**Breach Report**

**1 April 2015 - 31 March 2016**

1. **Introduction**

It is a requirement that all breaches of the standards of good clinical practice or of the study protocol are reported to the reviewing REC for the purpose of keeping the favourable ethical opinion under review in light of significant developments in the research. Breach notifications are managed centrally by the HRA and classified as a violation, serious breach, or (allegation of) fraud or misconduct. All breaches are managed individually but general data is also collected for the purpose of identifying themes and trends to enable the sharing of learning outcomes.

The following data fields are recorded for all breaches:

1. Whether the breach notification relates to one or multiple breaches for the same study or more than one study.
2. Whether it was a REC breach (REC not adhering to SOPs)
3. UK or non-UK breach
4. Whether recruitment was halted in response to the breach
5. (For CTIMPs) Whether there was an MHRA inspection, either triggered or routine
6. Study details (title, REC reference, EudraCT number etc.)
7. Sponsor, site & Chief Investigator details.
8. How the breach was initially identified (e.g. routine audit or monitoring)
9. Study type (CTIMP or Other)
10. Breach type (serious breach, violation or alleged fraud or misconduct)
* **Serious breach** - A serious breach of the protocol or of the conditions or principles of Good Clinical Practice (or equivalent standards for the conduct of non CTIMPs) which is likely to affect to a significant degree the safety or physical or mental integrity of the trial subjects, or the scientific value of the research.
* **Violation** - Variations from the protocol which are not agreed in advance or which deviate from the principles of Good Clinical Practice and are the result of error, but do not constitute a serious breach.
* **Fraud and/or misconduct** - Intentional behaviour by a researcher, either alleged or proven, that falls short of good ethical and scientific standards, or the generation of false data with the intent to deceive.
1. **Breach notifications**

The breach notifications received during the reporting period 1 April 2015 - 31 March 2016 are broken down in the following sections:

* 1. **Breach classification**

|  |  |  |
| --- | --- | --- |
|  | **2015 - 2016** | **2014 -2015** |
| **Category** | **No.** | **%** | **No.** | **%** |
| Serious breach | 135 | 53.36 | 86 | 41.75 |
| Violation | 115 | 45.45 | 118 | 57.28 |
| Fraud or misconduct | 3 | 1.19 | 2 | 0.97 |
| ***Total*** | **253** | **100.00** | **206** | **100.00** |

Table 2.1

* 1. **Type of study**

|  |  |  |
| --- | --- | --- |
|  | **2015 -2016** | **2014 -2015** |
| **Study Type** | **No.** | **%** | **No.** | **%** |
| CTIMPs | 166 | 65.61 | 147 | 71.36 |
| Other | 87 | 34.39 | 59 | 28.64 |
| ***Total*** | **253** | **100.00** | **206** | **100.00** |

Table 2.2

The number of breaches recorded centrally has increased in the last reporting period by 23%. This primarily relates to non CTIMP studies and may be due to various reasons. We have improved the breaches policy and procedure document to that staff are clearer in regards to what is required when they receive a breach and we have also updated the information which goes to applicants when they receive a favourable opinion to include reporting breaches for non-CTIMPs to the REC. The CTIMP number has not altered significantly as this requirement for reporting and the reporting mechanism via the MHRA has remained consistent.

* 1. **Other factors**

|  |  |  |
| --- | --- | --- |
|  | **2015 - 2016** | **2014 - 2015** |
| **Factor** | **No.** | **%** |  |  |
| Multiple breaches\* | 10 | 3.95 | 9 | 4.37 |
| REC breach\*\* | 5 | 2.12 | 2 | 0.97 |
| Study halted | 19 | 7.50 | 11 | 5.34 |

Table 2.3

\*Where one breach notification contains a number of individual breaches

\*\*Where the REC has breached Standard Operating Procedures

Summary of REC breaches

1. Relates to a PhD study. The REC suggested that the section at the bottom of the consent form, which detailed the person who was taking consent, was not required. However, this was misinterpreted in the provisional opinion letter to say that consent was not required. The student therefore did not take consent and subsequently there was a significant delay in awarding the PhD.

2. A breach notification was submitted to the REC and additionally, a substantial amendment was submitted to halt study procedures until the breach could be fully investigated. This is the process which is expected but the REC gave an unfavourable opinion for the substantial amendment. The REC was advised that a substantial amendment to inform the REC that study procedures had been halted would be considered good practice and there was no reason to issue an unfavourable opinion for this type of substantial amendment. The REC agreed and subsequently issued a favourable opinion.

3. A sponsor contacted the REC Manager to confirm whether a Site Specific Assessment (SSA) form needed to be submitted for an-NHS site. The sponsor was advised that this was not required but this information was incorrect. The MHRA later picked up during an inspection that the site did not have the appropriate SSA approval in place.

4. The REC gave a favourable opinion for a clinical trial involving children which involved payment to the child participants. However, the Clinical Trial Regulations explicitly states that children should not receive payment to take part in CTIMPs. A substantial amendment to not provide payment was subsequently submitted as the site rose the issue with the Sponsor that payment to children in a CTIMP is not allowed. The REC gave an unfavourable opinion stating that the payment should continue. The REC was advised that this is against the Clinical Trial Regulations. The REC Chair stated that the REC was not aware that such payment was not allowed and agreed to vary the opinion to a favourable opinion. A reminder note was issued to all RECs and also will be picked up in the CTIMP training for staff and members.

5. A REC Member e-mailed an excerpt of the REC meeting minutes to an individual who is not a REC member. The information related to the discussion which had taken place when reviewing the application which was submitted to a number of RECs as part of a review of REC consistency (The WHEAT study). The REC member concerned was spoken to and reminded about the need for confidentiality of discussions and documents.

Studies halted

|  |  |  |
| --- | --- | --- |
| 1 | No CTA obtained for trial of drugs used off-label. | Trial halted pending triggered MHRA inspection. Recruitment and use of data halted pending application for CTA. Ongoing. |
| 2 | Allegations made by staff member regarding poor PI oversight at one site. | Trial halted pending triggered MHRA inspection. MHRA found little foundation for allegations - trial restarted |
| 3 | No R&D approval – misunderstanding of process | Study halted pending R&D approval. No safety issues. |
| 4 | Study drug given to patient off-trial  | MHRA investigation concluded no safety issues. Study restarted |
| 5 | Monitoring visit revealed quality defects | Study halted pending resolution of issues. Now resolved to MHRA’s satisfaction so study restarted. |
| 6 | One participant given trial pack without being randomised. | Study halted, staff retrained and study restarted |
| 7 | Consenting issues. | Study halted then restarted – problems continued and study was closed. |
| 8 | IMP accountability and randomisation concerns. | Study halted then terminated. |
| 9 | No R&D approval. | Study halted pending R&D approval – now obtained and study restarted. |
| 10 | Procedure omitted from protocol though was described in the information for participants. | Study halted pending approval of amendment to amend protocol. Now restarted |
| 11 | IMP accountability – drug pack damaged. | Study halted pending MHRA triggered inspection. Outcome satisfactory and study restarted. |
| 12 | Dispute over whether CTIMP or not (reviewed by non-recognised REC).  | Study halted pending MHRA investigation. Concluded non-CTIMP – study restarted. |
| 13 | Consent forms lost. | Study halted temporarily pending investigation and implementation of preventative measures.  |
| 14 | IMP mis-labelled but none used. | Study halted temporarily pending investigation and implementation of preventative measures.  |
| 15 | IMP integrity – foreign body found during preparation. | Study halted pending issue of new batch of IMP. |
| 16 | Participant fatality. | Study halted pending investigation. Fatality unrelated to study which restarted. |
| 17 | CTIMP not reviewed as CTIMP (reviewed by recognised REC). | Study halted pending re-review as CTIMP – now has a favourable opinion |
| 18 | No R&D approval. Pre-screening scans conducted to test scanning protocol with healthy volunteers. | Study halted pending R&D approval – now obtained and study restarted. |
| 19 | One participant did not receive treatment in terms of study protocol. | Study halted at site indefinitely and is under investigation – study overall continues. |

* 1. **Type of breach**

|  |  |  |
| --- | --- | --- |
|  | **2015 - 2016** | **2014 - 2015** |
| **Type of breach** | **No.**  | **% of total**  | **No.**  | **% of total**  |
| IMP | 54 | 21.34 | 51 | 24.75 |
| Recruitment/informed consent | 85 | 33.60 | 75 | 36.41 |
| Record keeping | 9 | 3.56 | 11 | 5.34 |
| Safety reporting | 8 | 3.16 | 13 | 6.31 |
| No approval | 19 | 7.51 | 17 | 8.25 |
| Tissue | 10 | 3.95 | 6 | 2.91 |
| Data protection | 28 | 11.07 | 17 | 8.25 |
| Other | 75 | 29.64 | 71 | 34.47 |

Table 2.4

1. **Summary of actions taken**

The HRA maintains close liaison with the MHRA when managing breaches for CTIMPs. It follows the lead taken by the MHRA which considers breaches on the basis of their impact on patient safety and validity of trial data. However, the REC is asked to consider any ethical implication of the breach, particularly in relation to the information provided to participants and ensuring that any consent was, and continues to be, informed.

This generally involves a review by a Sub-Committee of the reviewing REC, which may request further information/action in the interests of participants. For research other than CTIMPs, the REC is asked to consider all aspects of the breach to ensure that the favourable ethical opinion which was issued remains valid.

* 1. **Examples of further information/action requested by RECs**
* Assurances that adequate action has been taken to rectify the problem and prevent recurrences for future participants in the research
* Confirmation that samples taken without appropriate consent for research have been destroyed.
* Confirmation that an amendment has been submitted to rectify the cause of the breach
* Confirmation that appropriate steps are in place to ensure patient confidentiality

*\*It is noted that effective monitoring and reporting procedures will inevitably result in the proactive sponsors and sites appearing more often than the sponsors and sites with the inadequate reporting procedures. It is therefore important to take a proportionate approach and ensure that proactive monitoring and reporting is not being penalised. The HRA is also keen to provide support and assistance when issues are highlighted rather than taking a heavy handed approach.*

* Reassurances about training, revisions to safety protocols etc.

Additional action is taken exceptionally where deemed necessary in the interests of participants.

Note is taken of multiple transgressions\*, whether occurring at a particular site or in association with a particular individual, and information is shared with the MHRA on such matters where appropriate.

Due to the relatively low number of breach notifications received, RECs review breaches infrequently. An information sheet was therefore produced and sent out to REC members to support them in their role when dealing with breaches.

1. **Position at end of year**

At the end of the year under review, the position of breaches received was as follows:

|  |  |  |
| --- | --- | --- |
|  | **2015 - 2016** | **2014 - 2015** |
|  | **Open** | **Closed** |  | **Open** | **Closed** |  |
| **Study type** | **No.** | **%** | **No.**  | **%** | **Total** | **No.** | **%** | **No.**  | **%** | **Total** |
| CTIMPs | 74 | 29.25 | 92 | 36.36 | 166 | 75 | 36.4 | 72 | 35.0 | 147 |
| Other | 34 | 13.44 | 53 | 20.95 | 87 | 30 | 14.6 | 29 | 14.0 | 59 |
| ***Total*** | **108** | 42.69 | **145** | 57.31 | **253** | **105** | **51.0** | **101** | **49.0** | **206** |

Table 4.1