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New Drug Advisory Committee (NDAC) Missions and Procedures

POL013

Version 1.2

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1 PURPOSE

This policy outlines the missions and tasks of the New Drug Advisory Committee (NDAC) as well as the interaction between NDAC and the Early Project Optimization Department (EPOD) at EORTC Headquarters (HQ).

2 DEFINITIONS

- ◆ **Early Project Optimization Department (EPOD):** A unit at EORTC HQ strategically dedicated to actively participating in the development of group strategy, offering project support and optimization, and conducting pro-active project development.
- ◆ **New Drugs Advisory Committee (NDAC):** An advisory committee that facilitates the introduction of new drugs into clinical trials within EORTC.
- ◆ **Protocol Review Committee (PRC):** An independent panel of experts. The PRC reviews and approves all clinical studies proposed by EORTC Groups prior to activation.
- ◆ **Translational Research Advisory Committee (TRAC):** An advisory committee that supports and provides expert advice from a scientific and practical perspective on translational research (TR) projects conducted within the EORTC.

3 THE ROLE OF NDAC

The New Drug Advisory Committee (NDAC) was implemented in October, 2002. Its role is to support and make recommendations to the clinical research groups in all aspects of New Drug Development including strategy approach and prioritization for development within the EORTC network.

4 THE TASKS OF NDAC

To ensure a consistent approach towards the pharmaceutical industry, NDAC acts as a reference body for all EORTC Groups and upon request can make recommendations to them in various aspects of drug development including benchmarking the choice of target/ agent and/or company. This includes the strategic approach and setting priorities regarding drug development within the entire EORTC Network as well as being a recipient of information from disease oriented groups at the earliest stages of their discussions about trials involving new agents.

The remit of NDAC are those agents that have not been registered and/or not yet with a role in oncology or possibly agents which come to the EORTC for the first time in a specific setting.

NDAC coordinates Advisory Boards/ partnership meetings performed with the pharmaceutical industry. NDAC also supports the EPOD regarding methodological issues inherent to innovative agents with new mechanisms of action in the approach of early studies design.

The missions of NDAC lie in three areas:

- (a) Advisory to Board for strategic and scientific review of projects;
- (b) Advisory to the groups during group strategy or project development;
- (c) Advisory to industry in the frame of advisory boards / partnership meetings.

4.1 NDAC review at Board level

NDAC is consulted very early on and in parallel to the Board submission. Study concepts are sent to NDAC Chair in parallel to the Board by EPOD. NDAC is only involved in projects involving new drugs, involving targeted/ biotherapies, or new/challenging combinations and specific clinical settings where NDAC review may be necessary. Sorting is done at EPOD internal meetings, and when in doubt, proposals are sent to NDAC Chair who can readily decide whether or not the project needs to be reviewed.

NDAC assesses the adequacy of a given new drug in the proposed setting (population, pathway/target, drug, industrial partner). NDAC is there to stop or re-orient inappropriately conceived projects.

In order to increase the usefulness of NDAC's advice in project development, NDAC's position should be provided to the Board prior to the Board's strategic review of a project. One week prior to the Board meeting, the EPOD secretary provides NDAC with the Board submission form of the proposal and any additional background information (Investigator Brochure if available, pipelines, other EPOD document...). The NDAC Chair reviews the proposal and involves additional relevant NDAC member(s) if judged necessary by him/her and sends his comments back to EPOD.

NDAC provides an official review (in free style) if possible prior to the Board review. The Board's endorsement of a proposal, including some of NDAC's recommendations, would then guarantee the implementation of NDAC's advice. EPOD routinely follows up to ensure that NDAC advice is taken.

In case a post-Board EPOD action is required (e.g. drug mining), a review is requested again before the PRC submission.

4.2 NDAC involvement in Strategic Project Development

EPOD supports some EORTC Disease Oriented Groups (DOG) in the development of their clinical strategy and/or project development. NDAC could have useful input.

4.2.1 PRE-Board: During the development of a group strategy

NDAC should be involved as soon as EPOD interacts with a group on the basis of a written document. This working document is initially developed by EPOD in collaboration with the Clinical Research Physician (CRP) assigned to the group. It might include a SWOT analysis of the respective group, an indication background, a clinical overview, a drug pipeline overview, and a list of clinical trials proposals serving as a supportive document for further strategy discussion with each DOG. This document may also be limited to a specific patient population, such as brain or bone metastases, or setting, such as the preoperative window of opportunity.

The NDAC Chair should be provided with a concise version of the document containing information on the relevant targets, the current pipelines, and the corresponding proposals as applicable. The Chair could at this stage decide whether/which other members of NDAC to involve and even reach out to external experts if deemed necessary (with no conflicts of interest). NDAC (via Chair) is asked to provide feedback to EPOD/DOG on the proposals (setting, target, drug, and industrial partner) and potentially gives support in interacting with industrial partners (company contact).

4.2.2 PRE -Board: During the development of a group specific project

NDAC is involved in case a group needs help in identifying a pathway, target, drug, and/or industrial partner. The NDAC Chair should be provided with the proposal and a "drug mining" document (prepared by EPOD) summarizing the possible pathway, target, drug, and/or industrial partner for this proposal. The Chair could at

this stage decide whether/which other members of NDAC to involve and even reach out to external experts if deemed necessary. NDAC provides feedback to EPOD/ DOG on the possibilities (setting, target, drug, and industrial partner) via e-mail and if necessary is asked to participate in interacting with industrial partners.

4.3 Advisory to industry in the frame of advisory boards and partnership meetings with pharmaceutical industry

The process for NDAC contact with industry is as follows: EPOD establishes the first contact, then an initial meeting with members of NDAC is arranged followed up by an advisory board/partnership meeting where the company presents its pipeline (or a specific drug or set of drugs) and possible collaboration is discussed (chaired by the NDAC Chair). If the groups have a clear strategy, they might be the ideal partners to help the pharmaceutical industry in registering their drugs. The DDC “Drug Development Committee” of the Pharmacological and Molecular Mechanism Group (PAMM) could also play a role, as they could easily support or further develop some of the company's drug pipeline (mechanism of actions, pharmacokinetic, pharmacodynamic, etc). This could apply to drugs at any stage of development from preclinical to late clinical stage.

5 FOR EXPERTISE / ADVISORY BOARDS

NDAC may be asked to provide general expertise for drug development to companies. This activity usually performed within the scope of advisory boards/partnership meetings is to be discussed on a case by case basis. The acceptance to conduct an advisory board/partnership meeting for an agent or a group of project(s) should be approved by the majority of NDAC full members. The practical organization of the advisory board/partnership meeting is the responsibility of EPOD. Ideally, NDAC members should attend such advisory boards/partnership meetings. The NDAC chair may appoint other participants according to required expertise and the ultimate goal of the advisory board/partnership meeting. NDAC should always recommend to industrial partners, that they consider performing part or all of the clinical development within the context of EORTC. EORTC group officers may be invited if tumor types to be explored are known in advance. If not, EPOD must report to the CRP and Chair of the disease oriented group and about the potential clinical trial openings. EPOD is responsible for following up the outcome of advisory boards/partnership meetings and the development of clinical trials emerging from such advisory boards/partnership meetings.

TRAC expertise should be present on advisory boards to facilitate the implementation of translational research projects alongside clinical development plans. The TRAC Chair nominates the persons to be present on advisory boards/partnership meetings according to level of expertise.

6 METHODOLOGY

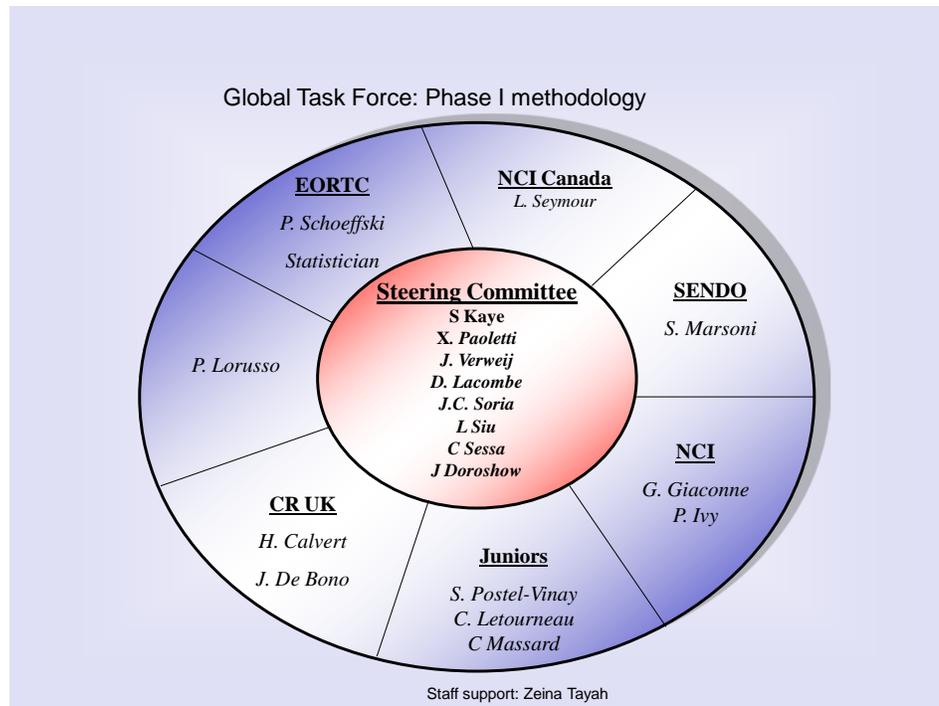
NDAC stimulates and provides expertise for methodological research addressing specific aspects of new drug development in cooperation with EORTC HQ.

Methodological research is one of the missions of EORTC HQ. New drug development is faced with a number of issues linked to specific target modulation, mild toxicity profile, biological surrogate end-points etc., which challenge current methodology. While end-points and statistical designs have to be re-visited, concerted actions are needed between the laboratory researchers, the clinicians, and the methodologists.

NDAC plays a role in promoting a position paper on methodology of phase I trials.

The proposal of having NDAC identify the best approach (e.g. working group, two day seminar, etc.) to position EORTC on challenging issues regarding methodology on early clinical trials (e.g. Dose Limiting

Toxicities (DLT) definition, DLT read-out frame (one cycle or more), chronic toxicity criteria in the era of targeted therapies) has been accepted by the EORTC Executive Committee and EORTC President in June 2010. This initiative is still ongoing.



Primary objectives of the initiative are to define new DLT criteria (which will require peer validation) for chronic dosing => chronic toxicity:

- to assess duration and timing of the DLT;
- to assess appearance of the chronic DLTs;
- to incorporate the new pattern of some toxicities such as asthenia, skin, unusual organ toxicities;
- to explore the possibility of having two sets of MTDs, an acute one and a chronic one.

7 NDAC MEMBERSHIP

NDAC is comprised of full members and additional ex-officio members (Appendix 1). There is a Chair appointed for a period of three years. The Chair of NDAC is a full member of the EORTC Board with voting rights. Chairmanship can be prolonged at discretion of EORTC Board. All members have to file a conflict of interest document and a confidentiality disclosure form.

7.1 Full members

They must dispose on extensive experience in new drug development; their individual background should comprise either clinical research such as medical oncology or laboratory research such as (bio-)chemistry, molecular biology, pharmacy or pharmacology.

7.2 Ex officio members

The EORTC Translational Research Advisory Committee Chair.

The EORTC Translation Research Division Chair.

8 ABBREVIATIONS

CRP	Clinical Research Physician
DOG	Disease Oriented Group
DLT	Dose Limiting Toxicity
EPOD	Early Project Optimization Department
NDAC	New Drug Advisory Committee
PRC	Protocol Review Committee
TRAC	Translational Research Advisory Committee
TRD	Translational Research Division

9 DOCUMENT HISTORY

Version number	Brief description of change	Author	Effective date
1.0	Initial Release	Denis Lacombe	01 Feb 2003
1.1	Transfer to new template; no further modification	Denis Lacombe	14 Feb 2005
1.2	Initiation methodological research on early clinical trials	Denis Lacombe	08 Jan 2013
1.2	No change	Anne-Sophie Govaerts	25 Jan 2016