LOOKING BACK AT 2019

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OUTLINE

- GCP inspection findings for 2019
- ICH E6 (R3)
- Launch of new HSA website

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

Classification of GCP Inspection Findings

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.

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
- Suggestions to improve quality or to prevent a non-compliance from occurring in future.

GCP Inspections over the past 10 yrs

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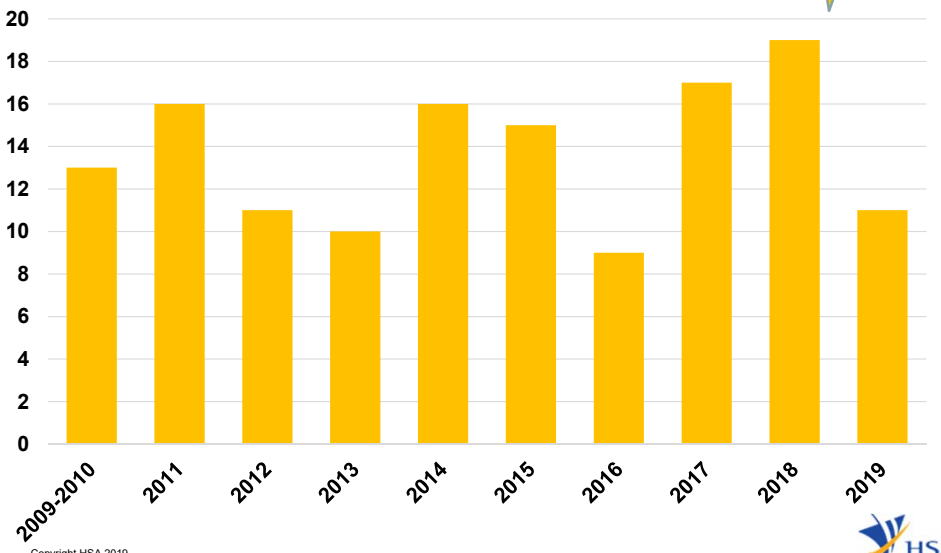

GCP Inspections in 2019

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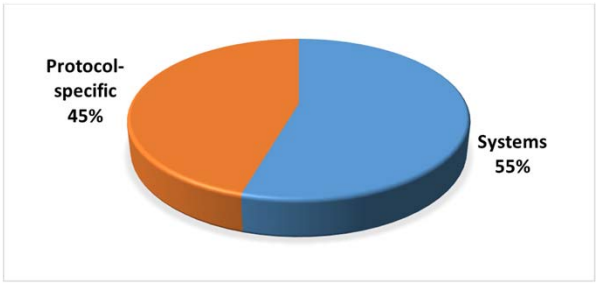
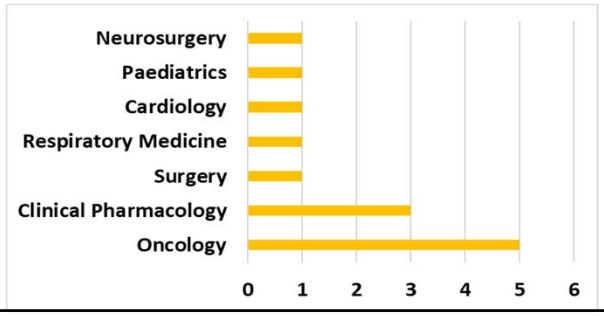
TYPE OF GCP INSPECTION (N=11)

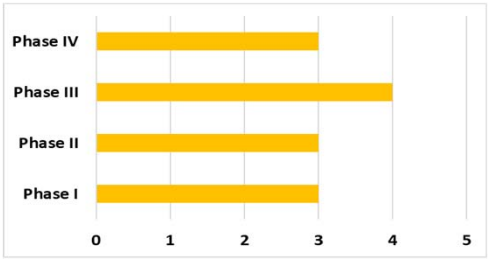


DISTRIBUTION BY THERAPEUTIC AREA (N=13)

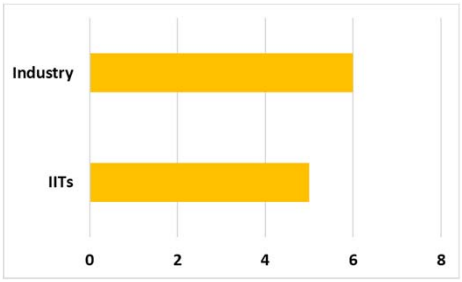


GCP Inspections in 2019

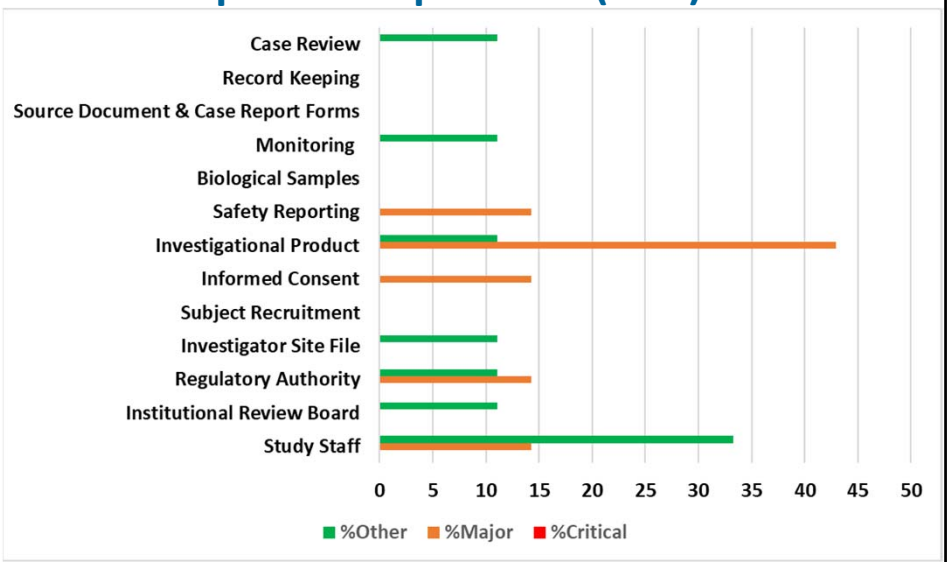
DISTRIBUTION BY PHASE OF CLINICAL TRIAL (N=13)



DISTRIBUTION BY SPONSOR (N=11)



GCP Inspection Findings in 2019
Protocol-specific Inspections (N=5)



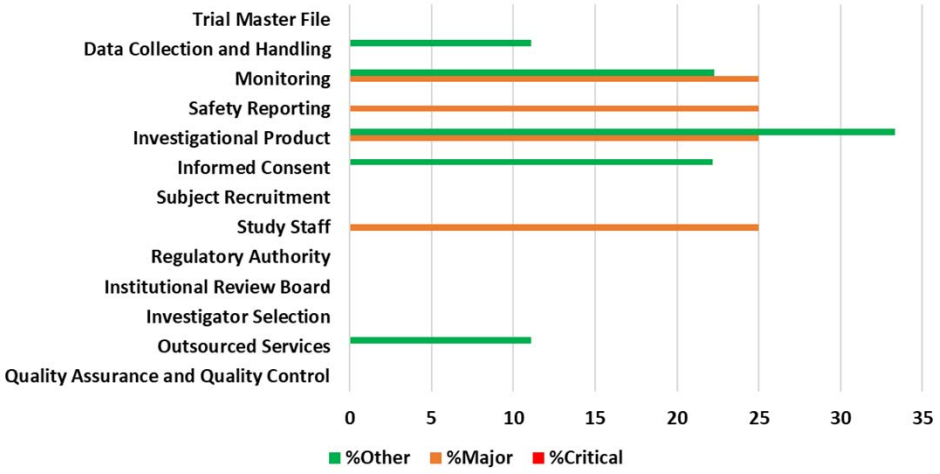
Protocol-specific Inspections

- **Investigational Product**
  - Delegation and training of study staff
    - *Lacking during IP receipt*
  - Written procedures for handling IP
    - *Lack of SOPs for handling IP*
  - IP documentation
    - *No document control*
    - *No ALCOA principles*
    - *Lack of traceability*
    - *Retrospectively created*
    - *Discrepancies*
  - IP repackaging and relabelling
    - *Non-compliance with GMP guidelines*
  - IP Labelling
    - *Non-compliance to clinical trials regulations*

Protocol-specific Inspections

- **Study Staff**
  - Lack of study-specific training.
- **Informed Consent**
  - Subject had signed on unapproved ICF.
- **Safety Reporting**
  - Delayed reporting of SAEs to sponsor.
- **Regulatory Authority**
  - Serious Breach not notified to HSA.

GCP Inspection Findings in 2019
Sponsor Inspections (N=4)



Sponsor Inspections in 2019

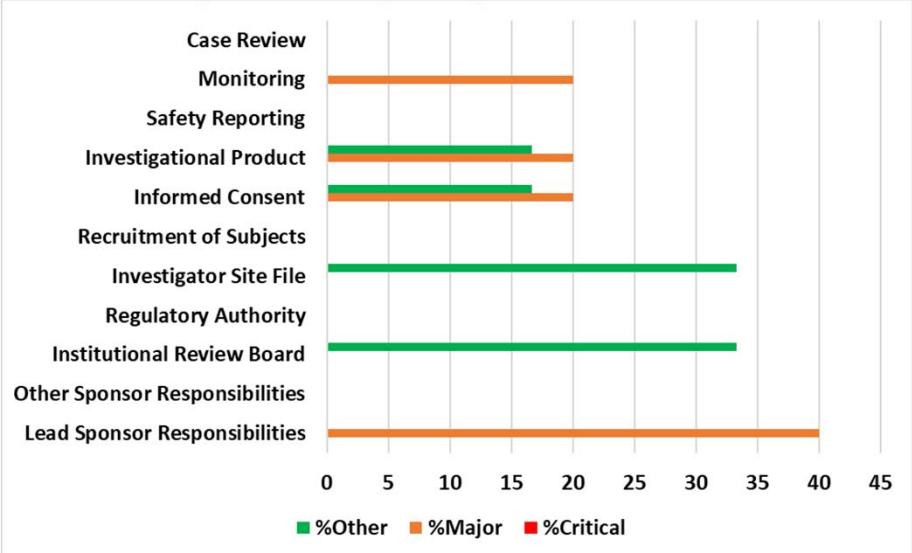
- **Study Staff**
  - Study staff had been delegated by Sub-investigator instead of PI.
- **Investigational Product**
  - Significant discrepancies in IP documentation.
    - *Lack of ALCOA principles*
    - *Discrepancies in IP accountability.*
    - *Discrepancies in IP preparation for calculation of volume of IP.*
- **Safety Reporting**
  - Lack of adequate oversight of safety review process by sponsor and CRO.
- **Monitoring**
  - Monitors had not reviewed eligibility criteria thoroughly and carefully.

Sponsor Inspections in 2019

- **Inadequate oversight of Investigator-initiated trials (IITs) by local sponsor**

- **Note:**
  - Institution is the local sponsor of IITs
  - Sponsors of IITs should ensure there are proper processes and systems in place to:
    - *Keep track of all clinical trials conducted within the institution*
    - *Screen clinical research studies to determine whether they are regulated by HSA*
    - *Ensure that non-compliances, serious adverse events and urgent safety measures are promptly notified to the local sponsor's Research Office / Clinical Research Unit*
    - *Monitor clinical trials*
    - *Maintain oversight of IITs under the mutual recognition of IRBs*

GCP Inspection Findings in 2019
MS IIT Inspections (N=2)



MS IIT Inspections in 2019

- **Lead Sponsor Responsibilities**
  - Lead sponsor did not promptly assess the impact of the breaches and notify HSA of the serious breaches.
  - Lead sponsor did not submit updated IB to HSA.
  - Lead sponsor did not submit CRM Notification to HSA.
- **Informed Consent**
  - Subject did not personally date the ICF.
  - Subjects were not provided with signed copies of ICFs.
  - Non-substantial amendments had been made to the ICF and used to consent a subject prior to IRB approval.

MS IIT Inspections in 2019

- **Investigational Product**
  - Study staff had not been delegated to handle IP.
  - Discrepancies in IP documentation
    - *No document control*
    - *Photocopies were not certified as true copies*
    - *Lack of traceability to Subject ID between IP documentation*
    - *Actual IP storage temperature was not recorded, but plotted in 5ºC intervals*
- **Monitoring**
  - Lead sponsor did not maintain adequate oversight of the satellite site.

ICH E6 (R3) – update of ICH E6

- Clinical trials have become more complex with respect to trial design, use of technology, quantity of data collected and involvement of central testing facilities or other service providers.
- ICH E6 (R1) was amended to ICH E6 (R2) in Nov 2016 to incorporate electronic data sources and quality risk management (e.g. Quality by Design, Risk-based Monitoring).
- ICH E6 (R2) will be amended to ICH E6 (R3) in future. The development of ICH E6(R3) will consider the flexibilities needed for a variety of trial designs and will focus on key principles.
- HSA is a member of the ICH E6 (R3) EWG.

ICH E6 (R3) – update of ICH E6

- **Concept Paper for ICH E6 (R3)**
  - **Annex 1 – Interventional clinical trials**
    - *Principles and objectives document; and GCP guidelines*
    - *Include use of unapproved / approved drugs in a controlled setting with prospective allocation of treatment to participants and collection of trial data.*
    - *NB: ~18-24 months to reach Step 1 (i.e. draft Technical Document).*
  - **Annex 2 – Additional considerations for non-traditional interventional clinical trials**
    - *Include designs such as pragmatic clinical trials, decentralised clinical trials, and trials that incorporate real world data sources.*
    - *NB: Work will commence when Annex 1 reaches Step 1.*
- **Stakeholder engagement**
  - Academia
  - Patient-advocacy groups – Not applicable for Singapore

Launch of new HSA website

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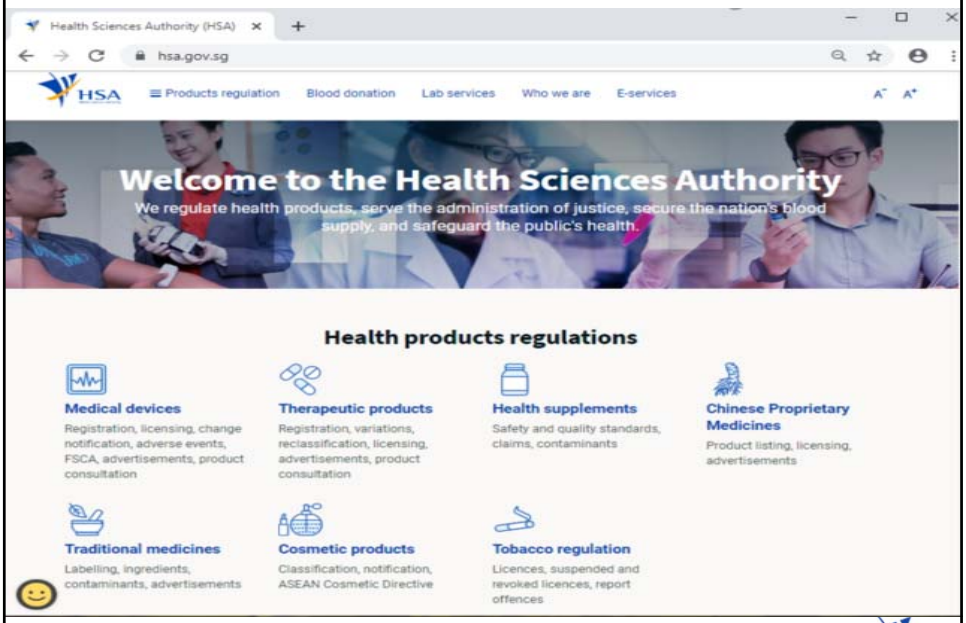

NB: FAQs have been incorporated into the webpages!

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Conclusions

- Both sponsors and site staff play a crucial role in maintaining the quality of clinical trials.
  - Quality systems should be implemented in every aspect of the clinical trial.
  - Risk-based approach should be adopted in quality systems.
  - Adequate oversight is key.
  - Sponsors and site staff should work in tandem to maintain the quality of clinical trials.
    - Be aware of non-compliances, and learn from them to prevent a recurrence.

We welcome your enquiries and feedback!

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THANK YOU!