



# **Current quality status of CABETs environmental laboratory and necessary steps to meet GLP requirements**

**June 18 – 22, 2007**

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**Sino – Dutch Pesticide Environmental  
Risk Assessment Project**

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## **1 Purpose of the trip**

Identify CABET's current situation with respect to:

- Quality system ISO 17025
- GLP system on management/staff level
- GLP on laboratory level.

Identify, describe and agree what steps are required to meet ISO 17025 and GLP.

## **2 Activities**

- Discussion with ICAMA/CABET staff on program
- Visit to the CABET laboratory
- a scan/audit of laboratory activities in CABET
- Discussion with lab workers
- A course "Principles of GLP" with included the following presentations/topics
  - The quality and environmental management in practice
  - GLP Introduction
  - Introduction OECD guidelines
  - Introduction SOP's on Facility Operations
  - Introduction study protocol
- Advice on GLP and ISO 17025 improvement and timeline
- Discuss the finding of visit and possibility of a follow up

See attached work programme for more details

## **3 Results / Observations**

This visit turned out to be a good eye opener for all those present at the presentations and a fertile discussion made clear that a lot of work and investment must be made to implement a GLP system within two years.

During the course "Principles of GLP" a survey was given over Good Laboratory Practice (GLP) and the possibility to implement this in CABET it became clear that;

- There was only very basic acquaintance of GLP
- There is no basic knowledge of the role of a QAU group
- No knowledge about OECD guidelines for management and QA

A big step was made by getting certified for ISO 17025 last year. This is a good basis for building a GLP system on management/staff level.

In spite of the fact that CABET is certified for ISO 17025 there is a lot of work to be done. When audited on this aspect incompleteness were pointed out on the following aspects.

- There were no safety cupboards for some hazardous chemicals
- Storage and transport of electronic acquired data (HPLC) is not documented.
- There were no validation plans of equipment used.
- Entrance SOP's of the GLP area were not present.

The QAU, including its archive, is not up to the level to work on the high level of GLP.

- The employees working as QA are not qualified and have not enough scientific research background to work at GLP level.
- There is no clearly division of chapters of SOP's to be used in GLP QA and GLP management.

There is no investment plan for an organisation who must act as an authority in China for contract laboratory.

## 4 Agreements for follow-up

For a follow up a plan of action must be set up for the next to years. For a good order these steps has to be taken for a good implementation of GLP and to get ready as an Inspection authority for pesticide contract laboratory in China.

### Step 1

The CABET laboratory is currently working on a list of SOP's written for use within the line of GLP regulations.

- Chapters of the SOP for management
- Chapters of the SOP for QA and archive

See appendix 3 for an example of SOP's in use at Alterra.

The current available SOP's also need a revision of their chapters. A management structure must be set up to work according to GLP. A division must be made in ; management SOP's, QA SOP's, Facility SOP's and Science SOP's based on methods and operations. An example is given in figure 1.

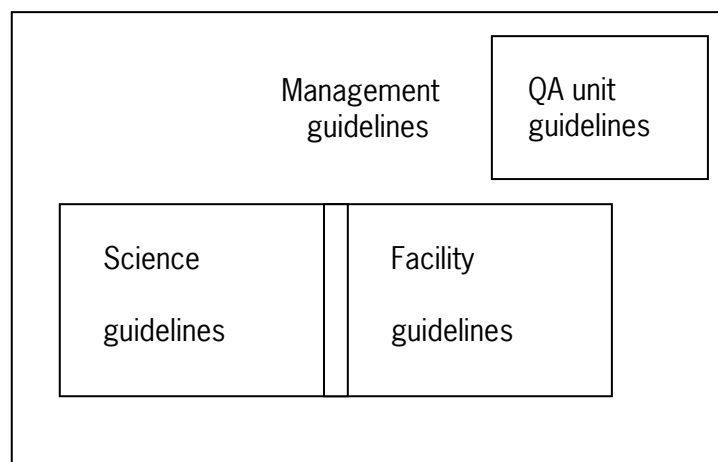


Figure 1 division of chapters used in GLP

### Step 2

As pointed out it is also necessary to setup a Quality assurance Unit (QAU) within CABET according to the OECD guidelines. Employees must be appointed, trained and SOP's must

be written according to the OECD management guidelines. The QA- unit may not be part of one of the research sections, it must be embed in the General management section or a new section.

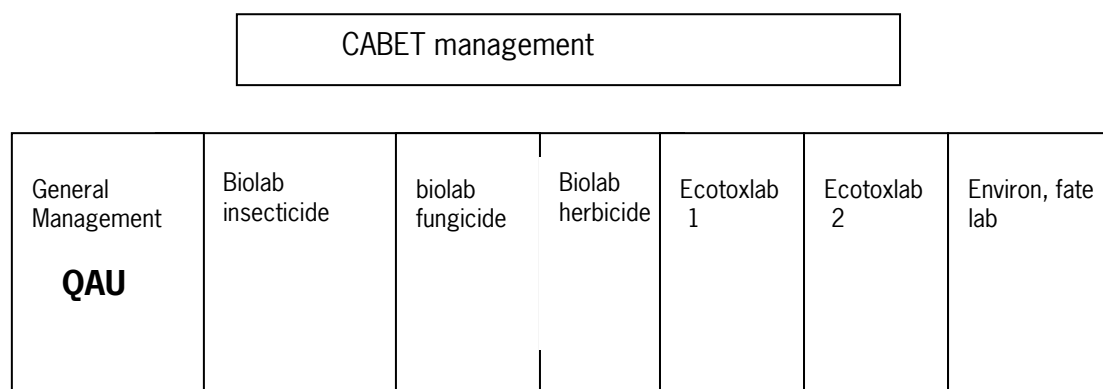


Figure 2 implementation of the QA-Unit in CABET

### Step 3

For the completion the personnel of the Quality Assurance Unit must have a scientific research background and has to have affinity with auditing on scientifically and management aspects. They also have to be trained by following a course in Quality Assurance and Auditing (in the Netherlands, CFPA or England, BARQA).

After step 1-3 an external auditing authority has to check that CABET can work according to the GLP-OECD guidelines. Before that Alterra will function as an advisor to assist and solving problems, answering questions and on side training/coaching.

### Step 4

The next step will be to be authorized to audit the contract labs. At this moment it is not clear how we will set up things. CABET need to get in contact with the SFDA. (A part of the Ministry of Health's State of China). They already have some kind of structure and are already auditing clinical contract laboratory in China.

- Get in contact and find out of the management, of there QAU structure is usable for CABET.
- Expand the QAU up to a authority for auditing contract laboratory in China.
- A workshop of both SFDA, CABET (ICAMA) and Alterra is a good start. The next step will be to be authorized to audit the contract laboratory in China.
- Look at the Dutch Food and Consumer Product Safety authority and use some parts of there management structure.

## 5 Plan of Operations

## CABET

- Set up a working group and work on steps 1-3
- clearly place a QAU within CABET
- appoint employees to set up a QAU
- train employees, they must take courses
- management SOP's must be written
- Operating SOP's and procedure SOP'S must be updated according to the OECD guidelines.
- Wil get in contact with SFDA to see if there management structure as authorized authority is usable for CABET.
- Wil take measures for the safety within laboratory (see observations)
- GLP-workplan for the next two years.

## Alterra

- Coaching within the framework of GLP part of the Sino-Dutch project.

## **Annex 1 Detailed programme**

### **Monday June 18, AM**

Discussion of the programme, check required preparations and agree on amendments if required.

Attendances: Paul, Ginger, Tao, Ye

### **Monday June 18, PM**

Visit to CABET laboratory to get a first general impression

Feedback of first impressions

Attendances: Paul, Ginger

### **Tuesday, June 19, AM**

Interview with management ICAMA and CABET

Presentation the quality and environmental management in practice and discussion

Attendances: management of ICAMA/ CABET and laboratory staff of CABET

### **Tuesday, June 19, PM**

Presentation explaining basic principles of GLP and discussion

Attendances: management ICAMA/CABET and laboratory staff CABET

### **Wednesday, June 20 AM**

Presentation Introduction OECD management guidelines and discussion

Attendances: staff of laboratory + lab workers CABET

### **Wednesday, June 20 PM**

Presentation of various example of management SOPs

Attendances: staff laboratory + lab. Workers CABET

### **Thursday, June 21 AM**

Presentation Introduction SOP's on Facility Operations

Attendances: staff laboratory + lab. Workers CABET

### **Thursday, June 21 PM**

Interview with laboratory personnel (lab. Workers) on the status of Testing Facility

Operations (this includes SOPs), using a checklist of questions.

Attendances: laboratory workers QA

### **Friday, June 22 AM**

Presentation of an example study protocol for an experiment under GLP

Attendances: staff laboratory + lab. Workers CABET

### **Friday, June 22 PM**

Main findings, conclusions and required future steps (Paul and Ginger) Will be the concept for Trip Report.

Presenting back to all and discuss and follow-up.

Continuation of Interview with laboratory personnel (lab. Workers) on the status of Testing Facility

## **Annex 2 Presentations / documentation**

Presentations;

A course "**Principles of GLP**" which included the following presentations

- The quality and environmental management in practice
- GLP Introduction
- Introduction OECD guidelines
- Introduction SOP's on Facility Operations
- Introduction Study Protocol

Documentation;

OECD Guidelines no I-10

Course "Introduction to GLP" (CFPA Amsterdam/New York)

Course "Conducting effective Quality Audits" (CFPA Amsterdam/New York)

Course "Quality Assurance in GXP" BARQUA (Cambridge)

Course "Study Director in GLP" BARQUA (Cambridge)



## **Annex 3 Management and QA SOP's**

A list of management and QAU SOP's based on the OECD management and QAU guidelines.

### **01 Formulating a formalized study protocol for GLP compliant studies**

For every study carried out according to GLP a Study Director will be appointed by management at a sufficiently high level, i.e. the board of directors. The Study Director formulates a study protocol based upon a previously devised format and consisting of 3 coherent sections. If a section is not applicable for the study under consideration, it will be explicitly labelled as "Not Applicable".

### **02 Protocol for entry and use of GLP endorsed rooms and facilities**

This procedure describes rules for the entry and use of rooms, terrains and facilities used during GLP studies. The goal is to endorse and maintain an environment in which experiments can be performed complying to GLP.

### **03 Inspections and reports produced by the QAO**

As described in, "Tasks and responsibilities of the QAO during GLP studies", the QAO or substitute QAO will carry out the following types of inspections. A more detailed description of the nature of the various types of inspections is given in the chapters noted between parentheses:

- inspection of study protocol
- assessment of Standard operating procedures
- inspection of experimental implementation of studies
- inspection of facilities
- inspection of data management systems
- inspection of reports
- duties of the QAO during externally performed studies All inspections are reported as described in this procedure.

### **04 Duties and responsibilities**

Duties and responsibilities of the Board of Directors during GLP studies

Duties and responsibilities of the Study Director

Duties and responsibilities of the Principal Investigator

Duties, responsibilities and authority of collaborators

Duties and responsibilities of the Quality Assurance Officer

Duties and responsibilities of the GLP archivist

Retaining test substances

- Administration and storage of chemicals
- Expiry dates of chemicals, reagents and solutions
- Protocol for the administration of reference chemicals used in GLP studies
- Administration and tracking system for dangerous chemicals

## **05 Delimitation and definitions used for GLP compliant investigations at Alterra**

Procedures ... up to and including ... are only applicable when, upon the request of a Sponsor, a study protocol is prepared that adheres to the rules of GLP. 'The GLP rules according to the OECD' refers to the rules established in the OECD Principles of Good Laboratory Practice, ENV/MC/CHEM(98)17, Paris 1998.

Alterra has established facilities to perform investigations according to the (OECD) GLP rules. By harmonizing the OECD rules applying to GLP and the quality system in place at ALTERRA, including the accompanying protocols, routines and Standard Operating Procedures according to NEIN-ENISO/IEC 17025:2000 and ISO-9001:2000 norms, assignments can be carried out complying to GLP.

## **06 Authority of personnel participating in GLP studies**

This procedure describes matters concerning the collecting of information with regard to personnel participating in GLP studies, comprising procedures for:

- Establishing comprehensive definitions of the functions of each collaborator.
- Obtaining relevant Curriculum Vitae.
- Establishing a description of the authority and responsibility of each collaborator.
- Establishing 'Knowledge and Experience' forms describing relevant knowledge and experience of each collaborator.
- Guidelines for establishing a list of signatures and initials used during the study.

## **07 Use of information technology facilities in GLP studies**

This procedure supplements the Quality Handboek, in particular the sections dealing with Quality Assurance Laboratories, and the Quality Handbook Laboratories.

## **08 GLP archive**

The GLP archive is only accessible by the GLP archivist and/or his substitute. Only they are in possession of a key that gives entry to the room containing the archive and the fire proof cabinets contained therein. These cabinets should be locked whenever nobody is present in the room.

All other employees of ALTERRA do not have access to the archive. An exception is made for a Study Director wishing to access a study that has been conducted under his responsibility, but only when accompanied by the GLP archivist or his substitute.

## **09 Operation and maintenance of the fire detector in the GLP archive**

Operation and maintenance of the fire detector in the GLP archive.

## **10 Protocol for updating various components in the framework of GLP-studies**

This procedure describes rules for updating the components mentioned under 3 at Alterra, the Centre for Water and Climate Research and the team Environmental Risk Assessment. The aim is to create and maintain a situation in which periodic controls assure that these components are updated on a regular basis.

Field of application

The GLP related components discussed in this update protocol are:

- Standard Operating Procedures Methods
- Standard Operating Procedures Equipment
- Registration / calibration
- Personnel files
- Archiving
- Quality Assurance program
- F forms
- B forms
- Operating instructions

### **11 Using, checking and administrating spreadsheets in GLP studies**

Recording the way in which employees involved in GLP studies make use of spreadsheets, and recording who is responsible for checking any spreadsheets used.

Spreadsheet: pages that are made using spreadsheet programs like e.g. Microsoft Excel, containing various types for data and formulae, and which are used to perform calculations in a project.

Standard calculation sheets: these are input only files, i.e. standard spreadsheets that can be used for entering analytical results, automatically performing the desired calculations. The formulae contained in the spreadsheet and used for the calculations can not be changed.

### **12 Checking and releasing measurements generated at the organic-chemical and ecotoxicological laboratories**

Independent checks of data generated in GLP studies at the organic-chemical and ecotoxicological Laboratories of Alterra.

Measured data obtained at the organic-chemical and ecotoxicological Laboratories of Alterra should comply with quality criteria, most of which are specified in Standard Operating Procedures. The collaborator generating the results is responsible for the quality of the data generated. It is the Study Director's responsibility that measured data are checked by an independent expert.