

The Release of FACTS 6.3

*To: FACTS Licensees
From: Berry Consultants
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Introducing FACTS 6.3

Berry Consultants is delighted to announce that FACTS 6.3 is ready for release!

Building on FACTS 6.2, FACTS 6.3 adds new features to FACTS Core to handle situations where the different arms being tested are best analyzed as being on a grid, improvements to Open Enrolment in FACTS Dose Escalation, and improvements to Hierarchical model fitting in FACTS Enrichment Designs and Ordinal toxicity model fitting in FACTS Dose Escalation.

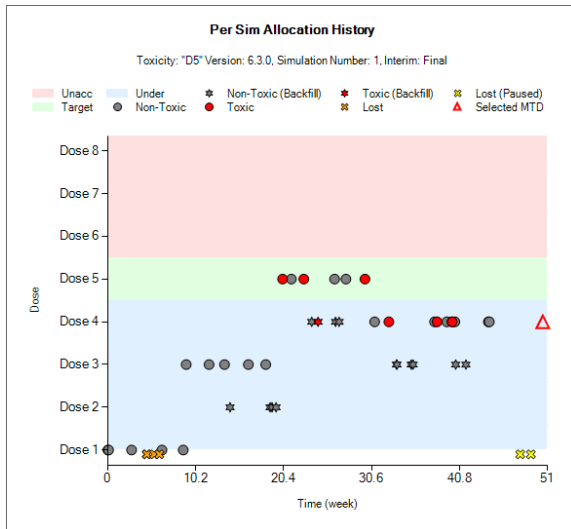
- FACTS Core and FACTS Staged (all versions except TTE) now have an option for modelling the treatment arms as being on a 2D-grid, with their strength defined by 2 factors (e.g. dose and treatment regime, or a combination of 2 drugs).
- FACTS Core and FACTS Staged now have 2D dose response models: 2D-NDLM, linear factorial and discrete factorial.

| Index (i) | Column Name | Effective Column Strength (μg/dl) |
|-----------|----------------|-----------------------------------|
| 1 | Ctrl (ATA 1.0) | 0 |
| 2 | ATA 1.5 | 0.5 |
| 3 | ATA 2.0 | 1 |
| 4 | ATA 2.5 | 1.5 |

| Index (j) | Row Name | Effective Row Strength (μg/dl) |
|-----------|----------|--------------------------------|
| 1 | No NBH | 0 |
| 2 | With NBH | 1 |

| Use | Dose Name | Effective Dose Strength (μg/dl) | Index (i) | Selected Dose Name | Effective Dose Strength (μg/dl) |
|-------------------------------------|---------------------|---------------------------------|-----------|---------------------|---------------------------------|
| <input checked="" type="checkbox"/> | Ctrl (ATA 1.0): 0 | 0 | 1 | Ctrl (ATA 1.0): 0 | 0 |
| <input checked="" type="checkbox"/> | ATA 1.5: No NBH | 2.6 | 2 | ATA 1.5: No ... | 2.6 |
| <input checked="" type="checkbox"/> | ATA 2.0: No NBH | 4.17 | 3 | ATA 2.0: No ... | 4.17 |
| <input checked="" type="checkbox"/> | ATA 2.5: No NBH | 5.92 | 4 | Ctrl (ATA 1.0): 5.4 | 5.4 |
| <input checked="" type="checkbox"/> | Ctrl (ATA 1.0): ... | 5.4 | 5 | ATA 2.5: No ... | 5.92 |
| <input checked="" type="checkbox"/> | ATA 1.5: With N... | 6.4 | 6 | ATA 1.5: With... | 6.4 |
| <input checked="" type="checkbox"/> | ATA 2.0: With N... | 7.76 | 7 | ATA 2.0: With... | 7.76 |
| <input checked="" type="checkbox"/> | ATA 2.5: With N... | 9.52 | 8 | ATA 2.5: With... | 9.52 |

- FACTS Dose Escalation N-CRM has improved the way that subjects are enrolled when using an Open Enrolment design. The limit on the number of subjects without a final result (which temporarily blocks enrolment when its reached) is now per dose rather on the trial overall, and two limits can be defined, one for when allocating to a new dose, and another when allocating to a dose that has been 'cleared' i.e. allocating to the dose that is the optimal target dose after a minimal number of subjects on it have completed.
- FACTS Dose Escalation N-CRM has more extensive and flexible options for the "run-in" options.



- FACTS Dose Escalation N-CRM has an option when using Open Enrolment to allow subjects to be allocated to lower doses than the current target, while the limit on the number of subjects without a final result had been reached. This allocation, referred to as “backfilling” allows allocation to doses that maybe be informative because they are close to the target, or may yet become the target if the trial has to de-escalate.

- In FACTS Enrichment Designs we have improved the fit of the Hierarchical models that has improved how these converge, generally leading to smaller credible intervals.

- In FACTS Dose Escalation N-CRM we have improved how the likelihood is calculated when using the Ordinal Toxicity model leading to smaller credible intervals.

FACTS 6.3 is fully backwards compatible with FACTS 6.2, 6.1, 6 and 5 – it can load and run all your FACTS 6 and FACTS 5 designs – and then use new FACTS 6.3 features with those designs.

You can have FACTS 6.3 and FACTS 6.2 installed on the same machine, so it’s easy to have a transition period as you move to the new version.

Key New Features

FACTS Core Continuous, Dichotomous and Multiple Endpoint and FACTS Staged Design Continuous, Dichotomous and Multiple Endpoint Dose Escalation, now have options for:

- Modelling treatment arms on a 2D grid,
- Analysis by 2D-NDLM of Factorial models.

FACTS Dose Escalation N-CRM

- Open Enrolment now handles the “maximum subjects without final result” on a per dose queue, allowing faster accrual in safe way.
- Open Enrolment now includes a “backfill” option for allocating subjects who would otherwise have to be excluded

FACTS Enrichment Designs

- Improved model fitting of Hierarchical Models across Treatment arms or across Control arms.