Session Two

Blood Safety & Quality Regulations

Learning Objectives

- The BSQR Standard
- The purpose & structure of the BSQR
- Documentation required by the BSQR
- Audit objective evidence

Public Expectations

Blood must be:

- Available whenever needed
- Safe and effective
- Zero risk of disease transmission
- Global Travel – same quality all over the world

What do the regulations say?

Article 1: Objectives of EU Directive 2002/98/EC

Status:-

This directive lays down standards of quality and safety of human blood and blood components in order to ensure a high level of human health protection.

What do the regulations say?

The regulations apply to:

- Collection and testing of blood and blood components whatever their intended purpose
- Processing, storage and distribution of blood and blood components when intended for transfusion

Where does GMP practice apply to Blood Banks

- Purchasing
- Testing
- Quality Control
- IT
- Storage
- Distribution

Blood Safety & Quality Requirements

An Overview to the Requirements

1. Introduction & Principles

- Quality system
  - Responsibility of all and managed systematically
  - Includes quality management systems, processes, people & infrastructure
  - Specify processes in instructions
  - Management reviews & corrective actions
- Quality assurance
  - Provide QA support
  - Procedures, premises and equipment that have an effect on safety shall be validated

Quality - Critical

- Functions include
  - Change management
  - Internal audit and self inspection
  - Non- conformance management
  - Contract management and supplier qualification

2. Personnel& Organisation

- Organisation & Structure
  - Adequate staffing levels
  - Organisation chart
  - Medical officer available

- Training
  - Induction and continuous
  - Recorded and competence assessed
  - Evidence of the effectiveness

- Hygiene
  - Instructions
  - Appropriate PPE

3. Premises

Factors that need to be considered include:

- Location, design, construction, security and maintenance
- Sufficient space for logical sequence of workflow
- Dedicated areas (Storage areas away from clinical areas)
- Environmental, temperature and humidity monitoring & cleaning records
- Adequate storage (segregation of stock)

4. Equipment & Materials

- Equipment shall be validated, calibrated & maintained
- Select equipment to minimise hazards
- Reagents & materials from approved suppliers
  - Critical materials to be released by qualified person
  - Meet Medical Device Directive (where required)
- Retain inventory records
- IT procedures to control use of hardware & software including control & back ups of data

5. Documentation

- Procedures – SOPs
- Records
- Document control
  - review, approval and change control
  - Archiving
- Benefits
  - Standardisation
  - Traceability

6. Blood Collection & Testing

Procedures to include:

- Laboratory testing
- Processing & validation
- Labelling
- Release of blood & blood components

Testing

Mandatory markers

- Minimises risk of disease transmission

Sampling & testing requires

- Defined written procedures
- Validated methods
- Qualified, calibrated , maintained equipment
- Approved reagents and test kits
- Validated data transfer procedures
- Documented acceptance / rejection criteria

ABO & RhD blood group testing

- Performed on first- time, repeat & regular donors
- Subject to requirements set by competent authority

Quality Monitoring

- Provides evidence of:
  - Process control

- Quality Critical Processes must be:
  - Validated
  - Evidence of control

- Monitoring should
  - be carried out on an individual donation (not pooled samples)
  - reflect single donor “batch” nature of components
  - be subject to periodic review

7. Storage & Distribution

- Procedures shall be validated
- Prevent mix ups
- Records of inventory & distribution
- Packaging to maintain integrity & temperature
- Control return of blood back into storage

Review & Release

Product status management
- Quarantine
- Released by authorised (against written specification)
- Accordance with a defined written procedure

Computer generated data
- system validated with access control
- earlier release from donor – consistency check

Rejected donations
- Securely quarantined pending destruction
- Associated components checked

8. Contract Management

- Define any contracted tasks in a written contract

9. Non Conformance

- Any deviation must be released only by exception with agreement of prescribing physician & blood establishment physician
- Complaints and other information including serious adverse reactions and event shall be investigated & controlled
- Effective recall procedure maintained
- Corrective & preventive action system

10. Self Inspection

- Audit system implemented to ensure the compliance with the BSQR
- Document results & close out actions in a timely manner

Audit ‘Objective’ Evidence

‘records, statements of facts or other information which are relevant to the audit standards’

Section 3.9.4

ISO 9000:2005

Session Three

Audit Planning & Preparation

Purpose of Session

To review audit planning activities including:

- Audit programmes
- Audit planning & preparation
- Setting objectives, criteria & scope
- Audit preparation & checklists

Definition: An Audit

'systematic, independent and documented processes for obtaining audit evidence and evaluating it objectively to determine the extent to which the audit criteria are fulfilled'

ISO 19011 Section 3.1

Types of Audit

TYPE OF AUDIT	DESCRIPTION	CONDUCTED BY
Internal	First Party	By Organisation on Itself
External	Second Party	By Organisation on Supplier
Independent (and external)	Third Party	Notified Body - MHRA

Internal Audit Objectives

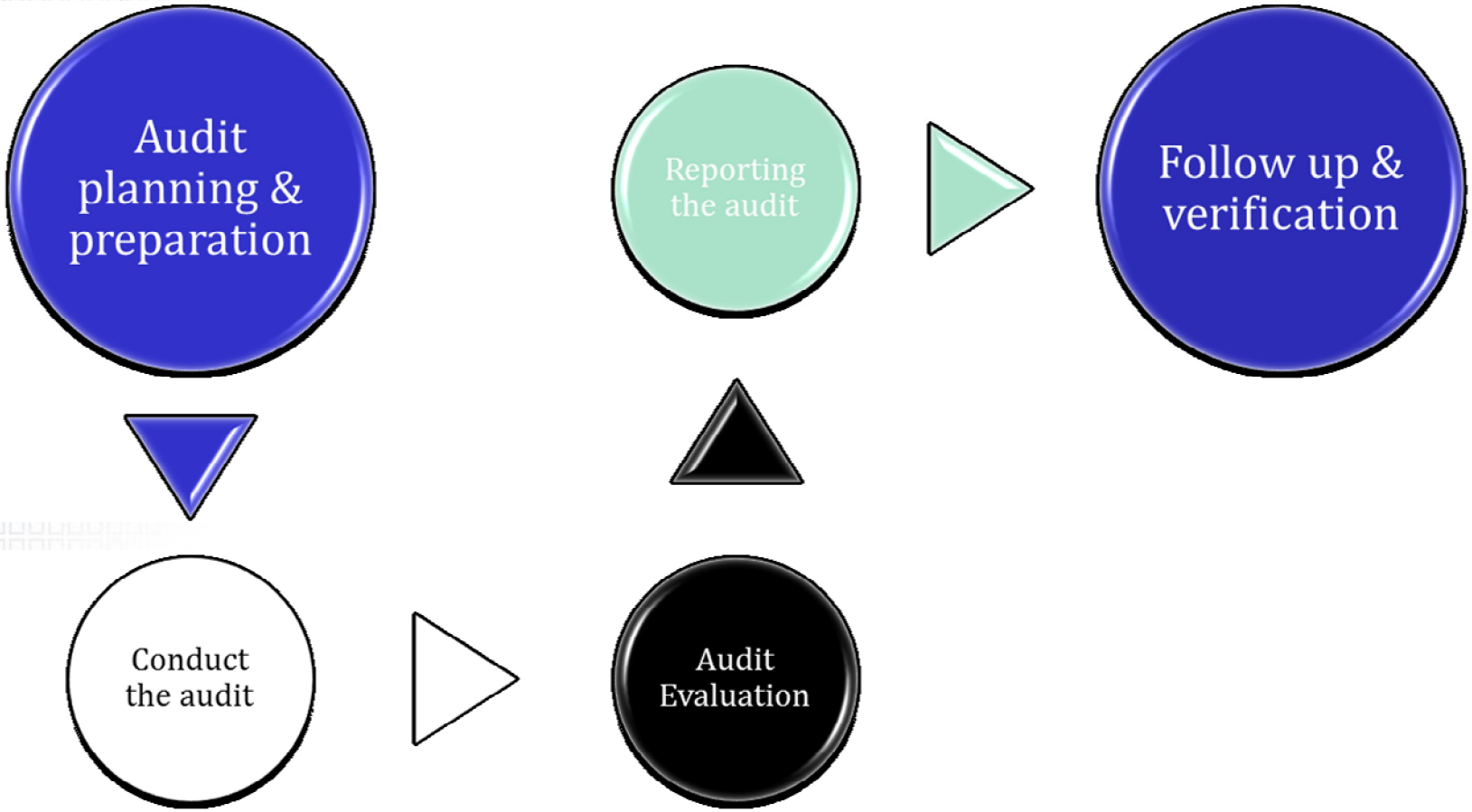
- Management priorities and objectives
- System requirements
- Regulatory requirements
- Compliance to BSQR
- Improvement Audits

Audit Programmes

Audit Programme: *Set of one or more audits planned for a specific time frame, directed towards a specific purpose*

ISO 19011

Audit Life Cycle



Audit Planning

- Defining the scope of the audit
- Defining the audit criteria
- Defining the overall audit objectives
- Contacting the area to be audited
- Review documentation
- Determine if expert help is required
- Produce audit plan (agenda)
- Prepare audit checklist

Audit Scope

‘Extent & boundaries of an audit’

Includes

- Physical location
- Organisation unit
- Activities
- Processes
- Documentation
- Time scale

Audit Criteria

'Set of policies, procedures or requirements used as reference'

- BSQR
- 'Orange Guide' & 'Red Guide'
- ICH 9,10
- Procedures (documented or otherwise)
- Specifications/standards
- Regulatory requirements

And many more…

Internal Auditor Responsibilities

- Plan the audit
- Contact the auditee & ensure availability
- Agree audit plan(agenda), scope and criteria
- Documentation review
- Checklist preparation

Checklist Contents

- Specific questions to criteria (BSQR)
- Documentation available
- Activities to observe
- Concerns/points to raise
- Records to verify
- Other considerations…
  - Previous audits
  - Changes
  - Know issues
  - Experience & knowledge

Process Checklist

BSQR	Checkpoint	Notes
5.1	Is the SOP in date? Is there a review date?	
5.1	Is the SOP clear and unambiguous?	
5.1	Is there an author, reviewer and authoriser?	
4.1	Is there a complete materials list?	
5.3 these	Are there any amendments or alterations to the SOP? Are dated and signed? Is there a reason given for the alterations?	
2.3	Are there training records available for the procedure?	
2.3/5.3	Have all staff been trained in the procedure?	

Examples of Questions....

Position	Sample Question	Guidance to Reply
All	**How was you trained and/or qualified to perform your job?**	**Mention how do you train**
All	**Are there training records that give evidence to this?**	**Answer Yes/No**
All	**Where are training records located?**	**With Manager, QA-HR-…etc**
All	**What forms and/or records do you use while performing your job?**	**According to your procedure you are following**
All	**How to store forms you are using?**	**Records are identified by address date, indexed and maintained according to control of records procedure**
All	**How long are they to be kept?**	**According to your procedure you are following**
All	**Who has the access of that records?**	**Your dept., members… any one who can access the record**

Examples of Questions....

Position	Sample Question	Guidance to Reply
BMS	Do you ever have problems come up? How do you handle them?	*According to the type of problems
BMS	When you find nonconforming part, what do you do?	Inform the Forman who follows the controlling of non conformity procedure
BMS	If you are responsible to perform Inspection? how do you record your results?	In Inspection Forms according to given from "XYZ" procedures
BMS	If your documentation says you should do something a specific way and someone else tells you to do it differently, what do you do?	Ask him to issue a change note
BMS	What do you do if your machine breakdown?	Make a Break down report according to procedure 123

Session Four

Conducting the Audit

Purpose of Session

At the end of the session you should have an understanding of:

- Use of checklists
- Process-based auditing
- Sampling and interviewing techniques
- Obtaining and recording objective evidence
- Effective audit practice

Use of Checklists

- Defines the scope and sample of the audit
- Use as an aide memoir
- Used to record audit evidence for:
  - You
  - The audit system
  - Objective evidence that you have done the audit

Process Audits

- Assess process risks
- Implementation of process controls
- Monitoring and measurement of the process
- Effectiveness of the process
- Continual improvement of effectiveness and efficiency

Always ask:

- Is the process implemented and maintained?
- Is the process effective?

Fact Finding not Fault Finding

Collect Objective evidence to:

- Compare
- Evaluate
- Inform

<u>Does the system conform to the criteria!</u>

Opening Meeting

May be formal or informal but will aim to:

- Confirm the audit plan
- Summarise how the audit will be conducted
- Confirm communication & reporting
- Provide opportunity for the auditee to ask questions

The Auditors 6 friends….

WHAT?

WHY?

WHEN?

HOW?

WHERE?

WHO?

The auditors 7th friend: SHOW ME!

Good Practices

- Speak clearly & simply
- Look at the person
- Body language
- Rephrase question
- Ask the right person
- Be relaxed, confident
- Impartial
- Apologise for interrupting
- Don’t look for issues
- Give positive feedback when deserved

Bad Practices

- Asking too many questions at once
- Saying you understand when you don’t
- Answering your own question
- Not giving enough time to answer
- Getting into an argument
- Relying on your memory
- Subjective opinions
- Taking sides
- Criticising individuals

Objective Evidence

- What was observed, examined or stated, where and when
- Details of requirement (standard, procedure, work instruction, specification etc.)
- Who made what statement(s)

Objective Evidence

- Evidence which exists
- Uninfluenced by emotions or prejudice
- Can be traced
- Does not need further clarifications
- Within the scope of the document

Observation

- People
- Product and service
- Processes
- Information systems

Taking Samples

When planning samples, consider:

- The major process of the department
- The other duties it undertakes
- What it does when things go wrong

Taking Samples

- Released products
- Raw materials
- In-process materials
- Inspector or sampler
- Number of samples and sample size
- Authorization

Look out for ...

- Employees understanding of the procedures that affect their work
- Managers understanding of their quality objectives and progress towards meeting these objectives
- What happens to the system when responsible person for a job is absent from work
- System integrity under an emergency

Session Five

Audit Evaluation

Purpose of Session

- Evaluating audit evidence against agreed criteria
- Writing clear nonconformity reports

Evaluating Objective Evidence

- Determine system components in full compliance and those which show best practice
- Identify nonconformities and rate them according to importance
- Identify areas of weakness where an opportunity for improvement should be raised to prevent future nonconformity or promote best practice.

Definition: Nonconformity

‘Non-fulfillment of a requirement’

ISO 9000:2005

Reporting Categories

Critical: **Has produced** a product harmful to a person, leads to a significant risk of harming a person.

Major: Has produced or may produce a product which does not comply with GMP, indicates a major deviation from GMP.

Other: A combination of several 'other' deficiencies none of which may be major but which may together represent a major deficiency and should be explained and reported as such. A departure from GMP.

Opportunity for Improvement: Minor weakness or potential improvement (optional)

Establish the facts

- Get help from the auditee
- Discuss concerns
- Verify the findings
- Record all the evidence:
  - Exact observation
  - Establish why a nonconformity or otherwise confirm
- State who (if relevant) – preferably by job title

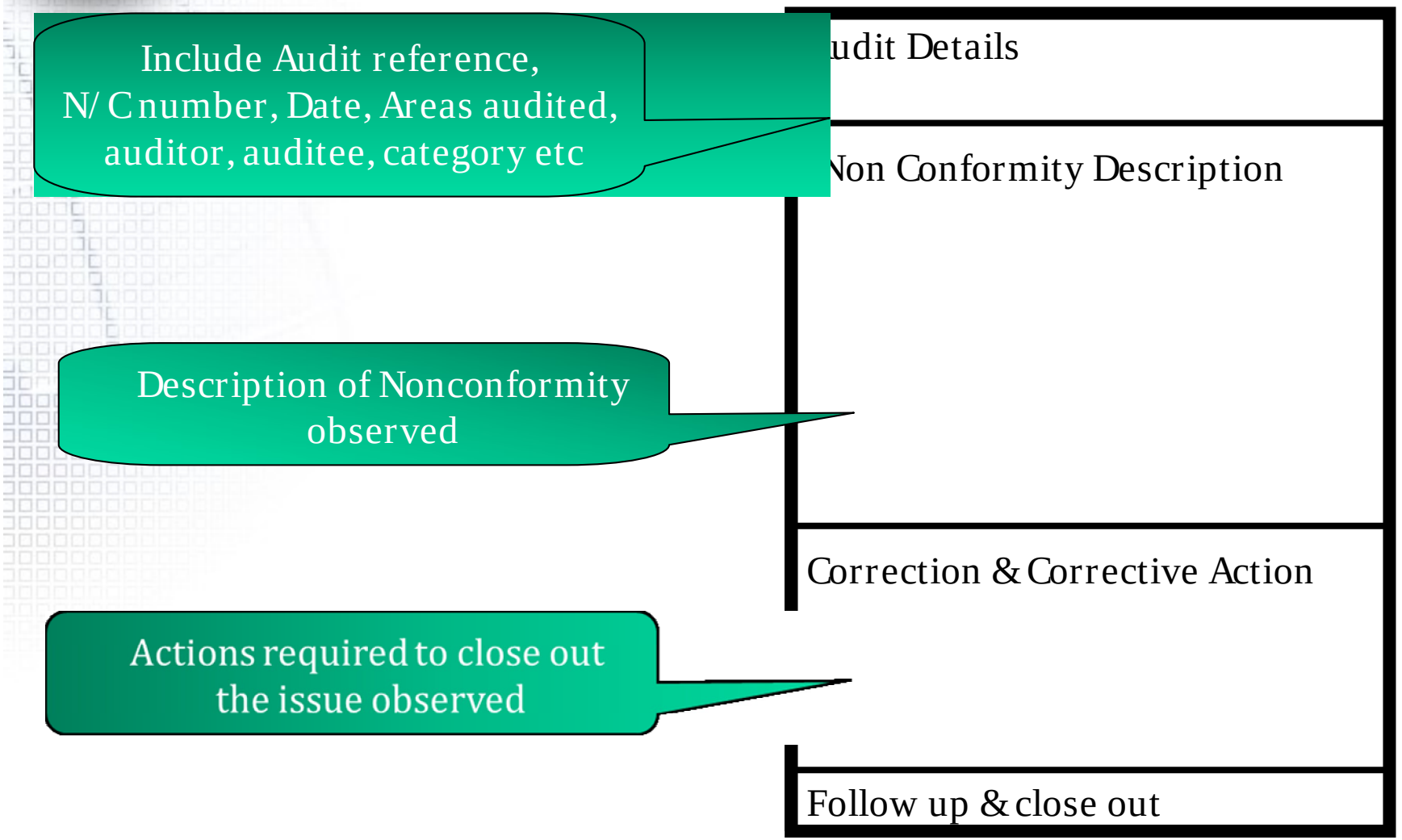
Consider the seriousness

Two questions to be answered:

1. What could go wrong if the nonconformity remains uncorrected?

2. What is the likelihood of such a thing going wrong?

Nonconformity report



Nonconformity Description

Anyone reading the nonconformity should know:

- What is the issue (location, details of issue)
- So What is wrong (stick to the facts)
- Why is it an issue (i.e. what criterion not met)

<u>Without having to ask the auditor!</u>

Writing a Nonconformity

State what you saw…

During an audit of the quality management audit system, corrective actions had not been established for nonconformities raised for audits performed in 2008 (i.e. Audits 01/08 to 06/08).

Writing a Nonconformity

State Why this is an issue

BSQR Section 10.2 states that action shall be taken to eliminate the cause of nonconformities without undue delay.