



The Global Health Network

National Skills Sharing Workshop



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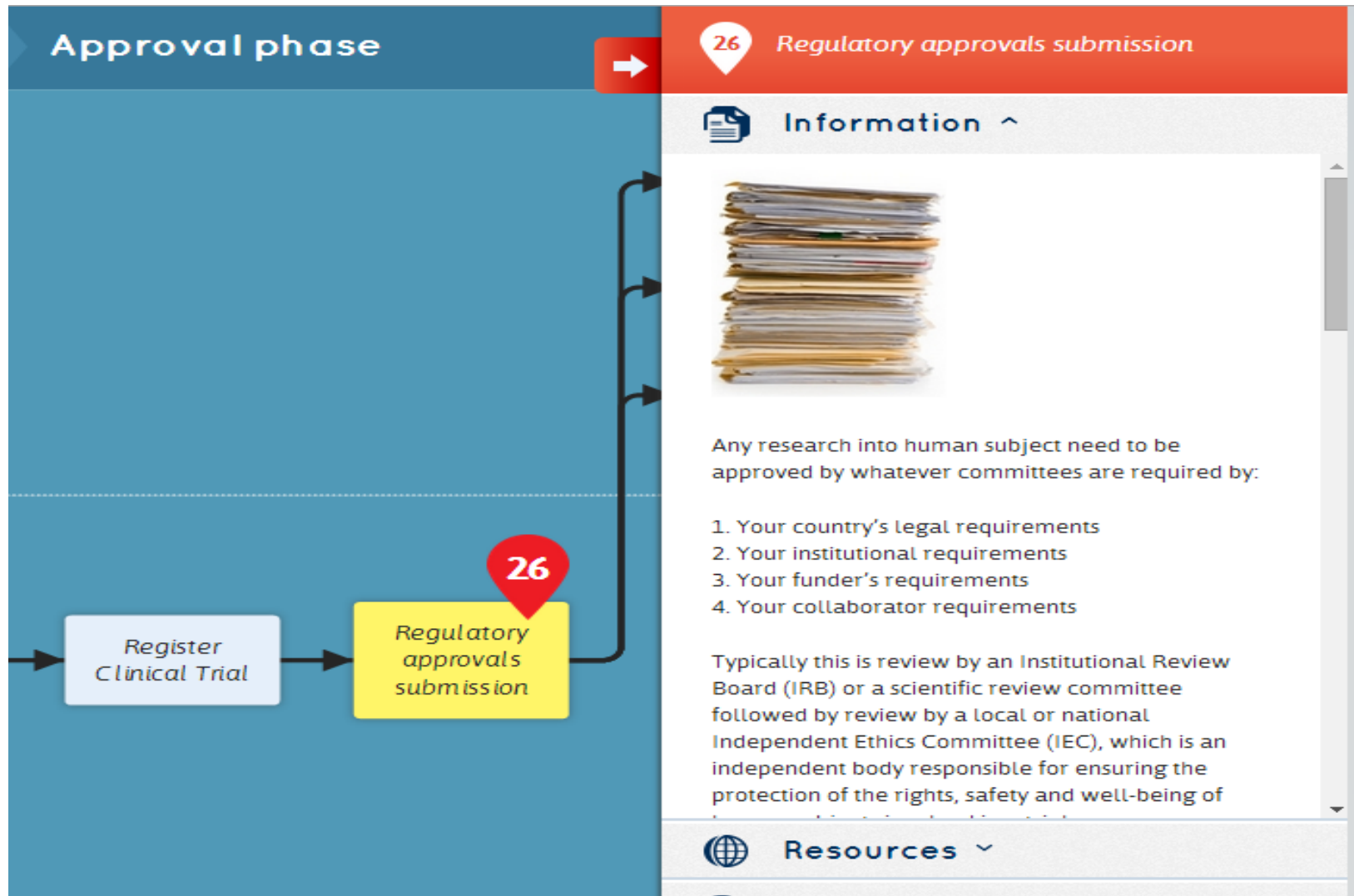
The MCC submission process for clinical trials: Tips and Tools

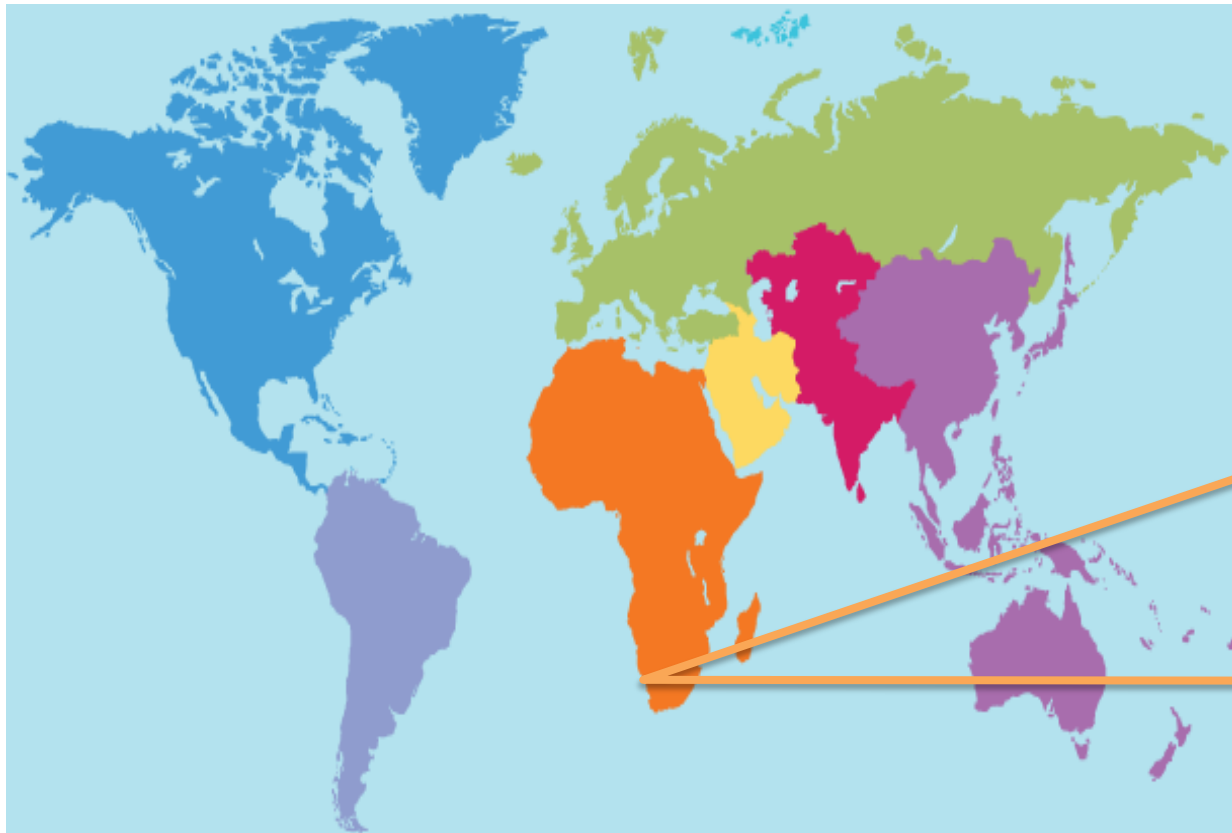
**Presented by: Ashley Veldsman (Regulatory Specialist, SATVI) and
Marilyn Solomons (Regulatory Advisor, CRC)**

Abbreviations and Acronyms

- CRC – Clinical Research Centre (UCT).
- CTC – Clinical Trials Committee
- CTU – Clinical Trials Unit
- CoCT – City of Cape Town (for research at any clinic)
- DoH – Department of Health (South Africa)
- DAFF – Department of Agriculture, Forestry and Fisheries (for studies involving a GMO)
- GMO – Genetically Modified Organism
- MCC – Medicines Control Council
- MRA – Medicines Regulatory Authority
- SACRA – South African Clinical Research Association

Regulatory Approvals





MCC is a statutory body that was established in terms of the Medicines and Related Substances Control Act, 101 of 1965, to oversee the regulation of medicines in South Africa.

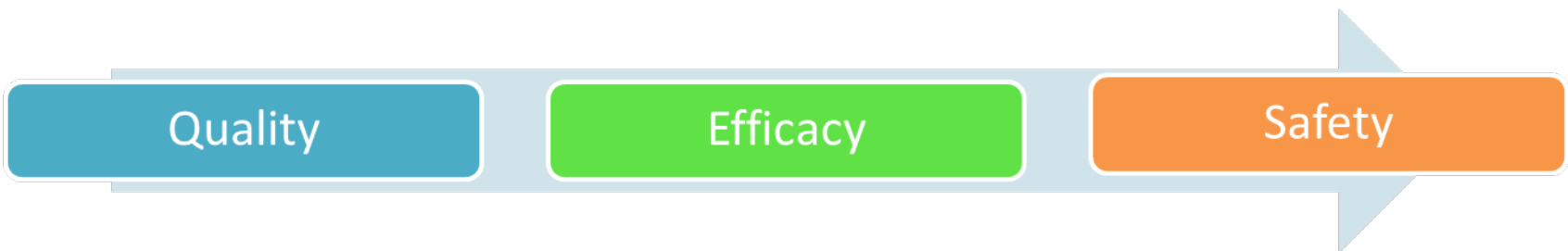
For more information on the MCC refer to <http://www.mccza.com>

Purpose

Its main purpose is to safeguard and protect the public through ensuring that all medicines that are sold and used in South Africa are safe, therapeutically effective and consistently meet acceptable standards of quality.

A Sponsor / Principal Investigator (PI) must apply for MCC approval to conduct a trial of a non-registered drug or a registered Drug with new indications

The MCC has an statutory obligation to ensure that all drugs available in the Country fulfil the necessary requirements for:



A photograph of two women and a young child. The woman on the left is wearing a blue sari and has her hand near her face. The woman on the right is wearing a blue sari and is holding the child. The child is wearing a yellow sleeveless top. The background is a plain, light-colored wall.

BEFORE you complete the CTF1

- This is not just about completing an application form. It's important to view the submission process holistically.

TIMELINE:

- Keep a copy of the annual MCC CTC Submission and Meeting Dates on hand. Use your network such as SACRA or the CRC to obtain this.
- Consider the timelines for submission. Dependant on the circumstances such as protocol complexity you would need at least 4 - 6 weeks to prepare.
- Factor in courier transport time - send 2 days before deadline if you can.

BEFORE you complete the CTF 1

MEDICINES CONTROL COUNCIL



CLINICAL TRIALS COMMITTEE MEETING AND SUBMISSION DATES FOR 2014

DATE OF SUBMISSION TO MRA	DATE OF CTC MEETING
15 November 2013	24 & 31 January 2014
17 January 2014	28 February & 14 March 2014
14 March 2014	25 April 2014 & 9 May 2014
16 May 2014	27 June 2014 & 4 July 2014
11 July 2014	22 & 29 August 2014
12 September 2014	17 & 24 October 2014
14 November 2014	January 2015

To all Applicants:

It is advisable to submit your clinical trial application before the due date.

- Sponsors / potential sponsors) cannot find these dates and will often ask you.
- SACRA (and Pharma) always seem to get this first-hand as they are listed on the MCC communication stakeholder list.
- There are approximately 6-7 submission dates annually. Approx. every 6-8 weeks. With 2 CTC meeting dates for every submission date i.e. approx. 12 CTC meetings per annum.
- Occasionally an extraordinary CTC meeting may be held if required.

BEFORE you complete the CTF 1

REVIEW THE PROTOCOL AND ICF

- A well written protocol is key. Local Investigator input is preferable and will assist immensely with your submission.
- Insist on a FINAL protocol version before you start any work. Do not work from a draft protocol. The study title will be written on all your documents – a change to 1 word and you will have to change it all!
- Is this a multi-national, multi-site study? Has the study been reviewed before, by whom, any comments? Is there a National PI and/or a local PI.

A photograph of two women and a young child. The woman on the left is wearing a blue sari and has her hand near her face. The woman on the right is wearing a blue sari and is holding the child. The child is wearing a yellow sleeveless top. They are all smiling and looking towards the camera.

BEFORE you complete the CTF 1

- Review key aspects such as Ethics, Regulatory, Safety Reporting in the protocol
- Is it in keeping with international and national guidelines such as ICH and SA GCP?
- Bear your research community in mind. Consult your CAB. An established CAB can be very helpful identifying potential pitfalls with for example new recruitment strategies & participant remuneration. CAB consultation should be mentioned in your application.

BEFORE you complete the CTF 1

- Are other approvals required: DAFF (GMO products), Regional DoH, CoCT? This is a linear process and approval is only granted when both MCC and EC approval is provided. Explain the implications of these additional requirements to the sponsor wrt timeline.
- Work with your lead Investigator to assist with the clinical aspects of the CTF1 and to identify and sort out any potential problems beforehand.

PREPARATION

WHAT DO YOU NEED TO PREPARE?

Allow staff sufficient time to prepare documentation for MCC. You will need to check each document beforehand.

For MCC **submit key staff only**: PI, all clinical investigators, the Study coordinator, all Pharmacists. You can submit others but that is not a requirement.

CHECK:

Cv – In MCC format. Create a standard template and use throughout for all staff. Latest GCP details consistent with certificate supplied. Are related studies listed to show experience. Is the publication list updated and adequate.

Declaration: In MCC format. Distinguish between PI, SI & other staff and Regional Monitor declarations. Both signature dates should be the same.

Workload: In MCC format. Applicable to clinical Investigators only. MCC will check to see if Investigator is overextended. 100% = 168 hours. Add up and ensure this is correct for each investigator. Add signature and date text to this document and ensure it is signed.

PREPARATION

WHAT DO YOU NEED TO PREPARE?

GCP certificate: Online courses such as NIH HSP NOT accepted. Must have gone through the HPCSA approval process so will be issued with a number which should be reflected on certificate. Valid within 3 years of date of issue.

All **Professional registration certificates/receipts** (HPCSA, SAPC and SANC) must be available and current. **Professional Indemnity** for Investigators such as MPS required.

Consider how you will pay the MCC. **Proof of payment** must be faxed through to MCC beforehand. Keep a copy of the payment and proof of fax for the submission file

Prepare your files – you will need 2 sets. How you do this is up to you but remember to include a Content Table (state Protocol Title, Protocol Number, Site and PI name) so that documents will be easy to find. As your documents are ready you can slot them in.

Prepare a **proof of delivery document**. MCC will not follow up on any query until you can prove that your submission was actually delivered to them. Liaise with your courier how best to do this.

PREPARATION

WHAT DO YOU NEED TO PREPARE?

Check that the PI will be available to sign the key documents such as:

- CV, Declaration etc.
- Protocol signature page
- Declaration of sufficient funds to cover the study. This must be signed by the sponsor as well.

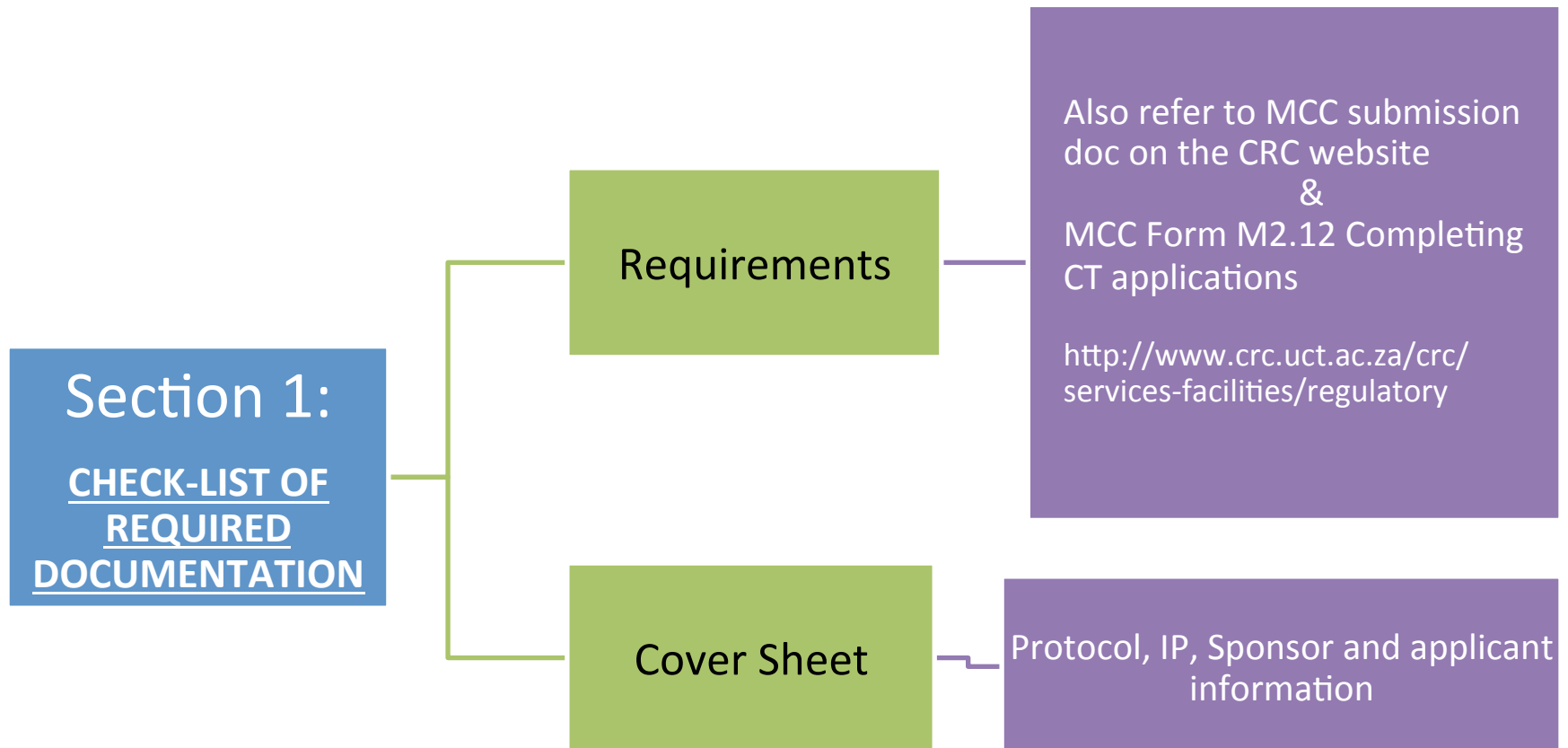
Types of Clinical trial applications forms

- CTF 1: Application to conduct clinical trial: - **6.05 CTF1 May03 v1.doc**
- CTF 2: Application for protocol amendment -**6.06 CTF2 May03 v1.doc**
- CTF 3: Application For Additional Investigator(s) Or Change Of Investigator(s) And Application For Additional Sites- **6.07 CTF3 May03 v1.doc**
- 6 Monthly Report
- For additional information – please see <http://www.crc.uct.ac.za/crc/services-facilities/regulatory>



Clinical Trial Application (CTF1)

Tips and Tools



IMPORTANT DOCUMENTS NOT ON THE MCC CHECKLIST

GCP, HPCSA, MPS or Professional Indemnity, Clinical Trial Insurance

Workload

Monitor(s) for the study - Add GCP certificate

GMP compliance that includes inspection of investigational product manufacture.

Provide the names and qualifications of members of the DSMB.

Evidence of laboratory competence should be provided, including GLP certification and evidence of test validation, where appropriate.

The protocol must be signed by the PI (where applicable)

Letter of Intent for EC approval – see CRC website

All MCC templates can be found in the MCC document 'Completing CT applications'.

Section 1:

CHECK-LIST OF REQUIRED DOCUMENTATION

CTF1 Application continued

Section 2: ADMINISTRATIVE AND SUPPLEMENTARY DETAILS

Section 2

Part 1: Contact details

Part 2: Details of
Investigational product

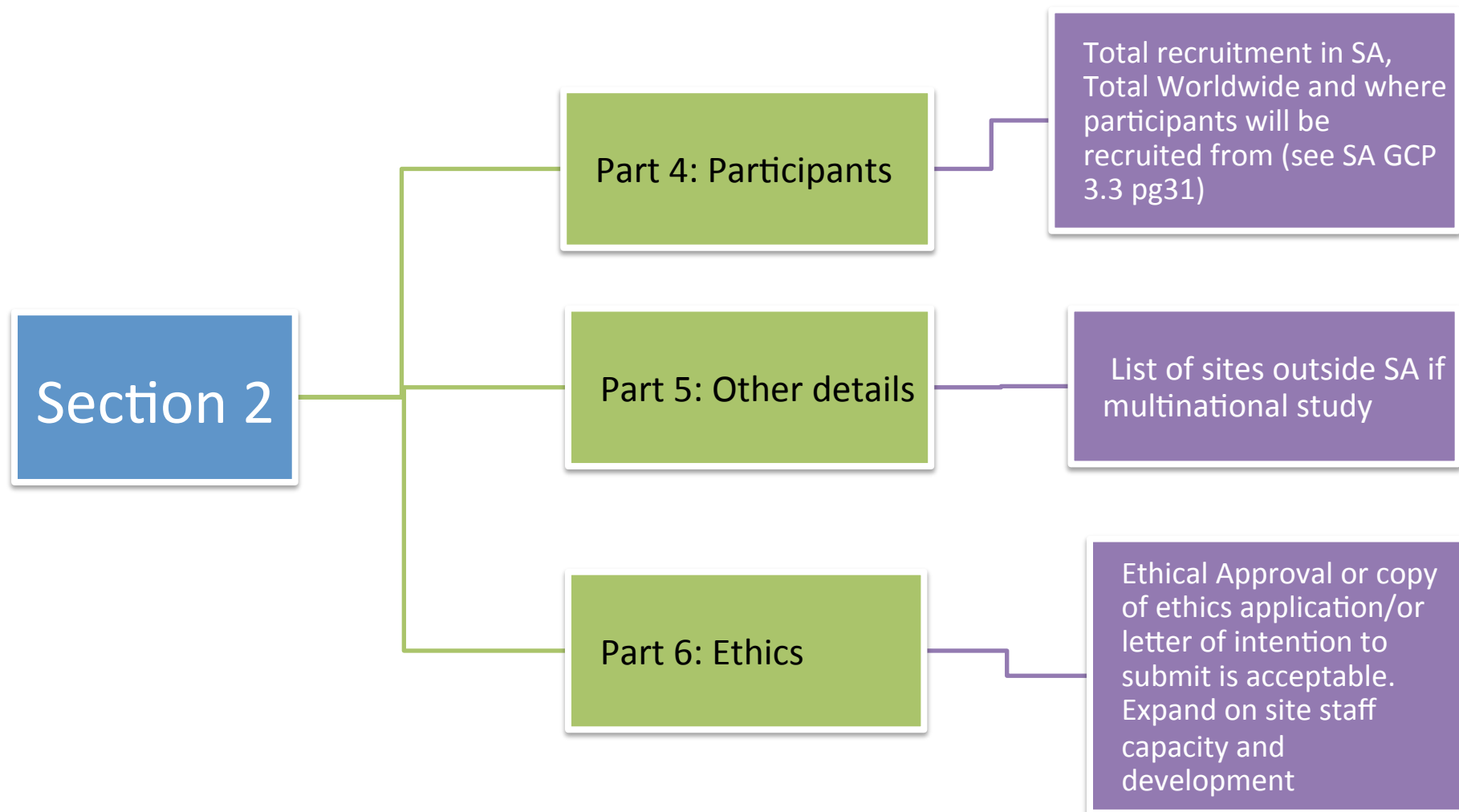
Part 3: Details of Trialists and
Sites

Your MCC approval letter is your permit!

Be sure to calculate the required IP + additional to allow for breakage (10%). Check the placebo/control and ensure that it has the same batch, lot number and expiry dates. This can be confirmed with supplier.

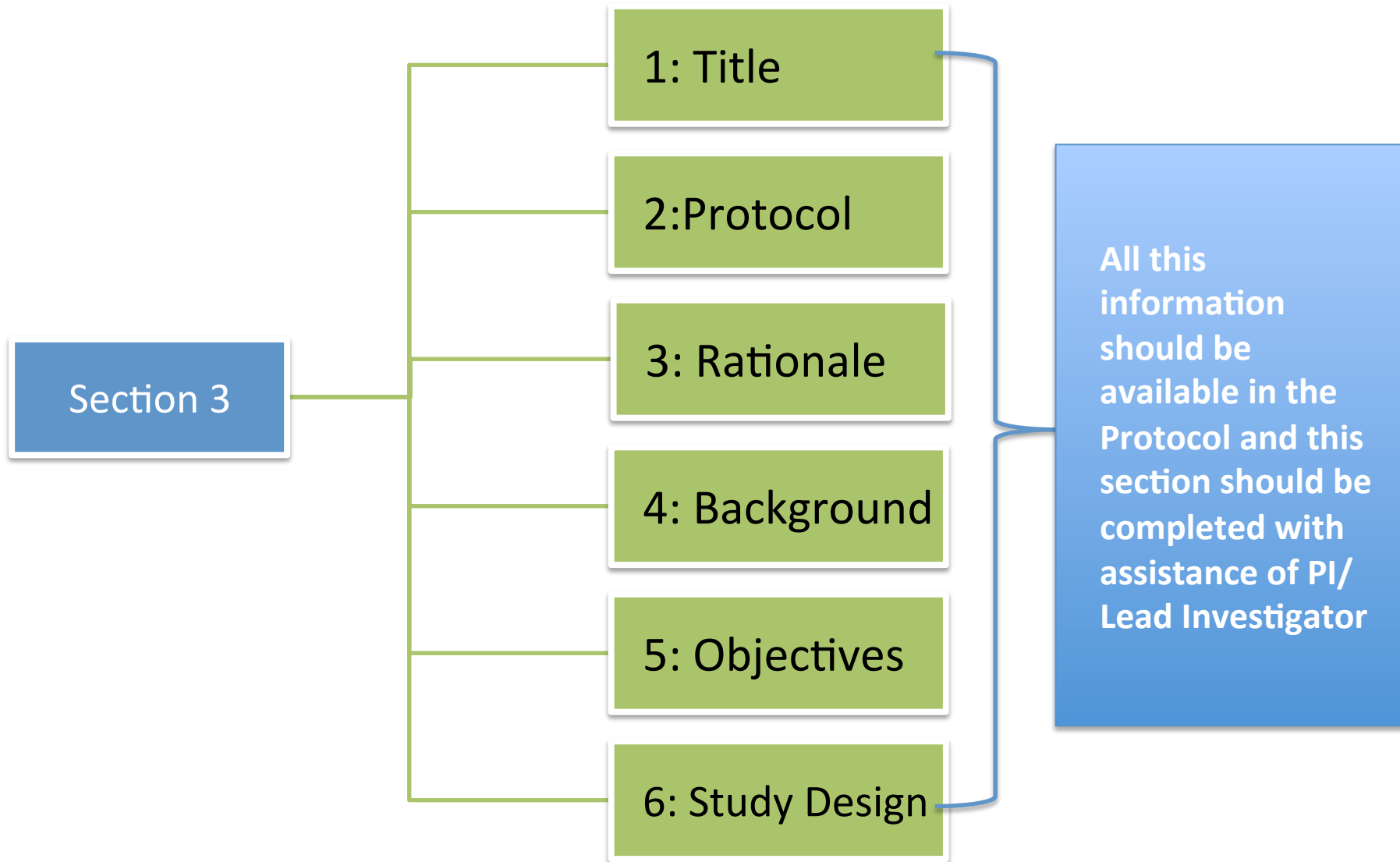
CTF1 Application

Section 2 continued



Section 3:

APPLICANT'S REPORT / PRESENTATION





Section 3: APPLICANT'S REPORT / PRESENTATION

Section 3

7: Participants

Total recruitment in
SA, Total Worldwide
and where
recruitment will be
from

8: Eligibility and enrolment:
(Inclusion and exclusion
criteria listed and justified)

9: Treatment modalities and
regimens, drug accountability

10: Outcome measurements/
variables (each clearly stated
and justified)



Section 3: APPLICANT'S REPORT / PRESENTATION

Section 3

11. Adverse events (prevention, definitions – including causality assignment, recording, reporting, time-lines, action to be taken, all clearly described)

12. Statistical measures

13. Ethical Issues

14. Other relevant information
not included above

WHAT TO EXPECT FOLLOWING SUBMISSION

- Following initial review of documents received, a checklist will be sent to site via facsimile as per applicant details. Ensure that the details supplied are correct and active.
- You will have 7 days within which to submit any outstanding documentation
- This will be the first communication with a MCC reference number (usually starts with the year of submission). To be used on all communication from thereon.
- Submit as before and keep proof submission (delivery note)
- Following CTC meeting a list of CTC comments/queries will be sent via fax. Again 7 days to respond.
- If approved, the CTC will recommend MCC approval at it's next meeting.
- Check the approval carefully: Study title; Protocol Version and date. List of investigators

MCC Checklist

**NEW SCREENING CHECKLIST
APPLICATION FOR THE CONDUCT OF
CLINICAL TRIALS IN SOUTH AFRICA**

COMPANY: SATVI

CONTACT PERSON: Ms Ashley Veldsman

FAX NO: 021-4066081

TELEPHONE: 021-4066991

DATABASE TRACKING NO: 20120534

PRODUCT & PHASE OF TRIAL

MCC RECEIPT DATE: 22 March 2012

MCC REF NO: 8.3.00 (2253)

PROTOCOL NO: HS 645

CTC MEETING DATE: 4 & 11 MAY 2012

ITEM	DOCUMENTS SUBMITTED WITH APPLICATION	YES	NO
1	Covering Letter/Date	✓ 22 March 2012	
2	Application form (30 Copies)	✓	
3	Checklist	✓	
4	Protocol Version and Date	version 1.1 15 March 2012	
5	Investigator Brochure/ Package insert	LS040 Rev D 31 Dec 2011	
6	Comparator Drug package insert		
7	Inform Consent & PIL	✓ version 1.1 15 Mar 2012	
8	Investigator CV's	✓	
9	Proof of GCP training (Certificates)	✓	
10	Proof of Current Malpractice insurance		Geldenhuys + Lucibeya
11	Signed declaration by Trialists (Crossing out 10&11 for PI's)	✓	
12	Pharmacist CV/Decl/GCP		
13	Letter of indemnity & insurance/Expiry date	✓ 01 Jan to 31 Dec 2012	
14	Copy of Ethics approval		✓
15	Copy of letter submitted to Ethics Committee	✓	
16	Reimbursement for Patients	R150 per visit	
17	Remuneration to Investigators		✓
18	National PI CV/ Decl / Malp/ GCP	✓	
19	Patients questionnaire		
20	Additional information Cert. Of analysis		✓
21	Disk	10 disk received	

CLINICAL TRIAL APPLICATION WITH OUTSTANDING DOCUMENTS, CDS AND NO SIGNATURES OR DRAFT DOCUMENTS
WILL BE REJECTED AND NOT CONSIDERED FOR REVIEW. THE ONLY OUTSTANDING DOCUMENTS THAT MAY BE
CONSIDERED ARE: ETHICS COMMITTEE APPROVAL AND CERTIFICATE OF ANALYSIS

Submit ^{of 10} HPCSA and MPS for all the investigators

PERSON RESPONSIBLE FOR THE CYCLE:

TEL: 012 312 8129

CTC Comments



health

Department:
Health
REPUBLIC OF SOUTH AFRICA.

MEDICINES CONTROL COUNCIL
The Registrar of Medicines, Private Bag X828, PRETORIA, 0001
Tel 012 395 8000 Fax 012 395 9201
Tel: Inquiries:
Fax: Reference:

FAX AND MAIL TO

Ms A Veldsman
SOUTH AFRICAN TB VACCINE INITIATIVE(SATVI)
Wehrner Beit South Building
Faculty of Health Science
Azino Road, Observatory
7925
Fax: 0214066081

Datum : Date

MR PHILIP MABILLE
N2/19/8/2 (2253)
07 June 2012

Tel: 0123958129
Fax: 0123958775

Dear Ms Veldsman,

Your application of the attached protocol has the following recommendations from the Clinical Trials Committee (CTC). Please respond to the attached recommendations within 7 days of receipt (07 June 2012), so as to assist the MCC in the timeous review and approval of your application.

- TWO copies of your response must please be forwarded to the clinical trials unit by mail OR hand delivered.
- Note that even if your trial category has 1 or 2, it still has to be ratified at the coming Medicines Control Council meeting.
- Please note that the study cannot commence until a final approval is obtained after the MCC meeting.

Please ensure that you indicate that it is a "RESPONSE" to the CTC meetings held on the 01 June 2012 for the Council meeting scheduled for the 08 June 2012

Yours faithfully,

MR PHILIP MABILLE
FOR AND ON BEHALF OF REGISTRAR OF MEDICINES

MCC TRIAL REFERENCE NO: 20120534




15 June 2012

The Registrar
Medicines Control Council
Hallmark Building
PRETORIA, 0001

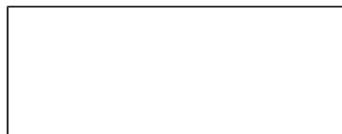
Dear Sir/Madam

RE: Response to the CTC meeting held on 01 June 2012 for the council meeting scheduled for the 08 June 2012 (?)

	MCC Reference Number: 20120534
Database Tracking number	N2/19/8/2 (2253)
Protocol Number:	HS 645
Protocol Title:	A randomized clinical trial in adults and newborns to compare the safety, <u>reactogenicity</u> and immunogenicity of BCG administration via a disposable syringe jet injector to BCG administration via syringe and needle Version 2.0 dated 15 June 2012

On behalf of the MCC I hereby acknowledge receipt of the documentation in support of the application for the above-referenced clinical trial.

MCC Stamp:



Additional MCC Applications

Protocol amendments (CTF2)

Follow the **CTF2 form** closely to ensure a successful application. Please contact the CRC if you are uncertain as to whether changes to your protocol constitute as amendment or otherwise.

Additional investigators (CTF3)

The MCC require that at least 80% of investigators are identified and included in the initial submission, and any new investigators cannot begin work until approved.

OTHER

ADDITIONAL PHARMACISTS

Adding a new pharmacist to the trial after the initial application requires a notification by letter (include an MCC-format CV, pharmacist's declaration, GCP certificate, Pharmacy Council registration document and insurance details). Once these have been submitted the pharmacist may start work on the trial immediately. No MCC response required. Maintain your correspondence and proof of delivery in the Investigator Site File.

MCC REPORTS

An MCC progress report is required every 6 months from the date of study start until the end of the trial, when the MCC is informed of trial closure (clinical aspects). A final SPONSOR study report should be submitted as soon as available.

SAFETY REPORTING

See CRC SOP 05 and the MCC's Reporting Adverse Drug Reactions in South Africa.

Points to consider:

- There is no set way to prepare and submit.
- For most applicants it's been a work in progress. Find what works for you (and them) and stick with it.
- Don't work in isolation. Develop your network and use the resources that are available such as the CRC.
- Your Mantra: The MCC is my friend! Get to know the MRA administrators – at some point you WILL be calling them everyday. Maintain your dignity – always be polite and courteous...Try!
- Document your process and any information you glean along the way. The study monitors/auditors will request this.

The MCC submission process for clinical trials: Tips and Tools

