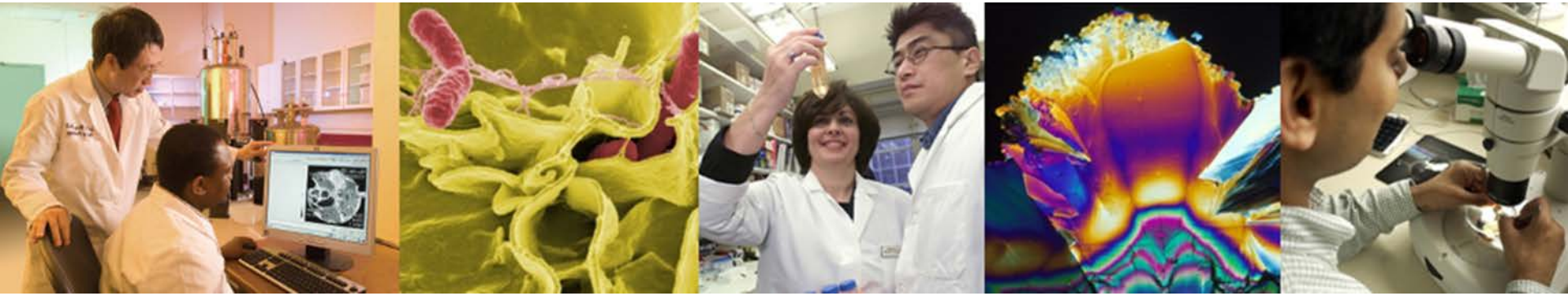
“Red Team”:
ACD Clinical Center Working Group

NIH Introduction

April, 21 2016



Francis Collins, MD, PhD
Director, NIH

Lawrence A. Tabak, DDS, PhD
Principal Deputy Director, NIH

Kathy Hudson, PhD
Deputy Director for Science, Outreach and Policy, NIH

Timeline I

- 5/19-29/15: FDA for cause inspection of Pharmaceutical Development Section (PDS) and Intravenous Admixture Unit (IVAU)
- 6/4/15: NIH announced response plans and suspension of sterile activities in PDS
- 6/4/15-12/10/15: NIH internal Task Force oversees response
  - Extensive internal investigation
  - Retrospective and prospective clinical monitoring of participants
  - Identifying safe sources for sterile products
  - Guidance for investigators
  - Oversight and retesting of quarantined products
  - Remediation and continued coordination with FDA
  - External expert report on PDS and IVAU
  - Hill inquiries on affected protocols and on events leading up to FDA inspection

Timeline II

- 12/10/15: Internal Task Force report and recommends formation of a Advisory Committee (to the NIH) Director (ACD) Clinical Center Working Group
- Ongoing NIH activities:
  - Short-term remediation of the Intravenous Admixture Unit
  - Establishing alternative sources of sterile products
  - Assessing all NIH sterile production facilities
  - Retraining PDS and IVAU staff
  - Hiring new Pharmacy Department Director (interviews pending)
  - Reviewing compliance oversight structures across the ICs and other institutions to inform scope and role of proposed NIH office

Reducing Risk and Promoting Patient Safety for NIH Intramural Clinical Research

The Clinical Center Working Group ("Red Team") Report to the Advisory Committee to the Director

April 21, 2016

NORM AUGUSTINE (CHAIR)
FORMER CEO, LOCKHEED MARTIN

LAURA FORESE, MD
EVP AND COO, NEWYORK-PRESBYTERIAN

ACD Clinical Center Working Group Roster

Norm Augustine (chair), Former CEO, Lockheed Martin

Victoria Christian, CEO, Duke Translational Research Institute

Laura Forese, EVP and COO, NewYork-Presbyterian

Donald Gagliano, Principal, Global Medical Innovation, Walter Reed National Military Medical Center

Harlan Krumholz, Professor, Yale School of Medicine

F. Kurt Last, Executive Vice President–Clinical Products Group, WorkingBuildings, LLC

Richard Marchase, Vice President for Research, University of Alabama at Birmingham

Edward Miller, Former CEO, Johns Hopkins Medicine

John Noseworthy, President and CEO, Mayo Clinic

Kathy Hudson (ex-officio), Deputy Director for Science, Outreach and Policy, NIH

Lawrence Tabak (ex-officio), Principal Deputy Director, NIH

Carrie Wolinetz (executive secretary), Associate Director for Science Policy, NIH

Kate Saylor (staff), Office of Science Policy, NIH

ACD Clinical Center Working Group Charge

To make recommendations about ways to enhance the **organization, financing, and management** of the clinical center to **improve the quality of patient care**, and **reduce the risk** of clinical research and research-related activities

To inform its deliberations, the working group may:

- Examine the **structural and cultural issues** at the CC that may have contributed to the deficiencies identified in the Pharmacy and Pharmaceutical Development Service
- Review other research activities at the CC that pose a **potential risk to research participants**

Clinical Center Working Group Process

- 3 in-person closed meetings, January-March
  - Presentations from NIH IC and CC leadership, and investigators and clinical staff working in the trenches
  - Tour of CC PDS and NCI Biopharmaceutical Development Program
- Reviewed extensive documents from the CC and NIH
- Deliberated on recommendations at meetings and via email
- Report to the ACD via public teleconference

Report Themes

I. NIH needs to fortify a culture and practice of **safety and quality**

II. NIH must strengthen **leadership** for clinical care quality, oversight, and compliance

III. NIH is obligated to address **sterile processing** of all injectables used in the Intramural program as well as the specifics of the sentinel event

I. Safety and Quality: Findings

- In some instances, patient safety was treated as secondary to research needs
- In multiple cases, there was a failure to report or address concerns related to safety and/or compliance
- There are inadequate research and clinical support systems in place
- There are variable standards across research programs

I. Safety and Quality: Recommendations

1. Adopt new CC mission and values statements that reflect synergism of science and safety
2. Establish a Research Support and Compliance Office
3. Establish systems to monitor, report, and enforce safety and quality standards

II. Leadership: Findings

- Fragmented governance, responsibility, authority and accountability has led to an unclear locus of responsibility for leadership of the CC
- There is a lack of funding transparency in the CC
- Outdated CC facilities fail to meet standards
- There is a lack of compliance and regulatory expertise within the intramural program

II. Leadership: Recommendations

4. Establish an external hospital board
5. Strengthen leadership authority and responsibility
   - Centralize authority for clinical research
   - Clarify responsibilities of CC leadership
   - Integrate patient safety in individual performance plans
6. Establish a Clinical Practice Committee
7. Identify and eliminate potential gaps among clinical services

III. Sterile Processing: Findings

- Compliance failures
- Failure to certify facilities
- Reporting failures
- Inadequate attention to capacity and prioritization
- Potential to expand use of NCI Biopharmaceutical Development Program

III. Sterile Processing: Recommendations

8. Do not rebuild the sterile PDS in the CC
9. Enhance resource sharing across ICs
   - Establish prioritization and governance for sterile products
   - Analyze future product needs
10. Ensure that the IVAU and non-sterile PDS are fully remediated
11. Assess all facilities at NIH producing sterile materials

Questions?

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NIH Response

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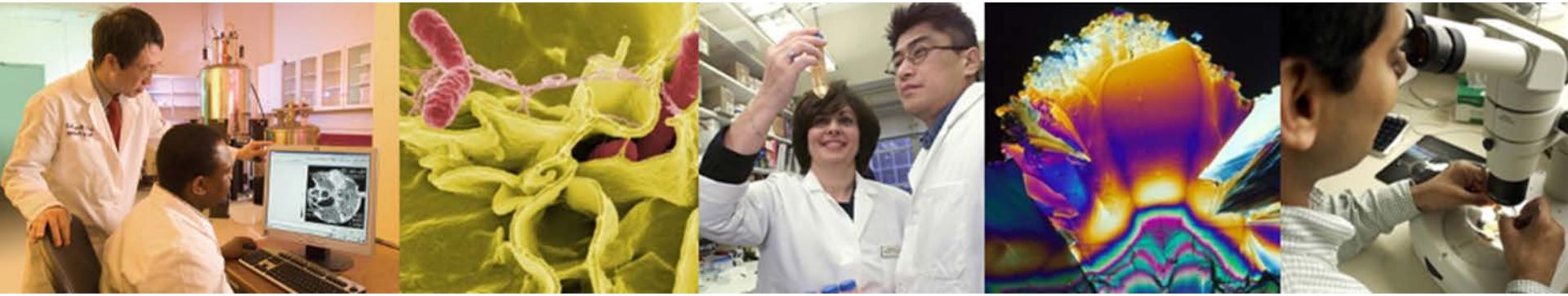

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Immediate Actions by April 21

- Create new external board and name chairperson
- Create compliance office and name interim director
- Schedule for assessment of all NIH sterile facilities with compliance consultant
- Changes to clinical staff performance plans
- Assign implementation plan for other recommendations

Hospital Board Chair: Laura Forese, M.D., M.P.H.

Executive Vice President and Chief Operating Officer, NewYork-Presbyterian

Interim office director: Kathryn C. Zoon, Ph.D.

Chief, Cytokine Biology Section,
NIAID

Longer-term Implementation

- If the proposed recommendations are implemented, the IRP can provide essential patient safety while continuing extraordinary scientific accomplishments

- Mission and values statements
- Monitoring, metrics and reporting systems implementation
- Improving coordination across the CC by the Clinical Practice Committee and other recommended actions
- Long-term plans for sterile production

Sterile Processing Facilities

NOTE: All facilities are undergoing a uniform review by Kurt Last and Working Buildings.

* FDA inspection complete
~ Other external inspection complete
^ Remediation in progress
XX Some operations suspended

- CC IVAU *^
- CC Sterile PDS *XX
- CC Cell Processing Section, DTM
- CC Radiopharmacy, Nuclear Med. Section, Radiology and Imaging Sciences
- CC Positron Emission Tomography Dept.
- NCI Leidos Radiopharmacy, Bldg 459 Frederick
- NCI BDP, ATRF bldg., Frederick ~^
- NCI Thoracic Epigenetics Lab, bldg. 10 ~XX
- NCI Surgery Branch Lab, bldg. 10 ~XX
- NIA Research Pharmacy, Baltimore
- NIAID Vaccine Pilot Plant, Frederick ~
- NIMH PET Radiochemistry Lab, bldg. 10 ~

Preliminary Findings of NCI Surgical Branch

- Unit devoted to development of cancer immunotherapies
- NCI engaged independent experts to review
- Report outlined substantial deficiencies
  - Lack of SOPs, quality unit, training, records
  - Equipment and facility issues
- NCI contacted FDA/IRB
- No new accrual, current participants continue treatment
- Inspected by Kurt Last on 4/18/16




NIH...

Turning Discovery Into Health