Production Assistance for Cellular Therapies

Educational Web Seminar

Contract Manufacturing by and for Academic Institutes

Tuesday, 15 December 2020

12:00 PM – 1:00 PM ET

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Speakers

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Interdisciplinary Stem Cell Institute, University of Miami

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Baylor College of Medicine

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Objectives

- Describe current technologies and trends in contract manufacturing and how they both affect the landscape of the current market.
- Identify what the quality assurance requirements are from steps in product development to the manufacturing of the clinical product.
- Identify the key elements of the technical requirements versus the legal requirements and how they both affect the technical, legal and pricing structure of agreements.
- Describe the necessary steps needed in the manufacturing phase and through the product administration phase to create a successful supply chain for cell therapy manufacturing.
- Describe the differences between academic contract manufacturing and commercial contract manufacturing and the importance of both in determining the need for services.

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Contracting: In and Out

Adrian Gee
Center for Cell & Gene Therapy
Baylor College of Medicine
Houston, Texas

Academic GMP Facility

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Outline

Contracting Scenarios

- Working for Biotech
- Contracting out services

Other considerations

Future directions

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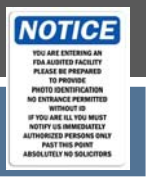
Working for Biotech



Selection based on:

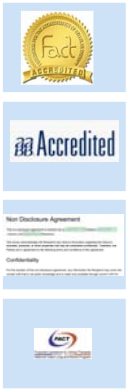
- Previous experience
- Accreditation
- FDA registration/audits

Preliminary meeting

- Review experience
- Examine capacity

Follow-up meeting

- Non-disclosure agreement



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Working for Biotech

Status Meeting

- IND Status
- Methods finalized or translational?
- Validated procedures
- Source of cells
- Informed consent
- Donor screening
- Incoming cell shipment
- Tech transfer / Staff training
- Timelines / Capacity

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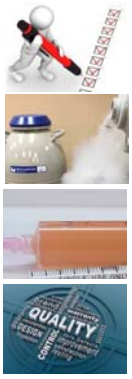
Working for Biotech

Who, where, when?

- Product testing and release
  - Certificate of Analysis
- Product shipping
- Preparation for administration
- Ongoing quality management



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Ongoing Quality Management

Quality audit

- Who, when, what, how long?

Quality Agreement

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Quality Agreements

Specifies all aspects of quality management

Assigns parameters to be met

Assigns responsibilities of each party

Section	Description
	Signature Page
1.0	Purpose
2.0	Scope
3.0	Policy Statements
4.0	Definitions
5.0	Regulatory Authorizations and Com
6.0	Equipment and Testing Facilities
7.0	Documentation
8.0	Materials Receipt and Storage
9.0	Reference Standard Management
10.0	Analytical Methods and Testing
11.0	Deviations, Discrepancies, OOS, an
12.0	Change Control
13.0	Data Acceptance and Disposition
14.0	Sample and Record Retention
15.0	Complaints and Recalls
16.0	Inspections and Audits
17.0	Annual Product Review (commercia
18.0	Subcontracting

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Quality Agreements

What to look for:

- Visit frequency
- Reporting
  - Frequency
  - Turnaround times
- Change control
- Regulatory involvement

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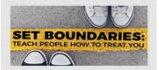
Major Issues

Legal contract
- Complex
- Takes time

Degree of involvement
- This is ONE project – not your ONLY project
- Charge for additional services & time
- Set boundaries



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Most important!

- Clear lines of communication
- Free and open communication
- Trust
- Ongoing collaboration
- Common problem solving

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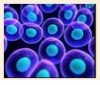
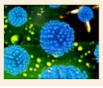
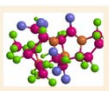
Contracting Out Services

Manufacturing
- Cell Products
- Intermediates
- Viral Vectors
- Plasmids
- Peptides







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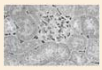
Contracting Out Services

Testing

- Viral testing
- Animal testing
- TEM
- Replication-competent virus
- Residual reagents



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Whom to Chose?

Manufacturing

- 128 Commercial companies
- 28 Academic Facilities
- Government-funded organizations

Testing

- Eurofins, BioReliance, WuXi AppTec, Charles River, ThermoFisher etc. etc.



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Manufacturing Companies

- Experience
- GMP Compliance
- Familiarity with regulations
- Do they have procedures in place
- Ability to source starting material
- Good working relationships
- Can provide customized solutions
- Additional services?
- Cost & turnaround times



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Testing Companies

- Familiar with regulations & current release assays
- Good working relationship with regulators
- GMP/GLP compliant
- Wide range of testing services
- Open working relationship
- Good problem solvers
- Costs and turnaround times?

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Manufacturing & Testing Backlogs

- Academic facilities generally have shorter wait time
- Consider foreign companies with FDA experience
- Bring in-house
- Bundle projects to create special relationships
- Consider governmental services

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Conclusions

- Academic facilities can benefit from contract activities
- Detailed negotiations with defined responsibilities are important
- Contracting out activities requires careful evaluation of multiple factors

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Tack
ju faleminderit
Asante
谢谢
Tak
mulţumesc
kiitos
Salamat!
Gracias
Terima kasih
Aliquam
Merci
Dankie
Obrigado
ありがとう
köszönöm
grazie
Aliquam
Go raibh maith agat
děkuji
Thank you

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MAYO CLINIC
IMMUNE, PROGENITOR, AND CELL THERAPEUTICS (IMPACT)
Contract Manufacturing at an Academic Medical Center
Allan B. Dietz, Ph.D.
PACT Webinar
November 2020

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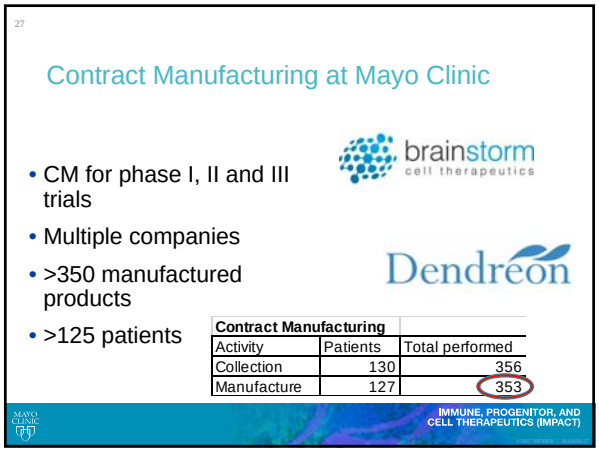
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Contract Manufacturing at Mayo Clinic
brainstorm cell therapeutics
Dendreon
• CM for phase I, II and III trials
• Multiple companies
• >350 manufactured products
• >125 patients
Contract Manufacturing
Activity | Patients | Total performed
Collection | 130 | 356
Manufacture | 127 | 353
IMMUNE, PROGENITOR, AND CELL THERAPEUTICS (IMPACT)

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Contract manufacturing

- What is it?
  - Trading your time, expertise, space and equipment
- Why would you do this crazy thing?
  - $
  - To fill gaps that occur in production runs/to get facility to capacity
  - To gain some expertise
  - To "fit" new product into a clinical program

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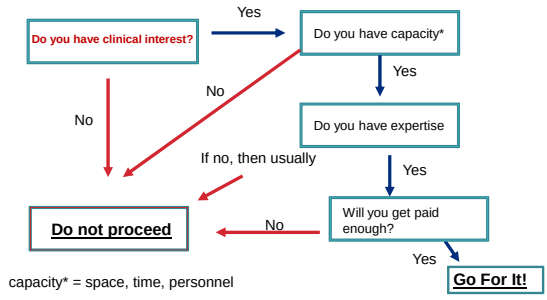
Decision Matrix for Contract Manufacturing



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Considerations in regards to contract manufacture…capacity

- Capacity calculations
  - Understand prioritization
    - Time is money for companies
  - Space
    - Dedicated clean room?
  - People and training
    - Train the trainer?
  - Expertise
    - Does the project need any development (validations, new SOPs, etc.)?

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Considerations in regards to contract manufacture…capacity

- How to decide if you have capacity?
  - Get as much detail as you can
    - Review SOP, data, requirements
  - Try to estimate gaps between what they need and what they have
    - Could be zero…could be a lot
  - BE REALISTIC on time
    - It will probably take more time than you think

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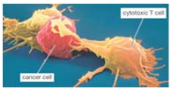
Capacity, budget, and time

- The calculus used to understand your capacity (infrastructure, people, development needs etc.) is the basis you use to start estimating both
  - Time
  - Budget



- Both of which (if they are excessive) will be non-starters for the company…

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Agreements

- You have a feel for the time and budget AND you think you have capacity
- Now time to figure out how you work together
- Technical Agreement
- Quality agreement
- *(Intellectual property, confidentiality, liability are not discussed here but should be addressed somewhere)*

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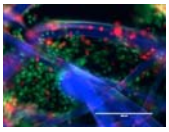
Technical Agreement Part 1

- What you are going to do?
  - How many runs
  - What release tests
  - Extra work if necessary (development, new release assays, equipment validation etc.)



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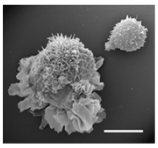
Technical Agreement Part 2

- What you need
  - List of SOPs (Document Matrix)
  - List of Critical Materials
  - Process specific equipment



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Quality Agreement

- The quality agreement describes who is responsible for the quality aspects of manufacturing
  - Ultimately – the Sponsor is responsible, however, *how they do that job via the interaction with the CRM* is what is outlined in the QA

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Quality Agreement

- Parts of a QA
  - Monitoring plan
    - What the Sponsor considers sufficient information to meet their regulatory requirements for example:
      - *Pre-audit*
      - *Review CoA*
      - *Scheduled batch record review*
    - Anything else is transferred to fall under typical CRM quality unit responsibilities
  - Communication plan

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Quality Agreement

- Parts of a QA - the Communication plan
  - What are you communicating?
  - When will it take place?
- Examples…
  - Product fails release testing – Immediate
  - Minor event during processing (verifier signature missed on one step of SOP – within 5 working days
  - Courier was late for scheduled pick up – at monthly meeting
- The Document matrix and critical materials list in TA are reference points for communication
  - Things on that list fall to higher urgency in communication

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Timing and budgets

- Proposal hits your desk…
  - Review for capacity, expertise, time
  - Do your best to estimate time and resource requirements for BOTH the Quality and technical agreements
  - Bid out in two parts; quality agreement work and technical work

They accept the bids…

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They accepted the bids – PART 1

- Start the QA agreement process
  - Get list of critical materials
  - Get a list of SOPS in document matrix
  - Agree on communication matrix
  - Get required equipment
- Once completed with the QA part – then should be good to go on the technical agreement
- Should be able to provide validated test runs of process – IND filings

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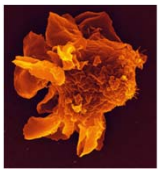
They accepted the bids – PART 2

- Initiate the TA agreement
  - With the QA done, this should be easy
  - Manufacture according to plan reviewed and approved SOP
  - Refer to the QA for communication/reporting issues
  - MEET THE TIMING MILESTONES



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The final steps

- Close out
  - Make sure the close out process is included in the agreements
  - Final transfer and sign off of all documents
  - Retained product transfers

IT'S THAT SIMPLE

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Contract Manufacturing By and For Academic Institutes

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