HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

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CLINICAL TRIALS GUIDANCE

MULTI-SPONSOR INVESTIGATOR-INITIATED CLINICAL TRIALS

GN-IOCTB-02 Rev. No. 002

HSA Health Sciences Authority

PREFACE

This document is intended to provide general guidance. Although we have tried to ensure that the information contained here is accurate, we do not, however, warrant its accuracy or completeness. The Health Sciences Authority (HSA) accepts no liability for any errors or omissions in this document, or for any action / decision taken or not taken as a result of using this document. If you need specific legal or professional advice, you should consult your own legal or other relevant professional advisers.

In the event of any contradiction between the contents of this document and any written law, the latter should take precedence.

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REVISION HISTORY

Guidance Version (Version Date)

GN-CTB-2-001B-001 (02 May 2017)

GN-IOCTB-02 Rev. No. 002 (01 Mar 2021)

SUMMARY OF AMENDMENTS

- Added a new category of health products, i.e., Cell, Tissue and Gene Therapy Products (CTGTPs), that is regulated under the Health Products Act
- Added a new section on Communication between Lead Sponsor and other sponsor(s) (Section 2.5)
- Amended the term “subjects” to “trial participants”

TABLE OF CONTENTS

1. INTRODUCTION

1.1. Purpose

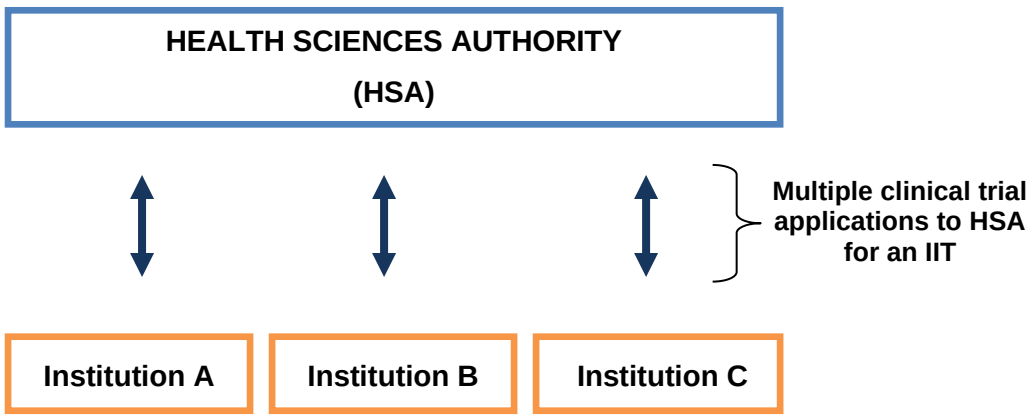
The purpose of this document is to provide guidance to institutions on sponsor responsibilities for multi-sponsor investigator initiated clinical trials (i.e. multi-sponsor IITs), where an investigator-initiated clinical trial (IITs) is conducted at more than one local trial site involving a single protocol.

1.2. Background

The sponsor of a clinical trial is responsible for the initiation, management or financing of the clinical trial. Clinical trials may either be initiated by the industry or investigators. For clinical trials initiated by investigators, the institution is the sponsor for investigator-initiated clinical trials (i.e. IITs).

Investigators from various local institutions may collaborate to conduct an IIT involving a single protocol. For such multi-sponsor IITs involving a single protocol, each institution has traditionally been the sponsor for each local trial site. Figure 1 summarises the previous workflow for multi-sponsor IITs involving a single protocol.

Figure 1. Previous Workflow for Multi-sponsor IITs involving a single protocol (prior to 2015)



The Health Products (Clinical Trials) Regulations and the Medicines (Clinical Trials) Regulations (henceforth referred to as "the Regulations") require that every clinical trial must have a single sponsor. The concept of a single sponsor for multi-sponsor IITs involving a single protocol was discussed with institutions in 2015 in order to streamline the management of safety information across the trial sites. However, feedback from the institutions indicated that such a change would pose difficulties in indemnity and insurance coverage across institutions.

As such, for multi-sponsor IITs involving a single protocol, HSA will continue to allow multiple sponsors (i.e. each institution sponsoring their own trial site) for a single protocol, however a lead sponsor must be nominated amongst the sponsors.

1.3. Scope

This guidance applies to clinical trials regulated by HSA, namely:

(i) Clinical trials of Therapeutic Products[1] and Class 2 Cell, Tissue and Gene Therapy Products (CTGTPs)[1,2] that are subject to the requirements for a Clinical Trial Authorisation (CTA) or a Clinical Trial Notification (CTN);

(ii) Clinical trials of Medicinal Products[3] that are subject to the requirements of a Clinical Trial Certificate (CTC).

[1] Therapeutic Product and CTGTP are defined in the First Schedule to the Health Products Act.

[2] Class 1 and Class 2 CTGTP are defined in the Health Products (Cell, Tissue and Gene Therapy Products) Regulations.

- Class 1 CTGTP means a CTGTP that —
  (a) is the result of only minimal manipulation of human cell or tissue;
  (b) is intended for homologous use;
  (c) is not combined or used with a therapeutic product or a medical device; and
  (d) is assigned by HSA as a Class 1 CTGTP due to a lower health risk to a user of the product.
- Class 2 CTGTP means a CTGTP other than a Class 1 CTGTP.

[3] Medicinal Product is defined in the Medicines Act.

1.4. Definitions

1.4.1. Sponsor

A sponsor, in relation to a clinical trial, means a person who takes responsibility for the initiation, management or financing of a clinical trial.

1.4.2. Investigator-initiated clinical trial (IIT)

An investigator-initiated clinical trial (IIT) is a clinical trial that is sponsored by the institution where the clinical trial is being conducted.

1.4.3. Multi-sponsor Investigator-initiated clinical trial (Multi-sponsor IIT)

A multi-sponsor investigator-initiated clinical trial (multi-sponsor IIT) is an investigator-initiated clinical trial (i.e. IIT) conducted at more than one local institution, involving a single protocol, and that has more than one sponsor.

1.4.4. Lead sponsor

A lead sponsor is a sponsor appointed by all the sponsors of the multi-sponsor IIT involving a single protocol.

1.4.5. Other sponsor(s)

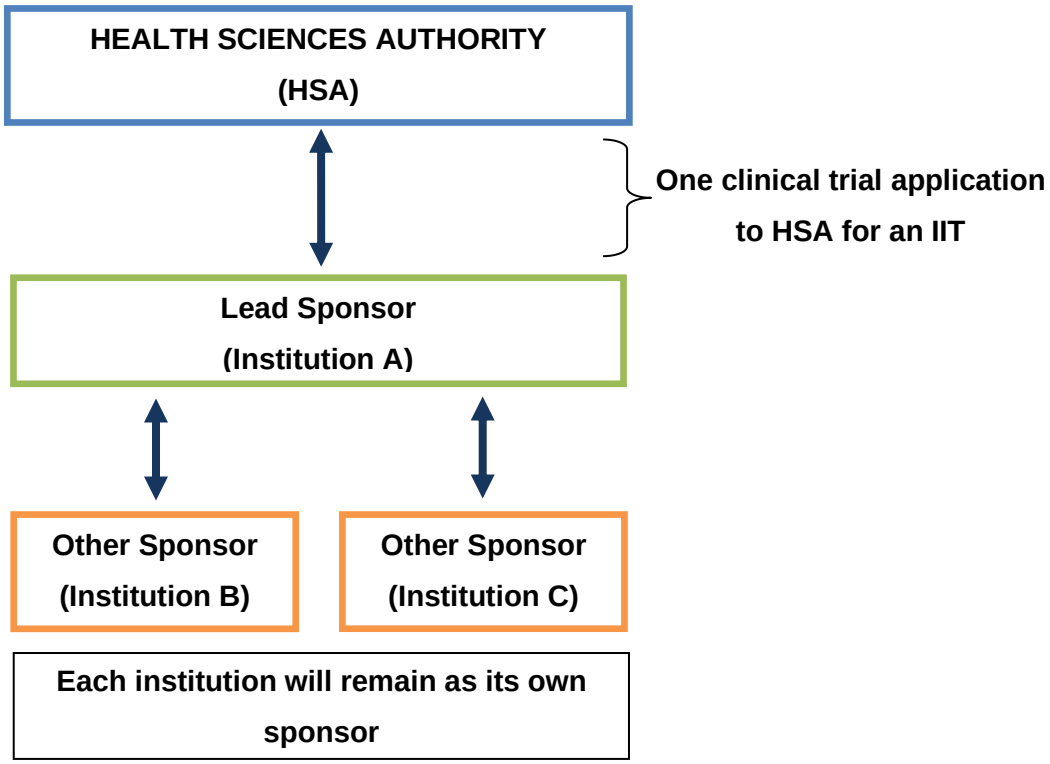
Other sponsor(s) means all other sponsors (excluding the lead sponsor) of a multi-sponsor IIT involving a single protocol. Such a sponsor may also be referred to as a ‘participating site sponsor’.

2. GUIDANCE

2.1. Workflow for multi-sponsor IITs

For multi-sponsor IITs involving a single protocol, each institution may be the sponsor for their respective trial sites involved in the conduct of the IIT. However, the sponsors must nominate a ‘lead sponsor’ amongst themselves to liaise with HSA; all other sponsors will be referred to as ‘other sponsors’. Figure 2 summarises the revised workflow for multi-sponsor IITs.

Figure 2. Revised Workflow for Multi-sponsor IITs involving a single protocol (w.e.f. 2015)



2.2. Objectives of the revised workflow for multi-sponsor IITs involving a single protocol

The objectives of the revised workflow for multi-sponsor IITs involving a single protocol include the following:

(a) To ensure a coordinated and effective management of safety information and trial updates between all the trial sites through the lead sponsor;

(b) To have a single point of contact through the lead sponsor for regulatory submissions for a more effective and streamlined communication with HSA.

2.3. Responsibilities for Lead Sponsor and other sponsor(s)

2.3.1. It is important to note that both the lead sponsor and other sponsor(s) remain the sponsor for their respective trial sites for multi-sponsor IITs involving a single protocol; and must comply with the sponsor responsibilities outlined in the clinical trials regulations and Good Clinical Practice.

2.3.2. Additionally, the lead sponsor and the other sponsor(s) must comply with the following additional sponsor responsibilities for multi-sponsor IITs involving a single protocol. Refer to Table 1 for further details.

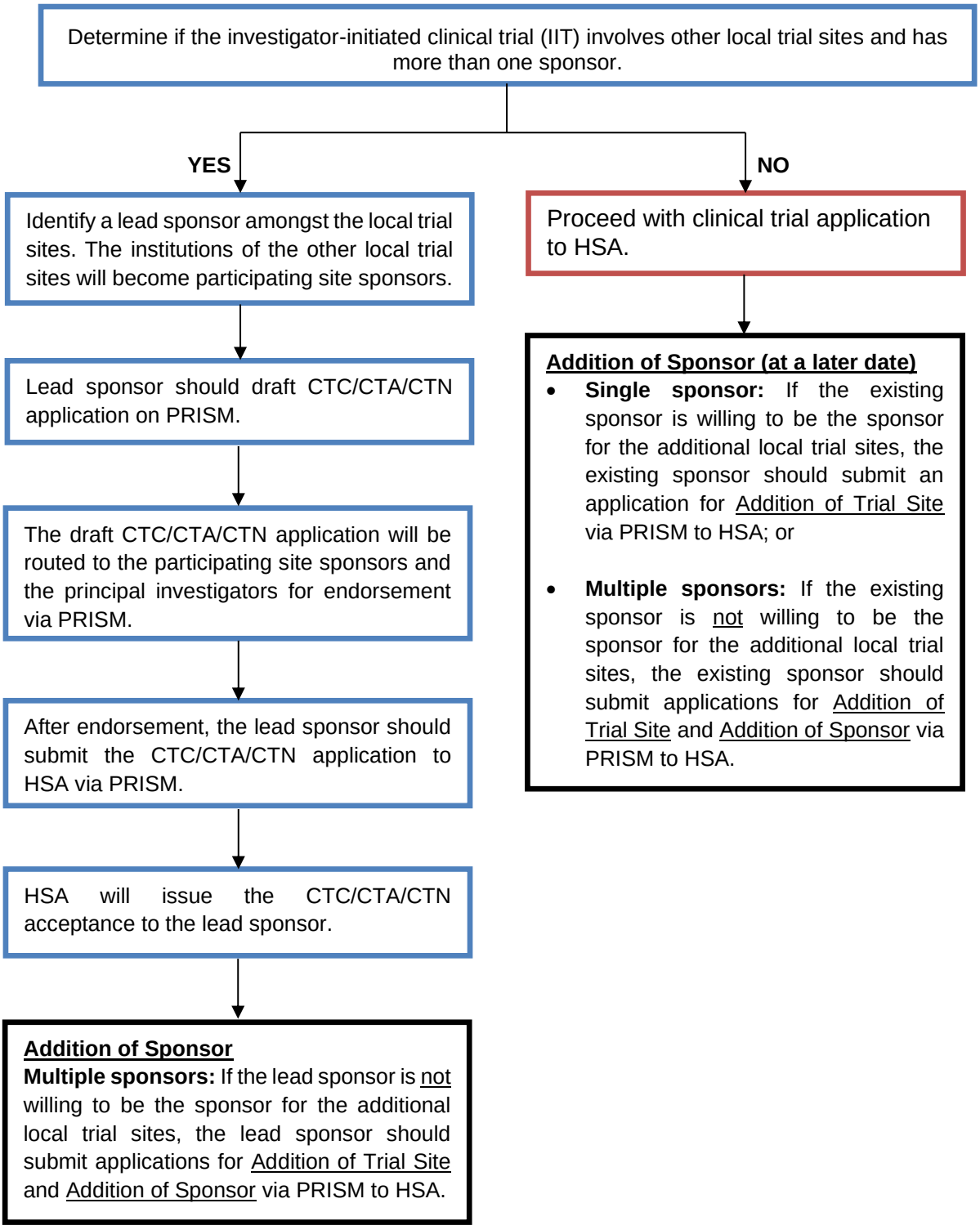
Table 1. Additional responsibilities for the lead sponsor and other sponsor for multi-sponsor IITs involving a single protocol

Additional Sponsor Responsibilities for multi-sponsor IITs involving a single protocol	Lead Sponsor	Other sponsor(s)
REGULATORY SUBMISSIONS / NOTIFICATIONS TO HSA		
CTA / CTN / CTC applications	✓	✗
Substantial amendments	✓	✗
Investigator's Brochure and updates	✓	✗
Clinical Research Material (CRM)	✓	✗
Change of Principal Investigator (PI)	✓	✗
Addition of Trial Site(s)	✓	✗
Serious Breaches	✓	✗
Urgent Safety Measures	✓	✗
Unexpected Serious Adverse Drug Reactions	✓	✗
Trial Status Reports	✓	✗
Final Report	✓	✗
MANAGEMENT OF SAFETY INFORMATION AND STUDY CONDUCT		
Ongoing safety evaluation of the study drug(s) administered to the trial participant	✓	✗
Prompt notification to all participating site investigators/institutions of findings that could adversely affect trial participant safety or impact conduct of trial.	✓	✗
Report immediately to lead sponsor any Serious Adverse Events (SAEs) at the participating site, or any finding that could adversely affect trial participant safety or impact conduct of trial.	✗	✓
Provide all relevant information to lead sponsor that is necessary for the lead sponsor to perform trial-related regulatory submissions and notifications to HSA.	✗	✓

2.4. Submission of multi-sponsor IITs to HSA

Figure 3 summarises clinical trial application process for multi-sponsor IITs.

Figure 3. Clinical trial application process for multi-sponsor IITs



2.4.1. Once it has been determined that the IIT involves more than one sponsor,

(a) A lead sponsor should be identified who would be responsible for submitting all clinical trial applications to HSA.

(b) The lead sponsor should draft CTC/CTA/CTN application on PRISM.

(c) The CTC/CTA/CTN application will then be routed to the other sponsors and the principal investigators for endorsement via PRISM.

(d) After endorsement by the other sponsors and the principal investigators, the lead sponsor should submit the CTC/CTA/CTN application to HSA via PRISM.

(e) HSA will issue the CTC/CTA/CTN acceptance to the lead sponsor.

2.4.1.1. If additional local trial sites and sponsors are included for the clinical trial at a later date, the lead sponsor should submit applications for Addition of Trial Site and Addition of Sponsor, respectively, via PRISM to HSA.

2.5. Communication between Lead Sponsor and other sponsor(s)

The Lead Sponsor and other sponsor(s) should maintain regular communication throughout the conduct of the clinical trial, including:

(i) Written instructions for conducting the clinical trial;

(ii) Amendments to the clinical trial;

(iii) Safety Reporting;

(iv) Urgent Safety Measures;

(v) Serious Breaches.

3. REFERENCES

(i) Health Products (Clinical Trials) Regulations

(ii) Medicines (Clinical Trials) Regulations

HEALTH SCIENCES AUTHORITY

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