# ADVERSE EVENT & SERIOUS ADVERSE EVENT COMPLETION GUIDELINES

## Contents



## Rationale for collection and reporting

The collection and reporting of adverse events (AEs) and Serious Adverse Events (SAEs) will be in accordance with Good Clinical Practice (GCP) and the Research Governance Framework 2005.

Safety will be assessed continuously throughout the trial. Safety monitoring has been delegated by the Sponsor (University of Birmingham) to the BCTU. There are no Investigational Medicinal Products being used as part of the PD COMM trial. A risk assessment of the PD COMM trial has been performed with the SLT interventions considered to be of low risk.

There may be a small increased risk of vocal strain or abuse, and this is stated clearly in the PIS. Every effort will be made to minimise the risk of vocal strain or abuse. Speech and language therapists are trained to identify and rehabilitate vocal strain so, if present, the therapist will be quick to identify and address it. No other risks are expected to arise from taking part in the trial. It is therefore reasonable to **collect only targeted AEs related to vocal strain or abuse**. No SAEs are anticipated as a unique consequence of participation in PD COMM, but reporting requirements are clearly outlined in this section.

## Adverse Events (AEs)

The standard AE definition is as below:

AE: Any untoward medical occurrence in a trial patient to whom a research treatment or procedure has been administered, including occurrences which are not necessarily caused by or related to that treatment or procedure.

AEs are commonly encountered in people with PD. However, very few are likely to be related to the SLT. As the adverse events seen in this population are well known, **only AEs relating to vocal strain or abuse will be reported**.

For participants on a therapy arm, any vocal strain or abuse believed to be associated with treatment will be identified by the therapists at the participants' therapy session. These AEs should be captured on the AE log (see section 10.4.1 of the protocol). BCTU will also check that no vocal strain or abuse has occurred following participants reporting out-patients appointments with ear, nose and throat (ENT) specialists on Resource Usage forms. The therapy notes will be checked and compared with the SLT treatment forms and AE Log for quality assurance.

Participants that are randomised to the control arm will have their AEs checked via the Resource Usage form - should the participant indicate they had an ENT referral, the Trials Office will query with site to clarify whether this was an SAE. At the 12 month clinical visit, the medical professional will also check whether any AEs have occurred since entering the trial,

## Serious Adverse Events (SAEs)

The definition of an SAE is an untoward event that:

- results in death;
- is life-threatening*;
- requires hospitalisation** or prolongation of existing hospitalisation;
- results in persistent or significant disability or incapacity;
- or, is otherwise considered medically significant by the Investigator

*The term "life-threatening" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
** Patients must be formally admitted – waiting in out-patients or A&E does not constitute an SAE (even though this can sometimes be overnight). Similarly, planned hospitalisations that clearly are not related to the condition under investigation or hospitalisations/prolongation of hospitalisation due to social reasons should not be considered as SAEs.

Investigators will only report AEs associated with vocal strain or abuse that meet the definition of an SAE (see '(S)AE Reporting Procedures - At Site' for details on how to report an SAE), SAEs that are expected and do not require reporting on an SAE form are listed in section 'SAEs that do not require reporting on a Serious Adverse Event Form'.

### *SAEs that do not require expedited (immediate) reporting*

SAEs that are not related to vocal strain or abuse are excluded from expedited notification during the course of the trial and do not need to be reported to the Trials Office – see 'SAEs that do not require reporting on a Serious Adverse Event Form' for examples. The only exception to this guidance is death – see section 9 of the protocol.

### *SAEs that do not require reporting on a Serious Adverse Event Form*

The following are expected SAEs for the purpose of the trial and should not be reported on an SAE form:

- Hospital admissions to control symptoms of any medications;
- SAEs that are related to a pre-existing condition;
- SAEs that are related to symptoms or progression of the participant's condition under study;
- Death as a result of the participant's standard treatment or from a pre-existing medical condition;

The above events are examples, this is not an exhaustive list. These SAEs are not considered related to the trial intervention and are therefore excluded from notification to the PD-COMM Trial Office as SAEs. These events should continue to be recorded in the medical records according to local practice.

Investigators should only report SAEs which are attributable to the trial protocol.

## AE Reporting period

Treatment related AEs associated with vocal strain or abuse will be documented and reported from the date of commencement of protocol defined SLT treatment until 30 days after the administration of the last treatment. AEs associated with vocal strain or abuse that are not considered treatment related (ie AEs experienced on the control arm) will be reported from randomisation until 12 months post randomisation via the resource usage questionnaire.

## (S)AE Reporting Procedure – At Site

### *AEs*

Treatment related AEs should be reported on the AE Log. The participant will also be asked if they experienced any AEs on the resource usage form. These will be returned to the PD COMM Trial Office by post.

### *SAEs*

SAEs which do not meet the criteria of 'expected' and are considered related to the trial intervention will be notifiable to the PD-COMM Trial Office **immediately and within 24hours of becoming aware of the event**. On becoming aware that a participant has experienced a trial related SAE, the Investigator (or delegate) must complete, date and sign an SAE Form. The form should be faxed to the PD COMM Trial Office using one of the numbers listed below. The Investigator will also be asked to provide a categorisation of seriousness and causality.

Fax SAE Forms to the Trials Office

and inform trial team of fax submission, via telephone or email

(please see page 3 of the protocol for contact details).

For SAE Forms completed by a member of the site trial team other than the Principal Investigator (PI), the PI will be required to countersign the original SAE Form to confirm agreement with the causality and seriousness/severity assessments. The form should then be returned to the Trials Office and a copy kept in the Site File.

Investigators should also report SAEs to their own Trust in accordance with local practice.

## SAE Causality assessment

AEs defined as serious and which require reporting as an SAE should be reported on an SAE Form. When completing the form, the PI will be asked to define the causality and the severity of the AE.

Causality (relatedness) will be categorised according to the following coding system:

**1**=Unrelated to trial treatment or procedure
**2**=Unlikely to be related to trial treatment or procedure
**3**=Possibly related to trial treatment or procedure
**4**=Probably related to trial treatment or procedure
**5**=Definitely related to trial treatment or procedure

Table 2 provides a definition for each relatedness category.

*Table 2: Definitions of relatedness.*

| Category | Definition | Causality |
|---|---|---|
| **Definitely** | There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out | Related |
| **Probably** | There is evidence to suggest a causal relationship, and the influence of other factors is unlikely | |
| **Possibly** | There is some evidence to suggest a causal relationship (e.g. the event occurred within a reasonable time after administration of LSVTLSVTiohexolLSVT). However, the influence of other factors may have contributed to the event (e.g. the patient's clinical condition, other concomitant events or medication) | |
| **Unlikely** | There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of LSVTLSVTiohexolLSVT). There is another reasonable explanation for the event (e.g. the patient's clinical condition, other concomitant events or medication) | Unrelated |
| **Unrelated** | There is no evidence of any causal relationship | |

## SAE Assessment of Expectedness

Expectedness will be assessed by the CI or designee using this study protocol as the reference document. Table 3 gives definitions of expectedness with respect to SAEs.

*Table 3: Definitions of expectedness*

| Category | Definition |
|---|---|
| **Expected** | An adverse event that is classed in nature as serious and which is consistent with known information about the study related procedures or that is clearly defined in this protocol |
| **Unexpected** | An adverse event that is classed in nature as serious and which is not consistent with known information about the study related procedures |

## SAE Provision of follow-up information

Participants should be followed up until resolution or stabilisation of the event. Follow-up information should be provided on a new SAE Form, making sure to include the SAE reference number, provided by the Trials Unit upon receipt of the initial SAE.