NIHR | Research Delivery Network

Clinical Trial Costing Guidance for Early Phase and Advanced Therapy Medicinal Products (ATMP) Clinical Trials

Version 1 (October 2024)

HSC Health and Social Care

Ymchwil Iechyd a Gofal Cymru Health and Care Research Wales

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Contents

Section 1 – Description of Document

Document Content

This document has been developed to assist the life sciences industry and the assigned NHS Study Resource Reviewer with costing commercially sponsored early phase Clinical Trials of Investigational Medicinal Products (CTIMPs) and clinical trials involving Advanced Therapy Medicinal Products (ATMPs) within the NHS.

It is intended to be used as a guidance document to assist with completion of the National Institute for Health and Care Research (NIHR) interactive Costing Tool (iCT) and should be read alongside the associated NIHR interactive Costing Tool guidance, NCVR SOP and relevant study documents (as a minimum the protocol and study manuals).

The guidance covers both the costs for activities that are specific to early phase and ATMP trials and which are not generally required for late phase CTIMPs. It also covers general iCT tariff items where further consideration needs to be given for early phase and ATMP trials.

Acknowledgements

This guidance has been developed with input from:

Northern Alliance Advanced Therapies Treatment Centre
Experimental Cancer Medicine Centre Network
Cell and Gene Cell Therapy Catapult
UK Clinical Research Facility Network
NHS England convened Early Phase and ATMP Clinical Trials Costing Guidance Working Group

Usage Disclaimer

The following document is intended for use as guidance only and has been compiled following full integration of early phase CTIMPs and trials of Advanced Therapy Medicinal Products into the National Costing Value Review (NCVR) business as usual process. It coincides with the October 2024 revisions to the NIHR UK interactive Costing Tool (iCT) tariff.

It has drawn primarily on the expertise of NHS centres specialising in early phase and ATMP trials in oncology. The content is subject to change and expansion, as ongoing feedback is sought from NHS centres with expertise in other disease areas.

Therefore, the document should be considered as a 'consultation in use' with anticipated quarterly updates during the first year following publication. Thereafter, it is envisaged that annual review/updates of this guidance will occur in conjunction with the NIHR annual review of the iCT tariff.

All suggested timings included herein are subject to change and amendment.

Recommendations for additions and amendments should be sent via this form. Updates will be made on a quarterly basis.

User support

All user support for the interactive Costing Tool, including the latest national tariff within the tool is accessed here. Information on the wider NCVR principles can be found on the NHS England Website and the NIHR Research Delivery Network website.

Information and tutorials to support the NCVR process is available through the NIHR Learn Life Science Customers Resource Centre in the 'Calculate the cost of your study at sites' section. The same details used to login to the Central Portfolio Management System (CPMS) give you access to NIHR Learn.

Further user support is available through the RDN or Devolved Nation central team via your local RRDN/DA contact.

Section 2 – Background

The key stages of the NCVR process for each multi-site commercial clinical study are:

1. The commercial sponsor populates (or Contract Research Organisation (CRO) as their delegate) the UK interactive Costing Tool (iCT) to reflect their initial interpretation of resource requirements to fulfil the study protocol.

2. The commercial sponsor is connected to an NHS costing expert who will conduct a study resource review to enable agreement by both sides on actual resource requirements.

3. Once approved, the iCT is shared with all participating NHS organisations to generate site-specific prices. This is a pre-defined, UK-wide methodology that ensures full cost recovery and accounts for aspects such as geographical variation, outsourcing costs etc.

4. Participating NHS Organisations are mandated to accept the agreed study budget. Updates have been made to the Market Forces Factor calculation across the whole of the UK to help smooth variation in trial delivery across participating NHS Organisations.

5. However, should there be any omitted activities in error these can be escalated via the NCVR Escalation process as set out in the NCVR Standard Operating Procedure if a threshold is met. The current threshold is >5% of direct per patient costs in England, Wales and Northern Ireland and >20% of the direct per patient costs in Scotland. Where a missing item is part of the Schedule of Activities the set thresholds do not need to be met for an escalation to be made.

For efficient study set up at all NHS sites and for full NHS cost-recovery, it is essential that the NCVR study resource review is robust, and the Study Resource Reviewer takes adequate account of the additional sites participating in the study. A recently developed NCVR Lead Site Review checklist is a helpful tool to ensure a comprehensive review.

Section 3 - Good practice recommendations (currently not mandated as part of the national NCVR process)

- It is acknowledged that ATMP and early phase studies can have a high level of complexity and/or stratification with ongoing change in study design (e.g. where additional/removal of cohorts is anticipated). For these types of studies, it is recommended that the Sponsor/CRO consult with the lead UK NHS site before constructing the study budget in the iCT, to discuss and agree its optimal format. This will facilitate the development of a high-quality initial budget and initial lead review and local site agreement, as well as subsequent 'during study' site level reviews following protocol amendments.

- Pharmacy costs relating to patient activity (dispensing etc) could be situated in a separate pharmacy per patient tab or as unscheduled activities. This would need to be agreed with the Sponsor/CRO at the time of the study iCT build.

- It is recommended for the Lead UK NHS site to consult with third party providers (for Example NHS Blood and Transplant; and associated national bodies) to consider third party service provision and capacity to meet the study requirements.

- It is recommended for the Study Resource Reviewer to download and save the version of the tariff used when constructing the iCT budget. This is important especially if local site reviews occur sometime later and after annual/biannual updates to the NIHR ICT tariff. Since whilst staff hourly rates and hence procedure fees will increase automatically; investigations and departmental fees will not and are often contested at subsequent local site reviews. It should be remembered that fees agreed at the time of the NCVR review hold for all participating sites.

- It is useful also to maintain a record of the rationale for decisions at lead site review to inform any subsequent participating site escalations. These decisions and rationale could be included in the checklist notes and distributed to participating sites by the sponsor/CRO at the time of iCT release.

- Where the protocol/budget is particularly complex, to facilitate individual site review/acceptance of the budget, or resolve issues relating to variation across sites, it may be pertinent to convene all participating sites to review some/all of the budget.

- As far as possible (subject to inter site variation and protocol specifics) include all mandated visit activities in the per participant section of the iCT and keep the unscheduled activities section for such potential additional unscheduled activities. This makes for a cleaner iCT and as per participant visit fees are usually driven by completion of the visit electronic case report form (eCRF) this facilitates site invoicing/payment for most of the incurred costs and decreases the need for additional tracking of activities for both the sponsor/CRO and the participating NHS organisation.

Section 4 – Per Participant Costs

The tables below provide guidance for consideration while reviewing the protocol:

- **Section 4.1** covers activities currently on the NIHR ICT tariff but which typically require more time when undertaken for early phase and ATMP trials.
- **Section 4.2** covers activities which are frequently required in early phase and/or ATMP trials and will be new additions to the NIHR iCT Tariff (October 2024)
- **Section 4.3** details activities related to pharmacy.
- **Section 4.4** details activities related to early phase and/or ATMP trials which could be considered for inclusion (not currently in NIHR iCT Tariff).

The notes section in the tables provide information/guidance for timing assignment and justification. However, it should be stressed that the protocol and relevant manuals should be consulted on a study-by-study basis to identify any adjustments required. The protocol schedule of events (or activities) and its footnotes are the starting point for the NCVR review, but it should be stressed that often additional requirements lay in the main text and appendices of the protocol which should be consulted. Where adjustments are made to standard tariff items justification for the change is captured in the iCT.

The NIHR iCT tariff is not exhaustive and where an appropriate tariff does not exist for a protocol required activity, it is perfectly acceptable and appropriate for the Sponsor/CRO and the study resource reviewer to make a 'new' manual entry into the study budget. Careful consideration should be given to all iCT entries and where necessary advice from clinical specialists, as relevant, should be sought.

The financial appendix within the model Clinical Trial Agreement (mCTA or CRO mCTA) is generated automatically from the iCT, therefore wording of manual entries should be concise, accurate, self-explanatory and generalisable to all participating NHS sites. Where activities are frequently being entered manually across multiple studies, these activities may be valid future additions to the NIHR iCT tariff and should be submitted for consideration via the UK iCT feedback form.

Section 4.1: Activities already in the ICT procedures but where additional time to current tariff recommendations may be required for early phase and ATMP trials.

General recommendations are made here where timings for activities may be increased. It is important to note that any changes to timings must be in line with protocol activity - the recommendations do not override the requirements for the study delivery. Therefore, timings may be increased or reduced depending on what is required to deliver the study according to the protocol.

Where activities are undertaken by different staffing groups/departments across research sites this must be addressed through organisational funding distribution models.

Section 4.1.1: General Activities/Procedures table

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
NIHR_GPC_046	Radiology presence at monitoring, audit or training visits (chargeable at the end of each visit)	0	450	0	These are related to Radiology review queries, image review queries and monitoring of radiology assessments. Where these activities are held outside the research team, an additional fee should be considered. Where these activities are held within the research team, additional time for trial monitoring should be considered.
NIHR_PRC_001	Informed consent	60	60		**Consider increasing to 120min clinician time and 120min nurse time** The PIS/ICF are lengthy and additional PIS/ICF often compliment the main document (e.g. pregnancy, pregnant partner, carer, assent for paediatric studies, genetic consent etc.). For ATMP studies consent will need to be taken for the cell collection procedure. The timing of the activity should be appropriate to cover all requirements for the study.

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					It may be advisable to have separate line entries for each PIS/ICF for transparency. Some may need to be in unscheduled activities as they may be related to optional protocol activities/sub-studies and/or only apply to certain cohorts. Early phase trials may be the last treatment option and/or participants and their family may be vulnerable. Adequate time (on several occasions pre-study) should be allowed to fully cover all trial aspects. For ATMPs this may be a one-off non-reversible treatment and negate any further gene therapy treatments. The consequences of which must be fully explained with the trial participant and family members, as appropriate. Consideration should also be given for the time needed for ongoing consent throughout the study lifecycle, a GCP requirement. Participants should be asked if they have any concerns and if they are happy to continue in the trial at each visit and this should be recorded in the medical notes. A separate line entry for ongoing consent should be considered. Reconsenting for updated PIS/ICF throughout the study is covered by NIHR_PRC_044.
NIHR_PRC_003	Medical history	30	30		**Consider increasing to 90-120 mins clinician time and 90-120 mins nurse time**

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					Consideration should be given to potential disease progression in participants at the point early phase and ATMP trials are offered. The resulting individual study medical history requirements (check eCRF), therefore may be extensive. In addition, participants often are referred into the specialist early phase/ATMP trial centre from another NHS organisation and therefore consideration needs to be given to the accessibility of the medical records and method and time to retrieve these. Consider ongoing medical history update line entry throughout the study.
NIHR_PRC_004	Blood sample -collection only		15		**Consider multiple units at each visit** Wherever possible a single blood draw should accommodate all samples required at that time point. However, PK samples usually involve a time course typically most frequently soon after dosing and so these visits will have multiple units. Consider separate line entries for PK sampling. Consideration should be given as to whether paediatric or vulnerable patient cohorts. Consideration should be given as to whether the timing should be increased when taking the above into consideration.
NIHR_PRC_005	Blood sample collection processing		30		**Consider variable timings** Early phase/ATMP clinical trials usually have high safety, PK, PD and biomarker blood sampling

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					requirements and consequently considerable local laboratory/research team sample processing time. Experienced staff should be consulted to review the laboratory manual (or key information extracted there from, if full lab manual not available) and provide blood processing timings for each visit. Depending on the specific study manual requirements, it may be possible to batch process or conversely, limited sample stability may require a special collection method e.g. directly onto ice, and rapid sample processing. Consider similar processing methods (batch centrifugation) for samples but also the sub-aliquoting requirements. For transparency and ease of future protocol required changes, consider separate line entries for safety, PK, PD and exploratory samples etc.
NIHR_PRC_006	Specimen dispatch by cost or courier		30		**Consider increasing the unit(s) per visit** This is recommended if samples need to be dispatched to multiple central laboratories and multiple couriers are being used. Since separate package preparation, separate courier liaison and separate pick-up times. **Consider increasing to 60 mins nurse time per dispatch.**

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					If sample dispatch preparation/transfer have special requirements e.g. barcode recording, temperature monitoring involving use of temperature probes, specialist packaging for e.g. higher risk biological hazards involving GMOs. Consult the study laboratory manual and consider any applicable national requirements. Consult a local Biological Safety Officer for advice (particularly relevant for ATMPs).
NIHR_PRC_007	Vital Signs measurements (Temp, BP, Pulse and respiration)	10	10	0	All vital sign collection per visit, and per collection should be appropriately captured. Where a particular visit requires multiple vital sign collections (for example, pre / post dose, and at different time intervals), each of these collection time points should be considered at 15 min nurse time each.
NIHR_PRC_011	Physical examination	30	20	0	In early phase/ATMP studies the physical exam is undertaken by a clinician, however the nurse is present to take notes from the examination. Where trial protocol requires additional examinations, appropriate additional costs should be considered
NIHR_PRC_016	Instruction/education for participant and/or care giver	15	15		**Consider increasing timing of clinician to 30min and nurse to 30-60 min** Due to complexity of early phase/ATMP trials the instructions to participant and caregiver, particularly with regards AEs etc. and general monitoring will be more extensive, and it may be necessary to include

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					this provision at the start of each cycle or visit. Rather than just once at the start of the study If electronic devices are involved, additional time needs to be considered if an older aged participant cohort is involved, and/or the participant cohort is cognitively impaired. **Consider increasing the unit(s) per visit** if multiple devices and instructions are required e.g. participant and carer.
NIHR_PRC_019	Concomitant medication check at screening	10	15		**Consider increasing to 20 min clinician time and 30 min nurse time** There are usually extensive medications requirements of participants on early phase trials, due in part to where they are in their disease progression, and the disease areas covered by ATMP therapies, which necessitate additional allocated times
NIHR_PRC_020	Concomitant medication checks on study		10		**Consider including 20 min clinical time per visit and increasing the nurse time to 30min.** The clinician needs to document concomitant meds, and relationship to disease/ symptoms/IMP or ATMP/side effects and co-morbidity For ATMP studies several new medications may be stopped and started each day, and will be the case if the subject is in a high dependency unit after the infusion of the product.

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
NIHR_PRC_021	Prescription for study	10	15		**Consider multiple units and/or separate line entries** The study drug/ATMP may require prophylactic treatments and or co-therapies. Some will require individual prescriptions for example if being dispensed from different pharmacy locations (often aseptic units are separate from main pharmacy). Consider adding multiple lines to cover lymphodepletion, prophylaxis, mobilisation drugs, rescue medication etc. which should also be added to unscheduled activities.
NIHR_PRC_022	Administer study drug in clinic	15	30		**Consider variable timings** The protocol should be consulted for the precise requirement for early phase study drug/ATMP administration. Consideration should be given to the route of administration and whether multiple staff need to be present. For example, all First in Human, sentinel participants drug administration should have additional staff provision. Intrathecal administration would require additional staff etc. Consider also administration of prophylactics and co-therapies and staffing requirements. Consider adding provision for slowing of infusion rates and therefore an extended drug administration time by a drug administration extension (per hour per staff member) entry in the unscheduled activities. This will also be appropriate for step-up dosing regimens. Consideration also needs to be given to post drug administration observation, which should be built into

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					the timing and take account of the number of staff needed. For Phase I studies consideration should be given as to whether the clinician time needs to be increased, in line with the Phase I risk assessment for the study. Administration of rescue medication should be covered in unscheduled activities
NIHR_PRC_025	Drug accountability and compliance		10		**Consider multiple units** If multiple drugs under participant own or carer's supervision
NIHR_PRC_026	CRF/eCRF completion including data transfer and query resolution	15	60		**Consider increasing to 120 min nurse time and 90 min clinical time.** **Consider multiple units if burden is particularly high on certain visits** For early phase/ATMP studies the query resolution time can be considerable and should be taken into account. Also consider where the eCRF input requirements are variable across visits eg.screening, early cycles and end of trial. A copy of the eCRF should be requested to determine the exact data reporting requirements. Timings should be sufficient for the visit. Having reduced timings in the per patient budget with the

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					option to add additional time required on an hourly rate from unscheduled should be avoided.
NIHR_PRC_027	Review/reporting of patient AEs/SAEs	10	30		**For complex studies add 120min clinician time and 120min nurse time for complex SAE reporting and follow up - to be added to unscheduled activities to charge when required.** Most early phase/ATMP trials require all AEs to be recorded separately (e.g. headache with associated nausea would be recorded separately as headache [AE1] and nausea [AE2]). SAEs are likely and are often complex and ongoing over several visits. The additional provision within unscheduled activities covers extraordinary and extended follow up and reporting when required. The IMP/advanced therapy profile should be considered along with the disease area of the patient population
NIHR_PRC_028	Handover to routine care (End of Trial)	15	0	0	Appropriate Nurse time (a minimum of 15 dependent on the protocol) to support the handover of routine care.
NIHR_PRC_040	Patient Eligibility Assessment	30			**Consider increasing to 60 min clinical time and adding 30 min nurse time.** **For ATMP studies consider increasing to 60 min clinical and adding 60 min nurse time.** Early phase/ATMP trials have a very long list of inclusion/ exclusion criteria where the clinician needs to confirm clinical tests and previous medical history.

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					The research nurse will source, compile and triage the potential participant's information ahead of the clinician's assessment.
NIHR_PRC_043	Reconsenting	15	15		**Consider increasing to 30 min clinical time and 30 min nurse time** Rationale as for NIHR_PRC_001 above - complexity and length of PIS/ICF for early phase and ATMPS. For reconsenting of non-main PIS/ICF standard timing may be sufficient. For all reconsenting the timings will be dependent on the extent of the changes in the PIS/ICF on each occasion. A potential way to accommodate this would be a unit increase provision in the unscheduled activities
NIHR_PRC_47	Archival Tissue Retrieval		60		**Consider increasing this to 90 min nurse time** If liaison with an external organisation is required, consider through cost payment**.** The external organisation may require payment for staff time incurred in the retrieval. This may sit best as an unscheduled activity through cost as NIHR_INV_117.

Section 4.1.2: Guidance relating to the adjustments of multiple NIHR iCT Tariff line items and Investigations

Activity Code	Activity Description	Cost (staff time or investigation fee)	Notes (including justification for any time increases)
Various	Tissue Handling	Various	Handling of trial tissues (blood, body fluids, soft tissue or any patient derived sample) as per lab manual and protocol should be appropriately costed. This is in addition to blood sampling, covered in NIHR_PRC_005 above). Early phase trials will have multiple processes of handling these tissues based on biomarker, pharmaco-dynamics and pharmaco-kinetic analysis. All activities required to process tissue post collection from the clinical area should be costed appropriately. Additional consideration should also be provided if tissue shipment is required in real-time, ad hoc or batched. Additional consideration should also be given to ATMP trials requiring tissue handling for human application.
Various	Play specialist (per visit, if required)	Various	Usually required for paediatric studies. Can be added as an adjustment within respective tariff line items e.g. Information Consent or Drug Administration. Recommended to add 30 mins admin time, plus cost of play specialist.
88182	Flow cytometry; cytoplasmic or nuclear marker; cell cycle or DNA analysis	£182	**Consider increasing cost to reflect time required for pathologist, Scientific staff time and per sample analysis** The study protocol should be reviewed to identify the need for input from other departments, especially for haematology and bone marrow investigations.

Section 4.2: New tariff activities (October 2024) which have been added for early phase/ATMP studies.

General recommendations are made here where timings for activities may be increased. It is important to note that any changes to timings must be in line with protocol activity - the recommendations do not override the requirements for the study delivery. Therefore, timings may be increased or reduced depending on what is required to deliver the study according to the protocol.

Where activities are undertaken by different staffing groups/departments across research sites this must be addressed through organisational funding distribution models.

Section 4.2.1: General Activities/Procedures table

Activity Code	Activity Description	Clinical time (min)	Nurse time (min)	Admin time (min)	Notes (including justification for any time increases)
NIHR_GPC_072	ATMP referral management	30	120		Additional time required if a site is set up as a treatment centre for dosing external patients. The clinical time and nurse time should be appropriately increased depending on clinical trial complexity and whether the trial is cellular therapy or non-cellular therapy and the patient population. Appropriate additional time for repeat apheresis must be considered.
NIHR_GPC_073	Cell therapy lab set-up (upon signature of agreement)		450	450	Cell Lab who stores IMP for cellular therapy trials on behalf of Pharmacy, appropriate time for set-up/close-down fee should be considered. Complex ATMP and GMO studies may require clinical input - consider adding 450 min clinical time and removing the admin time.
NIHR_GPC_074	Dietetics setup (upon signature of agreement)		450	450	Where protocols require specific meal plan, a set-up fee should be included. Additionally, per each visit, coordination of meal should also be considered

Activity Code	Activity Description	Clinical time (min)	Nurse time (min)	Admin time (min)	Notes (including justification for any time increases)
NIHR_GPC_075	IT support department set-up on site/remote monitoring		225	225	Remote monitoring requires several accesses provided to hospital systems, training, creation of IT accounts, and management of restricted accesses.
NIHR_GPC_076	Pre-screening activity, (discussion with local medical team, discussion with family)	240			Where protocols require pre-screening assessments.
NIHR_GPC_077	Receiving of ATMP at site		75		To ensure that quality checks are performed, temperature is checked, temperature data uploaded to central vendors etc. Where IMP are stored at ultra-low temperatures for cellular therapy trials, appropriate extra time (60min) should be considered when it comes to use of portals, providing temperature downloads to sponsor etc.
NIHR_GPC_078	Theatres set-up (upon signature of agreement)		450	450	This fee is required for trials requiring tumour collection for manufacturing of ATMP, where this would be undertaken as a standalone surgical procedure. Appropriate clinical/nursing time to be considered for scheduling of surgery, liaising with surgeons etc. Complex studies may require clinician input so consider adding 450 min clinical time and removing the admin time.
NIHR_GPC_079	Tissue preparation for processing/shipment		180		Tissue sample collection processing only (EXCLUDES collection - this is a separate line item). Times to be adjusted as per processing requirements in the protocol. The separate Specimen dispatch item should be selected if using an off-site lab (e.g. central lab). May need to consider time adjustments when collection is outside of normal working hours (e.g. access restrictions). Where applicable ensure investigator time is included for sign-off. Consider where there is a need for tumour collection for manufacturing of ATMP (e.g. TILS).

Activity Code	Activity Description	Clinical time (min)	Nurse time (min)	Admin time (min)	Notes (including justification for any time increases)
NIHR_GPC_080	Local completion and submission of genetically modified (GM) risk assessments (for each GM risk assessment conducted)	60	180		For trials involving genetically modified organisms such as CAR-T cells, appropriate clinical/nursing time should be considered.
NIHR_GPC_081	Annual Safety Maintenance fee – charged annually	1800		1800	Safety Meetings / CIOMS reviews / SUSAR reviews: Safety meetings are held every 2-3 weeks throughout the duration of the study. Decisions are made on increasing or expanding dosing, review of SUSARs / CIOMs reports in realtime, use of PV portals, reviewing, signing off relaying information to team, (minute, track, action where needed) in real time.
NIHR_GPC_082	R&D fee: tier 4 (upon signature of agreement)	1200	3000	3000	Variations to value (increase or decrease) may occur in relation to study or therapy area complexity. Tiers are given as guidance values which can be adjusted on a case by case basis. Tier 4 - 120 Hours (50 managerial, 50 admin, 20 medical) - Studies requiring additional safety committee review, above and beyond standard R&D confirmation of capacity and capability (including, but not limited to, GMO and Early Phase committees)
NIHR_GPC_085	Initiation Training fee: tier 3 (upon signature of agreement)	540	2400	960	To cover research team SIV plus any other study specific sponsor requested training at set-up. Times can be adjusted according to study requirements. Tier 3 - 65 hours (9hrs clinical, 40hrs managerial, 16hrs admin) - Early Phase (Phase I, II) - ATMP - Interventional, with 4 or more arms - Basket or platform trials requiring multiple set ups during course of study

Activity Code	Activity Description	Clinical time (min)	Nurse time (min)	Admin time (min)	Notes (including justification for any time increases)
					- Complex subcontracting is required (eg Hub and Spoke model)
NIHR_PRC_049	Apheresis/ Leukapheresis Delivery	960	1380		16 hours medical time (covers pre-apheresis consultation, vein access supervision, supervision of optia set up and apheresis, post apheresis consultation). 23 hours nurse time (covers pre-apheresis consultation, nurse assessment on the day, optia set up and apheresis, post apheresis consultation - all specialist nurse time) If necessary, the clinical time and nurse time should be appropriately increased depending on: ● clinical trial complexity ● if the patient needs to be mobilised ahead of the cell collection ● whether the trial is cellular therapy or non-cellular therapy ● patient population. Appropriate additional time for repeat apheresis must be considered.
NIHR_PRC_050	ATMP Preparation using Biosafety cabinet		120		Timings can vary according to product. Refer to pharmacy manual or ATMP handling manual, IMPD and IB. Consideration should be given to cleaning/preparation of area for preparation and cleaning post preparation. Disposal of waste is usually a separate line item.
NIHR_PRC_051	ATMP Product order request		30		The Clinical time and Nurse time should be appropriately increased depending on clinical trial complexity of whether the trial is cellular therapy or non-cellular therapy and patient population. Appropriate additional time for repeat/parallel requests must be considered.

Activity Code	Activity Description	Clinical time (min)	Nurse time (min)	Admin time (min)	Notes (including justification for any time increases)
NIHR_PRC_052	Autoclaving of Genetically Modified waste		60		Destruction of biohazardous waste via autoclave
NIHR_PRC_053	Blood transfusion (for study drug related anaemia)	30	45		Blood transfusion will include prescription, cost of blood products, blood tests and infusion time. In addition, the cost of blood products should be invoiced (pass through) as per local hospital costs.
NIHR_PRC_054	GP Eligibility Letter	10	15		Completion of eligibility request to GP practice to ensure volunteer medical history prior to Phase 1 study enrolment. May be required for healthy volunteer studies to determine eligibility prior to enrolment in early phase trials.
NIHR_PRC_055	Toxicity Management	60			Where additional toxicity management plans are required for early phase/ATMP trials.
NIHR_PRC_056	Neurocognitive Assessment	60			Required to monitor potential neurotoxicity following CAR T-cell/early phase therapy. Clinical time should be increased (and nurse time added) where additional testing such as handwriting tests are required. Clinical time should also be increased for paediatric or vulnerable patient groups.
NIHR_PRC_057	Pre-screening results management		120		To cover additional eligibility confirmation/study team communication/patient communication if non-eligible Where protocols require pre-screening assessments consider adding 30 min admin time for the management of results.
NIHR_PRC_059	The Over Volunteering Prevention Scheme (TOPs) registration		10	5	TOPS is required for all Phase I healthy volunteer studies.

Section 4.2.2 – Investigations table

Activity Code	Activity Description	Cost (Unit)	Notes (including justification for any time ranges)
NIHR_INV_187	Apheresis/ leukapheresis directly incurred Costs	1305	Includes one off payment of £1305 for Central venous catheter, one off payment of £350 for local anaesthesia and one off payment of £1,250 for the Apheresis kit (kit, saline nail, warmy coil, astotherm, 3 way connection, service etc) Please ensure that the procedure 'Apheresis/ leukapheresis delivery (NIHR_PRC_049)' is also added at the same time points as this activity Apheresis activities are generally managed by specialist nurses as this cost includes nurses time to plan/schedule and procedural costs.
NIHR_INV_188	Apheresis/ Leukapheresis Kits (additional)	1250	Additional cost to be considered as required by the protocol for example blood kits for central labs. Consideration should be given as to whether these are provided directly by the sponsor.
NIHR_INV_189	GP Eligibility Letter – Return of Medical history fee	40	Charged by some GP surgeries for return of medical history for healthy volunteers. Fees may be higher from some practices and should be negotiated on a case by case basis with Sponsor

Section 4.3 – Activities relating to early phase and ATMP pharmacy requirements

General recommendations are made here where timings for activities may be increased. It is important to note that any changes to timings must be in line with protocol activity - the recommendations do not override the requirements for the study delivery. Therefore, timings may be increased or reduced depending on what is required to deliver the study according to the protocol.

Where activities are undertaken by different staffing groups/departments across research sites this must be addressed through organisational funding distribution models.

Section 4.3.1: General Activities/Procedures table

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
NIHR_GPC_029 NIHR_GPC_030 NIHR_GPC_031	NIHR_GPC_029 - Pharmacy A setup: dispensary based dispensing only with no aseptic dispensing (upon signature of agreement) NIHR_GPC_031 - Pharmacy C setup: dispensary and aseptic dispensing (upon signature of agreement) NIHR_GPC_030 - Pharmacy B setup: aseptic dispensing only (upon signature of agreement)	0	1290-1800	0	Early phase studies are generally more time consuming to set up compared to late phase studies, therefore consider: - dose escalation studies - Novel agents (first in man) - risk assessments for handling - storage - preparation - transport after preparation - some require dilution steps at lower dose levels and no dilution at higher dose levels etc. Consideration to be given as to how dose changes, or changes to regimens decided via Cohort review meetings rather than protocol amendments, are resourced - these amendments may not be accompanied by a protocol amendment or pharmacy manual amendment.

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					For stratified trials (basket/umbrella) which may add new arms/IMPs which require full setup - currently set up fees are only chargeable at signature of CTAg. Some sponsors may submit full SA for addition of new arms/IMPs - in which case CTAg will be renegotiated at which time sites may locally add additional set up costs for new arm/IMPs.
NIHR_GPC_049	Pharmacy revision and implementation of relevant SOPs or documentation as a result of a protocol, Investigational Brochure or pharmacy manual amendment (chargeable at each amendment)	0	240	0	For early phase/ATMP studies – amendments are usually more complex and may require review of risk assessments, new dose levels, changes to dosing or need to implement additional safety measures. Reviewers needs to understand what this fee covers to amend as required: - time to review amendment, - update any pharmacy documents as required, - update PSF, - provide local C&C for amendment before implementing NB – not to be used for basket/umbrella trials which add new arms/IMPs as these should be attributed as new set up costs – see set up comments. Consideration for tiering may be given as set out against NIHR_GPC_045.
NIHR_GPC_067	Electronic prescription digital build fee	0	450	0	Electronic prescription build fee involves: - review of Protocol - associated dosing schedules / dose combinations. Consider adjusting time where:

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					- complex dose escalation study where multiple doses may need to be added - non-routine dose calculations which may add complexity - non-standard dose units which may add complexity - changes required for amendments, doses which were not pre-defined in protocol - complexity of regimen, number of IMPs across multiple days - charged per prescription add the electronic prescribing systems, charged multiple times for multiple dosing regimens for different cycles (i.e. loading doses, maintenance dosing etc.) Early phase/ATMP trials may require changes to electronic prescription during study as part of amendment or safety – It should be agreed with the sponsor that this can be charged again if changes are required. For IV IMPs review of BMI / safety etc are also required. Appropriate clinical time (120 min or more) Nurse time (180 min or more) are required.
NIHR_PRC_033	Dispensing time for standard agent or IMP/NIMP (excluding use of IVR/IWR)	0	70	0	Early phase trials may require complex dispensing of standard IMPs: - blinded trials where pharmacy is unblinded - multiple packs where dispensing multiple combinations of IMPs

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					- additional time for pre-meds, and or pre-med prescription amendments. - Dispensing time for IMP stored in Stem Cell Lab (ultra low temp) need to be considered Consider dispensing time for protocol required rescue/supportive medications which will require tracking. Time to be adjusted by lead reviewer; consider adding multiple manual iCT lines if timings may change depending on dose level
NIHR_PRC_034	Aseptic dispensing agent time	0	120	0	Early trials may involve: - novel compounds - may require larger numbers of vials per dose - take longer to prepare - may require specific thawing times - time to acclimatise to room temperature. Time to be adjusted by lead reviewer; consider adding multiple manual iCT lines if timings may change depending on dose level. NB. this fee covers: - pharmacist prescription clinical verification - aseptic unit to process prescription - generate worksheets - second check of worksheet - collection of correct preparation materials + IMP (taking into consideration some may be sponsor-provided or specialist items) - clean room procedures for transfer between rooms into isolator (including decontamination times, preparation time, second in-process checks, transfer

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					to labelling, final check release, segregation of packaging to ensure available for reconciliation by CRA, arrange transfer to admin area) Some trials may be risk assessed for the nursing team to prepare IMP in the clinical area (NB. this is not limited to early phase/ATMP trials) if this is permitted by sponsor. Consider adding both scenarios within NCVR iCT review with local sites to remove those that do not apply. This will need a manual line added to iCT to cover nurse preparation time. Expectation is that all other activity EXCEPT the preparation will require pharmacy resources and must be costed accordingly.
NIHR_PRC_036	Advanced therapy - additional preparation time [where relevant]	0	240	0	Consider adding this fee for ATMPs preparation where completed by pharmacy - time to be adjusted as required: - number of vials per dose prepared - complexity of dose preparation - if each vials requires reconstitution prior - if multiple diluents needed - specialist handling during preparation e.g. thaw time prior to preparation, use of water baths, incubators Early phase trials often require additional processes to follow, especially with freeze/thaw times, serial dilutions, coordination with start of IMP and post dose assessments, pre-IMP infusions etc.

NIHR coding	Activity Description	Current tariff Clinical time (min)	Current tariff Nurse time (min)	Current Tariff Admin time (min)	Notes - considerations and justification for time increases
					Appropriate staff time (Nursing and Pharmacy) should be considered. Where activity is undertaken by staff groups outside of pharmacy and/or in a different location, this should be covered via the organisational distribution model.
NIHR_PRC_039	Individual participant drug accountability time	0	35	0	To be charged per IMP dispensing episode/drug accountability performed. Early phase trials may: - Involve novel compounds - may require large numbers of vials per dose - take much longer to complete drug accountability - consider if nIMP/rescue medication accountability required and add as needed NCVR reviewer to consider adjusting current iCT baseline to account for additional time for specific early phase/ATMP IMPs - add manual additional iCT line to cover any specific IMP that this applies to. Where trials have oral IMPs, a minimum of 15 min nurse per visit should be included; per IMP for drug accountability activities. Additionally, where the IMPs are provided with different strengths and multiple bottles, additional time should be considered.

Section 4.3.2 – Investigations table

Activity Code	Activity Description	Cost (unit)	Notes (including justification for any time ranges)
NIHR_DEPT_042	Pharmacy storage space per month to cover additional space within each NHS Trust regardless of temperature requirements, monthly fee (annualised charge pro rata as needed)	60	Considerations to justify increase to iCT costs **per occurrence:** - Early phase/ATMP IMP received on dry ice/specialist shippers require significantly higher resource - Consider amending the iCT baseline costs so fee applies to each type of IMP or number of shippers received - If trials with multiple IMPs consider adding a manual line in iCT for each IMP type.
NIHR_DEPT_043	Pharmacy receiving shipment, per occurrence (chargeable quarterly in arrears)	60	Considerations to justify increase to iCT costs **per occurrence**: - Early phase/ATMP IMP received on dry ice/specialist shippers require significantly higher resource - Early phase/ATMP trials can require large numbers of vials to be unpacked, verified as part of receipt procedures - Consider amending the iCT baseline costs so fee applies to each type of IMP or number of shippers received - Consider arrangement of return via specialist shippers (including LN2 dry shippers and recyclable packaging) - IMP for cellular therapy trials of ten require extra resources to receive Imp in LN2 shipper. - any additional receipt procedures required - consider trials which require a 2-step release process due to shipping from outside the UK and needs UK QP oversight step (i.e. if needs to be quarantined prior to release). - If trials with multiple IMPs consider adding a manual line in iCT for each IMP type. NB. For some cell-based therapies, part/all this activity of this fee may be undertaken by the cell therapy labs
NIHR_DEPT_044	Pharmacy waste disposal management including paperwork, logs etc, per occurrence (chargeable quarterly in arrears)	49	Waste disposal of GMO's requires significantly more paperwork - consider adjusting iCT baseline cost accordingly. Consider adding a manual additional line in iCT to cover GMO waste disposal paperwork (i.e. if it needs to be autoclaved, reported to GMSC etc.)

Activity Code	Activity Description	Cost (unit)	Notes (including justification for any time ranges)
NIHR_DEPT_045	Pharmacy packaging returns for return to Sponsor, per occurrence (chargeable quarterly in arrears)	36	Consider activity associated with returning IMPs with specialist storage requirements and adjust cost. Sponsor to provide detail on returns procedures at NCVR review .
NIHR_DEPT_046	Pharmacy specialist storage requirements for advanced therapy/radiopharmaceuticals (e.g. dry shipper containing liquid nitrogen or minus 80C freezers) (annualised charge pro rata as needed)	TBC	To be added to iCT for each type of specialist storage - Consider separate additional manual lines in iCT to cover each IMP as required. - CAR-T/TILs require storage at ultra-low temperature, chargeable per occurrence. NB. Some cell therapies will charge this for IMPs stored at cell therapy facility
NIHR_DEPT_047	Pharmacy specialist transportation requirements for advanced therapy/radiopharmaceuticals (e.g. dry shipper, dry ice, spillage kits, courier costs) (per site charge) (chargeable quarterly in arrears)	TBC	Consider additional consumables required for specialist transportation around the site (either prior to preparation or after). Where not provided by sponsor, consider: - how IMP to be transferred between trials pharmacy and preparation area - how prepared IMP to be transferred between preparation area and clinical area for administration - Specialist transportation of Cell Therapies in LN2 per occurrence should be considered
NIHR_DEPT_048	Waste disposal as hazardous waste per container or Investigational Medicinal Product (IMP) destruction (chargeable quarterly in arrears)	30	Disposal of ATMPs likely require different waste streams or additional steps - consider time required and/or cost of waste stream for: - GMO gene therapy - non-GMO gene therapy - Cell therapy - Radiopharmaceutical To be charged per disposal occurrence of used/part-used IMP or unused/expired IMP NB. for unused/expired ATMP - this may be undertaken by cell therapy lab
NIHR_DEPT_059	Pharmacy study or Investigational Medicinal Product (IMP) specific consumables (total cost)	TBC	Consider what additional consumables required for handling, storage, preparation, packaging, disposal:

Activity Code	Activity Description	Cost (unit)	Notes (including justification for any time ranges)
			- cost of GMO spill kit contents (may be specific to IMP) - blinding materials - sponsor required infusion bags, syringes, needles, filters, CTSDs or vial adaptors - if sponsor provided, consider adding an additional line for time for validation/commissioning of these consumables as per NIHR_DEPT_043.
NIHR_DEPT_060	Pharmacy equipment purchase for specific Investigational Medicinal Product (IMP) requirements in storage space or conditions (total cost) (chargeable quarterly in arrears)	TBC	Consider time taken to order new equipment: - this does not include the purchase cost of any new equipment or specific enabling costs required for installation, e.g. new power supply points, removable of doors to install equipment etc; costs to be negotiated locally - to cover time taken to perform activities relating to QA time, validation documents To be charged per piece of new equipment including, but not limited to refrigerators, freezers, sponsor-provided preparation ancillary items, new temperature monitoring equipment

Section 4.4 - Activities related to early phase and/or ATMP trials which should be considered for manual iCT entry (not in the current NIHR iCT Tariff)

The activities within this section are to be added, as appropriate to the study budget, where the activity is deemed as direct research activity. Standard of Care, Indirect or Capacity build activities should never be added to the study budget.

For avoidance of doubt the Department of Health and Social Care (DHSC) guidance, Attributing the costs of health and social care research (AcoRD), sets out direct costs as attributable to three broad cost categories:

- research costs - the costs of the research and development (R&D) itself that end when the research ends. They relate to activities that are being undertaken to answer the research questions
- NHS treatment costs - the patient care costs, which would continue to be incurred if the patient care service in question continued to be provided after the R&D study had stopped
- NHS support costs - the additional patient care costs associated with the research, which would end once the R&D study in question had stopped, even if the patient care involved continued to be provided

For commercial studies full cost recovery for the above activities must be covered by the commercial sponsor.

The NIHR iCT Tariff document also sets out activities which may not be included in the study budget within the 'Non-chargeable activities' tab:

- Set-up of any finance and IT information systems as required
- Invoice generation for all departments
- Any standard tasks performed by the Trust as part of normal or routine patient care
- Any trial related communications
- Any standard administrative or management support and general maintenance of trial related paperwork (NOTE: this EXCLUDES data management)
- Pre-site selection or feasibility tasks
- Arrange/attend any introduction or qualification meetings
- Time research time spend preparing or attending inspections by regulatory bodies
- Time for any regulatory body inspections
- Medical record retrieval
- Internal contracts or paperwork for staff i.e. honorary contracts or University – Trust agreements for research staff
- PI duty of care responsibilities including Investigator review of safety reporting provided by COMPANY e.g. annual safety reports
- Storage space/co-ordination of equipment/notes

- Pre-screening (e.g. note searches) for non-stratified medicine/rare disease studies, however cost coverage for stratified medicine rare disease/study pre-screening resulting in significant workload for the participating organisation (e.g. data not recorded in routine patient notes) to be agreed on a study-by-study basis as required.
- Triggered company audits (if necessary Company and Trust can negotiate a cost for a company requested audit with above-standard time requirements for staff involved)

Section 4.4.1 - General Procedures/Set up table

Activity Description	Clinical time (min)	Nurse time (min)	Admin time (min)	Notes (including justification for any time ranges)
Dry run (post-consent and pre-treatment) per hour per staff member	180	180		Consider if dry run will account for apheresis, procedure, shipping, ATMP/GMO receipt and administration.
Amendment to ARSAC employer licence	225			If protocol necessitates changes to local licence
Medical Emergency Review (per hour)	60			Per occurrence
Completion of early phase/ ATMP Clinical Risk Assessment	240			One off
Amendment to early phase/ATMP Clinical Risk Assessment due to protocol/ IB amendment or emerging safety data	60			Per occurrence
Amendment to early phase/ATMP Technical Risk Assessment due to protocol / IB / pharmacy manual amendment	60			Pharmacy/Cell Therapy lab Per occurrence
Amendment to GMO Risk Assessment due to amendment	60			Per occurrence

Section 5 – Costs to Consider

5.1 Setup and closedown costs – ATMP studies

The cost of site set-up for ATMP trials is generally significantly more than for phase 2/3 CTIMPs, as the setup of ATMP trials often involves more steps (for e.g. site Genetic Modified Safety Committee [GMSC] review, HTA site registration, supply chain setup and management) and requires a higher level of co-ordination between stakeholders. In addition to the 'General R&D fee', additional pharmacy set-up costs for ATMP trials are incorporated within the iCT for the four broad categories of ATMP trials. The costs are based on the typical time required by the specialist staff involved and are derived from the collective experience of several NHS Trusts. Although itemised as 'pharmacy' costs, it is recognised that local arrangements vary, and these activities are not always carried out solely within pharmacy.

The four set-up costs available to select within the iCT (2024/25 tariff) are:

iCT Activity	Pharmacy D setup: specialist professions preparation for relevant advanced therapies and radiopharmaceuticals	Pharmacy E setup: virus based gene therapy (Hours)	Pharmacy F setup: somatic cell therapy (Hours)	Pharmacy G setup: tissue engineered product (Hours)
Time Required (hours)	385	102	256	256

NOTE: Depending on the formulation of the product and the logistics required to deliver the trial, the costs in the table above can be negotiated and agreed between sponsor and organisation. Within the organisation, these fees need to be negotiated internally depending on where the activity is taking place (e.g. pharmacy or cell labs).

As set out in the iCT tariff, the above tariff items cover the following activities:

- Review protocol
- Feasibility assessment
- Communication with the sponsor
- Participation in mandatory local review and approval processes
- Attendance at meetings & liaison with PI, Research Nurse, CRA
- Write bespoke SOPs, associated documents and worksheets
- Set up dispensing & stock control software systems and documentation
- Set up supply systems
- Train all relevant Pharmacy staff, as required
- Review contract including pharmacy costing

- Close down.

Out of Hours Costs

Out of Hours costs are currently not available in the NIHR iCT Tariff and, unfortunately, a resolution was not found before going live with Early Phase and ATMP integration into NCVR on 14th October 2024. Work will be undertaken to identify a suitable resolution in time for April 2025. In the meantime any Out of Hours costs related to the direct delivery of the study protocol (ie. is specified specifically within the protocol) should be picked up as a pass-through cost within the mCTA.

Any in-direct out of hours costs (ie. clinics running over-time outside of usual business hours) should be picked up via the study over-heads.

Coordination/support for participant appointments

Organising participant appointments (arranging a suitable date, organising travel and accommodation, arranging the visit around staff availability and the need to rearrange this if necessary) can take a lot of time and should be within the Per Participant costs. Discuss with the member of staff that will be responsible for arranging participant appointments/travel/accommodation etc. to agree an appropriate time per visit for visit coordination (this will depend on the demands of the study i.e. if accommodation needs to be booked, if coordination is required between several support departments), but a minimum of 30 min admin time per visit is advised.

IMP storage and management

Some advanced therapy IMPs need to be stored at cryogenic temperatures (liquid Nitrogen temperatures). The costs of this storage are generally substantially higher than the costs of fridge/freezer storage required for traditional IMPs.

The iCT provides an activity description for ‘Pharmacy Specialist storage requirements for advanced therapy/ radiopharmaceuticals. The costs are unspecified and should be incorporated by the site to cover the local costs, which will vary depending on the trial and any specific arrangements that have been put in place with the sponsor for IMP supply and/or local storage.

Consider sites where material may be held at one location and will require transport to another for infusion (multi-Location hospitals). You should also consider the collection labelling requirements (Patient’s full name, Patient’s date of birth, Hospital ID, SEC DIS) which will need to be applied at site.

Drug Reimbursement including rescue meds

Costs should be recovered at British National Formulary +VAT and will be included in the mCTA as a pass-through cost. Due to the confidentiality of NHS contract prices it is not possible to have them detailed specifically within the mCTA.

Waste Management - ATMPs

The site risk assessment undertaken for an ATMP trial involving genetically modified organisms (GMOs) will determine how waste (for e.g., IMP, clinical consumables) is to be managed at the site. This may require additional steps and/or waste segregation over and above those used for routine clinical waste. Arrangements can vary from site to site depending on local waste management infrastructure. Costs can be significantly higher than the standard iCT tariff for pharmacy waste management and will often be associated with specific patient visits where GMO based ATMPs are prepared and administered. The additional costs of waste management can be incorporated in the per patient visit costs, for example as additional staff time to manage the waste and as additional itemised costs where consumables (for e.g., additional waste packaging) and/or contracted waste disposal is needed.

Videotaping of assessments

If assessments need to be videotaped, time can be added within the Per Participant costs to allow for the additional burden (for e.g., for preparation/setup of equipment, recording the video, video transfer/upload). Time can also be added to the Additional Itemised costs to cover any additional work (for e.g. if there are any issues with set-up and image transfer).

Overnight stays

If participants are required to stay overnight this should be costed appropriately in the Per Participant costs for the relevant visits (for e.g., for study visits taking place over multiple consecutive days, visits starting early in the morning/lasting until late at night for participants travelling a long distance to the research site). Consider also adding an overnight stay to the Additional Itemised costs in case of an additional stay being needed. Consider whether the overnight stay can be in a local hotel. A preferential rate may be able to be negotiated if this is going to be a regular hotel used for booking overnight stays for study participants.

Unscheduled visits

On occasion, unscheduled visits need to take place (for e.g., to repeat an assessment or collect an additional blood sample). This should be addressed in the Additional Itemised costs/Clinical Trial Agreement, with a statement requesting that assessments that are conducted as part of an Unscheduled Visit will be costed as they appear in the Per Participant costs. Unscheduled visits can vary in complexity and coordinating these visits can be time consuming. Additional time can be charged for if appropriate (for e.g., under the unforeseen admin time item). Consider also if a Daily Facility Charge fee should be applied.

Coordination of participants to other departments

If the study involves the participant attending several departments within a hospital as part of their visit and a member of staff is required to accompany them, discuss this with the relevant member of staff and input time into the Per Participant costs accordingly to cover this. Consider how coordination of participants may be managed at different centres.

Support department costs

Include setup costs for the departments that are involved in the study in the Setup & Closedown Costs as appropriate. Without the support of different departments within hospitals it would not be possible to deliver research, so it is important that the relevant departments are paid for the work that they do. Discuss this with the appropriate support departments and with the R&D/Finance teams to ensure that costs are being allocated appropriately.

General consideration / other costs

As items costed as Additional Itemised activities are not routinely invoiced for in the same way as those entered as Per Participant activities, there is the potential for these items to be missed. Therefore, to make invoicing more straightforward, it can be useful to include as many elements as possible in the Per Participant costs (as long as this is appropriate).

Flexibility to adapt to changing circumstances

The Covid-19 pandemic has illustrated how clinical trials must be flexible to adapt to different circumstances. It is important to remember that sites must be paid for the work that they carry out to deliver studies, whether this is remotely, face-to-face, or a mixture of both. Consider whether, when circumstances change, re-costing is strictly necessary as this can take a lot of time and effort.

Upfront costs

Given the additional work needed to set-up and run an ATMP trial when compared to a typical phase 2/3 CTIMP, it may be appropriate for an organisation to request an upfront payment from the study sponsor to employ a member of staff to work on a study. This would need to be appropriately justified to reflect the percentage of a Whole Time Equivalent (%WTE) of the member of staff that is required, which can be calculated as follows:

Total staff time for relevant study assessments x number of expected recruits = total hours required (which can be converted into a %WTE)

Once a %WTE is determined this can be shared with the organisation's Finance department, who will provide the salary figure for the relevant staff, in turn enabling the Principal Investigator (PI) to submit the full request to the sponsor. If the sponsor agrees to fund the staff member, the associated timings for that member of staff should be removed from the Per Participant costs, and a lump sum cost for the staff salary should be entered into the costing tool (the Finance team can advise on the best place to put this within the study budget).

Upfront salary payments currently cannot be accommodated within the current version of the mCTA, so a separate salary agreement is needed to cover this.

Other guidelines that may help in costing ATMP trials are listed below:Northern Alliance Advanced Therapies Treatment Centre (NA-ATTC) Toolbox for Advanced Therapy Clinical Trials

Costing a study properly is important as it helps to ensure that appropriate time is allocated to carry out the tasks involved.