SOP-QA-35 V6

Title: Unblinding

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Document History

Version	Description of update	Date Effective
5	Minor updates throughout & reference to emergency unblinding at 3.7	09-08-23
6	Updated regulations at 1.2 Updated terminology at 3.5, 3.11, 3.12, 3.14 and 4.1	28-04-26

1. Scope

1.1 This SOP is applicable to Sponsor staff and research staff undertaking randomised blinded projects sponsored by the University of Aberdeen (UoA) and/or NHS Grampian (NHSG).

1.2 This includes Clinical Trials of Investigational Medicinal Products (CTIMPs) covered by the UK Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, or equivalent local legislation outside the UK.

1.3 This Standard Operating Procedure (SOP) details the procedures to:

- Unblind a subject in an emergency situation.
- Unblind data for the purpose of notification to the Data Monitoring Committee (DMC).
- Manage accidental unblinding.
- Unblind a research project for analysis purposes at the end of the trial.
- Unblinding due to other purposes

2. Responsibilities

Trial team	Ensure no unnecessary unblinding occurs.
Chief Investigator	Ensure the emergency unblinding process is in place, including out-of-hours access, and that all of the trial team are aware of the procedure.

3. Procedure

3.1 For the purpose of this SOP, 'Unblinding' is synonymous with 'Code Breaking' and with 'Unmasking'; all terms that are frequently used in research protocols.

3.2 Treatment codes shall be broken before reporting a Suspected Unexpected Serious Adverse Reaction (SUSAR) to the Medicines and Healthcare products Regulatory Agency (MHRA) and the Research Ethics Committee (REC).

3.3 Where appropriate, participants in CTIMPs shall be issued with 'In case of emergency' cards to be carried at all times. Minimum details on the card shall include the trial emergency

contact number, study identifier and details of the potential IMP (eg Bisoprolol 5mg or Placebo) and participant study number.

3.4 The Unblinding system shall be tested, including contact with the system, prior to recruitment of the first participant. The process shall be documented and reviewed at the Study Initiation Visit.

3.5 If the trial or a single participant is accidentally unblinded or unblinded due to a serious adverse event (SAE) the CI, or delegate, is responsible for promptly documenting the series of events and notifying the Sponsor (TMP-QA-26).

3.6 The details of all unblinding shall be included in the statistical report.

Emergency unblinding of individuals

3.7 If emergency unblinding is not required within a study, this shall be documented in the protocol.

3.8 Any member of the trial team, or a health care professional involved in the care of a participant, may unblind or request unblinding in an emergency situation. Following such a request, the information shall be transmitted to the requesting party.

3.9 All care shall be taken to ensure that the study team are kept blinded.

3.10 If the Clinical Trials Pharmacy, or an individual named on the Delegation Log, has performed the procedure, they shall inform the Sponsor (via pharmaco@abdn.ac.uk).

3.11 Details of any emergency unblinding shall be provided to Sponsor and documented fully in the Sponsor File, Investigator Trial Master File (TMF), Pharmacy File and Investigator Site File(s), as appropriate (see TMP-QA-26). This includes, but may not be limited to:

- Date
- Trial identifier
- Participant details
- Reason for unblinding
- The result of the unblinding (**when required**)
- Name and role of the individual requesting the unblinding
- Name and role of the individual carrying out the unblinding
- Details on the CI's decision for the participant to remain in the trial, or be withdrawn.

3.12 The Sponsor may instruct the CI, or delegate, to unblind a participant in an emergency situation. In this event the Research Governance Team or Sponsor Quality Assurance Manager shall be provided with the unblind. However, on a case-by-case basis a decision to unblind a wider team may be necessary.

Unblinding for DMC

3.13 A named statistician (ideally not involved with the final data analysis or with the study) shall receive the relevant codes, perform the interim analysis and prepare an unblinded report for the DMC if this is requested. A record shall be kept in the Investigator TMF of the name of the statistician, the date they were supplied with the relevant code breaks and the location of the results. The unblinded data and the results supplied to the DMC shall **not** be accessible to the CI **or** trial staff (see SOP-QA-17 - Project committees).

Accidental unblinding

3.14 Details of any accidental unblinding shall be documented fully. This includes, but may not be limited to:

- Date
- Trial identifier
- Participant details
- Reason for accidental unblinding
- Name and role of the individual responsible for the unblinding
- Action taken to prevent recurrence
- Details on the CI's decision for the participant to remain in the trial, or be withdrawn

The unblinding template should be completed (TMP-QA-26) and forwarded to Sponsor at pharmaco@abdn.ac.uk.

Unblinding at the end of trial

3.15 The Statistical Analysis Plan shall be provided in the protocol, or be finalised prior to the release of the randomisation codes. Any changes to the statistical analysis plan shall be version controlled.

3.16 A record shall be kept in the Investigator TMF to confirm when the randomisation code was requested and when provided.

Other Unbinding

3.17 There may be other cases where participants may be unblinded, for example:

- Real time unblinding for DMC.
- Legal instruction.
- Participant/GP request to know treatment allocation for planning future treatment.

Sponsor approval should be sought prior to unblinding. If approval is given, information should be provided to the requesting party and the unblinding template should be completed (TMP-QA-26) and forwarded to Sponsor at pharmaco@abdn.ac.uk. All care shall be taken to ensure that the study team are kept blinded.

4. Abbreviations and definitions

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
DMC	Data Monitoring Committee
MDCI	Medical Device Clinical Investigation
MHRA	Medicines and Healthcare products Regulatory Agency
REC	Research Ethics Committee
SAE	Serious Adverse Event
SUSAR	Suspected Unexpected Serious Adverse reaction
TMF	Trial Master File
TSC	Trial Steering Committee

Definition

4.1 A 'blind' study is a clinical trial in which the participant or the Investigator (or both) are unaware of which trial product/drug the participant is taking or which study arm the participant is in.

4.2 When only one is blinded to the treatment allocation this is a 'single blind' study. When both do not know the treatment, the study is 'double-blind'.

4.3 Unblinding is the process by which the allocation code is broken so that the CI and/or a clinician managing the participant and/or trial statistician and/or Sponsor delegate becomes aware of the intervention.

5. Related documentation and references

SOP-QA-15	Management of Medicinal Products used in research
SOP-QA-17	Project committees
SOP-QA-18	Randomisation and blinding for controlled trials
SOP-QA-22	Adverse Events in CTIMPs
TMP-QA-26	Emergency Unblinding Form