

Reproducibility in incurred samples

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Disclaimer

The outcome of CC-III with respect to the reanalysis of incurred samples has not been formally implemented at J&J to this time.

As for other companies, J&J is still evaluating how best to include the preliminary outcome of the CC-III meeting in their internal procedures. As a

consequence, this presentation does not reflect current business practices at J&J.

It's purpose is to stimulate the discussion within the industry to come to best practices with respect to both science and regulations, in line with regulatory expectations.

Aim of the workshop

Joined J&J Anapharm initiative - Organized via Anapharm
3 speakers - 1 topic

Anapharm

- Kris Kemper
- Scientific and regulatory overview

H - La Roche

- B. Lausecker
- Case studies of practical implementation

J&J

- P. Timmerman
- Challenge on real needs or added value
- EBF initiative

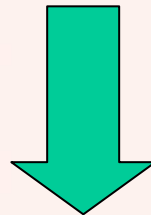
Ample time for discussion

CC-II : Going from 4-6-20 to 4-6-15

A lively discussion at CC-II followed by a...

....consensus not to do this.....but...

FDA decided otherwise.



a lot of controversy, maybe even anger, when
FDA adapted this without real consultation

5 years later....

A scientific perspective

- within Bioanalytical : better methods
- for our 'Clients' : Virtually no impact on any TK, PK or PK/PD assessment

5 years later....

An economic perspective

- Early development
 - Mdev/Mval :
 - increased effort to make methods more robust
 - e.g. in stability, acc. and pre. assessments,...
 - earlier use of STIL
 - more thorough investigation of Ion Suppression
 - Study support :
 - Limited added added workload (about 2% in ED)
 - time gained due to more robust methods
- Late development
 - Impact virtually zero, both on Mval and Study support

CC-III

CC-III outcome :

- Reproducibility of the method for the determination of analytes in incurred samples must be determined.

How FDA looks at things :

- Use scientific perspective + motivate and document your decision

CC-III : 'Reproducibility in incurred samples'

A example of a tiered approach

	<u>PRECLINICAL</u> <ul style="list-style-type: none"> • Random samples (IV/PO/SD/MD) • Pooled • Document in MVR 	<u>PRECLINICAL</u> <ul style="list-style-type: none"> • Random samples (IV/PO/SD/MD) • individual • Document in MVR 	<u>PRECLINICAL</u> <ul style="list-style-type: none"> • Random samples (IV/PO/SD/MD) • individual • Document in study 	<u>PRECLINICAL</u> <ul style="list-style-type: none"> • Predefined samples - All studies • Pooled • Document in PK study
<u>CLINICAL</u> <ul style="list-style-type: none"> • Random samples from a few selected studies - SAD/MAD - Special population • Pooled • Document in MVR 	<u>CLINICAL</u> <ul style="list-style-type: none"> • Random samples from a few selected studies - SAD/MAD - Special population • Pooled • Document in MVR 	<u>CLINICAL</u> <ul style="list-style-type: none"> • Random samples from a few selected studies - SAD/MAD - Special population • individual • Document in MVR 	<u>CLINICAL</u> <ul style="list-style-type: none"> • Random samples from a few selected studies - SAD/MAD - Special population • individual • Document in PK study 	<u>CLINICAL</u> <ul style="list-style-type: none"> • Predefined samples - All studies • individual • Document in PK study
+ 2 %*	----->			+ 21 %

* Hypothetical organization with 50 MVs/y and 200.000 samples/y (25% preclinical and 75 * clinical, divided over 250 and 100 studies respectively. Average sample batch size = 100 samples)

Questions to ask.....

- What do we (think we) prove by reanalyzing
 - will we pick it up ?
- What can cause non-reproducibility....
 - what did we do to prevent this in MDev?
- Why not focus more on increasing robustness of the assay....
 - where should our focus be ?
 - in early set up of the method
 - in late development
 - And how do we document this
- If we have a thorough Mval and study execution process,
 - doesn't reanalysis cfr. CC-III repeats any possible issue ?
- How about taking an orthogonal look at our methods?

Outcome

- In the Brussels meeting (mostly Pharma), there was a consensus that doing repeat analysis has value (although the majority of the people/companies present see only very limited added value)
- When implementing, the drivers of implementation should be around the science of a compound. Examples are (Physic)chemistry, metabolism, stability.....Reanalyzing arbitrarily any number of samples in all/majority of studies, often done to increase the comfort level, is not perceived as the best way forward. This may imply that it makes more sense to do reanalysis in an early phase of development rather than in a late phase of development
- A European Bioanalytical Forum is being formed to increase and facilitate interactions within the European Bioanalytical community and beyond

Above comment were sent to AAPS (Surendra Bansal) for further communication to FDA



Let's open the discussion

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