

## SLHD REQUIREMENTS REGARDING REQUESTS FOR THE USE OF ADVANCED THERAPY MEDICINAL PRODUCTS (ATMPs)

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#### 1. PROCESS OVERVIEW

An advanced therapy medicinal product (**ATMP**) is a medicine for human use that is based on genes, cells or tissue engineering. ATMPs can include gene therapy, cell therapy, applications of gene technology such as gene editing and tissue-engineered medicines. There exist legislative, regulatory and compliance requirements that must be adhered to in order to undertake any of these activities at Sydney Local Health District (SLDH).

All requests for the use of ATMPs within SLHD require early consultations with a range of Departments and Committees.

- The processes and steps involved are outlined in this document and in [Figure 1 and Figure 2](#).
- Information about how to undertake each step is provided in [Section 2](#).
- A questionnaire (the [ATMP Consultation Questionnaire](#)) is to be completed and submitted with preliminary information about the study.
- [Site visits must be approved by SLHD CE in advance](#)
- The contact details for each step are given in [Section 5](#).
- [Section 6](#) contains a list of prompts to assist Principal Investigators check that the required steps have been undertaken.

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## 1.1 Early consultations

In the first instance, the **RPAH Department of Cell & Molecular Therapies (CMT)** and the **RPAH Institutional Biosafety Committee (IBC)** must be consulted for technical and regulatory assessment. A Confidential Disclosure Agreement (CDA) (see section 1.3) should be put in place between the PI and sponsor before CMT feasibility can commence.

Preliminary details about the proposed study can be communicated initially by email. CMT must be included in meetings with Sponsor once a CDA has been put in place (Figure 2). Initial communications with CMT then must be followed as early as possible with completion and submission of the [ATMP Consultation Questionnaire](#). This must be done well in advance of the site being selected as a study site. Typically the requesting PI will also be invited to present the study formally for assessment by CMT management.

CMT will use the information from initial meetings with the Sponsor, the questionnaire, and the presentation to determine feasibility to service the project. This will be based on whether the ATMPs require storage, manufacture, formulation prior to administration, dispensation, etc. CMT's assessment will also cover areas such as sample processing and sample testing requirements, staff requirements, budget and timeframes.

Once CMT has completed its assessment it will notify both the requesting PI and the IBC in writing of the outcome of the ability to service the requested study (Decision 1 – Part 1). This process will indicate if and when further communication with, and an application to, the IBC is appropriate. Upon notification confirming feasibility, the IBC will provide details about the type of application required to the IBC and request further information if needed. Where possible, applications can be expedited in the event that there are deadlines or expectations of a trial completing before initiation at SLHD, such as may occur when recruitment is competitive between sites.

An agreement regarding authorship for publications resulting from study will be negotiated between CMT and the PI before the study is initiated. As a general guide, this agreement would require that the principal investigator meet SLHD requirements to undertake a clinical trial where contributions from laboratory and clinical departments are appropriately recognised.

After the CMT assessment, there must also be early consultation with RPAH Pharmacy to ensure Pharmacy's requirements are met, including regarding other medications that may be needed in the study. Please see below for more information about the IBC and Pharmacy.

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## 1.2 Details and documents to be provided in the early consultations above

Most studies have unique and diverse aspects that need to be specifically communicated. Please communicate these as well as basic details where known, such as the number of participants to be treated, budget and timeframes. Please also provide relevant documents. It is understood that some information and documents may be in development or not available at the time of early consultations. Please supply whatever information and documents you can as these will assist the Departments and Committees that need to be consulted to assess the study. The [ATMP Consultation Questionnaire](#) (see [3.1](#) below) contains a list of the types of documents that that can be supplied to assist the assessment.

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### 1.3 Confidential Disclosure Agreements

A **Confidential Disclosure Agreement (CDA)** should be obtained from the Sponsor by the PI. Once it is finalised and signed by the Sponsor, it will go to SLHD CE for signature. A CDA should be put in place prior to CMT performing a feasibility assessment.

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### 1.4 Site Visit Requests

Before Sponsors visit facilities at SLHD, [a formal request / brief must be submitted to, and approved by, SLHD CE.](#)

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### 1.5 SLHD policy applicable to the use of ATMPs

The use of ATMPs (including those with marketing authorisation) must follow the **SLHD Policy Directive on 'The Safe Introduction of New Interventional Procedures and Clinical Innovations into Clinical Practice'** (SLHD\_PD2015\_022) (See [4](#) below)

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### 1.6 Human Research Ethics Committee (HREC)

ATMPs may be sourced from an external supplier via RPAH CMT or they may be manufactured by RPAH CMT. They can be used as products with marketing approval or as investigational medicinal products within a clinical trial conducted at SLHD.

Unlicensed ATMPs without marketing approval must be assessed and approved by a Human Research Ethics Committee (HREC).

If the study is an early phase clinical trial (EPCT) (i.e., includes all clinical trial phases up to but not including Phase II, including studies with any Phase I component) it is reviewed under the **Early Phase Clinical Trials HRECs Scheme** (<https://www.medicalresearch.nsw.gov.au/early-phase-clinical-trials-2/>); whereby adult EPCTs are reviewed by Bellberry HREC and paediatric EPCTs are reviewed by Sydney Children's Hospitals (SCHN) HREC.

If the study is not an ECPT it is reviewed by the **Clinical Trials Sub-committee of the SLHD Ethics Review Committee (CTSC-ERC)**

(<https://www.slhd.nsw.gov.au/RPA/Research/ecp.html>).

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### 1.7 Pharmacy and the Drug and Therapeutics Committee (DTC)

After the CMT assessment, there must be early consultation with RPAH Pharmacy to ensure its requirements are met, including regarding other medications that may be needed in the study. An application to the RPAH Drug and Therapeutics Committee (DTC) will also be required for studies involving Genetically Modified Organisms (GMOs) to approve handling of investigational product outside of Pharmacy and ensure compliance with the **NSW Ministry of Health Medication Handling in NSW Public Health Facilities Policy Directive**. Pharmacy and RPAH CMT will advise on this and provide the correct forms.

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### 1.8 Institutional Biosafety Committee (IBC)

Review by the IBC is required for all GMOs, even if the GMOs are classed as exempt (or non-notifiable) under the Gene Technology Regulations 2001 (such as is the case for many cell therapy studies). Review by the IBC is also required even if there is an existing OGTR licence covering the study (regardless of whether RPAH IBC or another IBC reviewed the

licence application to the OGTR). This is to ensure risk management is in place at the local site. This type of application is referred to as a **Local Site IBC Application**.

If the study requires an OGTR licence (such as for a viral vector gene therapy or GM virus clinical trial), the process for obtaining an OGTR licence may take a number of months because the licence application must first go to an IBC for review before it goes to the OGTR for decision and the statutory time frame available for the OGTR decision is up to 90 days. Therefore it is very important to consult the IBC early on about requirements.

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### **1.9 Site-Specific Assessment, Governance and Site Authorisation**

Finally, after HREC approval, the Site-Specific Assessment (SSA) Form, Clinical Trial Research Agreement (CTRA) and other relevant documentation (such as approvals from the other Committees above (e.g. IBC, DTC)) are submitted to the Research Governance Officer (RGO) for site authorisation.

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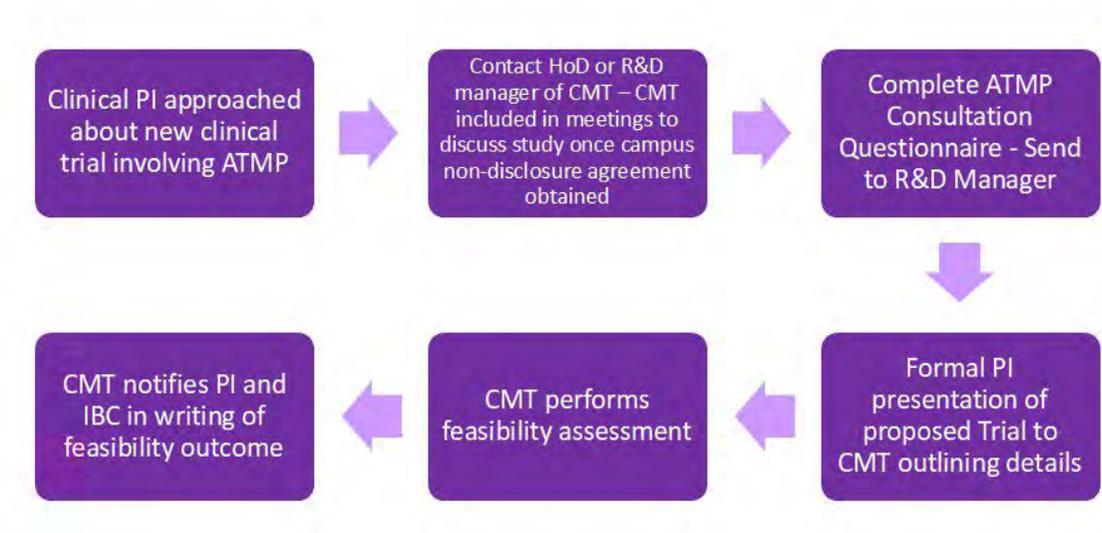
### **1.10 Schematic of overall process**

The overall process outlined above is depicted in [Figures 1 & 2](#) below. How to undertake each step in the process is outlined in [Section 2](#).



**Figure 2 – CMT Facility Engagement - Initial Consultation and Feasibility Assessment**

**Initial CMT Facility Engagement for use of Advanced Therapy Medicinal Products (ATMPs) in SLHD Prior to Clinical Trial Initiation – Decision 1 – Part 1**



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## **2. HOW TO UNDERTAKE EACH STEP IN THE PROCESS**

### **(1) Consultation with RPAH Cell & Molecular Therapies (CMT) & RPAH Institutional Biosafety Committee (IBC)**

Send initial details in an email to the Department of RPAH Cell & Molecular Therapies (CMT) (copying the CMT R&D Manager, Production Manager and the IBC Executive Officer). Arrange for CMT attendance at meetings with Sponsor once CDA is in place. Email the completed [ATMP Consultation Questionnaire](#) to the emails listed to assist in consultations. See [contact details](#) below.

### **(2) Confidential Disclosure Agreement (CDA)**

A CDA should be obtained from the Sponsor (unless an existing SLHD CE approved agreement is in place) and reviewed by SLHD legal. When satisfactory and signed by the Sponsor, it will go to SLHD CE for signature. This should be put in place before completion of the CMT feasibility review (3).

### **(3) RPAH CMT feasibility review**

After CMT has received the details of the study provided under (1) above, it will request further details to enable feasibility to be determined. Completion of feasibility will result in a letter to the PI and IBC committee.

### **(4) Consultation with RPAH Pharmacy**

Once consultations with CMT are in place, please consult Pharmacy to ensure its requirements are met and that other medications can be provided if required. See [contact details](#) below.

### **(5) Consultation with other Departments involved in the trial**

The Principal Investigator must consult their Department and other Departments involved in the trial or involved in the treatment and care of participants after treatment (e.g. radiology, apheresis and wards where participants will be cared for after treatment). RPAH CMT and the IBC can provide advice on this.

### **(6) Completion of Site Visit Request to SLHD CE**

Before Sponsors visit facilities at SLHD, [permission must be obtained from SLHD CE via formal request/ brief. The brief must include an approval chain that includes all relevant parties are aware of the details.](#) The brief can be submitted via email to SLHD Executive Support Unit [SLHD-ESU@health.nsw.gov.au](mailto:SLHD-ESU@health.nsw.gov.au) (copy to CMT [SLHD-RPACMT@health.nsw.gov.au](mailto:SLHD-RPACMT@health.nsw.gov.au))  
Urgent notifications may be handled via a phone call to the CE's Office on 02 9515 9641.

### **(7) Application to relevant Committees**

Consult the RPA Research Ethics and Governance Office website for information about applying to HREC and IBC and the schedule of meetings and closing dates. Consult Pharmacy for information about applying to the Drug and Therapeutics Committee (DTC). See [contact details](#) below.

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## **3. TEMPLATES**

### **3.1 ATMP Consultation Questionnaire**

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#### **4. REFERENCES**

**Policy Directive on 'The Safe Introduction of New Interventional Procedures and Clinical Innovations into Clinical Practice' (SLHD\_PD2015\_022) (SLHD Policies, SLHD Intranet)**

**Early Phase Clinical Trials HRECs Scheme**

<https://www.medicalresearch.nsw.gov.au/early-phase-clinical-trials-2/>

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#### **5. CONTACTS**

**RPAH Department of Cell and Molecular Therapies (CMT):**

**Research and Development Manager**

Dr Sharon Sagnella PhD

Tel 02 9565 6205 | [Sharon.Sagnella@health.nsw.gov.au](mailto:Sharon.Sagnella@health.nsw.gov.au) |

[Luigia.Manzoni@health.nsw.gov.au](mailto:Luigia.Manzoni@health.nsw.gov.au)

**Production Manager**

Dr Michelle Keir PhD

Tel 02 9515 4864 or 02 9515 4861 | [Michelle.Keir1@health.nsw.gov.au](mailto:Michelle.Keir1@health.nsw.gov.au) |

[SLHD-RPACMT@health.nsw.gov.au](mailto:SLHD-RPACMT@health.nsw.gov.au)

[https://www.slhd.nsw.gov.au/research/department\\_details.html?research=cmt](https://www.slhd.nsw.gov.au/research/department_details.html?research=cmt)

**RPAH Institutional Biosafety Committee (IBC):**

**Executive Officer**

Dr Gabrielle O'Sullivan PhD MPH

Tel 02 9515 6772 | Mob 0414 785 471 | [gabrielle.osullivan@health.nsw.gov.au](mailto:gabrielle.osullivan@health.nsw.gov.au)

<https://www.slhd.nsw.gov.au/rpa/research/IBChowto.html>

**RPAH Pharmacy and Drug and Therapeutics Committee**

**Senior Investigational Drug Unit Pharmacist**

Tel (02) 9515 8658 | Fax (02) 9515 3638 | [SLHD-RPAPharmacytrials@health.nsw.gov.au](mailto:SLHD-RPAPharmacytrials@health.nsw.gov.au)

**RPA Research Ethics and Governance Office:**

[SLHD-RPAEthics@health.nsw.gov.au](mailto:SLHD-RPAEthics@health.nsw.gov.au)

<https://www.slhd.nsw.gov.au/rpa/research/default.html>

<https://www.slhd.nsw.gov.au/RPA/Research/Committees.html>

**Sydney Local health District Executive Support Unit:**

[SLHD-ESU@health.nsw.gov.au](mailto:SLHD-ESU@health.nsw.gov.au)

<https://www.slhd.nsw.gov.au/>

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## **6. PROMPTS FOR THE PRINCIPAL INVESTIGATOR**

The following prompts are to assist Principal Investigators check that the required steps have been undertaken. This is not a form for submission but provided for the PI's own guidance.

1. Have you completed the [ATMP Consultation Questionnaire \(3.1\)](#)?
2. Have you consulted the RPAH Department of Cell and Molecular Therapies (CMT)?
3. Have you consulted RPAH IBC?
4. Have you obtained SLHD CE approval for site visits using the [Proposed Site Visit Request Brief \(3.2\)](#)?
5. Has an appropriate Confidential Disclosure Agreement (CDA) been executed?
6. Has a CMT feasibility assessment been carried out?
7. Has RPAH Pharmacy Department been consulted?
8. Has the Drug and Therapeutics Committee (DTC) been consulted?
9. Have other relevant Departments been consulted?
10. Is there any other Department or person that ought to be consulted? Yes  No   
*If yes, which Department(s):*  
*Have they been consulted? Yes  No*
11. Which approvals are required for this study? :
12. Have you applied to all relevant Committees for approval?
13. Is an OGTR licence required for the study? Yes  No
14. Is there a Clinical Trial Research Agreement (CTRA) in place for the study?
15. Has HREC approval been obtained?
16. Have you submitted the Site Specific Assessment (SSA) form to the Governance Officer?
16. Have you received Site Authorisation from the Governance Officer?
17. Have all required approvals and licences been obtained?

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### 3.1 - ATMP Consultation Questionnaire

Principal Investigator name:

Date:

Reference:

## ATMP CONSULTATION QUESTIONNAIRE & LIST OF DOCUMENTS PROVIDED

Date:

Reference:

The aim of this questionnaire is to assist RPAH CMT, IBC and Pharmacy to assess the details of the study and provide advice on it. Please complete the following as far as known at this stage

### A. STUDY IDENTITY & OVERVIEW

<b>1. Name of clinical study</b>						
<b>2. Principal Investigator (PI) name</b>						
<b>3. PI's organisational affiliation</b>						
<b>4. PI's department &amp; contact details</b>		Department:	Email:	Phone no:		
<b>5. International Sponsor</b>						
<b>6. Local Sponsor in Australia</b>						
<b>7. Local Contract Research Organisation (CRO) (if any)</b>						
<b>8. Lead HREC name</b>						
<b>9. HREC details (where known)</b>						
HREC reference:						
Title of HREC protocol:						
Name of PI on HREC application:						
<b>10. HREC approval status</b>		Approved <input type="checkbox"/>	Under review <input type="checkbox"/>	To be submitted <input type="checkbox"/>		
Date of HREC approval (if applicable):						
<b>11. Study phase</b>	First in human <input type="checkbox"/>	Phase 1 <input type="checkbox"/>	Phase 1/2 <input type="checkbox"/>	Phase 2 <input type="checkbox"/>	Phase 3 <input type="checkbox"/>	Phase 4 <input type="checkbox"/>
<b>12. Clinical trial registrations</b>	FDA IND <input type="checkbox"/>	ClinicalTrials.gov <input type="checkbox"/>	EudraCT <input type="checkbox"/>	MHRA <input type="checkbox"/>	ANZCTR <input type="checkbox"/>	Other <input type="checkbox"/>
<b>13. Reference for each registration above</b>						
<b>14. Type(s) of investigational product(s) to be used in this study<sup>1</sup></b>	Viral vector gene therapy <input type="checkbox"/>	Cell therapy <input type="checkbox"/>	Oncolytic virus <input type="checkbox"/>	Nucleic acid <input type="checkbox"/>	Interferin g RNA <input type="checkbox"/>	Other type <input type="checkbox"/>

<sup>1</sup> Usually there is one type of investigational product, but if more than one, please indicate.

### 3.1 - ATMP Consultation Questionnaire

Principal Investigator name:

Date:

Reference:

<b>15. Properties of each type of investigational product (above) to be used</b>	GMO Yes <input type="checkbox"/> No <input type="checkbox"/>	GMO Yes <input type="checkbox"/> No <input type="checkbox"/>	GMO Yes <input type="checkbox"/> No <input type="checkbox"/>	Synthetic Yes <input type="checkbox"/> No <input type="checkbox"/>	Synthetic Yes <input type="checkbox"/> No <input type="checkbox"/>	GMO Yes <input type="checkbox"/> No <input type="checkbox"/>
<b>16. Name(s) of investigational product(s) to be used:</b>						
<b>17. Please specify details of processing, formulation, and/or storage of investigation product required</b>						

### B. PARTICIPANT DETAILS

<b>18. Will study participants be treated or hospitalised at RPA?</b>	Treated at RPA:      Yes <input type="checkbox"/> No <input type="checkbox"/> Hospitalised at RPA:    Yes <input type="checkbox"/> No <input type="checkbox"/>
<b>19. How many patients are expected to be treated or hospitalised at RPA? (Please list approx. per month and total patient numbers)</b>	
<b>20. Which clinic/ward/department is running the trial?</b>	
<b>21. Will study participants be treated or hospitalised at another hospital within SLHD?</b>	Treated at another hospital within SLHD:                      Yes <input type="checkbox"/> No <input type="checkbox"/> <input type="checkbox"/> Hospitalised at another hospital within SLHD:                      Yes <input type="checkbox"/> No <input type="checkbox"/> <input type="checkbox"/> If yes, name of hospital:
<b>22. When will the trial commence patient accrual? What is the anticipated study duration?</b>	

### C. TYPES OF DOCUMENTATION PROVIDED

The following types of documentation may assist CMT, IBC and Pharmacy in their assessments. A CDA must be in place before the feasibility assessment and supplying confidential information.

### 3.1 - ATMP Consultation Questionnaire

Principal Investigator name:

Date:

Reference:

Some overlap may exist and not all are needed in initial consultations.

The most useful documents initially are the Protocol (1), Investigator Brochure (2), Pharmacy Manual or similar (3-6), MSDS or similar (7-8), Infusion Manual (9) and OGTR licence if applicable (17).

Please supply documents you consider relevant and indicate which types have been supplied.

1. CDA
2. Protocol
3. Investigator Brochure
4. Pharmacy Manual
5. Investigational Product (IP) Handling Instructions
6. Investigational Medicinal Product Manual (similar to Pharmacy Manual)
7. Investigational Product Preparation and Administration Instructions
8. Investigational Product/Material Safety Data Sheet (SDS/MSDS)
9. Safety Manual
10. Infusion Manual
11. Description of the Manufacturing Process and Process Controls
12. Approved Product Information (Australian or overseas)
13. Approved Consumer Medicines Information (Australian or overseas)
14. Patient Information Sheet (PIS)
15. Patient Consent Form
16. Site Initiation Visit (SIV) Presentation (if available)
17. IBC assessment (if applicable)
18. OGTR Licence (if applicable)
19. HREC Approval (if applicable)
20. Other  Name:
21. No documents supplied  Explanation:

Please complete this questionnaire and attach it with a cover email to RPAH Department of Cell & Molecular Therapies (CMT) and RPAH IBC at:

[Sharon.Sagnella@health.nsw.gov.au](mailto:Sharon.Sagnella@health.nsw.gov.au); [Michelle.Keir1@health.nsw.gov.au](mailto:Michelle.Keir1@health.nsw.gov.au); [SLHD-RPACMT@health.nsw.gov.au](mailto:SLHD-RPACMT@health.nsw.gov.au); [gabrielle.osullivan@health.nsw.gov.au](mailto:gabrielle.osullivan@health.nsw.gov.au)

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