NHSBT Board Meeting
24th May 2018

Annual Management Quality Review
April 2017 – March 2018

Status – Public

1. Executive Summary

1.1 External regulatory oversight was extremely high this year, with a total of thirty regulatory and accreditation inspections taking place. This compares to sixteen for the previous year. There were no critical and twelve major non-compliances raised, all by the Medicines and Healthcare products Regulatory Agency (MHRA).

1.2 The high number of overdue items has continued this year as one of the primary Quality Management System (QMS) issues. This has contributed to a number of Major non-compliances raised by the MHRA during site inspections and monthly compliance reports are now being sent to the inspectorate. Intense focus across directorates has yielded some promising improvements, however this needs to be accelerated and sustained in the longer-term.

1.3 It has been a demanding year preparing for regulatory change, with several new regulations and standards taking effect this year; and others being planned in early in 2018/19. The majority of regulatory changes have been dealt with effectively during the year.

1.4 There have been a number of changes to the reporting of both Serious Adverse Blood Reactions and Events (SABRE) and Serious Adverse Events and Reactions (SAEARs) reporting during the year following discussions with MHRA and HTA respectively. This has resulted in increased numbers of events being reported, but this does not reflect a deterioration in performance.

1.5 Work to transition NHSBT's diagnostic laboratories from Clinical Pathology Accreditation to the new international standard for medical laboratories (ISO 15189) has been completed successfully this year.

Actions Requested

The Board is asked to;

- Note the regulatory performance across NHSBT during the year.
- Note the plans for development and improvement activities in 2018/19.
- Comment and feedback on this report and recommend any areas for future improvement.

2. Purpose of the paper

2.1 Continued regulatory compliance is critical for NHSBT to maintain its licences and accreditations, including its Blood Establishment Authorisation, Human Tissue Authority (HTA) licences for Tissues, Cells and Organs, medicinal products licences and the Care Quality Commission registrations, all of which are essential to allow it to save and improve lives. This report provides an annual overview of regulatory activity, key trends, information and assurances in line with NHSBT's strategic targets for safety and compliance.

3. External Inspection Performance and External Reports

3.1 There were 15 MHRA inspections in 2017/18: 13 on-site visits and two desk-top inspections at Leeds and Bradford. The inspections took place across Blood Supply at various Centres, plus one Investigational Medicinal Products (IMP) inspection at Birmingham Advanced Therapies Unit (ATU). The Human Tissue Authority (HTA) performed four inspections and there were also 11 accreditation inspections.

There were no Critical inspection findings, however twelve Major MHRA findings were raised by MHRA. Seven of these were in Blood Supply; these were due to a range of issues, in particular the maintenance of QMS elements such as Change Control, Document Management and Incident reporting. The remaining five Majors were raised at the IMP inspection at Birmingham ATU, where significant GMP deficiencies in the management and monitoring of clean rooms were identified. NHSBT has submitted responses to all findings which the MHRA has accepted. Action plans are either complete or in progress to address all deficiencies.

3.2 Serious Adverse Blood Reactions and Events/Serious Hazards of Transfusion (SABRE/SHOT) reports; during 2017/18 there were a total of 47 events reported to SABRE, twice the number reported in 2016/17 (22). Stock reconciliation issues, errors in distribution and product irradiation, RCI testing errors, delayed product recalls, and omission of required discretionary donor testing each gave rise to several SABRE events. All events have been investigated and are being managed to conclusion on an individual or national basis. A significant proportion of the increase in numbers has been as a result of dialogue between NHSBT and the MHRA on triggers for reporting.

3.3 Human Tissue Authority Serious Adverse Events and Adverse Reactions (SAEARs): there were 41 Tissue and Cells SAEARs reports made in 2017/18 compared with 23 in 2016/17. This is a significant increase, however 12 of these were due to positive sterility test results, which prior to December 2017 were not required to be reported to the HTA; and an additional 13 SAEARs were graft failures (non NHSBT fault) for eight corneas, four stem cells and one cord blood product. The remainder were a mix of causes with no significant trends evident. There were 33 ODT HTA reports in 2017/18; this is a decrease on last year (54). Seventeen were due to retrieval damage resulting in no transplantation - there has been an increase of reported retrieval issues, however there has also been

a recent focus on improving the reporting of such events. All events are being investigated and managed to conclusion on an individual basis.

4. Quality Management System Performance Update

4.1 Critical and Major Internal Events: there have been no internal events classified as Critical during 2017/18. The number of Majors raised in blood and tissues has increased from 482 in 2016/17 to 544 in 2017/18. No new adverse trends have been detected. Decisions this year to record donor arm pain events and microbiology positive events detected during clean room environmental monitoring as Majors have contributed to the rise in numbers.

4.2 Patient Adverse Events (PAEs): numbers have increased slightly to 147 in 2017/18 from 138 during 2016/17. No new or significant trends have been identified among the reports received. All PAEs have also been reviewed regularly by the CARE groups where no significant issues have been noted.

4.3 Serious Adverse Events of Donation (SAED): there were 46 events in 2017/18, a decrease on the 53 during 2016/17. The SAED breakdown was similar to last year with; 16 needle insertion problems lasting more than 12 months, 13 fractures within 24 hours of donation, 12 hospital admissions within 24 hours, two acute coronary syndromes within 24 hours, one road traffic collision within 24 hours, one death within seven days and one “other” event.

4.4 Self Inspections: Across the year 73% of scheduled self-inspections were completed within one month of the scheduled due date, which is similar to the 74% achieved in 2016/17. The year therefore ended with 36/42 inspections completed; of the six outstanding, two have been carried forward into 2018/19 schedule and two are currently in progress.

4.5 Supplier Audits: Ten supplier audits were completed in the year, six were new suppliers, and the rest were routine re-audits. Implementation of the improved risk based approach to supplier management has continued throughout the year but is not yet complete in all areas of the business. A supplier audit schedule has been agreed for 2018/19.

4.6 Product Recalls: There has been an increase in the total number of recalls through 2017/18 (2346) compared with 2016/17 (1937). This is in part due to higher levels of bacteriology screening issues seen in Manchester and increased levels of donor-related recalls over the winter months. There was also a change to the way platelet recalls were recorded from January 2018 where pooled platelet recalls have four ”recalls” for each pool rather than one.

4.7 Document Management: The percentage of overdue document reviews at the end of 2017/18 was 1.3%, very similar to last year at 1.2%, although this peaked in Oct 2017 at 2.4%. A concerted effort from all Directorates has seen the rate reduce by almost 50% from this high.

4.8 Change Control Management: the percentage of overdue change controls ended the year at 12.8%, an increase on the 10.4% overdue at the end of 2016/17. However, there has been a high number of change controls opened and managed, reflecting the intensive change progressing within NHSBT, from both a regulatory and operational perspective. The challenge is to bring the overdue rate down significantly and then sustain this across the organisation.

4.9 Event Management (Quality Incidents, Hospital Complaints and Audit Findings): at the end of 2017/18 the number of overdue events had decreased by nearly 30%, with a total of 215 events overdue compared to 313 at the end of 2016/17.

5. Quality and Compliance Activities/Issues

5.1 A large number of quality and compliance activities/issues have been successfully dealt with over the year, these include;

5.2 Core Systems Modernisation (CSM) - QA continue to support the CSM Programme to ensure that processes developed are compliant with the complex suite of regulations within which we work and where software is developed to ensure it is safe and compliant. QA has fully supported the initial releases, plus the programme reset activities. Key processes such as the Software Development and Business Lifecycles and requirements traceability have been agreed and training to these processes is being delivered by QA across the programme. The Validation Master Plan for CSM has also been revised and tools for assessing software designs against the requirements of the updated In Vitro Diagnostic Device Directives (IVDD) have been drafted. The development/revision of key strategies and processes including Testing**,** Data Migration and Environment Management and the management of JIRA are all in progress. These all needed to be fully completed to assure compliance going forward. Blood Donation - the monitoring of specific event types and their trending through the MQR and CARE process prompted a number of National Quality Incidents to be raised to address potential concerns over areas of regulatory compliance/donor safety. These included missing donor health check (DHC) forms, failures to perform Haemoglobin testing at session, missing unit events and ongoing errors within the Discretionary Testing process. National reviews with key stakeholders were instigated and have been facilitated and supported by QA over the year. Missing DHC events and failures to perform Hb screening tests have, following completion of preventative actions, considerably reduced.

5.3 Transformation projects; The Supply Chain Modernisation project was effectively managed within the QMS through a suite of linked change control events (positively commented on at the Manchester external inspection). Other key activities requiring QA oversight have included the tendering, validation and procurement process linked to the Euro Blood Pack 2 project, the supply of PI treated non-UK plasma and the implementation of validated whole blood transport containers.

5.4 Data Integrity – Following completion of an extensive gap analysis and reviews of Quality Critical Software systems covered by EU Good Manufacturing Practice, compliance action plans were put in place to address compliance gaps. The initial agreed action plan timescales were not able to be met, consequently a revised plan was developed. MHRA has been notified and a risk based approach is being applied to prioritise the completion of these action plans by the revised target date of end of June 2018.

5.5 Advanced Therapy Medicinal Products (ATMPs) - a new National QA ATMP team has been created to provide expert support for ATMPs being developed and manufactured in the Advanced Therapy Units and the Clinical Biotechnology Centre (CBC). Following a challenging regulatory inspection at Birmingham, a number of improvements are being made to key systems, such as Environmental Monitoring, to improve regulatory compliance. The QA ATMP team has provided extensive input to ensure that the updated processes and procedures meet MHRA expectations and provide assurance regarding the safety of the final products from these facilities.

5.6 The HTA Import and Coding Directives came into force on the 1st April 2018. To comply with the Coding legislation, a Single European Code (SEC) must be applied by NHSBT to all its tissue and cell products issued for transplantation from 1st April 2018. This has required changes to core IT and label printing systems. The SEC has been implemented where required for all products apart from Cord Blood tissue and fresh unprocessed Cord Blood sent from Colindale to Filton. The delay for the latter product was caused by late notification (January 2018) from the HTA that a "partial" SEC would need to be applied when moving products between sites prior to processing. The subsequent software change required to implement this will not be available until November 2018. In the meantime, full product traceability will remain in place utilising current labelling procedures.

The Import Directive for Tissues and Cells requires an update to licences held by Tissue Establishments importing product from "third countries". To allow the future import of tissue such as heart valves from territories not considered part of the EU (Isle of Man and the Channel Islands), NHSBT has applied for a new HTA Import Certificate for Liverpool and the expectation is that the licence to import will be granted early in 2018/19.

5.7 Regulatory Licence changes – numerous licence changes have been required this year, including addition of the new centre at Basildon to the Blood Establishment Authorisation (BEA). The BEA was further modified to allow the commencement of apheresis platelet collections at West End Donor Centre and to reflect several responsible person changes.

5.8 UKAS Accreditation of Diagnostic Laboratories - work to transition NHSBT's diagnostic laboratories from Clinical Pathology Accreditation

to the new international standard for medical laboratories (ISO 15189) was completed successfully in 2017/18.

5.9 ODT Hub – In the past year ODT Hub has released new allocation schemes for heart, lung and liver. Following the release of the heart and lung schemes, several problems were identified which required QA support to perform root cause analysis. This resulted in improvements being identified for future releases.

5.10 HTA Codes of Practice – revised codes came into effect in April 2017. An audit and gap analysis of Non-Clinical Issue (NCI) indicated non-compliances regarding ethics approvals and information supplied to donor families for consent for research. The HTA were notified and an action plan was agreed and implemented. Progress has been made towards ensuring compliance and at the end of 2017/18, NCI were ready to accept new customers for product under their revised procedures.

5.11 Q-Pulse – A formal transformation project was completed during 2017/18 to improve performance issues and specifically resolve the problem of failures of the external reporting tool used by hospitals and transplant centres to report ODT incidents into Q-Pulse.

6. Improvement Plans for 2018-2019

6.1 "Document Revolution" - as part of the QA Strategy Deployment initiative to simplify and modernise the document control system we are assessing Microsoft 365 SharePoint as a viable option to be used for NHSBT's Document Control system and document library. This would prove better end user navigation and accessibility of documents at the point of use and can be accessed remotely. Methods for improving NHSBT's document formats is also being investigated by working with key stakeholders.

6.2 The Human Factors Group (HFG) has developed a plan for delivery in 2018/19 to further embed our HF approach. The key priorities will focus on improving serious incident investigations across the organization, selecting the external partner to work with NHSBT on development and integration of HF to enable acceleration of implementation across the organisation and roll out of the "Day 2 Day" Observation tool which has been successfully used in RCI and H&I.

6.3 New Medical Devices Regulations - these entered into force in May 2017 and will apply from May 2020 and May 2022 for medical devices and in vitro diagnostic medical devices respectively. NHSBT has contributed to the draft guidance and continues to be represented at the MHRA IVDR External Strategy Group. Work is ongoing within NHSBT to assess the impact of the revised regulations and to plan for and implement the required changes. This will have a significant impact in a number of areas, including existing systems and ODT Hub and CSM programmes.

6.4 Manufactured Red Blood Cells (mRBC): A submission to the MHRA for a Clinical Trail Application (CTA) to carry out a first-in-man clinical trial did not occur in 2017/18 as planned. The project was delayed for a number reasons which have now been resolved and three successful

pilot manufacturing runs have been completed. The submission of the CTA to the MHRA is now in the final stages of preparation and it is planned to submit this in Q1/Q2 of 2018/19, with a view to having authorisation to commence the clinical trial by Q3.

6.5 QA Workforce - One of the key objectives of the Quality Strategy was to perform a QA Workforce Review, this was completed and proposals for the future structure of the Quality Directorate were agreed with the ET. The key recommendations were setting up QA Direct, forming a national team to support ATMP, review of QA capacity and distribution of workload in the north and moving the regions to a Hub and Spoke management model. The National Team to support ATMP has been in place since December and the other recommendations are moving forward to plan.

7. Benchmarking

7.1 During 2017/18 QA worked with the European Blood Alliance (EBA) to develop a benchmarking questionnaire focussed on Quality Management Systems (QMS). This was distributed to EBA members in May 2017 and results compiled in September 2017. The exercise showed differences in the scope and extent of the quality management systems but demonstrated that NHSBT is in the forefront of using risk analysis to focus resource and efforts within the QMS.

7.2 QA has joined a similar exercise with the Alliance of Blood Operators which aims to complete during 2018/19.

NED Scrutiny N/A

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