Serious Breach Reporting Frequently Asked Questions 2025

Q1	**What constitutes a "Serious Breach" that requires reporting?** A "serious breach" is defined as deviation(s) from the approved clinical trial protocol, Principles of GCP, or any clinical trial-related regulations that is likely to have a significant impact on: 1. The safety, rights or well-being of any trial participants; or 2. The reliability and robustness of the data generated in the trial.
Q2	**What factors should be taken into account when assessing whether a breach is "serious"?** When assessing whether a breach should be classified as *serious*, sponsors should consider the **nature, impact, and consequences** of the incident. A breach is generally regarded as *serious* if it: ● **Significantly affects the safety, rights, or well-being** of one or more trial participants; or ● **Compromises the reliability, integrity or scientific value** of the trial data to a significant degree. In determining seriousness, sponsors should evaluate factors such as: ● The extent of deviation from the approved protocol, the Principles of GCP or applicable regulatory requirements; ● The potential or actual impact on participant safety, rights, and data credibility; ● Whether the non-compliance is systemic or an isolated case, and ● The timeliness, adequacy and effectiveness of corrective and preventive actions (CAPA) taken.
Q3	**Who is legally responsible for reporting a serious breach?** The **Clinical Trial Import Licence (CTIL) or Clinical Trial Exemption (CTX) holder** of the clinical trial is legally responsible for the reporting.
Q4	**What is the regulatory requirement for Serious Breach reporting?** The current requirements for reporting of a serious breach is stipulated under Section 14 (Protocol Deviation) of the *Malaysian Guideline for Application of Clinical Trial Import Licence and Clinical Trial Exemption (8.1th Edition)*, which states: *"Any deviation(s) from the protocol that significantly affect the credibility of study data or subject safety must be reported to the NPRA immediately upon the sponsor's awareness."* However, NPRA acknowledges that there are gaps in the current provisions and guidance for reporting of serious breaches. The relevant information is currently being provided through FAQ and will be incorporated into the forthcoming revision of the guideline.

Q5	**Do the Serious Breach reporting requirements apply to all phases of a clinical trial?** Yes. However, only serious breaches in clinical trials regulated by NPRA, i.e. those that require a Clinical Trial Import Licence (CTIL) or Clinical Trial Exemption (CTX), must be reported to NPRA.
Q6	**If a serious breach occurs outside of Malaysia, but the clinical trial is also running in Malaysia, does it need to be reported?** At present, the requirement to report a serious breach to NPRA applies only to clinical trial sites in Malaysia that conduct clinical trials under a valid Clinical Trial Import Licence (CTIL) or Clinical Trial Exemption (CTX). Serious breaches that occur at overseas sites are not required to be reported to NPRA. However, if the incident is assessed to potentially impact participant safety, data integrity, or the conduct of the clinical trial in Malaysia, the sponsor is required to notify NPRA accordingly**.**
Q7	**What is the timeline for reporting a serious breach to NPRA?** Reporting must be made **without undue delay and within seven (7) calendar days** of the sponsor becoming aware of a serious breach. If the reporting responsibility is delegated to a contracted service provider such as a Contract Research Organisation (CRO), the 7-day timeline applies to the delegated party.
Q8	**Is it necessary to wait until the investigation is complete before reporting NPRA of the serious breach?** **No.** If the Sponsor has obtained **clear and unequivocal evidence** that a s**erious breach has occurred**, they should report to the NPRA **without undue delay and no later than seven (7) calendar days after becoming aware of the breach.** The Sponsor **should not wait** for the completion of a full investigation or for all details to be confirmed before the initial reporting. The investigation and implementation of corrective and preventive actions (CAPA) may proceed **concurrently with or after the initial reporting** to NPRA.
Q9	**What is the process for submitting a Serious Breach report to NPRA?** Submission should be made electronically to the Head of Good Clinical Practice and Good Laboratory Practice Section via email at mygcp@npra.gov.my, using the template form available on the NPRA GCP webpage. Each submission should be accompanied by a signed cover letter. Depending on the nature and scope of the serious breach, the Sponsor or CTIL/CTX Holder should also consider whether other relevant NPRA sections or Ethics Committees need to be notified. For instance, if the breach involves **urgent safety measures**, a separate notification may be required in accordance with applicable NPRA procedures and ethical

	review requirements.
Q10	**What actions may NPRA take upon receiving a Serious Breach report?** Upon receipt of a serious breach report, NPRA will acknowledge, review, and assess the information to determine its potential impact on participant safety and data integrity. Based on the outcome of the assessment, NPRA may take one or more of the following actions: ● Request for additional information, clarification, or supporting documentation; ● Request submission of a Corrective and Preventive Action (CAPA) plan or progress updates; ● Initiate a for-cause inspection to verify compliance with Good Clinical Practice (GCP) if required; or ● Refer the case to the relevant internal section(s) within NPRA, such as the Investigational Product Evaluation and Safety Section, for further action(s).
Q11	**Does every deviation from the protocol or GCP constitute a serious breach?** **No.** Not every deviation from the approved clinical trial protocol or Good Clinical Practice (GCP) constitutes a serious breach. Protocol deviations occur frequently in clinical trials and are often minor or technical in nature, without significant impact on the safety, rights or well-being of trial participants, or on the reliability and integrity of the trial data. Such deviations should be documented, assessed and managed in accordance with the sponsor's internal procedures as Protocol Deviations. Please refer to Q2 for the criteria defining a serious breach.
Q12	**Can a protocol breach that results in a Severe Adverse Event (SAE) or Suspected Unexpected Serious Adverse Reaction (SUSAR) be classified as a serious breach?** SAEs and SUSARs that resulted from a breach of the GCP Principles or the trial protocol may constitute a serious breach. However, it is important to note that **not every SAE or SUSAR would be classified as a serious breach.** If a failure to comply with safety management procedures—such as **delayed or missed SUSAR reporting, inadequate safety oversight, or non-adherence to the protocol's safety requirements**—poses a significant risk to trial participants, such circumstances would be regarded as a *serious breach*.