Quality Control Document:

Finding Classification Grid

# Purpose

This grid allows compliance reviewers (auditors) to appropriately classify their audit findings. This tool has been developed to facilitate the review of research projects, Human Tissue Authority (HTA)-licensed tissue banks and Good Manufacturing Practice (GMP) facilities. Some adaptation may be required when using it to carry out reviews in other areas. The use of this classification grid is optional, but predefined classifications must be used to grade audit findings, as detailed in the Compliance Review SOP (UoB-CPR-SOP-001). The Clinical Research Compliance Team (CRCT) uses this findings classification grid when it carries out audits.

# Instructions

1. The compliance reviewer generates a report as per internal processes, capturing sufficient detail to allow for findings to be classified.
2. Consulting the tables within this document, the compliance reviewer assesses each individual finding to assign the appropriate ranking (high, medium, low) relating to its (i) impact, (ii) frequency and (iii) action.
3. The compliance reviewer then uses each of the finding’s assigned rankings to obtain the finding’s overall classification (critical, major, other) from the classification grid.
4. Where any graded finding has already been identified and reported (e.g. during a previous audit), and no corrective action has yet been taken, the compliance reviewer will assign an overall ‘finding classification’ that is one level higher than the previous reviewer’s overall classification (i.e. from ‘other’ to ‘major’ or from ‘major’ to ‘critical’).
5. The report detailing the compliance reviewer’s findings, and associated classifications, will be reviewed and approved by the independent, competent person as per the Compliance Review SOP (UoB-CPR-SOP-001).
6. The compliance reviewer files a copy of the report and distributes it to the reviewee, and all pre-agreed relevant parties.

# Related documents

* UoB-CPR-SOP-001 Compliance Review
* UoB-CPR-QCD-002 Site Visit Log

Access to the full UoB QMS for clinical research is available via the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx).

# Impact, frequency and action taken

## Impact

Assess impact on:

* data/documentation integrity
* participant confidentiality, rights, safety, dignity and/or wellbeing
* product safety
* regulatory requirements
* local policies and/or procedures
* contractual obligations.

|  |  |
| --- | --- |
| Impact ranking: | Description of impact: |
| High | The finding has impacted on, or has significant potential to impact on: participant confidentiality, rights, safety, dignity, wellbeing; data integrity and/or product safety. It may have also impacted on any of the other areas listed above.  |
| Medium | The finding has some potential to impact on: participant rights, safety, dignity, wellbeing; data integrity and/or product safety. However, evidence has not been observed during the audit. In addition, the finding may have impacted on any of the other areas listed above.  |
| Low | The finding has potential for minor impact on documentation integrity, regulatory requirements, local policies and/or procedures and/or contractual obligations. |

## Frequency

Assess the frequency of the finding, or the probability of the finding to happen again.

|  |  |
| --- | --- |
| Frequency ranking: | Description of frequency: |
| High | A high occurrence in the area (>49%), or in a single key document/participant data point, or it is very likely that the issue will happen again. Note: where only a sample of three was taken, high occurrence is where the finding occurred across all three samples.  |
| Medium | A medium occurrence in the area (25-49%), or neutral likelihood of the issue to happen again. Note: where only a sample of three was taken, medium occurrence is where the finding occurred in two of the three samples. |
| Low | Isolated incident or low occurrence in the area (<25%), or it is very unlikely that the issue will happen again. Note: where only a sample of three was taken, low occurrence is where the finding occurred in one of the three samples. |

## Action taken

Assess what action was taken by the compliance reviewee.

|  |  |
| --- | --- |
| Action ranking: | Description of action: |
| High | Finding (from any source) not previously identified and reported as a finding, or previously identified but no action has been taken. The finding is not immediately resolvable. For example, there is a discrepancy between a data field in the source data and the corresponding data field within the electronic database. On review, there is no entered data in the field on the source data, but there is an entry in the electronic database. Staff need to contact the site or participant to resolve this. This will take time and is therefore not resolvable immediately. |
| Low | Finding not previously identified and reported as a finding. Therefore, no action has been taken, but the finding is resolvable. For example, there is a discrepancy between data entered in a field on the source data and data entered in an electronic database. The data is present in both fields, and the electronic database can be corrected immediately by staff using the source data. This is resolvable immediately. |

## Classification grid

Note: A serious breach of GCP, the need to halt GMP production, fraud, and/or serious misconduct will be classified as ‘critical’ regardless of rankings below.

|  |  |  |  |
| --- | --- | --- | --- |
| Impact ranking | Frequency ranking | Action ranking | Finding Classification |
| **H** | **H** | **H** | **CRITICAL** |
| **H** | **H** | **L** | **CRITICAL** |
| **H** | **M** | **H** | **CRITICAL** |
| **H** | **M** | **L** | **MAJOR** |
| **H** | **L** | **H** | **MAJOR** |
| **H** | **L** | **L** | **MAJOR** |
| **M** | **H** | **H** | **MAJOR** |
| **M** | **H** | **L** | **MAJOR** |
| **M** | **M** | **H** | **MAJOR** |
| **M** | **M** | **L** | **MAJOR** |
| **M** | **L** | **H** | **OTHER** |
| **M** | **L** | **L** | **OTHER** |
| **L** | **H** | **H** | **OTHER** |
| **L** | **H** | **L** | **OTHER** |
| **L** | **M** | **H** | **OTHER** |
| **L** | **M** | **L** | **OTHER** |
| **L** | **L** | **H** | **OTHER** |
| **L** | **L** | **L** | **OTHER** |

## Example finding and scoring breakdown

SOP deviation: SOP v4.0 effective date 25-Aug-2018 section 9.1 Develop a Monitoring Plan states “The monitoring plan should document any oversight committees to be used for the trial including the Trial Management Group (TMG), Trial Steering Committee (TSC) Data Monitoring Committee (DMC)”.

Whilst reviewing monitoring plans for all three trials, the reviewer found no documentation to evidence the involvement of any oversight committee. However, during the audit, they interviewed staff who confirmed that oversight committees were involved in all three trials.

Grading:

|  |  |  |
| --- | --- | --- |
| Impact ranking – Low |  | Overall classification: **Other** |
| Frequency ranking – High |  |
| Action ranking – Low |  |

## Classification definitions

### GCP-related compliance reviews

The table below is an example of the classification definitions that may be used in the review of a research project and/or CTU. The definitions are adapted from the [MHRA grading of GCP inspection findings](https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#during-the-inspection).

|  |  |
| --- | --- |
| Definition: | Description: |
| Critical | Where practices or processes have resulted in a significant deviation and unjustified departure from: the protocol, the UoB quality management system (QMS), the area of Good Practice (GxP) reviewed and/or regulatory requirements. There is also evidence that: * participant safety or wellbeing has been jeopardised, or has significant potential to be
* the validity and/or integrity of data/documentation has been compromised
* the validity and/or integrity of clinical research conduct has been compromised
* the integrity of any external-sponsor/third-party contracts has been compromised (if applicable)
* there are a number of major findings, indicating a systematic failure in compliance
* inappropriate, insufficient or untimely corrective action has taken place in response to ‘major’ findings.

Notes * Where inappropriate, insufficient or untimely corrective action has taken place in response to previously reported major non-compliances, this would be classified as ‘critical’
* For CTIMPs and ATIMPs: where provision of the trial master file (TMF) does not comply with Regulation 31A 1-3 of The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006, this would be classified as ‘critical’. For example:
* the TMF is not readily available or accessible
* the TMF is incomplete to such an extent that it cannot form the basis of an audit, and impedes or obstructs auditors in their ability to verify compliance with the regulations.
* A serious breach of GCP and/or the protocol would be classified as ‘critical’.
* Where deliberate fraud and/or serious misconduct is confirmed, this would be classified as ‘critical’ (any impact on participant safety, data integrity, frequency of issue, or action taken notwithstanding).
* A classification of ‘critical’ requires immediate corrective action. Root cause analysis may be performed, and future preventative action is required.
 |
| Major | Where evidence exists that there is a significant deviation from the protocol, UoB QMS, GxP or regulatory requirements. There is also evidence that: * there is a risk to participant safety and/or dignity
* a finding has not yet developed into a ‘critical’ issue but may have the potential to do so unless addressed.

A ‘major’ finding may also be where evidence exists of a number of departures from the protocol, UoB QMS, GxP or regulatory requirements within a single area of responsibility, indicating a systematic failure in compliance. Notes * ‘Major’ findings may be escalated to ‘critical’ findings if any of the defined conditions as detailed in the ‘critical’ definition become apparent.
* A ‘major’ finding may be constituted from the combination of several ‘other’ findings, none of which is ‘major’ on its own. This type of ‘major’ finding should be explained and reported as such.
* Previously-reported findings, initially classified as ‘other’, should be escalated to ‘major’ where inappropriate, insufficient or untimely corrective action has taken place.
* A finding classified as ‘major’ requires prompt corrective action. Root cause analysis may be performed, and future preventative action is required.
 |
| Other | Where practices or processes result in a deviation from accepted standards, but the deviation does not adversely affect:* the safety or wellbeing of participants
* the integrity of the data/documentation
* clinical research conduct.

The deviation would not constitute a classification of either ‘critical’ or ‘major’. Notes * Findings classified as ‘other’ may be escalated to ‘major’ or ‘critical’ if any of the defined conditions as detailed in the ‘major’ or ‘critical’ definition become apparent.
* Corrective action is required within a timeframe appropriate to the issue found, in order to improve the quality of existing documentation/processes, or to prevent a potential negative impact on quality or compliance. Future preventative action may not be required.
 |

### HTA-related compliance reviews

The table below is an example of the classification definitions that may be used in a review of an HTA-licensed tissue bank. The definitions are based on the [HTA Research Licensing Standards and Guidance](https://www.hta.gov.uk/guidance-professionals/guidance-sector/research/research-licensing-standards-and-guidance).

|  |  |
| --- | --- |
| Definition: | Description: |
| Critical | A ‘critical’ finding (shortfall) is: * a shortfall that poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions; or
* a combination of several ‘major’ finding (shortfalls), none of which is ‘critical’ on its own, but which together could constitute a ‘critical’ finding (shortfall) and should be explained and reported as such.
 |
| Major | A ‘major’ finding (shortfall) is a non-critical shortfall that:  * poses a risk to human safety and/or dignity
* indicates a failure to carry out satisfactory procedures
* indicates a breach of the relevant CoPs, the HT Act and other relevant professional and statutory guidelines
* has the potential to become a ‘critical’ finding (shortfall) unless addressed; or
* is a combination of several ‘other’ findings (shortfalls), none of which is ‘major’ on its own, but when combined they could constitute a ‘major’ finding (shortfall) and should be explained and reported as such.
 |
| Other | A ‘other’ finding (shortfall) that: * cannot be classified as either ‘critical’ or ‘major’, but which indicates a departure from expected standards.

Note: the classification of ‘other’ is equivalent to ‘minor’ used by the HTA.  |

### GMP-related compliance reviews

The table below is an example of the classification definitions that may be used in a review of a GMP facility. The definitions are based on the [MHRA grading of GMP and Good Distribution Practice (GDP) inspection findings](https://www.gov.uk/guidance/good-manufacturing-practice-and-good-distribution-practice#grading-of-inspection-findings).

|  |  |
| --- | --- |
| Definition: | Description: |
| Critical | A deficiency which has produced, or significantly risks producing, a product which is harmful to humans or veterinary patients, or which could result in a harmful residue in a food-producing animal.Any departure from good distribution practice that results in a significant risk to patients. This includes an activity which increases the risk of counterfeit medicines reaching patients. |
| Major | A non-critical deficiency that:* has, or may produce, a product that doesn’t comply with its marketing authorisation
* indicates a major deviation from GMP or GDP, or from the terms of the manufacturer licence or wholesale licence
* indicates a failure to carry out satisfactory batch-release procedures, or (within EU) a failure of the Qualified Person or Responsible Person to fulfil their legal duties
* a combination of several ‘other’ deficiencies that on their own may not be ‘major’, but when combined may represent a major deficiency and should be explained and reported as such.
 |
| Other | A deficiency that cannot be classified as either ‘critical’ or ‘major’, or there is not enough information to classify it as ‘critical’ or ‘major’, but that indicates a departure from good manufacturing and distribution practice. |

# Reference and frameworks

* HTA Research Licensing Standards and Guidance: <https://www.hta.gov.uk/guidance-professionals/guidance-sector/research/research-licensing-standards-and-guidance>
* MHRA grading of GCP inspection findings: <https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#during-the-inspection>
* MHRA grading of GMP and GDP inspection findings: <https://www.gov.uk/guidance/good-manufacturing-practice-and-good-distribution-practice#grading-of-inspection-findings>