CareForum 2022

The WellSky® Conference

Tips and Tools to Overcome Challenges and Negotiate Partnerships for Biotherapy Trials

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Today's speaker

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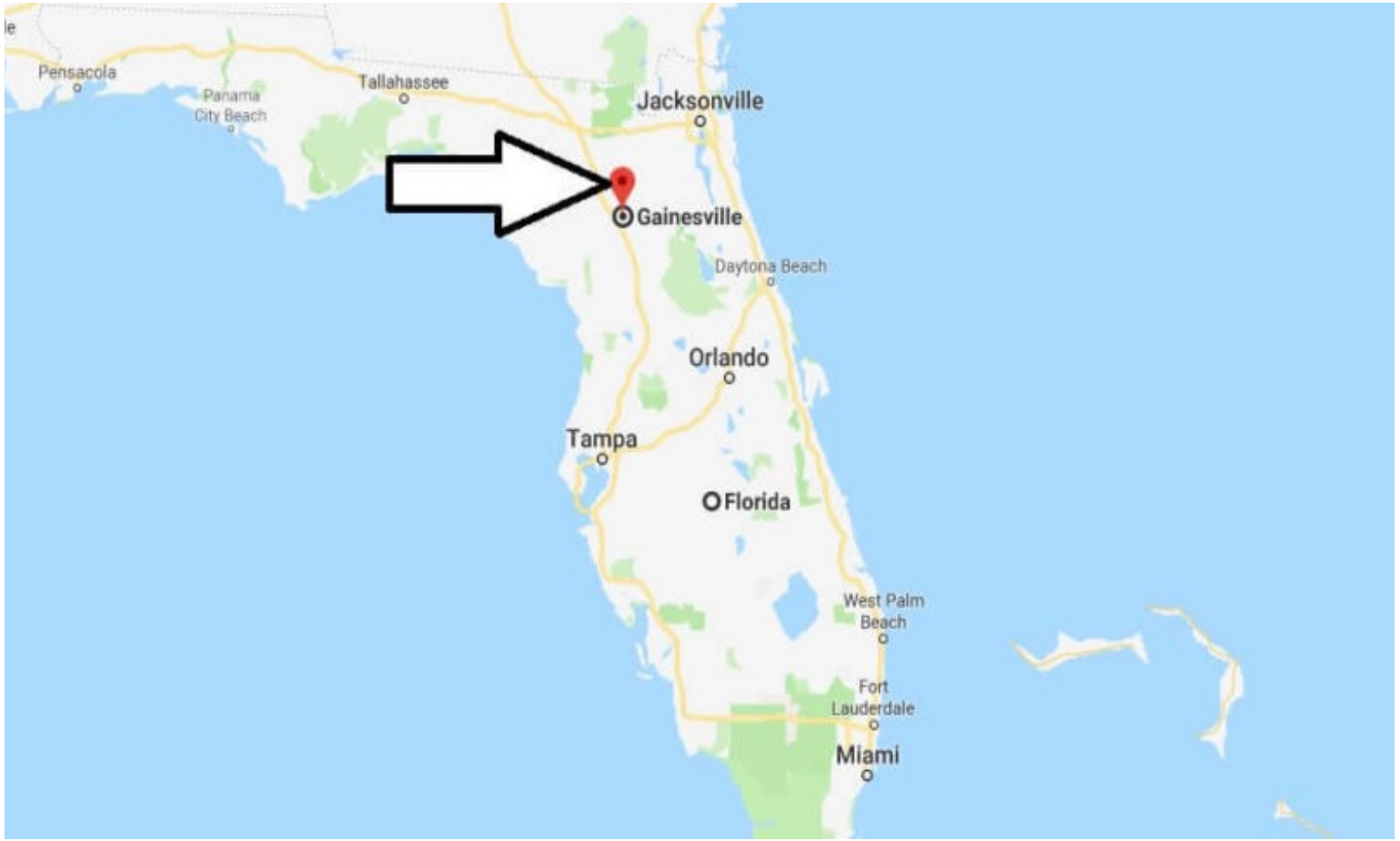
Disclosures

- No financial relationship with any sponsor or pharmaceutical company.
- The presenter’s opinion and experience is personal and does not represent any point of view or specific perspective from UFHealth Shands.

Objectives

- Discuss about how to develop partnerships with sponsors, manufactures and principal investigators to fully support and achieve success during the study of novel cell biotherapies.
- Describe practical solutions to overcome roadblocks that arise when supporting cutting-edge science and applying it in a clinical setting.

Where are we?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Introduction

- IRB (Institutional Review Board)

➢ According to the FDA "…an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, require modifications in (to secure approval), or disapprove research. This group review serves an important role in the protection of the rights and welfare of human research subjects."

➢ "The purpose of IRB review is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. To accomplish this purpose, IRB use a group process to review research protocols and related materials (e.g., informed consent documents and investigator brochures) to ensure protection of the rights and welfare of human subjects of research."

Areas to discuss

- This presentation encompasses two main areas:
  - ➢Collection facility
  - ➢Processing facility

Collection for further manufacturing

- **Apheresis**
  - Nucleated cells, including white blood cells may be obtained from the peripheral blood collected by apheresis
  - Donor may be mobilized or non-mobilized
  - Patients may donate for themselves: autologous
  - Donors may donate for patients or research: allogeneic
  - The patient or donor will be connected to a machine for several hours
  - The apheresis machine uses centrifugal forces to separate the cellular and plasma elements of blood
  - It can be specially programed to collect a targeted cell population

Requested products

- Products for research may target other cell populations (mononuclear cells, i.e. lymphocytes) and have variable collection targets
- Platelet loss can be considerable ~20-30%
- Advisable to check donor platelet count after the procedure
- Monitor donor/patient post donation
- Entities requesting products are advised to request a specific targeted cell population and total cell number, rather than specifying a particular device or blood volume passage

Processing in the Laboratory

- **Laboratory**
  - ➢Cryopreservation of the recently collected product
  - ➢Fresh: packing and shipping for further manufacturing to a central facility (i.e. GMP facility)
  - ➢Receipt of the manufactured product [either liquid (ready to infused) or cryopreserved]
  - ➢Receipt and storage of an investigational product (IP)
  - ➢Preparation for infusion (thawing, dilution, washing, labeling, transfer, etc.).

Who is Responsible for Compliance?

Although the study sponsor holds the IND and implements quality assurance systems to ensure compliance with mandatory (regulatory-FDA) and voluntary standards, the collection and processing facility share some of the responsibilities depending on the scope of the services provided:

- Personnel training
- Quality Management Plan
- Facility & equipment
- Containers & supplies
- Manufacturing records (batch records)
- Laboratory controls [product testing (release criteria) & stability]
- Packaging, labeling, and distribution
- Documentation

Compliance Responsibilities

- You are responsible to ensure compliance for your part (i.e. training, record keeping, collection, processing, labeling, tracking, documentation, etc.)
- Clarify what are the sponsor's responsibilities (i.e. documentation, training, testing, validation, product release, investigations, inspections/audits, etc.)
- If your facility participates as an active IP manufacturer, both you and the sponsor are responsible for assuring that the product is manufactured in compliance with cGMP or cGTPs.

The challenges

- Many different sponsors with different products & protocols
- Study onboarding process & communication with the research department(s)
- Navigating the regulatory environment
- Communication with collections, processing and transport schedulers
- Use of different sponsors portals (web based)
- Monitoring visits & audits
- **Staffing**
- Training
- Budget
- Freezer storage (bags, vials, tubes)

How to organize yourself?

- Communicate with stakeholders
- Get involved as early as possible
- Create a process or workflow
- Create SOPs, forms, worksheets, training modules
- Prepare a budget
- Assign tasks and responsibilities (divide and conquer!)

Know your stakeholders

- Build your department relationship with the research, pharmacy, and finance departments
- Learn the study onboarding and activation procedures in your institution
- Establish good relationship with your sponsors
- Get to know your principal investigators (PIs) and sub investigators.

Scheme for Study Activation

Get involved as early as possible

- Get your department involved in the study onboarding process as early as possible
  - Preferable, you should get some information before the pre-study visit
- The feasibility questionnaire is used by the sponsor to assesses your capabilities and qualifications to participate in the trial or study protocol
  - **It is also your opportunity to do the same with the sponsor**
- Be as informed as possible before the pre-study visit.
  - If a study manual is not available, you should at least have the protocol so you can review the required procedures and prepare questions to the sponsor.

Study / protocol details

- Determine feasibility (personnel, workload, schedule, cost, involvement, etc.)
- Meetings with stakeholders [sponsor, principal investigator (PI), collections leadership, providers (MDs, APPs)]
- Approval process [IRB, protocol, budget, COS (Cost of Services)]
- Pharmacy/Laboratory manuals
- Forms/labels templates
- Eligibility criteria (and exclusion criteria)
- Informed consents for subjects

Cost of Services

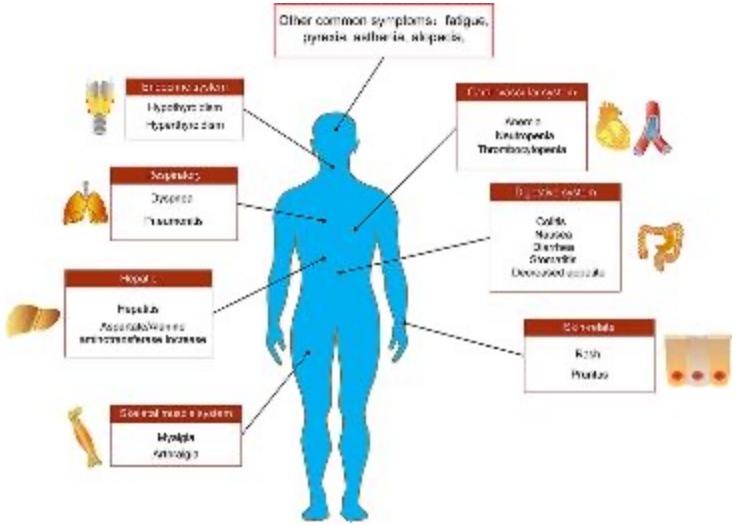
- Collection itself (to include cost of disposable apheresis kit, supplies, IV solutions required, **labor** and other ancillary items)
- Processing, including receipt, sampling, washing, diluting, packing, etc.
- MD or APP pre-evaluation for the subject
- Required lab tests (per your SOP and anything special required by the sponsor; i.e. CBC, Ca, Mg, P, BMP, CD3, CD34, TNC, etc.)
- Diagnostic tests (if applicable/required, i.e. EKG)

Cost of Services (cont.)

- Employee training
- Writing of study specific documents (SOPs, forms, worksheets, batch records, labels, etc.)
- Storage (refrigeration, liquid nitrogen)
- Dry / mock runs
- Administrative overhead (MD review, release, quality records, collection records, batch records, etc.)
- Monitoring visits / audits

Another required items

- Validation of equipment (if a specific instrument is required by the sponsor or if a new instrument is needed by your Lab)
- Depending of the clinical trial or study, the transportation temperature (shipping) and storage can vary
- Regardless of the temperature requirements, it is recommended to use a validated container or include a temperature monitoring device to ensure that proper temperature is maintained all the time
- Adverse events and occurrences
  - Define responsibilities of reporting to regulatory agencies, sponsor, etc.



Negotiations

- Always negotiate, negotiate, negotiate and clarify
- Don’t cut yourself short (but at the same time don’t over estimate or over charge), the amount of hours that your staff spends or will spent is very important
- Again, define responsibilities and accountabilities
- Don’t accept something that you can’t comply with
- Avoid pressure or resistance
- Make sure that you review the fine print on the contracts/agreements.

Negotiations (cont.)

- Get your administrators involved
- Get your legal team involved
- Follow rules and regulations (federal, state, local)
- Review / revise agreements at least every two years (or earlier if something critical changes)
- Perform periodic audits

Resources' management

- Always consider material, supplies and equipment used for a study or protocol
- Take in consideration items that you consider ‘normal/routine’ for your procedure (i.e. syringes, tubes, alcohol pads, saline solution, anti-acid tablets, calcium gluconate, ACD-A, tubes, bags, couplers, transfer sets, etc.)
- **Personnel** (RNs, Apheresis Technicians, Medical Technologists, clerical staff, etc.)
- Overhead expenses (i.e. space rent).

Example

Item	Performed / verified	Initials / date	Comments
Feasibility meeting			
Protocol / study review and approval by Medical Director			
SIV (site initiation visit) / tour of the facility			
Follow up meeting (if required)			
Budget approval / COS			
Submission of documentation (SOPs, worksheets, forms, etc.)			
Staff training			
Validation (if applicable)			
Materials and supplies provided by sponsor			
Mock/dry run			
Site activation			
Set up binder			
Audits			
Close out			

Summary

- Clinical trials are necessary to determine the safety and efficacy of cellular therapy products
- The involved facilities play an important role in ensuring the safe and efficient preparation of these cell therapy products to maintain their purity and potency
- It is utmost importance to maintain an open and effective communication between the sponsor/pharmaceutical/BioTech companies and the institution for the success of the endeavor and sustainability of the business.

Learn more about WellSky Biotherapies

Request a consultation today!

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Thank you.

Contact us:

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