Advanced Therapy Treatment Centres

LONDON ADVANCED THERAPIES

SCOTTISH NATIONAL BLOOD TRANSFUSION SERVICE

Standardisation of Procurement of Starting Materials by Apheresis for Advanced Therapies

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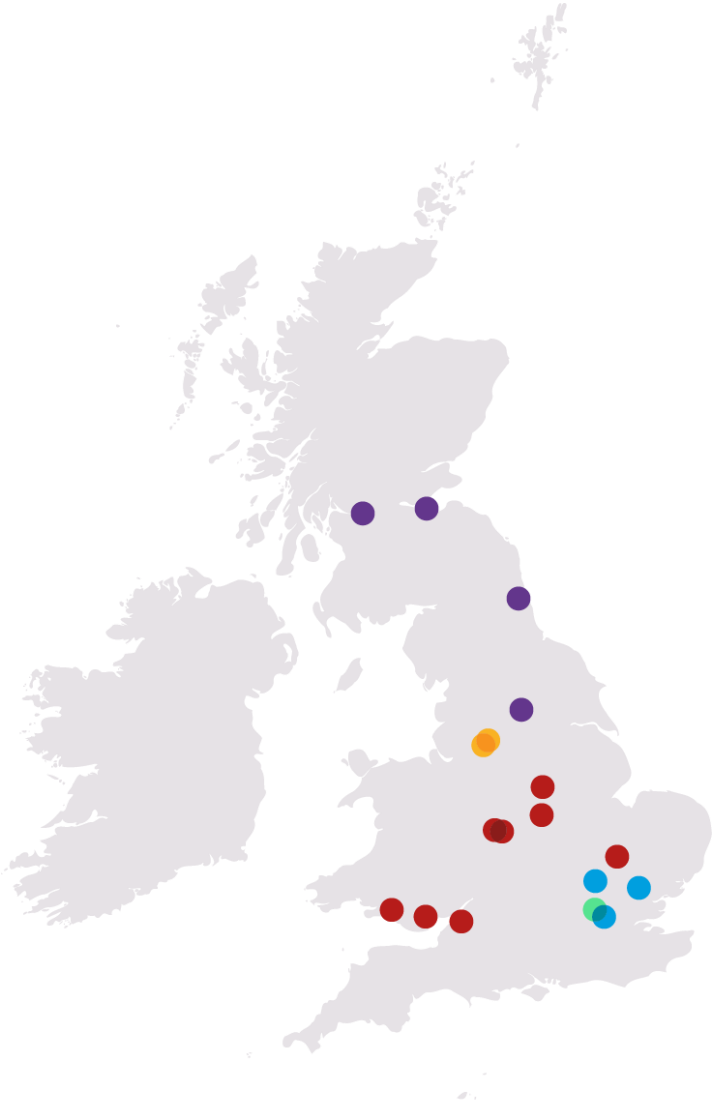

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Coordinated by

CATAPULT Cell and Gene Therapy

- **Disclosure of Interests :** none to declare

- NHS National Services Scotland is the parent organisation of the Scottish National Blood Transfusion Service

- Both are not-for-profit organisations facilitating the delivery of healthcare within the national health service in Scotland and beyond

- Personal perspective: cell collection, regulatory and accreditation environments

Objectives

- **Explore**
  - Why do we want to standardise?
  - What do we want to standardise?
  - What is currently standardised?
  - Is there tension and if so, why?
  - Moving forwards - next steps

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Why do we want to standardise?

- **Industry benefits -**
  - consistent quality
  - equivalent to other comparable products
  - underpins safety, interoperability and compatibility of goods produced
  - emphasis on repetition and sameness

- Disadvantages : boredom, loss of interest
  downturn on performance
  lack of innovative thinking

Why do we want to standardise?

- **Healthcare benefits**

- decreases variation
- reduces costs
- minimises risk of errors

- increases quality
- increases patient safety
- improves the patient experience

Why do we want to standardise?

- **Healthcare benefits**

- decreases variation
but is all variation bad?

Warranted v Unwarranted Variation

Warranted

- Reflects differences in patient-centred care
- Acceptable, good, desirable
- May reflect innovation
- Wide variation initially, reducing through health system adoption
- Fast rollout and spread of effective innovations and knowledge → reduces time to reach standardisation

Unwarranted

- Unacceptable
- Harmful to patients, families and carers, health system
- Difficult to define causes
- Complex delivery model, can't control all moving parts

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Why do we want to standardise?

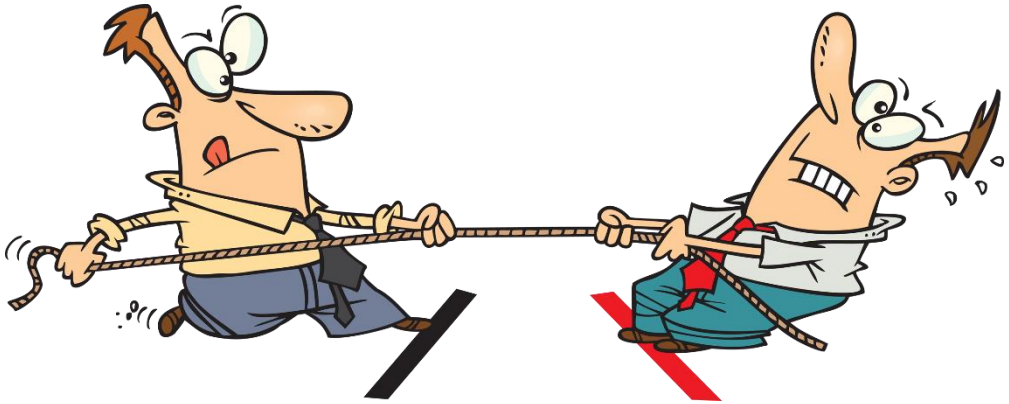
ATMP Manufacture (1)

- committed to safe, high quality products
- circular supply chain, not linear
- ideally, control each part of supply chain process
- quantitative and qualitative variation in starting material because of biological, patient-related factors – disease, treatment, current health
- so, control what we can control –

Why do we want to standardise?

ATMP Manufacture (2)

- control and standardisation of the collection process
- collaborative working between collectors and manufacturers



-variation in working practices amongst collection facilities

v

- variation in manufacturers' requirements

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Great Ormond Street Hospital for Children Jan 2016 – Dec 2019

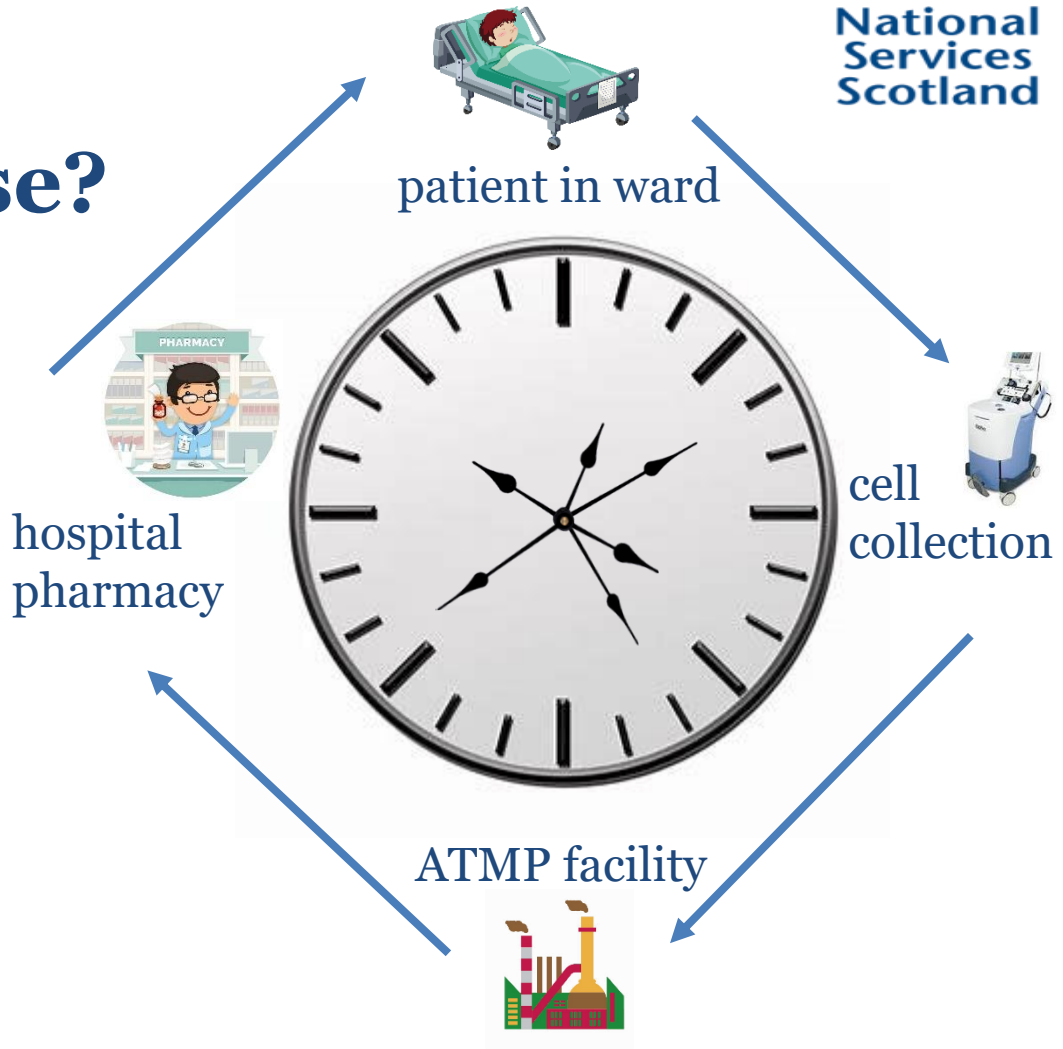
(O'Brien N, New H et al, BSH2020-392)

Patients	Collection Episodes	Collections
90	96	127
PBSC 30	33	56
Lymphs 60	63	71

Collection Episodes	Trials	Type
MNC		
31	8	Gene therapy for immunodeficiency
2	1	Gene therapy for thalassaemia
Lymphocytes		
45	3	CAR-T therapy (leukaemia, neuroblastoma)
16	™	Licensed product
2	2	Immunomodulatory therapies post PBSCT

What do we want to standardise?

- circular supply chain, not linear
- multiple stop-off points
- apheresis collection – one component part of that circle



What do we want to standardise? (All of it….?)

Accept and refer

Inform

Assess

Communicate

Collect

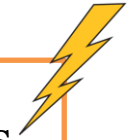
Label

Identify

Distribute

Communicate

Adverse events



Follow up

What is currently standardised?

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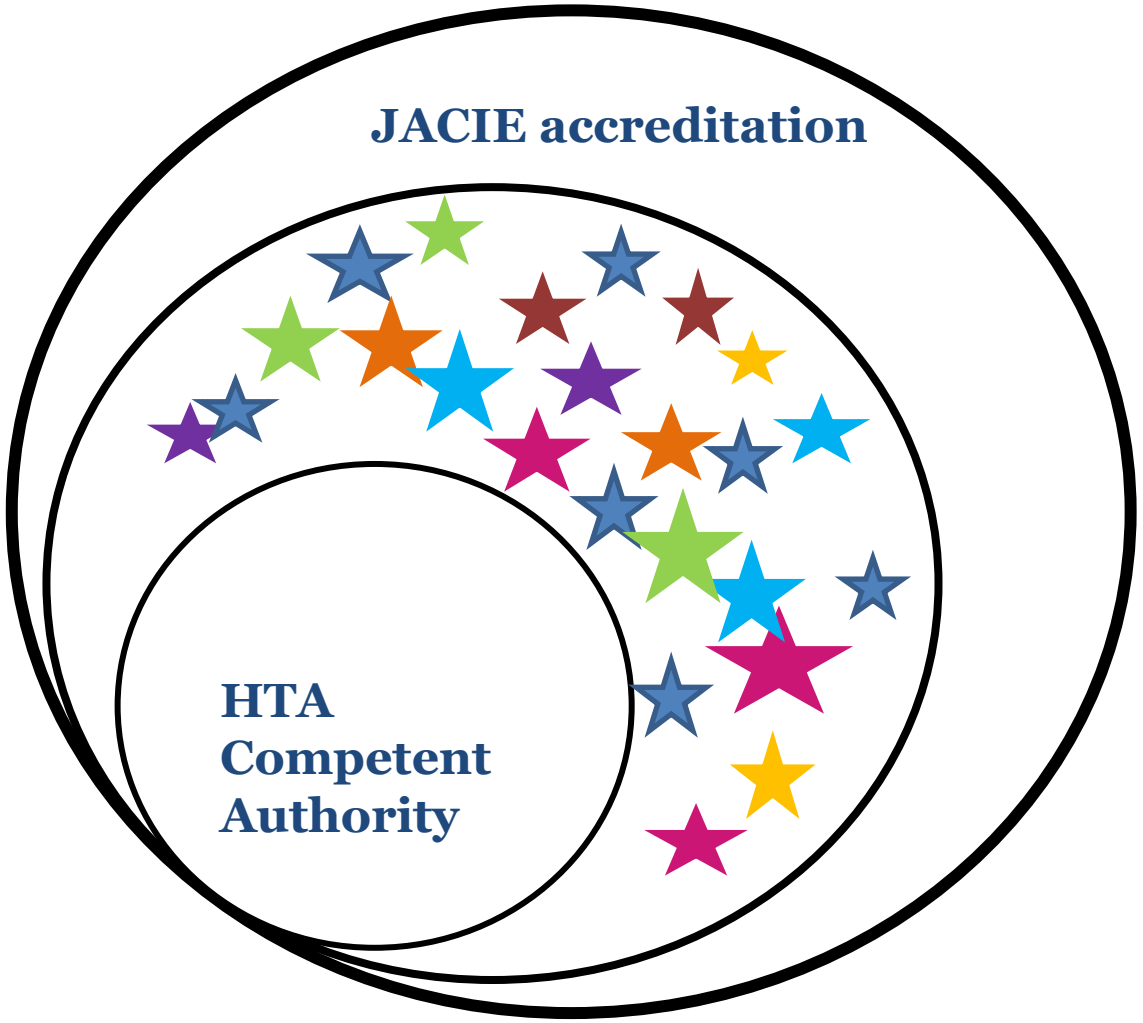
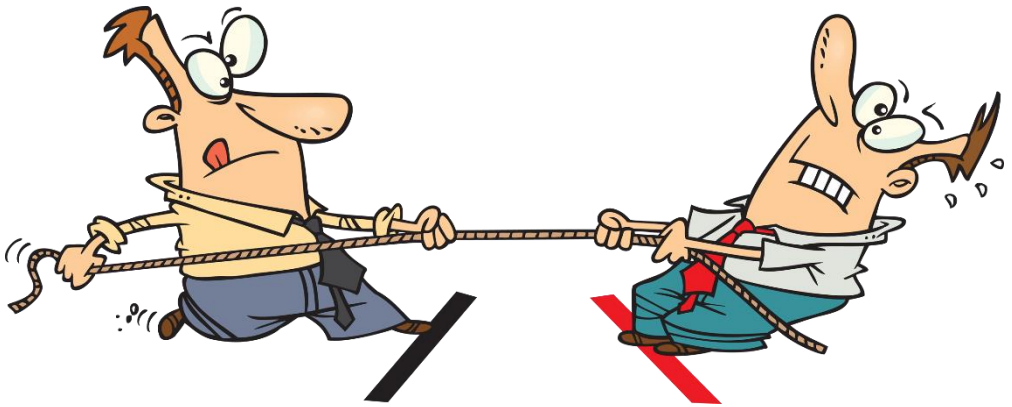
	Industry perspective	Collection perspective
Accept and refer 	✓	✗
Inform 	✓	✓
Assess 	✓	✓
Communicate 	✓	✗
Collect 	✓	✗
Label 	✓	(✗) ✓
Identify 	✓	(✗) ✓
Distribute 	✓	✗
Communicate 	✓	✗
Adverse events 	✓	✓
Follow up 	✓	✓
Process control	✗	✓

Is there tension, and if so, why?



the ‘scrutiny space’



Is there tension, and if so, why?

Examples

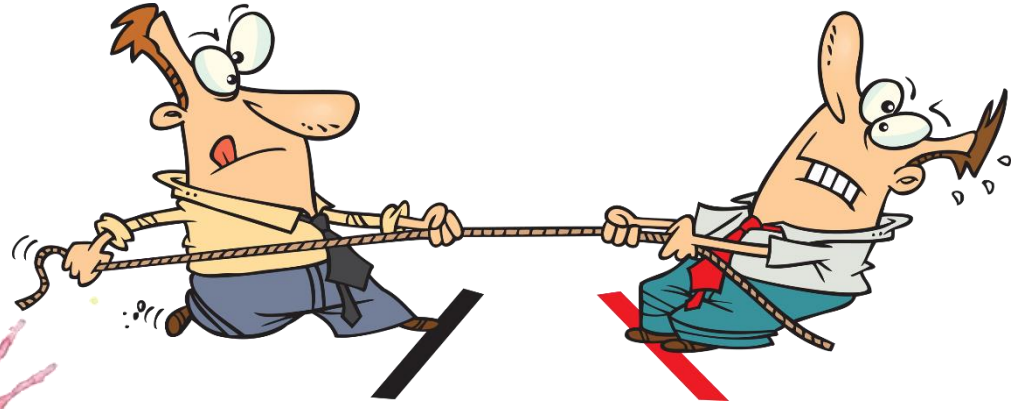
Site Qualification

HTA: consent, premises, collection process

JACIE: > 550 Stds

Industry partners:

On boarding site visits
JACIE Standards Site assessors
non JACIE Standards



Collection of Starting Material

HTA: focussed, fairly silent

JACIE: processes as per best practice; controlled, validated, verified.

Industry partners:

Target yield
TBV processed Peripheral counts
Apheresis manual

What is currently standardised (1)?

- Collection licensure
  - all collections carried out under HTA licensure
  - regulates to requirements of EUTCD (UK Competent Authority)
  - EUTCD refers frequently to 'stem cells' …but MNC, A for onward manufacture within scope

  * does ***not*** scrutinise to GMP
  * hybrid inspection model – trained auditors plus subject matter experts

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What is currently standardised (2)?

- Collection process control
  - entry level for ATMP collections – FACT-JACIE accreditation, 6th Ed Stds, v6.1 (IEC stds)
  - accreditation body, voluntary scheme;
  - MNC, A for onward manufacture within scope
  - clinical trial activity within scope

  * does ***not*** scrutinise to GMP
  * inspection model: volunteer inspectors, subject matter experts
  * variation in level of scrutiny applied by inspectors in determining applicant centre's compliance against Standards, and so level of process control and embedding of quality management system working into BAU activity. *Is this unwarranted variation?*

What is currently standardised (3)?

- Operational collection process - getting the cells into the bag

www.theattcnetwork.co.uk

What is currently standardised (3)?

- Operational collection process – getting the cells into the bag

Standard **A**pproach to AT**MP** tissue col**LE**ction:
SAMPLE initiative

WP1: (Collaborative) standardisation of apheresis collection

Objectives

- Reduce unnecessary complexity and variation in apheresis collection
- Improve efficiency in apheresis collection to increase capacity within the service and thereby AT delivery
- https://www.theattcnetwork.co.uk/wp-content/uploads/2021/04/PROCUREMENT-OF-STARTING-MATERIALS-BY-APHERESIS-20210425-v14.pdf

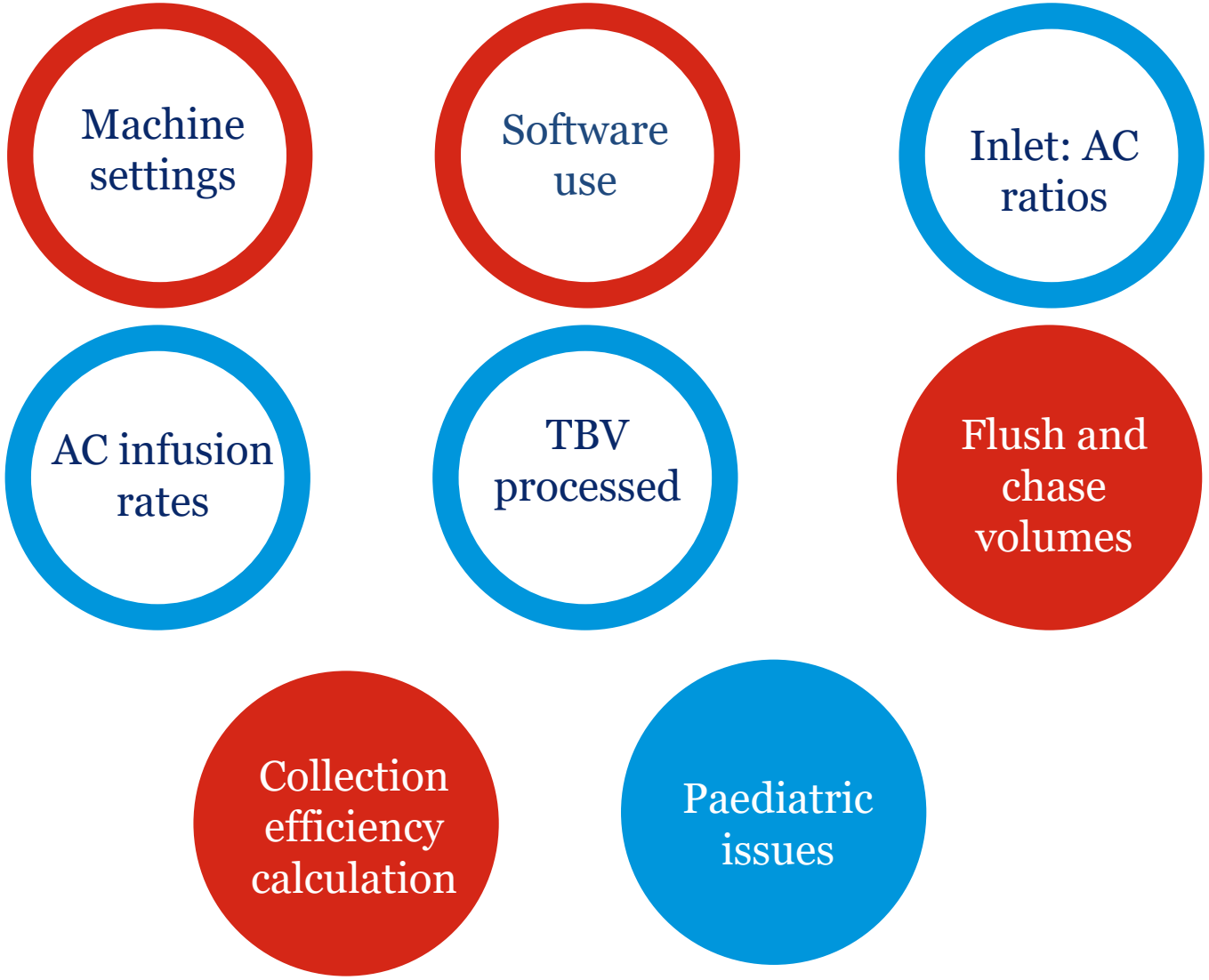
What is currently standardised (3)?

- Operational collection process - getting the cells into the bag

  - Uniformity of collection platform device……

  - ……but not uniformity of collection practice…..

What is currently standardised (3)?



Is there tension, and if so, why?

Mutual Understanding

Industry Colleagues

- There is process control within the collection facility
- The level of control is not to GMP standards
- What is the downstream impact on the GMP process of starting material collected within a controlled but non-GMP environment?
- Can this be accurately risk assessed, and to the Regulator's liking?
- Would GMP within the collection environment add value? Is it achievable, or desirable?

Collection Colleagues

- There is process control within the collection facility.
- There is process control within the manufacturing facility, and in some areas the Quality bar is higher.
- The extent of process control within each environment is different.
- Patients are managed safely within the collection facility.
- Manufacturers are every bit as wedded to patient safety as collection staff are.
- There is variation in the level of scrutiny applied by JACIE inspectors.
- JACIE inspectors do not assess to GMP.
- Industry needs assurance that JACIE accreditation is valid.

Moving forwards - next steps

- Ongoing collaborative initiatives moving towards a common goal
  - CGT CATAPULT IAG/ ATTC Network : unfinished business – standardisation of site qualification requirements, ISBT 128 Std-018 implementation, streamlining of logistics, end-to-end process IT solutions

  - EBMT GoCART initiative: reduce inspection burden through consensus-driven requirements and qualification standards

  - Standards Coordinating Body for Regenerative Medicine : developing cell collection standards for cell and gene therapies
    BSR/PDA Standard 08-202X Apheresis Collection for Cell and Gene Therapy Products, likely availability 2022-2025.

Summary

- Collection of starting material by apheresis for advanced therapies manufacture is a multi-stakeholder activity
- Mutual understanding and patience are key to effecting change.
- Continue to engage – across and within professional boundaries
- Collaboration engenders ownership, overcomes imposition
- Learn from what has been achieved so far – mistakes, best practice
- Challenge is essential – both of self and others

SAMPLE Working Group Members

- Bill Shingleton – Cytiva
- Chris Fong - Autolus
- Claire Brady – CGT Catapult
- Davina Potok – NHSBT
- Di Sweeny – Christies
- Dominic Reeks – GSK
- Doreen Condon – BlueBirdBio
- Douglas Watson - Novartis
- Drew Hope – Autolus
- Elia Piccinini – Kite Pharma
- Haili Cui – Kings College London
- Helen Delahaye – Autolus
- Helen Keane – UCL
- Jacqueline Barry – CGT Catapult
- Jennifer Armstrong – Terumo
- Jo Tomlins – Christies
- Joy Sinclair - BlueBirdBio
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