Clinical Trial Agreement

for Sponsored Clinical Trials

2012 HA Practical Workshop on Clinical Research Compliance

Henry Yau BSc (Biochemistry) MBA (Finance)

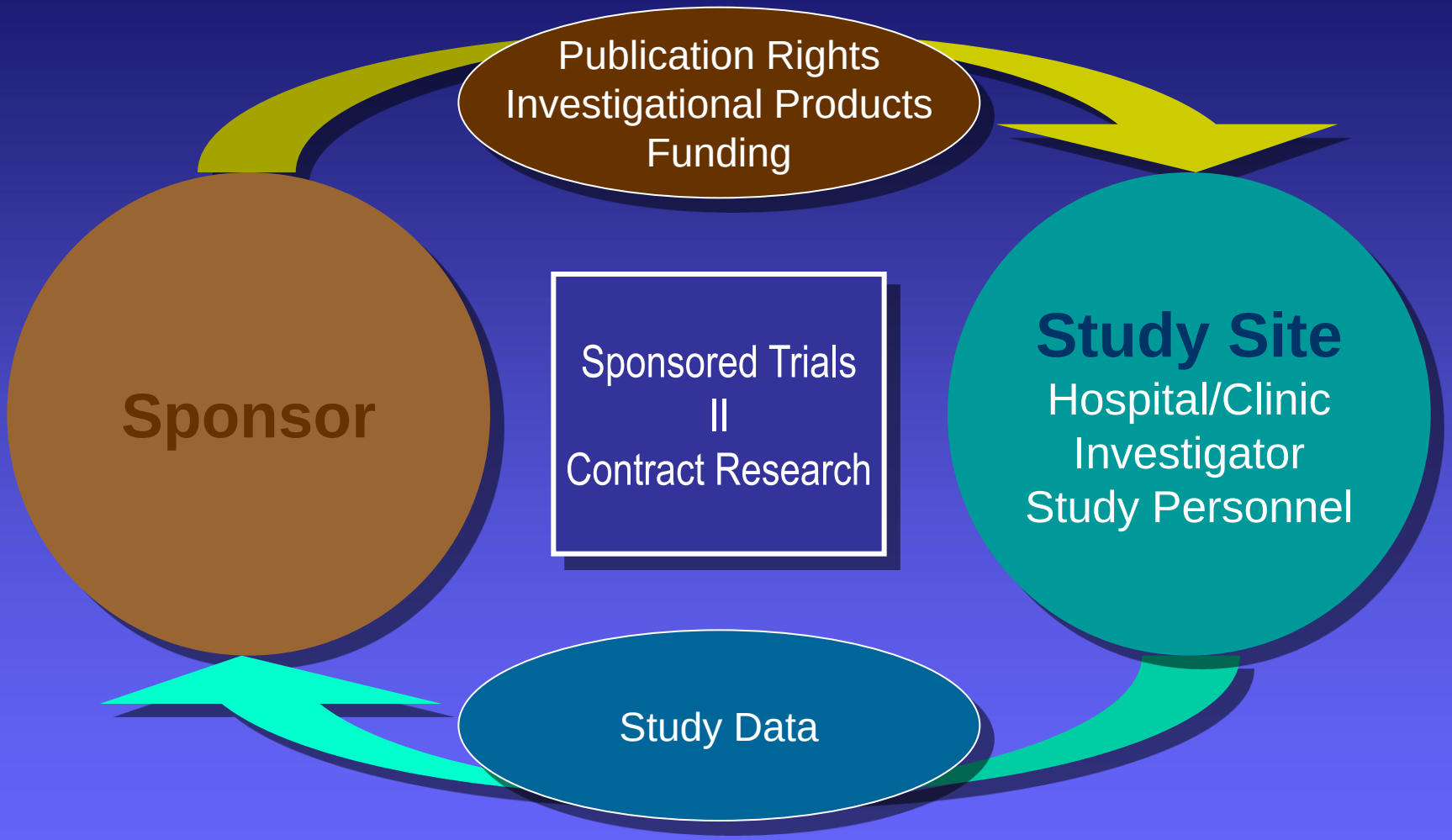
Tel: +852 9097 0567
Email: yauhenry@hotmail.com

Clinical Trial Agreement for Sponsored Clinical Trials

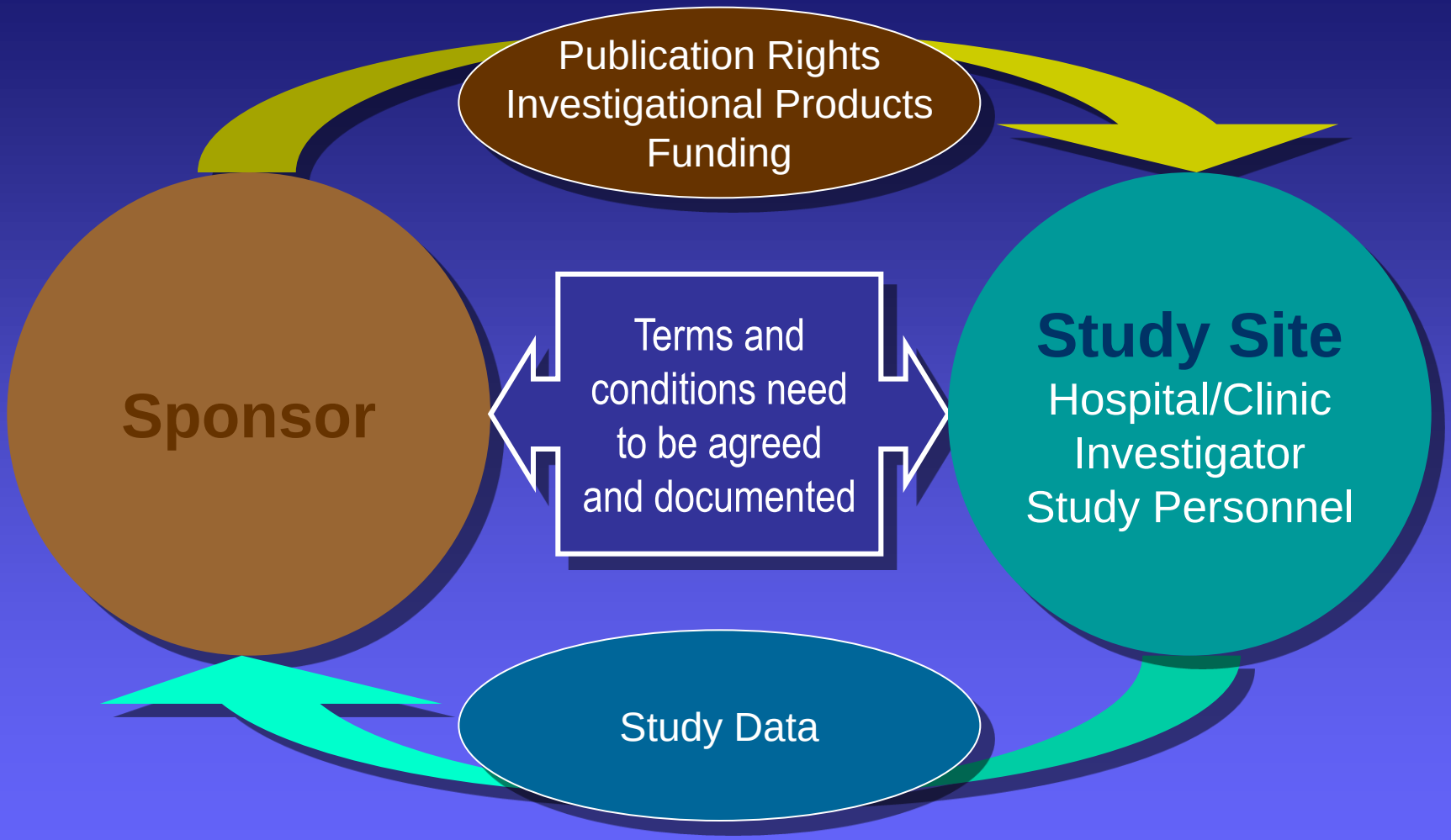
Highlights :

- Principles of clinical trial agreements
- Major contents in clinical trial agreements
- Management of clinical trial agreements

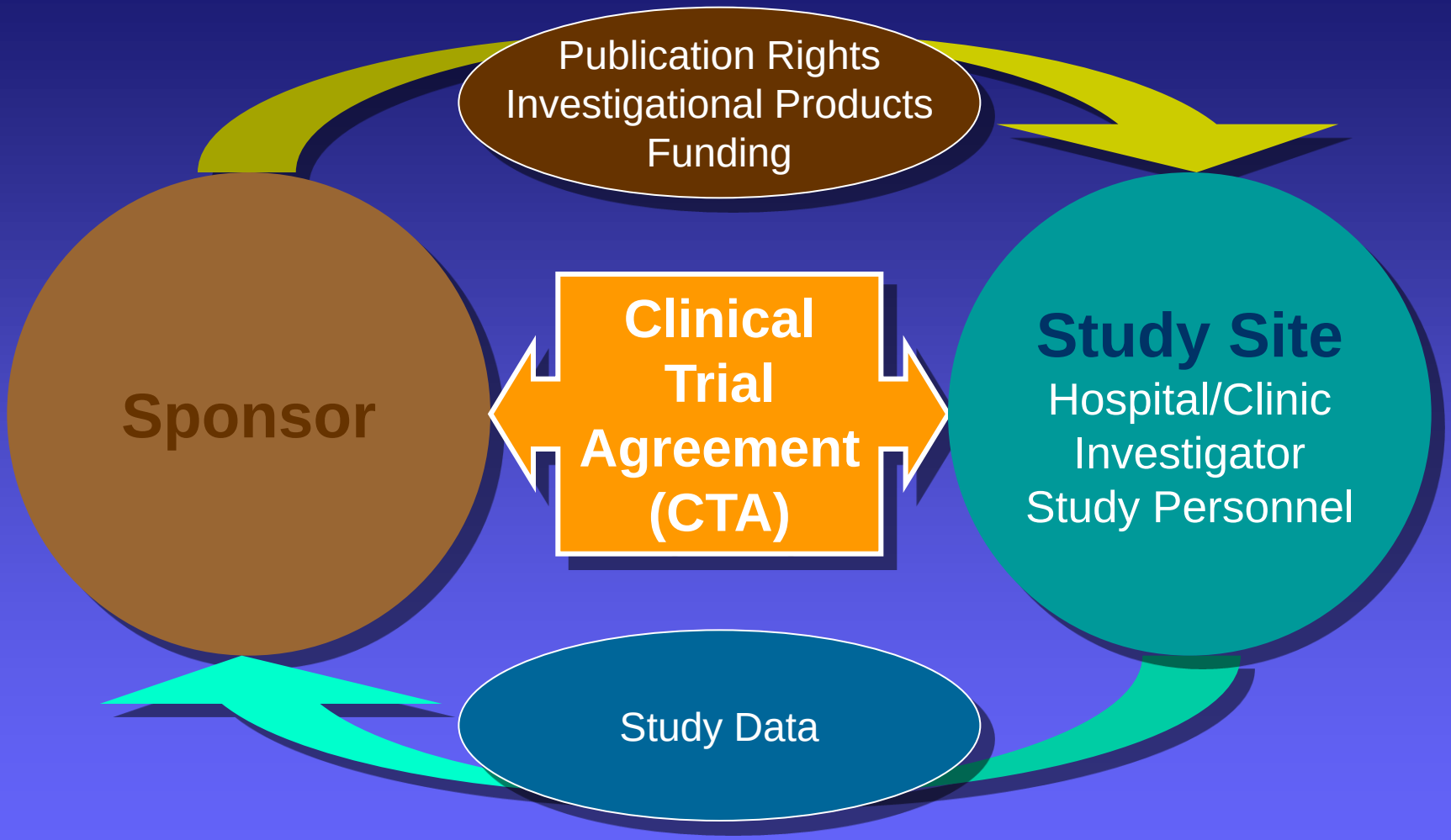
Sponsored Clinical Trials as Contract Research



Sponsored Clinical Trials as Contract Research



Sponsored Clinical Trials as Contract Research



Six Principles of Clinical Trial Agreements

Risk exposure of study site

Examples:

- Indemnity
- Insurance
- Limitation of liability

Six Principles of Clinical Trial Agreements

Practicality of operational requirements

Examples:

- Timeline for trial subject recruitment
- Time for case report forms submission
- Frequency of radiological imaging

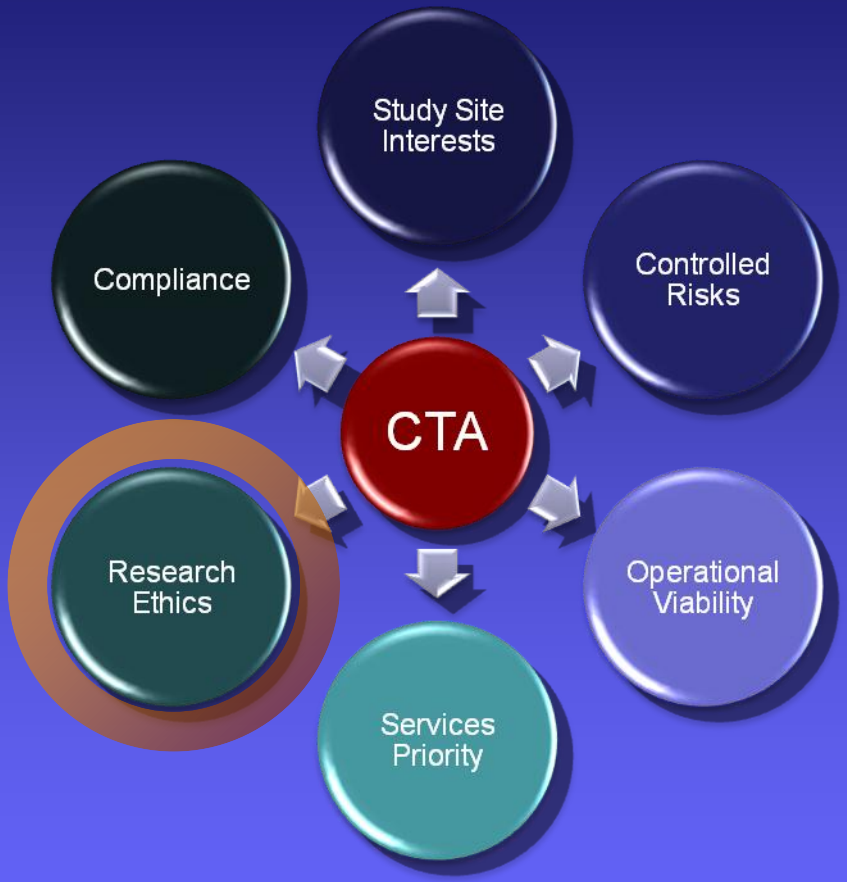
Six Principles of Clinical Trial Agreements

Influence on normal healthcare services

Examples:

- Patients' waiting time for hospital services
- Deviation from routine clinical operation
- Extra workload for hospital staff

Six Principles of Clinical Trial Agreements



Protection of subjects' rights, safety and well-being

Examples:

- Informed consent
- Coercive subject recruitment arrangement
- Reporting of safety data to study site

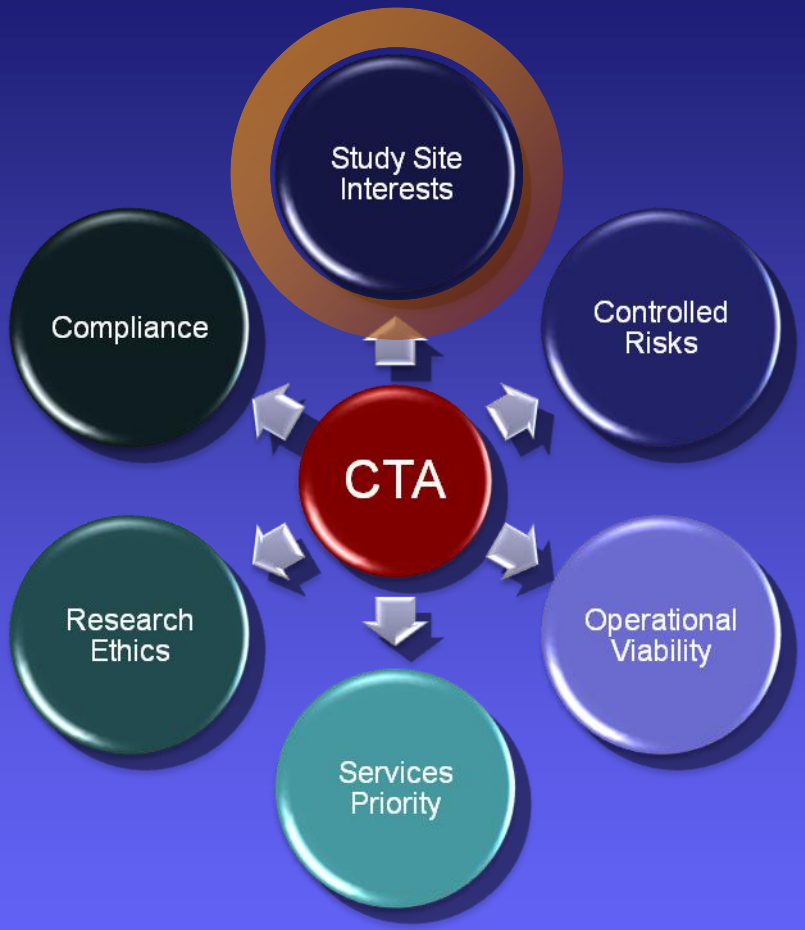
Six Principles of Clinical Trial Agreements

Consistency with laws, regulations, GCP & management policies

Examples:

- Access to subjects' medical records
- Long-term retention of medical records
- Application to DOH

Six Principles of Clinical Trial Agreements



Protection of study site's interests

Examples:

- Reimbursement for hospital services
- Rights to use study data for non-commercial purpose

Five Key Areas in a CTA

- Study Management
- Study Site Operations
- Handling of Study Information
- Liability Management
- Legal Procedures

Five Key Areas in a CTA

Study Management | Study Site Operations | Handling of Study Information | Liability Management | Legal Procedures

- Supply of investigational products and study materials
- Safety reporting
- Appointment of contract research organization (CRO), if applicable
- Monitoring, auditing and inspection
- Financial arrangements

Five Key Areas in a CTA

Study Management | **Study Site Operations** | Handling of Study Information | Liability Management | Legal Procedures

- Recruitment of human subjects
- Informed consent procedures
- Completion and verification of case report forms
- Archiving of study records

Five Key Areas in a CTA

Study Management | Study Site Operations | **Handling of Study Information** | Liability Management | Legal Procedures

- Ownership of study data and intellectual property rights
- Confidentiality of study information
- Registration of study with public clinical trial registries
- Publication of results

Five Key Areas in a CTA

Study Management | Study Site Operations | Handling of Study Information | **Liability Management** | Legal Procedures

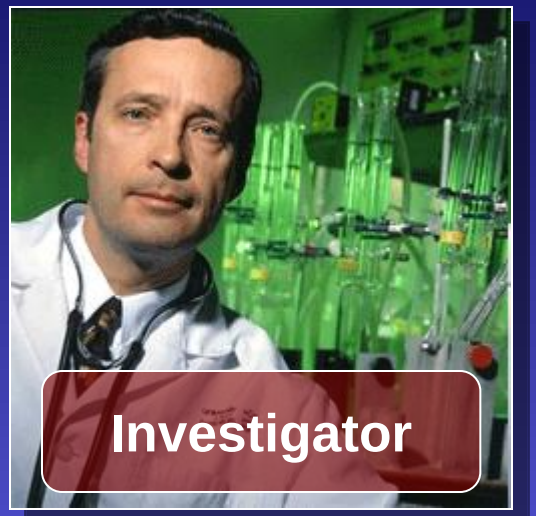
- Indemnity
- Insurance
- Limitation of liability

Five Key Areas in a CTA

Study Management | Study Site Operations | Handling of Study Information | Liability Management | **Legal Procedures**

- Amendment and assignment of agreement
- Termination of agreement / termination of study
- Disputes resolution
- Governing law

Who has the responsibility to manage a CTA ?

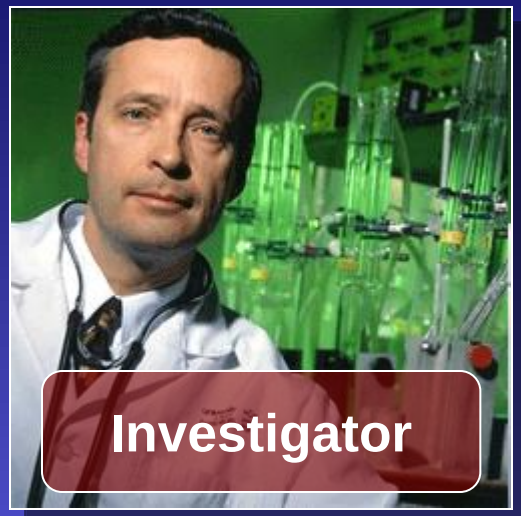


CTAs are legal documents
only lawyers can understand !

Who has the responsibility to manage a CTA ?

CTAs are signed by
the CCE / HCE / COS !

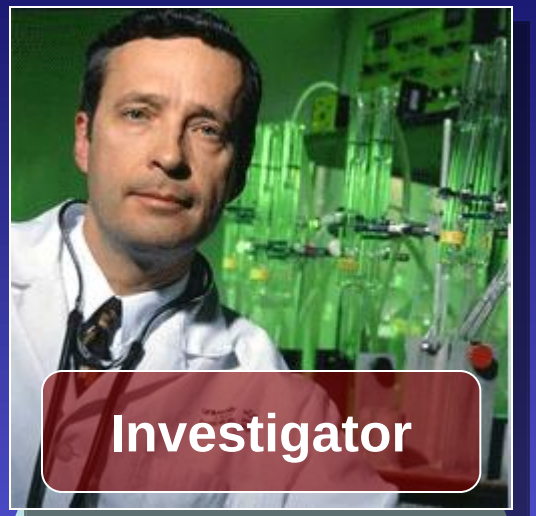
Who has the responsibility to manage a CTA ?



Clinical trials are conducted
by investigators !

Who has the responsibility to manage a CTA ?

- Legal languages
- Legal liabilities



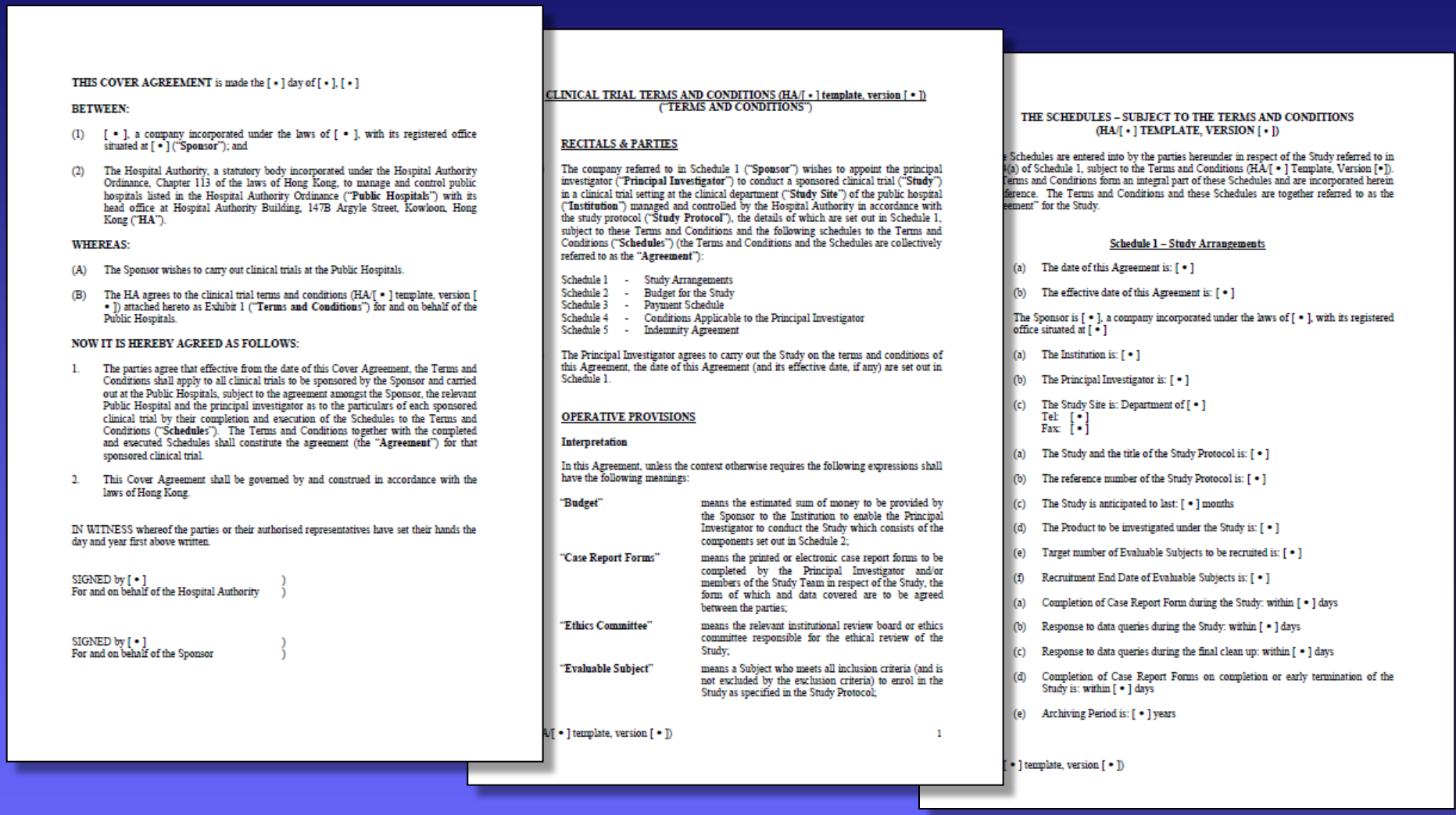
- Operational contents
- Funding arrangement
- Publication rights
- Protection of subjects' interests

- Resources allocation
- Influence on hospital services
- Protection of hospital's interests

Since
13 October, 2010

HA
Standard CTA

HA Standard CTA Template



THIS COVER AGREEMENT is made the [•] day of [•], [•]

BETWEEN:

(1) [•], a company incorporated under the laws of [•], with its registered office situated at [•] ("**Sponsor**"); and

(2) The Hospital Authority, a statutory body incorporated under the Hospital Authority Ordinance, Chapter 113 of the laws of Hong Kong, to manage and control public hospitals listed in the Hospital Authority Ordinance ("**Public Hospitals**") with its head office at Hospital Authority Building, 147B Argyle Street, Kowloon, Hong Kong ("**HA**").

WHEREAS:

(A) The Sponsor wishes to carry out clinical trials at the Public Hospitals.

(B) The HA agrees to the clinical trial terms and conditions (HA/[•] template, version [•]) attached hereto as Exhibit 1 ("**Terms and Conditions**") for and on behalf of the Public Hospitals.

NOW IT IS HEREBY AGREED AS FOLLOWS:

1. The parties agree that effective from the date of this Cover Agreement, the Terms and Conditions shall apply to all clinical trials to be sponsored by the Sponsor and carried out at the Public Hospitals, subject to the agreement amongst the Sponsor, the relevant Public Hospital and the principal investigator as to the particulars of each sponsored clinical trial by their completion and execution of the Schedules to the Terms and Conditions ("**Schedules**"). The Terms and Conditions together with the completed and executed Schedules shall constitute the agreement (the "**Agreement**") for that sponsored clinical trial.

2. This Cover Agreement shall be governed by and construed in accordance with the laws of Hong Kong.

IN WITNESS whereof the parties or their authorised representatives have set their hands the day and year first above written.

SIGNED by [•])
For and on behalf of the Hospital Authority)

SIGNED by [•])
For and on behalf of the Sponsor)

CLINICAL TRIAL TERMS AND CONDITIONS (HA/[•] template, version [•])
("TERMS AND CONDITIONS")

RECITALS & PARTIES

The company referred to in Schedule 1 ("**Sponsor**") wishes to appoint the principal investigator ("**Principal Investigator**") to conduct a sponsored clinical trial ("**Study**") in a clinical trial setting at the clinical department ("**Study Site**") of the public hospital ("**Institution**") managed and controlled by the Hospital Authority in accordance with the study protocol ("**Study Protocol**"), the details of which are set out in Schedule 1, subject to these Terms and Conditions and the following schedules to the Terms and Conditions ("**Schedules**") (the Terms and Conditions and the Schedules are collectively referred to as the "**Agreement**"):

Schedule 1 - Study Arrangements
Schedule 2 - Budget for the Study
Schedule 3 - Payment Schedule
Schedule 4 - Conditions Applicable to the Principal Investigator
Schedule 5 - Indemnity Agreement

The Principal Investigator agrees to carry out the Study on the terms and conditions of this Agreement, the date of this Agreement (and its effective date, if any) are set out in Schedule 1.

OPERATIVE PROVISIONS

Interpretation

In this Agreement, unless the context otherwise requires the following expressions shall have the following meanings:

"**Budget**"	means the estimated sum of money to be provided by the Sponsor to the Institution to enable the Principal Investigator to conduct the Study which consists of the components set out in Schedule 2;
"**Case Report Forms**"	means the printed or electronic case report forms to be completed by the Principal Investigator and/or members of the Study Team in respect of the Study, the form of which and data covered are to be agreed between the parties;
"**Ethics Committee**"	means the relevant institutional review board or ethics committee responsible for the ethical review of the Study;
"**Evaluable Subject**"	means a Subject who meets all inclusion criteria (and is not excluded by the exclusion criteria) to enrol in the Study as specified in the Study Protocol;

A/[•] template, version [•]) 1

THE SCHEDULES – SUBJECT TO THE TERMS AND CONDITIONS
(HA/[•] TEMPLATE, VERSION [•])

e Schedules are entered into by the parties hereunder in respect of the Study referred to in (a) of Schedule 1, subject to the Terms and Conditions (HA/[•] Template, Version [•]). erms and Conditions form an integral part of these Schedules and are incorporated herein ference. The Terms and Conditions and these Schedules are together referred to as the ement" for the Study.

Schedule 1 – Study Arrangements

(a) The date of this Agreement is: [•]

(b) The effective date of this Agreement is: [•]

The Sponsor is [•], a company incorporated under the laws of [•], with its registered office situated at [•]

(a) The Institution is: [•]

(b) The Principal Investigator is: [•]

(c) The Study Site is: Department of [•]
Tel: [•]
Fax: [•]

(a) The Study and the title of the Study Protocol is: [•]

(b) The reference number of the Study Protocol is: [•]

(c) The Study is anticipated to last: [•] months

(d) The Product to be investigated under the Study is: [•]

(e) Target number of Evaluable Subjects to be recruited is: [•]

(f) Recruitment End Date of Evaluable Subjects is: [•]

(a) Completion of Case Report Form during the Study: within [•] days

(b) Response to data queries during the Study: within [•] days

(c) Response to data queries during the final clean up: within [•] days

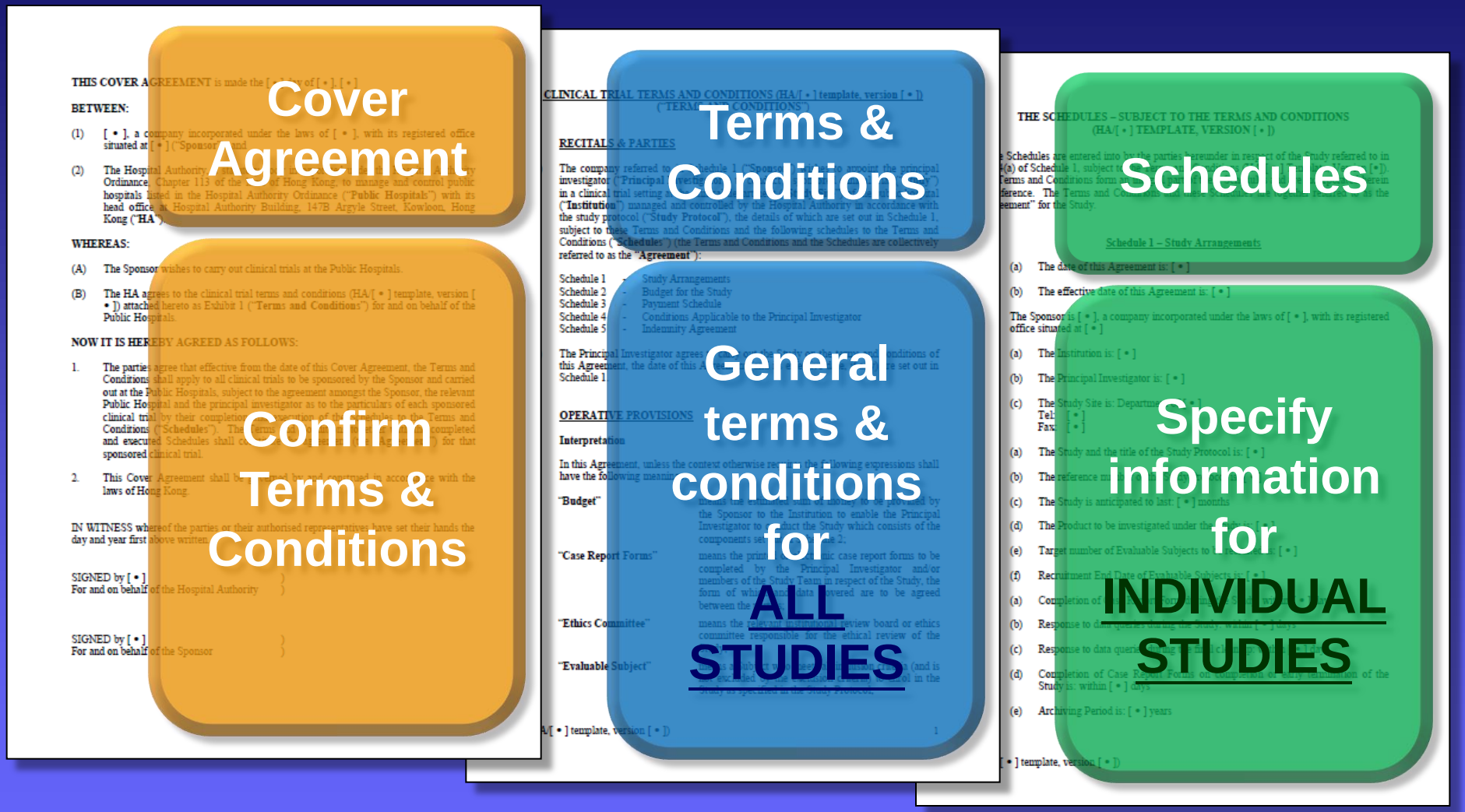
(d) Completion of Case Report Forms on completion or early termination of the Study is: within [•] days

(e) Archiving Period is: [•] years

[•] template, version [•])

Management of Clinical Trial Agreements

HA Standard CTA Template



HA Standard CTA Template

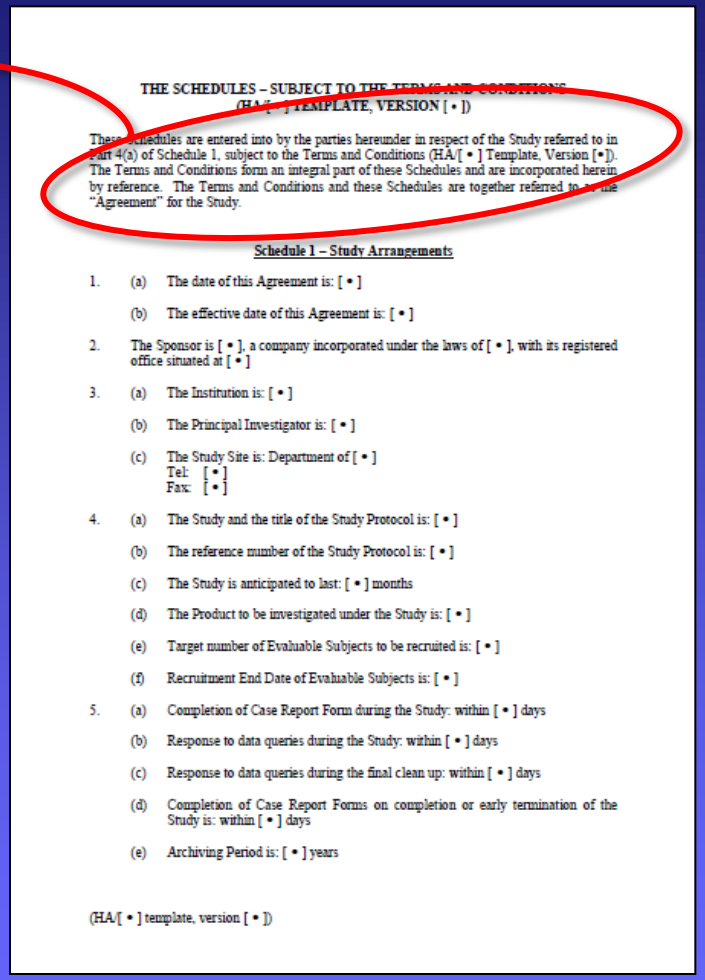
HA Standard CTA Template

Referring to the Master CTA

For each clinical study

Completing the Schedules

Signing of the Schedules constitutes a CTA



THE SCHEDULES – SUBJECT TO THE TERMS AND CONDITIONS (HA/[•] TEMPLATE, VERSION [•])

These Schedules are entered into by the parties hereunder in respect of the Study referred to in Part 4(a) of Schedule 1, subject to the Terms and Conditions (HA/[•] Template, Version [•]). The Terms and Conditions form an integral part of these Schedules and are incorporated herein by reference. The Terms and Conditions and these Schedules are together referred to as the "Agreement" for the Study.

Schedule 1 – Study Arrangements

1. (a) The date of this Agreement is: [•]
   (b) The effective date of this Agreement is: [•]
2. The Sponsor is [•], a company incorporated under the laws of [•], with its registered office situated at [•]
3. (a) The Institution is: [•]
   (b) The Principal Investigator is: [•]
   (c) The Study Site is: Department of [•]
   Tel: [•]
   Fax: [•]
4. (a) The Study and the title of the Study Protocol is: [•]
   (b) The reference number of the Study Protocol is: [•]
   (c) The Study is anticipated to last: [•] months
   (d) The Product to be investigated under the Study is: [•]
   (e) Target number of Evaluable Subjects to be recruited is: [•]
   (f) Recruitment End Date of Evaluable Subjects is: [•]
5. (a) Completion of Case Report Form during the Study: within [•] days
   (b) Response to data queries during the Study: within [•] days
   (c) Response to data queries during the final clean up: within [•] days
   (d) Completion of Case Report Forms on completion or early termination of the Study is: within [•] days
   (e) Archiving Period is: [•] years

(HA/[•] template, version [•])

Schedules for Individual Studies

THE SCHEDULES – SUBJECT TO THE TERMS AND CONDITIONS
(HA/[•] TEMPLATE, VERSION [•])

These Schedules are entered into by the parties hereunder in respect of the Study referred to in Part 4(a) of Schedule 1, subject to the Terms and Conditions (HA/[•] Template, Version [•]). The Terms and Conditions form an integral part of these Schedules and are incorporated herein by reference. The Terms and Conditions and these Schedules are together referred to as the "Agreement" for the Study.

Schedule 1 – Study Arrangements

1. (a) The date of this Agreement is: [•]
   (b) The effective date of this Agreement is: [•]
2. The Sponsor is [•], a company incorporated under the laws of [•], with its registered office situated at [•]
3. (a) The Institution is: [•]
   (b) The Principal Investigator is: [•]
   (c) The Study Site is: Department of [•]
   Tel: [•]
   Fax: [•]
4. (a) The Study and the title of the Study Protocol is: [•]
   (b) The reference number of the Study Protocol is: [•]
   (c) The Study is anticipated to last: [•] months
   (d) The Product to be investigated under the Study is: [•]
   (e) Target number of Evaluable Subjects to be recruited is: [•]
   (f) Recruitment End Date of Evaluable Subjects is: [•]
5. (a) Completion of Case Report Form during the Study: within [•] days
   (b) Response to data queries during the Study: within [•] days
   (c) Response to data queries during the final clean up: within [•] days
   (d) Completion of Case Report Forms on completion or early termination of the Study is: within [•] days
   (e) Archiving Period is: [•] years

(HA/[•] template, version [•])

THE SCHEDULES – SUBJECT TO THE TERMS AND CONDITIONS
(HA/[•] TEMPLATE, VERSION [•])

Schedule 2 – Budget for the Study

[EXAMPLE:]

1. Fixed cost to cover the basic costs to be incurred for the Study:

   [•] and the Institution's administrative costs of HK$15,000.00

2. Study costs for the Study:

   (a) Treatment cost per Evaluable Subject (up to the maximum number of Evaluable Subjects under this Agreement or additional Evaluable Subjects agreed by the Sponsor), provided that the Evaluable Subject completes the treatment and/or concludes with a "withdrawal/conclusion visit" in accordance with the Study Protocol, is: [•]

   (b) Follow-up cost per "Follow Up Visit" completed by the Evaluable Subject in accordance with the Study Protocol is: [•]

   (c) Screening failure cost per Subject screened according to the Study Protocol but who cannot be enrolled as an Evaluable Subject is: [•]

   (d) Additional assessment costs for each actual additional assessment performed for each Evaluable Subject in accordance with the Study Protocol is: [•]

   (e) [Nature of Assessment] [Cost]

   (f) Others (if any): [•]

3. The detailed breakdown of the Budget (if any) is attached to this Schedule 2.

(HA/[•] template, version [•])

Schedules for Individual Studies

THE SCHEDULES – SUBJECT TO THE TERMS AND CONDITIONS
(HA/[•] TEMPLATE, VERSION [•])

Schedule 3 – Payment Schedule

Payments due to the Institution under the Budget shall be made by the Sponsor according to the following schedule:

[EXAMPLE:]

1. The fixed cost of [HK$] shall be paid in full upon full execution of this Agreement.

2. The treatment cost, follow-up cost, screening failure cost and additional assessment costs shall be paid in March, June, September and December every year during the course of the Study. The amount of each payment due to the Institution shall be calculated in respect of the number of screened Subjects and Evaluable Subjects and the number of visits and additional assessments completed by each Evaluable Subject in accordance with the Budget in Schedule 2.

3. Payments are to be made payable to "Hospital Authority – [insert name]".

(HA/[•] template, version [•])

THE SCHEDULES – SUBJECT TO THE TERMS AND CONDITIONS
(HA/[•] TEMPLATE, VERSION [•])

Schedule 4 – Conditions Applicable to the Principal Investigator

I, being the Principal Investigator of the Study at the Study Site, have read and understood the Agreement.

I hereby agree to comply with the Agreement and following conditions during the period of the Agreement:

(i) I am free to participate in the Study and there are no rights which may be exercised by or obligations owed to any third party which might prevent or restrict my performance of the obligations detailed in the Agreement.

(ii) I am not involved in any regulatory or misconduct litigation or investigation by any relevant regulatory authority such as the Food and Drug Administration of the United States of America, the Medicines Control Agency of the United Kingdom or the European Medicines Evaluation Agency of the European Union. No data produced by me in any previous clinical study have been rejected because of concerns as to their accuracy or because they were generated by fraud.

(iii) I have considered, and am satisfied that, facilities appropriate to the Study are available to me at the Study Site and that I am supported, and will continue to be supported, by medical and other staff of sufficient number and experience to enable performance of the Study efficiently and in accordance with the obligations under the Agreement.

(iv) I am covered by appropriate medical liability insurance and details and evidence of the coverage will be provided to the Sponsor upon request.

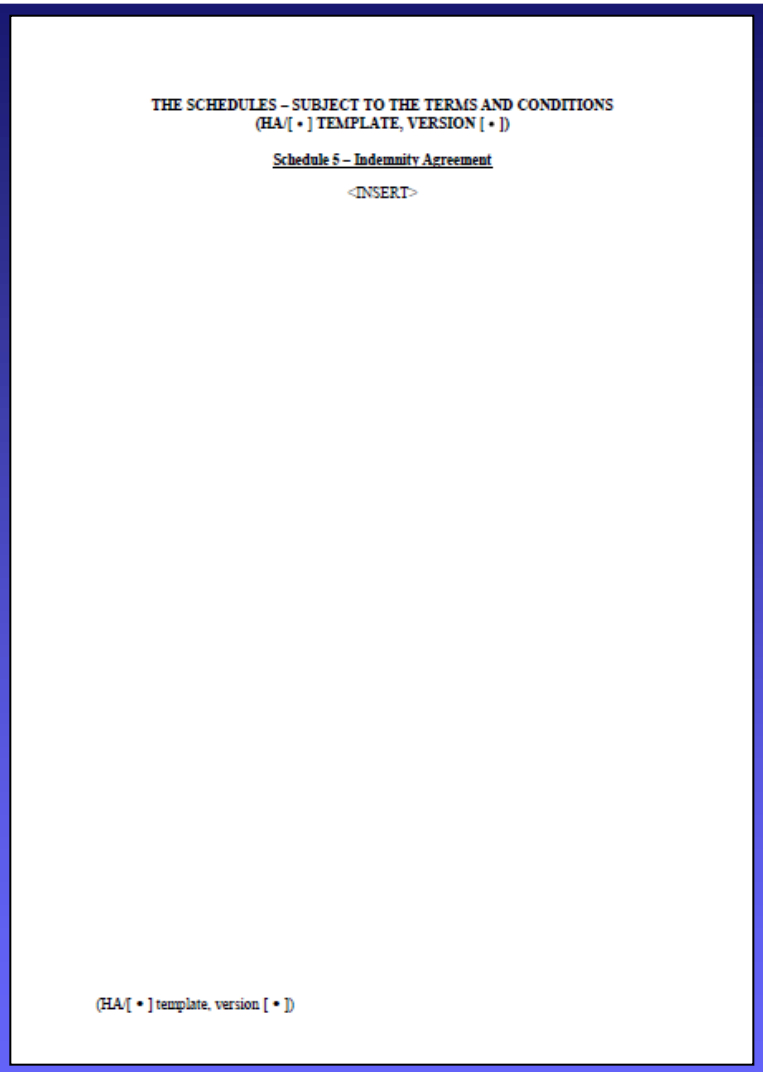
(v) Neither myself, nor my spouse nor any dependent children, have entered into and will not enter into any financial arrangements with the Sponsor to hold financial interests in the Sponsor and/or the Product that are required to be disclosed pursuant to the United States Code of Federal Regulations Title 21 Part 54 ("21 CFR 54"), namely: (i) any financial arrangement whereby the value of the compensation paid in respect of the performance of the Study could be influenced by the outcome of the Study (as more fully defined in 21 CFR 54.2(a)); (ii) any proprietary interest in the Product (as more fully defined in 21 CFR 54.2(c)); (iii) any significant equity interest exceeding US$50,000 in the Sponsor (as more fully defined in 21 CFR 54.2(b)); and (iv) any significant payments from the Sponsor (except for the Budget for the Study) such as grants to fund ongoing research, compensation in the form of equipment, retainers for ongoing consultation or honoraria (as more fully defined in 21 CFR 54.2(f)). In the case of subparagraphs (iii) and (iv), I understand that such prohibitions will be valid during the duration of my carrying out the Study and for one (1) year following completion of the Study.

_____
Signed by [Dr]

Date: _____

(HA/[•] template, version [•])

Schedules for Individual Studies



THE SCHEDULES – SUBJECT TO THE TERMS AND CONDITIONS
(HA/[•] TEMPLATE, VERSION [•])

Schedule 5 – Indemnity Agreement

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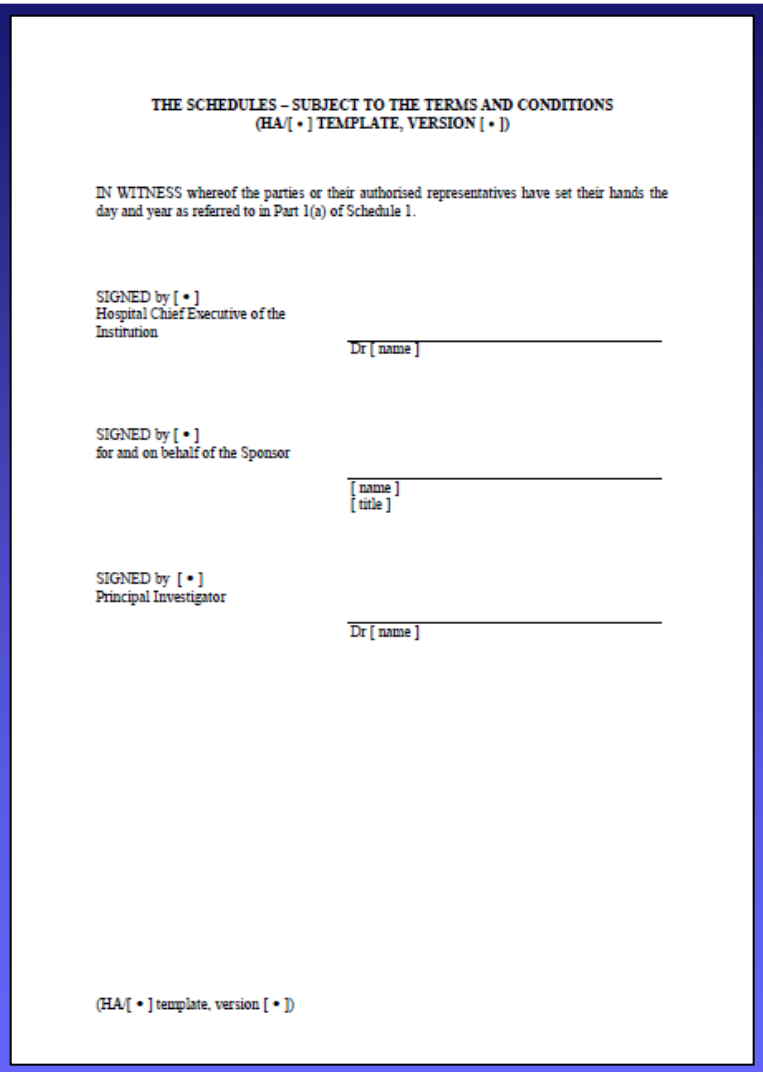

THE SCHEDULES – SUBJECT TO THE TERMS AND CONDITIONS
(HA/[•] TEMPLATE, VERSION [•])

IN WITNESS whereof the parties or their authorised representatives have set their hands the day and year as referred to in Part 1(a) of Schedule 1.

SIGNED by [•]
Hospital Chief Executive of the
Institution

Dr [name]

SIGNED by [•]
for and on behalf of the Sponsor

[name]
[title]

SIGNED by [•]
Principal Investigator

Dr [name]

(HA/[•] template, version [•])

Clinical Trial Agreement for Sponsored Clinical Trials

Highlights :

- Study sites need to consider 6 principles in CTA development
- Each CTA includes 5 key content areas
- CTA management is the joint responsibility of investigators, lawyers and hospital management
- When starting to plan for a sponsored study, check if a Master CTA with the sponsor is available.