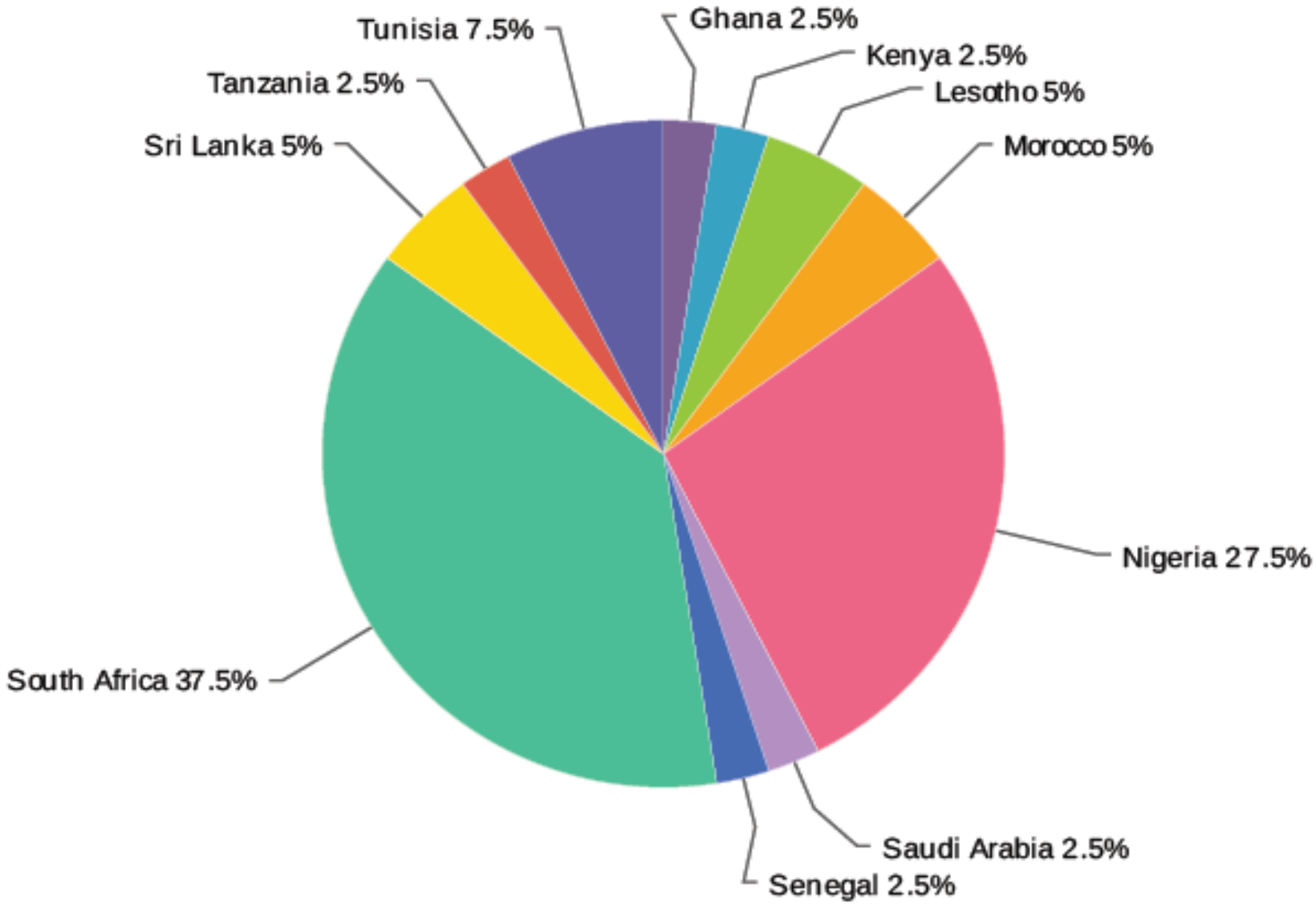
14.50-15.50	**Cell processing** **Chairs**: Mickey Koh (Singapore/UK) and Jackie Thomson (S Africa)
14.50-15:05	**Survey results of graft processing across – what is available** Mickey Koh (Singapore/UK) and Jackie Thomson (S Africa)
15.05-15:20	**Minimal requirements for a cell processing lab** Mickey Koh (Singapore/UK)
15.20-15:35	**Stem cell processing: method and graft characterization** Carolyn Taylor (USA)
15.35-15.50	**Roundtable discussion: How to successfully establish a cell processing facility** **Moderator:** Mickey Koh (Singapore/UK) **Panellists:** Adriana Seber (Brazil) Alok Srivastava (India) Carolyn Taylor (USA) Jackie Thomson ( ) LamiaTorjemane (Tunisia) Nina Worel (Austria)

Main functions:

-Overseeing the safe receipt/handling of donor stem cells
-Defining the product: its quality and characteristics----Carolyn Taylor
-any manipulation required for the transplant---- Carolyn Taylor

-Safe delivery back to the hospital/patient including infectious diseases

-quality assurance


Ghana 2.5%
Kenya 2.5%
Lesotho 5%
Morocco 5%
Nigeria 27.5%
Saudi Arabia 2.5%
Senegal 2.5%
South Africa 37.5%
Sri Lanka 5%
Tanzania 2.5%
Tunisia 7.5%

Survey

- 1/3 stem cell physicians; 1/3 physicians who refer, 1/3 transfusion /lab personnel

- **What is single biggest barrier to a transplant programme:**
- >40% financial
- 0% indicated blood safety or cell processing

- **2 biggest obstacles:**
- Donor availability and costs
- 15% govt or bureaucracy and 10% processing

- 40% have a functioning cell processing facility. 50% have access to freezing and storage facilities and 50% have a flow cytometry and able to count CD34
- 75% have reliable electricity
- 25% have no cell processing facility or trained staff

Transplant regulations:

20% none
7% national regulations in place
15% under blood transfusion or under cell processing/tissue.
Encouragingly: 33% under development
66% have a tissue, cell based regulatory framework

(Crucial for traceability and biovigilance)

- Transport and Cold Chain for Stem Cell Products

WBMT Graft Processing Workshop

Dr Mickey Koh
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Health Sciences Authority, Singapore

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Mickey_koh@hsa.gov.sg

Graft Processing

- Integral part of the transplant programme
- Specialised manpower and equipment: **?cost factored into transplant calculation**
- Minimal to advanced extensive processing
- Stem cell sources: BM vs PBSC vs Cord
- **Essential parameter in determining engraftment; graft versus host disease; immune reconstitution; relapse**

Minimal Requirements and Essential Features for Setting up a Stem Cell Processing Laboratory.

- **Thomas Leemhuis, Douglas Padley, Carolyn Keever-Taylor, Dietger Niederwieser, Takanori Teshima, Francesco Lanza, Christian Chabannon, Paul Szabolcs, Ali Bazarbachi, Mickey BC Koh (chair)**

- On behalf of the Graft Processing Subcommittee of the Worldwide Network for Blood and Bone Marrow Transplantation (WBMT).

Scope of Talk

- Physical premises and considerations
- Equipment/reagents and personnel needed
- Range of Processing Services offered
- Guidance documents and resources

Key Considerations

- Minimally Manipulated Products in support of a transplant programme: not Haplo-identical or advanced cell processing.
- improvements will be made as additional resources become available and as volume and scope of clinical transplant services increase

➢ Availability of a clean, temperature controlled and securable environment, with reliable electricity.

➢ Ability to purchase supplies suitable for clinical use.

➢ Staff have at least a basic understanding of medical laboratory practices.

➢ **Financial and Regulatory**

Physical Considerations

- **Does every transplant programme require a processing lab?**
- **Does centralising reduce costs and make best use of manpower?**
- **Number of centres; transplant numbers; distances from lab to centres**
- Hospital based vs involvement of the Transfusion Service
- Examples of processing labs in the UK and Singapore

Strengths of Transfusion Laboratories and Blood Banks

- Harvesting and handling of apheresis and cellular products
- Quality systems with a focus on “processes”
- Product safety focus including stringent donor testing
- Mulitidisciplinary: technologists, similar staff training; microbiologists
- Back-up power supplies

Scope of Talk

- Physical Layout and considerations
- **Equipment/reagents and personnel needed**
- Range of Processing Services offered
- Guidance documents and resources

Required Equipment:

Dedicated:

Biosafety Cabinet	Refrigerator	Balance (Scale)
Water bath	Centrifuge	Freezer (≤ -70^{o}C)
Hematology Analyzer	Tubing sealer	Personal computer
Plasma Extractor	SCD	
Pipette Aid	Hemostats	Tubing stripper
Cryo-transporter	Micropipettes	Label printer

Shared:

Hematology Analyzer	Flow Cytometer	Micro Lab
Microscope	LN_2 Freezer	Reference Thermometer

Equipment/Reagents

- Reliable Maintenance and Availability
- Qualification/validation and monitoring of equipment/reagents
- Back up/ Contingency:

Important Considerations

- Qualified staff and Training programmes
- How many lab staff are needed: minimum of 2
- to limit each workstation and each staff member to the processing of one product at a time
- Quality systems
- **Quarantine**

QC Testing

Attribute	Test Method	Specification
Donor Screening	Summary of Records; Donor Eligibility Form	Donor Eligible
Inf Disease Testing	Certified Laboratory	Negative (except CMV)
Infusion Volume	Measurement	≤20mL / Kg / Infusion
DMSO Volume	Calculation	≤ 1mL / Kg / Day
TNC Count	Cell Counter	As Measured
CD34+ Cell Count	Flow Cytometry	≥ 2 x 10^6 / kg
CD3+ Cell Count	Flow Cytometry	As measured
RBC Content	Cell Counter	≤25mL / Adult Infusion
Viability	Flow Cytometry	≥ 80% (pre-freeze)
Sterility	Bacterial Culture; Fungal Culture	No Growth

Clinical Focus

- Representation at Clinical Transplant Meetings
- Correlation with engraftment data and clinical outcomes (CD34; TNC; viability; microbiology)
- assurance that the clinical outcomes match the reliability of processing
- Apheresis /processing/ staff /equipment all contribute
- /Threshold of $2x10^6$ CD34/kg and a desirable $5x10^6$ CD34/kg

Auto vs Allo

- Autologous: freezing capacity and secure storage for the stem cell graft. Largely PBSC based with higher mobilisation failure
- Allogeneic: red blood cell (RBC) and plasma depletion services and be prepared to thaw and infuse cord blood products. DLIs

- Is Autologous processing more challenging? **Non cryopreserved an alternative?**
- Allo products if given fresh actually needs less doing than auto except for plasma/red cell depletion in ABO mismatched transplants. If PBSC-only plasma depletion and this often not mandatory

Key Partner Organizations:

AABB	www.aabb.org
ISCT	www.celltherapysociety.org
FACT/JACIE	www.factwebsite.org
ISBT	www.isbtweb.org
ICCBBA:	www.iccbba.org
WBMT:	www.wbmt.org
CTCLAG	
AHCTA	

World Health Organization

AIDE-MEMOIRE

for National Health Authorities*

Tissue and cell transplantation represent essential and rapidly developing therapies in modern healthcare. It is the responsibility of national health authorities to ensure that the needs of patients are met with a supply of safe tissues and cells of appropriate and consistent quality. A nationally supported legislative framework which defines consent requirements and supports donation and a regulatory system which authorises tissue and cell banks are prerequisites to achieving this goal. Donation and transplantation activities should be organised in a transparent way with the provision of adequate information and data to enable the public to make informed choices.

Tissue and cell transplantation carry risks of disease transmission. Viruses (including HIV, hepatitis B and C), bacteria, fungi, parasites

Access to Safe and Effective Cells and Tissues for Transplantation

☑ Checklist

National Oversight

- ❑ Legislative/Regulatory framework
- ❑ Appropriate national/international standards
- ❑ Inspection and authorisation of screening, testing, retrieval, processing, storage, distribution, import and export
- ❑ Surveillance and vigilance including transplantation transmitted disease
- ❑ Monitoring and reporting of donation, processing, distribution , import, export and transplantation activity data

Cell Processing Panel Discussion (15-20 min):

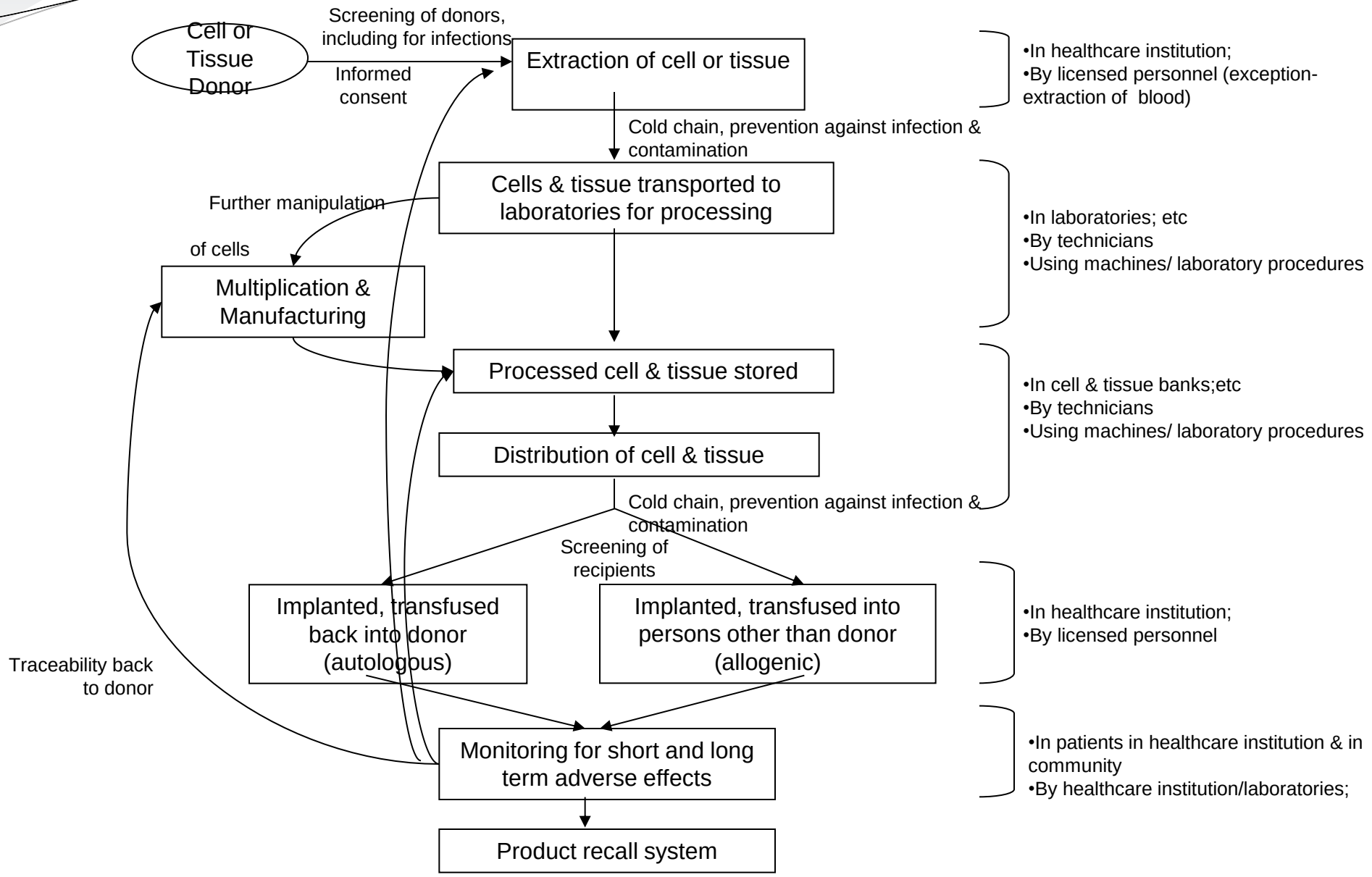
1. Where to set up such a facility?
   -hospitals vs blood banks (distance, infrastructure, expertise, lab testing, access to electricity)
2. Cost of Building and Maintenance.
3. Ability to source equipment and reagents amongst African countries
4. Capabilities, Staff expertise, Training across regions/countries. ?Twinning

Cell Processing Panel Discussion:

5. Clinical Interface between the Clinical Programme and the Processing Facility
6. Working within regulatory frameworks. What exists and what needs to be developed for each African country? Engaging govt officials and regulators
7. What innovative or novel cell processing solutions have the panellists been involved with or have encountered which could be of relevance to Africa?

Annex A

General flowchart of cell & tissues used for therapy from source to final usage



Transport. Import/Export and Regulatory Issues

- Labelling and Cold Chain Transport

- **Country Regulations.**
- Traceability of Stem Cell donations
- Infectious Disease Testing
- Required environment for cell processing

United States

- Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) regulated by US Food & Drug Administration
- HCT/Ps that meet ALL of the following criteria = “361” products
  - Minimally manipulated
  - Intended for homologous use
  - Not combined with drug or device
  - No systemic effect or not dependent on metabolic activity for primary function
  - ❖ No pre-market approval
  - ❖ Comply with Tissue Rules, including tissue establishment registration
- Other HCT/Ps = “351” products
  - Comply with Tissue Rules
  - Regulated as biologics or device (IND/BLA, IDE/PMA/510K)

Attribute	Test Method	Specification
Donor Screening	Summary of Records; Donor Eligibility Form	Donor Eligible
Infectious Disease Testing	Certified Laboratory	Negative (exclusive of CMV)
Infusion Volume	Measurement	≤20mL / Kg / Infusion
DMSO Volume	Calculation	≤ 1mL / Kg / Day
Total Nucleated Cell (TNC) Count	Automated Cell Counter	As Measured
RBC content (if ABO incompatible)	Automated Cell Counter	≤20mL-30mL /Adult Infusion
CD34+ Cell Count	Flow Cytometry	≥ 2 x 10^6 / kg
CD3+ Cell Count (if allogeneic)	Flow Cytometry	As measured
Viability (pre-freeze)	Flow Cytometry	≥ 80%
Sterility	Bacterial Culture	No Growth
Sterility	Fungal Culture	No Growth
Final Product Labeling	Observation	Labeled Correctly

Discussion

- Transplant programmes and graft processing labs: relationship
- Qualified manpower and training: twinning?
- How should one start? Auto vs Allo. The cell processing perspective
- Costs for running a cell processing lab
- Access to equipment/maintenance, reliability of power and qualified staff. Freezing capacity
- Advanced cell processing

Cell Processing Panel Discussion:

8. Any experience with setting up a stem cell processing lab with constrained resources? Panellists to share their involvement in this

What else to be considered

- Post thaw viability
- Sterility testing
- Non conforming product
- Bedside vs lab thawing
- Adverse effects
- Registry of all facilitites processing stem cells
- Cell Therapy for regenerative medicine and its knock on effects