CAPRA Education Day
May 31st 2007
DoubleTree International Plaza Hotel, Toronto

Meeting minutes from Breakout Session:
"Common Deficiencies in (A)NDS's, S(A)NDS's at TPD"
Speakers: Caroline Vanneste, Project Manager, Good Review Practices, TPD
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Issue #1:
Timelines for starting submission reviews:

- ***Why does the quality review start later than safety and efficacy review?***
- ***What happens when the target review time is nearing and the review is not completed?***
- ***Does Health Canada issue NONs instead of clarifaxes in order to meet target review times?***

- There are many more submissions to be reviewed by the quality divisions in TPD than by any one of the safety and efficacy review divisions. Therefore, many submissions sit in the queue before a quality reviewer has time to start the review.
- The performance target for review of submissions is 90% because it is recognized that some submissions may not be reviewed within the target review time.
- We have not analyzed the submission data to determine what prompts the issuance of a Notice of Non-Compliance near the target review time. We do know that most NONs are issued within 15 days of target, but most NOCs are issued within 15 days of target as well. More analysis is needed.

Issue #2:
Involvement of Regulatory Project Managers (RPMs) in review process:

- ***Why don't the RPMs always know what is happening with the reviews?***
- ***Why don't the RPMs in the quality area know what is happening in the safety and efficacy area, and vice versa?***

- The use of RPMs in the review process is still very new, and we still have improvements to make to ensure more interaction between RPMs and reviewers.
- Due to the large number of submissions requiring a quality review, coordination between RPMs and reviewers is even more difficult than in the safety and efficacy area.

Issue #3:
Use of the European Union (EU) Certificate of Suitability (CEP):

- ***What if the Sponsor stops supporting the drug substance Drug Master File (DMF) in the EU because of poor sales and Canadian product is available but TPD doesn't have the DMF?***
- ***How will TPD ensure that they have the necessary data?***

- This is not a Canadian-specific issue. The use of CEPs presents a challenge in the EU too. However, in Canada we only use the DMF (and therefore CEP) to look at the detailed method of synthesis. The submission sponsor provides batch data, specifications, validation of analytical procedures, etc.

- It is the responsibility of the submission sponsor to ensure that they, and/or Health Canada, have the appropriate data to support their product.

Issue #4:
Approvals in another jurisdiction:

- ***How is an FDA or EMEA approval of a product taken into consideration when reviewing that same product at TPD?***
- ***Do regulators from different jurisdictions discuss submissions for specific products?***

- Information or evaluations from other regulatory jurisdictions are looked at by TPD when available. TPD's decisions are however independent from other jurisdictions. There are various reasons why regulatory decisions differ between jurisdictions including differences in data interpretation or in risk management approaches.
- We cannot discuss submissions under review with other jurisdictions unless the sponsor agrees.

Issue #5:
Notification of status of review:

- ***Is it possible to receive a warning or early notification as to whether a product is going to be approved or not? When can the Sponsor receive information on a possible NOC?***
- ***When does TPD make approval decisions?***

- The RPM should be contacted for such questions. Ideally, TPD should contact the submission sponsor, but there are limited resources for this type of interaction.
- Many decisions are made within 15 days of the review target time.

Issue #6:
Clarifaxes versus NONs:

- ***How is the clarifax versus NON-decision made? This does not seem to be consistent.***
- ***Can the "show stoppers" in a clarifax be identified so that submission sponsors know what is most important to TPD?***

- It's recognized that there are inconsistencies across review divisions with respect to issuing a clarifax or NON, and this is currently being addressed by TPD.
- There is a proposal within TPD to have clarifax and NON-issues identified as major or minor.

Issue #7:
Submission classifications:

- ***If a company files for a line extension, i.e. new dosage form, and a trade name has not yet been established, why is this classified as an NDS instead of an SNDS?***

- Without knowing the specifics of this case, it is difficult to comment. This issue should be clarified with the RPM.

Issue #8:
Review of innovative versus generic biostudies:

- ***To what extent do biopharmaceutics reviewers get involved in the review of New Drug Submissions?***

- ***Are innovator biostudies (i.e. comparison of two formulations from the same company) held to the same standard as generic biostudies (i.e. comparison of the innovator product against the generic product)? Are non-prescription products held to the same standard as prescription products?***

- The review of NDSs is lead by "innovator reviewers", but generally the biopharmaceutics studies within NDSs are reviewed by "generic reviewers".
- Standards for bioequivalence are generally the same regardless of the type of submission, but more flexibility may be allowed in some areas due to other considerations. This is a very specific issue that should be discussed with the appropriate reviewers at TPD.

<u>Issue #9:</u>
Long-term studies to support long-term use:

- ***What studies are necessary to support long-term use of a product?***
- ***Do guidelines exist?***

- Generally 6 to 12 months of long term data would be needed.
- Submission sponsors should review ICH guidelines in this area.