

PALLAS Study: Research Project Proposals Workflow and Checklist (version 1.0)

Protocol Background

Described protocol objectives as well as future research project proposals (or RPPs) can generally be categorized into **projects requiring access to clinical study data only** versus **projects requiring access to study data and surplus samples or data generated from those samples**.

Multiple tissue- and liquid-based translational research projects are scheduled throughout the course of the PALLAS trial to evaluate potential markers of response and/or resistance in patients receiving endocrine therapy with palbociclib versus endocrine therapy alone. The companion TRANS-PALLAS Investigator Manual of Procedures was developed by the Translational Research Committee (TRC) and describes planned translational analysis, defined through the translational objectives in the PALLAS study protocol, in some detail. Additionally, examination of patient-reported outcomes (PRO)/quality of life in a sub-group of patients as well as adherence to oral therapy, and interaction of metabolic state and response to palbociclib will occur.

Any additional 'Clinical Study Data Projects' or 'Translational Research Projects' can be submitted as scientific research project proposals and brought to the attention of the study leadership after the primary analysis.

'Clinical Study Data Projects' (based on analyzing study data only) will be reviewed separately from 'Translational Research Projects' (involving study data and (surplus) study samples or data generated from those samples). 'Adherence/PRO/quality of life' research projects (requiring access to specific clinical study data only) will be reviewed through the workflow of 'Clinical Study Data Projects'. 'Translational Research Projects' are handled and reviewed by TRANS-PALLAS working groups and the Translational research committee (TRC), as defined in respective charters.

The submission process, review and endorsement of proposals is outlined in the applicable study charters and policies listed below and summarized within this document.

Charters and Policies

Access to PALLAS Study Data and Surplus Samples is defined in the globally harmonized „**PALLAS Policy for Access to Study Data or Surplus Samples for Research Projects not related to the Protocol**“ (please find attached)

The Policy differentiates between requests for access to:

- Data only (Clinical Study Data Projects) and for
- Data and surplus Samples or data generated from those samples ("TRANS PALLAS" Translational Research Projects)

All Research Project Proposals are to be submitted through the "Research Project Proposal Submission form" (please find attached) and are handled through the **RPP administrator**, who oversees the status and progress of proposals, and reports to the study sponsors. Timelines for the review process and the review workflow itself are defined within the above-mentioned PALLAS policy and relevant charters. The flow charts below summarize this information.

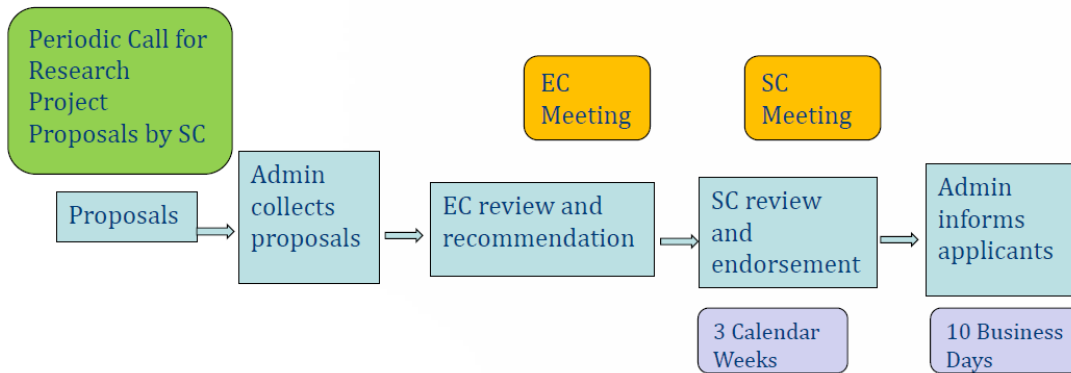
Committees involved in the approval process for such proposals are:

- Translational Research Committee (TRC; review and recommendations of translational RPPs)
- Executive Committee (EC; evaluation of all proposals and recommendations to SC/endorsement of TRCs recommendations)
- Steering Committee (SC; final endorsement of all proposals)

Workflow for handling Research Project Proposals

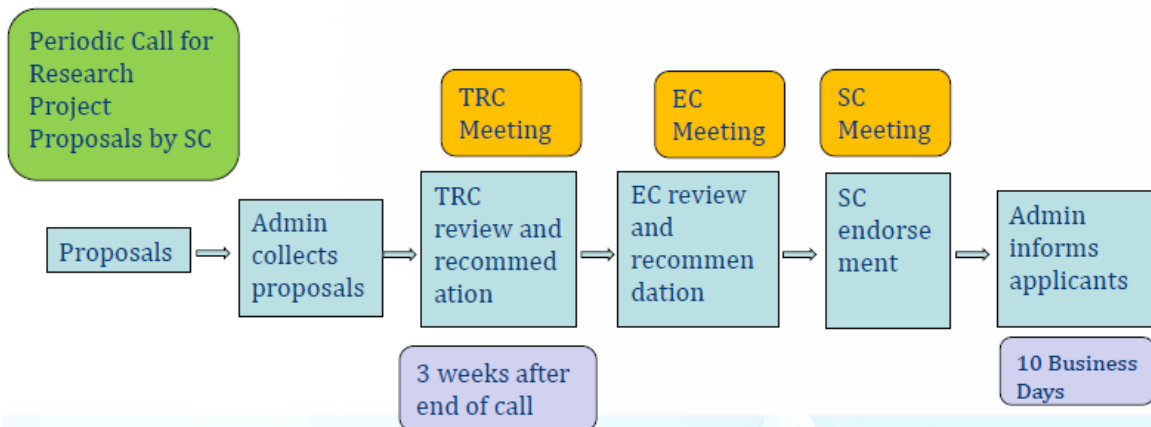
Proposal for Clinical Study Data Projects (Data only)

- Applicant completes „Research Project Proposal Submission Form”
- EC votes on each proposal: “Approve”, “Conditionally Approve” or “Reject”
- SC reviews and endorses the EC recommendation
- RPP Administrator will inform the Applicant about the SC decision



Proposal for Translational Research Projects (Data and Surplus Samples)

- Applicant completes „Research Project Proposal Submission Form”
- Each TRC Member decides based on scientific merit using the “Scoring Guidelines and Approvals Criteria”
- TRC finalizes recommendation together at call / meeting and votes on each proposal: “Approve”, “Conditionally Approve” or “Reject”
- EC evaluates / endorses this recommendation
- SC gives the final endorsement
- RPP Administrator will inform the Applicant about the SC decision



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Current “Checklist” and Guidance for Investigators submitting Research Project Proposals (RPPs)

Note: Analyses on PALLAS study data (submitted as RPPs) are only feasible after data of the primary objective analysis (on 469 iDFS events) has been released by the PALLAS Steering Committee. Due to contractual reasons, only PALLAS Investigators are eligible for submitting RPPs and any projects aiming at the development of any therapeutic product or at a diagnostic product in connection to therapeutic products aiming at the modulation of CDK4/6 are exempted from this research process.

General Guidance and preconditions for submitting RPPs

- Mind any currently open research calls and call deadlines for proposals (communicated by PALLAS Study Leadership)
- Mind publication guidelines (PALLAS Study Publication and Presentation Policy; available upon request)
- Mind contractual study timelines. A contractual “reservation period” prevents any experiments to be done on PALLAS surplus samples before a certain time period has elapsed, currently targeted for May 2022 (applicable only for RPPs requiring access to Samples and Data).
- Signed Data Access/Transfer Agreement (DTA) and/or Material Access/Transfer Agreement (MTA) will need to be implemented with the sponsors before any access to Samples and/or Data will be granted for endorsed RPPs
- Other legal agreements (e.g. COI, CDA, Data protection guidelines, contractual agreements with third parties) will be implemented with the sponsors as necessary for endorsed RPPs
- Any proposed analyses must be permitted per the valid Informed Consent Form (ICF) and patient data protection guidelines in affected countries and sites from which samples or patient data are planned to be used. This will need to be confirmed by the sponsors/study leadership for any endorsed RPPs. Information on ICF content can be provided by the sponsors upon request before proposal submission.

Necessary actions for research project proposals requiring access to study data only:

- Complete RPP Submission Form (Appendix A to the “PALLAS Policy for Access to Study Data or Surplus Samples for Research Projects not related to the Protocol” – please see attached)
- Ensure funding details and detailed projected timelines are included in your RPP
- Provide the RPP Submission Form to the RPP Administrator addressing it to pallas.research@abcsrg.at as well as pallas_AFT@alliancefoundationtrials.org in “cc”. The RPP Administrator will confirm receipt of the proposal and expected review timelines

Necessary actions for research project proposals requiring access to study data and surplus samples:

- Complete RPP Submission Form (Appendix A to the “PALLAS Policy for Access to Study Data or Surplus Samples for Research Projects not related to the Protocol” – please see attached)
- Ensure funding details and detailed projected timelines are included in your RPP
- Ensure details on project-specific logistics, technical requirements, sample requirements, sample preparations, etc. are included in your RPP, as applicable to your proposal.
- Keep in mind the scoring criteria for evaluation of your RPP, as outlined in the “PALLAS Policy for Access to Study Data or Surplus Samples for Research Projects not related to the Protocol”
- Provide the RPP Submission Form to the RPP Administrator addressing it to pallas.research@abcsrg.at as well as pallas_AFT@alliancefoundationtrials.org in “cc”. The RPP Administrator will confirm receipt of the proposal and expected review timelines

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Attachments to this document:

- RPP Submission form