Questions for the TAG Meeting

As can be seen by the last round of inspections at the control sites there is still a lack of understanding of the requirements of good practice. Can you update the group on the status of the development of Good Practice in Transfusion (Good Practice Guidance) document and the areas it covers?

‘Good Practice’ covers Tissues & Cells, and Blood.

A private Contractor, Alcimed, accepted a contract from the EU Commission to develop a Good Practice Guide from a number of existing tissues, cells and blood documents, and seek comment from EU Member States, blood establishments and tissue establishments. The project work was completed, but changed by the Commission to become a scoping document. We are still awaiting feedback from Commission on further progress. The final document will cover areas listed in the annex to Directive 2005/62/EC, taking into account GMP.

Can you explain why hospitals have been issued with conditional compliance status, post blood compliance report review rather than compliant?

An assessment of ‘conditional compliance’ gives a message that work is still needed, without the requirement for further inspection.

Helps HBB retain resource for on-going CAPA (evidence for senior management)

Ensures MHRA are applying the principles of the Hampton report (regulatory relief, and best use of resource).

The statement of conditional compliance is dependent upon one or more of the following (where applicable):

i. Adherence to commitments for remedial action:
   1. recorded in a submitted compliance report, and / or
   2. communicated to an inspector during the assessment process and /or.
   3. provided in response to previous inspection findings.

ii. Adherence with the Regulations of all transfusion laboratories within a legal entity:
   1. In the case where a different laboratory in a legal entity has been selected for inspection, the compliance status of all other transfusion laboratories within the legal entity remains undetermined until satisfactory closure of the relevant inspection.
   2. The subsequent determination of compliance will be conditional upon adherence at all other transfusion laboratories within the legal entity with relevant corrective actions identified during the inspection.

There is a development of pan-European standards and criteria for the inspection of blood establishments (EU-Blood-Inspection) – EUBIS. However there is no equivalent group for
hospital blood banks. Can you comment on whether hospitals would be inspected to these blood establishment standards and why there is no hospital blood bank equivalent? Are hospital blood banks inspected by the MHRA equivalent outside of the UK?

EUBIS is a project to provide support to training blood establishments and EU Member States in the inspection and operation of blood establishments and HBBs to Good Practice. It is not a Regulatory standard or requirement (therefore similar to CPA). MHRA will only inspect to the requirements of the Regulations, and the principles of Good Practice. These are relevant to HBBs, as stated in SI 2006/2013.

HBBs outside UK are managed differently. IMB require all HBBs to be accredited to ISO 15189. All EU CAs are responsible for compliance of hospital transfusion labs in their own territory – a requirement of 2002/98/EC. MHRA only inspect ‘for cause’ (with exception of compliance report controls). There is no routine programme for HBB inspections (in contrast with pharmaceuticals and Blood Establishments).

Hospital blood bank feel that there is significant variation between inspections that have occurred on varying sites. Can you clarify how the MHRA train their staff to ensure commonality and standardisation where there are no specific HBB standards?

Inspectors all come from a Regulated GMP background. Blood Directive 2005/62/EC states that GPs will take into account the detailed principles of GMP.

MHRA have inspected Blood Establishments since loss of Crown immunity in 1992 (including overseas sites), and inspected tissue banks under the 2000 DH Code of Practice until taken over under Tissues and Cells Directive by the Human Tissues Authority. The Agency therefore has experience in blood inspections. All inspectors go through a training programme for each speciality, including blood, and are not accredited to inspect solo until approved (peer review and competency log). There is also a competency assessment every 2 years with a senior / expert.

Team meetings, on-going training and regular liaison between colleagues ensures consistency.

‘Variation’ is sometimes cited by HBBs by applying ‘to the letter’ a deficiency identified at one site vs another, e.g. 4 probe temp mapping, which may be acceptable for a small fridge, but not a large walk-in. MHRA inspections focus on inspection outcome (working with sites towards compliance), pragmatism, and suitability for procedures to meet the intended outcome. {Note – this is the reason for the GMP guide being written in the way that it is}. It is difficult to comment on individual inspection findings out of context.

- Cleaning of blood fridges and plasma thawers – at one hospital the inspector was happy that there was a rota for cleaning which was signed and dated appropriately and the equipment looked clean, whereas in another hospital which also had this system in place they were asked for microbiological testing to prove that cleaning programme was effective.

This may be due to differences in equipment design, e.g. waterbath vs sahara, as the impact of contamination may be different. There may have been instances where components had
been implicated in microbiological investigations – cleaning may have been done, but this would call into question its effectiveness.

**EU GMP Annex 15 – para 36.** Cleaning validation should be performed in order to confirm the effectiveness of a cleaning procedure. The rationale for selecting limits of carry over of product residues, cleaning agents and microbial contamination should be logically based on the materials involved. The limits should be achievable and verifiable.

- **Traceability** – one hospital was put on special measures where they had to submit monthly traceability information to the MHRA whereas another hospital with the same traceability data was just given a comment about improving traceability.

This may be affected by site or Trust history – some sites have historically preformed badly in improving traceability figures. They may have been previously inspected, and not improved. The monthly updates can be used as a means to give HBB support – focuses the effort and resource of the Trust in compliance. Know non-compliance with traceability has lead to Regulatory action against hospitals.

The MHRA has carried out their first **unannounced** hospital blood bank inspection which resulted in an immediate "cease and desist" notice. Can you clarify whether when carrying out an inspection without notice there would be a different expectation with regards to immediate availability of paperwork, managers, quality personnel and why etc?

There is an expectation of the availability of records at all times for inspection. Unless otherwise stated in the Regulations (e.g. Traceability, and SABRE info), MHRA typically expect lifetime files for equipment, and 2 years of data for other records and procedures.

**BSQR Reg 9 (1)**

(d) maintain documentation on operational procedures, guidelines, training and reference manuals and reporting forms so that they are readily available for inspection under regulation 15;

Inspectors are aware of the ‘special nature’ of unannounced inspections, and act accordingly, although HBBs should be aware of the requirement to be able to demonstrate compliance, which cannot be easily done without the records.

MHRA was only meant to be the competent authority until 2010 and then RATE was planned to take-over. Is this still happening? If so, will RATE have the same criteria, training and standards?

No. The change to RATE has been cancelled, and MHRA are the permanent Competent Authority for blood. The standards applied are the Regulatory standards, not those of the MHRA, and therefore the standards would be the same.

One of the triggers previously stated for an inspection was the number of internally initiated recalls. Can you clarify if you think hospitals should perform a recall if a patient has had a transfusion reaction determined to be of clinical origin? If so should there be provision for clarification in the compliance report regarding the number of internal recalls performed due to quality related incidents rather than transfusion reactions due to physiological status?

The number of internal recalls is unlikely to be a sole trigger for inspection. MHRA consider a number of issues when determining whether inspection is necessary. Recalls are expected to be reported in the compliance report for quality-related issues. The BCR should not be a
reason for handling a component retrieval differently – the key factor is to protect the patient’s health. If the recall SOP needs to define all these reasons for recall, then it should do so. Clarification can be given in the BCR to state the number of recalls conducted due to clinical reasons (where it has been shown that this is not due to a lab testing failure).

Some hospitals use return tags on blood bags to confirm transfusion of a product. This information is then scanned into the LIMS. If there is a question regarding traceability then the LIMS is interrogated. Does the hospital need to keep the return tags?

Not if the primary info source is deemed to be LIMS. Must ensure 30 year accessibility of data.

A hospital has been reviewing their outstanding unit fates by review of patient notes and has been 98% successful. However there are still numerous outstanding unfated units. For the 2% outstanding for which there is no record contained within the notes is it acceptable to use an “assumed transfused” fate on the LIMS?

Not as routine practice. Regulatory requirement is 100%. Depending on the size of hospital, this could be a very low number (e.g. private hosp, with < 300 units per year vs large teaching hospital / DGH, issuing thousands per year). The system should be designed to succeed, not to accept a known level of failure. Remember that each failed traceability records could potentially affect the health of a number of patients in the case of impending a look back and trace back scenario.

It is accepted that occasionally (rarely), a component will not have confirmed final fate due to one or more failures in the system. The traceability records should be able to differentiate between these, and systems should be set up to act accordingly (e.g. raising an incident, etc).

Does the MHRA identify a quality incident threshold beneath which a root cause analysis is not necessary or feasible?

No. This is for the transfusion lab to assess, and justify. If full investigation not feasible, the issues should be recorded and trended, so that further action can be taken in the event of trends. Sites should consider resource when conducting investigations – the time and resource given to each investigation should be proportionate with the inherent risk of the error / incident, for example a single fridge alarm or lack of recording periodic cleaning of a fridge vs error in cross match.

What expectations / guidance does the MHRA have concerning the need to have a recognised full time permanent Transfusion Consultant within an organisation?

There is no specific requirement within the Regulations, which only state:

BSQR Reg 9 (1)
(a) ensure that personnel directly involved in the testing, storage and distribution of human blood and blood components for the hospital blood bank are qualified to perform those tasks and are provided with timely, relevant and regularly updated training;

Can you clarify why platelet incubators are not Medical Devices?
See response to transport boxes

Are there any plans to afford blood transport boxes a Medical Device status?

CE marking all relates to a manufacturers claim for the intended use of the equipment. MHRA do not specify when a certain piece of equipment requires a CE mark; except where a manufacturer states a claim (e.g. blood storage fridge, vs fridge for maintaining contents at 2-6C). CE marking has significant implications to manufacturers, therefore some may not be willing to do so. MHRA devices Division are happy to discuss any concerns.

The BSQR mandates adequate staffing in the blood transfusion laboratory. On two occasions the following phrase has cropped up in our inspection report: “…inadequate staffing to maintain and make progress with the quality management systems” I would like to know how the inspector assesses "inadequate" staffing. How does the MHRA conclude what the correct level is (numbers of staff, banding, rotational or fixed staff etc)?

Assessment of adequate resource is based on a number of factors, which together indicate whether the Quality System is in control. Some include the number of incidents, time to close out the investigations and CAPA, self inspection programmes up to date and issues closed out etc. All necessary change controls written, validations conducted on time, in the right order and written up, training up to date, completeness of procedures, equipment maintenance. MHRA inspection experience is often that a justification for not having these in place is ‘not enough time’.

A mature quality system will require less maintenance (and therefore resource) than a newly developing one. For this reason, there is no pre-defined number of staff required. The same issue for routine lab operations – depends on a number of factors, including amount of work outsourced, automation etc.

Does the MHRA have a position on training requirements in BT for non BT staff? How often should they attend training per month?

The baseline expectation for training is annual, unless otherwise justified. For lower criticality tasks, or more straightforward tasks, may justify a lesser frequency, so long as this is documented, and decision process is robust. Other external requirements (CPA, NPSA etc) may be different.

Can you clarify what the MHRA feel comprises a capacity plan?

Links back to resource – how much staff, equipment and space do you need to accommodate the workload (including the non-measurables in terms of service provision). In cases where there is obvious lack of resource to cope with work, a lack of capacity plan may be cited as a deficiency; or where labs are amalgamated, and one takes over the work of multiple sites. This has been seen during inspection with no site change control and no capacity plan, therefore leading to the potential for significant patient risk.

Can you clarify are the MHRA inspecting to ensure that the recommendations by the IBMS collaborative have been implemented in hospitals – staffing, education and automation?
No. While many of it’s recommendations may be helpful to transfusion labs, it is not a Regulatory requirement, and therefore will not be used by inspectors during inspections.

Can you please explain the MHRA’s thinking is developing their draft guidelines for Electronic Issue?

MHRA inspections of hospital blood banks have identified various situations where the practice of electronic issue of blood components has not been conducted in accordance with Good Practice or the relevant technical guidelines stated in the BCSH Guidelines for Blood Bank Computing (2006). This is due to procedural failures, lack of LIMS system functionality, or lack of system validation to verify the effectiveness of the control measures believed to be in place.

In some cases, this has resulted in the potential for incompatible blood components to be supplied to patients. The practice of electronic issue of blood components for transfusion without direct compatibility testing (cross match) between patient plasma and donor red cells is an inherently high risk operation, and therefore the administrative and technical arrangements for the control of this activity must be robust to protect patient safety.

The aim of the document is to clearly set out the GP requirements for implementing electronic issue, so that these do not come as a surprise to laboratories when discussed during inspections.

In the draft it does not mention the one/two samples requirement for EI. We currently do EI using two samples taken at separate times but other hospitals use one sample grouped twice (not always a forward and reverse). What is the MHRA’s position on this?

Two ‘samples separated in time’ does not necessarily ensure the correct blood for the correct patient. Compare to full cross match against a first-time sample – the components issued may be compatible with the blood in the tube, but not necessarily for the named patient, if the sample was bled from the wrong patient.

Why do the MHRA specify blood boxes to be validated 2-10 C rather then 2-6?

The Regulations state:

Transport and distribution of blood and blood components at all stages of the transfusion chain must be under conditions that maintain the integrity of the product.

There is no specific Regulatory requirement for temperature conditions during blood component transportation. The UK Transfusion guidelines state 2-10C for up to 12 hours. In the absence of specific GP or Regulatory requirements, the UK Transfusion Guidelines are used as the published set of standards. MHRA have requested work be carried out to demonstrate the suitability of the 2-10C limits.

What does the MHRA mean by saying testing of blood fridge alarms?

Making sure that the alarm will alert the user to an excursion (or impending excursion) in the required conditions for blood component storage.

How often do they think this needs to occur?
This depends on a balance of criticality of alarm with historical performance. Criticality increases with a decrease in other control measures.

Our hospital has introduced an electronic temperature monitoring system do we need to keep the charts on the fridges/freezers etc?

Not if the computer system is validated, data is retrievable, and is continuously monitoring temperatures. Procedures should clearly state the primary system, plus if a computer alarm state / excursion is ignored due to chart data which appears to be acceptable, then this causes a conflict in the justification.

Temperature challenges on FFP freezers, how often should they be performed?  (Currently we perform once a month, can be difficult to organise dry ice if we have full load)

This should be based on criticality. What are the risks, and what can be justified? Consideration should be given to protecting the equipment (and therefore the frozen components stored in the equipment) – handling and testing low temperature probes can cause damage and probe failure. The frequency of probe challenge should balance these risks with ensuring that the equipment is working properly.

Is it acceptable to allow a 10 second delay or other such minimum time with regards to core temperature alarms to prevent false alarms as a result of inherent electrical spikes?

Core temperature monitoring should not contain a delay. The laboratory should explore reason for electrical spikes. If this is a known problem, which has been shown to be transient (and not an indicator of potential failure), then a very brief (seconds) core delay could be justified, if clearly documented.

Is it mandatory to have an audible local alarm on a satellite fridges if the temperature control system is being monitored 24/7 by the transfusion laboratory?

Regulatory requirements are to store blood components at the correct temperature, and the Good Practice requirements would be having a system in place to monitor and record these temperatures. There is no mandatory requirement regarding how this should be achieved, although consider any delays between lab staff actioning the remote alarm, and satellite users being aware. A local alarm would alert the user as well as lab staff.