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

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

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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

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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

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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

‘s 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

<table>
<thead>
<tr>
<th>TYPE OF AUDIT</th>
<th>DESCRIPTION</th>
<th>CONDUCTED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal</td>
<td>First Party</td>
<td>By Organisation on Itself</td>
</tr>
<tr>
<td>External</td>
<td>Second Party</td>
<td>By Organisation on Supplier</td>
</tr>
<tr>
<td>Independent (and external)</td>
<td>Third Party</td>
<td>Notified Body - MHRA</td>
</tr>
</tbody>
</table>

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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*
Audit Life Cycle

- Audit planning & preparation
- Conduct the audit
- Reporting the audit
- Audit Evaluation
- Follow up & verification

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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
- 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

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

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

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### Examples of Questions....

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

Does the system conform to the criteria!
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

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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’
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

Include Audit reference, N/C number, Date, Areas audited, auditor, auditee, category etc

Description of Nonconformity observed

Actions required to close out the issue observed

Follow up & close out
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)

Without having to ask the auditor!

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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.*