

*Promoting Effective Drug Development Programs:
Opportunities and Priorities for FDA's Office of New Drugs*

1. Flipped Clinical Trials

2. One Indication, One Standardized Protocol, Multiple IMPs

Would FDA support those approaches?

Dr. Peter Schiemann

Managing Partner

Widler & Schiemann Ltd, Zug – Switzerland

FDA

White Oak Campus, Silver Spring, MD, November 7, 2019

Flipped Clinical Trials – The Problem Statement

- ▶ Usually, patients who do not suffer from a serious disease or suffer from a serious illness but are in stable conditions, e.g., MS, are not treated at large hospitals, but by their GPs
- ▶ Today, however, clinical trials in general take place at specialized clinics and, therefore, patients need to be convinced to change their treating physician in order to partake in a clinical trial
- ▶ For the patient this means disrupting the relationship with their treating physician, for the GP this results in losing a patient or not having access to the hospital records
- ▶ As a result, the GP may not very enthusiastically support participation of his/her patient in a clinical study and for the patient this could result in additional burden, e.g., for traveling to the institution, being exposed to an unknown environment, etc.

Flipped Clinical Trials – The Solution Part 1

- ▶ Patients are being treated by their local GP and remain with the physician who knows them best
 - However most GPs are not familiar with the conduct of clinical trials
 - Research from the Society for Clinical Research Sites (SCRS) has shown that about 40% of physicians will not continue their participation in clinical trials after the first one
- ▶ Thus, there is a need to leverage the proficiency in clinical trials conduct of the hospital treating physician in addition.
- ▶ **Is FDA open to the idea that “mixed” investigator teams can conduct a trial?** (GP-investigators might have only basic GCP knowledge or/and that GP-investigators can use systems that are not fully compliant, e.g., an EHR that does not meet 21 CFR Part 11 requirements)

Flipped Clinical Trials – The Solution Part 2

- ▶ We could design trials – especially longer-term trials – in such way that visits requiring specialized equipment or exams (e.g., baseline, end of treatment visits) are conducted at larger institutions that have extensive experience in the conduct of GCP trials while interim visits are conducted by the patients' GP
- ▶ We also need to challenge classic endpoints, e.g. in MS the T25-FW (Timed 25 Foot Walking Test), which is known to be unreliable and especially with patients where MS is in an early state, depends very much on the patient's "fitness" of the day. This alone introduces bias and loss of the sharpness of the signal.
- ▶ Here, we could use modern technology, and with the help of apps and other devices record the moving pattern of an MS patient 24/7, which could avoid filling in lengthy CRFs as the app will do this for the investigator and his/her team; push messages could be sent to patients and much more
- ▶ And all FU visits for safety could be done at the GP's office and not at the hospital anymore
- ▶ **Is FDA open for this approach to clinical trials and to changing established endpoints when it is supported by modern technology?**

One Indication, One Standardized Protocol, Multiple IMPs

Sharing Data from Standard Therapies

The Problem Statement

- ▶ Today, many resources are wasted in designing and reviewing clinical strategies and their studies as each sponsor manages their own. Not only on the sponsor side, but also on FDA's side
- ▶ Some sponsors have started using templates for clinical protocols, but we still see too much variety in the design and esp. data points to be collected
- ▶ General Practitioners are repelled by the complexity of clinical studies and what GCP demands of them. About 40% stop after their first participation in a clinical trial

One Indication, One Standardized Protocol, Multiple IMPs

Sharing Data from Standard Therapies

The Solution Part 1

- ▶ By using standardized protocols across a disease or therapeutic area, one would only change for a trial what needs to be changed based on latest research results, availability of a new biomarkers, innovative endpoint determination, etc.
- ▶ As a result of such standardization, the whole approval process of the protocol would be much easier and faster, i.e. IRBs would only need to review what is new or different and what these changes mean from a benefit-risk perspective
- ▶ In addition, also the reliability of the trials would increase as investigators would not have to re-learn "the Bible" every time when participating in a new trial

One Indication, One Standardized Protocol, Multiple IMPs

Sharing Data from Standard Therapies

The Solution Part 2

- ▶ The advantage:
 - For treating physicians and patients:
 - Increased familiarity of trial procedures within treating physicians incl. GPs
 - Over time optimization of trial conduct by implementing learnings from previous trials while being able to limit changes to the template
 - FDA would need to spend less time for review - standards could be endorsed by FDA
 - Advantage for sponsors:
 - Lengthy protocol development / writing iterations can be avoided on the basis of a recognized standard
 - Discussions with FDA on the design of a protocol could be accelerated
 - A protocol would undergo much faster FDA and IRB review and approval while avoiding “hobby-horse” comments by the reviewers
- ▶ Time and money could be saved and patients getting access to new medications much earlier.
- ▶ **Would FDA spearhead such an initiative, for instance leading a pilot in a “crowded” disease area?**

***We look forward to working on this with FDA
and relevant key stakeholders!***

WIDLER & SCHIEMANN LTD

Weinberghöhe 10B
CH-6300 Zug
Switzerland
www.wsqms.com
info@wsqms.com