Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Minutes for Blood Consultative Committee (BCC) Meeting
1st November 2016, 14:00-16:00
MHRA Buckingham Palace Road Offices, G4

Attendees:

Alison Watt
Angela Macauley
Ann Benton
Chris Elliott
Ian Bateman
Joan Jones
Rashmi Rook
Shubha Allard
Stephen Bassey
Ben Courtney
Jeremy Grindrod
Jan Stewart
Paddy Ford
Andy Ellis
Alan Morrison(telecon)

MHRA:

Mark Birse (IE&S)(Chair)
Michelle Rowson (IE&S)
Stephen Grayson (IE&S)
Vivian Rowland (IE&S)
Andrew Hopkins (IE&S)
David Churchward (IE&S)
Graham Carroll (IE&S)
Kevin Page (IE&S)
Chris Robbie (SABRE)
David Olszowka (IE&S)
Beverley Malin-Smith (IE&S)(minutes)

1) **Apologies Received**

Cyril Taylor, Jonathan Wallis, Karen Simpson, Liz Carroll, Marie McQuade, Paula Bolton-Maggs, Ian Rees, Sheila MacLennan, Tony Docherty, Etain Clarke

2) **Introductions and Apologies for Absence**

Mark Birse opened and chaired the meeting. He thanked everyone for attending, welcomed any new members, and noted the apologies.
Approval of Minutes of previous meeting held 17th March 2016. Matters arising from minutes:
Item 7 – BCC members to provide list of suppliers to Beverley Malin-Smith for Devices to follow up – Action completed

3) **SABRE Update**

Chris Robbie provided an update on SABRE. The key points of note were:

- Changes to reporting process have resulted in changes to the numbers of reports received in SABRE
- It will take at least another 12 months to assess the effect of these changes to analysis of the data
- Human error still remains the single largest cause of error
- The proportion of reports in the BSQR reporting categories remains broadly similar to previous years
- At least 10% of all reports are considered to be related to staffing and workload factors

- SARs are being classified and categorised by clinical experts in SHOT where the reporting function, for SAR to the EU, will remain with the MHRA as the UK competent authority. This will give a better idea of the UK SAR type and numbers reported to the EU Annually.

4) BCR Process Update

Vivian Rowland provided an overview of the BCR report and assessment process

5) Launch of on-line forum for blood stakeholders

Stephen Grayson presented the online forum which was launched yesterday.
There has been a post published on the Inspectorate Blog https://mhrainspectorate.blog.gov.uk to make people aware of the launch.
The inspectors will be monitoring and providing guidance on the forum.

6) Regulatory Update

David Olszowka, Senior Regulatory Advisor from IE&S Regulatory Advice Unit provided the following update:

- The next the meeting of the Competent Authorities for Blood and Blood Components will be held on the 1 and 2 December 2016, in Brussels
- Transposition of Commission Directives 2014/110/EU and 2011/38/EU is through SI 2016/ 604 which came into force on the 18 July 2016. These Directives allow testing for West Nile Virus ("WNV") as an alternative to a 28 day deferral period for prospective blood donors returning from WNV affected areas, and relaxed the quality control requirements for maximum pH values for platelets concentrates at the end of the shelf life
- DH is also currently considering the transposition of Directive 2016/1214, which amends Directive 2005/62/EC on quality system standards and specifications for blood establishments. The insertion of the revised Article 2.2 is the only change made by Directive 2016/1214. The new Article 2.2 requires MSs to ensure the adoption of good practice guidelines (GPGs). The GPGs can be found at the following link: https://www.edqm.eu/medias/fichiers/good_practice_guidelines_dec_2013.pdf

Post meeting note: David Olszowka will continue to provide regulatory advice support to the Inspectorate on blood related topics, following the sad death of colleague David Carter from a brain tumour.

Agency update

Mark Birse gave an update on Brexit and the work the agency has carried out following the outcome of the EU Referendum:

- A cross-agency taskforce has been set up which meets regularly to provide input and direction for the agency's Corporate Executive Team. The agency's current position statement is available at the following link:

https://www.gov.uk/government/news/medicines-and-healthcare-products-regulatory-agency-statement-on-the-outcome-of-the-eu-referendum

- Various scenarios have been worked through including:
  - A Norway-type model, operating within the EU regulatory framework
  - A Swiss/Canada model, acting as a sovereign regulator but following other regulators regulatory decisions
  - A US/Japan model acting as a sovereign regulator but providing added value
  - There has been wider stakeholder communication sent to key stakeholders in recent weeks explaining the work the agency is doing. In addition, the agency is liaising with

other international regulators that act as sovereign regulators to better understand how they operate
- For each of the scenarios the group are exploring how the agency would be affected and how to move forward once the Government decides the direction of travel to take
- MHRA confirmed that there are no routine activities that have been put on hold as a result of Brexit

Michelle Rowson gave an update on the agency's Digital Service Transformation project:

- MHRA's computer system known as sentinel is being replaced
- This is part of an agency wide IT refresh project to transform the way IT supports the work of the agency, as the IT systems in some areas are no longer fit for purpose and will be unsupported going forward
- IE&S Division want to use this opportunity to understand our end to end process and question why we do things the way we do, in order to identify and implement improvements and efficiency gains
- The IT kit we have available such as laptops and windows applications are also being updated which will make it easier to create, manage and access information
- IE&S are keen to engage with key stakeholders to receive feedback on how we can embrace technology more, in order to "future proof" the new systems and operating processes being developed

7) <u>Collaborative working – evolution of BCC</u>

Mark Birse reflected on the work that was initiated in March 2015 to review the BCC meeting format, members attending and establish effective two-way communication channels between MHRA and Blood stakeholders outside of the BCC meetings. The review had facilitated the launch of the on-line blood forum to improve communication throughout the blood community, not just relying on the BCC, and to provide a communication method that permits stakeholders to build contact networks and share experiences.

As future operational and regulatory updates will be communicated using the on-line blood forum, the BCC needs to develop a more strategic focus. Mark Birse explained that a survey of BCC members was planned, to identify what members wanted from the meeting, how this could be best achieved, consider whether the wants could be delivered by other means by linking into other meetings such as the UK Blood forum that has been set up involving, MHRA, HTA, UKAS and CEOs of the UK Blood Services, etc. The output from the survey would then be used to develop a new meeting format and terms and reference to meet the expressed needs of the group.

Post meeting note: The survey has been set up. BCC members are requested to complete the survey before 28th February 2017 using the following link. https://www.surveymonkey.co.uk/r/8KPQ86Z

8) <u>AOB</u>

a) A paper was submitted by Joan Jones relating to traceability considerations for allogeneic blood components and ex-vivo normothermic perfusion of organs for transplantation.

MHRA noted that the blood safety and quality regulations address blood for transfusion to a human, and that use in organ perfusion has specialist considerations. There remains a public health interest in maintaining blood component traceability. In the case presented, blood or a component is used to perfuse an organ and it would therefore be preferable to apply the appropriate record keeping requirements from the regulations. There are considerations in support of 'fating' blood components to either the organ donor or recipient.

MHRA is in favour of fating the blood component to the organ recipient, however it is understood that there may be operational challenges in reliably completing this traceability record as organs are

supplied to a wide variety of destinations. Traceability at the organ donor end might be more robust however the donor will not be affected by the blood or component used on the organ.
Ian Bateman noted that there may be a possibility for the national transplant team to act in the traceability chain, due to their visibility of both source and destination establishments. It was agreed to explore this possibility outside the meeting. Ian Bateman was requested to provide a description of this proposed model to David Olszowka, to enable an assessment of any consequential regulatory impact.

b) Discussion regarding the UKAS guests and the future of the work that was proposed regarding them attending.

Jan Stewart requested an updated on plans for UKAS and MHRA to work together to gain agreement on terminology and expectations. David Churchward confirmed that MHRA are not overly concerned about terminology and document titles, but are more concerned that a site understands the purpose of a given document in meeting a specific good practice requirement and has appropriate control systems in place around the generation, accuracy, and retention of documentation. MHRA is continuing to work with UKAS to understand where there may be commonalities in approach which might lead to a reduction in burden for HBBs; at the current time this is in the very early stages of discussion, and no timelines or specific outputs have been agreed.

c) Hospital Blood site inspections

Rashmi Rook commented that stakeholders had noted a reduction in MHRA inspections in recent years. David Churchward explained that a 2014 review of transfusion laboratory compliance outcomes from inspections and compliance report submissions demonstrated an improvement in compliance in the HBB sector. On this basis, the number of 'for cause' inspections had been reduced to acknowledge this improvement, and to comply with the regulatory requirement for 'for cause' inspections of HBBs. David Churchward explained that although MHRA has a legal obligation under the Blood Safety and Quality Regulations to ensure HBBs operate in compliance with the principles of Good Practice, there are no legal vires to implement a routine inspection programme. MHRA does however have powers to inspect 'for cause' to ensure compliance with the requirements of the Regulations and uses the BCR assessment process to assigns a risk score, which is used to trigger a 'for cause' inspection of the relevant HBB. The Inspectorate also has a responsibility to ensure that inspectorate resources are allocated to areas of greatest risk to public health, which includes oversight and inspection of a range of blood and pharmaceutical sites.

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SABRE BCC report Nov 2016

Chris Robbie MHRA

CPRD NIBSC MHRA

Reporting Activity

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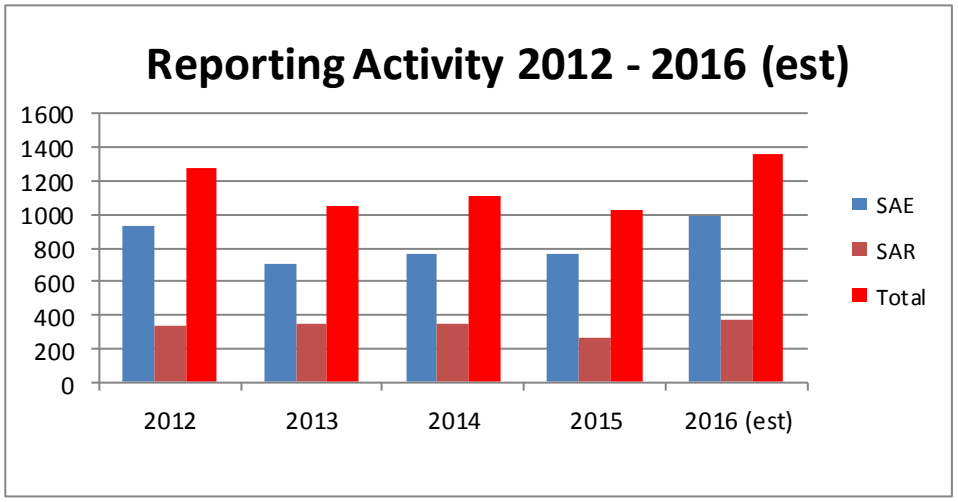
Confirmed Reports 2012 – Sep 2016

	2012	2013	2014	2015	2016 (8mths)	2016 (est)
SAE	931	705	764	765	653	980
SAR	343	345	346	262	251	377
Total	1274	1050	1100	1027	904	1357



2016 will be the first full year of data since phase 1 changes to SABRE/SHOT reporting process

Has led to an increase in reportable SAEs and SARs reported to MHRA

This increase in numbers should not be interpreted as a reduction in quality and safety in reporting establishments without further analysis

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SAEs by Deviation Jan 2016- Sep 2016

SAE Deviation	Total No	Product Defect	Equipment Failure	Human Error	Other
Whole Blood Collection	**14**	0	0	14	0
Apheresis Collection	**0**	0	0	0	0
Testing of Donations	**2**	0	0	2	0
Processing	**7**	0	1	6	0
Storage	**153**	0	2	150	1
Distribution	**14**	0	0	14	0
Materials	**0**	0	0	1	0
Other	463	0	7	456	0
Overall Total	**653**	**0**	**10**	**642**	**1**

The proportion of reports in each category remains broadly similar to previous years despite changes to reporting process

Human Error is still the highest single SAE deviation

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Other reports sub categories 2016

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Sub Category	2015	2016 (est)
Incorrect blood component selected and issued (IBCI)	137	188
Component labelling error (CLE)	86	108
Pre transfusion testing error (PTTE)	79	114
Sample processing error (SPE)	75	125
Data entry error (DEE)	48	51
Component collection error (CCE)	45	83
Failed recall (FR)	10	5
Incorrect blood component ordered (IBCO)	7	14
Component available for transfusion past de-reservation date (CATPD)	4	6
Unspecified (UNS)	4	2
Expired component available for transfusion (ECAT)	3	0
Handling Damage	1	1
Not Known (NKN)	1	2
Total	500	699

The increase in SAEs falling in the “other” category is largely a result of changes to SAE reporting arrangements where SHOT and MHRA see all reports. It is not thought to demonstrate a worsening of performance.

Selecting the right component, typically meeting special requirements continues to be the largest category and sample processing errors where discrepancies between sample and form details with LIMS are not picked up

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Human factors

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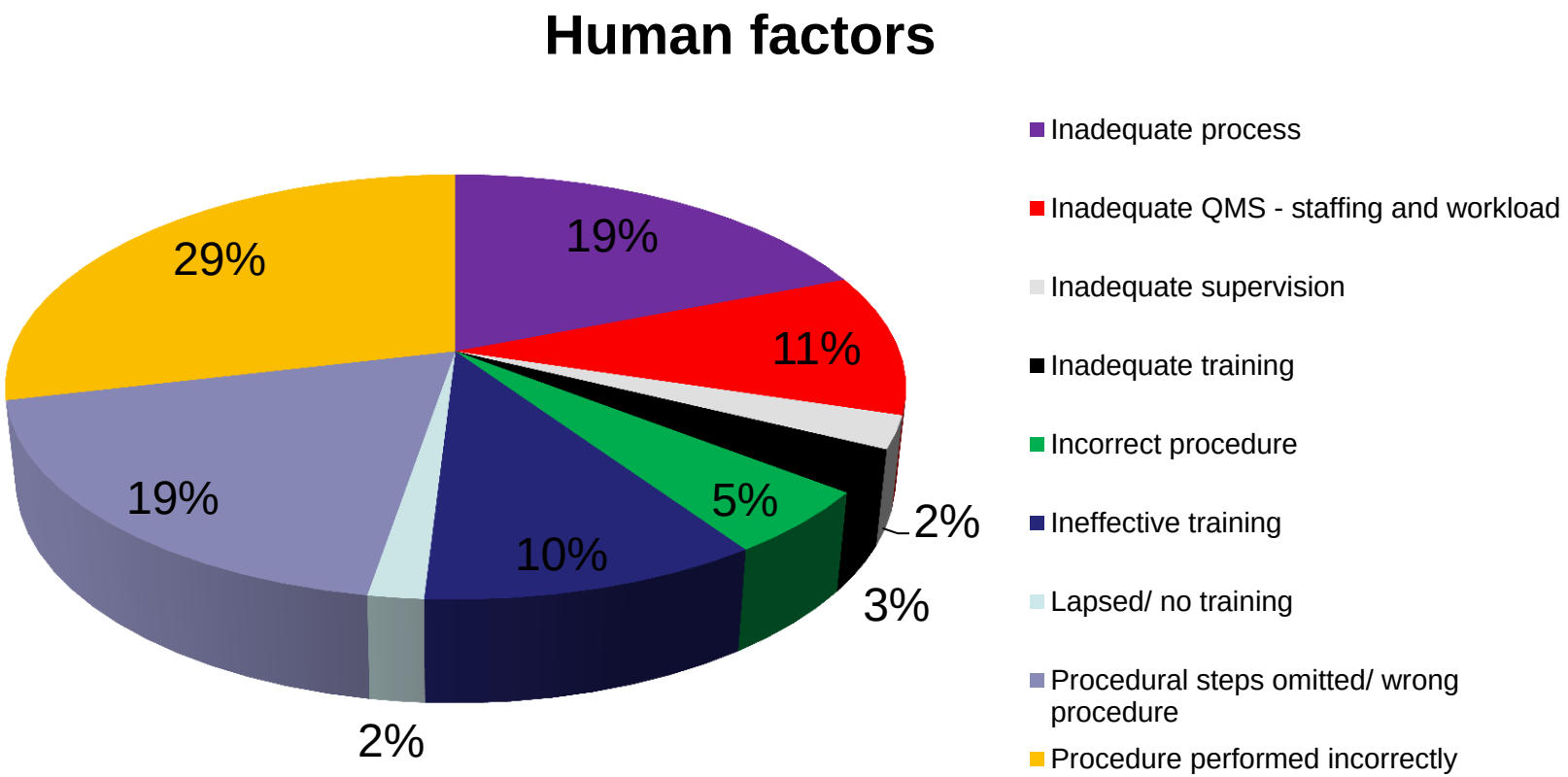

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Human factors

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- First year where reports have been assessed to identify significant staffing and workload problems
- 11% of reports are a result of errors made when workload was considered to be too high or staffing too low (these do not include reports where errors were made when staff were considered “busy”, but staffing and workload within accepted levels)
- Nearly 50% of all reports due to errors made by staff where procedures were performed incorrectly, the wrong procedure performed or steps missed with no other QMS failures identified
  - These are usually due to wrong decision making or unexplained slips and lapses rather than faults in the QMS
  - More thorough investigation or detailed reporting may have identified alternative human factors
- Nearly 20% of reports are considered to be due to the lack of a robust process

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Human factors

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- Reporters must continue to investigate thoroughly to identify all root causes and contributory factors
- Detailed CAPA needs to be produced to address human factors involved
- Work needs to be done to make processes more robust and SOPs written that are detailed enough for staff to know exactly what to do, even when tasks don’t go to plan

- MHRA will continue identify staffing and workload issues and inspectors often raise this at inspection
- MHRA will continue to support the industry in addressing it

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SAR Reporting

- Phase 1 of the Joint Haemovigilance Project was released on time with no major problems
- Phase 2 is under construction which will incorporate SAE reporting
  - Improvements to information to feedback to reporters following analysis of reports by SHOT or MHRA
  - Provide a seamless link between SABRE and Dendrite systems
  - Allow SHOT to update SABRE confirmation reports directly from Dendrite
  - Reduce SAR reporting burden on reporters (MHRA/SHOT – Centralised reporting system)
- Work is scheduled be completed and implemented before the end of the year
- Regular consolidation of figures by SHOT and SABRE
- Phase 3 is under investigation

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2016 Data Summary Points

- Changes to reporting process have resulted in changes to the numbers of reports received in SABRE
- It will take at least another 12 months to assess the affect of these changes to analysis of the data
- Human error still remains the single largest cause of error
- At least 10% of all reports are considered to be related to staffing and workload factors
- SARs are being classified and categorised by clinical experts in SHOT where the reporting function, for SAR to the EU, will remain with the MHRA as the UK competent authority.
- Will give a better idea of the UK SAR type and numbers reported to the EU Annually.

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Blood Compliance Report (BCR) Process Update

Vivian Rowland

01 November 2016

Topics for discussion

BCR April 15 – March 16 Outcome

Common Issues with Improvements

BCR April 15 – March 16 Outcome

2016 BCR Outcome

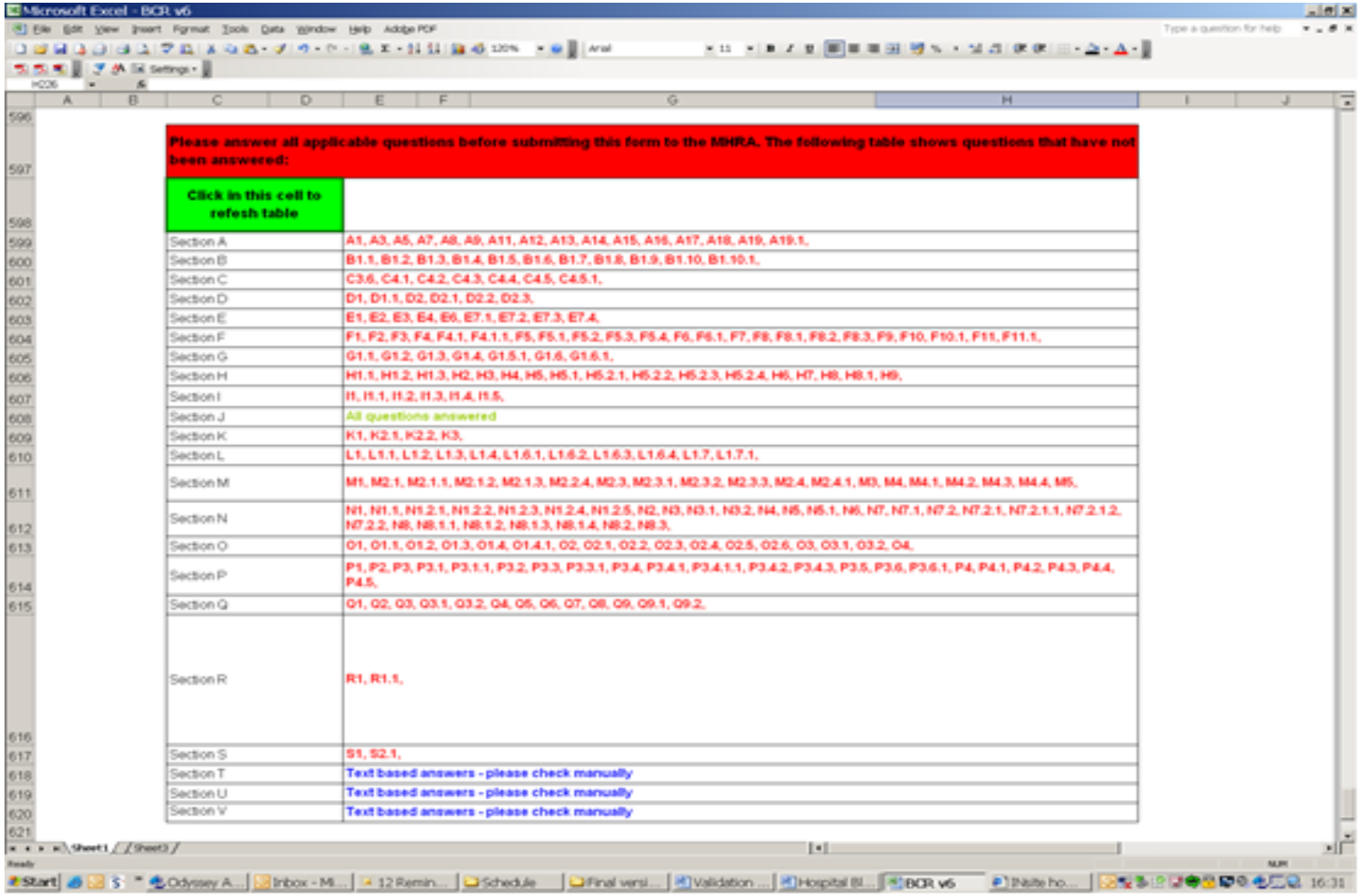
HBB BCR received	303
Late submission (after 30 April 2016)	52
BAT referral required	63
Site compliant	285
Site required further assessment	1
Site required inspection	17 (including 1 control site)

Common Issues

Common Issues

- Missing answers on BCR
- Late submissions
- Incorrect Hospital name or Trust / Private Healthcare Organisation Name
- Compliance letters not received

Missing answers on BCR



How to manage the issue

- Submitted BCR will be pre-reviewed on receipt
- Return to the HBB manager for completion

Late submissions

- Late submission of BCR or Declaration form

- Declaration form was not submitted with the BCR
  - CEO or Registered Person was not available

- Incorrect declaration form was used

Late submissions

Completing the declaration page

The declaration page is a separate document which can be downloaded from the GOV.UK. Signed declaration pages must be returned by email with the compliance report.

The report must be signed by the Chief Executive Officer (in the case of hospital blood bank located in a hospital managed by a health service body), or the Registered Person (in the case of an independent hospital).

The content of the declaration should be read carefully by the CEO or Registered Person before signing.

Late submissions

Blood bank managers must fill in the blood bank compliance report and declaration form and send it to MHRA.

Facility managers must fill in the blood facility declaration form and send it to MHRA.

Incorrect Hospital name or Trust / Private Healthcare Organisation Name

General Information	
Hospital name	
Trust / Private Healthcare Organisation Name (where applicable)	

How to manage the issue

- Revise Guidance Note
  - ➢ colour / bold text to highlight deadline and areas that require special attention
- BCR Admin Team request for Declaration Form if not submit with the BCR
- Further work instructions on the Blood Forum
- Interim compliance report for HBB

Compliance letters not received

Compliance letters were not delivered to the site contact or the department

General Information	
Hospital name	Arrowe Park Hospital
Trust / Private Healthcare Organisation Name (where applicable)	Wirral University Teaching Hospital NHS Trust
Address line 1:	Arrowe Park Road
Address line 2:	Upton
Town/city:	Wirral
County:	Merseyside
Post Code	CH49 5PE
Contact name	Steven Carter

How to manage the issue

- Revise the compliance letter templates
- Electronic issuance of compliance letters

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Thank you

Any questions?

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The Blood Forum

Stephen Grayson, Senior GMDP Inspector

Why

- The MHRA committed through the Blood Consultative Committee (BCC) to introduce a stakeholder communication tool
- The aim is to improve communication throughout the blood community, not just relying on the BCC
- To provide a communication method that permits stakeholders to build contact networks and share experiences

What

- The decision was made for the MHRA to develop and host a discussion Forum specifically for blood stakeholders
- A Forum was already in place for GCP stakeholders which has proved very successful
- Building on the GCP experience a blood discussion Forum has been developed.
- In addition to providing a discussion platform, the Forum has also been populated with guidance previously issued, and links to relevant websites

Who

- The Forum is intended to be usable by all stakeholders
- Includes those working in Blood Establishments, Hospital Blood Banks, Blood Facilities and others with an interest
- MHRA inspectors will monitor the Forum and provide guidance where needed, but it is expected that the majority of use will be by stakeholders, sharing experiences and helping to resolve issues

How

- Users will need to register to use the site
- The content will be moderated by MHRA blood inspectors. The target of releasing posts for viewing within 3 working days (as soon as possible)
- The Forum is not intended to replace the formal system of seeking specific guidance from the MHRA which is still in place, but as a means for stakeholders to highlight and discuss issues with the wider blood community

Where

- The Forum is hosted by the MHRA and can be accessed through the MHRA website: Blood Forum

- An MHRA Inspectorate Blog was published this morning, launching the Forum which also includes a link to the Forum: MHRA Inspectorate Blog site

When

- The Forum went live yesterday
- The Blog was published on the MHRA website today
- To be successful it needs stakeholders to use it
- **Now it is over to you**. Start using it and you should realise the benefits.

Thank You … Questions?