World Health Organization

TRAINING MANUAL

Quality practices in basic biomedical research (QPBR)

TRAINEE

TDR For research on diseases of poverty

UNICEF • UNDP • World Bank • WHO

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Quality practices in basic biomedical research (QPBR) training manual.

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QUALITY PRACTICES IN BASIC BIOMEDICAL RESEARCH (QPBR) TRAINING MANUAL

FOR THE TRAINEE

A tool for training and promoting
Quality Practices in Basic Biomedical Research (QPBR)
concepts in disease endemic countries

World Health Organization

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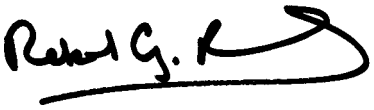
FOREWORD

A key aim of the Special Programme for Research and Training in Tropical Diseases (TDR) is to empower disease endemic countries (DECs) to develop and lead high quality research activities to internationally recognized standards of quality, and so contribute to TDR's primary mission of *"fostering an effective global research effort on infectious diseases of poverty in which disease endemic countries pay a pivotal role"*.

One way we have approached this is to produce guidelines and training manuals that will help institutions and researchers attain the highest international quality standards in their research. In 2006 we published a handbook on Quality Practices in Basic Biomedical Research (QPBR) which received worldwide acceptance and acclaim, from both industry and academia. It also created a demand for training, especially in DECs.

This manual (for *trainees*), and the accompanying manual (for *trainers*) will help meet this demand, and will assist institutions in implementing good quality practices. The two manuals, together with the QPBR handbook, now form a sister series to the highly popular series on Good Laboratory Practice (GLP), which has had an impact on the way that laboratory research is carried out in many institutions and countries.

We anticipate that this manual will be useful to all those who aspire to undertaking biomedical research to the best international standards. We believe it will be particularly useful when used with the trainers' manual in workshops and courses on good quality practices. Used together, the QPBR series will help institutions and researchers ensure that research work is produced, recorded, reported and archived appropriately and in a cost-effective and efficient manner.



Dr Robert Ridley, Director TDR,
Special Programme for Research and Training in Tropical Diseases
Executed by WHO and co-sponsored by UNICEF, UNDP, the World Bank and WHO

ABOUT THIS TRAINING MANUAL

Quality practices in basic biomedical research are of paramount importance when resources are limited and when the results of research are to be used to advance science, shape policies or aid decision making. This applies particularly to disease endemic countries (DECs), although quality practices in research are just as essential for other parts of the world.

Establishing good quality practices in research can only improve the quality of research and the veracity of data derived from it. Guidelines on quality of research also steer researchers towards approaching their work in a similar way, no matter where they are working. This is a critical element in research, allowing experiments to be reproduced more easily and the body of evidence on a particular research issue to grow.

In the absence of national or international guidelines on Quality Practices in Basic Medical Research, in 2006 TDR published at WHO a *Handbook on Quality Practices in Basic Biomedical Research (QBPR)* to help researchers throughout the world produce high-quality biomedical research. The handbook highlighted non-regulatory practices that can be easily institutionalized at very little extra expense.

The QPBR handbook was so well received and the demand for training so high (especially in DECs) that the decision was made to develop this brand new manual for ***trainees*** of QPBR and an accompanying manual for *trainers*.

The two QPBR training manuals are based on the QPBR handbook and are designed around a course/workshop on QPBR. They therefore outline the goals of the course/workshop and the topics that should be covered. The manuals include a set of power point slides, questions and case histories on QPBR. The QPBR handbook explains why QPBR is essential and also provides help (through illustrative examples and templates) on how QPBR can be implemented.

The training manuals can be used to conduct standardized and validated training; they provide institutions and researchers with the necessary tools for implementing and monitoring quality practices in their research. Training of trainers will lead to propagation of the number of individuals who can train others about QPBR.

The QPBR series supports TDR's long-term mission of helping DECs develop their own research activities. Training efforts throughout the world, especially in Asia, Latin America and Africa, will lead to the formation of a global culture of quality practice in research. This in turn should help institutions in their quest for partnerships with both the public and the private sector. Overall, the adoption of QPBR – facilitated by these training manuals – will have the effect of promoting cost-effective, accelerated research with a long-term positive effect on the development of products for the improvement of human health.

ACKNOWLEDGEMENTS

This manual for trainees is part of a suite of three documents produced by WHO/TDR:

1. *Quality Practices in Basic Biomedical Research Handbook* (orange)
2. *Quality Practices in Basic Biomedical Research Training Manual – for the Trainee* (turquoise)
3. *Quality Practices in Basic Biomedical Research Training Manual* – for the Trainer (brown)

Production of the two training manuals was made possible by the enthusiastic support of and contributions from WHO/TDR and the participants in scientific working groups set up under the auspices of WHO/TDR and collaborators.

Our thanks are also extended to those who helped in the production of the *Quality Practices in Basic Biomedical Research Handbook*, on which the training manuals are based. Sincere thanks go to Nadya Gawadi and David Long for their role in drafting this manual.

Comments and suggestions on all aspects of these QPBR training manuals are welcome for consideration in future revisions. Please contact:

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INTRODUCTION

The quality practices in basic biomedical research (QPBR) training manual is an accompaniment to a two-day training course on the subject. The course is divided into six sessions – sessions 1, 2 and 3 are structured for the first day and sessions 4, 5 and 6 for the second. The manual material has been put together to fit the six sessions (see contents page above).

How to use the WHO/TDR material

Course material:
WHO/TDR handbook on QPBR

Trainee manual, including:

- set of PowerPoint presentation slides
- list of goals for each section
- set of questions for discussion for each section
- workshop suggestions for each section
- case studies for discussion at the end of the training course.

Goals

Each section has a set list of ambitious pedagogical goals – at the end of the course you should be able to formulate the requirements of QBPR in order to transmit and implement them (in dialogue with your respective research institutions). The more lively the discussions and exchanges between you and the other participants during this course, the more you will learn; so contribute actively to all the workshop sessions and ask questions of the trainer.

The goals are set in a hierarchy from simple to complex cognitive skills: this is because you will be expected to complete an exceedingly complicated exercise (implementation of QPBR) when you return to your research institution. Simple knowledge of QBPR will not be sufficient for this task.

Bloom's taxonomy of learning domains* is used in the description of goals for each section. This system is not new but can be used relatively simply to categorize the level of abstraction of tasks that occur in educational settings.

*From Bloom, Benjamin *S. Taxonomy of educational objectives*. Boston, MA: Allyn and Bacon. Copyright (c) Pearson Education 1984. Adapted by permission of the publisher. Table copied from University of Victoria web site (http://www.coun.uvic.ca/learning/exams/blooms-taxonomy.html).

Competence	Skills Demonstrated
Knowledge	• observation and recall of information • knowledge of dates, events, places • knowledge of major ideas • mastery of subject matter *Question Cues:* list, define, tell, describe, identify, show, label, collect, examine, tabulate, quote, name, who, when, where, etc.
Comprehension	• understanding information • grasp meaning • translate knowledge into new context • interpret facts, compare, contrast • order, group, infer causes • predict consequences *Question Cues:* summarize, describe, interpret, contrast, predict, associate, distinguish, estimate, differentiate, discuss, extend
Application	• use information • use methods, concepts, theories in new situations • solve problems using required skills or knowledge *Questions Cues:* apply, demonstrate, calculate, complete, illustrate, show, solve, examine, modify, relate, change, classify, experiment, discover

Analysis	• seeing patterns • organization of parts • recognition of hidden meanings • identification of components *Question Cues:* analyse, separate, order, explain, connect, classify, arrange, divide, compare, select, explain, infer
Synthesis	• use old ideas to create new ones • generalize from given facts • relate knowledge from several areas • predict, draw conclusions *Question Cues:* combine, integrate, modify, rearrange, substitute, plan, create, design, invent, what if? compose, formulate, prepare, generalize, rewrite
Evaluation	• compare and discriminate between ideas • assess value of theories, presentations • make choices based on reasoned argument • verify value of evidence • recognize subjectivity *Question Cues:* assess, decide, rank, grade, test, measure, recommend, convince, select, judge, explain, discriminate, support, conclude, compare, summarize

SESSION 1

1.1 QUALITY PRACTICES IN BASIC BIOMEDICAL RESEARCH

Goals

At the end of the session, you should be able to:

- define basic biomedical research and place it in context with later stage research;
- describe changes in the social and natural environment that are accelerating health problems today;
- present the case for QPBR guidelines as an aid to selection of new projects and for the acceptance of new products/principles;
- describe and exemplify the difference between the scientific content and the practical performance of research studies;
- recognize the stages of biomedical research and give examples from everyday practice or examples that do not fit the model (include drug products, other products and/or principles for new therapies or strategies).

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QPBR – What is basic biomedical research?

What is basic biomedical research?

Session 1:1:1

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QPBR – What is basic biomedical research?

Basic biomedical research refers to activities to find means of detecting, preventing or treating human disease

- Such research covers:
  - discovery and exploratory studies that precede the regulatory phases of drug development*

  or
  - studies that precede programmes to develop other methods of disease control

* see (or skip) next 3 slides

Session 1:1:2

QPBR – What is basic biomedical research?

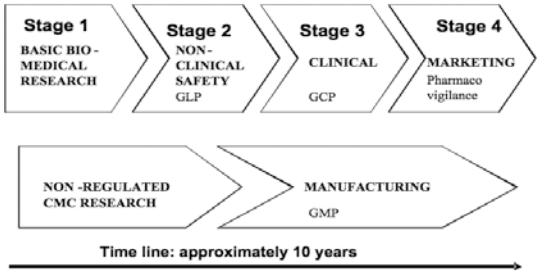
Drug development has four regulated stages:

1. Non-clinical stage: to establish drug safety (Good Laboratory Practice – GLP)
2. Clinical stage: to establish safety and efficacy in man (Good Clinical Practice – GCP)
3. Post-approval stage: drug monitored for safety (Good Pharmacovigilance Practice – GPvP)
4. Manufacturing during clinical development and post approval (Good Manufacturing Practice – GMP)

Session 1:1:3

QPBR – What is basic biomedical research?

Seen in context, the regulated quality systems complement or succeed one another as shown



Session 1:1:4

QPBR – What is basic biomedical research?

GXP* quality practices are supplemented by other guidelines

- WHO initiatives: standards for clinical chemical laboratories, chemical analytical laboratories and pathology laboratories (consult WHO web site)
- WHO quality assurance of pharmaceuticals (GMP) 2004
- ISO 25 guide, ISO 9000 and related documents

* GCP, GLP or GMP regulated quality practices taken as one, Irrespective of specific type

Session 1:1:5

QPBR – What is basic biomedical research?

Basic biomedical research: drug development model

Basic biomedical research comprises three stages:

- 1a – discovery per se
- 1b – transitional research*
- 1c – non-regulated, non-clinical research

* sometimes called translational research

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QPBR – What is basic biomedical research?

Basic biomedical research: drug development model

Stage 1a – discovery per se:

- researcher notices signs that a compound may have therapeutic potential
- finds ways to establish whether this is a fruitful lead
- observation, literature, knowledge of traditional practices, screening

Session 1:1:7

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QPBR – What is basic biomedical research?

Basic biomedical research: drug development model

Stage 1b – transitional research, researcher:

- tries to characterize active pharmaceutical ingredient (API)
- investigates how to produce and analyse API
- continues focused biological experimentation to investigate actions in cells, tissues or organisms

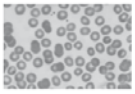
Session 1:1:8

QPBR – What is basic biomedical research?

Basic biomedical research: drug development model

Stage 1c – non-regulated, non-clinical research:

- biological tests on subcellular systems, tissues, whole animals provide evidence of efficacy – i.e. proof of principle (POP)*
- rigorously controlled studies with biological models
- demonstrates biological activity and potential for use in man
- requires sufficient supply of API



* not to be confused with field trials to demonstrate safety or clinical trials to demonstrate efficacy

Session 1:1:9

QPBR – What is basic biomedical research?

- Basic biomedical research: drug development model

Session 1:1:10

QPBR – What is basic biomedical research?

Basic biomedical research: products other than drugs

- Also comprises three stages of research:
  - 1a – discovery per se
  - 1b – transitional research*
  - 1c – practical proof of principle

* sometimes called translational research

Session 1:1:11

QPBR – What is basic biomedical research?

Basic biomedical research: products other than drugs

- Stage 1a – discovery per se:
  - researcher's observations verify that there is a phenomenon worth pursuing

Session 1:1:12

QPBR – What is basic biomedical research?

Basic biomedical research: products other than drugs

- Stage 1b – transitional research
  - Researcher works out strategies for exploiting the observed phenomena
  - Makes prototype equipment or discovers how to modify/ influence vectors, etc.
  - Performs preliminary experimentation

Session 1:1:13

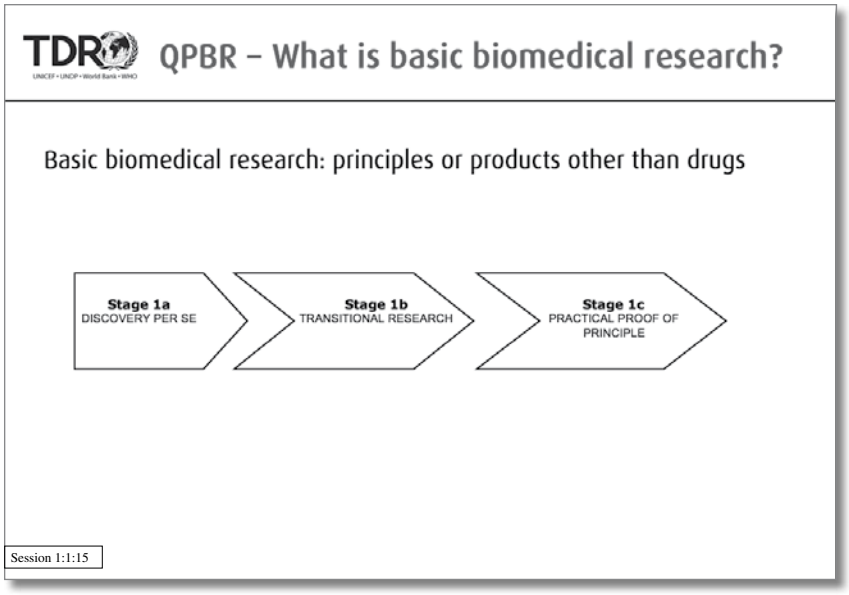
QPBR – What is basic biomedical research?

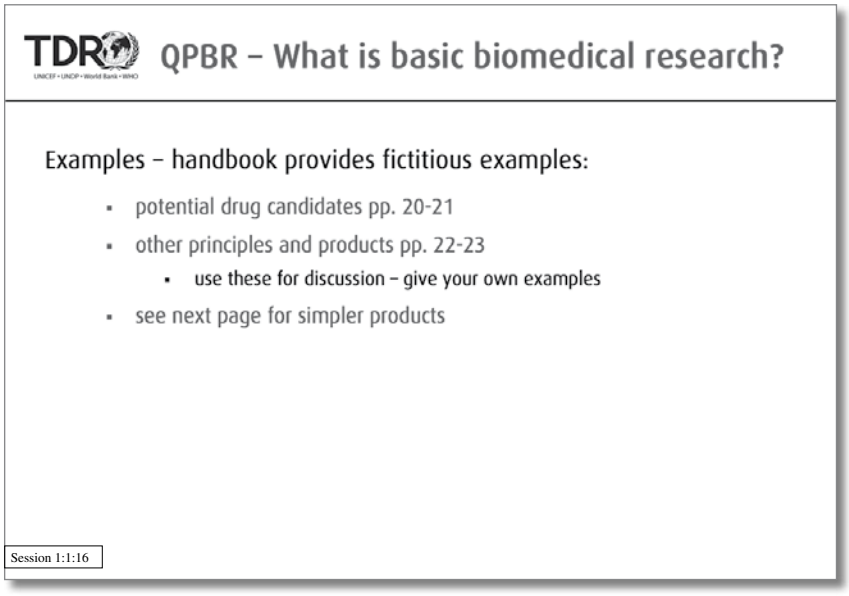
Basic biomedical research: products other than drugs

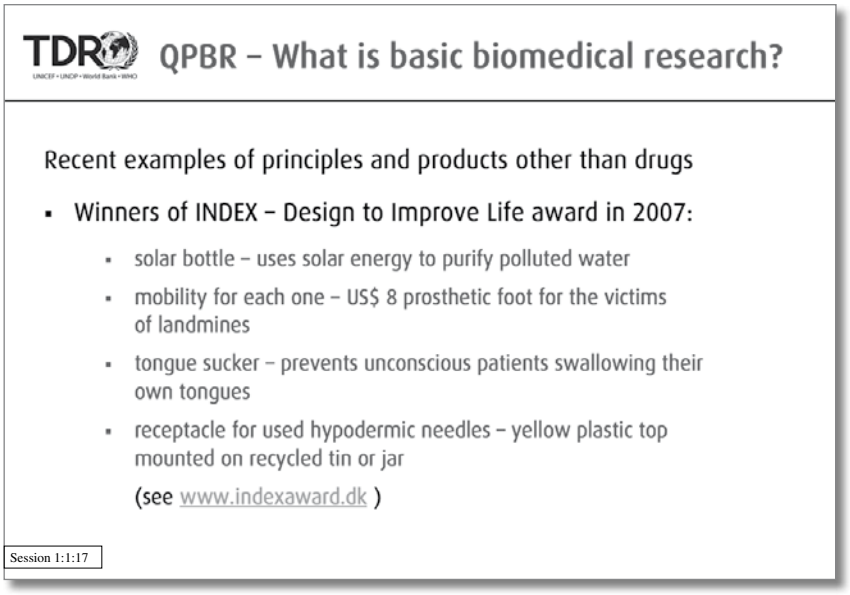
- Stage 1c – practical proof of principle (POP)*:
  - researcher uses an experimental model to demonstrate that the right relationships have been identified
  - may include studies to show potential applicability of these insights as practical methods for disease control

* not to be confused with field trials to demonstrate safety or clinical trials to demonstrate efficacy

Session 1:1:14


QPBR – What is basic biomedical research?
Basic biomedical research: principles or products other than drugs
Stage 1a
DISCOVERY PER SE
Stage 1b
TRANSITIONAL RESEARCH
Stage 1c
PRACTICAL PROOF OF PRINCIPLE
Session 1:1:15


QPBR – What is basic biomedical research?
Examples – handbook provides fictitious examples:
potential drug candidates pp. 20-21
other principles and products pp. 22-23
use these for discussion – give your own examples
see next page for simpler products
Session 1:1:16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QPBR – What is basic biomedical research?
Recent examples of principles and products other than drugs
Winners of INDEX – Design to Improve Life award in 2007:
solar bottle – uses solar energy to purify polluted water
mobility for each one – US$ 8 prosthetic foot for the victims of landmines
tongue sucker – prevents unconscious patients swallowing their own tongues
receptacle for used hypodermic needles – yellow plastic top mounted on recycled tin or jar
(see www.indexaward.dk)
Session 1:1:17

Questions

- What is basic biomedical research? Give an example from your own experience.
- What urgent health challenges is the world facing? Can you add more examples?
- Why is it difficult to match the needs for prevention and treatment with a supply of new products and/or principles to combat disease and other threats to health?
- Why are guidelines for basic research helpful in enabling the supply of new products and/or principles to combat disease and other threats to health?
- Describe the scope of the QPBR guidelines. Be specific about what is and what is not addressed.
- Why would guidelines facilitate the decision-making process for funding new projects?
- What is fraudulent research? Would the use of guidelines discourage fraud in basic biomedical research?
- What is meant by regulated research? Give examples of some of the regulations and what they cover.
- Where does QPBR fit into the stages of drug development research?
- What phases comprise basic biomedical research?

Workshops

1. Take an example of a research project from your everyday activity and place it in context as a stage in basic biomedical research. What activities preceded it and what will follow?

   What is the aim of this project and what studies are involved? How will you consolidate the results for transition to the next stage? Are all the studies in the project at the same stage of basic research?

   Present your discussion using the flip chart or board for diagrams, flow charts or any other presentation you prefer.

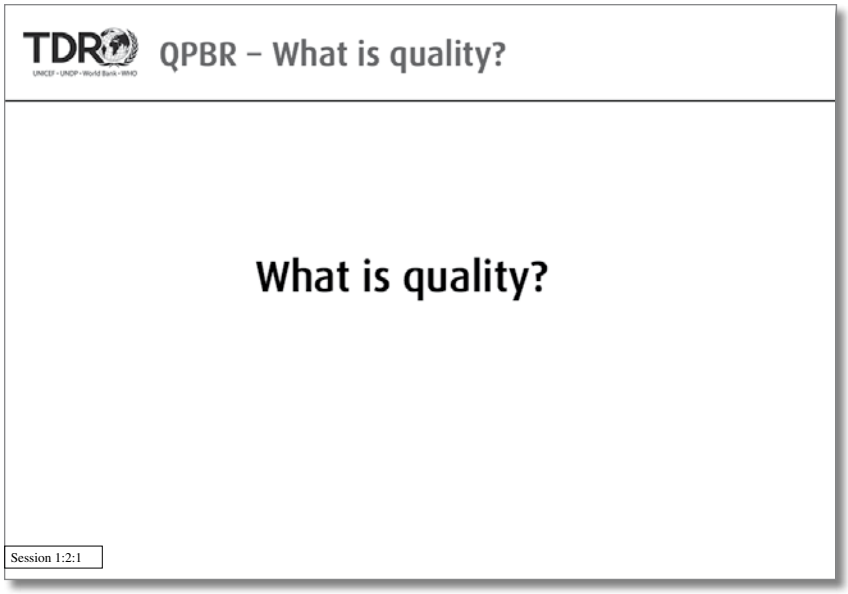
2. Use a flip chart to draw up a flow chart showing the different research and development stages for a new drug. Indicate the places at which QPBR and regulatory texts impact the development pathway.

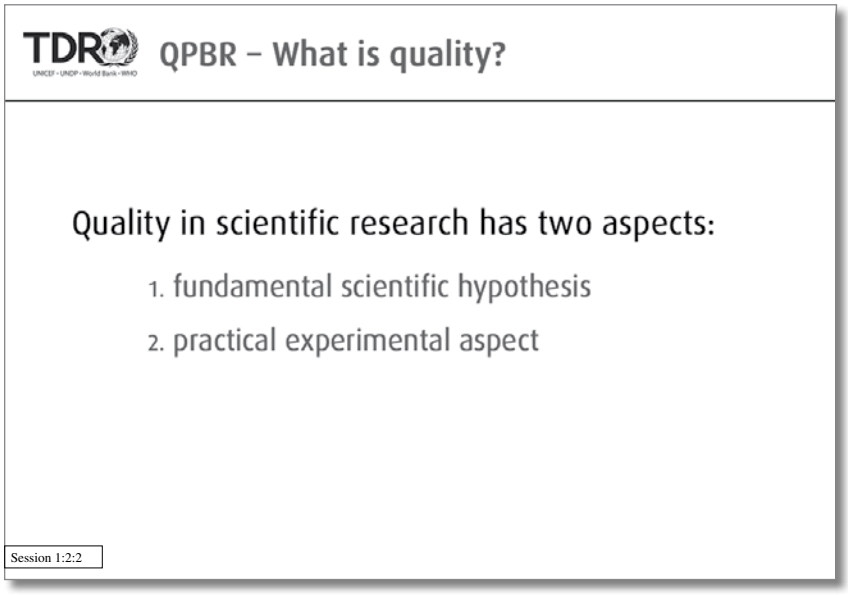
1.2 WHAT IS QUALITY IN RESEARCH?

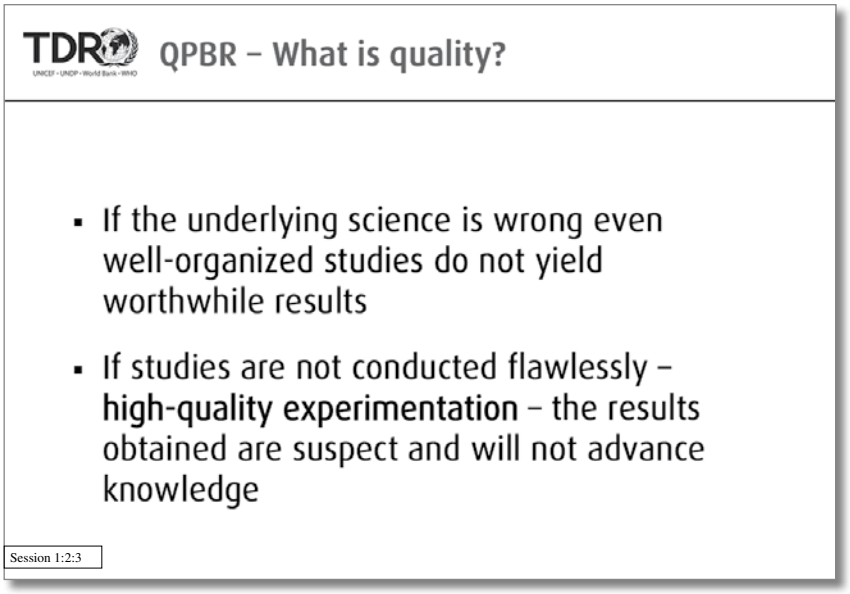
Goals

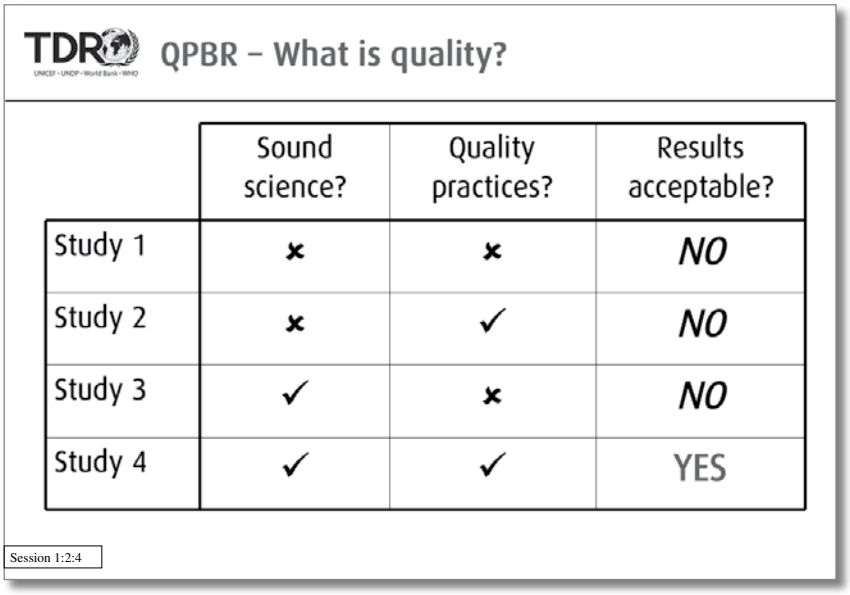
At the end of the session, you should be able to:

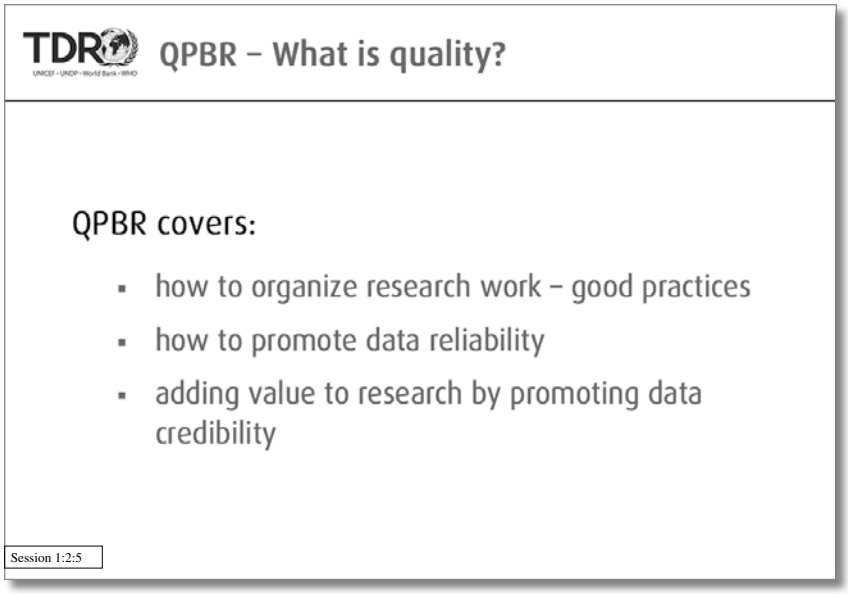
- define "quality" in general terms;
- explain the difference between the scientific content and the practical, organizational aspects of experimental science;
- define the purpose of QPBR in terms of data reliability and added value;
- list the quality attributes of basic biomedical research and outline their meanings;
- describe the sort of activity that the scientific community uses to validate studies and data;
- outline a set of variables affecting a study, possibly introducing bias;
- argue for the importance of careful planning and a written plan for each study;
- summarize the case for using standard procedures for routine activities;
- explain why a named individual needs to take high-level responsibility for the design and conduct of a study;
- explain the purpose of controls;
- assess critically how variables influence study results;
- describe the relationship between plan, study and data;
- describe a researcher's needs for repetition of a study, e.g. in terms of data and documents.


QPBR – What is quality?
What is quality?
Session 1:2:1


QPBR – What is quality?
Quality in scientific research has two aspects:
1. fundamental scientific hypothesis
2. practical experimental aspect
Session 1:2:2


QPBR – What is quality?
If the underlying science is wrong even well-organized studies do not yield worthwhile results
If studies are not conducted flawlessly – high-quality experimentation – the results obtained are suspect and will not advance knowledge
Session 1:2:3


QPBR – What is quality?
Sound science?
Quality practices?
Results acceptable?
Study 1 ✗ ✗ NO
Study 2 ✗ ✓ NO
Study 3 ✓ ✗ NO
Study 4 ✓ ✓ YES
Session 1:2:4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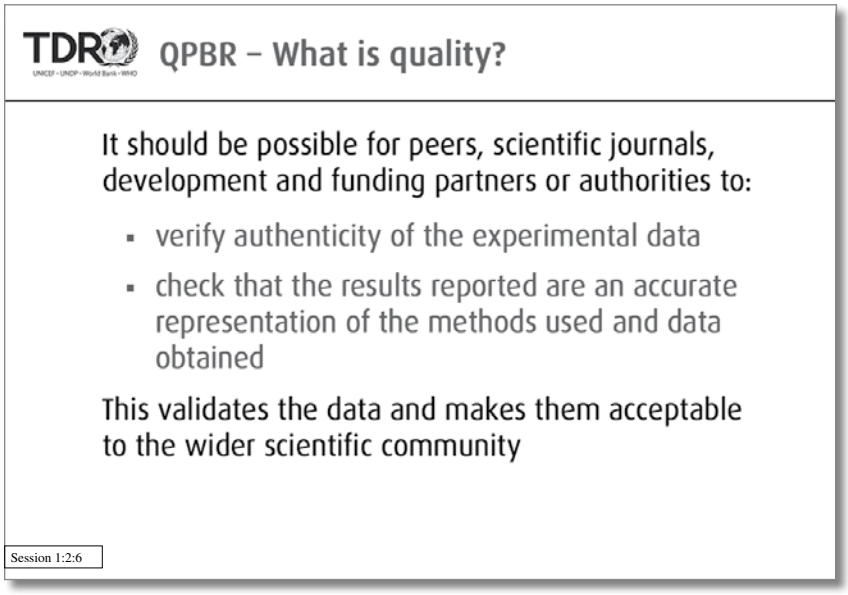
QPBR – What is quality?
QPBR covers:
how to organize research work – good practices
how to promote data reliability
adding value to research by promoting data credibility
Session 1:2:5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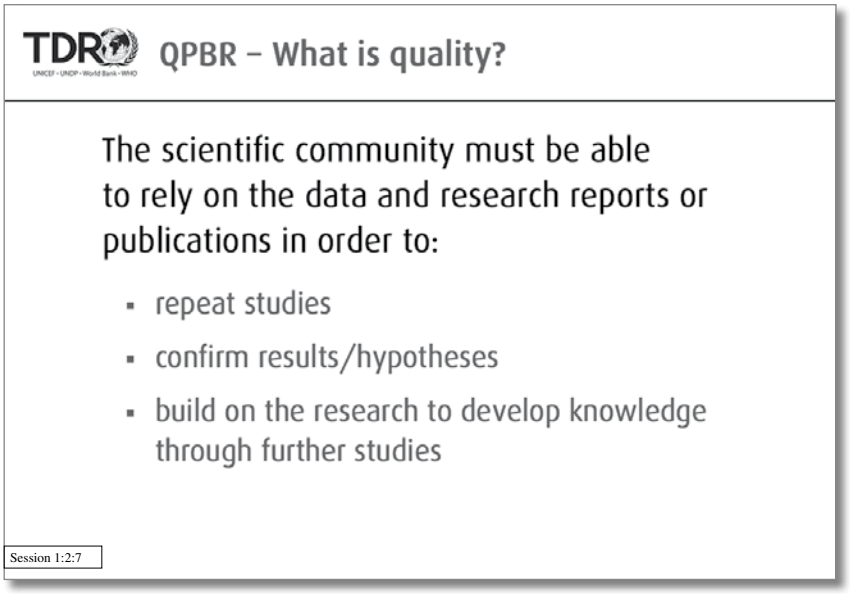
QPBR – What is quality?
It should be possible for peers, scientific journals, development and funding partners or authorities to:
verify authenticity of the experimental data
check that the results reported are an accurate representation of the methods used and data obtained
This validates the data and makes them acceptable to the wider scientific community
Session 1:2:6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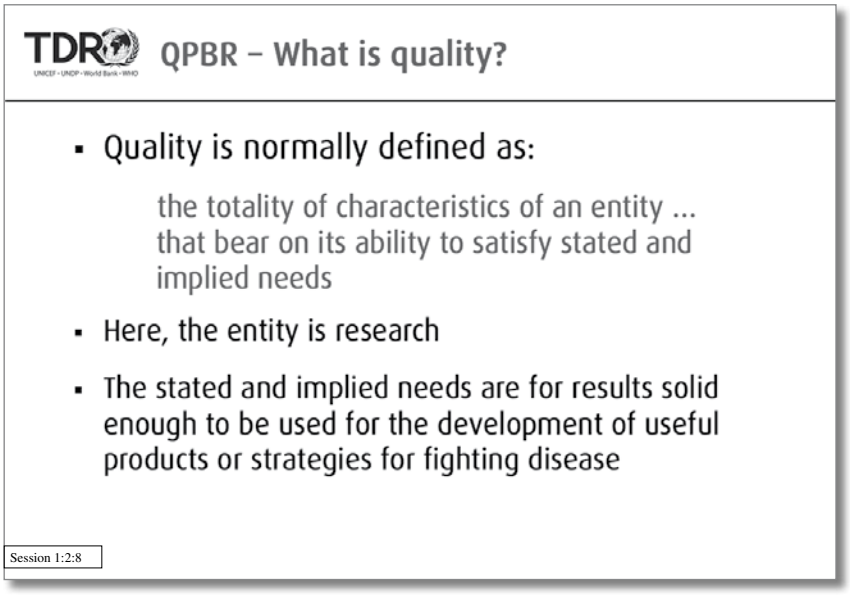
QPBR – What is quality?
The scientific community must be able to rely on the data and research reports or publications in order to:
repeat studies
confirm results/hypotheses
build on the research to develop knowledge through further studies
Session 1:2:7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QPBR – What is quality?
Quality is normally defined as:
the totality of characteristics of an entity ... that bear on its ability to satisfy stated and implied needs
Here, the entity is research
The stated and implied needs are for results solid enough to be used for the development of useful products or strategies for fighting disease
Session 1:2:8

QPBR – What is quality?

- To deliver these needs, scientific research must deliver results that are:
  - relevant
  - reliable
  - reproducible
  - ethical
  - auditable
  - in the public domain
- QPBR provides guidance on implementing practices that ensure that results have these characteristics

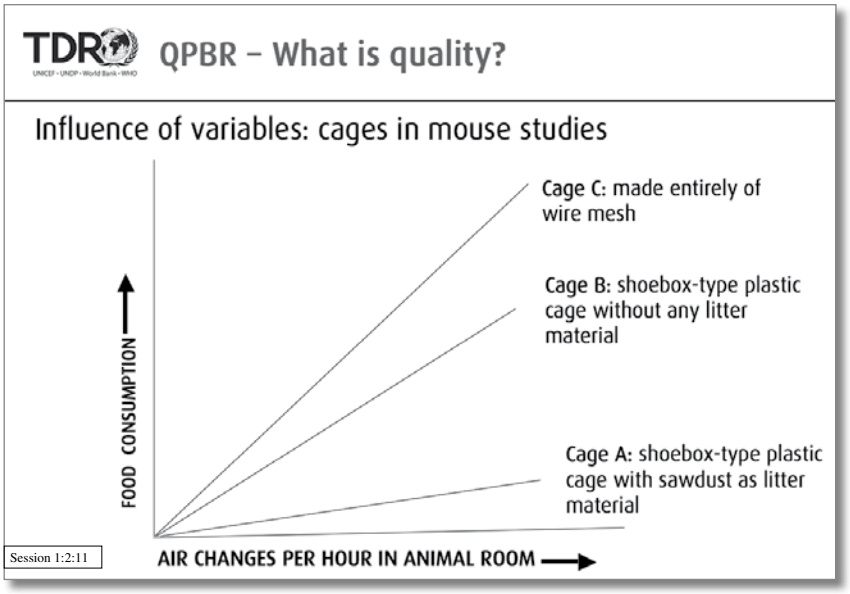
Session 1:2:9

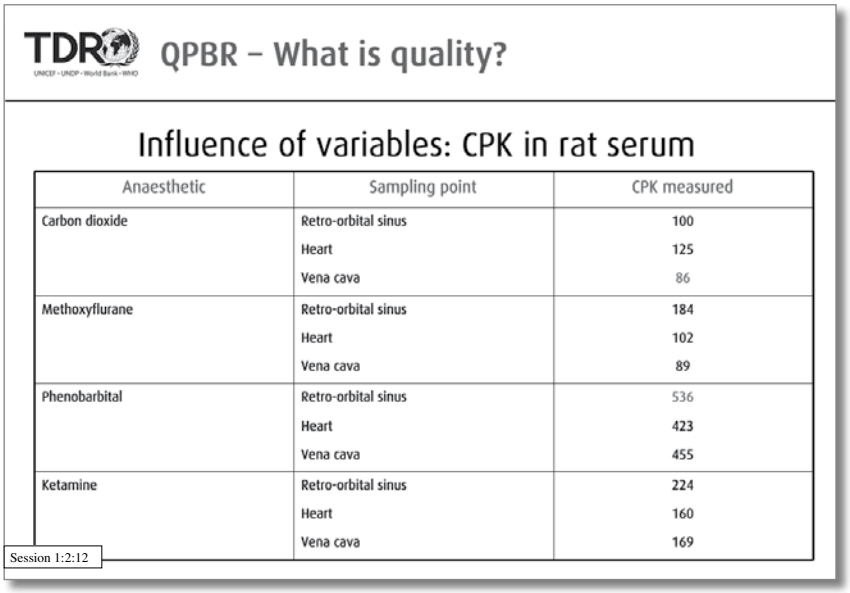
QPBR – What is quality?

Importance of variables

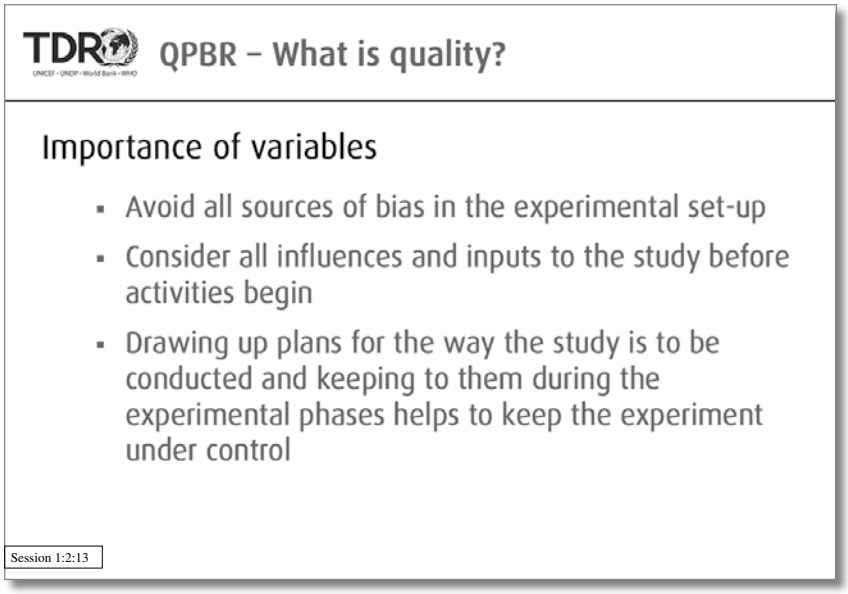
- Scientific activity must generate reliable data
- Meaningful scientific interpretation of results is possible only when founded upon reliable data
- Experimental variables must be kept under control in order to obtain reliable data
- Quality practices (like QPBR) are designed to help scientists to control the variables
- If variables are not controlled the research may yield false negative or false positive results

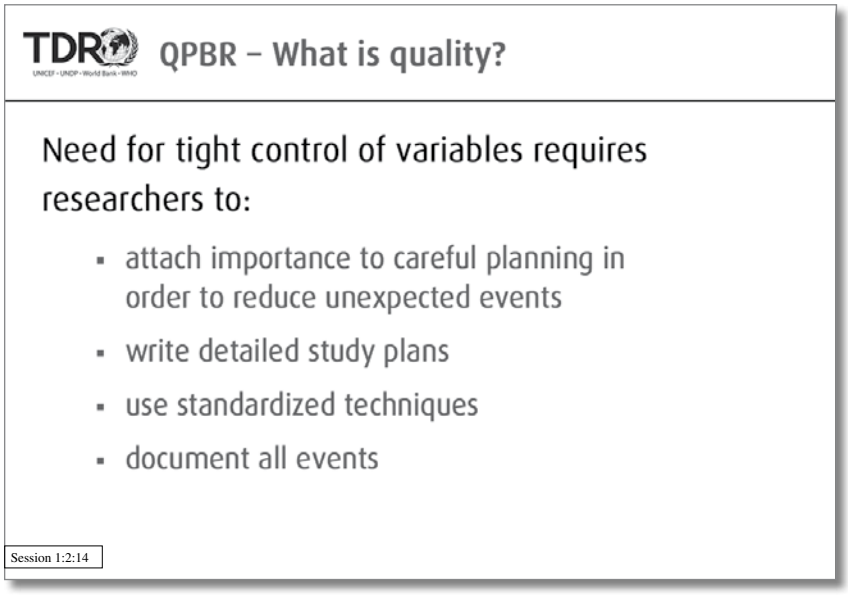
Session 1:2:10

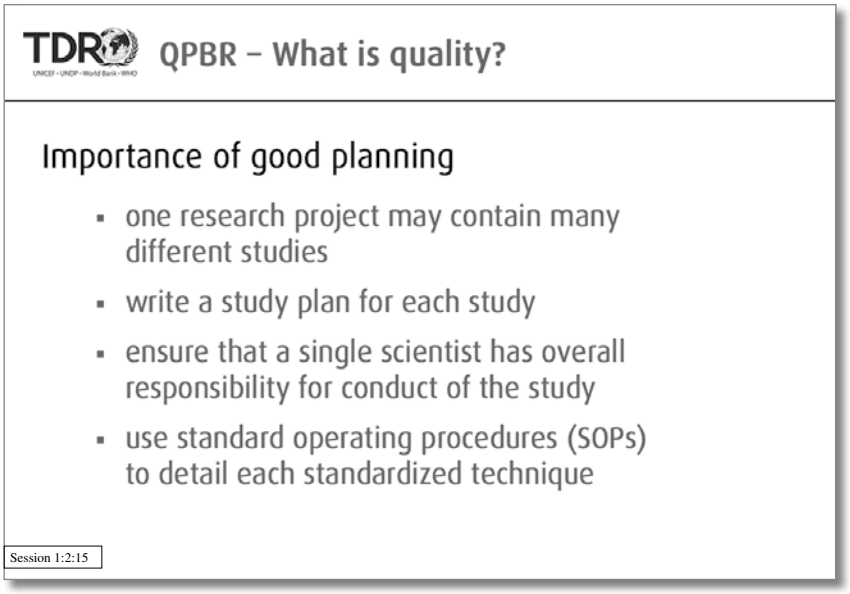


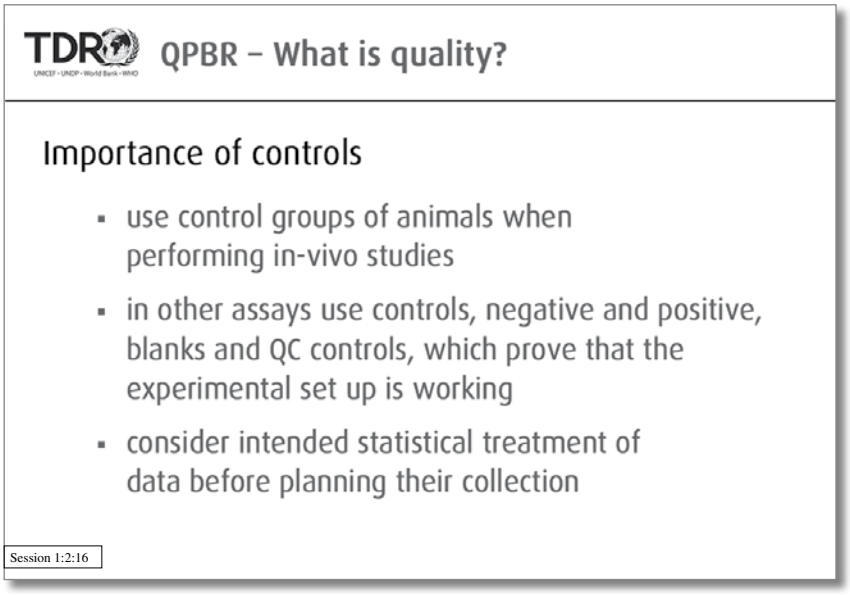


Anaesthetic	Sampling point	CPK measured
Carbon dioxide	Retro-orbital sinus	100
	Heart	125
	Vena cava	86
Methoxyflurane	Retro-orbital sinus	184
	Heart	102
	Vena cava	89
Phenobarbital	Retro-orbital sinus	536
	Heart	423
	Vena cava	455
Ketamine	Retro-orbital sinus	224
	Heart	160
	Vena cava	169


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – What is quality?
Importance of variables
▪ Avoid all sources of bias in the experimental set-up
▪ Consider all influences and inputs to the study before activities begin
▪ Drawing up plans for the way the study is to be conducted and keeping to them during the experimental phases helps to keep the experiment under control
Session 1:2:13

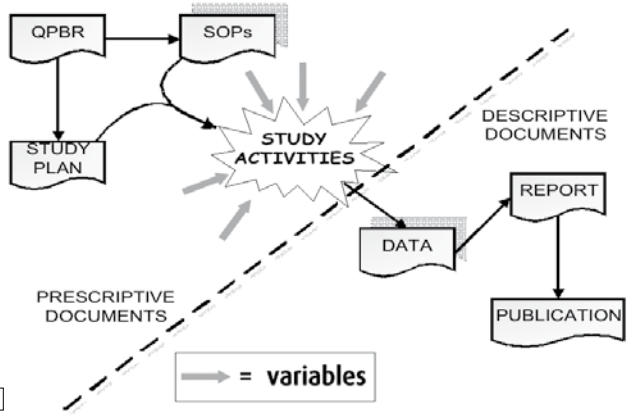

TDR
UNICEF • UNDP • World Bank • WHO
QPBR – What is quality?
Need for tight control of variables requires researchers to:
▪ attach importance to careful planning in order to reduce unexpected events
▪ write detailed study plans
▪ use standardized techniques
▪ document all events
Session 1:2:14


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – What is quality?
Importance of good planning
▪ one research project may contain many different studies
▪ write a study plan for each study
▪ ensure that a single scientist has overall responsibility for conduct of the study
▪ use standard operating procedures (SOPs) to detail each standardized technique
Session 1:2:15


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – What is quality?
Importance of controls
▪ use control groups of animals when performing in-vivo studies
▪ in other assays use controls, negative and positive, blanks and QC controls, which prove that the experimental set up is working
▪ consider intended statistical treatment of data before planning their collection
Session 1:2:16

QPBR – What is quality?

Relationship between study and documentation



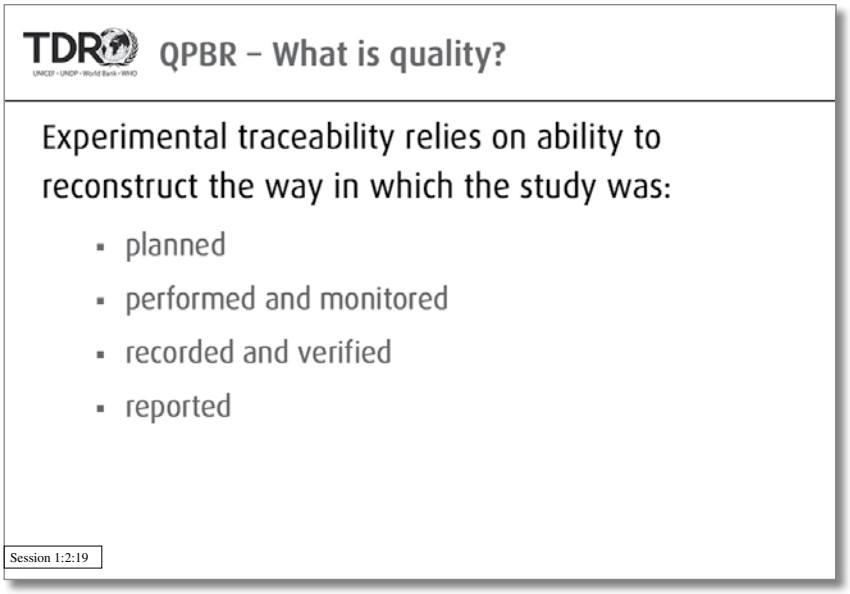
Session 1:2:17

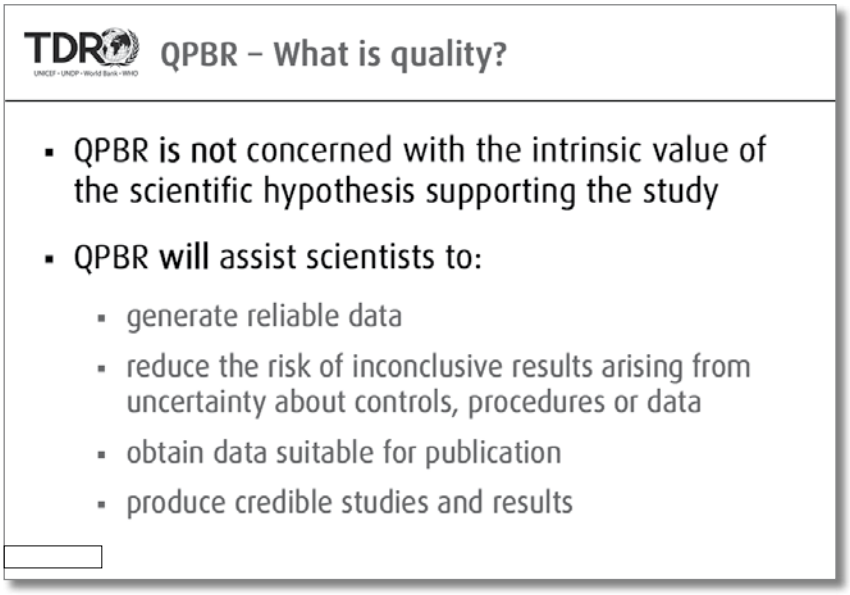
QPBR – What is quality?

Importance of reproducibility

- ability to repeat a study is a classic way of testing the reliability of methods and data
- valuable, unexpected or controversial results will almost certainly require confirmation
- repetition of a study requires conduct of the first experiment to have total traceability

Session 1:2:18


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – What is quality?
Experimental traceability relies on ability to reconstruct the way in which the study was:
planned
performed and monitored
recorded and verified
reported
Session 1:2:19


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – What is quality?
QPBR is not concerned with the intrinsic value of the scientific hypothesis supporting the study
QPBR will assist scientists to:
generate reliable data
reduce the risk of inconclusive results arising from uncertainty about controls, procedures or data
obtain data suitable for publication
produce credible studies and results

Questions

- What are the two aspects of research quality? What does each aspect contribute to the total quality?
- What is the purpose of QPBR?
- Is there a practical advantage to making sure that your research work is well-organized?
- What value does well-organized research hold for other researchers?
- What is the definition of "quality" in QPBR? Do you agree? Are there other meanings?
- What are the quality characteristics of scientific research?
- Can you briefly define each one?
- What are experimental variables?
- What is the message of the two examples given?
- Why should you spend time on a written plan?
- What sort of information would you include to describe/control variables? Give two or three examples.
- How does the information in the study plan differ from the information in the data?
- Explain the intended scope of QPBR, including what is not covered.

Workshops

1. List the quality attributes of two or three everyday products or services (e.g. a drinking cup, cup of coffee, road, weather forecast, organizing a holiday). Could different examples of the same sort of product have different quality attributes? List your examples and their quality attributes on the flip chart.

2. List the quality attributes for basic biomedical research. Is this an exhaustive list? Write down what each attribute means in practical, behavioural terms.

3. Taking one or two studies from your everyday experience write a list of possible sources of bias and discuss measures you could take to minimize artefact to ensure the validity of your data. Present your discussion schematically on the flip chart/board.

4. Give an example of doubtful scientific results in your everyday activity or from the scientific literature. Was the failure due to scientific problems? Problems with experimental conduct/data? A mixture of both? Or something quite different? Use the flip chart to summarize your discussion as a table showing the type of failure and the actual circumstances.

SESSION 2

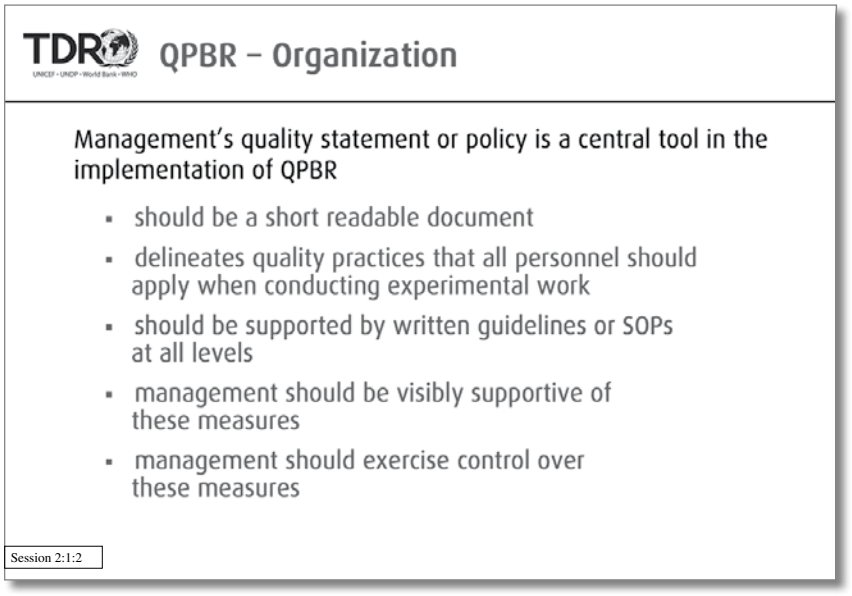
2.1 ORGANIZATION

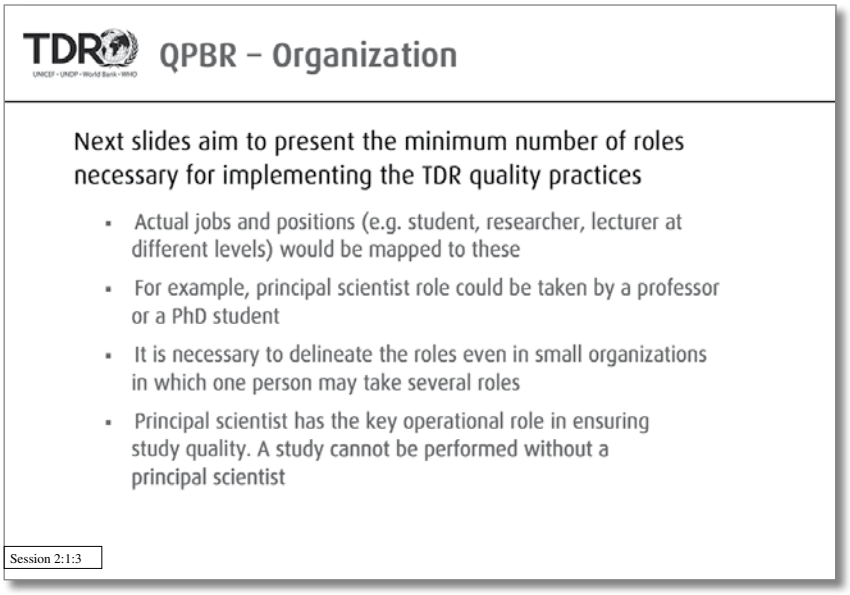
Goals

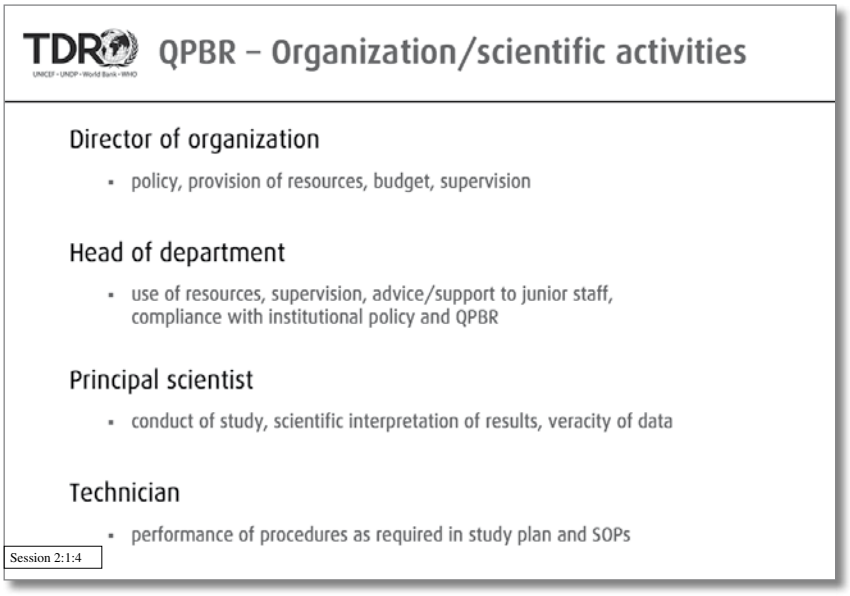
At the end of the session, you should be able to:

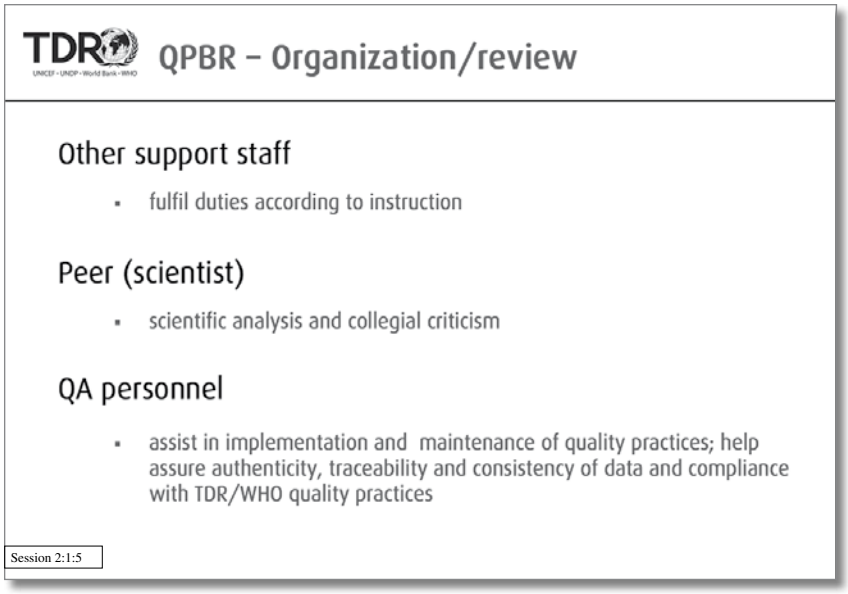
- explain why a formal organization is needed;
- argue for the advantages of a clear allocation of responsibilities and activities;
- describe management's roles and responsibilities;
- summarize the checks and balances implicit in the use of peer review and quality assurance (QA) surveillance;
- explain the practical purpose of the documents involved: quality policy, organizational chart, job description, curriculum vitae (CV);
- produce a model job description for three different roles.

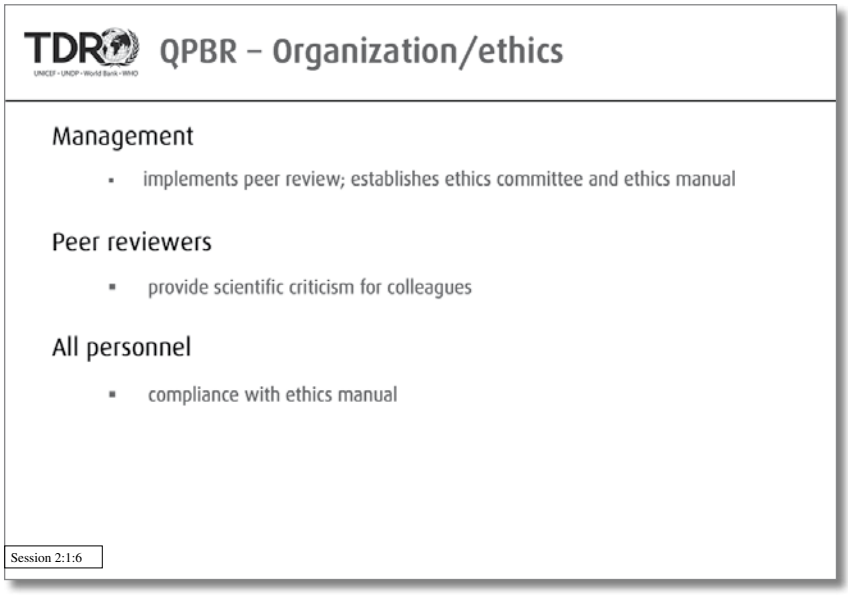

TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Organization
Organization & quality
Session 2:1:1


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Organization
Management's quality statement or policy is a central tool in the implementation of QPBR
▪ should be a short readable document
▪ delineates quality practices that all personnel should apply when conducting experimental work
▪ should be supported by written guidelines or SOPs at all levels
▪ management should be visibly supportive of these measures
▪ management should exercise control over these measures
Session 2:1:2


QPBR – Organization
Next slides aim to present the minimum number of roles necessary for implementing the TDR quality practices
Actual jobs and positions (e.g. student, researcher, lecturer at different levels) would be mapped to these
For example, principal scientist role could be taken by a professor or a PhD student
It is necessary to delineate the roles even in small organizations in which one person may take several roles
Principal scientist has the key operational role in ensuring study quality. A study cannot be performed without a principal scientist
Session 2:1:3


QPBR – Organization/scientific activities
Director of organization
policy, provision of resources, budget, supervision
Head of department
use of resources, supervision, advice/support to junior staff, compliance with institutional policy and QPBR
Principal scientist
conduct of study, scientific interpretation of results, veracity of data
Technician
performance of procedures as required in study plan and SOPs
Session 2:1:4


QPBR – Organization/review
Other support staff
fulfil duties according to instruction
Peer (scientist)
scientific analysis and collegial criticism
QA personnel
assist in implementation and maintenance of quality practices; help assure authenticity, traceability and consistency of data and compliance with TDR/WHO quality practices
Session 2:1:5


QPBR – Organization/ethics
Management
implements peer review; establishes ethics committee and ethics manual
Peer reviewers
provide scientific criticism for colleagues
All personnel
compliance with ethics manual
Session 2:1:6

QPBR – Organization

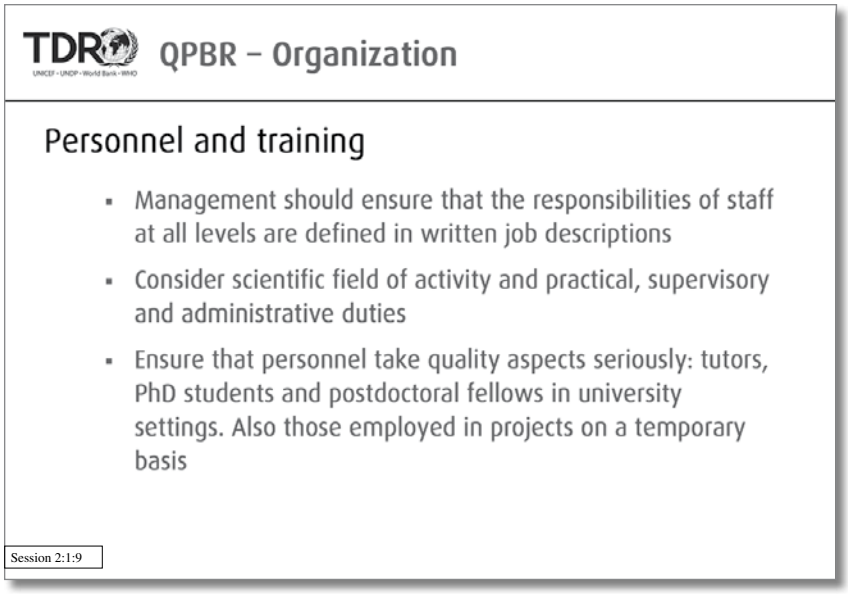
- QA personnel are not employed routinely at research establishments
  - Role is becoming more widespread but not compulsory
  - QA personnel take an active role in implementing and maintaining quality measures
  - Through auditing activities QA keeps management informed of the level of compliance with quality requirements
  - Most effective to organize QA personnel independently of study activities

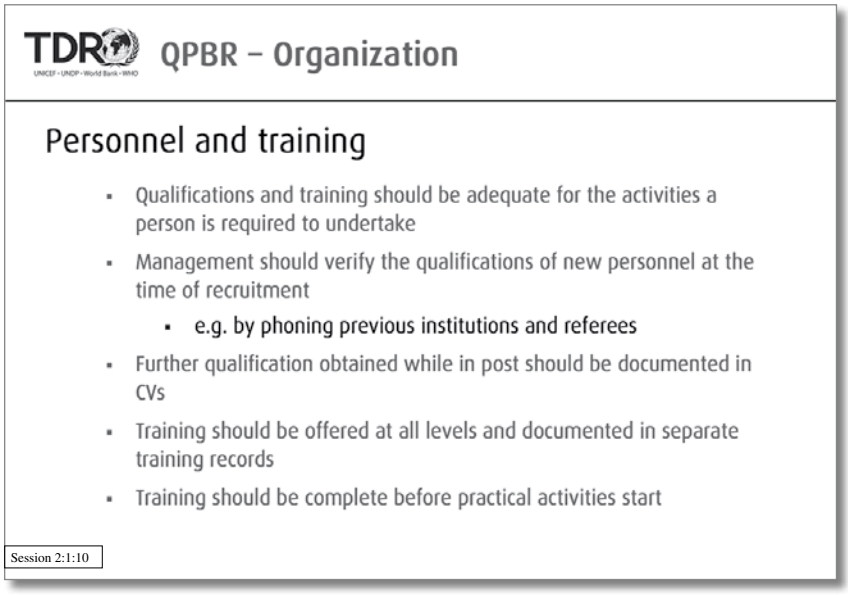
Session 2:1:7

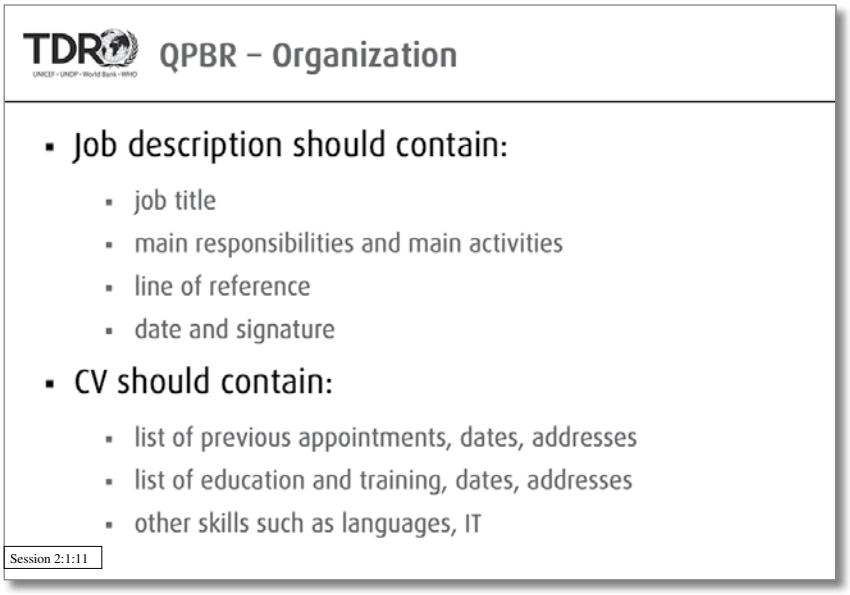
QPBR – Keynote

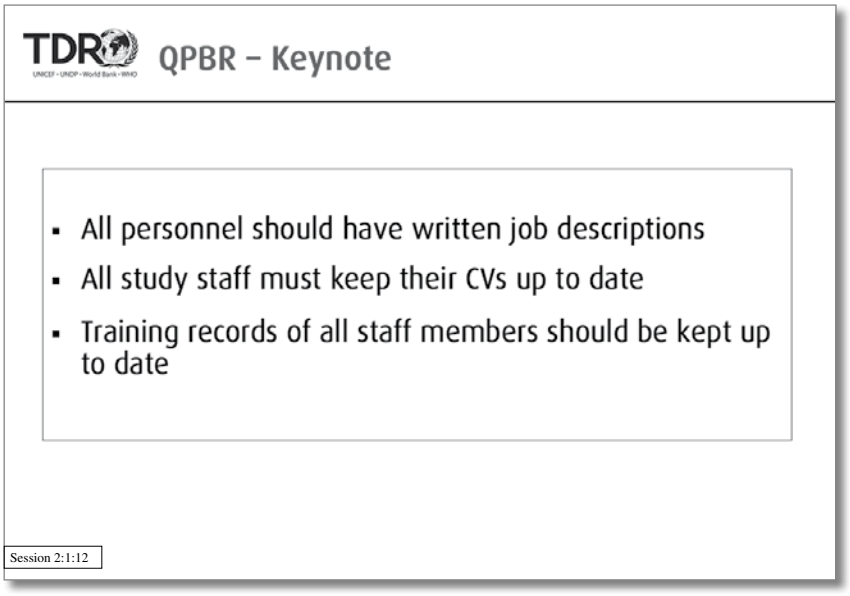
- Research institution should establish a written policy that describes its quality practices
- Responsibilities of each level of personnel should be defined and documented

Session 2:1:8


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Organization
Personnel and training
Management should ensure that the responsibilities of staff at all levels are defined in written job descriptions
Consider scientific field of activity and practical, supervisory and administrative duties
Ensure that personnel take quality aspects seriously: tutors, PhD students and postdoctoral fellows in university settings. Also those employed in projects on a temporary basis
Session 2:1:9


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Organization
Personnel and training
Qualifications and training should be adequate for the activities a person is required to undertake
Management should verify the qualifications of new personnel at the time of recruitment
e.g. by phoning previous institutions and referees
Further qualification obtained while in post should be documented in CVs
Training should be offered at all levels and documented in separate training records
Training should be complete before practical activities start
Session 2:1:10


QPBR – Organization
Job description should contain:
job title
main responsibilities and main activities
line of reference
date and signature
CV should contain:
list of previous appointments, dates, addresses
list of education and training, dates, addresses
other skills such as languages, IT
Session 2:1:11


QPBR – Keynote
All personnel should have written job descriptions
All study staff must keep their CVs up to date
Training records of all staff members should be kept up to date
Session 2:1:12

Questions

- Who should issue a quality statement/policy? Why should they do this?
- What are the minimum roles needed for studies performed under QPBR?
- Why is the principal scientist a key position? Describe the responsibilities and activities of this person.
- Who is QA? What are QA's main responsibilities? Ideally, QA should be independent of the organization performing scientific study activities – why?
- What are the purposes of a job description?
- Why does an institution need to keep CVs for all staff?
- Why is training a core activity for achieving high quality in basic biomedical research?
- Why should training be documented?
- Why is it important to keep training records for personnel?

Workshops

1. Taking one of your own (or your department's) studies as an example, describe what roles are active and who (job title) occupies these roles. Tabulate responsibilities, roles and job titles. Identify any roles that are missing; situations in which two people appear responsible for the same activity; or responsibilities that are not covered.

2. In your discussion group, for each of your institutions, make a chart showing the incidence of the following: a quality policy, a QA group, routine use of peer review, use of job descriptions, use of training records. If any of these are missing, how would you propose to introduce them?

3. Write job descriptions for one or two persons in the group (bullet points rather than full text), using the points mentioned in slide 11 of the PowerPoint presentation on organization and quality.

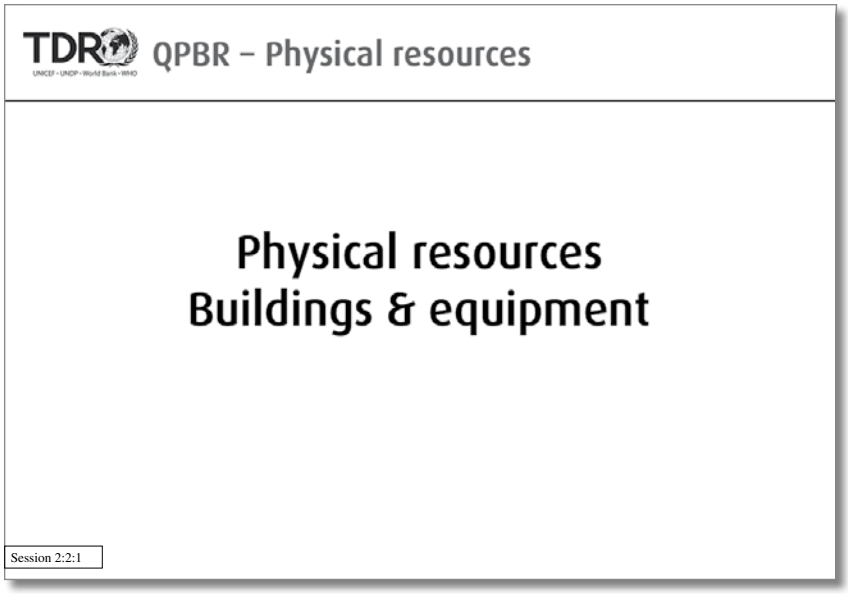
4. Write a job description for the managers or assistants of one or two other persons in the group.

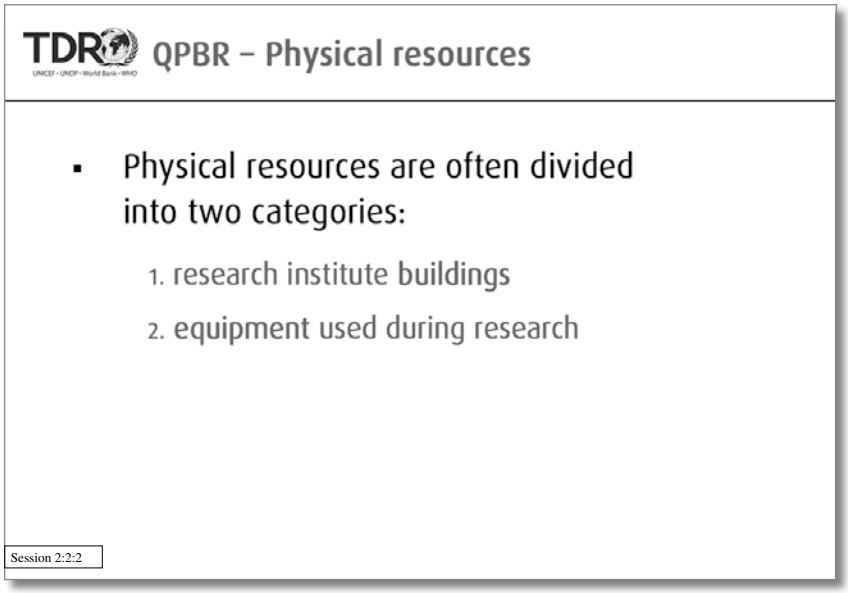
2.2 PHYSICAL RESOURCES

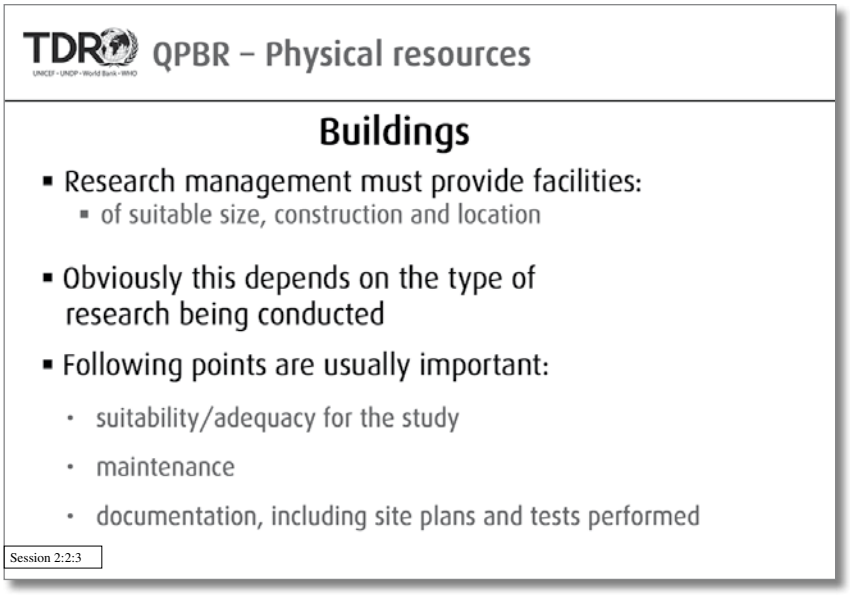
Goals

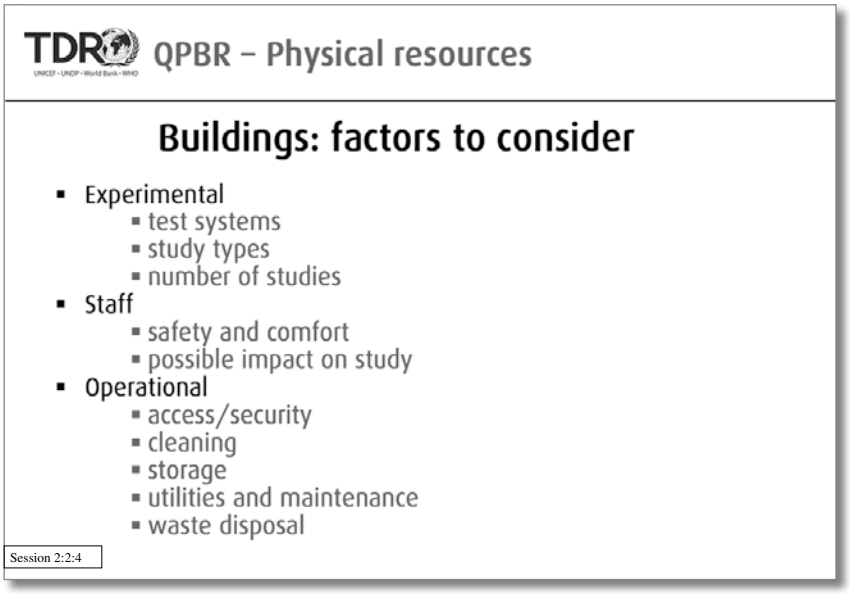
At the end of the session, you should be able to:

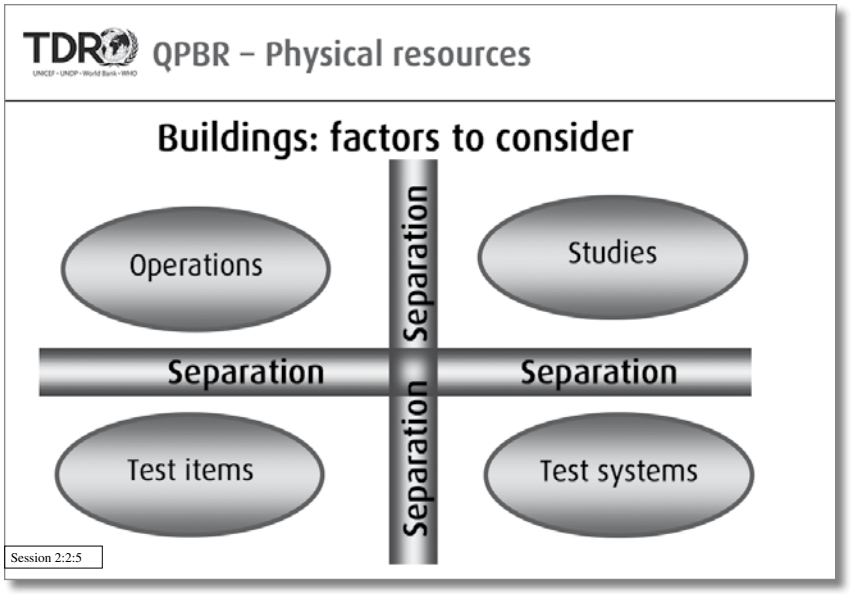
- describe important factors to consider when building new facilities;
- argue for the importance of separating activities in research facilities;
- define different ways of separating activities;
- provide examples in which separation of research activities is fundamental to the integrity of research;
- differentiate between the scientist's responsibility for deciding what equipment to use and the need to ensure that all equipment functions correctly;
- argue for the need to implement calibration and maintenance procedures within a research organization;
- distinguish between preventive maintenance and repair;
- describe what documents are needed to ensure full traceability of calibration and maintenance;
- describe the content and use of a fault action report.

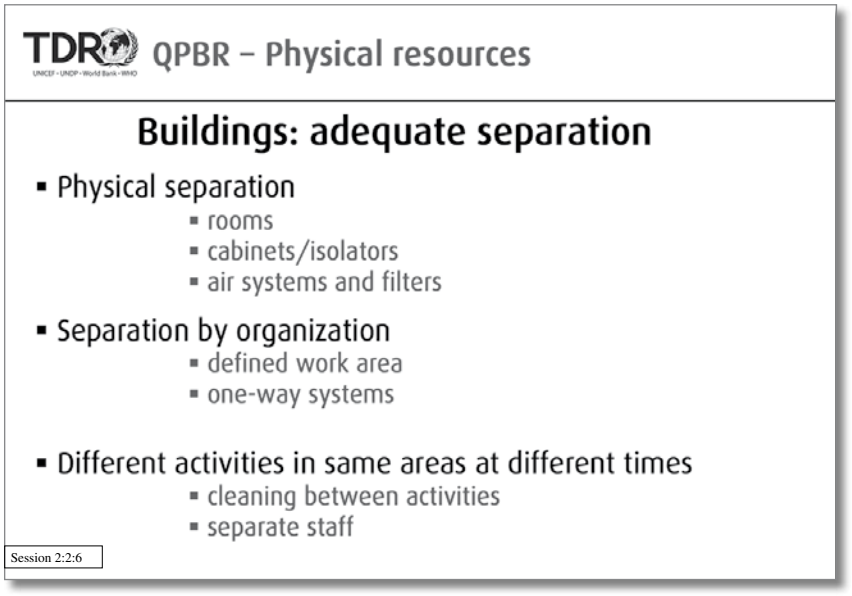

TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Physical resources
Physical resources
Buildings & equipment
Session 2:2:1


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Physical resources
Physical resources are often divided into two categories:
1. research institute buildings
2. equipment used during research
Session 2:2:2


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Physical resources
Buildings
Research management must provide facilities:
of suitable size, construction and location
Obviously this depends on the type of research being conducted
Following points are usually important:
suitability/adequacy for the study
maintenance
documentation, including site plans and tests performed
Session 2:2:3


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Physical resources
Buildings: factors to consider
Experimental
test systems
study types
number of studies
Staff
safety and comfort
possible impact on study
Operational
access/security
cleaning
storage
utilities and maintenance
waste disposal
Session 2:2:4


TDR
QPBR – Physical resources
Buildings: factors to consider
Operations
Studies
Separation
Separation
Separation
Separation
Separation
Test items
Test systems
Session 2:2:5


TDR
QPBR – Physical resources
Buildings: adequate separation
Physical separation
rooms
cabinets/isolators
air systems and filters
Separation by organization
defined work area
one-way systems
Different activities in same areas at different times
cleaning between activities
separate staff
Session 2:2:6

TDR UNICEF • UNDP • World Bank • WHO QPBR – Physical resources

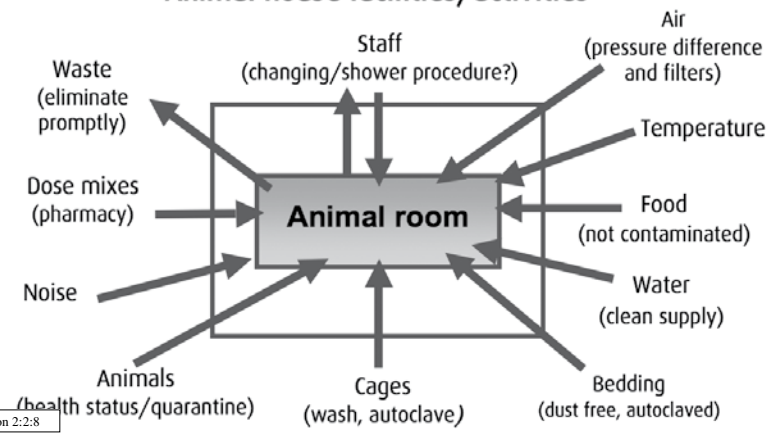
Buildings: adequate separation

- Animal house facilities provide a good example of organizational constraints and separation
- There is a requirement to:
  - ensure adequate separation of animals and studies
  - prevent unintended movement of contaminants by personnel, air flow, waste products etc
  - provide adequate environmental conditions (temperature, humidity, light, air flow etc)
  - ensure correct husbandry (feed, water, care etc)

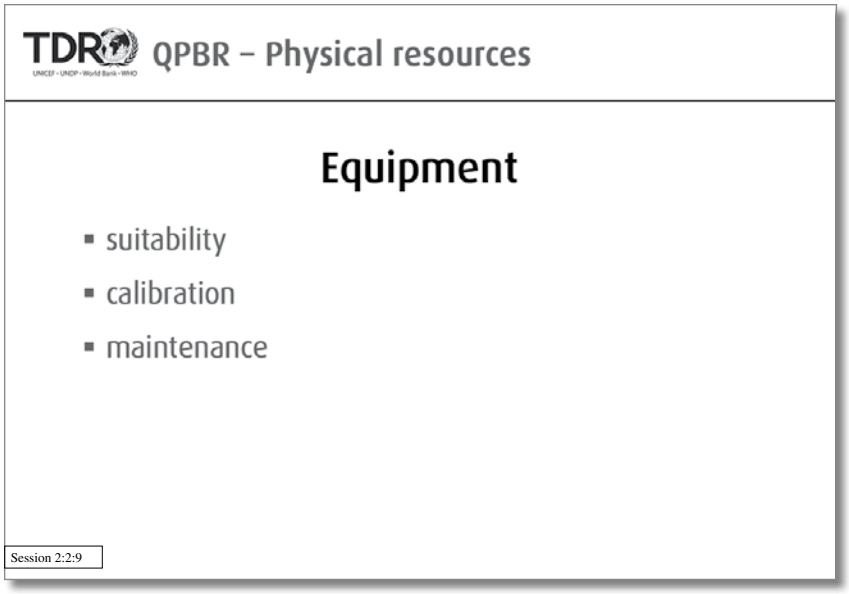
Session 2:2:7

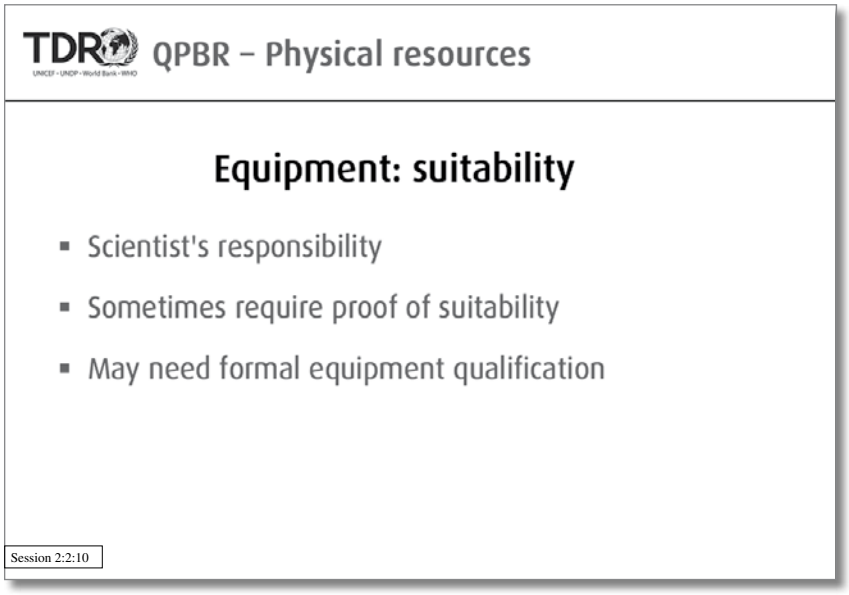
TDR UNICEF • UNDP • World Bank • WHO QPBR – Physical resources

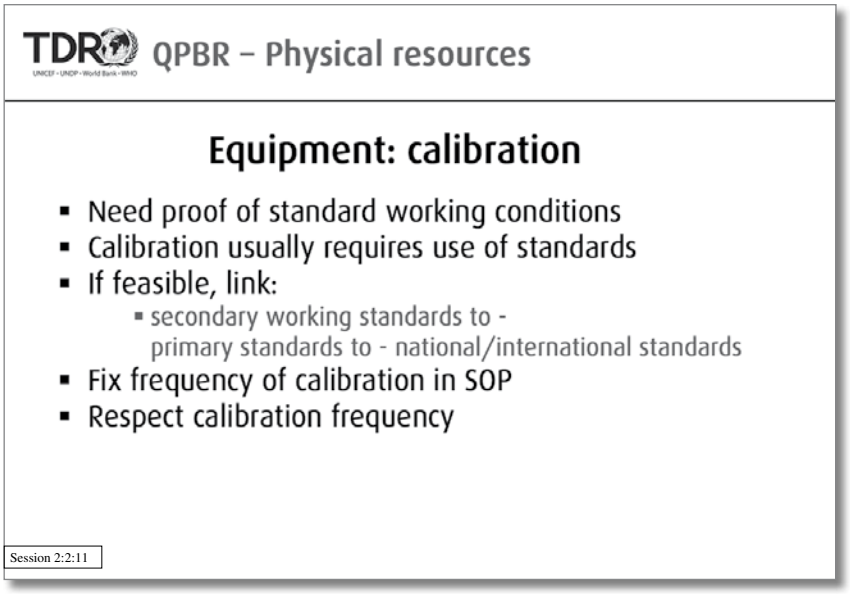
Animal house facilities/activities

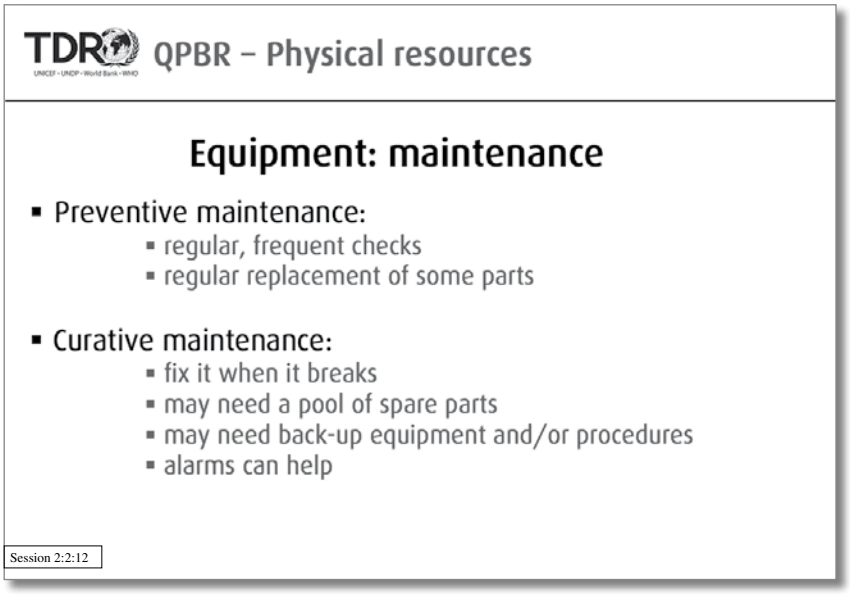


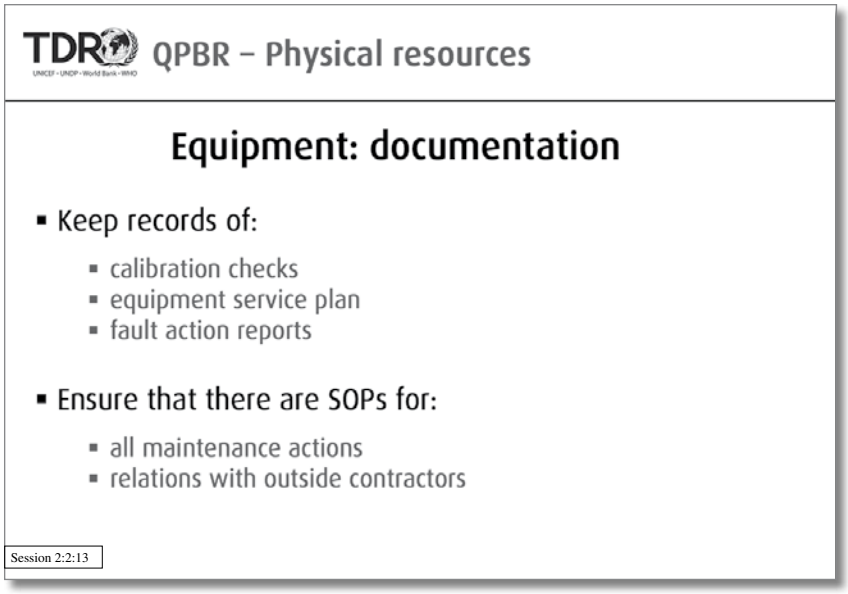
Session 2:2:8

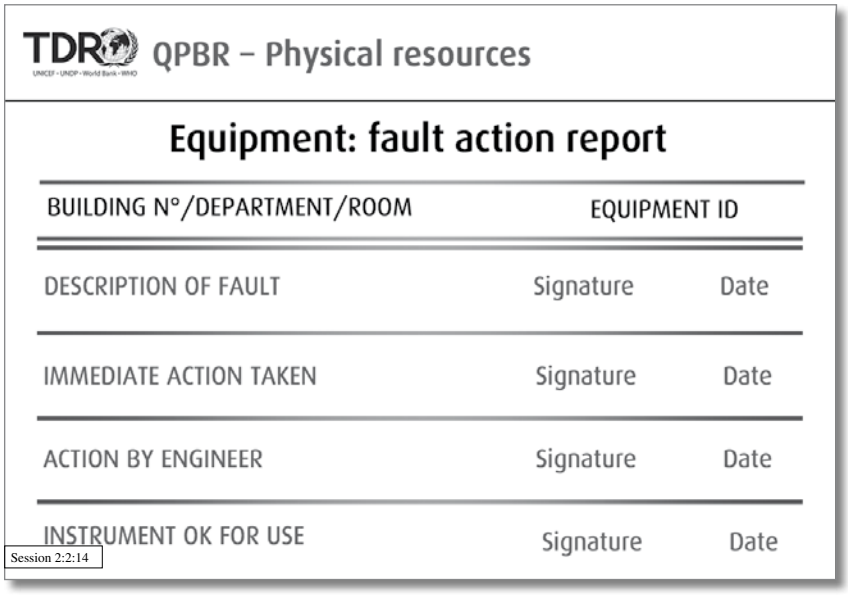

TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Physical resources
Equipment
suitability
calibration
maintenance
Session 2:2:9


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Physical resources
Equipment: suitability
Scientist's responsibility
Sometimes require proof of suitability
May need formal equipment qualification
Session 2:2:10


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Physical resources
Equipment: calibration
Need proof of standard working conditions
Calibration usually requires use of standards
If feasible, link:
secondary working standards to -
primary standards to - national/international standards
Fix frequency of calibration in SOP
Respect calibration frequency
Session 2:2:11


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Physical resources
Equipment: maintenance
Preventive maintenance:
regular, frequent checks
regular replacement of some parts
Curative maintenance:
fix it when it breaks
may need a pool of spare parts
may need back-up equipment and/or procedures
alarms can help
Session 2:2:12


TDR
QPBR – Physical resources
Equipment: documentation
▪ Keep records of:
▪ calibration checks
▪ equipment service plan
▪ fault action reports
▪ Ensure that there are SOPs for:
▪ all maintenance actions
▪ relations with outside contractors
Session 2:2:13


TDR
QPBR – Physical resources
Equipment: fault action report
BUILDING N°/DEPARTMENT/ROOM
EQUIPMENT ID
DESCRIPTION OF FAULT
Signature
Date
IMMEDIATE ACTION TAKEN
Signature
Date
ACTION BY ENGINEER
Signature
Date
INSTRUMENT OK FOR USE
Signature
Date
Session 2:2:14

TDR QPBR – Physical resources

Equipment: service label

INSTRUMENT N°

DATE OF LAST SERVICE

NEXT SERVICE DUE

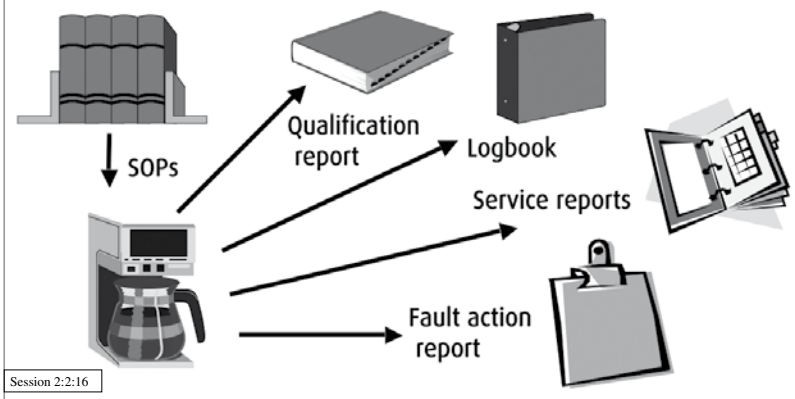
NAME RESPONSIBLE METROLOGIST

Signature/date

Session 2:2:15

TDR QPBR – Physical resources

Documentation for buildings/equipment



Session 2:2:16

Questions

- What is separation of activities within a facility? Why is this concept important for the integrity of research?
- Give examples to show how a research project could be compromised by failure to separate research activities.
- Give examples of physical separations frequently found in a research environment.
- Does separation of activities always require physical separation? In what other ways could this separation be achieved?
- Why is the suitability of equipment said to be a scientific responsibility rather than an aspect of quality management?
- What is the difference between a primary and a secondary working standard?
- What SOPs do you think are required for equipment used in a laboratory?
- Give some examples of preventive maintenance performed in your own organization.
- What headings should be included in a fault action report? Who would write it? To whom should it be sent?
- What would a standard logbook contain?
- What would a standard apparatus file contain?

Workshops

1. Taking as examples two different pieces of equipment with which you are familiar, use a flip chart to describe:
   a. how you would determine suitability for use
   b. how you would recommend that calibration be performed
   c. documents you would consider necessary to support the traceability of all actions involving the equipment.

2. Consider a secondary standard used in your laboratory. Use a flip chart to map out the process by which it is linked to (a) a primary standard; and eventually (b) a national standard.

3. List on a flip chart the information/documents that you would require from an outside contractor called in to service an identified piece of equipment that has broken down. What would you do with these documents?

4. Design a standard fault action report for your facility.

5. You have been asked to design and equip a laboratory which will be used for analytical work, including general analysis (potentiometry, high performance liquid chromatography [HPLC] etc.), microbiology and stability studies. List the points that you consider essential for drawing up a requirements document that will form the basis for requests for tenders from architects.

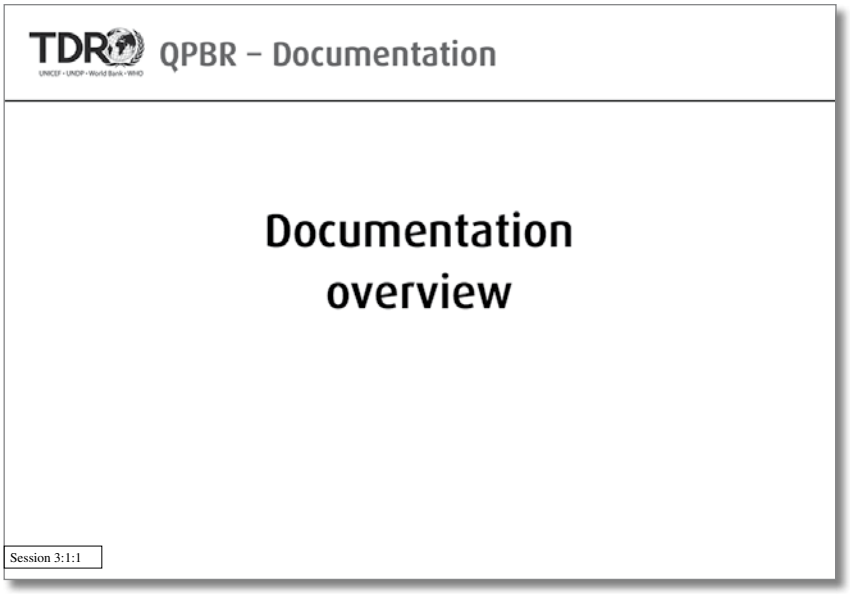
SESSION 3

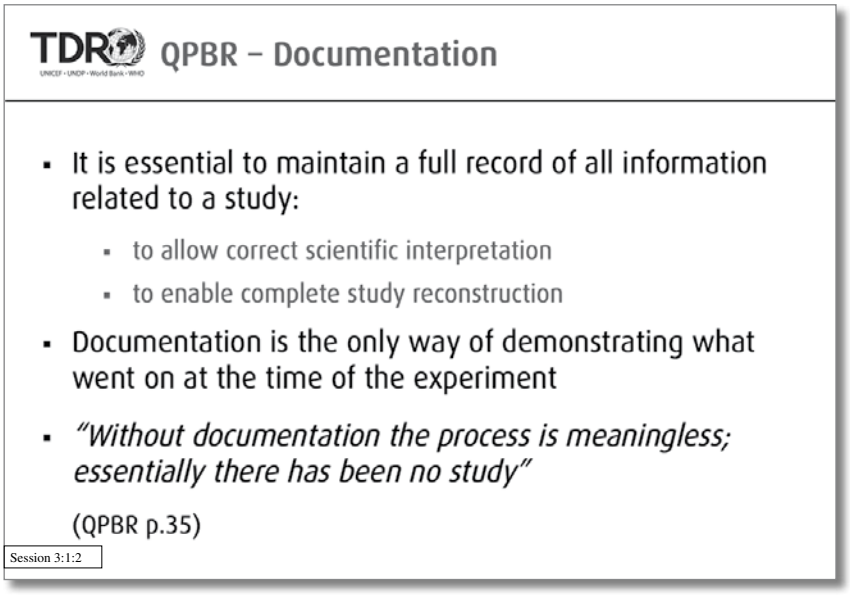
3.1 DOCUMENTATION – OVERVIEW

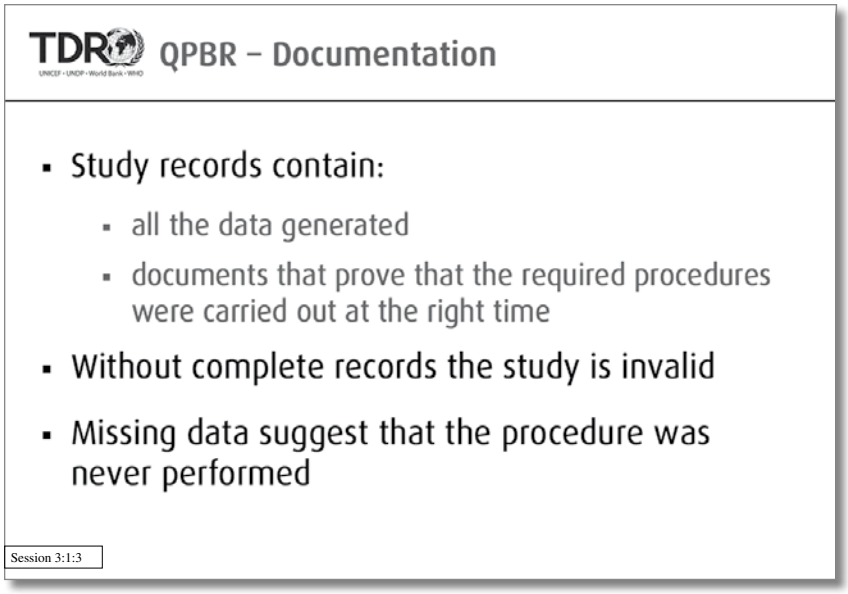
Goals

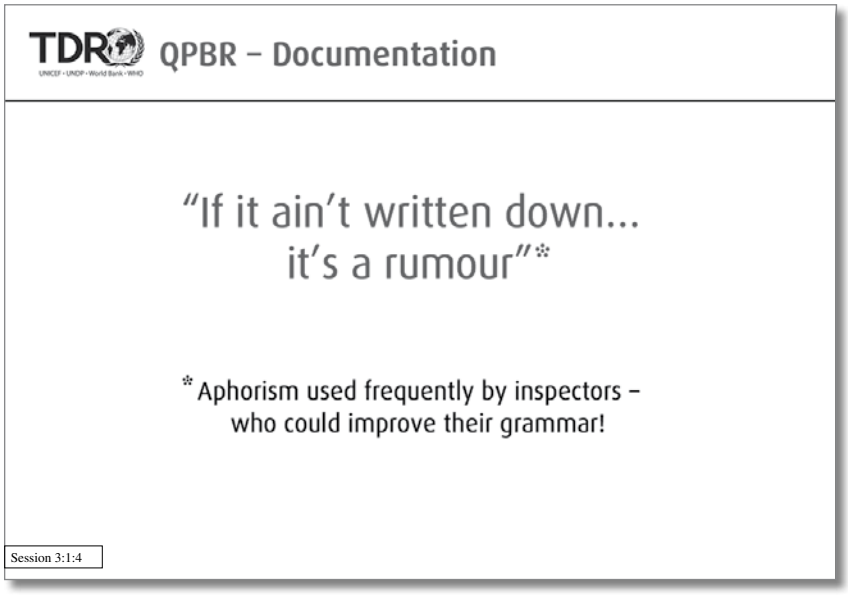
At the end of the session, you should be able to:

- explain why full documentation is central to the value of a study;
- define prescriptive and descriptive documents and give examples of each type;
- provide in schematic form the relationship between prescriptive and descriptive documents and their relationship to the practical study activities;
- explain why full records are necessary for study reconstruction;
- describe the relationship between study data and the study plan and explain what a study file is;
- describe the relationship between a study report and a publication;
- argue for formalized storage of study documentation.


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Documentation
Documentation overview
Session 3:1:1


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Documentation
▪ It is essential to maintain a full record of all information related to a study:
▪ to allow correct scientific interpretation
▪ to enable complete study reconstruction
▪ Documentation is the only way of demonstrating what went on at the time of the experiment
▪ "Without documentation the process is meaningless; essentially there has been no study"
(QPBR p.35)
Session 3:1:2


QPBR – Documentation
Study records contain:
all the data generated
documents that prove that the required procedures were carried out at the right time
Without complete records the study is invalid
Missing data suggest that the procedure was never performed
Session 3:1:3


QPBR – Documentation
"If it ain't written down... it's a rumour"*
* Aphorism used frequently by inspectors – who could improve their grammar!
Session 3:1:4

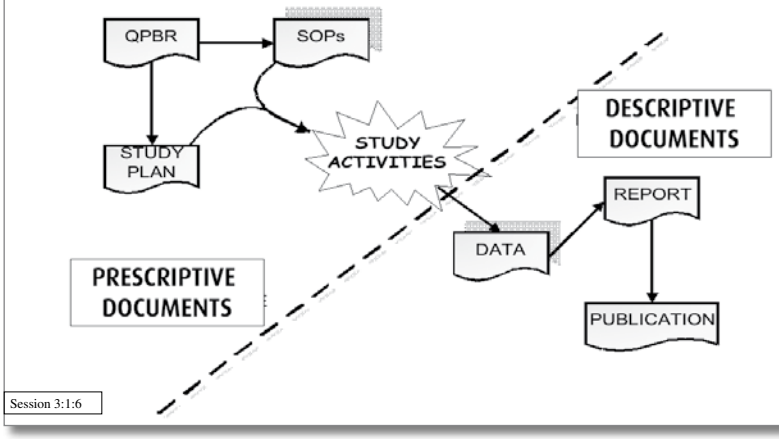
QPBR – Documentation

- Documentation may be divided into two broad categories:
  1. Prescriptive documents – give instructions on what is to happen during the study
  2. Descriptive documents – describe what actually happened during the study

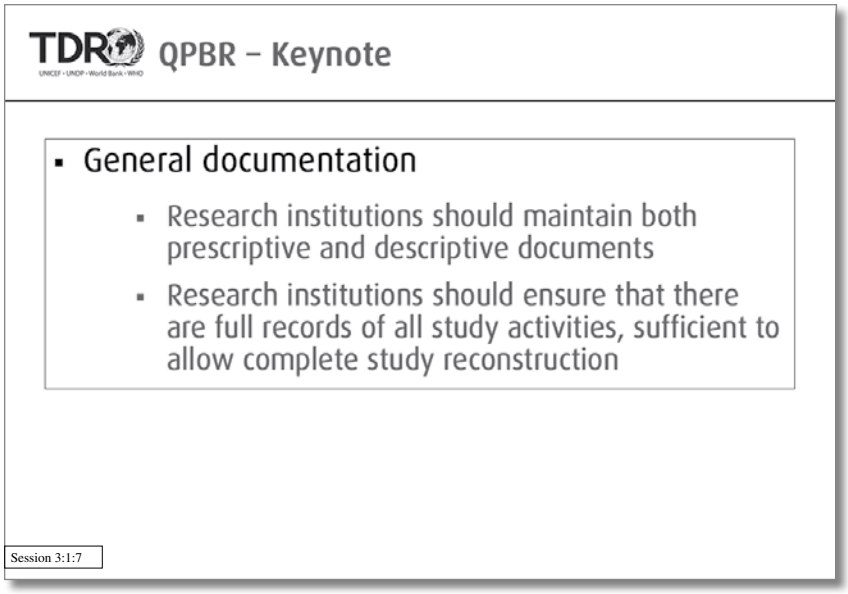
Session 3:1:5

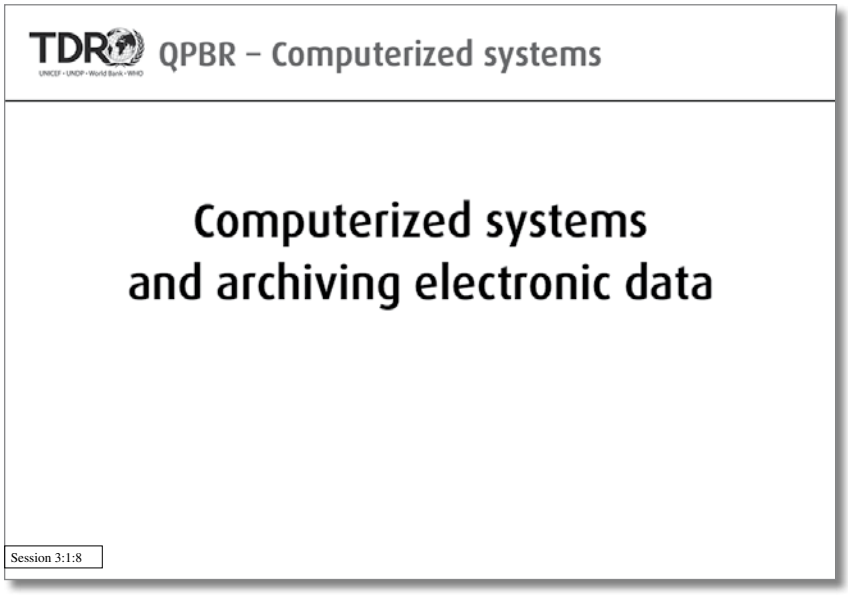
QPBR – Documentation

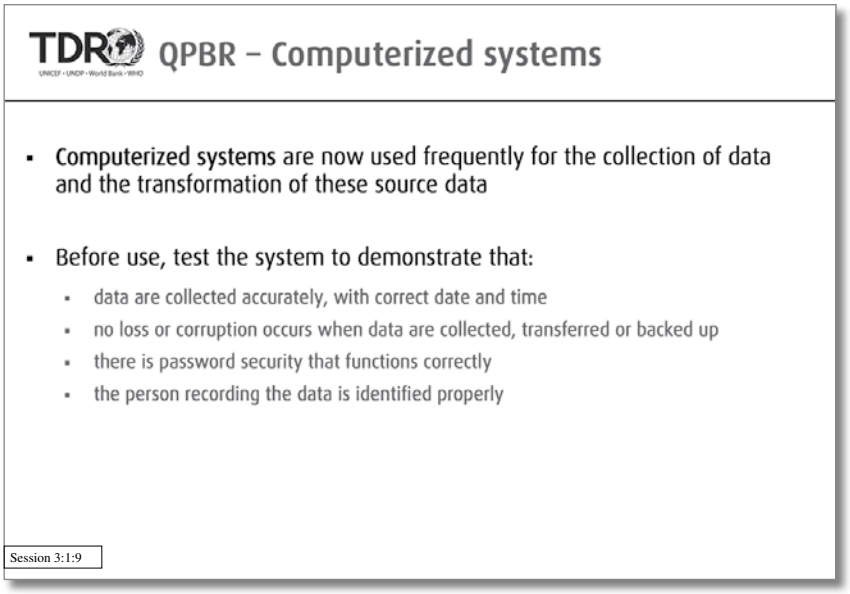
Relationship between study and documents

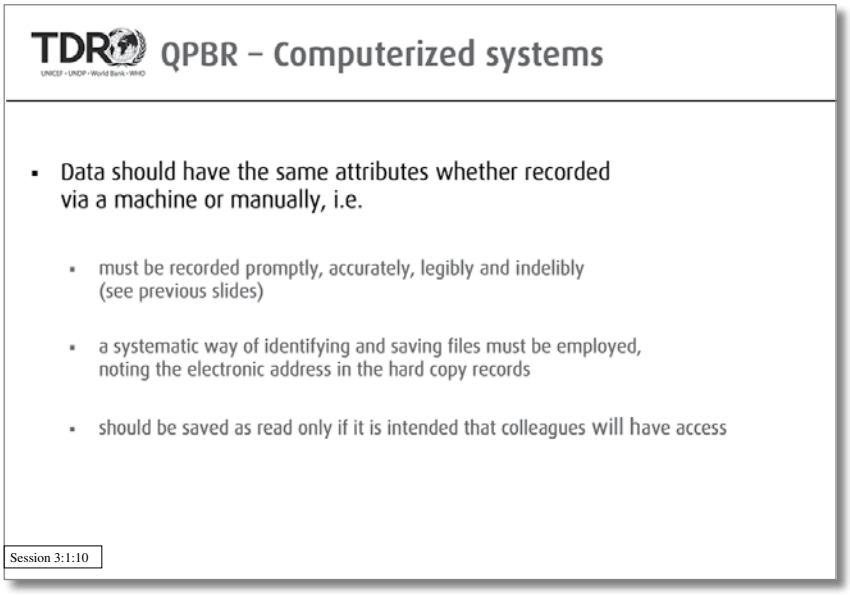


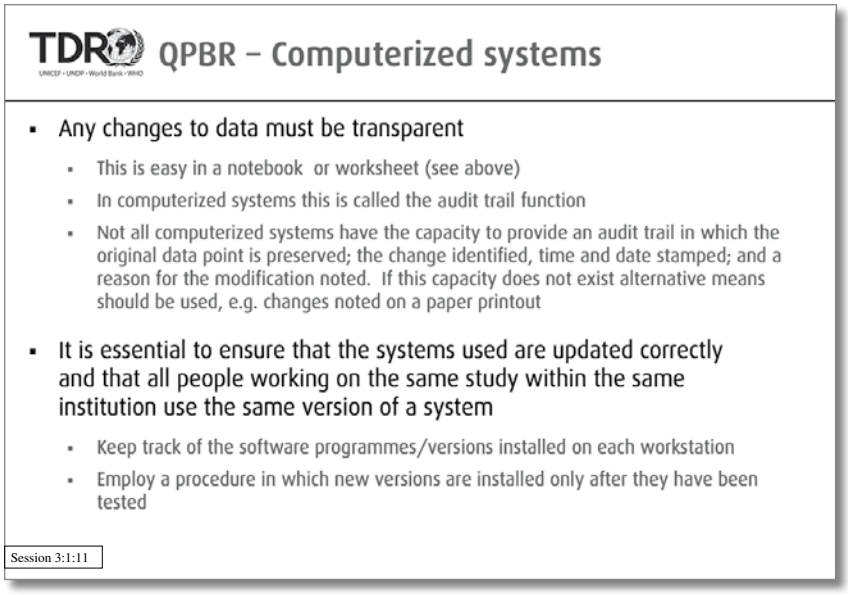
Session 3:1:6

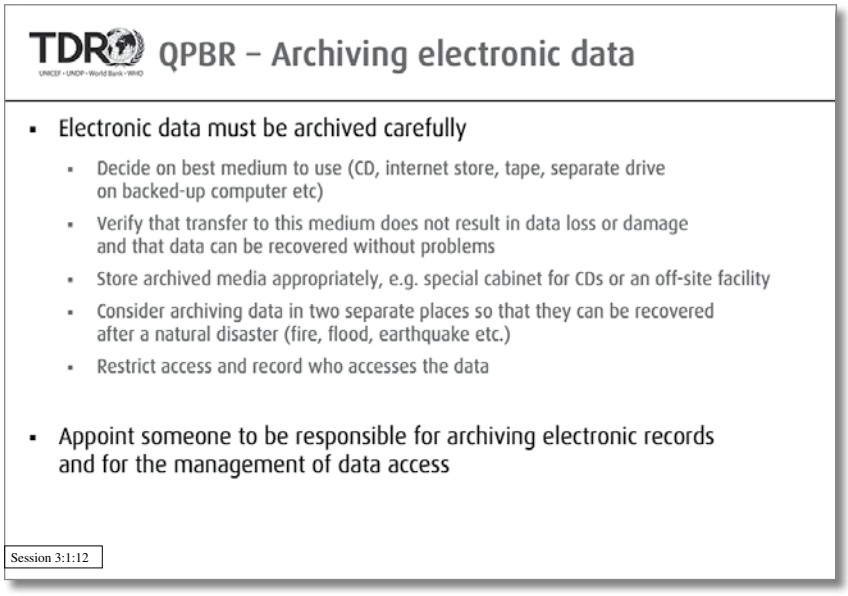

QPBR – Keynote
General documentation
Research institutions should maintain both prescriptive and descriptive documents
Research institutions should ensure that there are full records of all study activities, sufficient to allow complete study reconstruction
Session 3:1:7


QPBR – Computerized systems
Computerized systems and archiving electronic data
Session 3:1:8


QPBR – Computerized systems
Computerized systems are now used frequently for the collection of data and the transformation of these source data
Before use, test the system to demonstrate that:
data are collected accurately, with correct date and time
no loss or corruption occurs when data are collected, transferred or backed up
there is password security that functions correctly
the person recording the data is identified properly
Session 3:1:9


QPBR – Computerized systems
Data should have the same attributes whether recorded via a machine or manually, i.e.
must be recorded promptly, accurately, legibly and indelibly (see previous slides)
a systematic way of identifying and saving files must be employed, noting the electronic address in the hard copy records
should be saved as read only if it is intended that colleagues will have access
Session 3:1:10


QPBR – Computerized systems
Any changes to data must be transparent
This is easy in a notebook or worksheet (see above)
In computerized systems this is called the audit trail function
Not all computerized systems have the capacity to provide an audit trail in which the original data point is preserved; the change identified, time and date stamped; and a reason for the modification noted. If this capacity does not exist alternative means should be used, e.g. changes noted on a paper printout
It is essential to ensure that the systems used are updated correctly and that all people working on the same study within the same institution use the same version of a system
Keep track of the software programmes/versions installed on each workstation
Employ a procedure in which new versions are installed only after they have been tested
Session 3:1:11


QPBR – Archiving electronic data
Electronic data must be archived carefully
Decide on best medium to use (CD, internet store, tape, separate drive on backed-up computer etc)
Verify that transfer to this medium does not result in data loss or damage and that data can be recovered without problems
Store archived media appropriately, e.g. special cabinet for CDs or an off-site facility
Consider archiving data in two separate places so that they can be recovered after a natural disaster (fire, flood, earthquake etc.)
Restrict access and record who accesses the data
Appoint someone to be responsible for archiving electronic records and for the management of data access
Session 3:1:12

Questions

Why is full study documentation essential to the validity of a study?

- Can you give examples of studies in which the scientific interpretation was doubtful because records were incomplete?
- What are the essential characteristics of prescriptive and descriptive documents?
- Give examples of prescriptive and descriptive documents that are used in your laboratory.
- What is the function of each document in slide 6 of the lecture on documentation?
- Where does your institution ask you to keep study records?

Workshops

1. Use a flip chart to draw up a flow chart that shows the relationships between a research proposal, study plan, study data, study report and publication(s) concerning the research programme. List some of the materials you would expect to have generated by the end of a study (the study file). How soon after the end of the study should the material be archived? For how long should each type of material be stored?

2. In practical terms, how would management ensure the safe keeping of study documentation? Use the flip chart to draw up a to-do list for management.

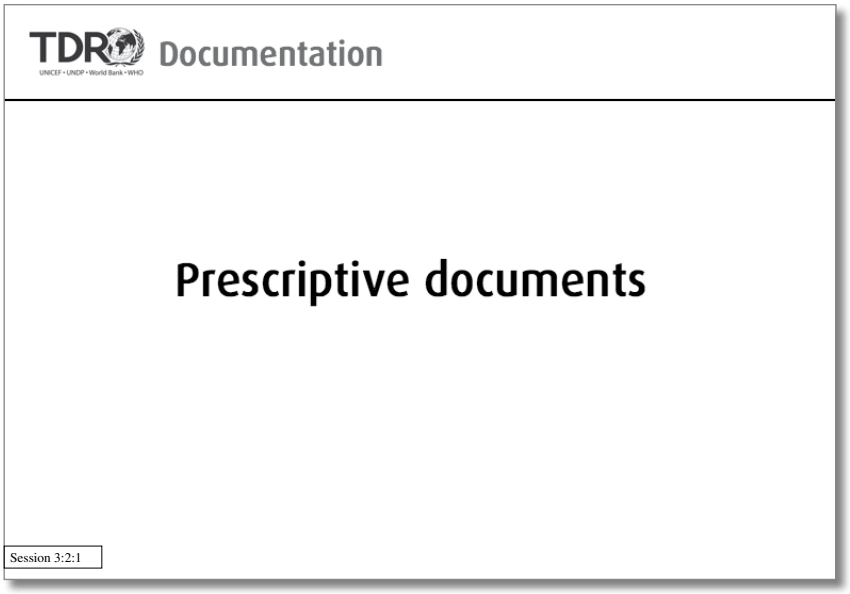
3. In practical terms, how would management ensure the safe keeping of study documentation? Use the flip chart to draw up a to-do list for management.

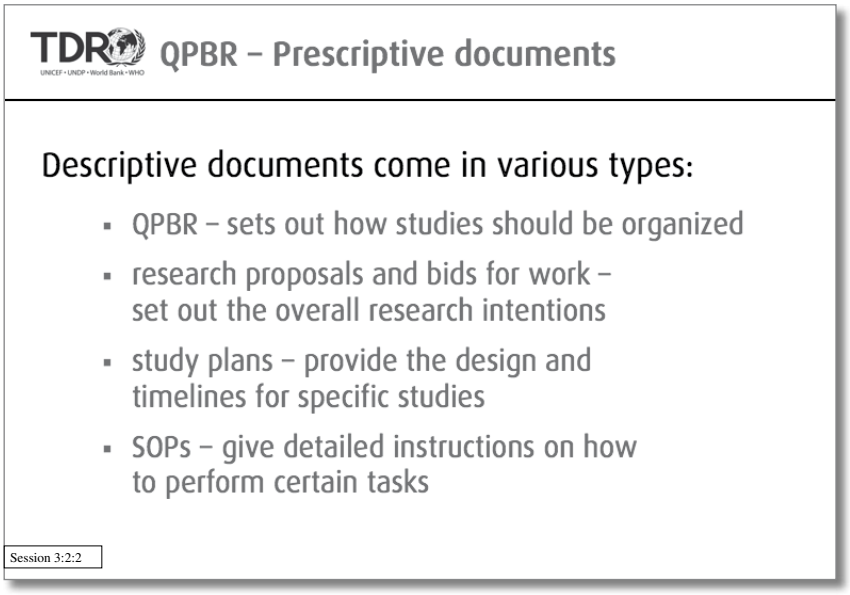
3.2 PRESCRIPTIVE DOCUMENTATION

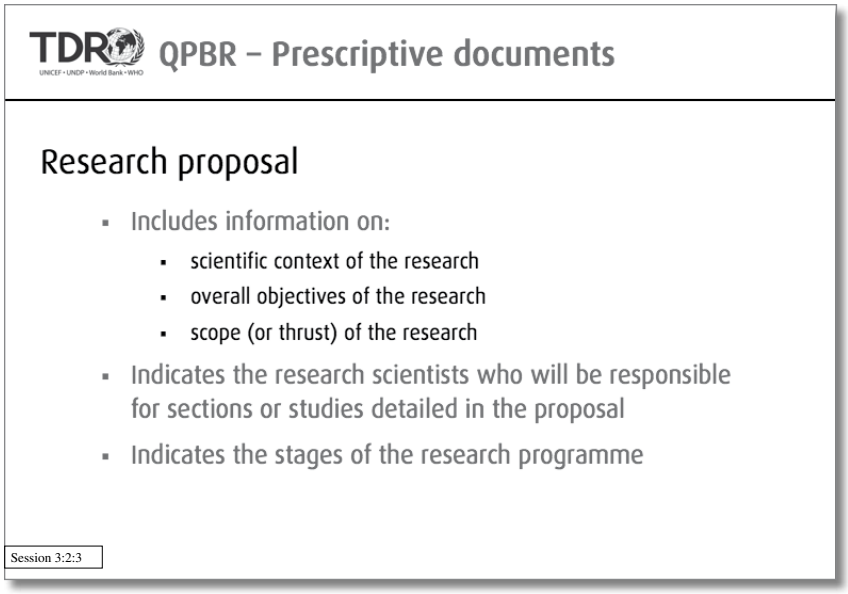
Goals

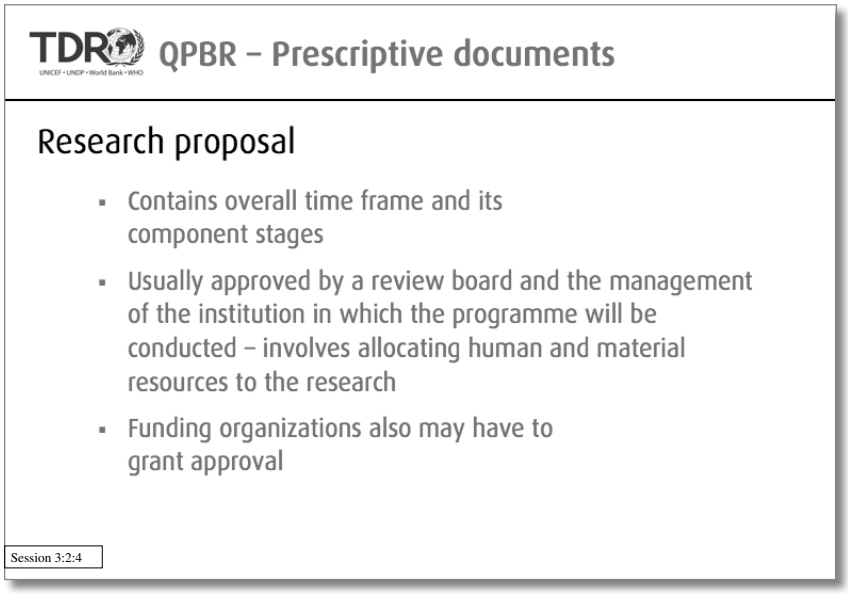
At the end of the session, you should be able to:

- define prescriptive documentation and its relationship to the practical activities of studies;
- name the different layers of prescriptive documentation and describe their relationship to one another;
- describe the purposes of these types of documents and outline the approval process for each;
- define template, layout, format and content;
- give an outline of the types of information typically found in research proposals and in study plans and define the relationship (using a diagram) between these two documents;
- define the responsibilities necessary for the approval and issue of a study plan;
- distinguish between study plan amendments and study deviations;
- describe situations in which study plans and SOPs should be used;
- give examples of SOPs;
- describe the attributes of an SOP management system;
- understand how SOPs contribute to the basic research process;
- argue for the freedom and integrity of the creative research process, despite the use of SOPs.


TDR
UNICEF • UNDP • World Bank • WHO
Documentation
Prescriptive documents
Session 3:2:1


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
Descriptive documents come in various types:
QPBR – sets out how studies should be organized
research proposals and bids for work – set out the overall research intentions
study plans – provide the design and timelines for specific studies
SOPs – give detailed instructions on how to perform certain tasks
Session 3:2:2


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
Research proposal
Includes information on:
scientific context of the research
overall objectives of the research
scope (or thrust) of the research
Indicates the research scientists who will be responsible for sections or studies detailed in the proposal
Indicates the stages of the research programme
Session 3:2:3


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
Research proposal
Contains overall time frame and its component stages
Usually approved by a review board and the management of the institution in which the programme will be conducted – involves allocating human and material resources to the research
Funding organizations also may have to grant approval
Session 3:2:4

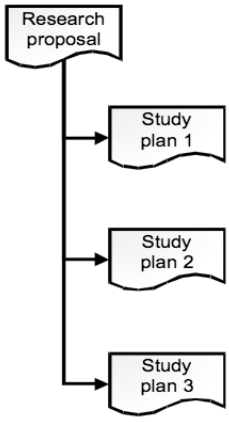
QPBR – Prescriptive documents

Study plan (protocol)

- Provides design and timelines for an individual study that forms part of the research proposal package
- Key document for communicating study intentions to all contributing staff and sponsors – content and layout should be clear
- Every study must have a study plan that is in line with the objectives of the research proposal

Session 3:2:5

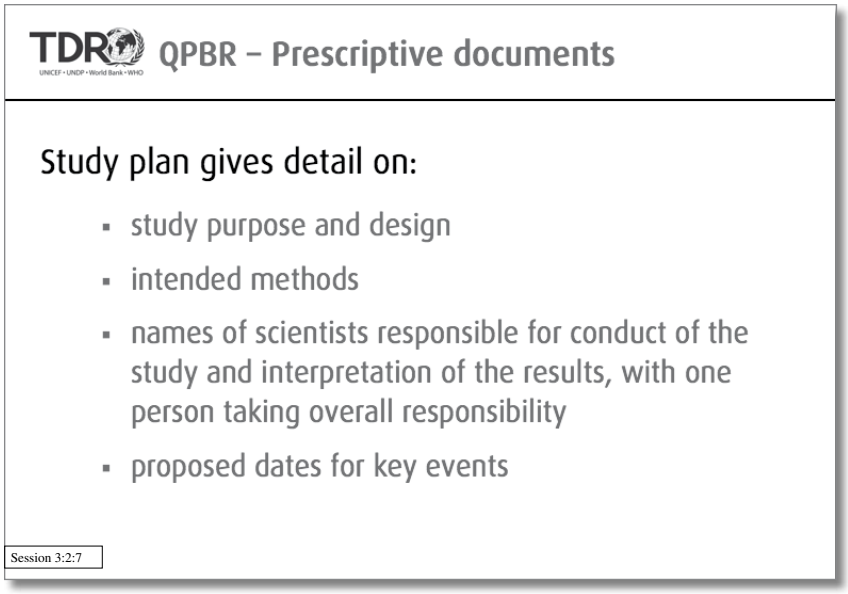
QPBR – Prescriptive documents

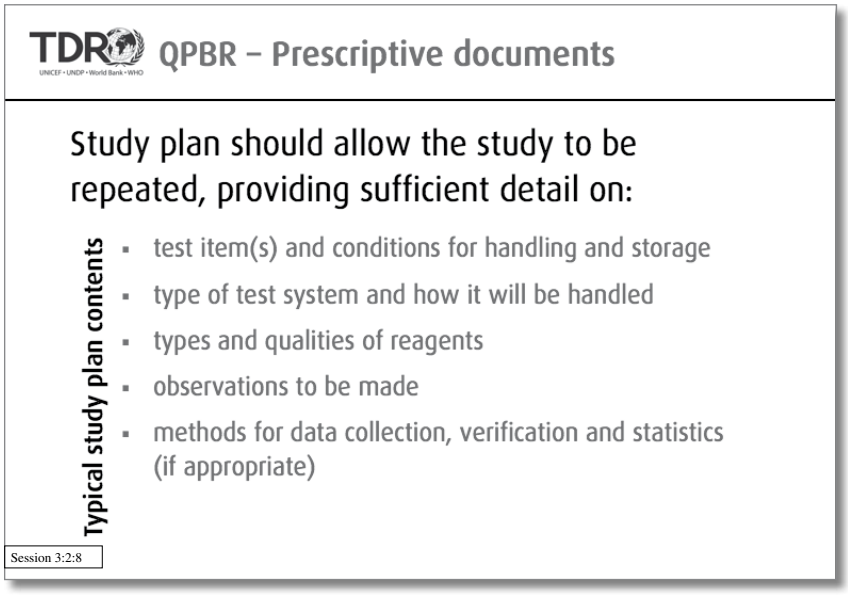


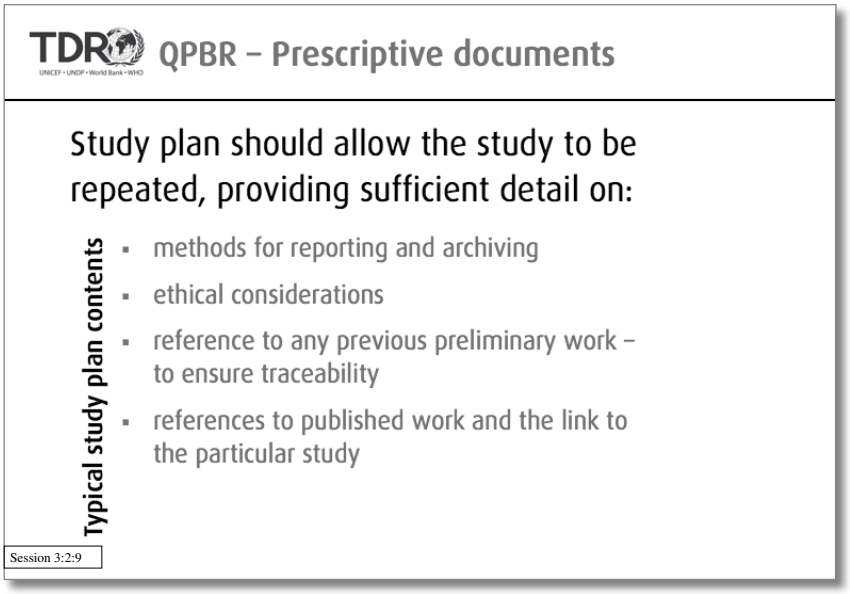
Relationship between research proposals and study plans

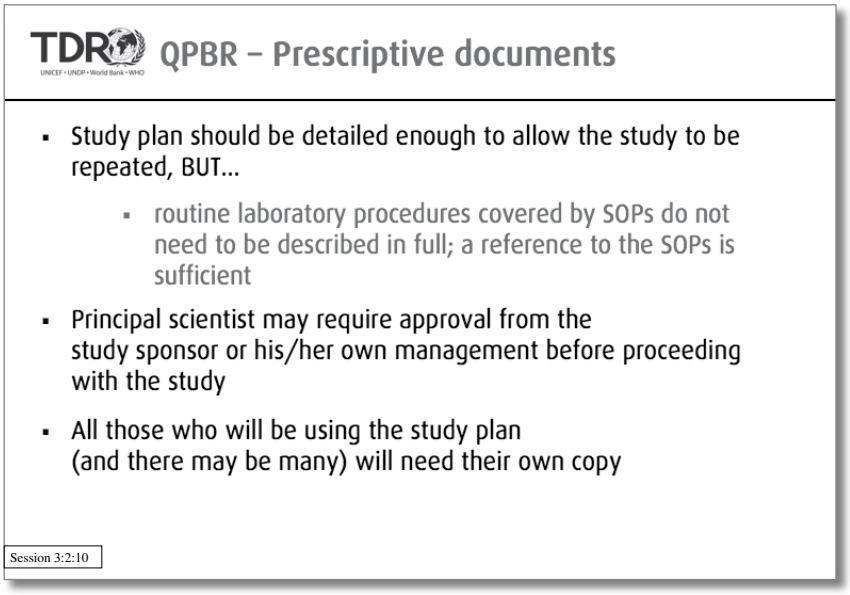
- A single research proposal may comprise several studies, each requiring a separate study plan
- Each study plan may be under the responsibility of a different scientist – possibly working in separate institutions

Session 3:2:6


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
Study plan gives detail on:
▪ study purpose and design
▪ intended methods
▪ names of scientists responsible for conduct of the study and interpretation of the results, with one person taking overall responsibility
▪ proposed dates for key events
Session 3:2:7


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
Study plan should allow the study to be repeated, providing sufficient detail on:
Typical study plan contents
▪ test item(s) and conditions for handling and storage
▪ type of test system and how it will be handled
▪ types and qualities of reagents
▪ observations to be made
▪ methods for data collection, verification and statistics (if appropriate)
Session 3:2:8


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
Study plan should allow the study to be repeated, providing sufficient detail on:
Typical study plan contents
▪ methods for reporting and archiving
▪ ethical considerations
▪ reference to any previous preliminary work – to ensure traceability
▪ references to published work and the link to the particular study
Session 3:2:9


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
▪ Study plan should be detailed enough to allow the study to be repeated, BUT...
▪ routine laboratory procedures covered by SOPs do not need to be described in full; a reference to the SOPs is sufficient
▪ Principal scientist may require approval from the study sponsor or his/her own management before proceeding with the study
▪ All those who will be using the study plan (and there may be many) will need their own copy
Session 3:2:10

QPBR – Prescriptive documents

Use a distribution check-list to ensure that all staff receive the study plan

Study plan distribution list	Date received	Signature
Principal scientist Sponsor Technician in charge Analytical laboratory Clinical pathology Necropsy Statistician Quality assurance		

Session 3:2:11

QPBR – Prescriptive documents

Study plan should be approved by the principal scientist

- Signature of the study plan signifies that the study will be performed in strict compliance with the plan and with QPBR
- Principal scientist assures that all staff are aware of the plan and associated SOPs

Session 3:2:12

QPBR – Prescriptive documents

Changes to the study plan

- Subsequent major, intended modifications to the study plan:
  - require study plan amendment – authorized and signed by the principal scientist
- Minor, unintended deviations are recorded either in the laboratory notebook or on deviation sheets drawn up for the purpose

Session 3:2:13

Keynote

Research proposal and study plan

- Research institution should:
  - define the difference between the research proposal and the study plan
  - have guidelines for the production, review and approval of research proposals
  - have guidelines for the production, review and approval of study plans
  - make it clear that the principal scientist's signature on a study plan indicates that he/she takes full responsibility for the conduct of the study according to the plan and to QPBR
  - should provide a format and a list of minimum contents for a study plan in accordance with QPBR recommendations
- Each individual study should be the subject of a single detailed study plan (one study = one study plan)

Session 3:2:14

QPBR – Prescriptive documents

SOPs:

- provide very detailed instructions for repetitive work – routine
- help to ensure that standard procedures are always performed in the same way, thus removing experimental bias and helping to reduce false negatives and false positives
- all research institutions already have SOPs in various forms – recipes for preparation of solutions, directions for operating equipment, step-by-step instructions for technical troubleshooting etc.

Session 3:2:15

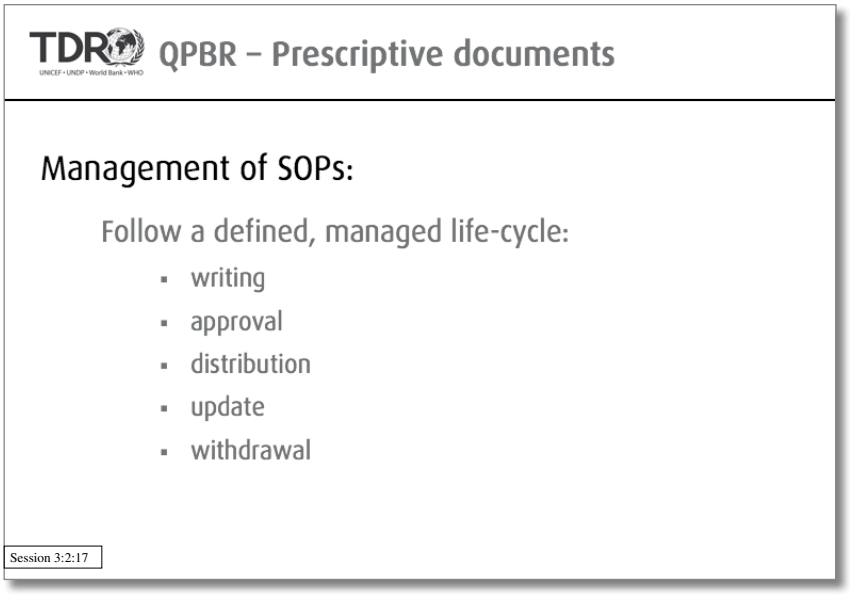
QPBR – Prescriptive documents

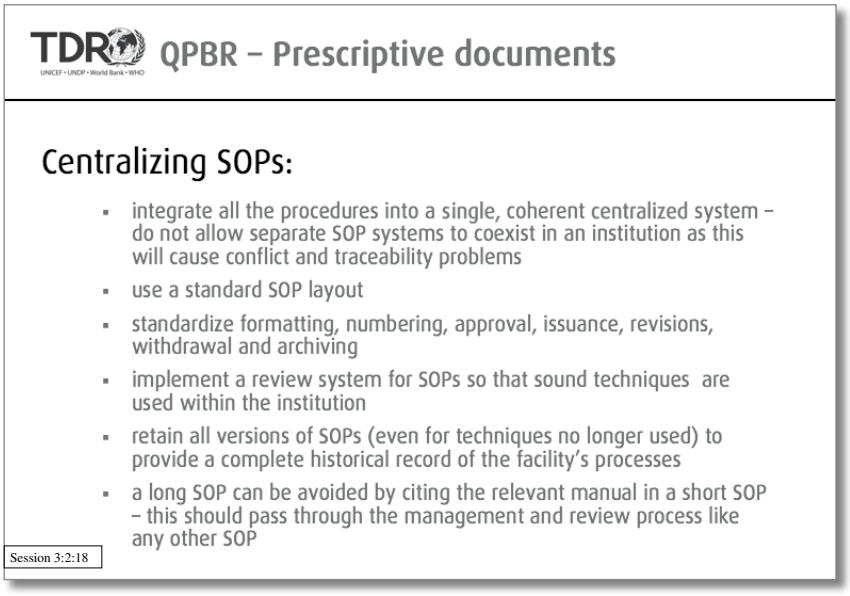
One-off or non-standard techniques do not require SOPs BUT must be documented

"Use Standards (i.e. SOPs) as the liberator that relegates the solved problems to the field of routine, leaving the creative faculties free for the problems that are still unsolved"

Quotation generally attributed to Dr Joseph M Juran, based on an idea of Dr W Edwards Deming (two quality gurus)

Session 3:2:16


QPBR – Prescriptive documents
Management of SOPs:
Follow a defined, managed life-cycle:
writing
approval
distribution
update
withdrawal
Session 3:2:17


QPBR – Prescriptive documents
Centralizing SOPs:
integrate all the procedures into a single, coherent centralized system – do not allow separate SOP systems to coexist in an institution as this will cause conflict and traceability problems
use a standard SOP layout
standardize formatting, numbering, approval, issuance, revisions, withdrawal and archiving
implement a review system for SOPs so that sound techniques are used within the institution
retain all versions of SOPs (even for techniques no longer used) to provide a complete historical record of the facility's processes
a long SOP can be avoided by citing the relevant manual in a short SOP – this should pass through the management and review process like any other SOP
Session 3:2:18

QPBR – Prescriptive documents

- SOP systems provide the greatest benefit if there is comprehensive coverage of:
  - standard scientific techniques
  - equipment, disposables and reagents
  - all critical stages of study design, management, conduct and reporting
  - scientific administrative policies and procedures (format, safety and hygiene, security, personnel management etc.)
- Ideally, the person most familiar with a technique should write the associated SOP – even if a senior person signs off the final approval
- Impose a minimum period for SOP review to avoid clogging up the system with waiting documents

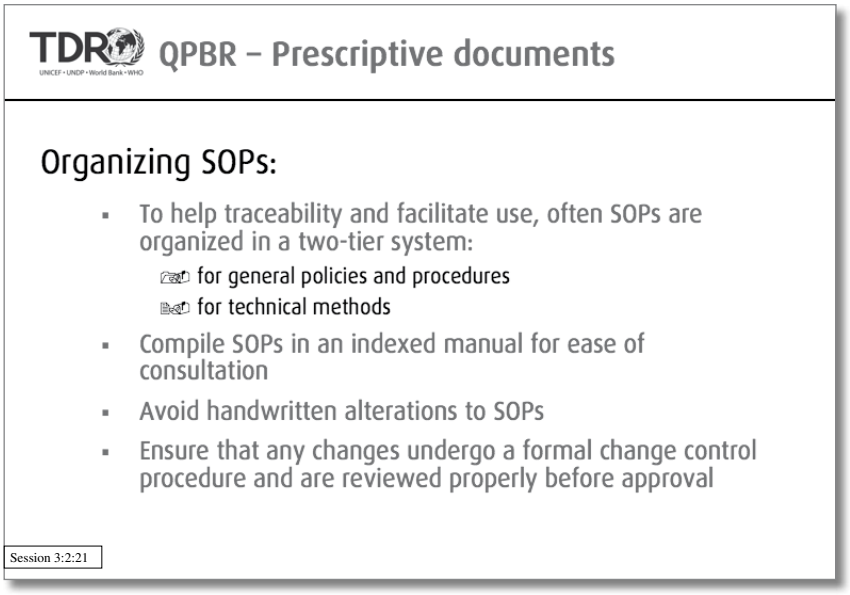
Session 3:2:19

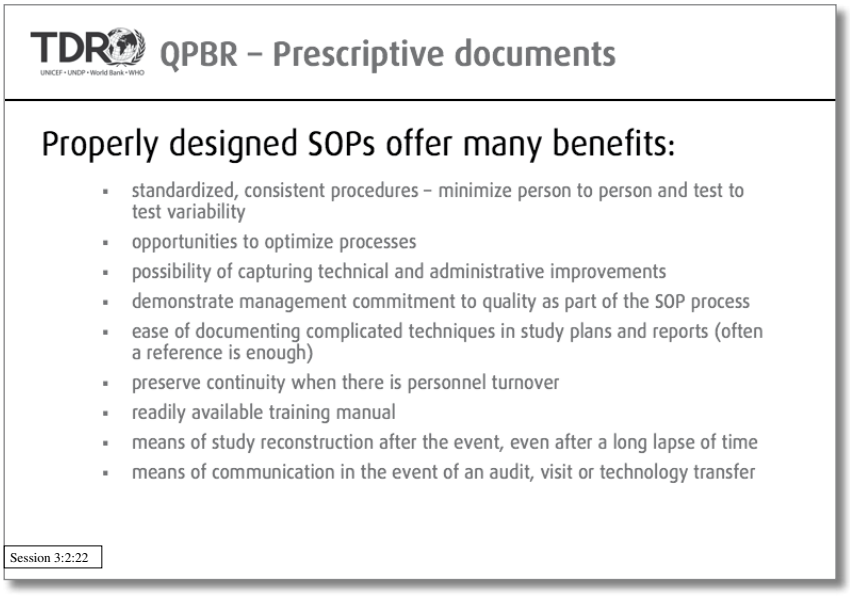
QPBR – Prescriptive documents

Use of SOPs:

- SOPs must be available immediately to staff when they need them
- Staff must fully understand the SOPs they use – this may involve specific training for any that are new or complex
- Staff must rigorously follow the SOPs they employ
- During study conduct, any deviation from the SOP must be documented – this may be the only way of explaining an unexpected result
- When documenting a deviation ensure that it is fully described, explained, signed and dated – the only way to preserve credibility

Session 3:2:20


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
Organizing SOPs:
To help traceability and facilitate use, often SOPs are organized in a two-tier system:
for general policies and procedures
for technical methods
Compile SOPs in an indexed manual for ease of consultation
Avoid handwritten alterations to SOPs
Ensure that any changes undergo a formal change control procedure and are reviewed properly before approval
Session 3:2:21


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Prescriptive documents
Properly designed SOPs offer many benefits:
standardized, consistent procedures – minimize person to person and test to test variability
opportunities to optimize processes
possibility of capturing technical and administrative improvements
demonstrate management commitment to quality as part of the SOP process
ease of documenting complicated techniques in study plans and reports (often a reference is enough)
preserve continuity when there is personnel turnover
readily available training manual
means of study reconstruction after the event, even after a long lapse of time
means of communication in the event of an audit, visit or technology transfer
Session 3:2:22

QPBR – Prescriptive documents

Successful implementation of SOPs requires:

- sustained support at all levels of management
- commitment to establishing SOPs as essential part of institution's culture
- SOP-based education and training so that all personnel perform the procedure in the same way
- effective SOP management system to ensure that SOPs are available in the right place

Session 3:2:23

Keynote

SOPs:

- Each research institution must establish appropriate SOPs covering the activities of the research institution and the study
- Content of SOPs should follow a standard format set by the research institution
- Institution must implement a system for the management of SOPs – to cover writing, signature, issuance, modification, withdrawal and archiving
- Institution provides and records SOP-based training

Session 3:2:24

Questions

- Why do you need to document your research activities?
- How would you know that time points had been kept/missed or that data are complete/missing?
- What is a template? What is the difference between a standard research proposal (an official form) and the content of a standard research proposal?
- What does a study plan contain? Contrast with a research proposal.
- Who takes overall scientific and organizational responsibility for the study plan and the conduct of the study?
- How do you deal with changes to the study plan?
- Give an example of what could constitute a study plan amendment and what would be classified as a study deviation. How would each of these be documented?
- How could you present instructions for detailed, repeated processes?
- Why is it important to have SOPs?
- Who should write standard operating procedures?
- What are the characteristics of a well-managed SOP management system?
- Can you give some examples of practical SOPs and administrative SOPs?
- Who approves the content and use of SOPs – and why?
- How do you deal with changes to SOPs?
- What is the difference between an SOP and an instruction left for a colleague?
- Would it be reasonable to write an SOP for a procedure that is a one-off in your laboratory? If not, how would you document this?
- Can a manual be used to guide (e.g. use of apparatus)? How would this knowledge be accessed some years after the event?

Workshops

1. Taking two or three everyday processes as examples (e.g. making coffee, cleaning a bathroom, preparing a dinner party) make an outline for an SOP. Who would use these? Present the outline on the flip chart.

2. You are an expert in a technique which is a standard practice in your research institute. You are asked to write an SOP that will become the standard used by all the technical personnel who perform this technique.

   Choose your domain of expertise and write an SOP (in summary form) for one particular standard procedure for the technique in question. You are not expected to write the SOP in detail but should provide an outline of the sections you would include and the contents of each section. An annotated table, organized set of bullet points or a detailed flow chart would be effective responses.

   You may wish to look at the SOP template in QPBR for guidance on the format.

3. A non-controlled photocopy of an SOP was found pinned to the wall near the machine for which the SOP had been written. What are the possible unfortunate consequences?

4. Sometimes it is claimed that the use of a study plan or the use of SOPs limits the creative imagination and weakens the research process. Do you agree? What are the arguments for or against this view?

5. For very short assays or tests it may be difficult to decide whether to use SOPs or study plans. Give examples and outline solutions. Discuss how to manage a one-off instruction.

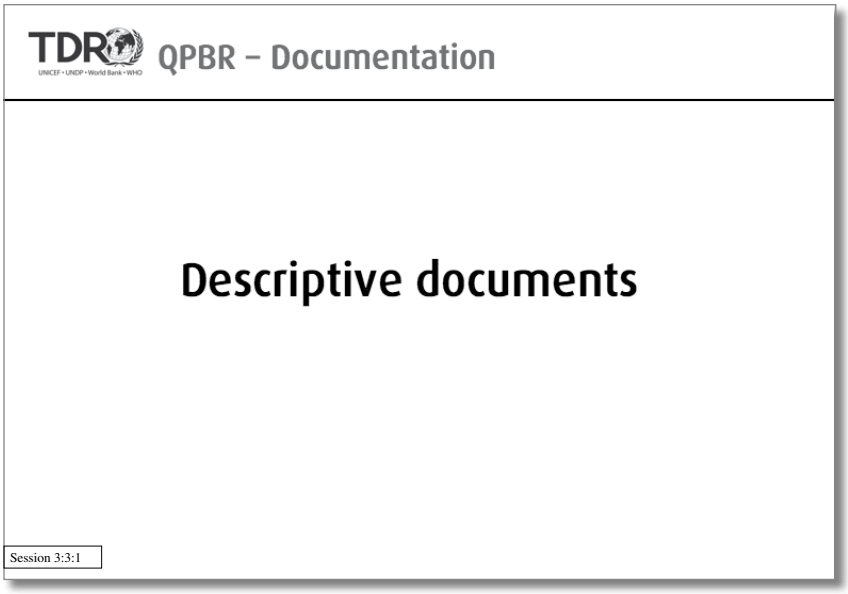
6. Go through the SOP template and discuss the sections (including header and footer). Use the flip chart to tabulate the sections and the purpose of each. If you were to implement SOPs at your workplace would you add more sections, leave out sections or do something else entirely? For example, some organizations like to sign each page, some use electronic signatures, some keep to one page and some include a section on safety. Argue for your choice.

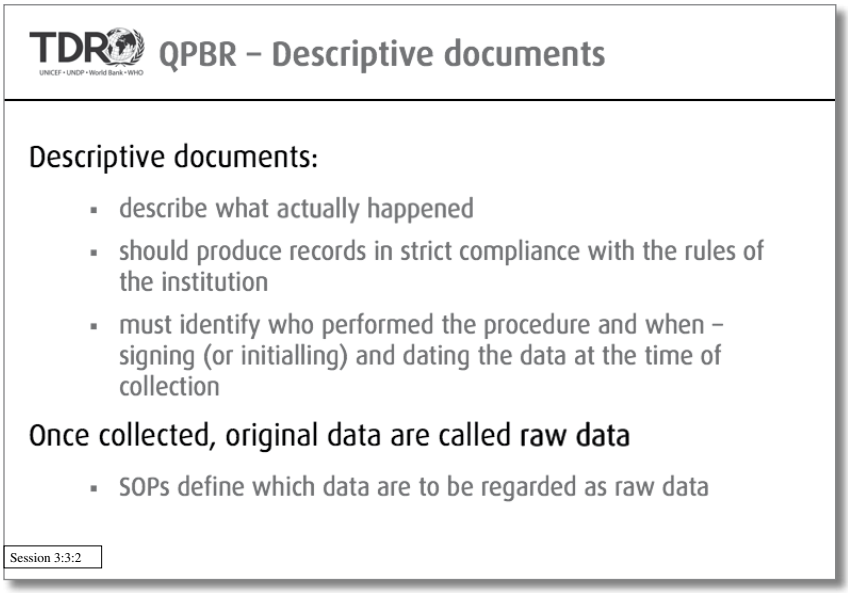
3.3 DESCRIPTIVE DOCUMENTATION – RAW DATA AND RECORDS

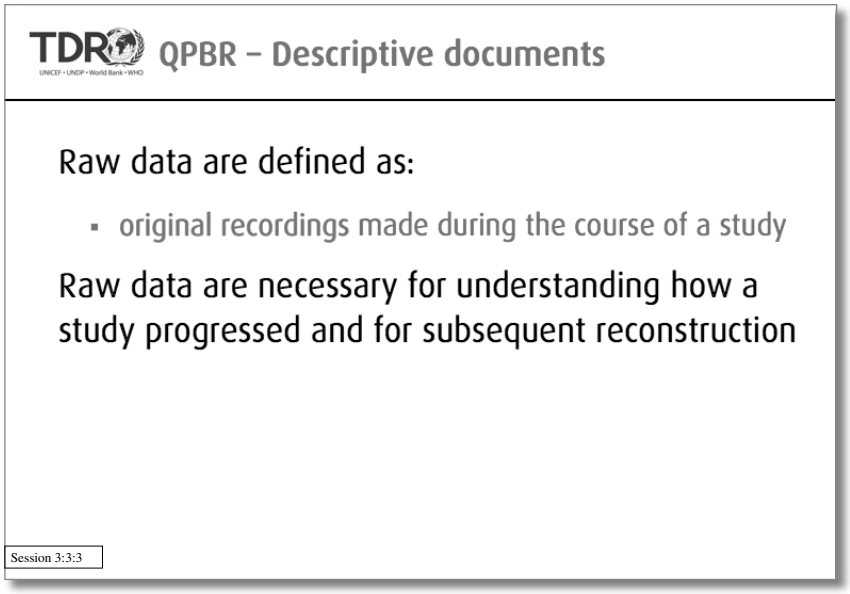
Goals

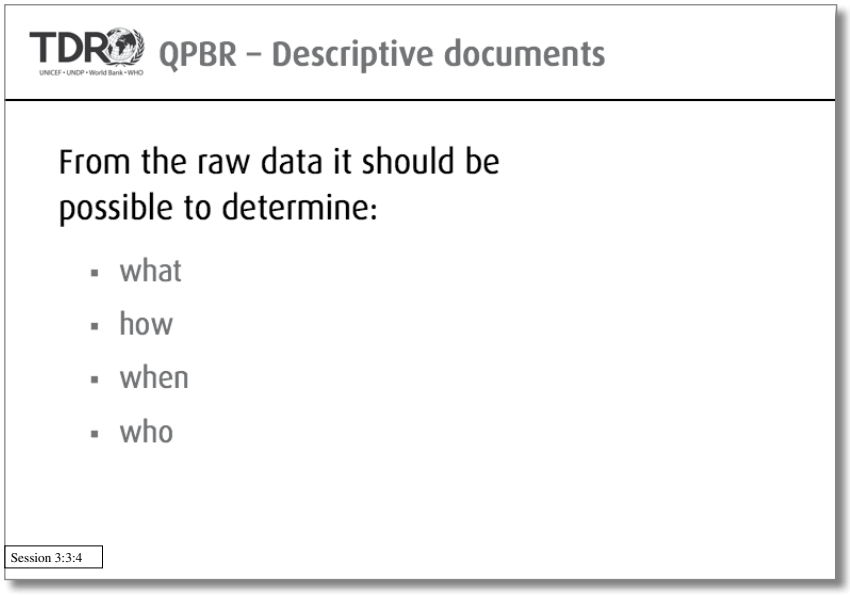
At the end of the session, you should be able to:

- define descriptive documentation and its relationship to the practical activities;
- name the different layers of descriptive documentation and describe their interrelationships;
- describe what is meant by raw data and provide examples of raw data and derived data in a study from your everyday experience;
- explain what is meant by authenticity;
- assess the advantages and disadvantages of any given data collection method;
- outline the advantages and disadvantages of using computers to collect data;
- discuss how to organize contributions from several scientists;
- describe the contents of study records and their interrelationships.


QPBR – Documentation
Descriptive documents
Session 3:3:1


QPBR – Descriptive documents
Descriptive documents:
describe what actually happened
should produce records in strict compliance with the rules of the institution
must identify who performed the procedure and when – signing (or initialling) and dating the data at the time of collection
Once collected, original data are called raw data
SOPs define which data are to be regarded as raw data
Session 3:3:2


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Descriptive documents
Raw data are defined as:
▪ original recordings made during the course of a study
Raw data are necessary for understanding how a study progressed and for subsequent reconstruction
Session 3:3:3


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Descriptive documents
From the raw data it should be possible to determine:
▪ what
▪ how
▪ when
▪ who
Session 3:3:4

QPBR – Descriptive documents

From the raw data it should be possible to determine:

- what was done – demonstrating compliance with the study plan

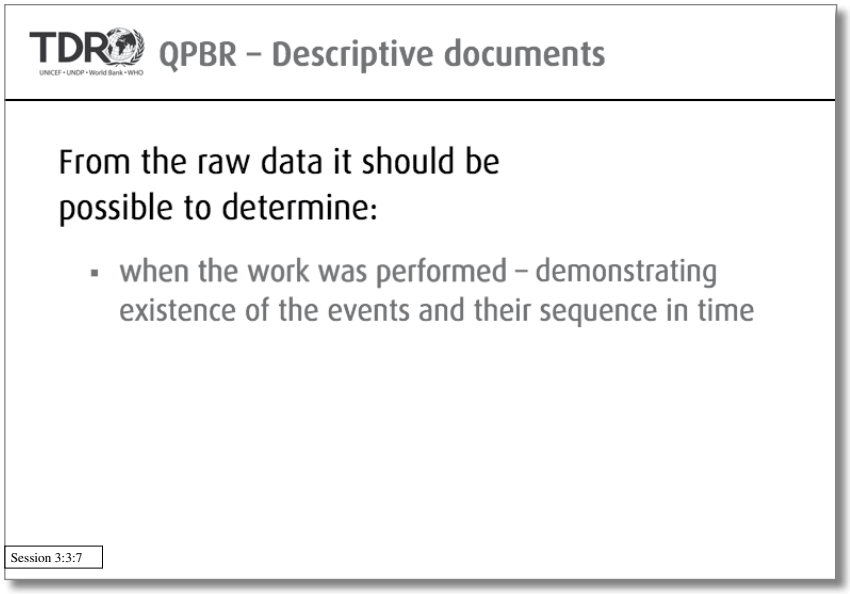
Session 3:3:5

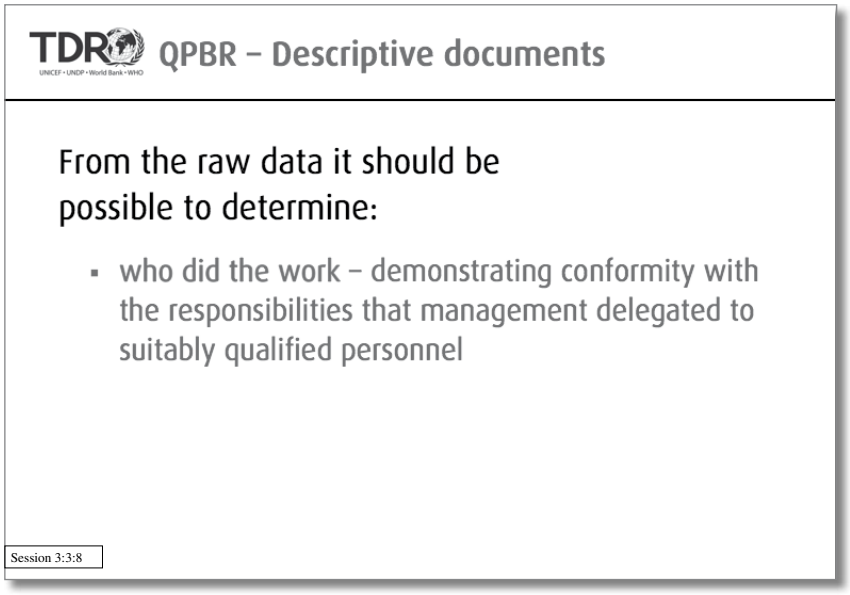
QPBR – Descriptive documents

From the raw data it should be possible to determine:

- how it was done – demonstrating practical compliance with instructions in the study plan and detailed SOPs

Session 3:3:6


QPBR – Descriptive documents
From the raw data it should be possible to determine:
when the work was performed – demonstrating existence of the events and their sequence in time
Session 3:3:7


QPBR – Descriptive documents
From the raw data it should be possible to determine:
who did the work – demonstrating conformity with the responsibilities that management delegated to suitably qualified personnel
Session 3:3:8

QPBR – Descriptive documents

Characteristics of the collection of good raw data

- Attributability – data can be traced to their source e.g. by study number, sample number, parameter etc:
  - unique identification of data relating to an individual study helps to prevent mix ups
- Originality – raw data constitute the first record of the observation:
  - data should not be collected on scraps of paper and then transcribed in their final form
  - when a computer is used to collect data it is necessary to define whether the signed printout or the electronic recording is the raw data
  - if electronic data are designated as raw data, the computer must be protected by password and backed-up regularly

Session 3:3:9

QPBR – Descriptive documents

Attributability and originality are assured by recording data:

- promptly – record immediately the observation is made, not some time after finishing, as memory is notoriously defective
- accurately – raw data must be a true record of the observation; this is central to the integrity of the study
- legibly – data that cannot be read are useless; records that are difficult to decipher raise doubts about their credibility
- indelibly – do not use media that can be altered without leaving trace (pencil)
  - any changes should be made in a way that does not obscure the original
  - all changes should be explained; person responsible for making the change should sign and date it

Session 3:3:10

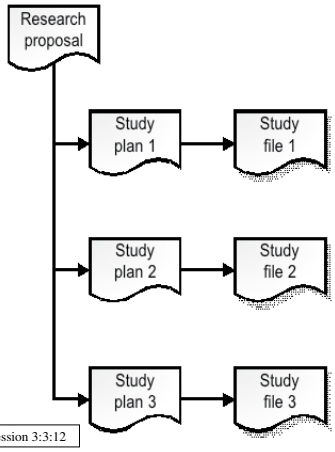
QPBR – Descriptive documents

Compilation of data

- Data should be recorded and organized to facilitate subsequent processes:
  - data processing and statistical analysis
  - interpretation
  - reporting
  - auditing
  - archiving
- Raw data for the study include:
  - handwritten observations
  - electronic data and printouts
  - analytical traces
- Total study records include:
  - raw data
  - data analyses and statistics
  - notes made during the study

Session 3:3:11

QPBR – Documentation



- All the study records, the study plan and amendments and (later) the study report should be compiled in the **STUDY FILE**
- Study file, complete with all relevant documents, is archived as the study progresses (for long-term trials) or at the end of the study

Session 3:3:12

QPBR – Keynote

Good record keeping

- Each research institution must implement rules for the recording of raw data
- Raw data and other records should be sufficiently detailed and complete to ensure study traceability and reconstruction
- If computers are used to acquire, modify, manipulate or archive raw data, the raw data must be clearly defined

Session 3:3:13

QPBR – Descriptive documents

Notebooks

- Some organizations require notebooks to be used during studies, particularly during the very early stages of discovery
- Notebooks are usually numbered sequentially – sometimes by the laboratory's own organization, sometimes by an outside authority
- Notebooks can offer advantages for research that is a continuous process (small daily additions):
  - everything is in the same place, nothing gets lost
  - notebook is always at hand and is practical in the field
  - each person is responsible for his/her own notebook
  - consecutive numbering of notebooks is easy
  - in some countries patent laws require the use of paginated notebooks

Session 3:3:14

QPBR – Descriptive documents

Notebooks

- Disadvantages
  - Planning (prescriptive) and records (descriptive) are intermingled and it is difficult to see any amendments to a study plan
  - Sometimes one notebook contains data from different studies or technicians use their own notebooks when working on the same study. This complicates data compilation at the end of a study and makes it very difficult to be certain that all the study data have been reported
  - Notebooks do not contain everything. Data are also captured on other media (e.g. assay printouts, gels, slides) but this may not be clear from the notebook
  - When different notebooks are also used to record the status of laboratory equipment, it is difficult to follow the life-cycle of each apparatus

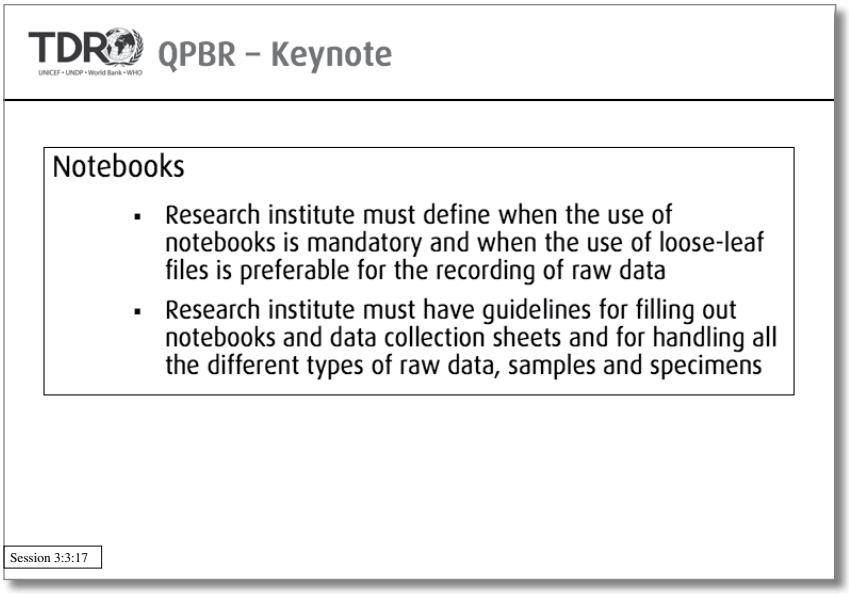
Session 3:3:15

QPBR – Descriptive documents

Use notebooks with caution:

- ideally use a separate notebook for each study
- number all notebooks and pages consecutively before they are circulated
- keep first page clear for compiling an index when the book is full
- ensure that plans (prescriptive parts) are easily distinguished from records (descriptive parts)
- make clear when the line of enquiry is finished and you are ready to report
- reference any related activity and locations of data and specimens
- sign and date each day's work and make corrections following the rules of the institution – never tear out pages
- principal scientist should review and countersign the work promptly
- store notebooks safely when not in use
- notebooks and pages accessed must be referenced exactly in the report

Session 3:3:16


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Keynote
Notebooks
Research institute must define when the use of notebooks is mandatory and when the use of loose-leaf files is preferable for the recording of raw data
Research institute must have guidelines for filling out notebooks and data collection sheets and for handling all the different types of raw data, samples and specimens
Session 3:3:17

Questions

- Why do you need to document your research activities?
- What aspects of the research process do the data support?
- What is meant by raw data?
- Are there other types of data?
- What are the minimum identifiers of authentic raw data?
- Why is it important to collect data promptly? What else characterizes good raw data capture?
- What are the advantages/disadvantages of using loose, pre-printed data sheets?
- What are the advantages/disadvantages of using notebooks?
- What would you do if you realized that the raw data were incorrect?
- What is meant by study file? What is the minimum content of a study file?
- How do study reports relate to raw data?
- Do you use computers to capture data?
- Do you store raw data on the computer? Are there any special precautions to observe, given that a study loses validity if data are lost?
- What other raw data might be necessary (other than raw data pertaining to the study?)

Workshops

1. Taking one of your own studies as an example, make a list of the raw data parameters you collected and the format in which they were collected (i.e. data sheet, notebook, computer, machine output). Use a flow chart to follow the route of each parameter to the report (i.e. conversions, computer processing, statistics).

2. Design a raw data form for the collection of blood samples that are to be sent to a bioanalytical laboratory for analysis.

3. Do you perform the experiments with other people? If so, how is data collection organized? How can the scientists understand each other's contribution and how is data checking performed? In your discussion group compare your ways of organizing this process. Present verbally.

4. How does your organization check the authenticity of data? How does it check accuracy? Make a list of activities on the flip chart.

5. What would you do if you realized the data were incorrect – at the moment of collection? A day later? One month later? After the report is issued? After publication? Use the flip chart to tabulate these time points and the sort of action you consider appropriate.

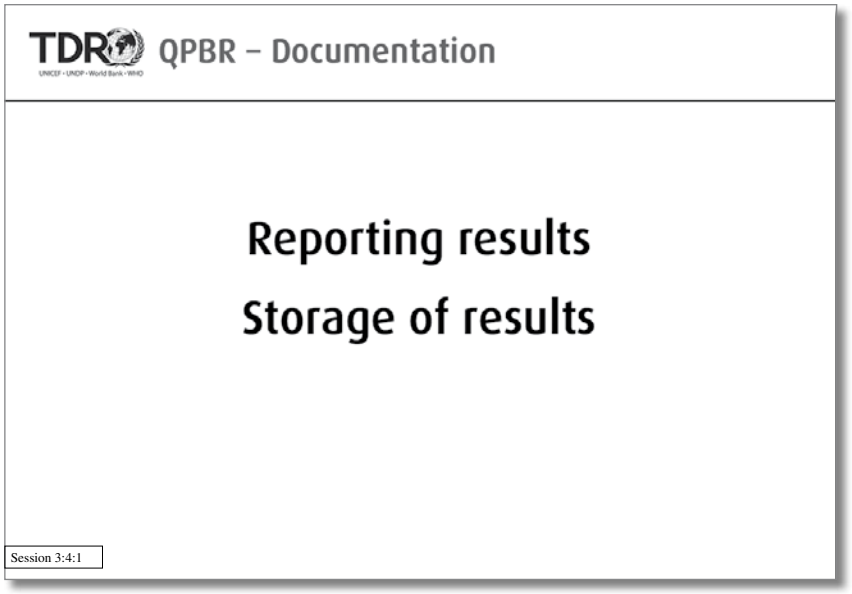
6. Taking one of your own studies as an example, list the contents of the study records (= study file) and present on the flip chart. Divide the documents into prescriptive and descriptive.

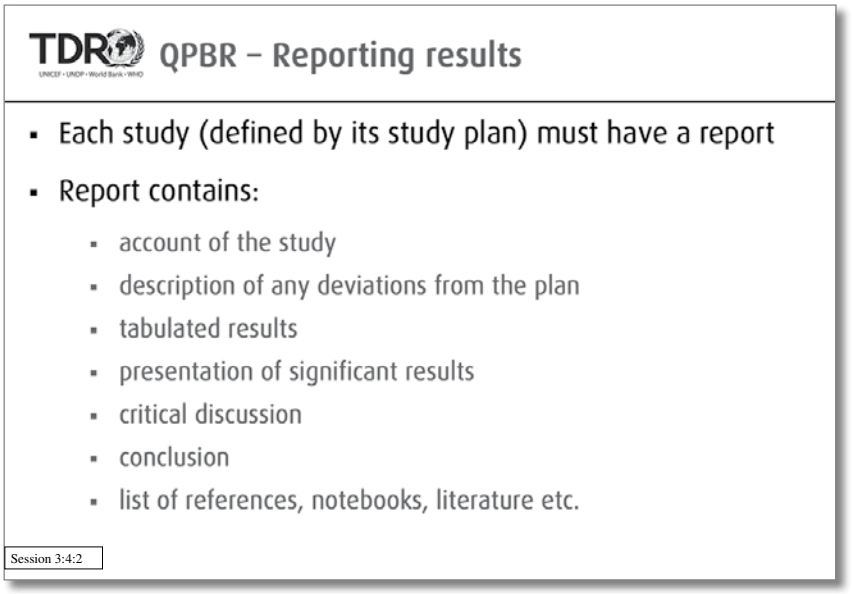
3.4 DOCUMENTATION – REPORTS AND STORAGE

Goals

At the end of the session, you should be able to:

- explain why it is important to protect study documentation during the whole course of the study and after the report is complete;
- categorize reports into prescriptive and descriptive documents;
- explain the relationship between individual study reports, articles in the literature and the global account of an entire research project;
- describe in general terms what comprises a study report;
- specify the individual responsibilities of those who author, review, edit and approve a study report;
- explain management's role in generation and issue of reports;
- argue for the necessity of allocating human and physical resources to archiving activities;
- distinguish between archiving and storage in a locked/ fireproof cabinet;
- explain management's role in ensuring the integrity of study documentation.


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Documentation
Reporting results
Storage of results
Session 3:4:1

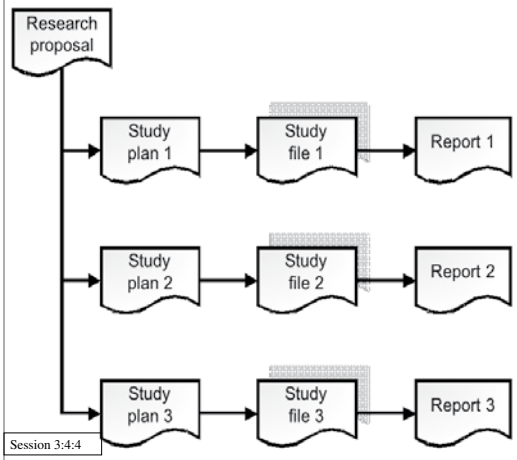

TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Reporting results
Each study (defined by its study plan) must have a report
Report contains:
account of the study
description of any deviations from the plan
tabulated results
presentation of significant results
critical discussion
conclusion
list of references, notebooks, literature etc.
Session 3:4:2

QPBR – Reporting results

- When there are contributions from several colleagues:
  - each of the scientists retains responsibility for the veracity and quality of their own contribution
  - principal scientist takes responsibility for the overall scientific content of the report and interpretation of the results as a whole
- Writing the report:
  - do so as soon as the practical work is complete – while the study is fresh in the mind
  - evaluate all the results
  - do not omit results without providing an argued justification in the report

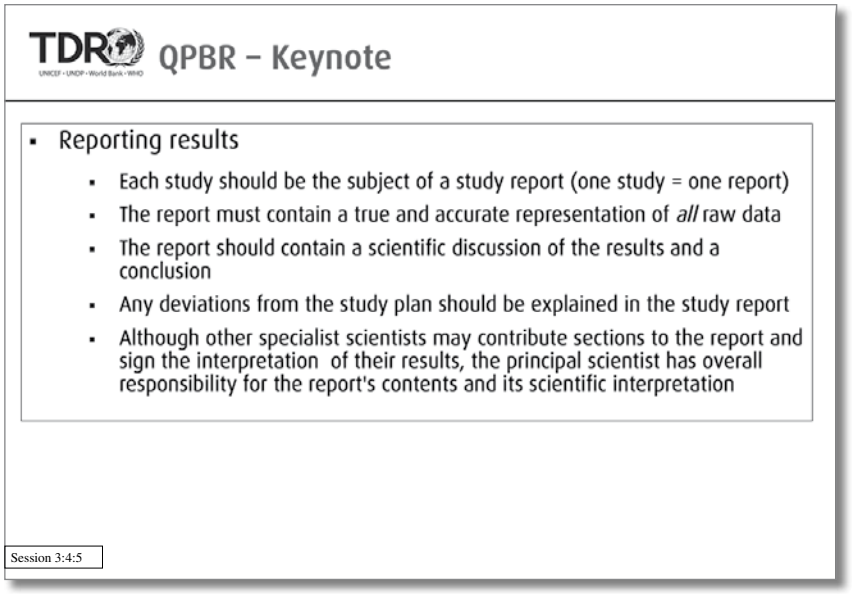
Session 3:4:3

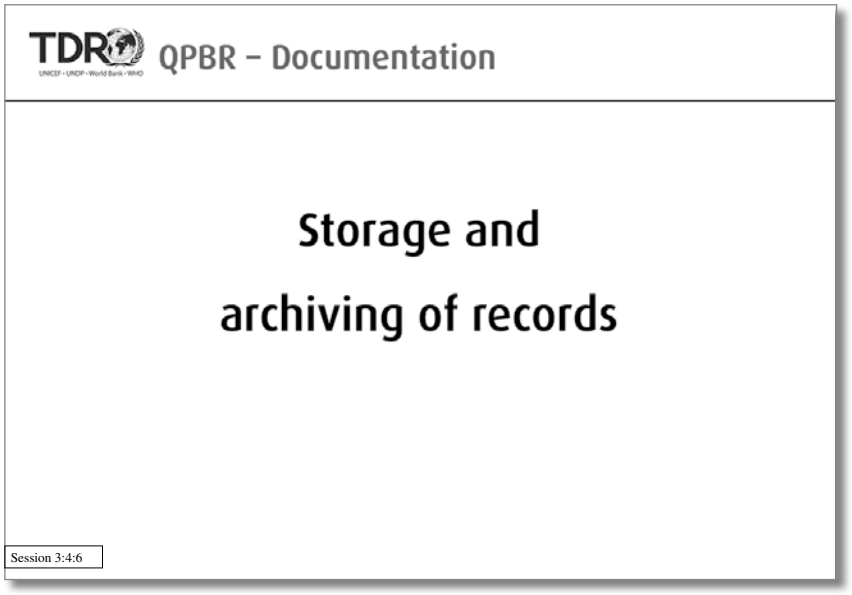
QPBR – Documentation

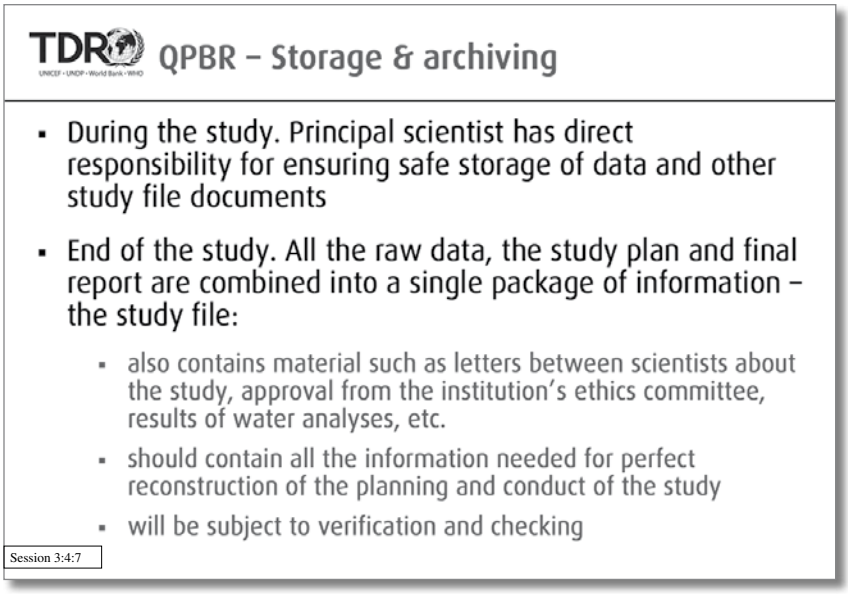


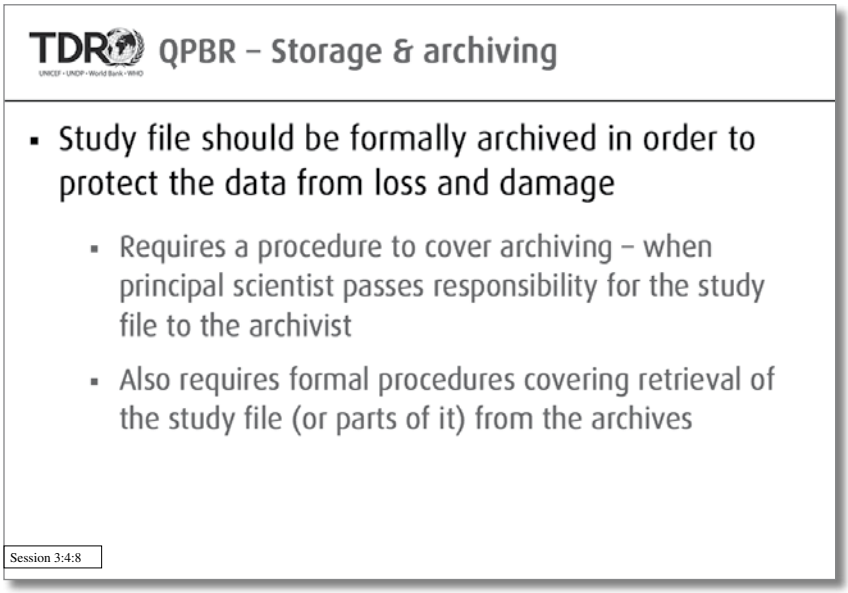
- Each study has a single study plan and a single report
- A research proposal may require many individual study reports

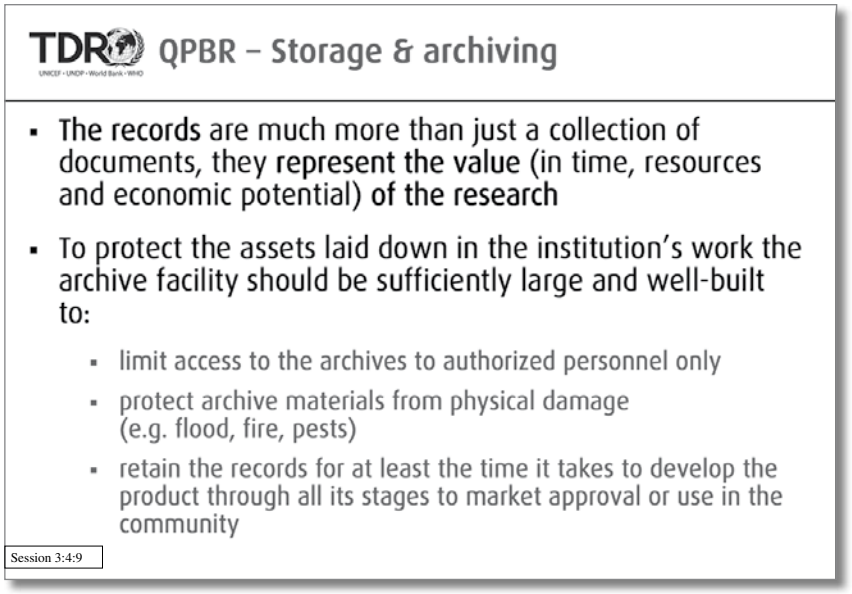
Session 3:4:4

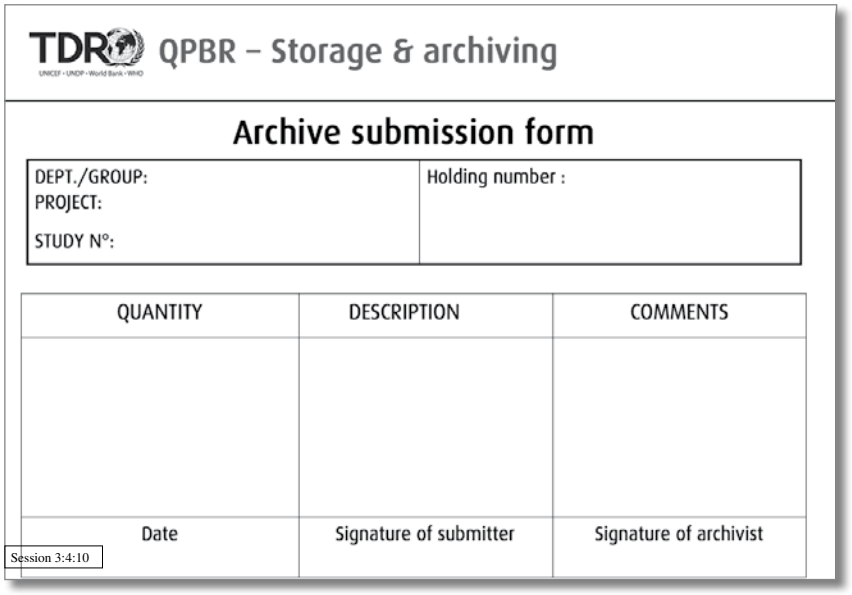

TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Keynote
Reporting results
Each study should be the subject of a study report (one study = one report)
The report must contain a true and accurate representation of *all* raw data
The report should contain a scientific discussion of the results and a conclusion
Any deviations from the study plan should be explained in the study report
Although other specialist scientists may contribute sections to the report and sign the interpretation of their results, the principal scientist has overall responsibility for the report's contents and its scientific interpretation
Session 3:4:5

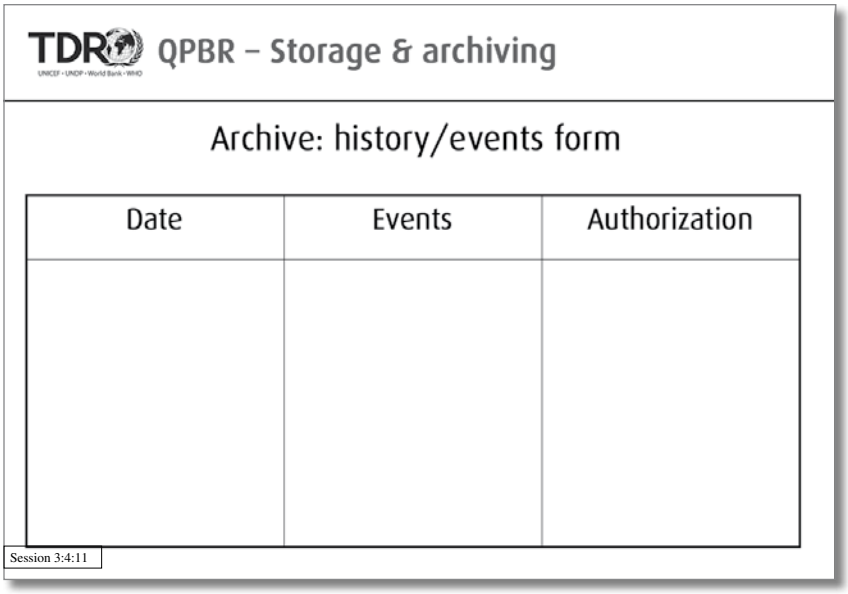

TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Documentation
Storage and
archiving of records
Session 3:4:6

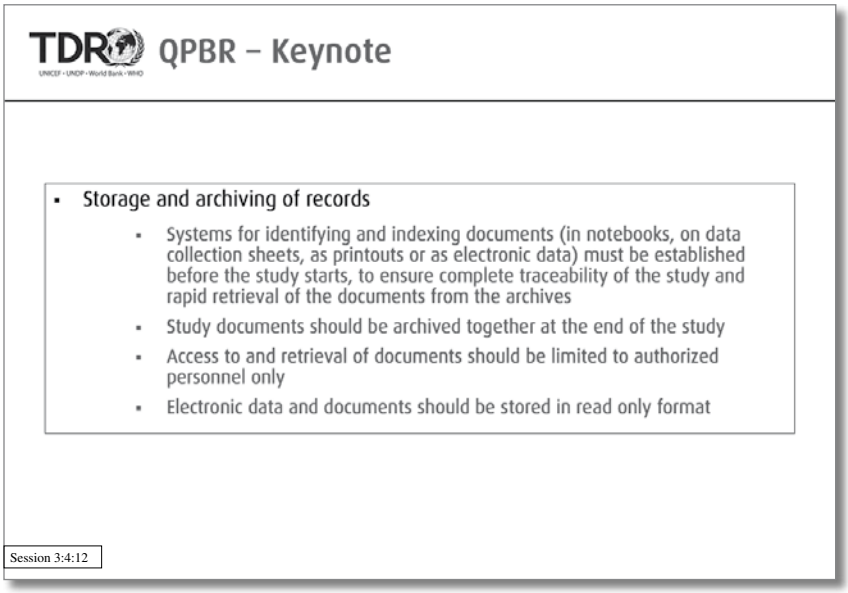

QPBR – Storage & archiving
During the study. Principal scientist has direct responsibility for ensuring safe storage of data and other study file documents
End of the study. All the raw data, the study plan and final report are combined into a single package of information – the study file:
also contains material such as letters between scientists about the study, approval from the institution's ethics committee, results of water analyses, etc.
should contain all the information needed for perfect reconstruction of the planning and conduct of the study
will be subject to verification and checking
Session 3:4:7

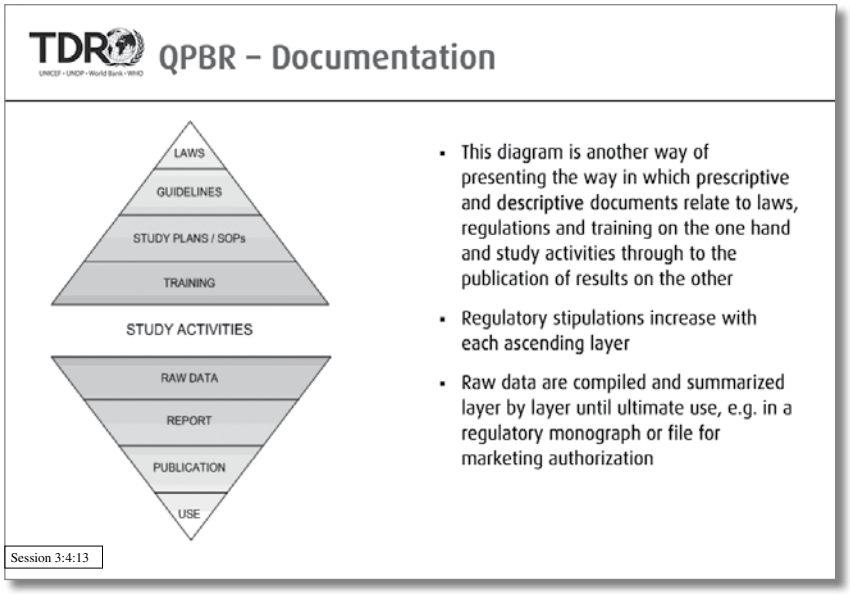

QPBR – Storage & archiving
Study file should be formally archived in order to protect the data from loss and damage
Requires a procedure to cover archiving – when principal scientist passes responsibility for the study file to the archivist
Also requires formal procedures covering retrieval of the study file (or parts of it) from the archives
Session 3:4:8


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Storage & archiving
The records are much more than just a collection of documents, they represent the value (in time, resources and economic potential) of the research
To protect the assets laid down in the institution's work the archive facility should be sufficiently large and well-built to:
limit access to the archives to authorized personnel only
protect archive materials from physical damage (e.g. flood, fire, pests)
retain the records for at least the time it takes to develop the product through all its stages to market approval or use in the community
Session 3:4:9


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Storage & archiving
Archive submission form
DEPT./GROUP:
PROJECT:
STUDY N°:
Holding number :
QUANTITY
DESCRIPTION
COMMENTS
Date
Signature of submitter
Signature of archivist
Session 3:4:10


QPBR – Storage & archiving
Archive: history/events form
Date
Events
Authorization
Session 3:4:11


QPBR – Keynote
Storage and archiving of records
Systems for identifying and indexing documents (in notebooks, on data collection sheets, as printouts or as electronic data) must be established before the study starts, to ensure complete traceability of the study and rapid retrieval of the documents from the archives
Study documents should be archived together at the end of the study
Access to and retrieval of documents should be limited to authorized personnel only
Electronic data and documents should be stored in read only format
Session 3:4:12



Questions

- Why is it necessary to have a procedure for protecting study documentation?
- Where should study materials (data, samples, specimens etc.) be stored during the practical activities; during writing/editing of the report; after the report has been issued?
- What is management's role in the generation and management of study documentation?
- How soon after completion of the practical activities should the report be written?
- How do study reports relate to the protocol?
- How do study reports relate to raw data?
- What are the main sections of the study report?
- Who should review the report before approval and issue?
- What does the reviewer's activity actually mean in terms of what they have reviewed or checked? What does their signature signify?
- Who is responsible for the completeness of the study file?

- What are the characteristics of a well-managed archive system? How are these different from the characteristics of the fireproof cabinet?
- What sort of documentation should an archivist keep to show that the archive is properly managed?
- Besides study documentation, what other documentation might an archive contain?
- How does your facility approach the need for archiving electronic data?
- For how long should study documentation be kept? What about specimens, samples, test item(s)?
- Should it be possible to remove materials from the archive?

Workshops

1. Describe the ideal writing, review, editing and approval process for scientific reports produced in an imaginary research facility. Use the flip chart to tabulate authors and reviewers according to job title, activity, responsibility, meaning of signature.

2. Design a form for transferring materials to the archive.

3. Draw up a flow chart to describe the handover of documentation and material from the laboratory to the archive, showing when (during/after the study) this would be done.

4. List the SOPs necessary to ensure effective management of the archive.

5. List the records required to document that the archive is kept under control during the whole lifetime of the stored documents.

6. How is it possible to prevent the archive from becoming a repository for unwanted materials? Discuss how to keep the archive functional and how to remove obsolete materials. Tabulate the persons who would give permission for removal/destruction of material in the archive.

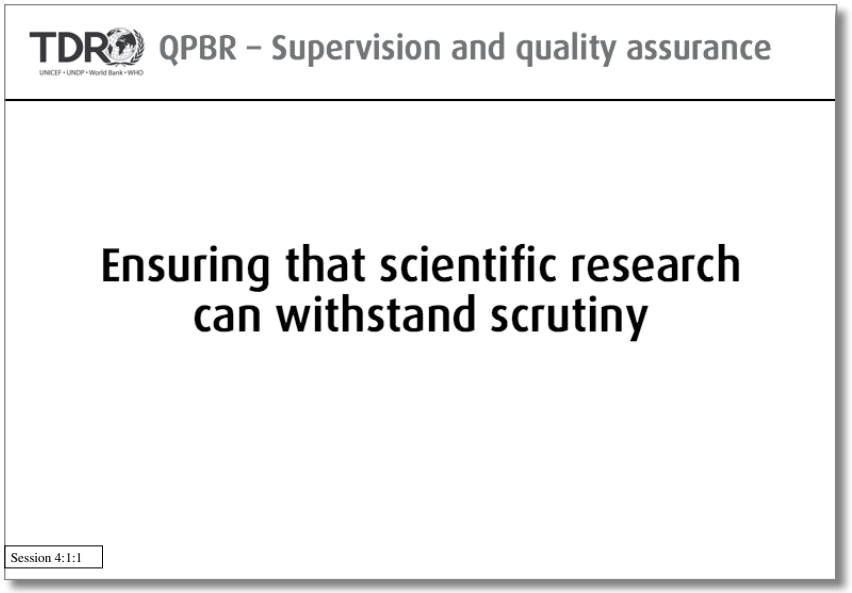
SESSION 4

4.1 SUPERVISION AND QUALITY ASSURANCE

Goals

At the end of the session, you should be able to:

- argue for the contribution that different supervisory and review roles bring to the quality of the research activities and results;
- explain the necessity for formalizing both scientific and process (QA) review;
- explain the relationship between the documentation in section 3 (CVs, training records) and supervision/QA;
- make a plan for a model review;
- suggest improvements in supervision at your own institution (if necessary);
- read the scientific literature and analyse the reports of scientific studies in terms of science and process.



QPBR – Supervision and quality assurance

An earlier slide listed the quality attributes of scientific data:

- relevant
- reliable
- reproducible
- ethical
- auditable
- in the public domain

This means that:

- the scientific content fits the research proposal and the design and conduct are likely to produce a result that can be believed and built on
- independent staff can verify the generation and existence of the results

Session 4:1:2

QPBR – Supervision and quality assurance

It is already common practice for scientists to review one another's work before publication

- A supervisor usually helps a researcher to formulate the study hypothesis and practical plan of action. But here there is a difference of rank. It is not clear who would routinely review a senior researcher's hypothesis and plan of action
- A researcher may ask a colleague to review a report or paper for publication. This might function well. However, the colleague may not have the time to do this thoroughly; may not be rewarded for it; may not know how to do it; or may be too polite to make a stringent review
- It is certainly very unusual to challenge the results of a study by checking back to raw data or (for example) apparatus logs

Session 4:1:3

QPBR – Supervision and quality assurance

In order to bring supervision into the realm of routine activity, management's quality policy must include provision for:

- review of staff qualifications
- institution's procedures for scientific review
- organization and procedures for technical review
- technical (QA) review

Session 4:1:4

QPBR – Supervision and quality assurance

- It is important that policy and provisions for review are formulated to make it clear that this is a routine and non-threatening activity
- It must be clear that all the scientific staff contributes to review activities
- And that all scientific activities are subject to review
- Scientific review is so important that the peer reviewer should sign for his/her activity

Session 4:1:5

QPBR – Supervision and quality assurance

- Clearly, staff must be qualified to do their job well in order to take primary responsibility for the quality and reliability of their own data
- Staff must be qualified enough to contribute to the review activities
- The CV and the training record provide documentary evidence of the suitability of staff qualifications
- Management must implement a procedure for checking staff qualifications and training

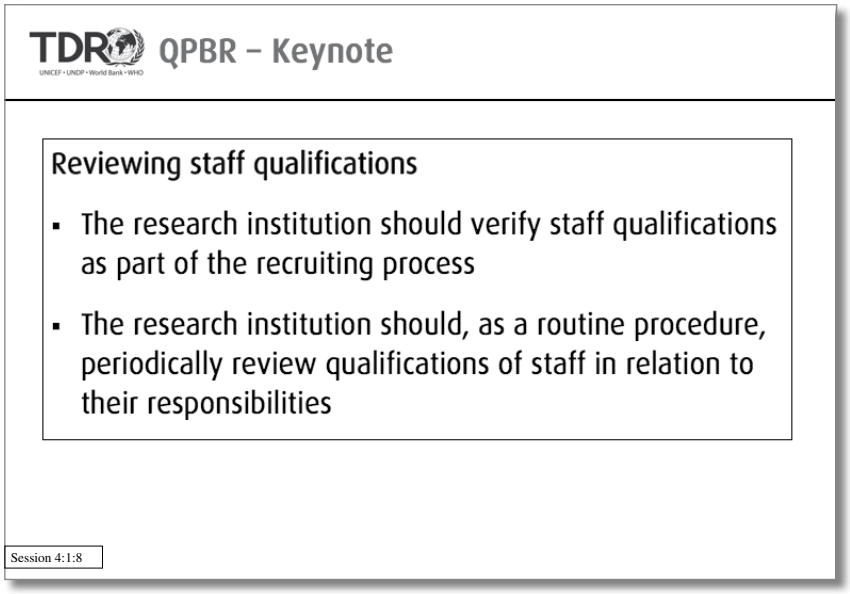
Session 4:1:6

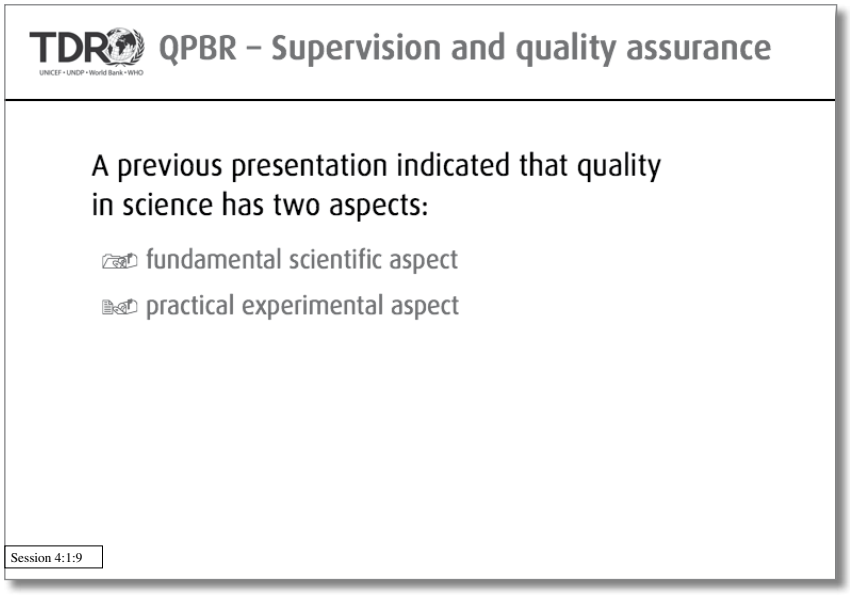
QPBR – Supervision and quality assurance

At the moment of recruitment, management need not be afraid of verifying CV information by:

- verifying the existence of previous workplaces or educational institutions
- checking publications
- contacting referees

Session 4:1:7


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Keynote
Reviewing staff qualifications
▪ The research institution should verify staff qualifications as part of the recruiting process
▪ The research institution should, as a routine procedure, periodically review qualifications of staff in relation to their responsibilities
Session 4:1:8


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Supervision and quality assurance
A previous presentation indicated that quality in science has two aspects:
fundamental scientific aspect
practical experimental aspect
Session 4:1:9

QPBR – Supervision and quality assurance

- When the underlying science is wrong even well-organized studies do not yield worthwhile results
- If studies are not conducted flawlessly (high-quality experimentation) the results obtained are suspect and will not lead to an advance in knowledge

Session 4:1:10

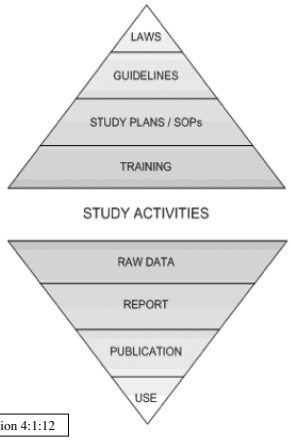
QPBR – Supervision and quality assurance

- The flawless conduct of the studies (the experimental work) can be subject to QA review
  - Undertaken by QA staff or an external auditor, this review would cover:

  - comparison of study plan and raw data from the study
  - comparison between ongoing activities and the study plan and SOPs
  - presentation of raw data in the final report
  - procedures for generating, capturing, processing, storing and retrieving data
  - physical framework for the study

Session 4:1:11

QPBR – Supervision and quality assurance



- During review, both the scientific and the technical reviewers are aware of the layered nature of the documents they deal with
- Much review compares information in different layers of both prescriptive and descriptive documentation
- This assures management that:
  - study activities are on course
  - raw data are compiled and summarized layer by layer until ultimate use (e.g. in a regulatory monograph or file for marketing authorization)

Session 4:1:12

QPBR – Supervision and quality assurance

Does the scientific review overlap the QA review?

- Not in principle
- In practice, scientific and QA reviewers sometimes examine the same aspects of a study... and disagree
- In such cases the findings may be discussed constructively

Session 4:1:13

QPBR – Supervision and quality assurance

Ideally, both scientific and QA reviewers should be independent of the study activities

- Principal scientist is primarily responsible for the quality of the study and performing his/her own checks
- Principal scientist's staff are responsible for the quality of their contribution and do their own checking
- Scientific reviewer should have no direct interest in the performance of the study
- QA reviewer should be independent of all study activities
- Allows reviewers to take a dispassionate view

Session 4:1:14

QPBR – Supervision and quality assurance

Confidentiality and the external auditor

- External auditors must understand their obligations concerning confidentiality of data
- It is good practice to write a confidentiality agreement outlining what the auditor may see and what he/she is at liberty to reveal. This should be signed by the institution and the auditor before the audit

Session 4:1:15

QPBR – Supervision and quality assurance

Evaluation and review of the final report

- Institution should have a policy or guidelines for evaluation of the final report
- Reviewer (superior or peer) should read the report carefully and also compare it with the raw data
- Reviewer should be able to assure management that the report is a fair and complete account of the scientific activities
- Circulation of the report to other scientific staff for discussion and comment helps to ensure that the report is of an acceptable standard

Session 4:1:16

QPBR – Keynote

Verification of results and reports

- Principal scientist has primary responsibility for the quality, integrity and reliability of the study results
- Senior management has responsibility for ensuring the timely and routine review of study data
- Research institution should arrange for verification of study activities and results by persons independent of the study
- It must be possible to audit the report and to trace all results to the raw data of the study

Session 4:1:17

Questions

- What is understood by scientific quality? What aspects are emphasized in this presentation?
- It is claimed that quality means that an entity complies with its specifications (attributes). What are the quality attributes of scientific data? Can you add any more?
- What provisions does the scientific community already make (more or less formally) to ensure reliable scientific results? Is this a successful strategy?
- Why should management propose both scientific and process (QA) supervision?
- Why should management verify staff qualifications at recruitment? Why should management insist that staff and human resources update CVs and training records during subsequent work at the institution?
- What is the difference between scientific and process supervision?
- What do peer reviewers look for?
- What do QA reviewers look for?
- Ideally, both the peer reviewer and the QA reviewer should be independent of study activities – why?
- Can you describe the process for reviewing a final report?
- Why would an institution call in an external auditor?

Workshops

1. Make a plan for the review of a final report (or for an experimental process e.g. dosing or weighing). What tools would the peer reviewer and the QA reviewer use for the review? What would they look for? Write a to-do list for each role or present the plan as a tabulation or diagram on the flip chart.

2. Do you expect the scientific review and the QA review to overlap? Give reasons for your answer. If yes, give examples from your own practice. If they overlap, what can be done to resolve differences between the parties?

3. In your discussion group, make a frequency chart covering the presence of the following in the institutions represented: requirement to use peer review, description of this review, signature of peer reviewer, requirement for QA review, description of process review, provision for resolving differences.

4. How do the underlying science and the flawless experimental process contribute to the quality attributes? How does one know what comprises the underlying science? How does one know anything about the execution of the experiment? From your own everyday activities, or from the literature, give some examples of instances where either the science or the process seems to have failed. Use the flip chart to note: approximate date and place of the study; focus of the study; the result; and what seemed to be wrong.

4.2 PUBLISHING PRACTICES

Goals

At the end of the session, you should be able to:

- argue for the necessity of moving scientific results into the public domain;
- explain the necessity of a formal policy and procedure for this process and the issues that management would address in these documents;
- explain the relationship between studies and publications and the advantages and disadvantages of multiple publications of the same work;
- argue for the necessity of allocating defined responsibility to authors;
- appraise current publishing practice and (if necessary) suggest improvements;
- choose critically the most advantageous forum for any given publication;
- protect the potential for patenting (where relevant).

TDR UNICEF • UNDP • World Bank • WHO QPBR – Publishing practices

Bringing scientific results into the public domain

Session 4:2:1

TDR UNICEF • UNDP • World Bank • WHO QPBR – Publishing practices

- An earlier slide listed the quality attributes of scientific data:
  - relevant
  - reliable
  - reproducible
  - ethical
  - auditable
  - in the public domain

- This means that the results must be moved from the laboratory setting to the wider community
- Without publication, the scientific research might just as well have never been done

Session 4:2:2

QPBR – Publishing practices

It is good practice to publish results in a timely way

Advantages:

- results are moved into the public domain while the activities are relevant and state of the art
- timely publication is part of the scientific process – the public (directly or indirectly) funded the activity and have a legitimate interest in the outcome
- researcher becomes exposed to peer review and scientific challenge
- other researchers can build on the results and avoid repetition of the same study
- scientists become known in their field and increase the chances of funding and further research

Session 4:2:3

QPBR – Publishing practices

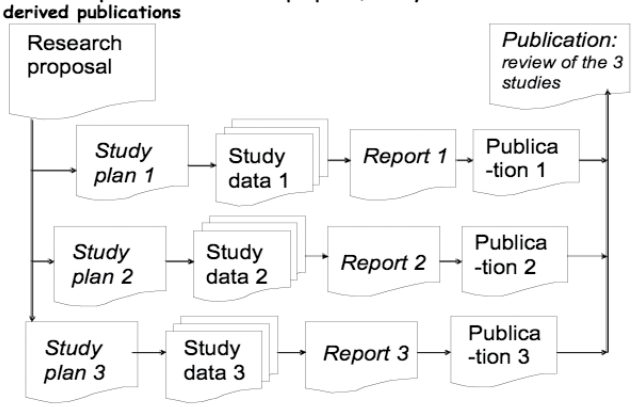
Since publication is the essential process for moving ideas into the public domain, the institution should have a policy covering issues such as:

- at what point in a project it is advisable to publish
- institution's procedures for review
- conventions for coauthoring papers
- necessity of including significant data fairly and accurately in publications
- whether research data are the intellectual property of the research institute (or the grant giver)
- ownership of patent rights

Session 4:2:4

QPBR – Publishing practices

Relationship between research proposal, study documentation and derived publications



Session 4:2:5

QPBR – Publishing practices

It is customary to make one publication from one set of study data

Session 4:2:6

QPBR – Publishing practices

- But it is possible to produce more than one publication
  - Advantages:
    - allows elucidation of unexpected observations or follow-up studies
    - allows full and detailed exploration that may be too long for a single publication
  - Disadvantages:
    - lengthens author's publication list BUT adds to the volume of scientific publications without adding new knowledge or insight
- It is not acceptable to publish the same material in slightly different ways in different journals

Session 4:2:7

QPBR – Publishing practices

- Advantages of publishing review articles:
  - present overview of similar studies, sometimes with conflicting results
  - help colleagues to orient themselves quickly
  - may present materially new interpretation of known data
- Disadvantages of multiple reviews:
  - same as previous slide – unless materially new insight is presented

Session 4:2:8

QPBR – Publishing practices

- It is rather unusual to publish negative (inconclusive) results
  - If the study was well-controlled and well-executed, the negative results are valid and interesting
  - Publication prevents resources being wasted trying to replicate the same study
  - Researchers have been reluctant to publish
  - Journals have also been reluctant to publish
- But the scientific community is beginning to understand the importance of knowing what did not return expected results

Session 4:2:9

QPBR – Publishing practices

Assigning credit to contributors

- Always give credit to others who contribute work, ideas or results
- Published sources: quote loyally and give names and full bibliographic reference
- Unpublished sources: obtain permission from author and give acknowledgment. Show consideration for his/her own publication strategy
- Consider including the author of the unpublished source in the list of authors – if the contribution is significant

Session 4:2:10

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QPBR – Publishing practices

List of authors

- If the paper is the result of a collaboration, follow institution's policy or agree in advance who will be an author and who will be principal author
- Principal author: person who generated idea and undertook most of the work
- Do not include people who made only a modest contribution or contributed activities as part of a routine job
- A very long list of authors dilutes individual responsibility for the integrity of the results
- There is no particular reason for automatic inclusion of the head of the laboratory

Session 4:2:11

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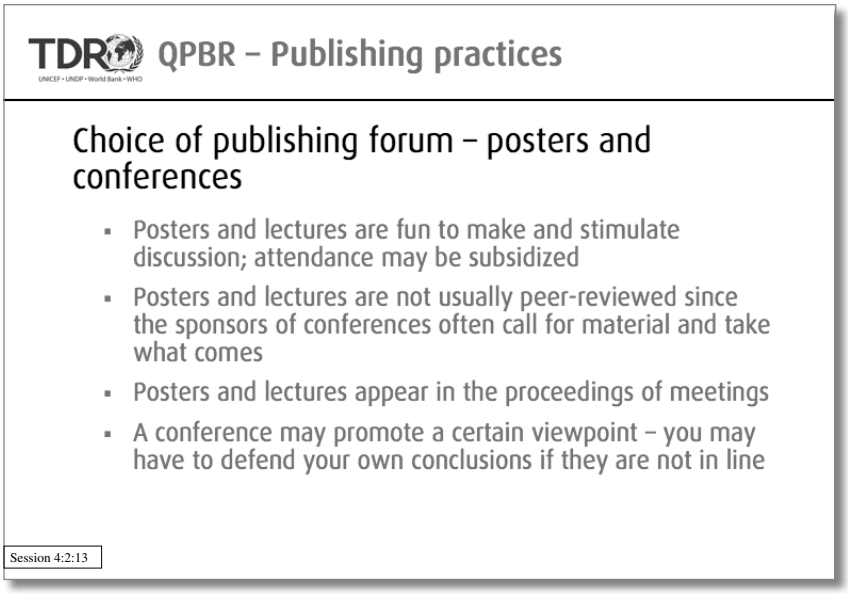
QPBR – Publishing practices

Choice of publishing forum – scientific journals carry most weight

- There is considerable competition to have results accepted
- Journals provide instructions on format, style, content, length, position of principal author – follow these instructions carefully
- Takes time for review – revisions may be requested and take more time
- Final result is considered reliable and earns respect for the author

Session 4:2:12


TDR
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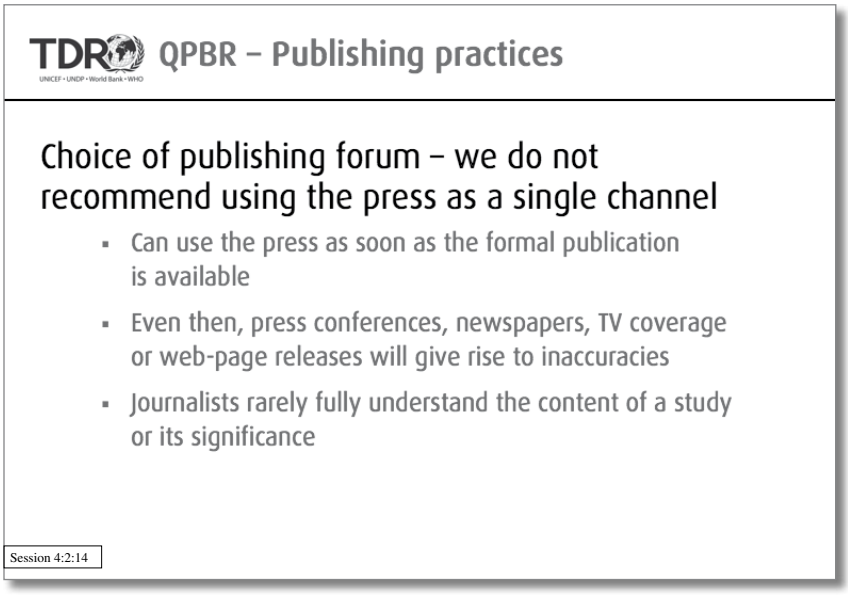
QPBR – Publishing practices
Choice of publishing forum – posters and conferences
Posters and lectures are fun to make and stimulate discussion; attendance may be subsidized
Posters and lectures are not usually peer-reviewed since the sponsors of conferences often call for material and take what comes
Posters and lectures appear in the proceedings of meetings
A conference may promote a certain viewpoint – you may have to defend your own conclusions if they are not in line
Session 4:2:13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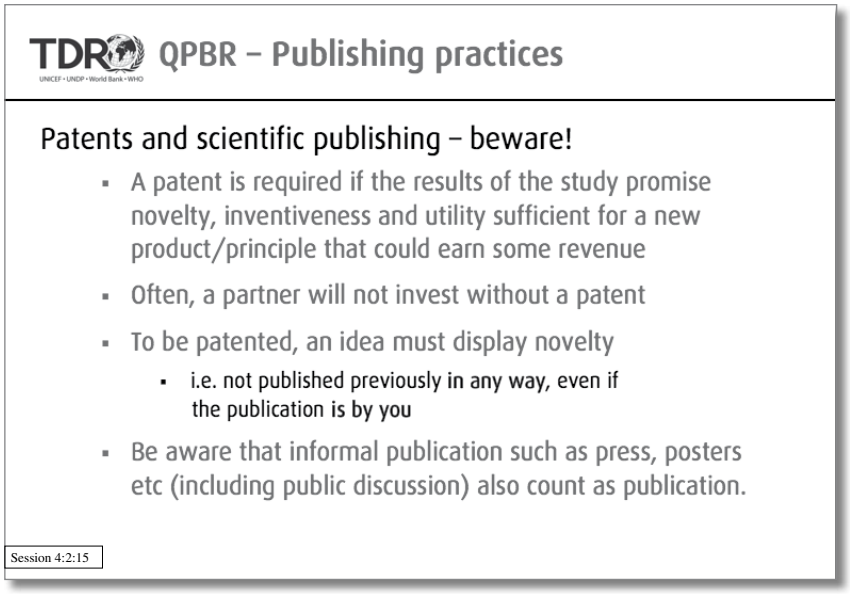
QPBR – Publishing practices
Choice of publishing forum – we do not recommend using the press as a single channel
Can use the press as soon as the formal publication is available
Even then, press conferences, newspapers, TV coverage or web-page releases will give rise to inaccuracies
Journalists rarely fully understand the content of a study or its significance
Session 4:2:14


TDR
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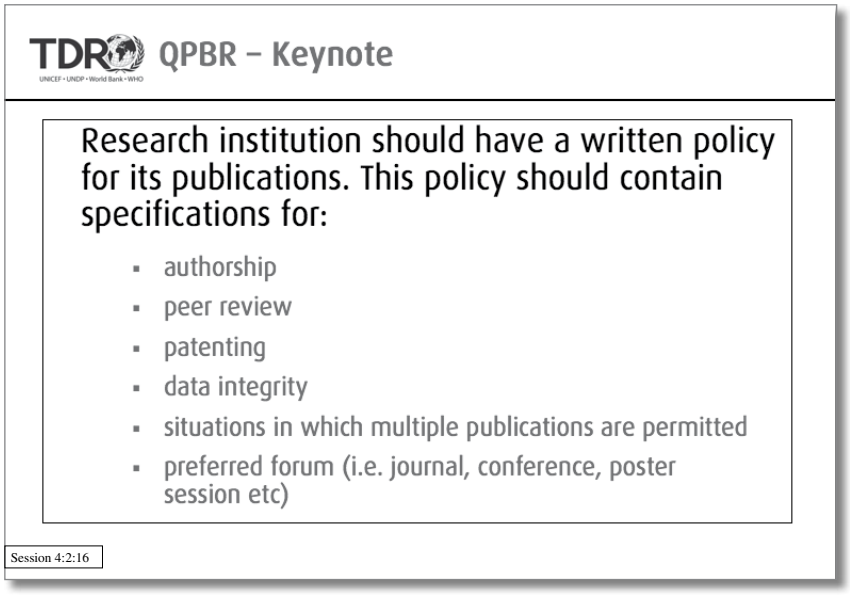
QPBR – Publishing practices
Patents and scientific publishing – beware!
A patent is required if the results of the study promise novelty, inventiveness and utility sufficient for a new product/principle that could earn some revenue
Often, a partner will not invest without a patent
To be patented, an idea must display novelty
i.e. not published previously in any way, even if the publication is by you
Be aware that informal publication such as press, posters etc (including public discussion) also count as publication.
Session 4:2:15


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Keynote
Research institution should have a written policy for its publications. This policy should contain specifications for:
authorship
peer review
patenting
data integrity
situations in which multiple publications are permitted
preferred forum (i.e. journal, conference, poster session etc)
Session 4:2:16

Questions

- What is understood by public domain?
- Why is "in the public domain" one of the quality attributes of basic scientific data?
- What is the purpose of moving results into the public domain?
- What sort of issues would be addressed in an institute's publishing policy?
- One study: one publication – is this idea tenable?
- Why should anyone publish negative results? Give an example if you can.
- What are the different methods of publishing? Give examples.
- Why does the need to move results into the public domain sometimes conflict with the need to patent a finding?
- Where can you find authoritative advice on the presentation and format of publications?

Workshops

1. QPBR claims that moving results into the public domain is an integral part of the basic research process. Why does QBPR make this claim? Whose interests are involved? Why should management have a formal policy and procedure in place to cover this part of the process?

2. In your discussion group, for each of the institutions represented, indicate the number and the level of staff normally represented in the author list of a publication in a scientific journal. Tabulate your information on the flip chart. Indicate the level of staff represented in the acknowledgements list. Is a holder of a specific rank automatically listed as an author? Is anyone automatically thanked? What are the pros and cons of your present practice? For each institution indicate the presence or absence of a publication policy. If you wanted to implement a publication policy, where would you seek support?

3. Taking an anonymous or fictitious study suggested by your everyday experience, draw a diagram on the flip chart showing the plan, study, the report, proposed publication and the review publication or posters you have planned (do not ruin your chances of patenting with this activity!).

4. List the advantages and disadvantages of the different publishing fora identified in the questions above or in the manual. Give examples from your own experience.

4.3 ETHICAL CONSIDERATIONS

Goals

At the end of the session, you should be able to:

- define "ethical" in the context of basic biomedical research;
- summarize the case for a formal policy and procedure for ethics (including ethics committee);
- perform a simple risk analysis;
- outline a draft charter for an ethics committee and its line of reference in the organization;
- list the relevant guidelines for Good Clinical Practice (GCP), animal welfare, safety, biosafety and environmental protection in order to facilitate access and enable consultation;
- explain why human experimentation is governed by, and requires, special standards (GCP, data and personal privacy);
- anticipate controversy and participate in discussions on ethical issues.


TDR
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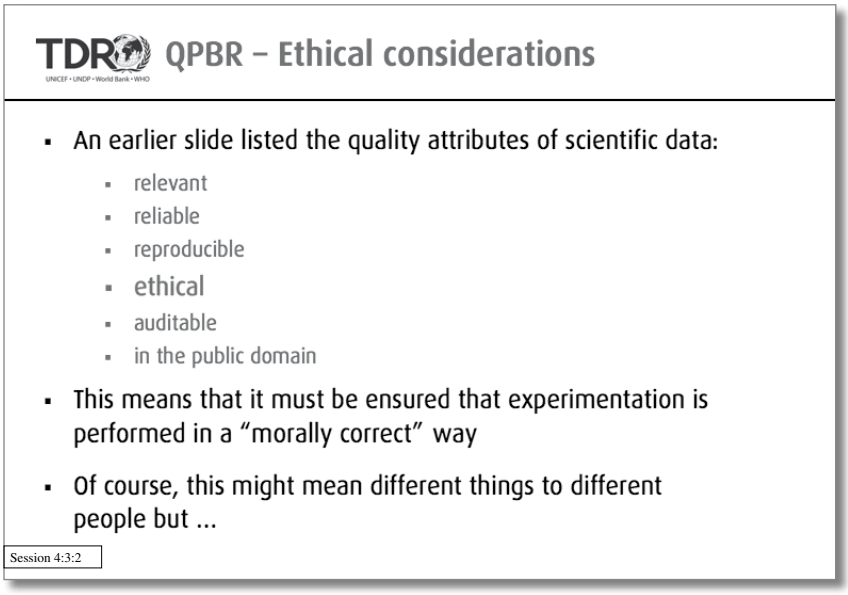
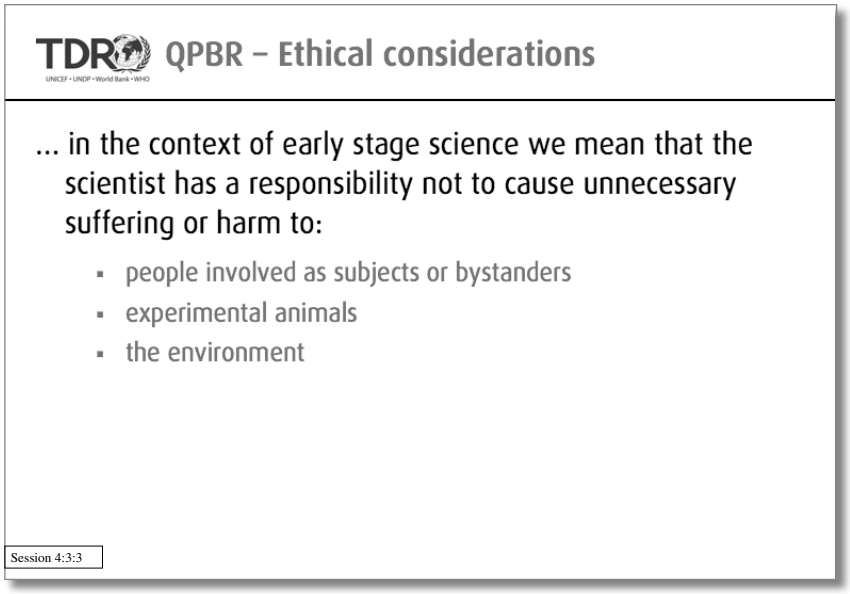
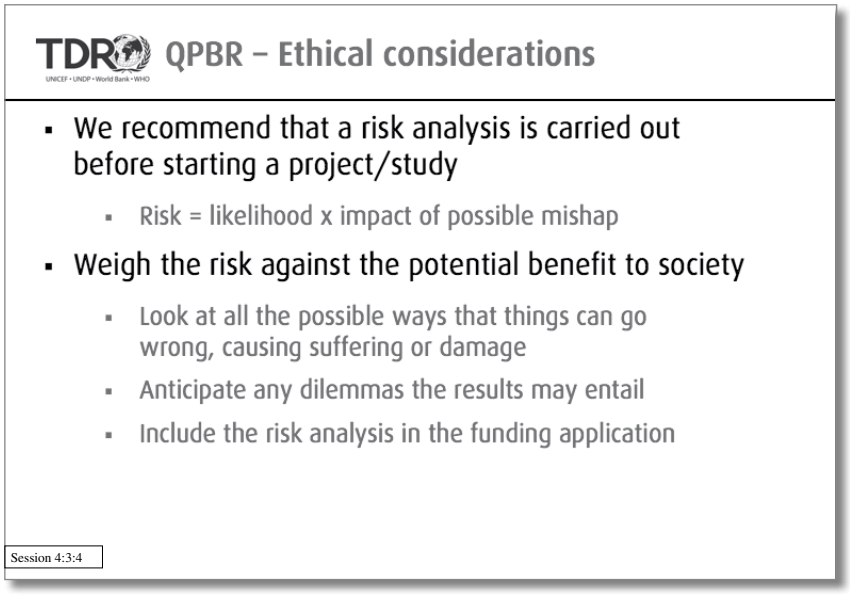
QPBR – Ethical considerations
Honouring ethical responsibilities
Session 4:3:1

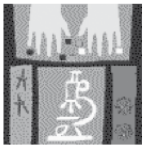

TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Ethical considerations
An earlier slide listed the quality attributes of scientific data:
relevant
reliable
reproducible
ethical
auditable
in the public domain
This means that it must be ensured that experimentation is performed in a "morally correct" way
Of course, this might mean different things to different people but ...
Session 4:3:2


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Ethical considerations
... in the context of early stage science we mean that the scientist has a responsibility not to cause unnecessary suffering or harm to:
people involved as subjects or bystanders
experimental animals
the environment
Session 4:3:3


TDR
UNICEF • UNDP • World Bank • WHO
QPBR – Ethical considerations
We recommend that a risk analysis is carried out before starting a project/study
Risk = likelihood x impact of possible mishap
Weigh the risk against the potential benefit to society
Look at all the possible ways that things can go wrong, causing suffering or damage
Anticipate any dilemmas the results may entail
Include the risk analysis in the funding application
Session 4:3:4

QPBR – Ethical considerations

- Working in the laboratory entails a fair amount of risk for personnel



- Consider risks from:
  - apparatus, chemicals, allergens
  - accidental infection from microorganisms or test animals
  - accidents while working alone
- DO ensure that there is/are:
  - SOPs
  - contingency plan
  - training

Session 4:3:5

QPBR – Ethical considerations

- For studies involving human subjects, GCP is the proper ethical and procedural standard
  - GCP studies involve the use of investigational medicinal products produced according to GMP
  - Supportive data from laboratories should be GLP standard or similar
- Consult:
  - TDR ethical guidelines
  - TDR SOPs for clinical studies
  - ICH guidelines for GCP

Session 4:3:6

QPBR – Ethical considerations

- A non-invasive, observational study may not need GCP but it will still be necessary to consult the local ethical committee if:
  - study may invade personal privacy
  - study may influence the behaviour of subjects or of the health instances involved (practising physicians, clinics, practitioners of traditional medicine etc.)

Session 4:3:7

QPBR – Ethical considerations

- Use of laboratory animals
  - Study itself must not entail unnecessary suffering
  - Do not include too many animals – but sufficient to give meaningful power in the results
  - Timing – animals must not arrive too soon and die needlessly
  - Train personnel in handling and caring for animals
- Read and follow available guidelines for animal welfare

Session 4:3:8

QPBR – Ethical considerations

- Ancillary data may involve a dilemma
- For example, your in vitro study needed only human blood or tissue but you have noticed a pathological state in some donor blood/tissue
  - Will you inform the donor? Or were the samples blinded?
  - Have you written into the institutional ethics charter that no medical opinion would be given in this situation?

Session 4:3:9

QPBR – Ethical considerations

Field trials may unintentionally involve bystanders:

- compounds or methods to control insect or other vectors may affect surrounding population
- by affecting water or food supplies

Session 4:3:10

QPBR – Ethical considerations

Unexpected effects on the environment

- Knock-on effects of controlling the identified vector
- Escape of microorganisms/organisms into the environment (follow WHO or national guidelines)
- Escape of chemicals or metabolites into the environment
- Changes in water supplies, food chains, ecological balance

Session 4:3:11

QPBR – Ethical considerations

Some aspects of the results may have an extreme and unforeseen impact on society:

- use as weapons
- effects on future generations, individuals or populations

Session 4:3:12

QPBR – Ethical considerations

Institution should establish an ethics committee that:

- must have management support (right to veto)
- represents all levels of personnel – not just scientific
- takes time for deliberation and records minutes
- may seek support from local community ethics committee

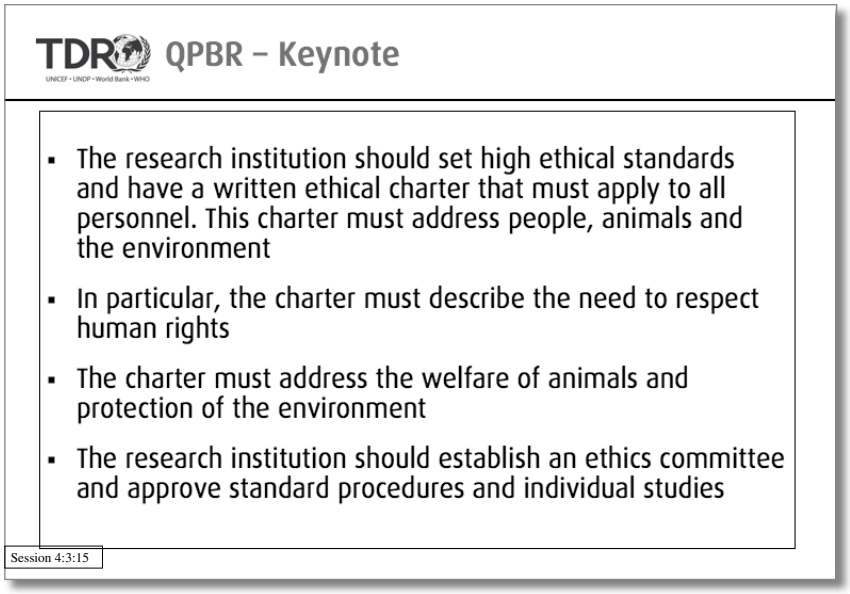
Session 4:3:13

QPBR – Ethical considerations

Ethics committee – activities:

- writes the charter for adoption by management, taking regard of human rights, animal welfare and environmental protection
- reviews actual practices and ensures that these are documented (SOPs)
- reviews individual study plans
- discusses ad hoc issues that may arise

Session 4:3:14



Questions

- Why is "ethical" part of the QBPR quality attributes of basic biomedical research?
- What does "ethical" mean in this context? What types of issues are involved?
- What is a risk analysis?
- What sorts of risks are entailed in laboratory work? For whom?
- Is your institution governed by national or international guidelines/regulations for safety at work, animal welfare, environmental protection, GCP? Where can you access these? Is an individual at your institution responsible for finding such guidelines and advising management on compliance?
- What is the special standard for studies involving humans? Is it always relevant?
- Why is Good Laboratory Practice the standard for laboratory work supporting clinical studies? Is this always the case?
- How could you prevent unnecessary suffering for laboratory animals in your studies? Does this cover all types of animal?

- Do incidental observations (e.g. tissue samples taken for another purpose) engender any ethical problems?
- What is an ethics committee?
- What sort of work do they do?
- Are any of their activities controversial? Give examples.

Workshops

1. Your institution needs to set up an ethics committee. How many members are required? Who (which groups) should be represented? Use the flip chart to list the essential components of a draft charter for an ethics committee.

2. For one or more studies from your experience, brainstorm the risks involved for people, animals and the environment. Tabulate on the flip chart. Assess risk by indicating the impact and likelihood of each.

3. For one or more human studies from your experience or from your reading, discuss the relevance of using the special guidelines (on GCP, ethics, privacy) for human studies. Why should this be necessary?

4. For a study from your experience, list the factors that impact negatively on the welfare of the animals involved. What could you do to prevent or minimize these effects?

SESSION 5

5.1 CASE STUDIES

This session consists entirely of discussions around case studies. These are based on actual events but have been modified slightly. Discuss what happened, identify the real issues and suggest solutions to the problems.

You may be asked to present a case of your own.

5.1.1 Test item in animal model

You are the responsible research scientist running a study to determine the efficacy of a test item in an animal model, using treated groups and an untreated control group. When the bioanalytical results are reported it is shown that some blood samples from control group animals contain traces of the test item.

What are the likely causes of this situation?

What should you do?

What can you do to ensure that this is unlikely to happen in the future?

5.1.2 Results not to be reported

You are a researcher running a study which is part of a larger project. Your results run contrary to results from other scientists performing other studies for the project. When you report your results the project leader informs you that he would like you to repeat certain parts of the study and, should you obtain results more "favourable" to the project, report only the second set of results.

How would you deal with this situation?

5.1.3 Unreported values

When examining a report and the data from a study that one of your subordinates has been running you find several instances in which out of range values have not been cited in the report.

How should you react to this?

5.1.4 Technology transfer

You are about to embark on a new type of study within your department. This involves analytical techniques of which your technicians have no experience. The techniques are well-mastered by a group in another department and the director of your institution has requested that you organize a technology transfer between the two laboratories.

How would you proceed? How would you document this? How would you ascertain whether the transfer has been successful?

5.1.5 Blood sample logistics and handling

Your study will entail repeated collection of blood samples (every month for nine months) from a population and subsequent transfer to a laboratory for analysis. Transfer will be carried out by a company said to be specialized in handling biological materials which claims that it can guarantee cold storage conditions throughout the transport period.

Design a raw data form covering the collection of blood samples and chain of custody to the analytical laboratory.

5.1.6 Multisite multi-headaches

A funding organization has agreed to fund a study for which you will be the overall responsible scientist. This will be a multisite study involving the collection of similar data from different geographical areas. All the data generated by the sites will be sent to you for scientific interpretation and inclusion in a final report. The sites have adopted different methods for collecting data – notebooks, loose-leaf files or data collected directly on computers (electronic data).

How will you ensure that all the data from the various sources are sent to you without problems and that the data you receive are reliable?

How will you organize the data so that you can compile your report easily?

How will you deal with the archiving of raw data and other documents at the end of the study?

5.1.7 Scientific peer review

As a well-known senior scientist in a specific field of research you have been contacted to review the work of a scientist working in a different research institution.

How would you go about reviewing this researcher's work?

5.1.8 Preparing a policy document

The director of your institute has asked you to lead a group to write a policy document on the process for publishing the results of the institute's scientific research.

What points would you ensure are discussed during group meetings before preparation of the policy document?

5.1.9 Investigating the unexpected

You are running a study in which an analytical result is unexpectedly out of specification for a parameter that usually remains constant.

What investigations would you perform to elucidate whether or not the result is valid?

5.1.10 Implementation case study

You have been appointed chairman of a small team charged with implementation of QBPR at your research institution.

Where will you start? What will be the main steps to implementation? What pitfalls can you anticipate on the way to implementation?

On the flip chart, construct a plan that shows the main sections of your project (no more than ten steps). Before starting the exercise decide whether you prefer to discuss QPBR for a small team, a larger institution or the discovery departments of a larger company. If there is sufficient time, the task can be repeated for one of the other settings. Discuss any differences.

SESSION 6

6.1 WRAP-UP AND EVALUATION

This session concludes the workshop. Having discussed what you have liked or disliked about the entire workshop you will be asked to complete an evaluation form. This can be submitted anonymously.

6.2 ISSUING OF CERTIFICATE AND CLOSURE

Only those who attend the entire workshop receive a certificate of participation. This should be signed by the organizer and the TDR programme coordinator.

End of the workshop.

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