Health Canada Santé Canada

Therapeutic Products Directorate

Health Products and Food Branch

Direction des produits thérapeutiques

Direction générale des produits de santé et des aliments




Submission Review Challenges

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Canada

Presentation Objective:

- **Provide information on issues that cause difficulties during the review of submissions, and hence facilitate the review process.**

Sources of Information

- **TPD's NOD and NON analysis (NDS, SNDS, ANDS)**
- **Results from a feasibility study on "scorecards" to measure critical aspects of quality performance**
- **Reviewers' experiences**

Design and methodology issues

- **Symptomology Vs Diagnostic confirmation.**
- **Unvalidated endpoints.**
- **One pivotal study only; two studies are usually required for NDS.**

Design and methodology issues (cont'd)

- **Clinical practice guidelines for control group.**
- **Insufficient number of patients in studies.**
- **Exposure data; long-term indications need to be supported by long-term studies.**

Design and methodology issues (cont'd)

- ***Post hoc*** **analysis, e.g., pooling of study results, sub-population analysis.**
- **Statistical significance Vs clinical significance.**
- **No dose-response studies.**
- **Excluding data without adequate justification.**

Design and methodology issues (cont'd)

- **Secondary endpoint to support an indication**

- **Literature studies to support a new indication**

PM/ Labeling issues

- **Clinical trial section information must support an approved indication.**
- **PMs should be provided in clean and annotated versions.**
- **Rationale to support labeling changes (NCs, SNDSs)**

Communication issues

- **Rounds of clarifaxes on the same issues;**
- **Transparency with status of submission in other regulatory jurisdiction**
- **Extension of timelines for clarifax responses**

Quality issues

- **DMF issues**
- **Incomplete analytical methods**
- **Manufacturing and validation of drug process**
- **Incomplete stability data**
- **Innadequate characterization of impurities**

What might help us all…

- **Consultation meetings and communication**
  - **Discussions on endpoints and study design if possible.**
  - **Discussions on the data package.**
  - **Upfront discussions on issues with the product.**
  - **Seeking clarification on information requests.**