SCTO PLATFORMS

White Paper:

SCTO statisticians in Independent Data Monitoring Committees of academic studies

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Background

Our objective in this statement is to describe the role of a statistician from a Swiss Clinical Trial Organisation (SCTO) associated body when taking on the role of independent statistician in an Independent Data Monitoring Committee (IDMC)[1] for a study conducted with the participation of a SCTO network partner or a similar institution. We propose a framework for efficient collaboration between SCTO network partners to the assignment of statisticians to this role.

IDMC members are independent of the study team, potentially with access to unblinded study data and treatment allocation. They review clinical trial data and oversee patient safety, data quality, and progress of the trial on a regular basis. The focus of the IDMC is patient safety and scientific integrity of the study. The study sponsor is responsible for organizing an IDMC if deemed necessary and remains the body responsible for the study. The IDMC usually consists of independent experts in the respective medical field and in biostatistics and/or trial methodology.

A detailed description of the role and responsibilities of the independent statistician in an IDMC must be defined in the study protocol and in the IDMC charter of the trial, including the statistician's name.

Throughout this document, we refer to organizations associated with the SCTO as CTUs (as listed on the SCTO members list, the department of biostatistics at the University of Zurich and the Swiss Group for Clinical Cancer Research, SAKK). We refer to statisticians employed by SCTO network partner as "SCTO statisticians" and to statisticians with the role of independent statistician in IDMC as "IDMC statistician".

Roles of the independent SCTO-statistician in IDMCs

The independent IDMC statistician is an expert in statistics/methodology who assists the IDMC members to understand and interpret the reports. Upon request, the independent IDMC statistician may perform simple ad-hoc analyses instead of the trial statistician. In specific cases, they may supervise or perform planned interim analyses. The IDMC statistician may or may not have voting rights with respect to decisions that the IDMC may take.

Preparation of the reports for the IDMC, potentially also performing interim analyses for efficacy or futility, might be done either by the trial statistician or by the IDMC statistician. This distinction has implications on the voting rights of the IDMC statistician, on the scope of work required and the possible compensation and must be determined by the sponsor when defining the structure and role of the IDMC.

The work of the IDMC members is often not paid apart from, e.g. travel costs, if relevant. However, the time-costs of SCTO statisticians need to be covered if participation in an IDMC is via their position as a statistician in a CTU. This poses a challenge for CTUs, which are financed by basic funds and fees per working time. ***In case an SCTO statistician serving as IDMC statistician prepares the reports and/or interim analyses, the work costs (salary per hour) should be covered by the sponsor of the study.*** Guidelines to this end are listed in the section 'finances' below.

Scope and types of studies in which SCTO statisticians may act as independent statistician

This document refers to trials managed or conducted by CTUs for which an independent statistician from an SCTO network partner is required. It includes trials in which CTUs are acting as project managers, statisticians, study center etc. To this end, a CTU-statistician may act as IDMC statistician for studies managed by a different CTU in:

- Randomized phase II to IV trials
- Proof-of-concept phase I and phase II trials

Ensuring independence

CTUs are typically requested to assist the sponsor in the organizational aspects of studies including the

[1] Often also called Data Safety and Monitoring Board (DSMB)

organization of IDMCs. Ensuring the independence of the IDMC statistician when coming from within the same CTU requires special considerations and might not ensure complete independence.
The SCTO Statistics & Methodology Platform can maintain a network of qualified statisticians ready to fulfil the role of IDMC statisticians for another CTU. By organizationally belonging to a different CTU, we ensure the independence of the IDMC statistician from the study team.

Collaboration between SCTO network partners

This document offers a platform for agreement and coordination between CTUs in order to facilitate the collaboration between CTUs in assigning IDMC statisticians for trials managed by CTUs. We define that CTUs will reciprocally assist each other in providing personnel to serve as IDMC statisticians according to their time and financial capabilities.
To this end, we define:

- *The requesting CTU* is the unit contracted by the trial sponsor to manage the trial; the requesting CTU has working and financial agreements with the sponsor and provides them with study specific services.
- *The host CTU* is the employer of the statistician intended as IDMC statistician.

We distinguish between cases in which IDMC service costs are covered by the host CTU or the statistician's institutional funding and those cases where the scope of the work for the IDMC statistician is larger and an additional agreement is made between the sponsor and the requesting CTU to cover the working costs of the IDMC statistician. See section **finances** below.
In the first case (costs covered by the host CTU), the requesting CTU approaches the host CTU to assign a statistician. The reciprocal nature of taking over these tasks between CTUs would ensure that, over time, costs are equally shared by the different CTUs. Thus, funding of the IDMC statistician is via the host CTU internal budget, according to its capacities.
To this end:

1. The requesting CTU conveys the request for IDMC statistician to the representative of the host CTU (typically team leader)
2. The request clearly states the tasks required from the IDMC statistician, the expected time-scope of the work and includes a synopsis of the trial.
3. The host CTU provides written confirmation to take over the task under its own costs under the reciprocal SCTO agreement.

In the latter case, an additional working agreement is required. The requesting CTU ensures a working agreement with the sponsor, which determines the financial compensation to the requesting CTU. The costs should take into account the working costs at the host CTU (since these differ between CTUs).
To this end:

1. The requesting CTU conveys the request for IDMC statistician to the representative of the host CTU. A trial synopsis and a list of tasks required from the IDMC statistician is added to the request.
2. The host CTU statistician generates a cost-estimate of the required work, conveying this to the requesting CTU.
3. The requesting CTU ensures that the costs for the relevant tasks are included in the budget and an agreement is signed between the sponsor and the requesting CTU.
4. An agreement is signed between the requesting CTU and the host CTU determining the details of funding transfer (e.g. timing of transfer – once per year/half-year; costs; reporting etc.).

The SCTO, via the statistics platform, will build and maintain a network of qualified statisticians to participate in IDMCs. The list would be open to all SCTO network partners (CTUs). The SCTO Statistics & Methodology Platform takes no further responsibility on the coordination of IDMC statistician tasks or appointments.

Finances

The CTU statistician's salary while performing duties for the IDMC will be covered using the following rules:

1. If the IDMC statistician only acts as expert advisor on the IDMC but does not perform statistical analysis, the expenditure of time is rather low, and funding is usually not foreseen. We suggest that for time expenditures up to 10 or 15 hours, the host CTU will cover the CTU statistician's salary

excluding potential travel costs. The final work time free of charge will be determined per case by the two involved CTUs.

2. If the IDMC statistician only acts as expert advisor on the IDMC but does not perform statistical analysis, but more than 10 to 15 hours are expected to be spent in total (including preparation time in reading the protocol and reading/reviewing the IDMC charter), the study grant should fund the work. Typically, this will be the case when the study requires intensive safety monitoring and many IDMC meetings. A budget is necessary and should be discussed with the sponsor in the planning phase.
3. If the IDMC statistician prepares a statistical report for the IDMC, the study grant should fund the work. A budget is necessary and should be discussed with the sponsor in the planning phase.

Of note, the sponsor needs to be informed if more time is spent inside the IDMC than anticipated, in particular in case where no payment from the budget of the trial was anticipated and agreed upon. In this scenario, a solution needs to be discussed between the IDMC statistician and the sponsor to cover these additional costs.

Role of the SCTO Statistics & Methodology Platform

The SCTO Statistics & Methodology Platform takes upon itself to define the role of the IDMC statistician when coming from a partner organization, as defined in this document. This can serve as a basis for discussion between the CTU and the sponsor and clarifies the position of CTUs regarding this role.
The SCTO Statistics & Methodology Platform will assist in coordinating the reciprocal assignment by generating and maintaining a list of qualified statisticians with interest and experience, who can take the role of IDMC statisticians. Statisticians interested in entering the list must confirm their obligation to fulfil the training requirements (see below).
The SCTO Statistics & Methodology Platform maintains a template for an IDMC charter, including the role definition of the statistician for the use of CTUs from the network. The platform will make this template available to all CTUs.

Training of SCTO IDMC statisticians

The SCTO defines specific training requirements from statisticians listed in the platform's IDMC list. These include the following sources, this training program includes reading at least one guideline and one journal paper from the following list:

- "FDA: Guidance for Clinical Trial Sponsors – Establishment and operation of Clinical Trial Data Monitoring Committees" (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/establishment-and-operation-clinical-trial-data-monitoring-committees)
- EMA Guideline on Data Monitoring Committees (https://www.ema.europa.eu/en/data-monitoring-committees)
- Herson, Jay. Data and safety monitoring committees in clinical trials. Chapman and Hall/CRC, 2016.
- DeMets D, Califf R, Dixon D et al. Issues in regulatory guidelines for data monitoring committees. Clinical Trials. 2004; 1(2):162-169
- DeMets D and Ellenberg S. Data Monitoring committees – expect the unexpected. New England Journal of Medicine. 2016; 375:1365-71
- Schöffski, P. Importance and role of independent data monitoring committees (IDMCs) in oncology clinical trials. BMJ Open 2021 Oct 25; 11(10)

Upon completion of the training, the statistician will enter the date of completion in the IDMC list as confirmation.