

# Challenges involved with using legacy clinical trial study data during integration

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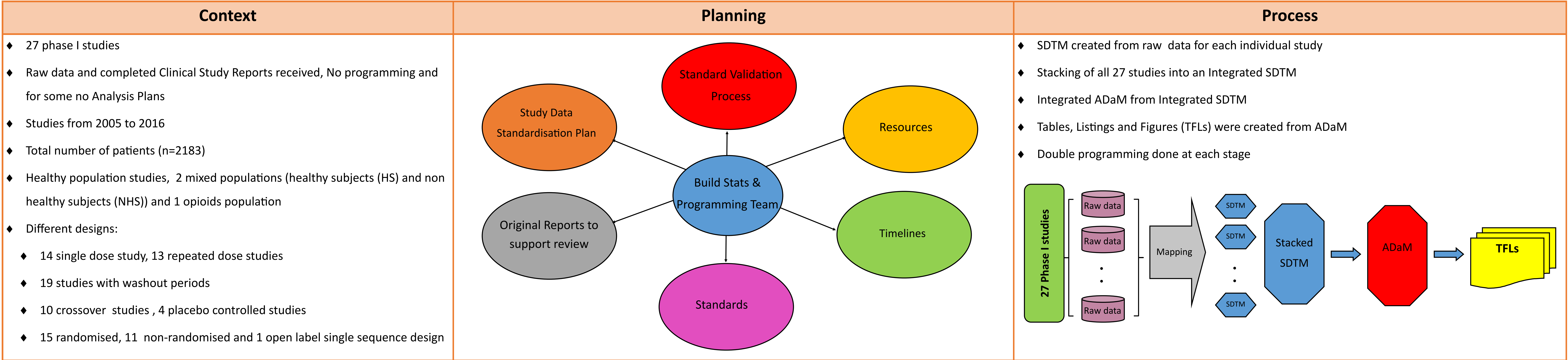


## Introduction

The purpose of an Integrated Summary of Safety (ISS) analysis is to help the reviewer understand the overall evidence for drug safety for a particular drug. This poster will give an insight into the integration of 27 different legacy phase I studies to produce an Integrated package and the challenges faced during ADaM data integration for a compound that was acquired by GSK.

## Objectives

- ◆ Create analysis datasets (ADaM) to support the analysis defined in the ISS Summary Document Analysis Plan (SDAP)
- ◆ Support potential re-production of selected CSR outputs which were previously created for individual studies
- ◆ Deliver a quality Integrated Summary of Safety



| Challenges                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Solutions                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                             |                                                                                                                   |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| <ul style="list-style-type: none"><li>◆ Varying study designs for the 27 studies</li><li>◆ Various treatment groups in different studies</li><li>◆ Mapping the study level data to pooled data whilst enabling recreation of CSR outputs from pooled data</li><li>◆ Dealing with missing values from the different studies</li><li>◆ Windowing or imputation rules</li><li>◆ Consistency of codelists, formats and units across studies</li><li>◆ Summary statistics for some lab, PK and vital signs to match original CSRs</li></ul> | <ul style="list-style-type: none"><li>◆ Simplified treatment group to capture all patients needed<table><tr><td rowspan="6">Main Treatment Arms</td><td>HS TRT Alone</td><td>Treatment period with treatment given alone</td></tr><tr><td>TRT + Other</td><td>Treatment period with treatment co-administered with at least one other drug</td></tr><tr><td>TRT NHS</td><td>NHS who received at least one dose of treatment within the treatment period</td></tr><tr><td>Any TRT</td><td>Treatment period with treatment given alone or with others, i.e. any treatment given within this treatment period</td></tr><tr><td>Placebo</td><td>Treatment period with Placebo only</td></tr><tr><td>Total</td><td>Total treatment or Placebo. (If other drug in treatment period alone, this is not included)</td></tr></table></li><li>◆ CSR vs ISS variable<table><tr><th>CSR Variable (s)</th><th>ISS Variable (s)</th></tr><tr><td>APERIOD</td><td>IPERIOD</td></tr><tr><td>APxxSDT</td><td>ISSxxSDT</td></tr></table></li></ul> | Main Treatment Arms                                                                         | HS TRT Alone                                                                                                      | Treatment period with treatment given alone | TRT + Other | Treatment period with treatment co-administered with at least one other drug | TRT NHS | NHS who received at least one dose of treatment within the treatment period | Any TRT | Treatment period with treatment given alone or with others, i.e. any treatment given within this treatment period | Placebo | Treatment period with Placebo only | Total | Total treatment or Placebo. (If other drug in treatment period alone, this is not included) | CSR Variable (s) | ISS Variable (s) | APERIOD | IPERIOD | APxxSDT | ISSxxSDT | <ul style="list-style-type: none"><li>◆ Harmonisation at the ADaM level instead of the integrated SDTM level<ul style="list-style-type: none"><li>◆ The ADaM datasets set up to support both standard CSR reporting as well as ISS specific analysis</li><li>◆ One mapping definition for all studies for windowing, codelists, units and missing values</li></ul></li><li>◆ Reproduction of CSR outputs from pooled data and compared to individual study CSR outputs<ul style="list-style-type: none"><li>◆ Creation of new parameters to match original reports not required for Integrated outputs</li><li>◆ Documentation of discrepancies</li></ul></li><li>◆ Production of Analysis Data Reviewers Guide as part of the production process meant a detailed document was produced (107 pages)</li></ul> |
| Main Treatment Arms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | HS TRT Alone                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                             | Treatment period with treatment given alone                                                                       |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | TRT + Other                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                             | Treatment period with treatment co-administered with at least one other drug                                      |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | TRT NHS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                             | NHS who received at least one dose of treatment within the treatment period                                       |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Any TRT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                             | Treatment period with treatment given alone or with others, i.e. any treatment given within this treatment period |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Placebo                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                             | Treatment period with Placebo only                                                                                |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Total                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Total treatment or Placebo. (If other drug in treatment period alone, this is not included) |                                                                                                                   |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| CSR Variable (s)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | ISS Variable (s)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                             |                                                                                                                   |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| APERIOD                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | IPERIOD                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                             |                                                                                                                   |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| APxxSDT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ISSxxSDT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                             |                                                                                                                   |                                             |             |                                                                              |         |                                                                             |         |                                                                                                                   |         |                                    |       |                                                                                             |                  |                  |         |         |         |          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

## Conclusion

- ◆ Plan early and in detail
- ◆ Implement solution at the ADAM level (Use data standards)
- ◆ Consistency between integrated data and individual study data
- ◆ Cross check outputs from ISS data to original individual study reports