Infrastructure and Cultural Changes Occurring Since the Red Team Report: An IC's Perspective

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NIH National Heart, Lung, and Blood Institute

Clinical Research in the NHLBI DIR

Major emphasis

- First-in-human new therapeutics and diagnostics for heart, lung, and blood-related diseases
- Characterizing the pathophysiology of common and rare diseases

Clinical Research in the NHLBI Division of Intramural Research (DIR)

NHLBI DIR has the 2nd/3rd largest clinical research program within **the NIH intramural program**

199 IRB-approved clinical research protocols

Phase I	-	35 studies
Phase I/II	-	13 studies
Phase II	-	54 studies
Natural History	-	97 studies

} Greater than minimal risk with prospect of direct benefit to the patient

FDA-regulated Trials (IND/IDE):
61 studies with an IND/IDE
Average 12 new IND/IDE protocols approved annually

- 4,296 total clinical trial-related inpatient days at the Clinical Center and 9,954 annual clinical trial-related outpatient visits to NHLBI clinics

NHLBI DIR Clinical Research Branch Structure

Cardiovascular Branch

Pulmonary Branch

Translational Vascular Medicine Branch

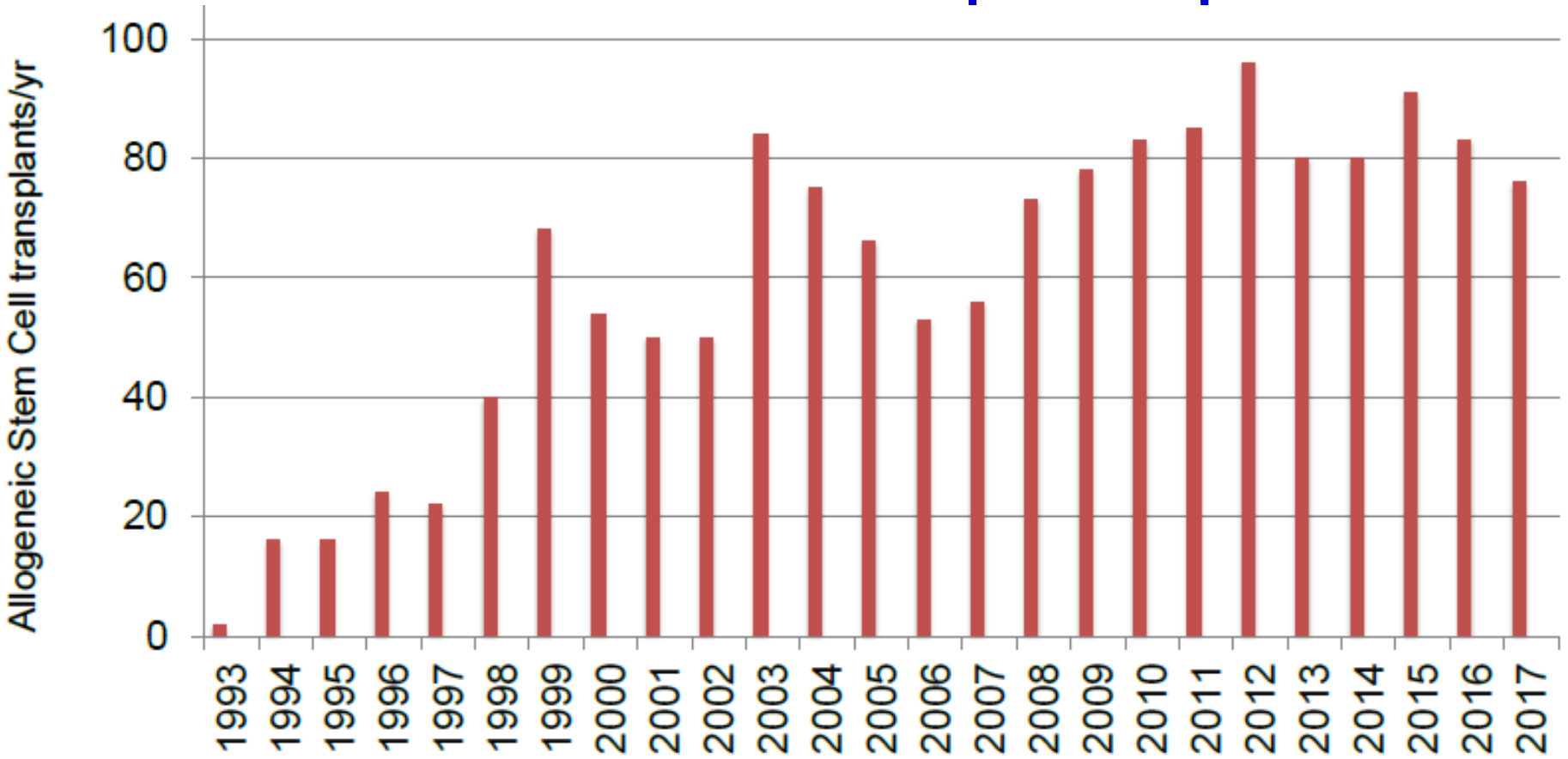
Hematology Branch

Sickle Cell Branch

- First in human research
- Interventional trials enrolling “high-risk” pts undergoing “high-risk” procedures
  - Allogeneic stem cell transplantation
  - Umbilical cord blood transplantation
  - Gene therapy of hematopoietic stem cells
  - Caval-Aortic non-surgical heart valve replacement (TAVR)

Allogeneic Transplants in high-risk patients at the NIH

Total = 1501 pts transplanted



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Diverse Group of PIs Conducting Clinical Research in the NHLBI DIR

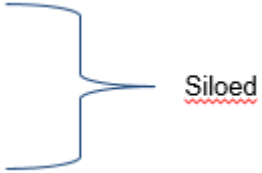
N=42

- Tenured PIs
- Tenure Track PIs, including Lasker Fellows
- Assistant Clinical Investigators (ACIs)
- Staff Clinicians
- Fellows in Training (Hematology/Oncology/Cardiology)

DIR Clinical Research in 2011

Systematic overview of the DIR clinical program identified a lack of a comprehensive and standardized clinical research infrastructure and oversight to support our clinical research enterprise:

- research nurse support
- FDA oversight-protocol navigation
- patient care coordinators
- data managers – nonexistent
- poor compliance with regulatory monitoring
- lack of a standardized clinical research database that met FDA standards



Strategic Plan to Support Clinical Research in the NHLBI DIR: Major Elements

Centralize, standardize and enhance the infrastructure supporting clinical research out of the Office of the Clinical Director (OCD):

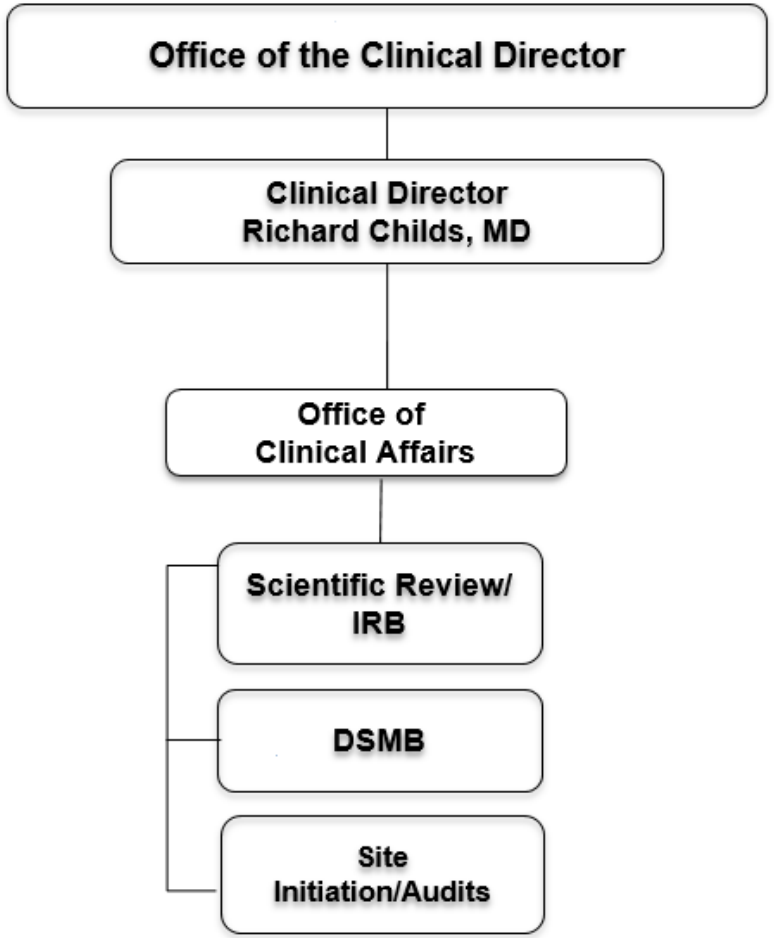
Goals:

- Optimize regulatory compliance
- Optimize the efficiency by which we conduct research
- Do more with less by:
    - **Centralizing research nurses in the OCD**
        - Workload assessments and scope of practice reviews
    - **Create an Office of Research Education and Patient Outcomes**
        - Ensure all nurses and practitioners are trained in GCP
        - Centralized oversight of adverse event/SAE/unanticipated problem reporting
    - **Create an Office of Clinical Research Support Services in the OCD**
        - *Centralized FDA Regulatory Experts (Navigators) in the OCD*- expertise with IND/IDE and FDA-mandated reporting
        - *Centralized monitoring/auditing:*
            - FDA-regulated studies
            - Interventional studies that are not FDA regulated

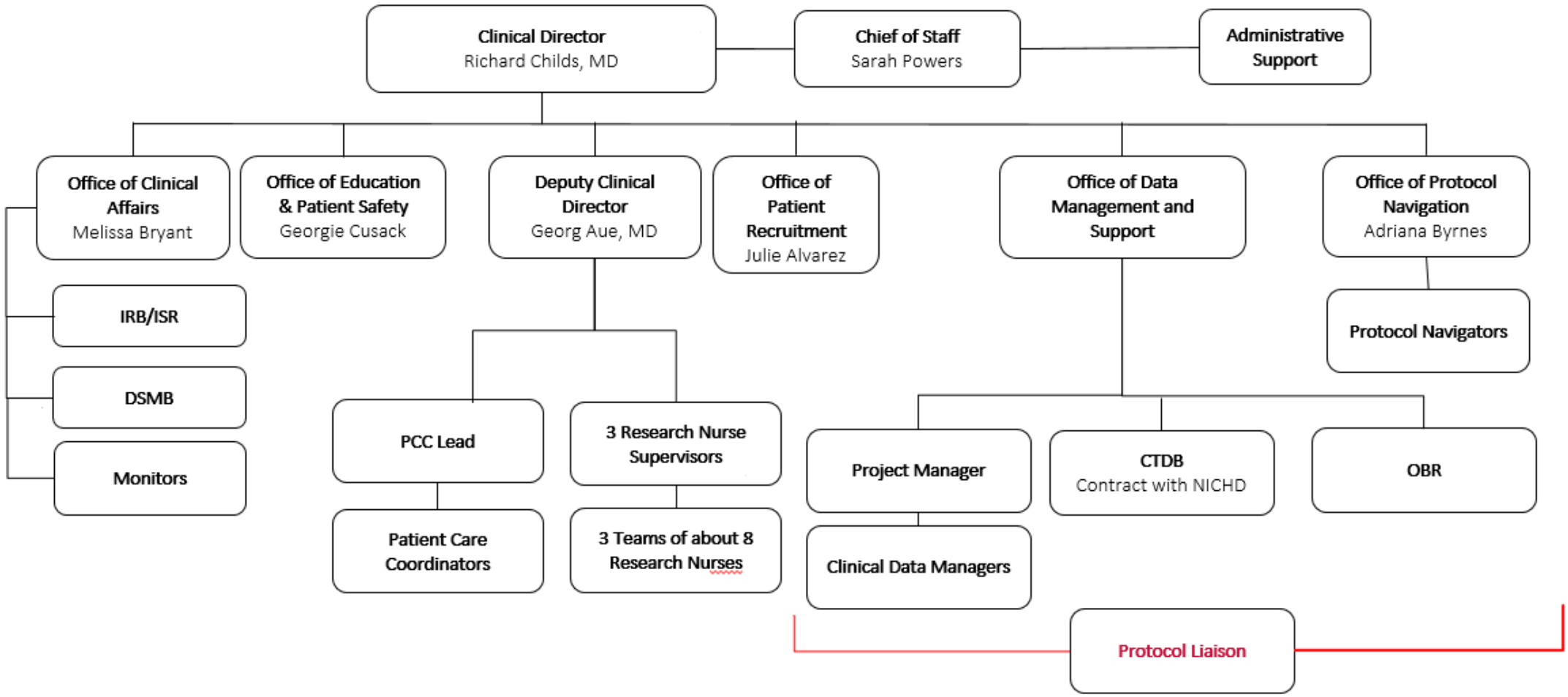
Realization

- A robust clinical research infrastructure is needed to assure compliance with good clinical practice and maximize the safety of patients involved in clinical research
- This infrastructure is
  - Necessary
  - Costly but worth the investment
  - Has many components that need careful integration to function well
  - Ever changing
- Preemptive changes initiated by the NHLBI since 2012 have put us in a good position to meet or exceed requirements for the practice of good clinical research

NHLBI Office of The Clinical Director: 2012



NHLBI Office of The Clinical Director: 2018



RED Team Report

- Many of the concerns addressed in the red team report were actively being addressed by our IC when the report came out
  - Validated our efforts
  - Momentum on these efforts was enhanced
  - A cultural change regarding patient safety became readily apparent in short order
  - Observation: Efforts to reinforce patient safety, spearheaded by the Clinical Center, became contagious across ICs at all levels of staff supporting clinical research
    - CC- Patient safety huddle
      - Attendance by CEO reinforces safety as a priority
    - Development of a drastically improved reporting system
    - The expectation that any event impacting safety needed to be not only documented but addressed in a timely fashion
    - Attitude change amongst clinicians
      - Past- “That was a freak event; it will probably never happen again”
      - Present- “OMG, we need to make sure that never happens again”

Patient Safety Effort has become contagious in our IC

- Patient Safety added to the title of our Education Office but also changes at a local level in the ICs
  - Creating a safety office
  - Review of SAEs by an extra set of eyes
  - Systematic review/auditing of NHLBI clinicians notes to make sure documentation is in accordance with CC guidelines
  - More formalized review of occurrences or STARS events by our office
    - Emphasis not only on documentation, but on follow-up

Clinical Examples of Progress

- Events being reviewed related to NHLBI have nearly doubled over the past 2 years
- Patient huddle leads critical events to be addressed immediately
  - Root cause analysis conducted quickly
  - Remediation more timely
    - I.e., the quick fix followed by the perfect fix

Case #1: Neutropenic Fever

- Critical near miss involving a pediatric patient and delayed administration of antibiotics
- Immediate Root Cause Analysis revealed:
  - Communication lapses
    - Failure to escalate issues (nursing, medicine, pharmacy)
    - Unclear communication within pharmacy re: availability and location of drug
  - Pharmacy staffing issues (e.g., off-tour mix, new hires)
  - Complex process for preparation and delivery of non-formulary medications

Case #1: Neutropenic Fever

- Improvement Strategies
  - Immediate Actions
    - “Deep Dive” conducted to evaluate timeliness of all STAT antibiotics
    - Communication pathways improved – clarifying process for escalation of issues; internal pharmacy information exchange
    - First-line antibiotics made available on patient care units

Case #2: Neurologic Emergency – Brain Code

- Adult patient with acute cerebral edema-impending herniation
- Clinical response to neurologic emergency was suboptimal
- Root Cause Analysis revealed:
  - Lack of urgency during acute response
  - Communication lapses
    - Failure to escalate issues (fellow to attending)
    - Delay in notification of neurology consultants
  - Variable nursing, medicine, and pharmacy awareness of availability of critical medications (e.g., mannitol) in the ICU

Case #2: Neurologic Emergency – Brain Code

- Improvement Strategies
  - Interdisciplinary team developed “Brain Code” algorithm
    - Immediate engagement of neurology and radiology to streamline diagnosis and treatment
  - Implementation of “neurological care bundle” in ICU
  - Active engagement of Suburban Stroke Team

Conclusions

- Webster Dictionary: Definition-Cultural: “relating to the ideas, customs, and behavior of a group or society”
  - Cultural change, for the better, has occurred in terms of how patient safety is prioritized amongst all NIH staff
- This is a process
- In my opinion, the right people are spearheading this effort
- We’re not perfect, but we are aiming for perfection