Policy for Access to MINDACT Biological Materials and Data

Public Version 9

EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

BIG
Breast International Group

Contents

1. Introduction

In the context of the MINDACT clinical trial, *biological materials*, *molecular data, clinical data, outcome data and (central) pathology data* from each of the 6,600 patients participating in the trial have been collected. These materials and data will be used for the purposes of the study as outlined in its protocol, as well as for future research by investigators who have contributed to MINDACT and by the wider scientific community.

This Policy for Access to MINDACT Biological Materials and Data (the "policy") describes the principles and procedures for submitting proposals that are not described in the MINDACT protocol. This policy is in line with the principles of the EORTC POL008 ("Release of data from EORTC studies for use in External Research Projects"[1]) of the European Organisation for Research and Treatment of Cancer (EORTC).

The latest approved version of this *Policy for Access to MINDACT Biological Materials and Molecular Data*, including appendices is publicly available on the EORTC and Breast International Group (BIG) [2] websites.

2. Glossary

TRANSBIG
MINDACT was initiated by TRANSBIG, a translational research consortium partially supported by the European Commission 6th Framework Program (FP6) and coordinated by BIG. The trial is legally sponsored and run by the EORTC, also member of TRANSBIG. Although TRANSBIG disbanded in February 2011 when FP6 funding ended, BIG, the EORTC and several TRANSBIG partners continue their collaboration under the leadership of the MINDACT Steering Committee. The responsibilities and obligations from TRANSBIG were transferred to the MINDACT Steering Committee, which is legally represented by BIG and EORTC.

MINDACT Biological Materials
The MINDACT biological materials consist of frozen breast cancer tissue, tissue microarrays (TMAs), cores, paraffin slides, blood, and serum.
The exact number of samples can be provided upon request[3].
All these samples are stored in an independent facility ("the biobank"), which was set up by BIG with support from the Breast Cancer Research Foundation and maintained with support of the EORTC.

[1] http://groups.eortc.be/radio/res/membership/pol008.pdf
[2] http://www.breastinternationalgroup.org/our-research/clinical-trials/big-3-04-mindact and http://www.eortc.org/investigators/data-sharing/
[3] mindact@bigagainstbc.org and mindactRP@eortc.be

MINDACT Clinical Data
The clinical data available comprise data that were collected by the means of the MINDACT case report forms[4]. These are kept in the MINDACT clinical database located at the EORTC Headquarters (HQ).

MINDACT Molecular Data
The molecular data comprise the 70-gene (Mammaprint®) test results[5] as well as raw genome-wide expression data (44k Agilent arrays) from all patients. These data are kept at the Swiss Institute of Bioinformatics by BIG and the EORTC on behalf of the MINDACT Steering Committee.

MINDACT Central Pathology Data
The central pathology review data consist of histology, grade, ER, PgR, Ki67 and HER2 status analysed at the Istituto Europeo di Oncologia in Milan for all MINDACT samples as indicated in the MINDACT protocol.

MINDACT Steering Committee
The MINDACT Steering Committee (SC) consists of the study principal investigators, the trial's leading scientists, and representatives from each of the following entities: the EORTC HQ, BIG HQ, countries participating in the trial, the pharmaceutical companies that have contributed to the trial, Europa Donna-European Breast Cancer Coalition. The role of the MINDACT SC is manifold. First, it is responsible for maintaining the scientific integrity of the trial, for example, by recommending changes to the protocol in light of emerging clinical or scientific data from other trials. Second, it is responsible for the translation of recommendations of the Independent Data Monitoring Committee into decisions. The SC is also responsible for reviewing and approval of any publications, presentations and official communications using data from the MINDACT study. Finally, it is the body responsible for taking the scientific decisions about internal or external research proposals requesting access to MINDACT materials or molecular data as described in this policy. The list of the MINDACT SC members is available upon request[6].

MINDACT Executive Committee
The MINDACT Executive Committee (ExCo) consists of a subset of the SC, namely the study principal investigators, the leading trial scientists, and representatives of the EORTC HQ, BIG HQ, and of the 5 highest-recruiting countries. The ExCo is responsible for the day-to-day management of the trial and reports to the SC. It is also involved in the review process of internal or external research proposals requesting access to MINDACT materials or data, reporting its decision to the MINDACT SC that endorses its decision.

EORTC TRAC
EORTC Translational Research Advisory Committee: an advisory committee that supports and provides expert advice from a scientific and practical perspective on translational research projects conducted within the EORTC.

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[4] See MINDACT protocol which is available upon request by contacting EORTC (contact form on the EORTC web-site)
[5] Nota Bene : MammaPrint proprietary information will not be shared.
[6] mindact@bigagainstbc.org

Data Sharing Coordinator: The EORTC staff member responsible for the coordination of the review, approval and follow up of the data sharing requests.

Internal and External Proposals
Internal proposals are proposals that include at least one member of the MINDACT SC (formerly TRANSBIG SC). External proposals refer to all others.

Majority approval
Majority Approval means the affirmative vote of at least 51% of the individual members of a given committee who are present or represented at a meeting of such committee. For a vote to be valid at least 60% of the members of a committee have to be present or represented (60% quorum).

3. Governance and responsibilities

The use of the MINDACT biological materials and data for research is decided by the MINDACT SC in accordance with this policy.

The SPONSOR of MINDACT trial acts as the custodian for the MINDACT biological materials and data and hence has the final authority over their use.

The MINDACT clinical data, outcome data and central pathology data recorded in the EORTC central clinical database are under the responsibility of the EORTC as legal sponsor of the trial. The MINDACT Biological Materials stored in the MINDACT biobank and the MINDACT molecular data are under the responsibility of BIG and the EORTC.

The EORTC is the legal entity that will represent the MINDACT SC and as the need arises conclude a contract with institutions of approved projects for the transfer of materials and data[7].

Diagram of the review processes for research proposals can be found in Appendix 1, and the detailed procedure in section 5 of this policy.

4. General principles

1. For each randomization step, no access to outcome data pertaining to the randomization will be given before publication of the results.
2. If similar proposals are submitted (similar objectives and equal scientific merit), the MINDACT Executive Committee will encourage collaboration and a revised joint submission. If collaboration is not possible, priority will be given to internal proposals.
3. Priority will be given to proposals that use the existing clinical and molecular data. All proposals will undergo evaluation as described in Section 5. The amount of biological material made available to any approved proposal will be limited to the minimum necessary to complete the project. Special attention will be given to proposals that involve re-contacting patients.

[7] See section 6 for more information on this contract.

4. The MINDACT Molecular Data will not be used to validate retrospectively RNA gene expression measurements with prognostic value directly competing with Mammaprint® or to validate retrospectively any RNA gene expression measurements with predictive value or with prognostic value directly competing with any service using RNA conducted on the Agilent platform and covered by Agendia's patent rights.
5. The RNA from MINDACT Biological Materials will not be used for any activity, commercial or non-commercial, to validate retrospectively RNA gene expression measurements with prognostic value directly competing with Mammaprint®, or to validate retrospectively any RNA gene expression measurement with predictive value or with prognostic value directly competing with any service using RNA conducted on the Agilent platform and covered by patent rights, unless strikingly superior results are foreseeable with other RNA gene expression measurements, for the benefit of patients, and such validation is performed using as measure outcome of disease exclusively and not Mammaprint® results or results using RNA conducted on the Agilent platform and covered by patent rights. Any raw results or any processed data generated within MINDACT-related projects must be sent to EORTC and can be used for future (internal and external) research projects.

5. Review Procedures

1. The proposal is sent to the EORTC HQ using the Request Form from Appendix 2. The form can be found on the EORTC website (http://www.eortc.org/investigators/data-sharing/) and BIG website (http://www.breastinternationalgroup.org/our-research/clinical-trials/big-3-04-mindact).
2. A feasibility check will be performed by the EORTC as (the MINDACT sponsor), to exclude potential legal or intellectual property issues related to existing contractual commitments and existing ethical approvals for the trial.
3. If no major issue is identified during the feasibility check, EORTC data sharing coordinator transmits the proposal
    - to the EORTC TRAC extended with MINDACT-specific reviewers (projects involving access to samples)
    - to MINDACT-specific reviewers (other projects).
4. Following EORTC TRAC evaluation, the Request Form and EORTC TRAC / MINDACT-specific reviewers' recommendations are sent to the MINDACT Executive Committee for evaluation (approval / conditional approval / rejection) and indication of the priority for execution. The EC will discuss and make recommendations at the earliest possibility at the regular MINDACT ExCo TC or face-to-face meeting.
5. The ExCo recommendations will be submitted to the MINDACT SC by email by EORTC MINDACT PM for endorsement. If concerns expressed, the project will need to be evaluated again by MINDACT ExCo. MINDACT SC members will have 2 weeks to endorse/express their concerns.
    a. If project is "rejected", the applicant will be informed within 10 working days by EORTC HQ.
    b. If project is "conditionally approved", the applicant will be informed within 10 working days by EORTC HQ. It is the responsibility of the applicant to ensure that the Research Project is adapted according to the ExCo and SC

comments and resubmitted within 1 month via EORTC HQ to the EORTC TRAC and ExCo and SC for a final decision (depending which body expressed the concerns).

c. If project is endorsed by MINDACT SC, EORTC will inform the applicant about the final decision, at the latest within 10 working days.

6. For approved projects that will require data transfer or use of samples, data transfer agreements (DTA) or material transfer agreements (MTA) will have to be negotiated between EORTC HQ and the Applicant institution.
7. Proposals that are "Rejected" may be re-submitted after suitably addressing the concerns and comments raised by the MINDACT ExCo and SC. The process will stop after the second rejection of the Research Project by the ExCo and SC.

6. Instructions for applicants

1. For access to the MINDACT data and/or biological samples**,** applicants must submit **a Request Form** which can be found in **Appendix 2 of this policy**. This form is to be submitted to EORTC HQ via e-mail (mindactRP@eortc.be).
2. EORTC HQ sends an acknowledgement of receipt to the applicant. The applicant may be asked to address concerns and comments raised during the review process and to submit a revised proposal before a final decision is taken.
3. Within maximum six months after the date of submission, the applicant(s) will receive a final formal written response from EORTC HQ on behalf of the MINDACT SC relaying the decision about the proposal. A project cannot be implemented without first having received formal written approval.
4. If the proposal has been approved, the following applies:
    a. Before samples / data can be released,
        i. the responsible investigator(s) must demonstrate that all applicable approvals (e.g. ethics committee) have been received
        ii. **a data / material transfer agreement** must be signed between the EORTC and the institution(s) of the responsible investigator(s). The agreement will cover issues such as use of data and/or biomaterial (its use in a manner not specified in the agreement/ proposal is strictly prohibited), confidentiality, data ownership, intellectual property rights, publication / presentation, and financial issues. Note that a financial contribution for the management of the biobank and clinical database may be requested.
    b. Publications / presentations related to the project must comply with the **MINDACT Publication Principles**[9] which comply with the EORTC Policies: "Disclosure of Results and Publication Policy" (POL009). Among other aspects, these foresee but are not limited to:
        i. All publications / presentations must be submitted to EORTC and BIG for review prior to their submission to a journal, a congress or any presentation.
        ii. All MINDACT funding bodies are to be acknowledged in all presentations and publications. The clause will be included as well in the data / material transfer agreement.

iii. Co-authors include EORTC Headquarters' staff who contributed to the analysis and publication (if any). Other co-authors are selected amongst the other scientific contributors to the research project and/or investigators who contributed patient and data to the study and/or MINDACT Steering Committee members. The list of co-authors must be approved by MINDACT Steering Committee.

iv. If the authorship list does NOT contain any EORTC Headquarters' staff AND if it was NOT agreed upfront that the publication would be "on behalf of EORTC" or as "EORTC research", the EORTC must be acknowledged for sharing the data for the research and the publication/presentation must contain the following disclosure "The contents of this publication and methods used are solely the responsibility of the authors and do not necessarily represent the official views of the EORTC".

v. All publications/presentations must acknowledge the source of the Study Data/Biological Samples (MINDACT), and mention that MINDACT is sponsored by EORTC, conducted in collaboration with BIG.

[9] provided upon request to mindact@bigagainstbc.org

7. Applicable fees

The MINDACT access fees are mandated and determined by the EORTC Headquarters. The MINDACT Executive, Steering Committee and Investigators are not responsible for this request. Any discussion regarding the fees should be directed to mindactRP@eortc.org.

7.1 For MINDACT investigators who enrolled more than 100 patients for research projects that will be done at their institution

Type of requested access	MINDACT clinical data	MINDACT clinical data + samples	MINDACT clinical data + genomic data	MINDACT clinical data + genomic data + samples
Clinical data access fee	2500E	2500E	2500E	2500E
Samples access fee		2300E + sample handing (75E + 1.13E/sample + dry ice shipments)		2300E + sample handing (75E + 1.13/sample + dry ice shipments)
Genomic data access fee			1000 E for academic requestor	1000 E for academic requestor
TOTAL	**2500E**	**4875E +1.13E/sample**	**3500E**	**5875E +1.13E/sample**

7.2 For any non-commercial requestor

Type of requested access	MINDACT clinical data	MINDACT clinical data + samples	MINDACT clinical data + genomic data	MINDACT clinical data + genomic data + samples
Clinical data access fee	5000E	5000E	5000E	5000E
Samples access fee		2300E + sample handing (75E + 1.13E/sample + dry ice shipments)		2300E + sample handing (75E + 1.13/sample + dry ice shipments)
Genomic data access fee			1000 E for academic requestor	1000 E for academic requestor
TOTAL	**5000E**	**7375E +1.13E/sample**	**6000E**	**8375E +1.13E/sample**

For commercial requestors the fees may vary. Please contact EORTC HQ (mindactRP@eortc.org) for details.

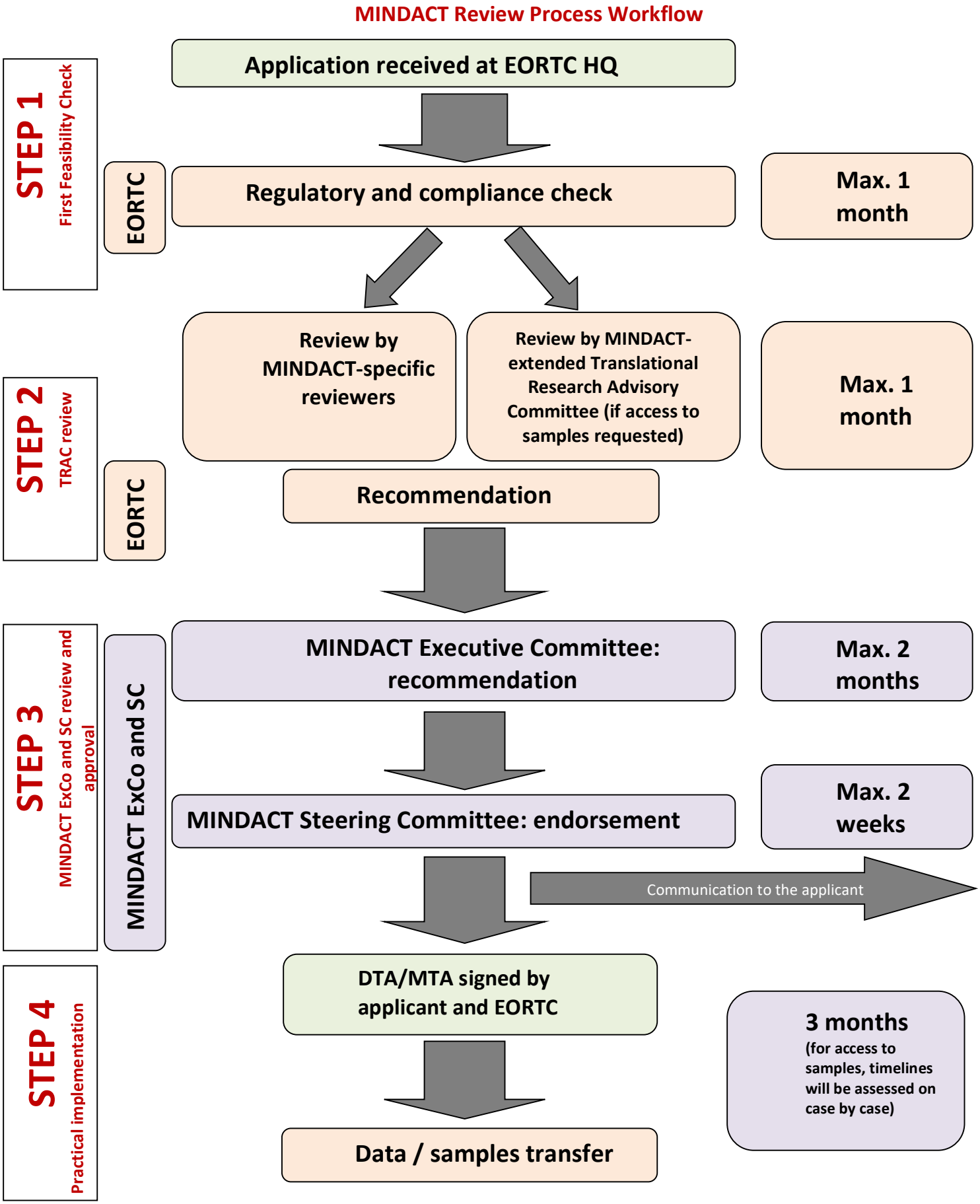
8. Confidentiality

The content of all project proposals will be kept confidential by all parties involved in the review process. The members of the Executive Committee and Steering Committee are bound to confidentiality as referred in the committee's guidelines. The TRAC and MINDACT-specific reviewers will sign a confidentiality agreement prior to receive the proposals.

All MINDACT ExCo and SC members and TRAC and MINDACT-specific reviewers must treat as strictly confidential, the research proposal, meetings discussions, minutes and any information related to the review of research proposals.
All MINDACT ExCo and SC members and TRAC and MINDACT-specific reviewers shall be responsible for the breach of any of the terms hereof by any member of their institution.

In the event it becomes necessary for a MINDACT ExCo or SC member, or a TRAC or MINDACT-specific reviewer to disclose confidential information related to research proposals to third parties (including members of his/her Institution), such disclosure shall be made only with the approval of the MINDACT ExCo and under obligation of secrecy no less restrictive than the obligations of the member hereunder. Such member remains responsible for any third party's breach of confidentiality.

Appendix 1: Diagram of the review process workflows



<u>Appendix 2</u>: Request form for access to samples and/or data

REQUEST FORM
Biological Samples and/or Data

Applicants are invited to submit additional documentation that may facilitate review of their proposal as supplementary appendices.

This form and any accompanying documents must be submitted to:
mindactRP@eortc.be

PROJECT TITLE:

PROPOSAL REQUEST DATE:

REQUESTOR NAME:

INSTITUTION WHERE THE RESEARCH IS CONDUCTED:

WHAT IS THE MAIN SCOPE OF YOUR PROJECT (Meta-analysis, translational research, statistical or methodological research):

CONTACT DETAILS (Scientific Leader):

NAME :	
ADDRESS:	

TEL:	
E-MAIL:	

CONTACT DETAILS (Involved Team member(s)):

NAME :	
ADDRESS:	
TEL:	
E-MAIL:	

CONTACT DETAILS (Statistician):

NAME :	
ADDRESS:	
TEL:	
E-MAIL:	
CV:	If not an EORTC statistician, please provide the CV

1 – PRELIMINARY INFORMATION

Any raw results or any processed data generated within MINDACT related projects should be sent to EORTC and can be used for future (internal and external) research projects.

Does the proposal require the use of biological material from the MINDACT biobank?
Yes / No

if yes, please:
Specify the type of samples and estimated quantity: ☐ _____frozen tumour ☐ _____blood ☐ _____Serum ☐ _____TMA ☐ _____RNA

Explain explicitly why MINDACT samples are required for your research (as opposed to samples that were collected outside of a clinical trial)

Does the proposal imply re-contacting the patient? (e.g. ICF, questionnaire)	
Yes No	if yes, specify & justify reason for doing so:

Does the proposal require the use of the clinical data collected during the MINDACT trial?	
Yes No	If yes, list the variables requested: • baseline/patient characteristics • treatment data • outcome data • other (safety, QOL…)
Does the proposal require the collection of additional clinical data?	
Yes No	If yes, please be informed that the patient will need to be re-consented. If yes, please specify which type of molecular data: (gene expression, etc.) Do you need those data from: all patients selected patients

Does the proposal require the use of molecular data?	
Yes No	if yes, specify: all genes selected genes all patients selected patients

2 – PROJECT DESCRIPTION

RESEARCH QUESTION(S):

ABSTRACT OF RESEARCH PLAN (including BACKGROUND, OBJECTIVES AND (IF APPLICABLE) EXPERIMENTAL TECHNIQUES TO BE APPLIED ON THE SAMPLES i.e. sequencing, IHC) max. 300 words

SAMPLE SIZE AND PARTICIPATING SITES & COUNTRIES

STATISTICAL METHODS AND ANALYSIS PLAN:

PROPOSED TIMELINE (START AND COMPLETION DATES):

3 – PRACTICAL IMPLEMENTATION

Please note that a financial contribution will be requested. For the details please refer to the "Policy for Access to MINDACT Biological Materials and Data".

PLAN FOR THE TRANSFER OF DATA (Please fill in if applicable. By default, the trial data are transferred to you in the form of a SAS-readable set of files. However, if you are unable to read that format, please specify an alternative format you prefer (Excel, Text..). Specify here which variables you need. Indicate "all data" if you need the complete database. Please indicate the suggested date of the data transfer):

Note that a Data Transfer Agreement between the EORTC, BIG and the applicant's institution is required. See Policy for Access to MINDACT Biological Materials and Data for more details.

PLAN FOR THE TRANSFER OF SAMPLES (if applicable):

Note that a Material Transfer Agreement between the EORTC the applicant's institution is required. See Policy for Access to MINDACT Biological Materials and Data for more details.

HAVE YOU ALREADY OBTAINED THE ETHICAL COMMITTEE APPROVAL FOR THIS PROJECT? If yes, please attach all documents that were sent/required by your EC for the approval of this project as well the approval document itself. If no, please justify why the approval is/will be not requested.

BUDGET (also specify source(s) of funding and involvement of any participating third parties, i.e. company, collaborating group):

EXPECTED PUBLICATIONS (also specify the preliminary titles and timeliness of first publication):

AUTHORSHIP (for the EORTC, BIG and MINDACT representatives)

PLANNED EXPLOITATION AND OWNERSHIP OF INTELLECTUAL PROPERTY RIGHTS OF RESEARCH RESULTS (if applicable)

SUPPLEMENTAL APPENDICES (please list):
