Policy for Access to Residual Biological Samples and Data in the ALTTO and NeoALTTO Studies ("Policy")

Version 3

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version 3 to amalgamate the "Procedure for Access to Biological Materials and Genomic / Clinical Data in the ALTTO Trials" and "Procedures for Data Collection, Data Sharing and Data Access".

Policy for Access to Residual Biological Samples and Data in the ALTTO and NeoALTTO Studies

1. Introduction

GlaxoSmithKline Research and Development Limited ("**GSK**"), Breast International Group – aisbl ("**BIG**") and Institut Jules Bordet ("**IJB/BrEAST**") entered into a Clinical Trials Agreement with an effective date of 19 April 2007 which was subsequently amended by various amendments (the "**CTA**"). The CTA was assigned from GSK to Novartis Pharma AG (**"Novartis"**) effective as of 30 November 2015.

Unless otherwise defined below, all capitalized terms in this Policy shall have the meanings as defined in Appendix 8 - Definitions.

Within the framework of the ALTTO and NeoALTTO studies, originally sponsored by GSK and now sponsored by Novartis, and conducted under the auspices of BIG and IJB/BrEAST, Data and Residual Biological Samples were collected, stored and later made available to carry out Follow-on Studies, for the purpose of correlative science research. The Alliance for Clinical Trials in Oncology (**"Alliance**") (previously North Central Cancer Treatment Group ("**NCCTG**")) is a partner for the ALTTO study and SOLTI is a partner for the Neo-ALTTO study. The Biological Samples and Data are available for analyses as outlined in the Studies' Protocols, as well as for new, independently-funded research projects (conducted outside the Studies' Protocols, using Residual Biological Samples and/or Data,) that may be proposed by investigators participating in the Studies and by the wider scientific community, hereinafter referred to as "**Research Project Proposal(s)**"or "RP Proposals" (RP Proposal(s).

A strict, fair and scientific review process of RP Proposals is set up to ensure precious Residual Biological Samples and Data collected in the Studies are accessed appropriately. A distinction is made between RP Proposals requiring access to Residual Biological Samples (with/without Data) and RP Proposals requiring access to Data only (without Residual Biological Samples). This Policy provides the guidelines for the review and approval of such RP Proposals.

This Policy does NOT cover translational research analyses that are already part of the Studies' Protocols and/or Sub-Study.

This Policy is NOT applicable to the results generated by the approved (under this Policy) Research Project (hereinafter referred to also as "Research Project" or "RP"). The terms governing the use of the results of the R Pare described in section 4 of this Policy (Results generated by the approved (under this Policy) RP) and further defined in the contract covering the transfer of the Residual Biological Samples and/or Data (materials/data transfer agreement / material use agreement).

2. General Principles

2.1 Research Project or Follow-on Study

"Research Project" or "Follow-on Study" refer to studies conducted outside the Study Protocols, using Data and/or Residual Biological Samples as specifically i) approved by the Steering Committee (on Executive Committee (EC) recommendation as the case may be) when it concerns Data only and ii) allowed by the TRANSALTTO Committee and endorsed by the Steering Committee when it concerns Data and Residual Biological Samples, including for example translational research studies.

2.2 Residual Biological Samples

"Residual Biological Samples" means any left-over part of Biological Samples remaining after the processing and analyses carried out according to the Study Protocol and/or Sub-Study as well as any Biological Samples initially collected, processed and stored for Follow-On Studies. Residual Biological Samples include but are not limited to: formalin-fixed paraffin embedded (FFPE) tumour tissue, tumour tissue microarrays (TMAs), snap frozen tumour tissue, extracted tumour RNA/DNA as well as blood, plasma and PGx samples (blood and/or DNA). The samples collected for ALTTO are stored at Instituto Europeo di Oncologia (IEO) in Milan and the samples collected for NeoALTTO at Vall d'Hebron Institute of Oncology (VHIO) in Barcelona. Shipping costs of the requested Residual Biological Samples are under the investigator'(s') responsibility.

2.3 Data

"**Data"** means all data collected regarding the patients recruited within the framework of the Studies, in any format whatsoever, whether such data was reported in the Case Report Forms ("**CRFs**"); or, on ancillary data collections forms; or, whether captured by electronic means, including but not limited to electronic (scanned) images of stained slides already available (i.e. no cutting of new slides is needed).

Compliance with Applicable Laws: all RP Proposals shall comply with applicable laws, rules, regulations, guidance, guidelines and standards relating to data protection (including the European Data Protection Directive 95/46/EC, the General Data Protection Regulation EU2016/679 and the EU-US Privacy Shield as applicable), as amended from time to time, with respect to the processing and securing of Data.

Personal data of applicant, co-applicant and institution's employees: the institution and applicant expressly consent to authorize the collection, processing and transfer of institution's and applicant's personal data to countries other than institution's and applicant's own country, even though data protection may not be as developed there. Novartis shall use reasonable efforts to achieve an appropriate level of confidentiality, when reviewing the RP Proposal.

2.4 Custodianship and Ownership

All Residual Biological Samples are stored on behalf of the Studies' Steering Committee ("**SC**"), which is the custodian of the Biological Samples and Residual Biological Samples, in various independent facilities specified by the relevant Studies' clinical trial documents.

All Data are owned by BIG and IJB/BrEAST.

Governance:

The SC is the ultimate governing body of the Studies and makes the final decision on the approval of the RP Proposals.

The TRANSALTTO Committee ("**TrAC**") is a group of clinicians and scientists, with demonstrated expertise in translational research, that will be involved in the translational aspects of the ALTTO studies (for both Neo-ALTTO and ALTTO). Endorsed by, and functioning under the governance of the SC, the TrAC is an advisory body for translational projects that are already embedded within the Study Protocols, in addition to being a reviewing body for RP Proposals (refer to TransALTTO Committee Guidelines version 1.1 from 12th of June 2015 for details).
The responsibilities of the TrAC include the following:

- Provide advice (and any necessary recommendations) on translational research projects already embedded in the Study Protocols to the Joint Study Management Team, EC and SC when required
- Review, vote on and recommend RP Proposals requiring the use of Residual Biological Samples for final approval by the SC.
- Provide advice on RP Proposals NOT requiring the use of Residual Biological Samples (ie: Data only) to the EC and SC (if required)

2.5 Review of RP Proposals

All RP Proposals, in addition to representing outstanding scientific merit in order to obtain approval, must:

- Specify exactly what types and amount of Data and/or Residual Biological Samples are needed, based upon the proposed analysis and the statistical rationale;
- Be compatible with all current Studies' informed consent forms ("**ICFs**"), as well as related policies and contractual commitments developed for the Studies (including but not limited to Principles Guiding Publications and Presentations (including abstracts and posters (the "((Neo)ALTTO Publication Guidelines)" (see Appendix 6), Intellectual Property Rights (IPR));
- Be self-funded with description of potential funding sources.

If a RP Proposal requires additional ethical-scientific review (as decided by the scientific reviewers), ethical-legal experts will be appointed by the TrAC chairs (for RP Proposals requiring Residual Biological Samples with/without Data) or by the EC chairs (for RP Proposals requiring Data only). RP Proposals requiring access

to Residual Biological Samples with/without Data or Data only require confirmation from the Novartis Precision Medicine (assoc.) Director (on behalf of the Tykerb global program team) that the scope of the RP Proposal is covered by the ICFs signed by the patients.

In case researchers are asked to make any changes to their RP Proposal, every effort should be made to implement the changes within 5 working days, in time for re-evaluation during the same call. Otherwise the modified RP Proposal needs to be submitted with the next call.

The content of all RP Proposals shall be kept confidential by all reviewers.

There are two different types of RP Proposals:

1) *RP Proposals requiring Residual Biological Samples (with/without Data)*

As a general principle, the SC will propose a given number of calls per year for RP Proposals requiring access to Residual Biological Samples (with/without Data), depending on the Residual Biological Samples availability.

All RP Proposals requiring Residual Biological Samples submitted within the same call will be reviewed by:

- 2 (two) TrAC members. In case one of the designated TrAC members has a conflict of interest with a specific RP Proposal, another reviewer will be proposed for that proposal.
- 1 (one) of the Studies' statisticians, independent from the RP Proposal;
- 1 (one) external scientific reviewer appointed by the TrAC chairs, if necessary.

On the basis of these reviews, the TrAC makes a recommendation to the SC, which will take the final decision to grant or deny access to the Residual Biological Samples (with/without Data). Under special circumstances, if requested by the TrAC chairs, the SC can delegate the final voting to the EC. Such special circumstances could include an unexpected backlog of RP Proposals, or an extraordinary RP Proposal requiring rapid decision-making.

In case funding is not secured, conditional approval can be given by the SC for an initial period of up to 6 (six) months. During this time, the applicant must secure the required funding. Any request for an extension to the conditional approval will be considered on a case-by-case basis only.

A distinction shall be made between internal and external RP Proposals, as follows:

a) Internal RP Proposals: These are proposals made by researchers who have contributed to the Studies in any form or manner, such as investigators and members of any Studies committees (EC, SC, TrAC, Cardiac Advisory Board (CAB). Internal proposals will be granted 2 (two) additional points during the review process.

b) External RP Proposals: These are proposals made by researchers from the wider scientific community not involved with the Studies.

In addition, RP Proposals which request access to the Alliance Residual Biological Samples will also need to be submitted to the National Cancer Institute ("**NCI**") for additional scientific review and approval. NCI review will be performed on all such RP Proposals which have been already approved by the SC. This process is under the responsibility of the researcher.

The data set used in analyses for all abstracts and publications should be the one provided by the Independent Statistical Team, which has been derived from the IJB/BrEAST Data Center database. The RP Proposal must also clearly identify the statistician involved in the RP design and performing the analyses.

2) *RP Proposals requiring Data only*

As a general principle, the SC will propose two to three calls per year for RP Proposals requiring access to Data only. Should it be deemed appropriate, additional calls can be issued, after SC approval.

All RP Proposals requiring access to Data only submitted within the same call will be reviewed by 3 (three) voting members of the EC (independent from the RP Proposal), who have been appointed by the EC chairs as the designated reviewers for that call. In case a reviewer has a conflict of interest with a specific RP Proposal, another reviewer will be proposed for that proposal. The three independent designated EC voting

members will make a recommendation to the EC for all requests. The EC then makes a recommendation to the SC, which will make the final decision. The SC, taking into account the EC recommendation, will decide to either grant or deny access to the Data.

The data set used in analyses for all abstracts and publications should be the one provided by the Independent Statistical Team, which has been derived from the IJB/BrEAST Data Center database. The RP Proposal must also clearly identify the statistician involved in the RP design and performing the analyses.

2.6 Changes to a RP Proposal

BIG HQ must be informed of any changes that an investigator intends to apply to an approved RP Proposal. Administrative changes that do not affect the scientific aspects of the RP, the number of Residual Biological Samples required or the amount of Data requested, do not need to be re-evaluated by the TrAC, EC and/or SC. If the changes affect the scientific aspects of the RP, the number of Residual Biological Samples required or the amount of Data requested, BIG HQ will submit the changes to the EC chairs (Data only proposals) or TrAC chairs (proposals requiring Residual Biological Samples with/without Data) who will decide whether a new RP Proposal needs to be submitted during the following call, or whether the changes can be sent to the SC for endorsement. The appointed evaluators (i.e. EC or TrAC chairs) will need to have no conflict of interest with the RP Proposal.

2.7 Appeal process

If a request for Data or Residual Biological Samples with/without Data is denied by the SC, the applicant may appeal the decision. In the case of an appeal, the SC can charge the EC with the responsibility to investigate the appeal case in detail. The decision of the EC in such cases will be deemed final.

2.8 Contractual Commitments

All RPs will require a materials transfer agreement ("**MTA**") /data transfer agreement ("**DTA**") /material use agreement ("**MUA**") to be signed by the applicant which will detail data ownership, intellectual property rights, publication, confidentiality, possible exploitation issues and budget.

BIG shall ensure that:

(a) the terms of the MTA/ DTA/ MUA provide Novartis with all rights granted in the CTA (including any and all amendments thereto) and that the terms of the MTA / DTA / MUA contain those provisions of the CTA (including any amendments thereto) which safeguard Novartis' interests. Such rights and interests include without limitation all rights and interests relating to intellectual property, ownership and confidentiality; and that the MTAs/DTAs/MUAs are consistent with the terms of the CTA; and

(b) the items listed below, shall be incorporated *mutatis mutandis* in the MTA / DTA / MUA:

Regardless of when or what type of Data/ Residual Biological Samples are released, the following conditions will apply:

1. The Data/ Residual Biological Samples shall only be used for the purpose for which they have been approved. If the researcher(s) later wish(es) to use the same Data/ Residual Biological Samples for another purpose, another request is required to be submitted. Data/ Residual Biological Samples should be kept secure after transfer to the researcher(s).
2. The researcher(s) must not share the Data/ Residual Biological Samples with anyone else without the prior permission of the SC.
3. The Data must be kept confidential.
4. All regulatory and legal requirements for the use and/or processing of Data/ Residual Biological Samples must be met.
5. If a patient withdraws consent and the site submits a sample destruction form, IJB/BrEAST shall ensure that any remaining Residual Biological Samples from that patient are destroyed. IJB/BrEAST shall inform BIG of the request for sample destruction.

2.9 Left-over Residual Biological Samples

After completion of the RP, any and all left-over Residual Biological Samples shall be returned to the relevant tissue repository that the Residual Biological Sample was taken from under the responsibility and at the expense of the investigator(s). Only with written permission from the SC can left-over Residual Biological Samples be stored in the Investigator's laboratory. Such permission shall detail the future handling and storage of the Residual Biological Samples. Any additional usage of the left-over Residual Biological Samples, beyond the initial RP Proposal, must undergo another review process (including feasibility review) and be approved by the SC.

2.10 Publications / Presentations

All publications arising out of the use of the Data/ Residual Biological Samples are subject to the (Neo)ALTTO Publication Guidelines (see Appendix 6).

Prior to submission of a publication or an abstract, including oral presentations, NOVARTIS and the sponsor(s) of the RP, shall have the right to review and comment on the content of the material to be published or presented, Novartis shall have the right to have deleted any confidential information provided by Novartis to a Partner pursuant to the Clinical Trial Agreement or any amendment thereto. This is applicable for Internal Proposals since external researcher will not receive any confidential information. The time frame to complete the review shall not exceed thirty (30) calendar days. However, during this review period, NOVARTIS may request delay of submission for an additional period up to a maximum of ninety (90) calendar days from the original submission to NOVARTIS. This is for the sole purpose of deciding on Patent filing. If such a delay is imposed, NOVARTIS will notify the principal author.

All RP must properly acknowledge the source of the Data and Residual Biological Samples in all presentations and publications. Acknowledgement of particular individuals may be requested on a case-by-case basis.

3. Procedure

The procedures are summarized in Appendix 1. The SC will periodically issue a "Call for Research Project Proposals" and informs the Frontier Science (FS) Research Project Proposals Coordinator ("RPPC"). This call will also be announced via various means, including but not limited to, the BIG, IJB/BrEAST website, email notification to all study Principal Investigators and in study newsletters. A deadline will be specified, and only electronic submission of RP Proposals before the deadline will be accepted, using the Research Project Proposal Submission Forms ("RPPS Form" – see Appendix 2 and 3 of the Policy).

3.1. RP Proposals requiring access to Residual Biological Samples (with/without Data)

1. *RP Proposal Submission*
   - A group, institution or researcher who would like to have access to the Studies' Residual Biological Samples with/without Data should submit their RP Proposal to the **RPPC** using the RPPS Form (see Appendices 2 and 3). Only RP Proposals submitted after a call for RP Proposals is announced and within the set timeline, will be reviewed. The RPPC is the primary point of contact for RP Proposals.
   - A RP Proposal number will be allocated which will be also used in all related communication and contractual arrangements.
   - The RPPC checks within 3 (three) working days the RPPS Forms for completeness and returns incomplete forms to the researcher who submitted them. The researcher has to return the complete RP Proposal within 5 (five) working days.
2. *Feasibility review*
   - Within 3 (three) working days after the submission deadline, the RPPC sends the RP Proposals to representatives from IJB/BrEAST, FS and to the Precision Medicine (assoc.) Director for Tykerb-Novartis for data management, statistics and ICF compliance review.
   - The representatives from IJB/BrEAST, FS and Novartis will provide their comments within 10 (ten) working days to the RPPC.

    - If Novartis confirms that the RP Proposal is not covered by the ICF, the RPPC will inform the researcher that the RP Proposal needs to be modified accordingly. If the RP Proposal can't be modified to comply with the ICF signed by the patients, it will be rejected.
  - In addition, the RPPC forwards any questions, requests or concerns received during this step to the researcher who will then modify the RP Proposal as necessary and return it to the RPPC within 5 (five) working days.
  - Within 5 (five) working days after the feasibility review deadline, the RPPC sends the reviewed RP Proposals to the TrAC chairs, copying BIG HQ.

3. *Appointment of Reviewers*
   - Within 5 (five) working days after receiving the documents, the TrAC chairs appoint 3 (three) (scientific) independent reviewers to evaluate all RP Proposals submitted within the call and inform the RPPC. The reviewers may be members of the TrAC and/or external reviewers. One of the reviewers must be one of the Studies' statisticians, independent from the RP Proposal.
   - Within 3 (three) working days after being informed by the TrAC chairs, the RPPC provides the reviewers with the RP Proposals and scoring guidelines (see Appendix 4).

4. *Scientific Review*
   - The scientific reviewers may request additional ethical-legal review. In such a case, the TrAC chairs appoint the appropriate independent experts.
   - The scientific reviewers score the RP Proposals from 1 to 5 on six different criteria.
   - The scientific reviewers return their formal review to the RPPC within 10 (ten) working days.
   - A RP Proposal will be proposed for approval to the TrAC Chairs if all obligatory criteria are met and the average scientific score is ≥ 24 or for rejection if the score is <24.
   - The RPPC compiles and provides the TrAC chairs, copying BIG HQ, with an overview of those RP Proposals which are recommended and those which are not recommended within 5 (five) working days.

5. *Recommendation by the TrAC chairs*
   - Within 5 (five) working days, the TrAC chairs check the RP Proposals for overlaps and similarities and present a summary of the evaluated RP Proposals, a suggested decision (approve / reject / conditionally approve / collaborate (for example, in case of overlapping scope)) and a priority for implementation to RPPC.
   - Within 3 (three) working days, RPPC provides all TrAC members with a copy of the RP Proposals and the TrAC chairs' recommendation.

6. *TrAC review*
   - Within 5 (five) working days, the TrAC members provide their feedback (approve / reject / conditionally approve / collaborate (for example, in case of overlapping scope) and a priority for implementation) to the RPPC and TrAC chairs.
   - Voting is by simple majority. In case of voting by e-mail, a "no-reply" by the deadline will be considered as an approval.

7. *Final TrAC recommendation*
   - Within 3 (three) working days, the TrAC chairs and RPPC will liaise to finalize the summary for the SC.
   - RPPC sends the summary and final TrAC recommendation (approve / reject / conditionally approve / collaborate (for example, in case of overlapping scope) and a priority for implementation) to the SC within 3 (three) working days copying BIG HQ.

8. *Steering Committee approval*
   - Within 10 (ten) working days, the SC will endorse (or not) the RP Proposals.

9. *Feedback to researcher*
   - The RPPC will inform the researcher within 3 (three) working days about the approval status of their RP Proposal, copying BIG HQ.

- In case a proposal is conditionally approved, the updated proposal can be resubmitted outside of a call for proposals. The TrAC chairs decide whether the updated proposal needs to go back to the reviewers or can immediately go to the whole TrAC for recommendation and subsequently the SC for endorsement.
- An investigator of a rejected proposal can only resubmit an updated proposal during a new call for proposals.

10. Submission to the NCI (only for proposals requesting access to US samples)

- After formal SC approval, the researcher should complete section A-2 of the RPPS Form and submit it to the NCI to request access to the US samples. The submission process to the NCI is the responsibility of the researcher.

*11. Materials transfer agreement ("**MTA**")*

- For Non-US samples, BIG HQ and the researcher will liaise with each other to set up a MTA. The MTA will need to be signed by the investigator's institution, BIG, IJB/BrEAST and any other Principal Investigator indicated in the RP Proposal.
- For RPs involving US samples, after having received the NCI approval, the researcher will contact Mayo Clinic's biobank directly to set up a MTA/MUA for the US Residual Biological Samples & Data.
- BIG will ensure that any MTA / MUA that will be established provides Novartis with all rights granted in the CTA (including any and all amendments thereto) and is consistent with the terms of the CTA.
- BIG informs IJB/BrEAST and FS when the signature process of a MTA has started. FS will then liaise with the investigator in order to establish the format of the data transfer.
- BIG informs IJB/BrEAST, FS and IEO/VHIO (for ALTTO/NeoALTTO respectively) when a MTA is fully executed. For sake of clarity, no data or Residual Biological Material will be transferred to investigators conducting RPs without a previous confirmation from BIG that the MTA is fully executed.
- Dataset(s) will be prepared by IJB/BrEAST and FS after they receive the confirmation from BIG that the MTA is fully executed. In addition, the investigator/research statistician shall discuss and agree the required variables with the FS statisticians. After that, investigators (or their representatives) will receive the dataset via IJB/BrEAST. To allow FS and IJB/BrEAST to prioritize this in their workload and accommodate all requests, FS and IJB/BrEAST have up to 4 calendar weeks to deliver the data to investigators. The 4 calendar weeks period will start the moment that the investigator and the FS statistical team have fully agreed on the needed variables and not at the moment of MTA signature
- Each time datasets are transferred to the investigators, FS and IJB/BrEAST shall inform BIG about this transfer within 1 calendar week by providing the specific date of transfer.
- Each time ALTTO / NeoALTTO Residual Biological Samples are transferred to the investigator by IEO / VHIO respectively, the biobank representatives shall inform BIG about this transfer within 1 calendar week by providing the specific date of transfer.

3.2. RP Proposals requiring access to Data only

1. RP Proposal submission

- A group, institution or researcher who would like to have access to the Studies' Data, should submit their RP Proposal to the RPPC using the RPPS Form (see Appendix 2 and 3). Only RP Proposals submitted after a call for proposals is announced and within the set timeline, will be reviewed. The RPPC is the primary point of contact for RP Proposals.
- A RP Proposal number will be allocated which will be also used in all related communication and contractual arrangements.
- The RPPC checks, within 3 (three) working days the RPPS Forms for completeness and returns incomplete forms to the researcher who submitted them. The researcher has to return the complete RP Proposal within 5 (five) working days.

2. *Feasibility review*
    - Within 3 (three) working days after the submission deadline, the RPPC sends the RP Proposals to representatives from IJB/BrEAST, FS and to the Precision Medicine (assoc.) Director for Tykerb-Novartis for data management review, statistics and ICF compliance.
    - The representatives from IJB/BrEAST, FS and Novartis will provide their comments within 10 (ten) working days to the RPPC.
        - If Novartis confirms that the RP Proposal is not covered by the ICF, the RPPC will inform the researcher that the RP Proposal needs to be modified accordingly. If the RP Proposal can't be modified to comply with the ICF signed by the patients, it will be rejected.
    - In addition, the RPPC forwards any questions, requests or concerns received during this step to the researcher who will then modify the RP Proposal as necessary and return it to the RPPC within 5 (five) working days.
    - Within 5 (five) working days after the feasibility review deadline, the RPPC sends the reviewed RP Proposals to the EC chairs, copying BIG HQ.

3. *Appointment of Reviewers*
    - Within 5 (five) working days after receiving the documents, the EC chairs appoint, 3 (three) voting independent members of the EC to evaluate all RP Proposals submitted during the call and inform the RPPC.
    - Within 3 (three) working days after being informed by the EC chairs, the RPPC provides the RP Proposals and scoring guidelines (see Appendix 4) to the 3 (three) designated EC members for review.

4. *Designated EC members review*
    - The reviewers may request additional scientific and/or ethical-legal review. In such case, the EC chairs appoint the appropriate independent experts.
    - The scientific reviewers score the RP Proposals from 1 to 5 on four different criteria.
    - A RP Proposal will be proposed for approval to the EC if all obligatory criteria are met and the average scientific score is ≥ 16.
    - The scientific reviewers return their formal review to the RPPC within 10 (ten) working days.

5. *EC Review*
    - The RPPC compiles and provides the EC with an overview of those RP Proposals that are recommended and those that are not recommended within 3 (three) working days, copying BIG HQ.
    - Within 5 (five) working days, the EC members provide their final recommendation (approve / reject / conditionally approve) for each proposal.
    - The RPPC will forward the overview of the RP Proposals and the EC recommendations to the SC within 5 (five) working days, copying BIG HQ.

6. *Steering Committee approval*
    - The SC will adjudicate the EC's recommendations within 10 (ten) working days and has the final decision.

7. *Feedback to researcher*
    - Within 3 (three) working days of the SC's formal answer, the RPPC will inform the researcher about the SC's decision, copying BIG HQ.
    - In case a proposal is conditionally approved, the updated proposal can be resubmitted outside of a call for proposals. The EC chairs decide whether the updated proposal needs to go back to the reviewers or can immediately go to the whole EC for recommendation and subsequently the SC for endorsement.
    - An investigator of a rejected proposal can only resubmit an updated proposal during a new call for proposals.

8. *Data transfer agreement ("**DTA**")*
    - The researcher will liaise with BIG HQ to set up a DTA. The DTA will need to be signed by the investigator's institution, BIG, IJB/BrEAST and any other Principal Investigator of the RP Proposal.
    - BIG will ensure that any DTA that will be established provides Novartis with all rights granted in the CTA (including any and all amendments thereto) and is consistent with the terms of the CTA.
    - BIG informs IJB/BrEAST and FS when the signature process of a DTA has started. FS will then liaise with the investigator in order to establish the format of the data transfer.
    - BIG informs IJB/BrEAST and FS when a DTA is fully executed. For sake of clarity, no data will be transferred to investigators conducting RPs without a previous confirmation from BIG that the DTA is fully executed.
    - Dataset(s) will be prepared by IJB/BrEAST and FS after they receive the confirmation from BIG that the DTA is fully executed. In addition, the investigator/research statistician shall discuss and agree the required variables with the FS statisticians. After that, investigators (or their representatives) will receive the dataset via IJB/BrEAST. To allow FS and IJB/BrEAST to prioritize this in their workload and accommodate all requests, FS and IJB/BrEAST have up to 4 calendar weeks to deliver the data to investigators. The 4 calendar weeks period will start the moment that the investigator and the FS statistical team have fully agreed on the needed variables and not at the moment of DTA signature.
    - Each time datasets are transferred to the investigators, FS and IJB/BrEAST shall inform BIG about this transfer within 1 calendar week by providing the specific date of transfer.

3.3 Data access by individual non-profit academic institutions / Participating Groups for internal research purposes or for publications of results from their affiliated sites

Participating Groups and individual non-profit academic institutions shall be allowed access to the Data of their Participating Group/institution in accordance with the (Neo)ALTTO Publication Guidelines (see Appendix 6):

a) for their own internal research projects, for purposes of education and training;
b) for abstracts/publications using subsets of the entire database.

The timing of such access will be determined in collaboration with FS and is subject to the approval of the SC. The timing will not be unreasonably delayed, but could be delayed for scientific/statistical reasons.

Individual institutions / Participating Groups requiring access to data from their site / affiliated sites, will have to send their request by email to FS at: alttoreasearchproposals@frontier-science.co.uk

Individual institutions / Participating Groups will receive access to their site data, only after signing a DTA.

After the publication of the results of the primary research questions/endpoints, Participating Groups/ individual institutions might be allowed to publish/present the data and results from their site(s), provided the following conditions are met:

a. The proposed publication/presentation is first submitted to the SC (including the National Cancer Institute) and the sponsor of the research for review and comments, in line with point 6 of the (Neo)ALTTO Publication Guidelines document.
b. The publication/presentation cannot be made in the name of the ALTTO or Neo-ALTTO studies, but can make reference to the fact that patients had been enrolled in the ALTTO or Neo-ALTTO studies.

Any individual investigators who have access to data of their patients by virtue of being the treating physician or otherwise, may not publish any material (be that data, Data, Results or otherwise: (a) before publication of the results of the primary research questions/endpoints; (b) without first submitting their proposed publication to Novartis who shall have the right to review and comment on the content of the material to be published or presented and the right to have deleted any Novartis confidential information; (c) unless it

is in line with the (Neo)ALTTO Publication Guidelines and section 2.11 of this Policy; and (d) that is in the name of the ALTTO or Neo-ALTTO studies, but may make reference to the fact that patients have been enrolled in the ALTTO or Neo-ALTTO studies.

4. Results generated by the approved (under this Policy) RPs

Results mean all data, including raw data, collected, generated or derived from the RP, conducted by a Partner or a Third Party.

To the extent that the investigator of the RP does not have contractual restrictions from a funding party regarding the disclosure of Results, Novartis shall receive a copy of such Results, within sixty (60) days of completion of the RP. Novartis shall retain the Results in confidence and use such Results for its and its Affiliates own internal Research and Development purposes only. Novartis shall not otherwise use or disclose the Results until such Results are published or become part of the public domain, whichever occurs first, except for Novartis to comply with global laws and regulations.

All investigators of the RP Proposals approved under this Policy must agree with making the Results generated by their R P available to the wider scientific community through the (Neo)ALTTO Data Center, which will use a platform approved by the SC for the purposes of data sharing.

5. Appendices

1. Summary of review and approval process
2. Research Project Proposal Submission Form - completion instructions
3. Research Project Proposal Submission Form
4. Scoring Guidelines and Approval Criteria
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