

GPG2/GCP Quality Management and Performance Measurement System design workshop

Hosted by the Centre for Genetic Resources (CGN), the Netherlands
16-19 October 2007, Lunteren, The Netherlands

GCP's Laboratories brainstorming

The brainstorming was initiated by T. van Hintum, moderated/animated by D. Galsworthy. Notes were taken by C. Billot. Report was written by C. Billot and amended by all participants. Two presentations were given during this brainstorming: T. Metz reported on the data file organisation at IRRI, and S.M. Quilloy on the molecular marker's lab at IRRI. These are not specifically documented in this report.

1. Participants

Thomas Metz, IRRI (Los Banos, Philipines)

Claire Billot, CIRAD (Montpellier, France), Population geneticist, genotyping data, sorghum and rice GCP genotyping data.

David Galsworthy, CIP (Lima, Peru), present position quality manager at Central Science Laboratory (York, UK), previous position UK national accreditation service (private and public), working at CIP for one year (march '07-march '08) to implement the Germplasm quality management system

Sheila May Quilloy, IRRI (Los Baños, Philipines), managing the IRRI's genotyping data in the GCP

Michael Baum, ICARDA (Alepo, Syria), barley, lentil and fababean. Biotechnology work.

Alice Muchugi, ICRAF (Nairobi, Kenya). Molecular characterisation and germplasm.

Rajeev Varshney, ICRISAT (Hyderabad, India). Genomic laboratory. GCP-SP2 leader, comparative genomics.

Rheinhard Simon, CIP (Lima, Peru). Head of research informatics, data quality, genomics in potato.

Theo Van Hintum, CGN (Wageningen, Netherlands), GCP-SP4 leader. Bioinformatics crop information.

Quality certification of the CGN genebank.

2. Objectives of the brainstorming session

- Define the scope of the activities to cover
- Input and output of the process
- International standard as a framework for the process map: key aspects of the standard
- Output in terms of help given by GCP (SP4 mainly)

3. Main target

Molecular laboratories involved in the Generation Challenge Programme (GCP), are involved in three main activities:

- research,
- data production
- training

Data production can be considered as a service, whether working directly as a service facility or for research aspects,. For the purpose of this workshop, only the service aspects of the GCP laboratories were considered.

There is a clear process for this involving receiving the sample (as matrix or dna) through to the reporting of data to the client.

A client should expect a service laboratory to provide :

- fit for the purpose, accurate and reproducible data production methods
- efficient level of service in terms of delivery time
- give a complete dataset
- evidence of competency in term of quality system, infrastructure and staff.

4. General workflow of the process: Inputs and outputs

The general workflow is summarised in Figure 1 – **where is figure 1 ?**

Three mains steps were identified in the workflow :

1. initial client contact with the laboratory
2. data production and delivery,
3. client feedback.

The first step ensures that the client and the laboratory completely agree on the type of service requested and on the output of the process. The third step ensures that the client has the opportunity to report their satisfaction with the service provided.

The service laboratory should define a non-negotiable minimum quality level of service. This could include :

- the use of lab standards to quantify error rate (10% data repeated for ex, outsourcing)
- control genotypes (>1)
- reference sample
- missing data rate (below 5%)
- time delivery.

For a service laboratory, this level of quality is a non-adjustable parameter, whereas time and cost can be adjusted. Customer expectations are taken into consideration if possible a written Service Level Agreement (SLA) produced. The SLA should define :

- the laboratory procedure (DNA characteristics -quality, quantity, process-, markers choice, processes)
- output files (format of the data) with quality controls
- reports on any problem encountered, staff performance, infrastructure, record tracks
- confidentiality level of the data and publication terms.

5. Quality system requirements for laboratories

The International Standard ISO/IEC 17025:2005 “General requirements for the competence of testing and calibration laboratories” was used to structure this discussion. The standard is available online in 3 languages, English, French and Spanish (<http://www.iso.org/iso>) at a cost of 114 CHF.

The core of the Standard is given in Sections 4 and 5. Section 4 does covers Management Requirements and Section 5 covers Technical Requirements. The key points from each subsection within 4 and 5 were discussed.

a. Section 4 : Management Requirements

Section 4.2 Management System

Two key roles need to be defined in the Quality System :

- technical management role: person or group of people who take the responsibility that the data be generated by the laboratory (high level of responsibility)
- quality manager: person responsible for the maintenance of the system including control of documentation and the management of the audit system.

Section 4.3 Document control

The document control system in place must ensure staff in the laboratory have the most up-to-date documentation available to use for their work. A document review process is also required where the frequency of review needs to be defined. Critical documents would be checked annually whereas non-critical documents could be checked every four years.

Section 4.4 Review of requests, tenders and contracts

Systems need to be in place to ensure agreement is reached between the client and the laboratory on the work to be carried out and that communication with the client is recorded.

Section 4.5 Subcontracting of tests and calibration

Examples of sub-contracting could include sequences, external quality control, and the sharing of the work. The expectation of the work to be delivered by the sub-contractor should be clearly defined and the relationship with other organisation formalised. There may be an expectation that the sub-contractor has implemented a quality system.

Section 4.6 Purchasing services and supplies

Systems for the purchasing of critical services and supplies need to be defined in terms of the quality of the supplied materials and the expected level of quality system implementation of the supply companies.

Examples would include critical chemicals, reagents, equipment and software.

Where required checks may be necessary to be carried out to ensure the quality of the services and supplies. Companies used for services and supplies may also be checked to assess the procedures used and accreditation/ certification status.

Sections 4.7 Service for the customer 4.8 Complaints

These two section deal with service to customers. Clients should be encourage to give feedback or complains in a written form. Complains should be seen as official but should be used in a constructive way.

Encouragement should be given for clients to give their feedback in a proactive way.

Sections 4.9 to 4.11

These section of the Standard deal with the discovery, evaluation and correction of things that have gone wrong. These non-conforming situation can be found in a number of ways through audits, complaints, internal quality control failures and reports from staff. Once a non-conformance has been detected, the situation needs to be assessed and action taken if necessary. Examples of actions could include stopping the work, implementing an investigation and informing the client that there is a problem. Corrective actions should be then be decided upon and implemented. System implemented should be open and not used as part of a blame culture.

Section 4.13 Control of the records

The records system within the laboratory should give complete traceability from receipt of the sample through to the dispatch of results / data. This can be tested by checking the chain of records for a sample where it should be possible to re-create as far as possible the conditions under which the sample was analysed.

Sections 4.14 Internal Audit

The entire system should be monitored through the use of an internal audit system. Staff from the laboratory can be used as auditors provided they do not audit their own work. The audit programme identifies non-conformances against the ISO 17025 standard and the quality system requirements that have been defined by the laboratory. The audits should also be used to highlight areas for improvement. The definition of specific performance indicators to monitor systems can be a great help to identify areas where improvements can be made.

4.15 Management review

The Management review is a meeting normally held on an annual basis where management assess performance indicators to establish if the quality system needs to be changed. Long term trends and problems are addressed at this meeting.

b. Section 5 Technical requirements

Section 5.2 Personnel

Training records of the staff need to be produced, retained, organised and made available. They should make explicit the experience of staff and the activities that each person is authorised to carry out. Different stages of activity can be defined. For example the formation stages, carry out with someone, carry out alone, being able to run and take responsibility. For staff undergoing training, objective evidence of competence should be produced before final authorisation to carry out a process or procedure. Internal quality control checks can be used to monitor staff performance. Training records should be organised within the working units and it is not normally done as a function of human resources.

Section 5.3 Accommodation and Environmental conditions

Good housekeeping of the organisation in the laboratories should be formalised and monitored if necessary. An example of this is the need to define a strategy to prevent resistances to transparency. Safety does not normally form part of the quality system provided it does not affect the quality of the data being generated.

Section 5.4 Test methods and validation

Selection of methodology

The source of the methodology is important since it defines the expected level of validation required.

Sources of methodology can be :

Standard methodology that has been collaboratively trialled

Modified Standard methodology – specific amendments made to reflect local conditions in the laboratory.

In-house methodology – methods developed by the laboratory

It was felt that in the area of the molecular laboratory Standard methodologies do not exist. Therefore the methods are either modified standard or in-house developed methods. Sources of information for the methods include equipment manufacturers instructions and published papers.

Documentation of the methodology

Methodology needs to be documented to ensure consistency of operation between operators. Methods can be documented as stand-alone procedures containing all the information for a specific operation or a series of building blocks that can be linked together in a number of ways. The second approach is more suited to the type of work being carried out in a molecular laboratory. An overarching document can be used to describe how the building blocks are linked together to give the overall process.

Validation of methodology

Methodology needs to be validated to demonstrate fitness for purpose. A number of tools are used as part of the validation process. These can include :

Comparison with alternative methodologies

Comparison with other laboratories carrying the same procedure

Multiple analysis of a the same material

Use of reference materials

Assessment of robustness by the variation of the conditions of analysis and measuring the changes that occur in the data produced.

Assessment of sensitivity by diluting the sample concentration before analysis

The data produced for the validation needs to be assessed and a report produced that includes this assessment of the validation data.

Data manipulation software should also be validated where possible with the use of known data sets to check the data outputs are correct.

5.4.7. Control of data

The Standard stresses the importance of managing the data and where possible validating the data transfer steps. Practical ways of checking software performance are required.

Section 5.5 Equipment

Equipment records need to be set up for all significant equipment. Section 5.5.5 of the Standard defines what should be included in an equipment record.

The functionality of equipment should be checked. Examples of equipment requiring checks include auto-pipettes, PCR block temperatures , oven and incubator profiles.

Section 5.6 Traceability

Where physical measurements have a significant effect on the data being generated, traceability to the national/international measurement standards should be produced through calibration.

For molecular work, traceability requirements will be limited. Procedures should be place for the use of reference standards and materials. Size standards are an example of these.

Section 5.7 Sampling

Where a sub sample is taken from a large sample then sampling procedures should be formalised to ensure a representative sample is taken.

Section 5.8 Handling the tests items

Procedures need to be in place to document how the sample is received, stored and processed through the system.

A unique identity is needed for each sample which accompanies the sample through the system.

Section 5.9. Quality control

Systems need to be place to monitor the performance of the methodology on a on-going basis. The specific technologies available for this will be vary but will include use of reference materials and the repeat analysis of samples. Where possible the results of quality control checks should be monitored using statistical techniques to look for out of control situations and trends. Wherever possible, materials used for calibration should be independent from those used for quality control.

Section 5.10 Report the results

Results need be reported accurately, clearly and in an unambiguous manner.

6. Main conclusions concerning the GCP further involvements in Quality Management

GCP definitely should involve into quality management, and general processes to obtain data of good quality, which include proofs of the quality of the data.

Specific issues, actions, outputs and responsible persons are given in the following table.

Wrapping Up

Thanks to DG

Issue	Description	Actions
Laboratory Information Management System	<p>GCP has already contributed to the improvement of existing LIMS (CIP, ICARDA), transferability of LIMS (ICRISAT's transferred to IITA, Nairobi, Kenya) and establishment of an open source community (Workshop organised at ICRISAT in august 2007). However, taking into consideration the amount of money involved and the time dedicated, institutional commitment is particularly important.</p>	<p>Reviving the importance of the open source community give physical support to LIMS development (ICRISAT, CIP, ...)</p>
Raising capacity and staff concern	<p>GCP will support in organising workshops (practical and theatrical) dedicated to middle level staff on data management, interpretation, and data analysis... It will involve statisticians, and attendants should have as a prerequisite a complete knowledge of their workflow (presentation of their work to be made).</p> <p>GCP is concerned about the high turnover of staff people and its implication on the data quality, but cannot substitute to institutional decisions.</p>	

<p>GCP's help promoting quality management systems</p>	<p>It will raise the awareness of data quality, at a management level... Put a note in the GCP Newsletter to summarise the workshop Have a space in the GCP website: coordinates the build in of a website, which would indicate a road map of implementing a quality management workflow, links with resource person (D Galsworthy), resource sites (CIP, ICRISAT, ILAC), resources documents (world wide standards for laboratory operations, EU documents).</p>	<p>Quality project workshop, linked with the GCP website (D. Galsworthy). Possibility of bringing people to CSL (Central Science Laboratory) (a week workshop for 30 people, quality system running in place, bioanalytical work, presentation of the participant of their knowledge, implementation of the quality system), august 2008 aiming at a decision level (lab management or above). Thomas Metz and Rheinhard Simon would be the contact points for GCP. Auditing/assessment/consultancy of D Galsworthy (and/or Rebecca Weekes) possibly visits 4 places (one week each) after the workshop.</p>
<p>GCP requirements for the projects</p>	<p>Statistical set-up (involved at the beginning), 10% of the material reproduced on a separate, method proven to be useful Quality standards for GCP work List to be checked for Good quality data (like professional body), could we take into account "paternity analysis" Clear criteria in terms of performance of the system, standards?</p>	

	<p>We need to decide what the criteria are such as Miami standards (Dave Marshall, Steve Kresovitch, JF Rami...)?</p> <p>Other major donors that could ask for service level agreement?</p>	
Quality indicators	<p>See Dave Marshall's commitment...</p> <p>JF Rami, Fred van Eijk...</p> <p>Have in the GCP repository a quality report: not possible, or possible and generated. Written in R (missing data, frequencies, etc...). Make the software available in the depository.</p> <p>Have different quality data set: complete dataset.</p> <p>Every version should be with data quality.</p> <p>Missing data, allele frequencies, data resolution implemented in R</p>	
Central Registry Repository	<p>See with GenDiversity (Manuel Ruiz and JF Rami)</p> <p>Msat data</p> <p>Should be done next year</p>	
Reproducibility of data analysis/ Research	<p>Standard analysis protocols</p> <p>R script (opfweaf and sweaf)</p> <p>which exists to export different</p>	

	analysis (to openoffice) R Gentleman R and Bioconductor project, reassessing major mice project Possum (Keygenes) open standards for exchanging scientific data and data analysis	
Training material	Microarray data + SSR analysis comparison (R Simon, R Varshney, JC Glaszmann) (2 nd wave analysis, march 2008) SP4 project	
3- Exploratory data analysis (missing data etc....)		
Statistics should be involved at the beginning		
Financial resources to GCP		
What type of requirements needed for genotyping? Generic service level, including requirements for dataset (templates)?		