EORTC COORDINATION COSTS

APPLICATION GUIDELINES

CANCER RESEARCH UK

1. PURPOSE OF THESE GUIDELINES

These guidelines explain how to request funding from Cancer Research UK (CRUK) for the coordination of a UK-led intergroup study in mainland Europe by the European Organisation for the Research and Treatment of Cancer (EORTC) Headquarters. They should be read in conjunction with our Clinical Trial Application guidelines. If you have any questions about these guidelines, please email the CRUK Research Programme Manager.

2. REMIT

You can apply for funding for a UK group-led EORTC study where the study is being coordinated by a UK Clinical Trials Unit (CTU) but the EORTC HQ is supporting agreed components of the EU coordination of the study. The UK CTU is eligible to apply to CRUK for:

- the UK associated research costs (as per a normal funding application)
- eligible (see below) EORTC HQ costs associated with supporting coordination of the study in mainland Europe

CRUK also supports collaboration with the EORTC in the following ways, but these are not within the scope of this guidance:

- EORTC-led intergroup study with UK group involvement: The study will be led by the EORTC (primary sponsor) but a UK CTU will coordinate the UK component of the study. The UK CTU is eligible to apply for the UK-associated research costs through normal CRUK funding processes. No funding passes from the UK CTU to the EORTC.
- EORTC-led study: The study is being led by the EORTC and UK members are participating, but not as part of a national group. The EORTC wishes to open UK sites but there is no UK CTU involvement and the EORTC HQ intends to contract directly with sites. CRUK contributes to an EORTC liaison officer in the UK who assists with regulatory aspects and the UK CI can apply to CRUK for NHS Research Part A costs as per AcoRD, including any costs associated with transporting samples to central labs and with uploading medical images or radiotherapy plans to central platforms.

In these cases, you are encouraged to contact the CRUK Clinical Research team at clinicalresearch@cancer.org.uk to request an Expression of Interest form which will need to be completed for the team to assess whether the proposed research is in scope.

3. WHAT IS FUNDED

You can request funding for EORTC HQ staff costs associated with coordination activities, and trial overheads associated with the HQ management of the trial. Appendix 1 sets out the types of activity that the EORTC would be responsible for coordinating in mainland Europe.

Costs can be requested to cover the periods of study activation, enrollment, follow up to primary endpoint, and study closure. Costs must be trial specific

The following are examples of the types of costs which are eligible for inclusion:

Eligible:

- EORTC HQ staff costs associated with coordination activities within the EORTC HQ
- Ethics Authority costs
- Competent Authority costs
- Translation fees
- EORTC HQ site monitoring fees

Ineligible

- Trial development and EORTC HQ Board/Protocol review committee review time
- Site payments
- Insurance
- FAR/publication review

4. THE APPLICATION PROCESS

If you would like to consider requesting funding for a UK-led intergroup study to be coordinated in mainland Europe by the EORTC, please contact the CRUK Clinical Research Liaison Manager to discuss your application. We strongly encourage you to do this well in advance of the application deadline so that the relevant collaboration arrangements can be implemented.

You should then follow our Clinical Trial Application guidelines, noting the following:

- You should include the EORTC HQ coordination costs in your UK funding application, for transfer to the EORTC HQ if the trial is funded.
- You should work with the EORTC to complete the costing template (see Appendix 2) and use this to complete your eGMS application. Please be aware that the EORTC does not take inflation into account.
- Our grants management system is set up for UK salaries only so EORTC costs should be included in the **running costs** section of your eGMS application and be clearly labelled as 'EORTC salary' or 'EORTC overheads' to distinguish them from UK running costs. Justification of the costs should be provided in the justification section of the research upload, clearly distinguishing UK and EORTC costs (see Appendix 3).
- All costs should be in pounds sterling and the exchange rate used should be set out in the application.

5. POST COMMITTEE PROCESS

You will be provided with a feedback letter from the Clinical Research Committee, letting you know the outcome of the Committee's review. You should share this feedback with the EORTC HQ and, where applicable, liaise with them to respond.

Please note that for UK-led intergroup studies with EORTC involvement that have been successful in obtaining funding from CRUK, we may provide the peer review, and your response, to the EORTC Protocol Review Committee to support their review of the European component, unless advised by you not to do so.

APPENDIX 1

Guide to the delegation of responsibility to the EORTC for coordination in mainland Europe

Activity	UK CTU	EORTC HQ
Application & feasibility		
Application preparation & submission to approval committee	X	X
Evaluation of feasibility among national centres		X
Protocol, GSA & amendments		
Protocol preparation	X	
Protocol review	X	X
GSA development	X	X
Protocol & GSA finalisation and approval by sponsor committee/PRC	X	
Protocol & GSA distribution		X
Agreement between EORTC and UK CTU/Sponsor		
Draft preparation	X	
Review	X	X
Signature	X	X
Sponsorship & insurance		
UK legal sponsor	X	
EU applicant		X
Clinical trial insurance	X	?

Patient information sheet/GP letter		
Development of the PIS/IC and GP letter adapted to national requirements & translations		X
Review of the PIS/IC and GP letter by the sponsor	X	
Selection of EU investigators		
Selection of investigators in EU (unless already identified by UK CTU)	?	X
Confirmation of selected centres	X	
Release of authorised centres (informs centres)		X
EudraCT		
Request of EudraCT number	X	
General XML preparation	X	
Competent Authorities		
Preparation of documentation needed for submissions, including adaptation of XML	X (MHRA)	X (EU)
Submission of dossier for initial approval and amendments to national regulatory bodies	X (MHRA)	X (EU)
Ethics Committees in UK		
Preparation of documentation needed for submissions to MREC	X	
Submission of dossier for initial approval and amendments of MREC	X	
Contracts with Group investigators/centres & local approvals (where applicable)		
Preparation of template		X (EU)
Review of template	X	
Communication with centres and signature		X

Collection of R&D approvals		X
CRFs (RDC)		
System used	X	
CRF & guidelines design	X	
CRF & guidelines review	X	X
Data management		
Randomisation / Treatment allocation system	X	
CRF receipt and query distribution at centres (via RDC system)	X	
Data capture / entry (into RDC)	Investigators	Investigators
Methodological validation and update of CRFs	X	
Final clinical validation of cases	X	
Pharmacovigilance management		
Location of the main safety database	X	
Preparation of SAE/pregnancy forms + guidelines	X	
SAE notification/pregnancy notification to Pharmacovigilance Unit in real time by fax	X	X (site)
SAE notification/pregnancy notification to the Company in real time by fax	X	
Expectedness assessment of SAE	X	
Issue of queries for SAE/pregnancy	X	
Forwarding queries to the EU sites	X	
Sending back replies on queries to UK sponsor		X (site)
Distribution of SUSAR to the PV contact of EORTC	X	

SUSAR reporting to EudraVigilance Clinical Trial Module (EVCTM)	X	
SUSAR Reporting to Competent Authorities in EU	X	
SUSAR Reporting to Investigators and Central Ethic Committees in EU	X	
Preparation of Development Safety Update Report (DSUR)	X	
Distribution of DSUR to the PV contact of EORTC	X	
Distribution of DSUR to Competent Authorities in EU	X	
Distribution of DSUR to Central Ethic Committee in EU	X	
Distribution of Safety Alerts/ periodic safety reports to the PV EORTC contact, if applicable	X	
Distribution of Safety Alerts/ periodic safety reports to Investigators and Central Ethic Committee in EU, if applicable	X	
Tissue and human samples management		
Logistics for EU centres		X
Communication with the industry and drug distribution		
Communication with drug suppliers / distributors	X	
Triggering drug supply	X	
Quality Assurance: audit		
Site audit organisation and performance (if required)	X	
Communication of major findings (if any) to EORTC	X	
Trial end		
Termination of centres	X	X
Trial discontinuation	X	X
Communication to Investigators in EU		X
Communication to CA in EU		X

Communication to EC in EU		X
Reporting		
Providing semiannual trial status report	X	
Generating end of trial report	X	
Generating other trial related reports (other than final report and PV related reports)	X	
Statistical analysis	X	
Trial report (final)	X	
Review of the trial report	X	X
Documentation keeping / archiving		
Collection Regulatory Documents and keeping of copies for EU	X	X
Regulatory Documents for EU	X	X
Archiving Regulatory Documents for EU	X	X
Publications		
Publication draft preparation	X	
Publication review	X	X
Publication submission	X	
Database compatibility in case of transfer		
Compatibility testing.	X	X
Database transfer	X	

APPENDIX 2

Costing template for completion with the EORTC

Category	Additional Information	Cost Y1	Cost Y2	Cost Y3	Cost Y4	Cost Y5	Cost Y6	Cost Y7	Cost Y8	Cost Y9	Cost Y10	TOTAL
EORTC Clinical Research Physician (FTE salary £x)	Year 1: 0.00 FTE (Study activation)											
EORTC Statistician (FTE salary £x)	Year 1: 0.00 FTE (Study activation)											
EORTC Project Manager (FTE salary £x)	Year 1: 0.00 FTE (Study activation) Year 2-5: 0.00 FTE (Enrolment) Year 6-9: 0.00 FTE (Follow up) Year 10: 0.00 FTE (Closure)											

EORTC Data Manager (FTE salary £x)	Year 1: 0.00 FTE (Study activation)											
EORTC Regulatory Affairs Manager (FTE salary £x)	Year 1: 0.00 FTE (Study activation) Year 2-5: 0.00 FTE (Enrolment) Year 6-9: 0.00 FTE (Follow up) Year 10: 0.00 FTE (Closure)											
EORTC Clinical Research Associate (FTE salary £x)	Year 1: 0.00 FTE (Study activation)											

EORTC Clinical Trials Assistant (FTE salary £x)	Year 1: 0.00 FTE (Study activation) Year 2-5: 0.00 FTE (Enrolment) Year 6-9: 0.00 FTE (Follow up) Year 10: 0.00 FTE (Closure)											
EORTC RT-QA Manager (FTE salary £x)	Year 1: 0.00 FTE (Study activation)											
EORTC Contracts Manager (FTE salary £x)	Year 1: 0.00 FTE (Study activation)											
EORTC Competent Authority submissions	Year 1: x countries initial application: £x per country. Year 2-4: potential amendments: +/- 0.75 amendment per year of accrual)											

EORTC Ethics Authority submissions	Year 1: x sites initial application: average of £x per site Year 2-4: potential amendments: +/- 0.75 amendment per year of accrual)											
EORTC translations	Year 1: x countries (average of x per unit)											
EORTC onsite monitoring	£x per visit staff costs and £x average travel/accommodation. Based on x visits											

APPENDIX 2

Example of the costs justification section of the research upload.

EORTC HQ Costs

This application includes a funding request for EORTC HQ support to coordinate this trial in mainland Europe. If funded, EORTC HQ costs will be paid to the UK CTU for transfer to the EORTC HQ. CRUK's electronic grants management system is set up for UK salaries so it has been agreed that EORTC HQ costs should be included in the running costs section. The exchange rate used to calculate EORTC costs was [x].

EORTC Clinical Research Physician (Y1 0.06 FTE)

- Y1 (study activation)
  - Protocol review from leading group and development of Group-Specific Appendix, including support to review and approval by EORTC approval bodies (Protocol Review Committee).
  - Review and country specific adaptation of the PIS/IC.
  - Support in design of feasibility questionnaire (medical aspects).
  - HQ review of leading group CRFs and CRF completion guidelines.

EORTC Statistician (Y1 0.03 FTE)

- Y1 (study activation):
  - Protocol review from leading group and development of Group-Specific Appendix, including support to review and approval by EORTC approval bodies (Protocol Review Committee).

EORTC Project Manager (Y1: 0.50 FTE, Y2-4: 0.087 FTE, Y5-8: 0.044 FTE, Y9: 0.1 FTE)

- Y1 (Study activation):
  - Attendance at meetings & conference calls with leading Group for start-up activities.
  - General project planning and follow up on milestones.
  - Protocol review from leading group and development of Group-Specific Appendix, including support to review and approval by EORTC approval bodies (Protocol Review Committee).
  - Ensuring review and country specific adaptation of the PIS/IC, including translations for EORTC countries.
  - Design of the feasibility questionnaire, communication with EORTC network, review of feasibility responses, final selection of sites, communication with selected & non-selected sites.
  - Ensuring that appropriate clinical trial insurance is put in place for EORTC countries.
  - Preparation of documentation (other than general) for initial submissions to regulatory bodies.

- Collection of EORTC site commitment documentation and follow up on site contracting process.
- Review and input to any study specific manual to be developed.

- Y2-4 (Enrolment):
  - General coordination of the project at EORTC.
  - Protocol amendment review from leading group and development of Group-Specific Appendix, including support to review and approval by EORTC approval bodies (Protocol Review Committee).
  - Providing assistance to leading Group in case of problems with EORTC sites.
  - Ensuring proper study reporting within the EORTC network and communication with EORTC sites.

- Y5-8 (Follow up):
  - Providing assistance to leading Group in case of problems with EORTC sites.
  - Ensuring proper study reporting within the EORTC network and communication with EORTC sites.

- Y9 (Closure):
  - Close out activities for all EORTC sites and closure at EORTC HQ.

EORTC Data Manager (Y1: 0.01 FTE)

- Y1 (Study activation):
  - Review of leading Group CRFs and CRF completion guideline.

EORTC Regulatory Affairs Manager (Y1: 0.42 FTE, Y2-4: 0.095 FTE, Y5-8: 0.048 FTE, Y9: 0.3 FTE)

- Y1 (Study activation):
  - Assisting in site/country selection process.
  - Preparation & collection of essential study documents: identification of necessary country- (and site-) specific documentation required for the study submissions and initiation of the collection process.
  - XML preparation: tailoring to national specifications.
  - Preparation of initiation packages for sites: identification of necessary site initiation documentation (TMF) and documentation needed for local EC review, compilation into initiation packages and sending to the sites, follow up on collection of documentation to be returned.
  - Submission and follow up of dossier to Ethics Committees
  - Submission and follow up of dossier to Ethics Committees & Competent Authorities: development of master cover letters EC/CA, compilation of country-adapted submission dossiers, follow up on responses and final approvals (central and local), creation of regulatory database.

- Y2-4 (Enrolment):
  - Submission and follow up of protocol or trial amendments to Ethics Committees & Competent Authorities for EORTC territories.

- Y5-8 (Follow up):
  - Submission and follow up of trial amendments to Ethics Committees & Competent Authorities for EORTC territories.

- Y9 (Closure):
    - Notification of end of trial to regulatory bodies for EORTC territories.

EORTC Clinical Research Associate (Y1: 0.04 FTE)

- Y1 (Study activation):
    - Review of leading Group monitoring plan.
    - Study-specific training (by leading Group and self-training).

EORTC Clinical Trials Assistant (Y1: 0.14 FTE, Y2-4: 0.02 FTE, Y5-8: 0.01 FTE, Y9: 0.3 FTE)

- Y1 (Study activation):
    - Development of feasibility questionnaire into web-based form, communication with EORTC network, collection of responses in access database.
    - Setup of trial master file, initiation of EORTC tracking, defining and initiating e-TMF structure.
    - Assisting in the preparation and sending of initiation packages for site activation and collection of site documents.

- Y2-4 (Enrolment):
    - TMF filing of study documentation.

- Y5-8 (Follow up):
    - TMF filing of study documentation.

- Y9 (Closure):
    - TMF filing of study documentation.

EORTC RT-QA manager (Y1: 0.09 FTE)

- Y1 (Study activation):
    - Development/review of relevant chapters in protocol from leading Group, RT-QA guidelines as necessary.
    - Site accreditation: Facility Questionnaire and Beam output audit.

EORTC Contracts Manager (Y1: 0.07 FTE)

- Y1 (Study activation):
    - Contracting with all partners: e.g. leading Group and EORTC sites (tailoring of template site agreement to be in line with upstream (leading Group) agreement, communication/negotiation with sites, translation to local languages (where applicable).
    - Setup of financial tracking: Definition of income/expense in contract management tool for management of upstream/downstream invoices & payments.

EORTC Competent Authority submissions

- Year 1: Initial application for 10 countries: estimation of £633.90 per country - compensation to be requested will be based on actual expenses.

- Year 2-4: potential amendments: +/- 0.75 amendment per year of accrual.

EORTC Ethics Authority submissions

- Year 1: x sites, initial application: average of £x per site. Some sites will not charge a fee, in some countries there is only a central ethics committee to review; hence the compensation to be requested will be based on actual expenses.
- Year 2-4: potential amendments: +/- 0.75 amendment per year of accrual.

EORTC translations:

- Year 1: x countries (average of £x per unit) for translation of patient consent form and protocol summary to local languages for EORTC countries.

EORTC onsite monitoring

- £x per visit (staff time) and £x average per visit (travel/accommodation-to be based on actual expenses).
- Estimated 12 visits to be used in case of major problems on site.
- Staff time: 1 day of CRA time for preparation and follow up + 1 day of travel + 1 day on site, + 20% of cases 2-day visits + 0.5 day Head of CRA oversight).