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COMMON GCP INSPECTION FINDINGS 2016

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GCP Inspection Framework

- **Launched in Sep 2009;**
- **Completed 90 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)*
  - *2014: 15 (Protocol-specific), 1 (Systems on ICF and IP)*
  - *2015: 15 (Protocol-specific)*
  - *2016 : 8 (Protocol-specific), 1 (Systems on ICF and IP)*

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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.

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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.

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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.

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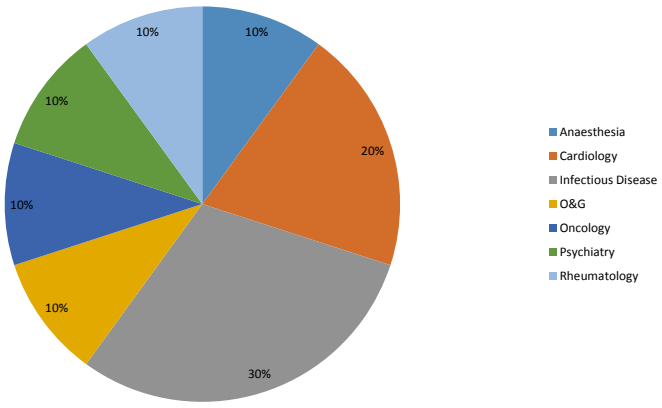
GCP Inspections in 2016

- Distribution of Therapeutic Areas (N=10)



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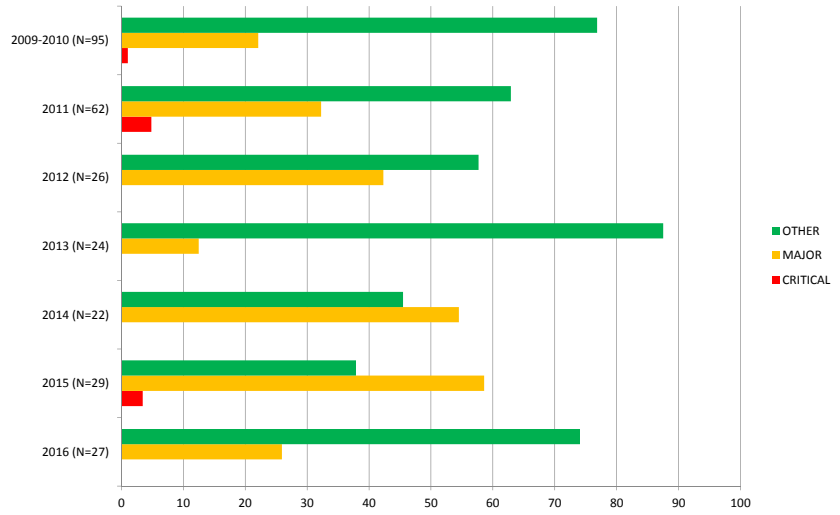
Distribution of GCP Inspection Findings 2009-2016



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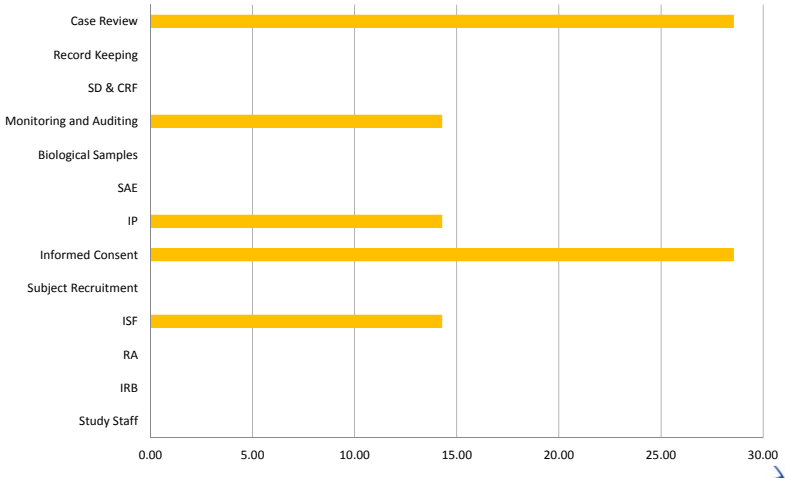
% MAJOR GCP Inspection Findings (N=7)



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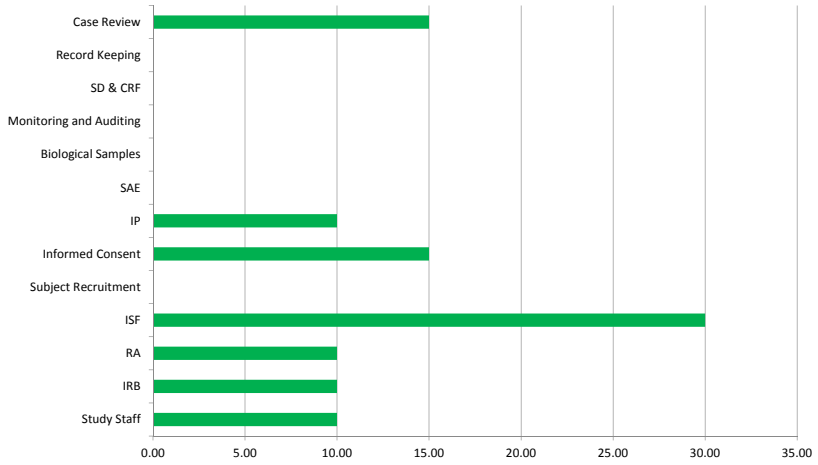
% OTHER GCP Inspection Findings (N=20)



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CASE REVIEW

- Subjects were not eligible for enrollment into the clinical trial
  - *SGGCP 4.5*
- Data was not recorded in an accurate manner
  - *SGGCP 2.10, 4.9.2*
- Lack of protocol compliance
  - *SGGCP 4.5*
- Protocol non-compliances were not documented and explained
  - *SGGCP 4.5.3*
- Discrepancies between Source Documents and Case Report Forms
  - *SGGCP 4.9.3*

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CASE REVIEW

Helpful Tips

- Traceability
- Subject Identifiers required if DCF is used as SD.
- Data should be captured in accordance with study protocol.
- Document and report non-compliances.
- CRF data should be consistent with SD.
- Version Control

Protocol ABC

DATA COLLECTION FORM

Subject ID: *59001*
Visit No.: 1

Subject Initials: *ABC*
Visit Date.: *1 Dec 2016*

- **Study Procedures**

- A – Attributable
- L - Legible
- C -Contemporaneous
- O - Original
- A – Accurate

- Amendments should be initialled and dated

Completed by: _____

Version Dated: 1 Nov 2016 **Page 1**

- Purpose: SD / CRF?
- Requires IRB approval
- Should be compliant with protocol
- May be required to be updated for protocol amendments.

NB: SD = Source Documents; CRF = Case Report Form

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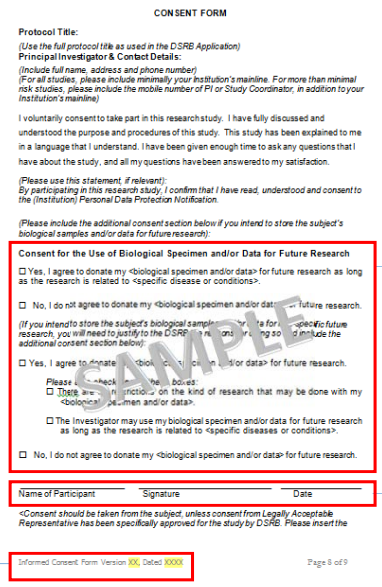
INFORMED CONSENT

- Some study-specific procedures had been performed before obtaining informed consent.
  - *Regulation 11(1) of the Medicines (Clinical Trials) Regulations and SGGCP 4.8.8*
- Subject had signed on an unapproved version of the ICF.
  - *Regulation 11(4) of the Medicines (Clinical Trials) Regulations and SGGCP 4.4.1*
- Signature of the investigator on the ICFs was inconsistent with the Signature Sheet.
  - *SGGCP 4.9.2*
- Subjects did not personally date the ICF.
  - *Regulation 11(4) of the Medicines (Clinical Trials) Regulations and SGGCP 4.8.8*
- Discrepancies in date of informed consent.
  - *Regulation 11(4) of the Medicines (Clinical Trials) Regulations and SGGCP 4.8.8*
- Investigator had signed as an impartial witness.
  - *Regulation 11(5) of the Medicines (Clinical Trials) Regulations and SGGCP 4.8.9*
- Lack of impartial witness although subject was unable to read the ICF.
  - *Regulation 11(5) of the Medicines (Clinical Trials) Regulations and SGGCP 4.8.9*

Helpful Tips

INFORMED CONSENT

- ICF must be approved by IRB and HSA.
- ICF amendments must be approved by IRB.
- Substantial amendments to ICF must be submitted to HSA for approval (for CTA and CTC) or acceptance (for CTN).
- Develop a tracking log to track IRB and HSA approvals.
- Develop a tracking log to track the version(s) of the ICF signed by the subject.



CONSENT FORM

Protocol Title:

(Use the full protocol title as used in the DSRB Application)

Principal Investigator & Contact Details:

(Include full name, address and phone number)
(For all studies, please include minimally your Institution's mainline. For more than minimal risk studies, please include the mobile number of PI or Study Coordinator, in addition to your Institution's mainline)

I voluntarily consent to take part in this research study. I have fully discussed and understood the purpose and procedures of this study. This study has been explained to me in a language that I understand. I have been given enough time to ask any questions that I have about the study, and all my questions have been answered to my satisfaction.

(Please use this statement, if relevant):
By participating in this research study, I confirm that I have read, understood and consent to the [Institution] Personal Data Protection Notification.

(Please include the additional consent section below if you intend to store the subject's biological samples and/or data for future research):

Consent for the Use of Biological Specimen and/or Data for Future Research

☐ Yes, I agree to donate my <biological specimen and/or data> for future research as long as the research is related to <specific disease or conditions>.

☐ No, I do not agree to donate my <biological specimen and/or data> for future research.

(If you intend to store the subject's biological samples or data for specific future research, you will need to justify to the DSRB in the applications and include the additional consent section below)

☐ Yes, I agree to donate my <biological specimen and/or data> for future research.

Please check the boxes:
☐ There are no restrictions on the kind of research that may be done with my <biological specimen and/or data>.

☐ The Investigator may use my biological specimen and/or data for future research as long as the research is related to <specific diseases or conditions>.

☐ No, I do not agree to donate my <biological specimen and/or data> for future research.

Name of Participant Signature Date

<Consent should be taken from the subject, unless consent from Legally Acceptable Representative has been specifically approved for the study by DSRB. Please insert the

Informed Consent Form Version XX, Dated XXXX

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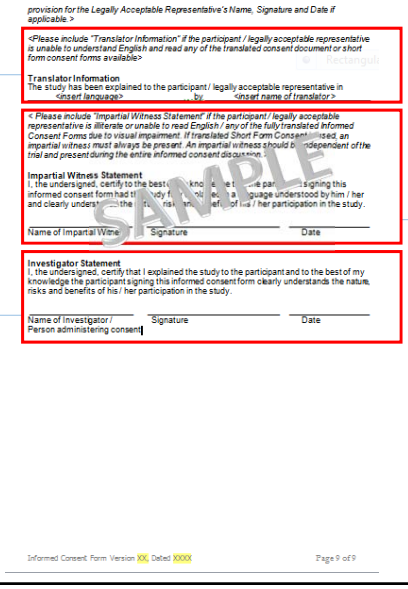
SAMPLE

- Subject to personally complete check boxes.
- Informed consent must be obtained before any study procedures.
- Subject to personally sign and date the ICF.
- Signature and date stamps are not allowed.
- ICF date should be consistent.

Helpful Tips

INFORMED CONSENT

- Translator should be used if subject and investigator are unable to communicate in the same language.
- Study staff may act as a translator.
- Investigator, who is a qualified physician, must obtain informed consent.
- Investigator must be authorised by PI to obtain informed consent.
- Investigator must personally sign and date the ICF.
- The signature of the investigator should be consistent with the Signature Sheet.
- Signature and date stamps are not allowed.
- ICF date should be consistent.
- Consent should be documented in medical records.



provision for the Legally Acceptable Representative's Name, Signature and Date if applicable.>

<Please include "Translator Information" if the participant / legally acceptable representative is unable to understand English and read any of the translated consent document or short form consent forms available>

Translator Information
The study has been explained to the participant / legally acceptable representative in <insert language> by <insert name of translator>

< Please include "Impartial Witness Statement" if the participant / legally acceptable representative is illiterate or unable to read English / any of the fully translated Informed Consent Forms due to visual impairment. If translated Short Form Consent is used, an impartial witness must always be present. An impartial witness should be independent of the trial and present during the entire informed consent discussion.

Impartial Witness Statement
I, the undersigned, certify to the best of my knowledge that the participant signing this informed consent form had the study explained to him / her in a language understood by him / her and clearly understood the risks involved of his / her participation in the study.

Name of Impartial Witne Signature Date

Investigator Statement
I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his / her participation in the study.

Name of Investigator / Person administering consent Signature Date

Informed Consent Form Version XX, Dated XXXX

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SAMPLE

- Impartial witness must be used if subject is unable to read the ICF or unable to sign/date the ICF.
- Study staff must not act as the impartial witness.
- Impartial witness must personally sign and date ICF.
- Signature and date stamps are not allowed.
- ICF date should be consistent/
- Subject should get a signed copy of the ICF.

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INFORMED CONSENT

INFORMED CONSENT TRACKING LOG

PROTOCOL TITLE:		
PROTOCOL NO.:	PRINCIPAL INVESTIGATOR:	SITE NAME:

Subject ID	Subject Initials	ICF version ref. (include language used)	Informed Consent Date	ICF version ref. (include language used)	Informed Consent Date	ICF version ref. (include language used)	Informed Consent Date

Version Date: Page 1

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INVESTIGATIONAL PRODUCT

- Lack of written instructions for calculation of dose of IP based on body weight of subject.
  - *SGGCP 5.14.3*
- Lack of IP shipping records.
  - *SGGCP 4.6.3*
- IP was not stored in a designated storage space.
  - SGGCP 4.6.4
- Discrepancies in documenting the IP Storage Temperature.
  - *SGGCP 2.10, 4.9.2*
- Discrepancies in IP documentation.
  - *SGGCP 2.10, 4.6.3, 4.9.2*
- IP was not used in accordance with the protocol.
  - *SGGCP 4.6.5*
- IP label did not comply with regulatory requirements.
  - *Regulation 18(1) of the Medicines (Clinical Trials) Regulations and SGGCP 4.6.3*

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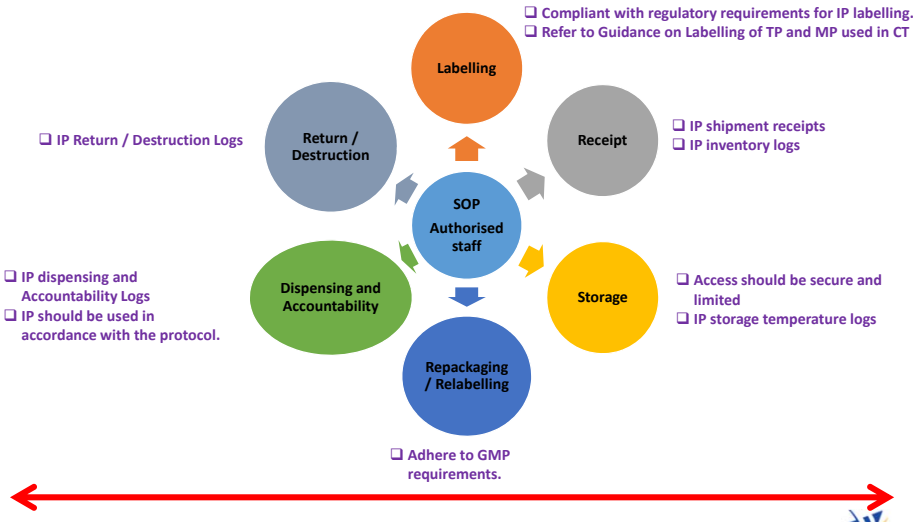
Helpful Tips

INVESTIGATIONAL PRODUCT



ATTRIBUTABLE, LEGIBLE, CONTEMPORANEOUS, ORIGINAL, ACCURATE

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INVESTIGATOR'S SITE FILE

- Breach in subject privacy and data confidentiality as sponsor had retrieved copies of essential documents bearing subject identifiable information.
  - *SGGCP 2.11*
- Lack of clinical trial insurance
  - *SGGCP 5.8.1*

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INVESTIGATOR'S SITE FILE

Protocol ABC

Name: John Smith
NRIC: S91234567Z
Address: 10 Care Bear Road, Singapore 612345

- Subject Identifiers should be obscured if essential document is to be sent to the sponsor.

DATA COLLECTION FORM

Subject ID: 59001 Subject Initials: ABC

Visit No.: 1 Visit Date.: 1 Dec 2016

SAMPLE

Version Dated: 1 Nov 2016 Page 1

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MONITORING

- Lack of verification that the investigator had only enrolled eligible subjects.
  - *SGGCP 5.18.4 (i)*
- Lack of verification of the accuracy and completeness of source documents and trial records.
  - *SGGCP 5.18.4(k)*
- Lack of verification of the discrepancies between the Case Report Form entries and the source documents during site monitoring visits.
  - *SGGCP 5.18.4(m)*
- Lack of verification as to whether the investigator had maintained the essential documents.
  - *SGGCP 5.18.4(p)*
- Significant discussions regarding trial conduct had not been documented.
  - *SGGCP 8.3.11*

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MONITORING

Site Selection Visit → Site Initiation Visit → Site Monitoring Visit → Site Closure Visit

- Follow monitoring plan.
- Review the subject's source documents in its entirety before performing source document verification.
- Determine compliance with protocol, SOPs, ICH E6 (R2) GCP and applicable clinical trials regulations.
- Comply with monitor's responsibilities outlined in Section 5.18 of ICH E6 (R2) GCP guidelines.
- Document significant discussions with trial site.

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REFERENCES

- Medicines (Clinical Trials) Regulations
- Singapore Guideline for Good Clinical Practice (SGGCP)
- CTB FAQs

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WE WELCOME YOUR ENQUIRIES AND FEEDBACK!

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www.hsa.gov.sg