ECTU Central Office WPD ECTU_ST_W4: Additional Guidance on the Contents of a Statistical Analysis Plan (SAP)

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Authorship and Approval			
Name and Designation	Author/Reviewer /Approval/ Authorisation	Date	Signature
Richard A. Parker Senior Research Fellow	Author	11-Dec-2025	Richard Parker Richard Parker (11-Dec-2025 15:51:28 GMT)
Aryelly Rodriguez Senior Statistician	Reviewer	11-Dec-2025	
Christopher Weir Statistics Team Lead	Approver	11-Dec-2025	Christopher Weir (11-Dec-2025 16:23:31 GMT)
Tanya Tharakan QA Manager	QA Authorisation	11-Dec-2025	Tanya Tharakan (11-Dec-2025 16:40:35 GMT)

Document Revision History		
Version No.	Effective Date	Summary of Revisions
1.0	13th March 2017	Initial creation/New Document
2.0	20th February 2019	Updated at scheduled review. Document moved to new WPD template. Changes to wording in Introduction and previous text now section 2.1. Document renumbered throughout
3.0	25 March 2021	Minor edits at scheduled review to sections 2.1.1 to 2.1.7. "Data sharing" has been moved from "Optional Contents" to "Essential Contents".
4.0	16 Oct 2023	Major edits at scheduled review. Many of the items previously included in the WPD have been moved to the

		SOP. Some items in the SAP template have been moved to the WPD. The WPD is now focussed on SAP contents and what to put in a SAP. The title of the WPD has been changed as a result.
5.0		Minor edits at scheduled review. Additional clarification provided regarding data sharing. Item added relating to the need to refer to the SPIRIT and CONSORT checklists when writing the SAP.

1. INTRODUCTION

This Working Practice Document (WPD) provides additional guidance on the contents of a Statistical Analysis Plan (SAP), and should be read in conjunction with ECTU Central Office SOP ECTU_ST_04: Statistical Analysis Plans.

2. INSTRUCTIONS and GUIDANCE

2.1 The SAP should provide full details of all planned summaries and analyses.

2.2 The SAP should define the analysis populations (e.g., intention-to-treat, safety population, as randomised, etc.) to be used, and it should be clear in the SAP which analysis population should be used for each analysis.

2.3 All primary and secondary outcomes should be clearly identified in the SAP.

2.4 The SPIRIT and CONSORT checklists (and any applicable extensions) should be referred to when writing the SAP (https://www.consort-spirit.org/). It is also recommended to follow the guidelines for the content of statistical analysis plans presented in the following paper: Gamble C, Krishan A, Stocken D, et al. Guidelines for the content of statistical analysis plans in clinical trials. *JAMA.* 2017 Dec 19;318(23):2337-43.

2.5 For some randomised controlled trials, particularly large multi-centre randomised controlled trials, it might be beneficial to explicitly define the estimand (as per the ICH E9(R1) addendum, a precise description of the treatment effect to be estimated), corresponding to the primary analysis in the SAP. This should at least be considered by the statistician writing the SAP, but it is not an essential requirement. For further guidance on incorporating estimands into SAPs, please see article by *Kang et al., Incorporating estimands into clinical trial statistical analysis plans. Clinical Trials. 2022;19(3):285-291.*

2.6 The SAP should include details of appropriate statistical methods that will be used to analyse each primary and secondary outcome measure.

2.7 For any statistical methods that are particularly unusual or complex, references from the literature should be provided (if applicable).

2.8 It is only necessary to list the first choice analysis. Details of how assumptions will be checked might be given in the SAP

2.9 Consideration should be given to the following:

- how the outcomes will be measured
- rules for calculation of derived variables
- any transformations of the outcome likely to be required before analysis
- methods for handling multiple observations
- methods for point and interval estimation
- checking method/model assumptions
- levels of statistical significance (one-tailed or two-tailed)
- methods for handling more than two treatment groups or multiple testing

- how missing data will be accounted for in the analyses
- any applicable imputation strategy
- use of baseline values and covariate data – in particular it is often useful to describe any stratification or minimisation variables that are used in the statistical analysis, and state whether these will be adjusted for.
- methods for handling multi-centre data
- treatment interactions, particularly with centre
- interim or sequential analyses
- rules for stopping the trial early, and allowance for them in the analysis
- methods for handling outliers
- any sensitivity analyses
- any subgroup analyses
- methods for analysing and reporting adverse events and treatment harms
- MedDRA coding requirements
- the impact of non-compliance, protocol deviations, and protocol violations on the analysis populations and/or analyses and/or estimands (if applicable).
- tabulated numbers of patients where blind was broken early

2.10 If the study is to be adjusted for centre, consider how this will be done, and specify this in the SAP. Adjusting for centre as a random effect may be of particular benefit if there are many centres, particularly if there are few outcome events, some centres are small, or if there are treatment imbalances. To enable estimation of the between centre variability, if there are ≤5 centres, a fixed effect approach might be best, but for >5 centres, a random effect should be considered.

2.11 The statistical package/software (or packages/softwares) to be used could be defined in the SAP, but this is optional. If defining the statistical package/software, avoid using specific version numbers as these are likely to change over the course of the trial.

2.12 If any analyses listed in the protocol are not covered by the SAP, then this should be stated, for example, exploratory analyses, health economic analyses, genetic analyses.

2.13 Consideration should be given to current registry reporting guidelines (if applicable) regarding appropriate data splits e.g. age groupings.

2.14 For adverse events that have been MedDRA-coded, the SAP should specify that summary table(s) be presented showing these events, grouped by MedDRA code. Applicable AE listing(s) should also include the corresponding MedDRA code for each event.

2.15 The SAP should describe the plan for validating results. This will usually consist, as a minimum, of separate programming and checking of the primary analysis of the primary outcome; although specific details will vary depending on the type of trial design.

2.16 The SAP should describe the plan for data sharing for secondary research (i.e. research outside the scope of the current study), or explain why data cannot be shared. Our usual process is to generate a pseudonymised version of the analysis dataset(s) to form a data sharing pack, which is created at the end of the study, after the primary results report has

been generated. This pack is shared via controlled access through the ECTU Data Sharing Committee. To add an extra layer of security, data de-identification/anonymisation may be undertaken. However, discussion with the Chief Investigator may be required to confirm that this approach aligns with their expectations.

2.16.1 This data sharing plan should be consistent with the procedures described in ECTU_SOP_DM_15: In Study Data Reports, Exports, Sharing and Transfers and, where applicable, with the data sharing plan submitted at the funding stage.

2.16.2 It is important to check whether any participants have opted out of sharing anonymised data, either in consent or withdrawal. If any have opted out, then their data must not be included in any dataset for sharing.

3. RELEVANT DOCUMENTS AND REFERENCES

On ECTU Website

- ECTU_SOP_ST_04 Statistical Analysis Plans
- ECTU_SOP_DM_15: In Study Data Reports, Exports, Sharing and Transfer.
- ST004 - SAP Template (Shared Drive location:\ECT Unit\SOPs\Finalised SOP and WPD\ST\Supporting Document and Templates\Current)

Others

- Gamble C, Krishan A, Stocken D, Lewis S, Juszczak E, Doré C, Williamson PR, Altman DG, Montgomery A, Lim P, Berlin J. Guidelines for the content of statistical analysis plans in clinical trials. Jama. 2017 Dec 19;318(23):2337-43.
- Hopewell S, Chan AW, Collins GS, Hróbjartsson A, Moher D, Schulz KF, et al. CONSORT 2025 explanation and elaboration: updated guideline for reporting randomised trials. BMJ. 2025; 388:e081124. https://dx.doi.org/10.1136/bmj-2024-081124
- Hróbjartsson A, Boutron I, Hopewell S, Moher D, Schulz KF, Collins GS, et al. SPIRIT 2025 explanation and elaboration: updated guideline for reporting randomised trials. BMJ. 2025;389:e081660. doi:10.1136/bmj-2024-081660
- ICH E9(R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials
- https://www.ema.europa.eu/en/ich-e9-statistical-principles-clinical-trials-scientific-guideline
- Kang M, Kendall MA, Ribaudo H, et al. Incorporating estimands into clinical trial statistical analysis plans. Clinical Trials. 2022;19(3):285-291. doi:10.1177/17407745221080463.

ECTU_SOP_ST_04, W4, ST004 Statistical Analysis Plans

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