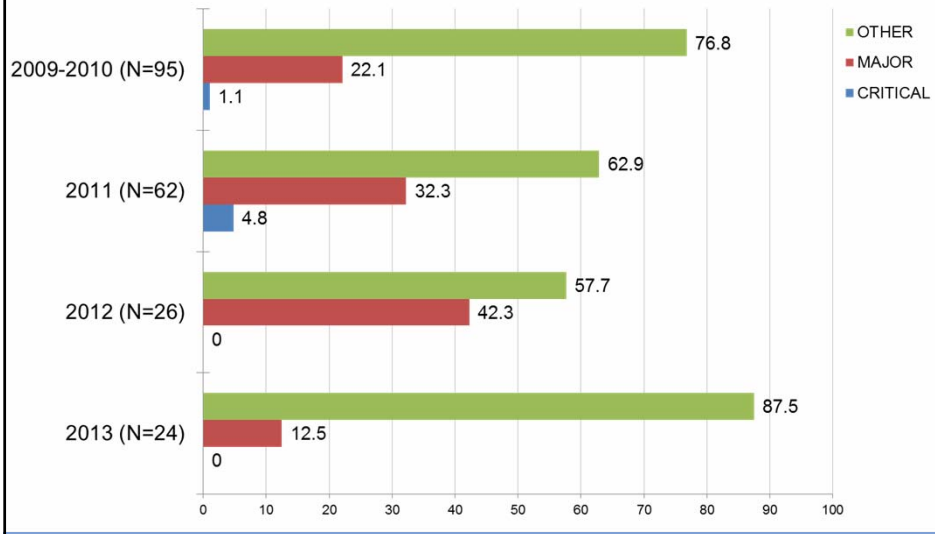
- **Other**: Conditions, practices or processes that would not be expected to adversely affect the rights, safety or well being of the subjects and/or the quality and integrity of data.
- **Comments**: The observations might lead to suggestions on how to improve quality or reduce the potential for a deviation to occur in the future.

GCP Inspections in 2013

Distribution of Therapeutic Areas (N=10)



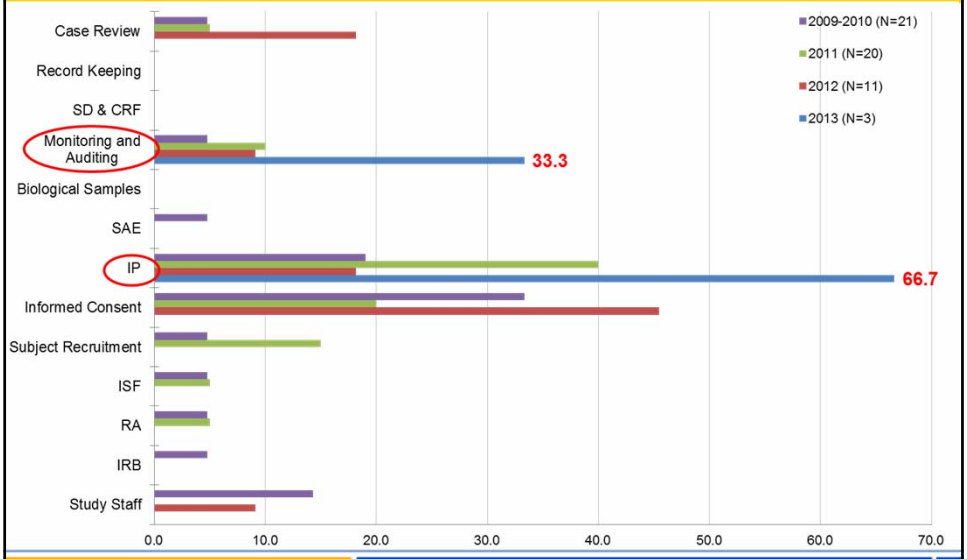
Distribution of Inspection Findings



GCP Site Inspections (2013)
CRITICAL GCP Inspection Findings

None ☺

Distribution of Major Findings



Major Findings in 2013

- Investigational Product (IP)
- Monitoring and Auditing

Major GCP Inspection Findings
Investigational Product

- IP had not been labelled in accordance with SGGCP and local regulatory requirements
  - ► *Medicines (Clinical Trials) Regulation 18(1), SGGCP 4.6.3*
- Lack of quality systems in IP Management
  - ► *SGGCP 2.10, SGGCP 2.13*

Regulatory Requirements for IP Labelling
Medicines (CT) Reg 18

Test materials' particulars, identification and storage
18. —(1) The holder of a certificate shall ensure that all test materials have the following particulars written on the containers:

(a) the designation, reference number or other identification mark of each item of such material;

(b) the name and address of the manufacturer;

(c) the production batch number of the material;

(d) name or other identification mark of the subject for whom the test material is intended;

(e) the date of manufacture and the expiry date of the test material;

(f) the storage conditions appropriate for each item of test material as may be indicated by the manufacturer; and

(g) the words: "This product shall only be used under strict medical surveillance" or "This product shall only be used under strict dental surveillance", as the case may be.

(2) No test material shall be used in a clinical trial if the container in which the test material is stored is not marked and labelled with the particulars specified in paragraph (1).

Potential Challenges in IP Labelling

- **Randomized, Double-blind Clinical Trials**

Test materials' particulars, identification and storage
18. —(1) The holder of a certificate shall ensure that all test materials have the following particulars written on the containers:

(a) the designation, reference number or other identification mark of each item of such material; → Drug A / Drug B

(b) the name and address of the manufacturer; → Name and Address of Sponsor

(c) the production batch number of the material; → Dummy Batch No.

(d) name or other identification mark of the subject for whom the test material is intended;

(e) the date of manufacture and the expiry date of the test material; →
- Request for a waiver from HSA for omission of manufacturing date.
- Use a dummy expiry date or an earlier expiry date.

(f) the storage conditions appropriate for each item of test material as n

(g) the words: "This product shall only be used under strict medical su
used under strict dental surveillance", as the case may be.

(2) No test material shall be used in a clinical trial if the container in which the test material is stored is not marked and labelled with the particulars specified in paragraph (1).

Lack of quality systems in IP documentation

- IP Management SOPs
  - *Sponsor should ensure that written instructions for handling and storage of IP and documentation thereof are available.*
    - *SGGCP 5.14.3*

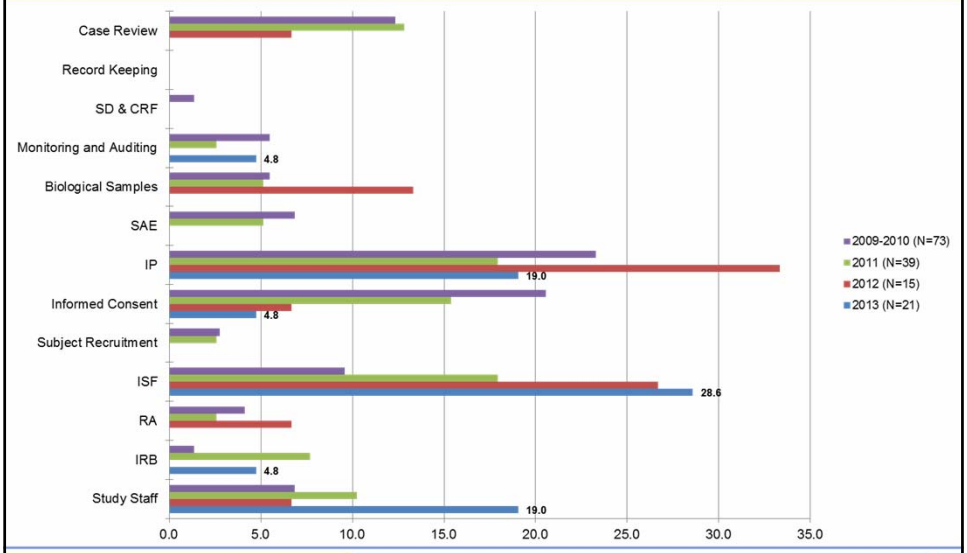
- IP Documentation
  - *IP Shipment and Receipts*
  - *IP Inventory Logs*
  - *IP Storage Temperature Logs*
  - *IP Repackaging and Relabelling Forms*
  - *IP Dispensing and Accountability Logs*
  - *IP Return and Destruction Logs*

- Version Control (SGGCP 2.13)
- Complete accurately (SGGCP 2.10)
- Include dates, quantity, batch numbers, expiration date (if applicable) and unique code numbers assigned to the IP and trial subjects (SGGCP 4.6.3)

Major GCP Inspection Findings
Monitoring and Auditing

- Lack of systems that assure quality in every aspect of the clinical trial
  - *SGGCP 2.13, SGGCP 5.18*
    - *Sponsor should be aware of its responsibility to implement systems / procedures (e.g. monitoring) to ensure trial quality.*

Distribution of Other Findings



Top 3 Other Findings in 2013

- Investigator Site File
- Investigational Product (IP)
- Study Staff

Other GCP Inspection Findings
Investigator Site File

- Inaccuracies in translated documents
  - *SGGCP 2.10*
    - *Ensure that the translated documents are referenced accurately.*
    - *Ensure that the version of translated documents used is the version approved by the IRB.*
- Missing essential documents on file
  - *Examples:*
    - *Protocol Signature Page (SGGCP 8.2.2)*
    - *Approval email from HSA (SGGCP 8.2.9 and SGGCP 8.3.3)*
    - *Record of retained body fluids (SGGCP 8.3.5)*

Other GCP Inspection Findings
Investigational Product

- Lack of written procedures for IP procedures
  - *SGGCP 5.14.3*
    - *Written procedures should be available for the handling and storage of IP*
    - *Refer to HSA website for template IP Management SOP.*
- IP Documentation for shipment, receipt, dispensing, accountability, return and/or destruction did not fulfil the requirements.
  - *SGGCP 4.6.3*
    - *Dates, quantities, batch numbers, expiration date (if applicable), unique code numbers assigned to the IP and trial subjects should be included in IP Documentation.*

Other GCP Inspection Findings
Study Staff

- Deficiencies in signed signature sheet
  - *Medicines (Clinical Trials) Regulation 19(3), SGGCP 2.13, SGGCP 4.1.5, SGGCP 4.9.1, SGGCP 8.3.24*
    - *Ensure that version control is present.*
    - *Responsibilities and roles of study team members should be accurately reflected.*
    - *Ensure that there are study members delegated for important trial activities e.g. informed consent, physical examination, medical history, eligibility assessment, randomization, communication with IRB, IP management , handling biological samples, ISF maintenance (where applicable).*
- Lack of training records/ Curriculum Vitae for study team
  - *SGGCP 4.2.4*
    - *Ensure that training of study staff is documented and available on file.*
    - *CV for all study team members should be available on file.*

Quality Improvement Initiatives

- Training
- CTB FAQs uploaded on HSA website
- Meetings with cluster Research QA and monitoring staff
- Observation of GCP Site Inspections
- From The GCP Inspector's Desk Newsletter
- Upstream consultation on IP management
  - *16 clinical trials in 2013*
- Sharing of Best Practices

Upcoming Initiatives for 2014

- Systems GCP Inspections
- Templates Repository
- Monitoring Framework for IITs

References

- Medicines Clinical Trials Regulations
- Singapore Guideline for Good Clinical Practice
- HSA GCP Compliance Inspection Framework
- HSA Guidance and Templates
- HSA CTB FAQs
- From the GCP Inspector's Desk Newsletter

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