Update: NIH Sterile and Non-Sterile Processing Facilities

2\textsuperscript{nd} Meeting of the NIH Clinical Center Research Hospital Board

October 21\textsuperscript{st}, 2016

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Principal Deputy Director, NIH
Inspection and Assessment of Facilities

- Following PDS event, an in-depth inspection of all sterile and non-sterile processing facilities occurred.
- Many activities are ongoing, but all facilities are in control.
- New Office of Research Support and Compliance (ORSC) has been established within the Office of Intramural Research (Michael Gottesman, MD, Deputy Director for Intramural Research).
  - Led by Andy Griffith, MD, PhD; Bruce Burnett, PhD; and Val Bonham, JD.
  - Responsible for ongoing monitoring of these facilities and related activities.
Intravenous Admixture Unit (IVAU)

- **Role:** Supply sterile pharmaceuticals by prescription
- **Status:**
  - Operating under a moderate level of control
  - Construction and process improvements complete
  - Constructing an interim-IVAU (I-IVAU) in former PDS space
  - Once I-IVAU is operational, current IVAU will be closed for renovation (~2 yrs)
  - After renovations, IVAU operations will be returned to renovated facility and I-IVAU space will be used for additional cell processing

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
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<tbody>
<tr>
<td>Oct 2016</td>
<td>I-IVAU Construction Complete</td>
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<tr>
<td>Nov 2016</td>
<td>I-IVAU Facility Commissioning Complete</td>
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<tr>
<td>Nov-Dec 2016</td>
<td>I-IVAU Qualifications Complete</td>
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<tr>
<td>Jan 2017</td>
<td>I-IVAU Fully Operational</td>
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<tr>
<td>Early 2019</td>
<td>IVAU Renovations Complete</td>
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Department of Transfusion Medicine (DTM)

- **Role:** Supply infusible materials for cell-based therapies including engineered immune cells and gene therapies

- **Status:**
  - Operating under minimum physical control with robust administrative controls currently
  - July 2016 unannounced FDA inspection – no formal findings
  - Constructing a new facility (2J) and then will renovate current facility (3T)

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Oct 2015
Contamination Found

Aug 22, 2016
2J Construction Complete

Aug-Dec 2016
Compiling Administrative Controls

Early 2017
2J Operational

Early 2017
3T Renovations Begins
Positron Emission Tomography (PET) Facilities

- **Role:** Produces sterile PET radiopharmaceuticals for human scanning studies

- **Status:**
  - **CC Facility:** Monitoring continues and most physical concerns have been resolved
  - **NIMH Facility:** Consolidating manufacturing activities with the CC PET Department

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- April-May 2016
  - Repairs to CC Facility

- May 2016
  - NIMH Facility Permanently Closed

- Ongoing
  - Hot Cell Installation & Testing (CC Facility)
Nuclear Medicine Department Radiopharmacy

- **Role:** Provides only commercially available nuclear medicine radiopharmaceutical products purchased from local sources

- **Status:**
  - Has not manufactured product directly
  - Construction to enable sterile manufacturing

- **Timeline:**
  - Summer 2016: Construction Enabling Sterile Manufacturing
  - Dec 2016: Construction Complete
  - Early 2017: Media Fills & Performance Qualification begins
  - Mid 2017: Facility Fully Operational
NCI Surgery Branch Cell Processing Laboratory (Located in CRC 3 West)

- **Role**: Investigational cell and gene therapy products

- **Status**:
  - Construction/renovations to remediate the space, as well as administrative efforts (e.g., SOPs, equipment)
  - Reopened with restricted manufacturing with moderate facility control

- April 2016: Facility Closed
- May 2016: Physical & Administrative Remediation
- June 2016: Facility Reopened (1 pt/wk)
- Summer 2016: Independent Assessment
- Sept 21, 2016: Accommodating 6 pts/month
NCI Surgery Branch Cell Processing Laboratory (Expansion Space in Building 53)

- **Role:** Same role as CRC 3 West; this project improves capacity
- **Status:**
  - Building 53, an unused facility on the Bethesda campus, will house a cGMP facility constructed with prefabricated modular components
  - Project will significantly increase the volume of cell processing
  - Working Buildings will develop Basis of Design, attend Type C Meeting, provide design and construction surveillance, and provide facility qualification support

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<tr>
<td>Oct 2016</td>
<td>Basis of Design Completed</td>
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<td>Dec 2016</td>
<td>Type C Meeting w/FDA</td>
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<tr>
<td>Feb 2017</td>
<td>Procurement &amp; Design</td>
</tr>
<tr>
<td>April 2017</td>
<td>Construction Begins</td>
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<tr>
<td>Aug 2017</td>
<td>Construction Complete</td>
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<tr>
<td>Oct 2017</td>
<td>Facility Operational</td>
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NCI Surgery Branch Vector Production Laboratory and Thoracic Epigenetics Laboratory

**Role:**

- **Surgery Branch Vector Production (SBVP) Lab:** Produced vectors for use in manufacture of engineered cells
- **Thoracic Epigenetics (TE) Lab:** Produced experimental cancer vaccines

**Status:**

- **SBVP Lab:** Concerns about physical plant and layout; Trailer 1 purchased to enable work to continue
- **TE Lab:** Irresolvable space layout deficiencies; Trailer 2 designed to enable work to continue, plus the work of 2 other researchers

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April 2016
SBVP and TE Labs Closed

Summer Fall 2016
Trailer 1 & 2 Design and Planning

Dec 2016
Trailer 1 Delivered

Early 2017
Trailer 1 Operational; Trailer 2 Delivered

2017
Trailer 2 Operational
NCI Biopharmaceutical Development Program (BDP) and Leidos Radiopharmacy

- **Role:**
  - **BDP:** Produces monoclonal antibodies, recombinant proteins, immunotoxins, oncolytic viruses, and vaccines
  - **Leidos Radiopharmacy:** Prepares radiopharmaceuticals (short-lived PET agents)

- **Status:**
  - **BDP:** Remediation ongoing and production continuing
  - **Leidos Radiopharmacy:** Operating at a high level of control; minimal remediation

- **Timeline:**
  - April 2016: Indep. Audits & BDP Partially Suspended
  - Aug 2016: Leidos Radiopharmacy Repairs Complete
  - Oct 2016: Indep. Audit Revisit Leidos Radiopharmacy
  - March 2017: BDP Remediation Complete
  - 2017: Independent Audit Revisit BDP
NIAID Vaccine Stock Manufacturing

- **Role:**
  - Manufactures viral seed stock drug substance that is then sent to Charles River Labs for additional processing, purification, and release

- **Status:**
  - Administrative controls changed to allow for continued operation until renovations could be completed
NIAID Vaccine Research Center (VRC) Vaccine Pilot Plant and Malaria Vaccine Laboratory

- **Role:**
  - **VRC Vaccine Pilot Plant:** Produces vaccines, monoclonal antibodies, and placebo products
  - **Malaria Vaccine Laboratory:** Being considered to produce malaria vaccine

- **Status:**
  - **VRC Vaccine Pilot Plant:** Operating at an exceptionally high level of control
    - No remedial actions were recommended or undertaken
  - **Malaria Vaccine Laboratory:** Consultation with CDC
    - Cancelled on-campus planning
    - Planning to perform this work at off campus location
Comments/Questions?

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