Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Delivering Advanced Therapy Medicinal Products (ATMPs) in Hospitals

Anne Black
Regional QA Specialist Pharmacist – North East and North Cumbria
Prof Nicola Stoner
Consultant Pharmacist, Oxford

11.10.2018

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Introduction

- Delivering ATMPs in Hospitals
- Background and governance
- Gene therapy/Genetically Modified Organisms
- Risk Assessment
- Preparation/reconstitution activities
- Practical barriers to near-patient delivery
- Implications for clinical pharmacy
- Car-T Cell therapy

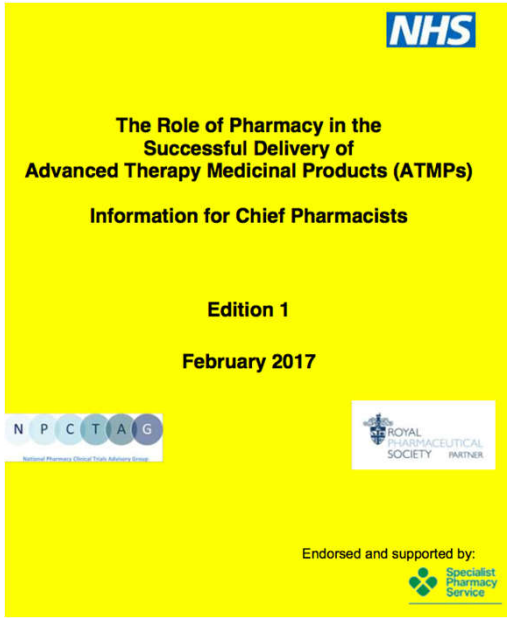
Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

The role of pharmacy in the successful delivery of ATMPs - Information for Chief Pharmacists

- Issued February 2017 (Ed 1)
- NHS Pharmaceutical Quality Assurance Committee (ATMP Working Party) with National Pharmacy Clinical Trials Advisory Group



Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Role of Pharmacy

- ATMPs subject to the same requirements as other medicinal products
- Chief Pharmacist is responsible for governance and management of ATMPs
- Ensures ATMPs are of appropriate quality for intended use
- Collaborative working with Human Tissue Authority (HTA) designated individual within organisations to develop process and appropriate handling of ATMPs.
- Most current usage is in clinical trials, but ATMPs are beginning to become available as licensed and unlicensed medicines.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Governance

- Many organisations have embraced the advice and have ATMP policy detailing approval process.
- Gene Therapy Requirements is less well understood with many queries re how to undertake a first Gene therapy clinical trial.
- Governance of Preparation Aspects

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Gene Therapy Governance Considerations

- Scrutiny by organisational multidisciplinary committee e.g. Medicines Management or New Interventional Procedures committee
- Review by Genetic Modification Safety Committee

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Considerations When Handling Gene Therapy In Clinical Settings

- Regulatory bodies and regulations
- Classification of risk & risk assessment
- Biological containment level
- Routes of exposure
- Minimise staff exposure, risk to patient and contamination of environment
- Integrity of product
- Accepted national practice
- Standard operating procedures (SOPs)

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

HSE Genetically Modified Organisms (Contained Use) Regulations 2014

- Came into force on 1st October 2014
- Describes the law applying to GMOs
- Containment measures & controls
- Role of the competent authority (HSE)
- Risk assessment
- Classification of contained use work
- Accident reporting

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Classification of Risk

- GMOs are classified as one of four classes (1, 2, 3 and 4), based on the risk to human health and the environment.
- Class 1 activities involve the least and class 4 the highest risk.
- Class 1 activities are unlikely to result in harm to humans or the environment (no or negligible risk).
- Work with any agent able to cause human disease is categorised as class 2 (low risk) or higher (class 3 = moderate risk; class 4 = high risk).

Containment

- Classification determines the level of containment required to control the risk.
- Four corresponding levels (1, 2, 3 and 4) of containment.
- Class 1 requires containment level 1.
- Class 2 requires containment level 2.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Genetic Modification Safety Committee (GMSC)

- Requirement for competent advice on risk assessments
- Person with expertise or GMSC for class 1
- GMSC for ≥ class 2

HSE

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

HSE GMO Contained Use 2014 Requirements for GMSC

- To carry out an assessment of the risks to human health and the environment, & to obtain competent advice on that assessment before contained use starts.
- To make a notification to the competent authority before starting a contained use with GMOs, for first use of a premises.
- To adhere to safety principles and apply appropriate containment and control measures.
- To inform HSE when accidents occur.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

HSE GMO Contained Use 2014 Regulations for GMSC's

- These regulations do not apply to any activity in which GMOs are contained in a medicinal product for human use marketed in accordance with the European Medicines Agency (EMA).

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

HSE GMO 2014 Guidance – Genetic Modification Safety Committee (1)

- The person responsible for contained use must obtain advice on a risk assessment from either a person (biological safety officer/advisor) or a GMSC (if class 2 or above).
- For class I use in a clinical environment, it may be more appropriate for a GMSC to advise.
- GMSC – no specific rules to govern its make up.
- One single GMSC within a single institution can cover separate GM premises.

HSE GMO 2014 Guidance – Genetic Modification Safety Committee (2)

- GMSC Members:
  - Representation from management and employees
  - Representatives of all people or groups with access to the GM facilities or who will be exposed.
- Committee can also consider other H&S matters if it has appropriate expertise.
- Advice can be provided by a shared committee or another institution's GMSC, if there is written agreements in place confirming the arrangements to provide this advice.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Genetic Modification Safety Committee - Membership

- Trust Biological Safety Officer
- Local Biological Safety Officers/ staff representatives
- Consultant Microbiologist
- Consultant in Infectious Diseases
- Consultant in Occupational Health
- Senior Pharmacist
- Senior Nurse
- Infection control representative
- Management representative
- Technical expert
- Estates representative
- Lay member

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Establishing a GMO Safety Committee

- Terms of Reference
- Membership, Chair, Deputy Chair
- Notification of premises
- Approval of projects, premises, SOPs, training
- Planned projects
- Risk Assessment documentation
- Risk Assessment review
- Regular meetings, agendas, minutes
- Trust Structure – sub-committee of Clinical Governance or Health & Safety Committees

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Genetic Modification Safety Committee Responsibilities

- Co-ordinate communication with Health & Safety Executive
- Risk assessment of gene therapy studies
  - Assess risk to human health and safety to environment
  - Containment and control measures
  - Classification to organism appropriate
  - Ensure appropriate SOP's written
- Ensure local Biological Safety Officer appointed
- Review of facilities for handling and administration
- Ensure ethics approval and indemnity for clinical trials
- Review of licensed gene therapy medicines to advise D&T committee

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Risk Assessments (1)

- Risk assessments must take into account all aspects of the planned work:
  - Storage
  - Handling
  - Transport
  - Work area decontamination
  - Inactivation of GMOs
  - Disposal and waste management
  - Spillage

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Risk Assessment (2)

- Cross references to any established guidance.
- Assignment of risk level.
- Containment measures based on the level of risk.
- How and where the contained use will be undertaken.
- Identification and severity of any potentially harmful effects.
- The likelihood of any potentially harmful effects occurring and any control measures required.

Occupational & Environmental Safety

- Risks to human health & the environment arising from contained use have to be reduce to the lowest practicable level.
- Measures must include general principals of good microbiological practice and of good occupational safety and hygiene.
- Barriers to limit contact of GMOs to humans and the environment must be consistent with the level of risk.

Waste

- Risk assessment should specify whether inactivation of waste is required at class I, and the methods required to achieve this.
- Validated means of waste inactivation include:
  - Disinfection
  - Incineration
  - Autoclaving
- The method must be proven as efficacious.
- Control measures must be in place for the safe transport and storage of the waste material.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Staff Training

- All staff handling gene therapy must be appropriately trained.
- Employees must be aware of the risk associated with the therapy and have an option not to be involved.
- Staff handling gene therapy should not be pregnant, breastfeeding or immunosuppressed.
- Document & update staff training.
- Involve Occupational Health.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Near patient delivery of gene therapy

- No pharmacy aseptic facilities
- Pharmacy storage and dispensing
- Nursing handling and administration
  - Class 1 handled in clinical areas
  - Class 2 handled in side rooms
- Class 1 & 2 defrosted & drawn up at bedside
- Personal protective clothing
- Dilutions at bedside with pharmacy prepared worksheets – undertaken by nursing staff

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Practical barriers to near patient delivery of gene therapy medicines

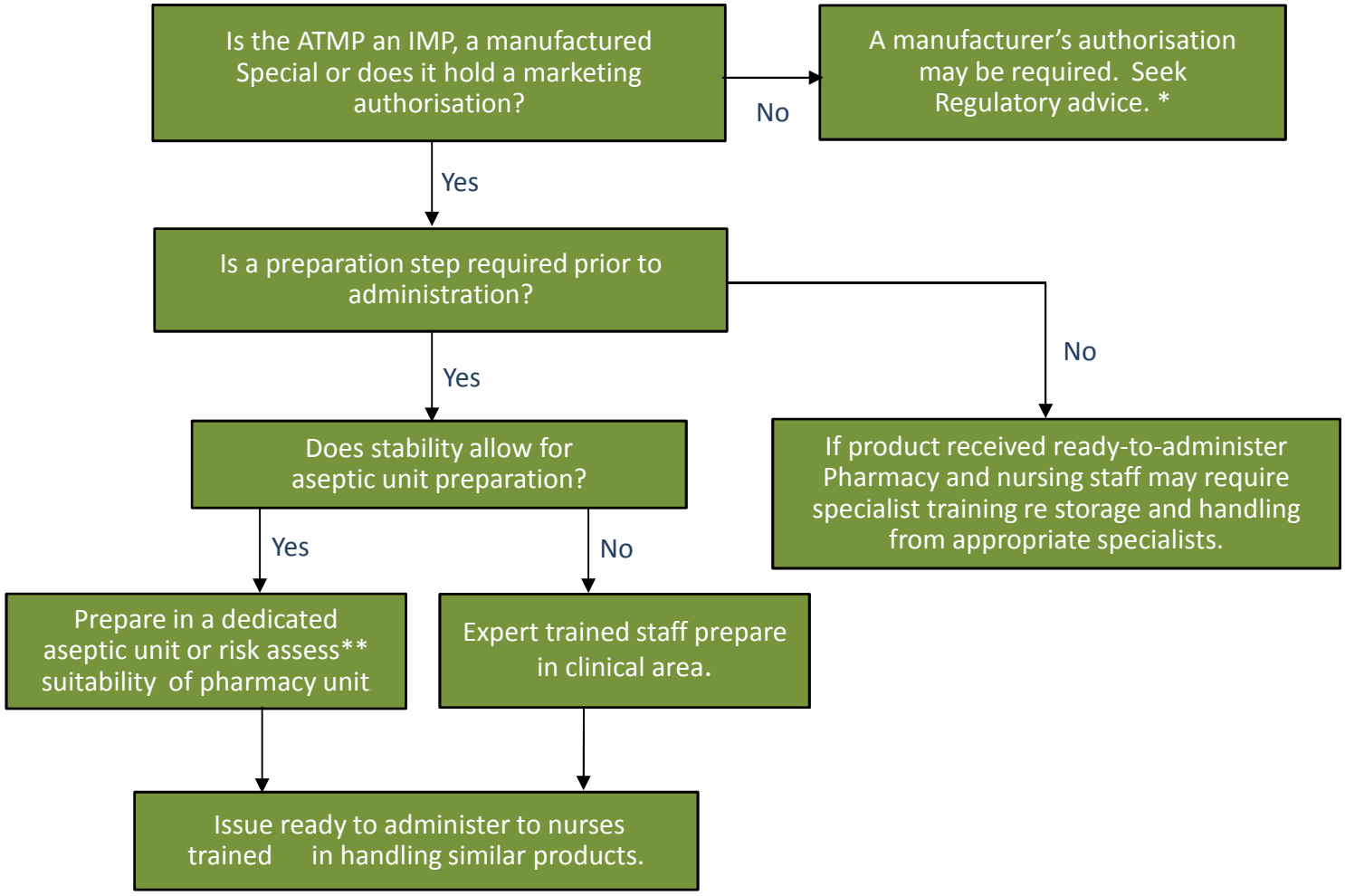
- Risk assessments
- Standard Operating Procedures
- Safe storage – pharmacy or clinical area?
- Temperature monitoring
- Transport
- Training and competency assessment
- Spillage and waste disposal

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Technical Assessment



Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

What is Preparation?

- Preparation is the process of making the product ready-to-administer.
- Often referred to reconstitution activity.
- Reconstitution can occur either in a clinical area or in aseptic facilities

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

What is reconstitution?

- Traditional Pharmaceuticals:
  - Adding a diluent to a freeze dried powder / dilution of a concentrate to produce a rta presentation
- ATMPs:
  - Thawing, washing, buffer exchange, DMSO removal, mixing with patients cells, splitting the product for doses, loading into a delivery device
  - Eudralex Volume IV Part 4 GMPS for ATMPS

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

What are preparation Risks?

- Traditional Pharmaceuticals
  - NPSA 20 risk assessment tool. High risk prepare in aseptic unit. (PN and cytotoxics mandated unless closed system).
- ATMPs
  - Complex manipulation +++
  - Inherent risks of cell death
  - Competence in handling is key.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Is Pharmacy Aseptics competence relevant?

- Nicholas Moyse: Senior Pharmacy Technician Cytotoxics for 10 years (RVI, Newcastle)
- Current Position: Healthcare Sciences Team Manage (Newcastle Cellular Therapies Facility)

"Cells are delicate and require more thoughtful handling than standard pharmaceuticals"

"Pharmacy Aseptics provides a good grounding for this specialism but competency training needed"

"You only have one chance – you can't go to the fridge to get more cells. This is always in the back of your mind"

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Aseptic practices with cells

Technique:

Avoid the use of syringes and needles where possible – use sterile pipettes

- If using syringes, do so with utmost care and pull/push plunger back slowly
- When measuring multiple volumes of cells in the same process, use the same syringe – to prevent cell loss which can adversely affect the finished product

- Moving products in and out of the cabinet during the same process is common
- Critical processes include centrifuging cells, microscope work
- Manufacturing processes take days
- You have 2 lots of regulations to think about – MHRA and HTA (consent is required)
- There is more in-process QC testing

“My pharmacy background in GMP and QMS fits well into the team in cell therapies”

What Facilities are Required

- Preparation should occur in a grade A environment.
- Background should be grade B if LAF or BSC II cabinet
- Background should be grade D if an isolator is used.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Environment for Preparation of ATMP

Product	Grade A Device	Background Required	Aseptic Suite considerations
Cellular Therapy (non GMO) e.g. dendritic cell	BSC class II or HLAF	Grade B	+ve cascade
	+ve pressure isolator	Grade D	
Cellular Therapy Product (GMO class1) e.g. CAR-T cells	BSC class II or VLAF	Grade B	+ve cascade
	-ve pressure isolator	Grade D	
Gene Therapy (GMO Class 2) e.g. xxxxxx	-ve pressure isolator (non recirculating/ externally ducted)		Containment suite with positive air bubble or negative air sink
		Grade D	

A. Black October 2018 Personal Opinion

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

What Facilities do we have in the UK?

- Pharmacy Aseptics
  - National aseptic services review (England)
  - 180 aseptic units
  - Most operating under S10* and are A/B (LAF) or A/D (isolator)
- Stem Cell Laboratories/ HTA processing
  - HTA licences (approx 30)
  - Often A / C (BSC class II)

*Section 10 of the Medicines Act enables a Pharmacist to supervise preparation of products against a prescription without needing a Licence from the MHRA;

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Medicines Act Considerations

- Section 10 exemption allows preparation under the supervision of a pharmacist without a manufacturing licence

- Supervision for ATMPs requires clarification.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Is there capacity?

Pharmacy Aseptic Services Review:

"Aseptic preparation is a labour intensive process and many Aseptic Facilities face significant problems with workforce recruitment, training, and retention. Lack of staff capacity is preventing c.60% Aseptic Facilities from offering desired services and a standard method to calculate capacity is needed to plan for national and local workforce requirements"

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Can Pharmacy Facilities be used for ATMP preparation?

Risks to Facility

- Microbiological contamination including viral.
- Mitigation: cleaning validation, campaign preparation and segregation

Risks to Product Quality

- Skilled workforce requires cellular knowledge and training

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Optimal Arrangements?

- For Patient Benefit consider…
  - A/B or A/D Facility
  - Stem Cell Workforce to handle ATMP
  - Pharmacist supervision or MS
  - Pharmacovigilance
  - QA expertise

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

The Pan – Pharmacy ATTC Group will support this collaboration and develop this thinking with the ATMP Working Party.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Is this really an issue?

Marketed ATMP	Preparation Required
Holoclar	None: Ready to Administer
Imlygic	THAW and draw up into a syringe
Strimvelis	None: Ready to Administer
Zalmoxis	None: Ready to Administer
Spherox	None: Ready to Administer
Alofisel	None: Ready to Administer
Kymriah	THAW
Yescarta	THAW

Clinical Trials Consideration: Needs Regulatory rigour at assessment to ensure expectation is clear via a Pharmacy Manual or equivalent.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Status Quo?

- Pharmacy workforce needs to
  - understand ATMPs sufficiently to allow receipt of ambient and fridge RTA product
  - competent to thaw items received in dry shippers.
- Cellular Therapies workforce
  - needs to receive and store any items requiring cryo storage, and to thaw such items
  - prepare or undertake complex reconstitution activities with Pharmacy oversight / supervision in the optimal local facility.
- Further work required to establish impact of outsourced ATMP activity for MA products and IMPs.

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Implications for Clinical Pharmacy

- Licensed product introduction
- Staff training
- Multidisciplinary working
- Standard Operating procedures
- Pharmacy clinical checks
- Medicines reconciliation and interactions
- Incident reporting

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Talimogene Laherparepvec

- Genetically modified Herpes Simplex oncolytic replication competent virus encoding GMCSF
- Licensed and NICE approved for melanoma
- Amgen training required prior to Trust use
- Class 1 gene therapy medicine
- Institutional SOPs on handling gene therapy
- Trust governance and approvals

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Pre-implementation Planning

- Multidisciplinary meeting – nurse, medical, pharmacy (purchasing, dispensary, cancer pharmacy, technicians & pharmacists)
- Pre-implementation action plan
- Medicine implementation in line with Medicines Policy
  - D&T application
  - Paperwork for pharmacy electronic systems

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Standard Operating Procedures

- Talimogene Laherparepvec (Imlygic®) Pharmacy Standard Operating Procedure
- Implementation and Management of Advanced Therapy Medicinal Products (ATMP) Standard Operating Procedure
- Handling Advanced Therapy Medicinal Products (ATMP) Gene Therapy Medicines Standard Operating Procedure

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Talimogene Laherparepvec SOP

- Personnel & Personal protective clothing
- Ordering & stock receipt
- Storage
- Clinically screening prescriptions
- Dispensing
- Accidental exposure & waste disposal
- Training

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Implementation and Management of ATMPs SOP

- Introduction of ATMP
- Risk Assessment
- Committee Assessment and Approval
- Occupational Health
- Training

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Handling ATMP Gene Therapy Medicines SOP

- Handling procedure
- Administration – class 1 and class 2
- Waste disposal
- Spillage decontamination
- Accidental Exposure
- Incident reporting
- Training

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Disclaimer Form

- Gene Therapy Medicines disclaimer form
- All current and new staff working in pharmacy
- “I have been told not be involved in the prescribing, screening, dispensing, receipt, release, checking or administration of gene therapy medicines unless I have been specifically trained and been given a Certificate of Competence by this Trust.”

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Talimogene Laherparepvec Governance Approvals

- Genetic Modification Safety Committee
- Medicine Management and Therapeutics Committee
- Technologies Advisory Group
- Pharmacy Clinical Governance
- Oncology Clinical Governance

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Implementation

- Approvals from all committees
- Freezer and temperature monitoring in place
- Patient identified with planned start date
- Stock ordered and delivered
- Successful dispensing and administration
- Review of SOPs
- Ongoing staff training

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Training

- Amgen
- Gene therapy background information
- Risk Assessments
- Handling and considerations
- Regulations
- Risk classification and containment
- Occupational and environmental safety

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Training

- Waste
- Spillage
- Storage
- Transport
- Incidents
- Training requirement
- SOPs

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Implementation Reflections

- Clinical trial experience & SOPs
- Pharmacist biological safety officer
- MDT working
- Organisational requirements - first in class
- EMA pre-order training requirements
- Amgen Imlygic® training, website and information for all professional groups

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Car-T Cell Therapy

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Car-T Cell Therapy

- Patient-specific (autologous) cell therapies
- Patient's own T lymphocytes - genetically modified to express a chimeric antigen receptor to confer antigen specificity
- Genetic modification by manufacturer
  - Using viral vector derived from a retrovirus or a lentivirus, which carries the new gene for the chimeric receptor (ex vivo gene therapy)

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Car-T Cell Therapy

CHIMERIC ANTIGEN RECEPTOR T CELLS

A briefing document for Chief Pharmacists

Issued by: The ATMP Working Party – a subgroup of the Pharmaceutical QA Committee

December 2017

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

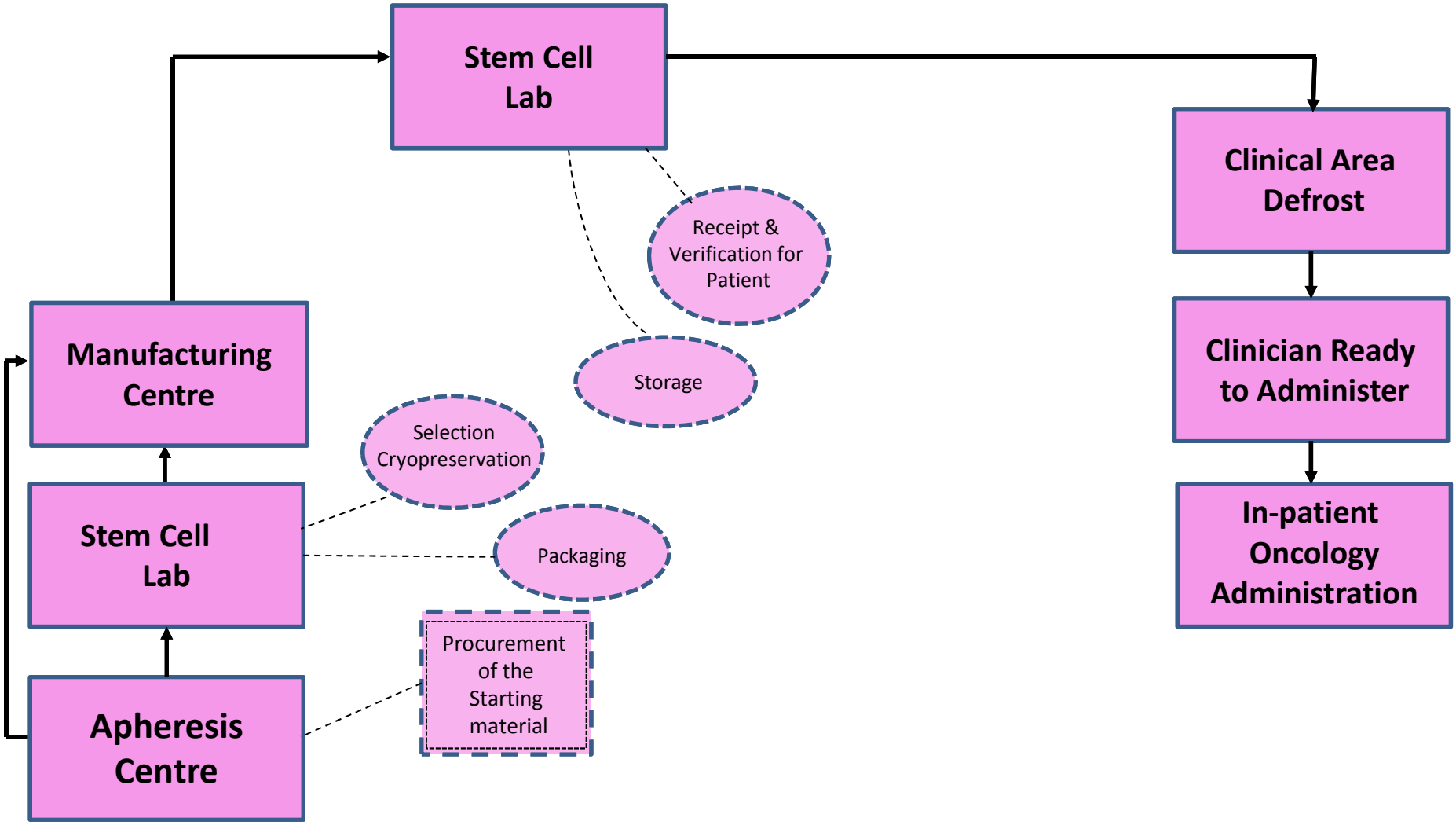
Pharmacy Institutional Readiness for Marketed CAR-T Therapy: Guidance for Chief Pharmacists

CAR-T Therapies are newly authorised products within Europe and currently undergoing review via the NICE Technology Appraisals process. They are classed as Advanced Therapy Medicinal Products (ATMPs) and as such, require governance and management by Chief Pharmacists. They present risks which Chief Pharmacists should ensure are minimised. The greatest risks are around tracking and traceability as CAR-T is an individualised therapy with disastrous consequences if not administered to the patient it was intended for. Whilst collaboration with expert cellular product handling colleagues will be key operationally, it may present challenges for Pharmacy to embed this new working relationship. Additionally, CAR-T therapies are associated with toxicities which must be well understood and managed in a timely fashion.

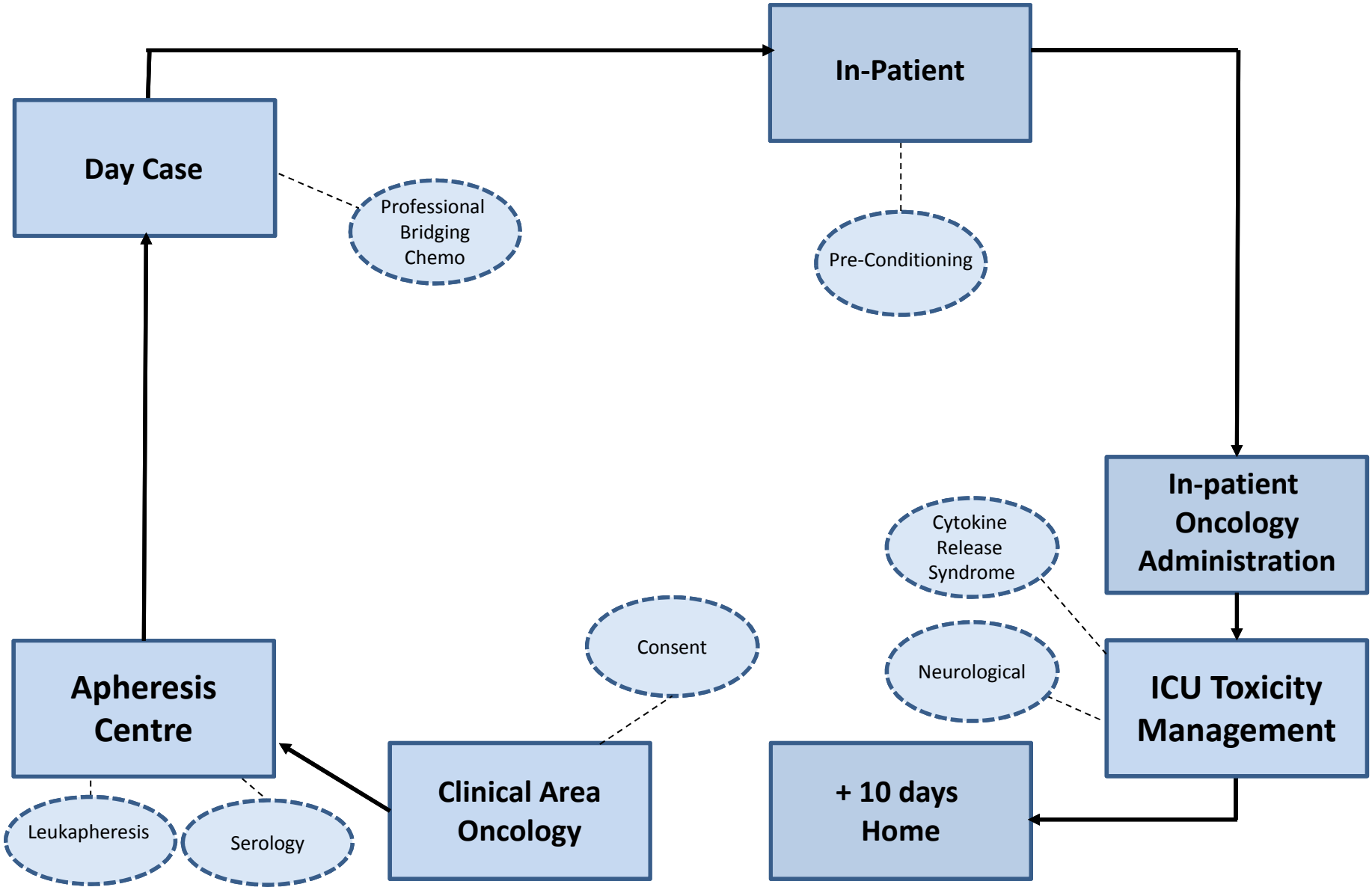
It is advised that the following areas require Pharmacy input prior to an organisation implementing CAR-T Therapy. It is recognised that Pharmacy does not currently have the expertise to handle the products and that, routinely, Pharmacy may not come directly into product contact. However, where Pharmacy is not directly performing the procedures agreed, then roles should be clearly documented in an overarching technical agreement with reference made to approved SOPs.

September 2018

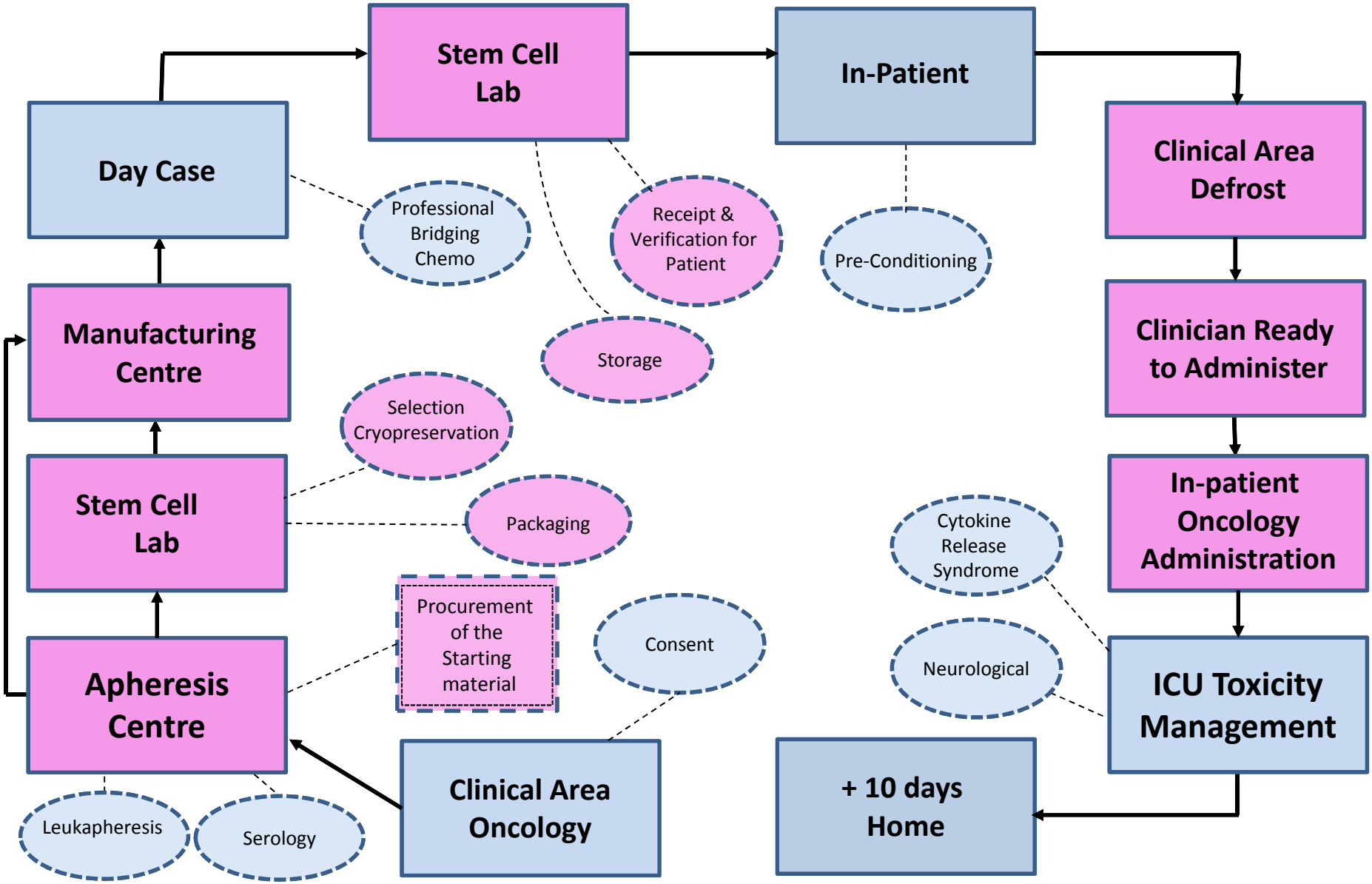
CAR-T PRODUCT JOURNEY

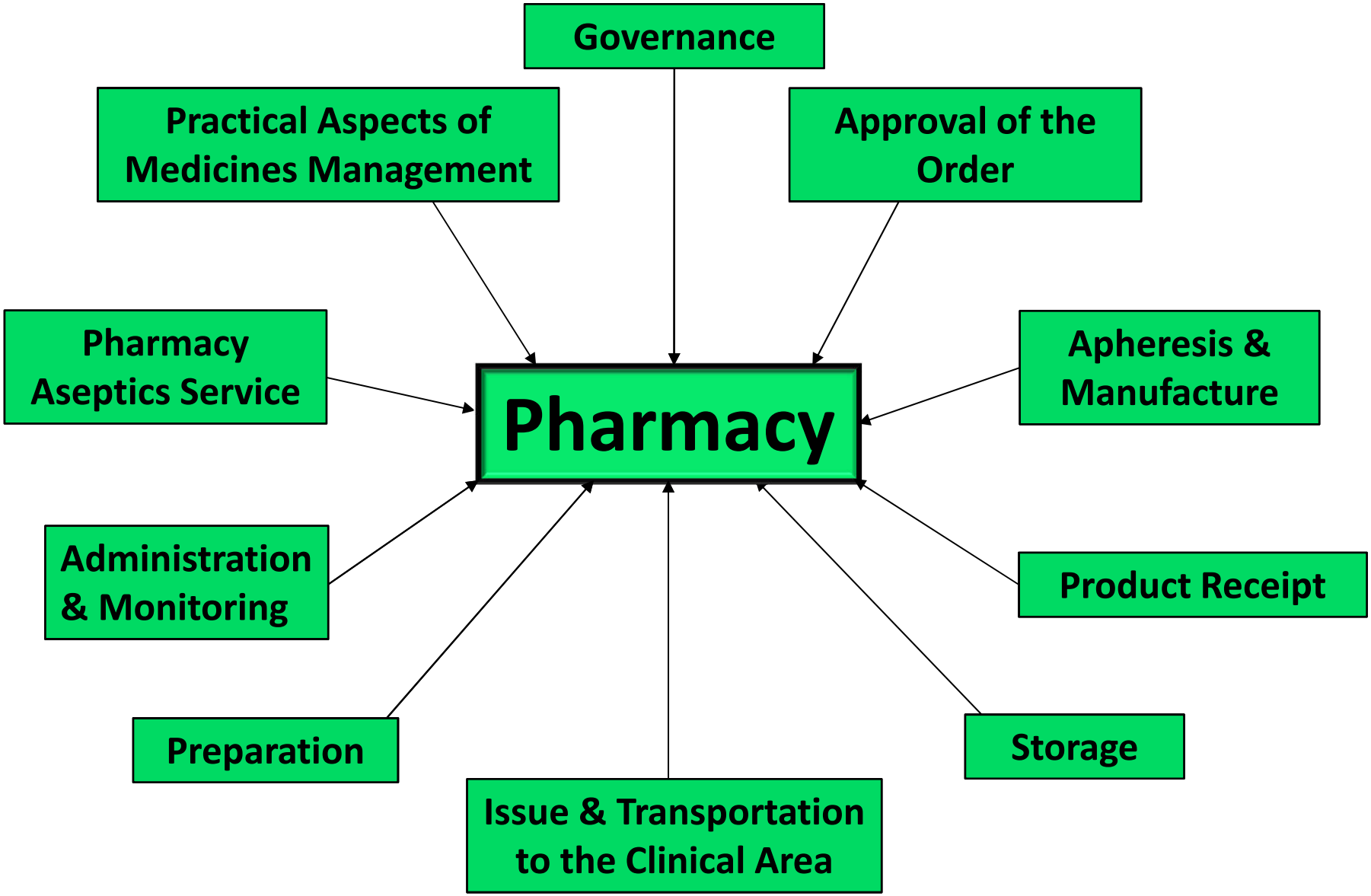


CAR-T PATIENT JOURNEY

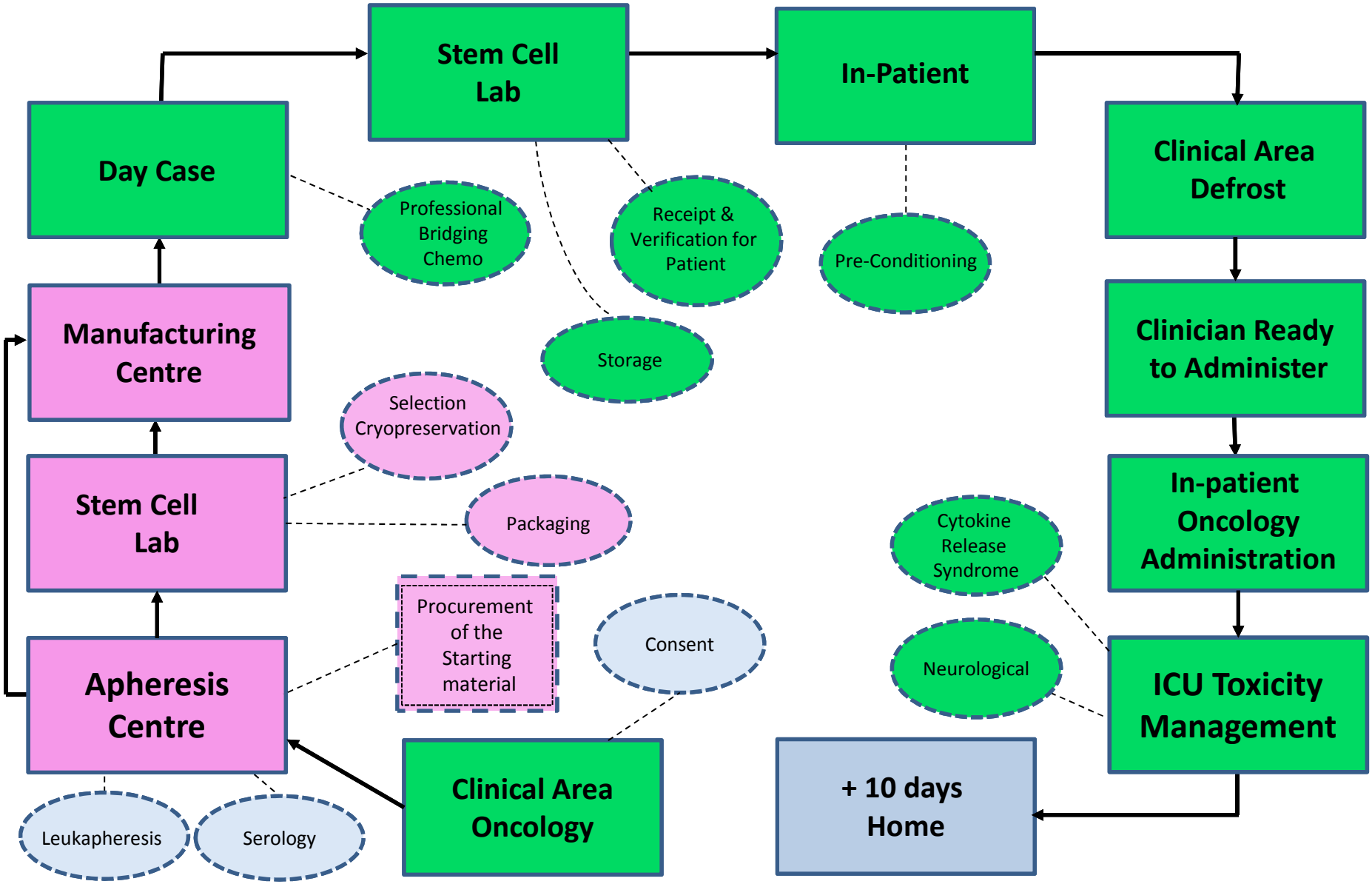


CAR-T COMBINED JOURNEY




Governance
Practical Aspects of Medicines Management
Approval of the Order
Pharmacy Aseptics Service
Pharmacy
Apheresis & Manufacture
Administration & Monitoring
Product Receipt
Preparation
Storage
Issue & Transportation to the Clinical Area

PHARMACY INVOLVEMENT IN MARKETED CAR-T THERAPY



Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Summary

- Delivering ATMPs in Hospitals
- Background and governance
- Gene therapy/Genetically Modified Organisms
- Risk Assessment
- Preparation/reconstitution activities
- Practical barriers to near-patient delivery
- Implications for clinical pharmacy
- Car-T Cell therapy

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

NHS
Oxford University Hospitals
NHS Foundation Trust

Questions?

Specialist Pharmacy Service
www.sps.nhs.uk

Northern Alliance
Advanced Therapies Treatment Centre

Oxford University Hospitals
NHS Foundation Trust

Delivering Advanced Therapy Medicinal Products (ATMPs) in Hospitals

Anne Black
Regional QA Specialist Pharmacist – North East and North Cumbria
Prof Nicola Stoner
Consultant Pharmacist, Oxford

11.10.2018