

Critical Knowledge and Tools- (Revised March 3, 2010)

**3.2.4.3 Critical Knowledge and Tools Subgroup (Preliminary draft kindly provided by Gerhard Walzl; additions kindly provided by Barbara Laughon)**

**Objectives:**

This subgroup aims to promote the development of knowledge critical to evaluating the most promising new TB drug candidates for entry into clinical trials. Moreover, this subgroup aims to promote the development of tools that will support the discovery, testing, or improvement of new TB drugs or treatment strategies that can ultimately be combined into novel TB regimens that correspond to the WGND aims. Its objectives are:

- To identify gaps in current knowledge and tools that are needed to support new drug development. As the subgroup is not able to address these gaps itself, its main objective will be to recognize the areas of need, to identify organizations capable of implementing the necessary actions and to identify appropriate funding sources to enable such implementation.
- To promote and support:
  - Compiling knowledge required at the interface of preclinical and clinical development, in particular the data required by multiple regulatory authorities;
  - the establishment of animal models for TB treatment evaluation, including animal models of combination drug therapy; Shorten the evaluation of drug candidates in animal models by advocating and facilitating the use of reporter strains, QC-PCR methods and devising new methods for short term animal models.
  - Studies of PK/PD of TB drugs and drug candidates, particularly regarding bioavailability alone and in combination;
  - Improvement of existing regimens and optimization of existing drugs;
  - research into biomarkers for TB treatment outcome and drug efficacy including research into imaging technologies to improve understanding of TB pathophysiology and treatment response, and preclinical biomarkers of toxicity, especially hepatotoxicity;
  - research into alternative drug delivery technologies;
  - Standardization of procedures related to all stages of TB drug research, including clinical and laboratory standard operating procedures such as specimen handling and processing, data definition, study design, analytical methodologies and development of a critical path for candidate TB drugs to regulatory approvals in collaboration with the Clinical Trials Group.
  - development of new PK/PD methodologies to assist in clinical trials of new TB drugs that are specifically tailored to different drug candidates or mechanisms of action and derive the rules to better select preclinical drug leads including studies of drug/drug interactions, between TB drugs and drug candidates and, for example, between TB drugs/drug candidates and ARVs
  - research to assist in validation of diagnostic technologies in collaboration with the New Diagnostics Working Group
  - Facilitate information sharing of centralized resources such as biobanks, strain collections and reference isolates.

- To promote and support the implementation of validated tools for new drug development into clinical trials and eventually clinical practice when such tools are validated and become available.

**Tasks:**

The Critical Knowledge and Tools Subgroup serves as a technical advisory body to the WGND and the Stop TB Partnership. Its primary tasks are:

Organize subgroup **meetings** to promote the objectives as outlined above.

To review guidance's and requirements issued by regulatory authorities for new TB drug development, and promote the coordination of research efforts to develop new tools for new TB drug development through workshops and discussion forums;

- Regular teleconferences to ensure progress in pursuing subgroup objectives
- Annual subgroup meetings during appropriate conferences, including IUATLD meetings to align subgroup strategies to achieve its objectives
- To compile and share lessons learned in chemistry, manufacturing, safety and efficacy studies by developers of recent candidate TB drugs;
- To explore resources available to the pharmaceutical industry and the wider TB research community on toxicology and predictors of toxicities ;
- To study available knowledge on PK/PD of existing TB drugs and new candidates;
- To identify and share information on drug-drug interactions likely to exist in TB prevalent settings.
- **Information exchange:**
  - Establishment of a publicly accessible **Tools Subgroup website** to facilitate information exchange including meeting coordination and maintaining a calendar of events in the following areas :
    - Survey of the most important global activities in the field of tools for new TB drug development and generation of a member activity list. The information will be collected through a customized questionnaire that will be sent to major role players in the field.
    - Posting of links to key references relating to tools for new TB drug development.
    - Presentations from scientific conferences and meetings
    - Posting of clinical and laboratory standard operating procedures, study design and analytical methodologies for the testing of new TB drugs and evaluation of appropriate tools with a commentary on inferior methods or products.
    - The existence of this web site and the appropriate links will be advertised through fliers at conferences and emails to Stop TB Partnership group participants.
  - **Providing a liaison with other working groups and subgroups**, including New Diagnostics Working Group and Subgroups Biological Targets, New Drugs in Clinical Trials and Clinical Trial Sites. This interaction will be facilitated by core group members.
  - To **engage funding bodies and policy makers** to advance research into tools for drug development, including the establishment of biobanks that will allow the discovery and validation of biomarkers for TB treatment response; (Please note: this is a major initiative for collaboration with other Stop TB WGs as well)

- Production of **white papers, review articles, and power point presentations** to increase the visibility of advances in tools for the development of new TB drugs. This will include advising regulatory bodies, the pharmaceutical industry and the wider TB research community through publications, workshops and web based communication about implementation of validated tools for new drug development when such tools become available.

***Members:*** The Critical Knowledge and Tools Subgroup comprise representatives with specific programmatic, clinical, advocacy, scientific, regulatory and managerial expertise. Its membership rests with individuals with specific areas of expertise relevant to tools for drug development.