May 27, 2016

TO: Francis Collins, M.D., Ph.D., Director, National Institutes of Health
    Michael Gottesman, M.D., Deputy Director for Intramural Research, NIH

FROM: Clinical Directors, Medical Executive Committee

SUBJECT: Response to Red Team Report

We are writing on behalf of the Medical Executive Committee (MEC) of the Clinical Center (CC) which includes the Clinical Directors of sixteen NIH institutes, the Surgeon-in-Chief, and directors of the Critical Care, Pediatric and Nursing departments in the CC. This is in response to the Red Team Report on “Reducing Risk And Promoting Patient Safety For NIH Intramural Clinical Research” conducted by a subcommittee of the Advisory Committee to the NIH Director (ACD) and the implementation plan being developed to address the issues and recommendations in the report. We have carefully reviewed the report and each of the recommendations. We have had several meetings to discuss all aspects of the report and its implications.

As active participants and directors of the clinical programs, which conduct the vast majority of the clinical research and provision of care in the CC, we embrace the need for enhancing our culture of safety and for standardizing clinical practices outlined in the committee report. Indeed, we have always believed that patient safety and the highest quality of clinical care are an integral part of clinical research in the NIH intramural research program (IRP). Several critical elements related to these issues are in place and should be preserved as we implement the new recommendations. This is an integral function of the MEC and reflects the unique nature of the IRP where patients must be enrolled in a research protocol to receive treatment at NIH compared with other academic centers where the primary objective is service to their community through patient care. Some of the measures go above and beyond the recommendations of the ACD.

Several distinguishing aspects of patient care at the NIH IRP provide additional built-in safety measures that support monitoring and implementation of quality of care. For example, all patients are seen on a research protocol and therefore require careful review of their medical records for their medical condition and eligibility, ensuring they meet inclusion criteria. A specific plan for investigation and/or treatment is outlined prior to patient arrival or at the time of the screening visit. For the majority of treatment protocols there is oversight by a data safety and monitoring board, or independent medical examiner, institutional review board (IRB) and quality assurance committees at all stages of protocol development and implementation. Investigators are required to report all serious adverse events (SAEs) for monitoring by Clinical Directors and the IRB annually at the time of continuing review. Unexpected events are reported within 7 days if they are serious and within 14 days if non-serious. In some institutes, serious, unexpected or recurrent SAEs and problems are discussed at clinical care meetings and morbidity and
mortality conferences within the ICs. For all serious events that occur at the CC, root cause analyses are performed by the CC Office of Patient Safety and Quality. Extensive metrics and documentation of these assessments of quality of care at the CC are maintained and are available for review.

The MEC is comprised of Institute Clinical Directors and selected CC Department heads and plays a critical role in oversight of activities and implementation of change. In particular, we have the following concerns and present options for implementing the recommendations of the ACD subcommittee report to the NIH and IRP leadership for consideration.

1. **Clinical Practice Committee (CPC):** We support the idea of forming a CPC to increase vigilance in critical areas, to longitudinally track progress, and to make recommendations to the CC leadership. However, after extensive discussion, we have reached consensus that the oversight and policy-making for the seven areas delineated in the ACD report are beyond what a 6-8 member committee could effectively accomplish. Several of the proposed CPC functions that overlap with current activities of the MEC could be leveraged in a collaborative way. The MEC is the current policy making board of the CC and is uniquely positioned to effectively set and enforce policies for clinical care, patient safety and research across ICs. Policies and practices decided upon by the MEC are carried out because the Clinical Directors and department heads are responsible for the conduct of the clinicians within their institutes and departments. The new proposed PMAP elements for clinical care and compliance, which we endorse, will greatly facilitate this oversight.

We suggest that the 7 topic areas outlined in the ACD report be divided among 3 to 4 committees which could be subcommittees of the CPC. As recommended in the ACD report, these committees should be comprised of experts in clinical care and practice, with representation from the Clinical Directors and department heads where appropriate. The present subcommittee structure of the MEC should be examined and revised to minimize overlap between the present subcommittees and the new CPCs. The chairs of these committees will prepare reports for the hospital board and other NIH leadership who will in turn communicate with the MEC for a discussion and implementation of the recommendations. It is essential that appropriate administrative support be given to the CPC subcommittees to perform these functions successfully.

2. **Membership and Responsibilities of the MEC** To facilitate information exchange and cooperative decision making between other stakeholders and the MEC, we propose that the directors of the Office of Compliance, Human Subject Protections, and Intramural Clinical Research, the CC and the new Chief Medical Officer be made full voting members of the MEC.

3. **Compliance Office:** We support the creation of an independent Office of Compliance to bring together various compliance activities for clinical research
under one roof and enable them to be independently evaluated and administered. Setting NIH-wide standards and establishing standard operating procedures (SOPs) for activities such as risk-based monitoring of clinical protocols and trials and FDA reporting, as previously done for human subjects protection, would be a valuable function of this office. A number of institutes support offices and subdivisions that have experienced staff with regulatory expertise who perform these activities; they also have existing standards and SOPs for these activities that the leadership of the compliance office can review. We suggest that in the search for a Director of the office, priority be given to finding someone with extensive experience in conducting clinical research as a principal investigator, or have similar experience working for an agency such as the FDA.

4. **Pharmaceutical Development Service (PDS).** The NIH CC Pharmacy and staff are an integral part of all therapeutic trials in the NIH IRP and play critical roles in allowing innovative trials while ensuring the highest standards of pharmaceutical quality and safety. We appreciate the difficulties outlined in the report of re-establishing the sterile preparation unit of the PDS in the current physical plant of the CC. We suggest that if the function of the PDS to produce and control the quality of non-sterile medications and placebos can be performed safely and effectively, this service should be continued, since it is one of the special features of the NIH CC that enhance the ability to do therapeutic clinical trials. If a new wing of the CC is built to accommodate the needs of Radiology and Surgery, we suggest that reconstituting the sterile unit of the PDS in this new space be considered. Since the closure of the PDS, institutes are being asked to pay the costs of preparing sterile and non-sterile investigational therapeutics and matched controls. Consideration should be given to a funding model in which the institutes and the CC share costs for producing these critical pharmaceuticals.

5. **Governance and Funding Model for the Clinical Center.** As Clinical Directors, we are at the center of discussions among Scientific Directors, IC Directors and the CC leadership about funding and cost-efficiency issues under the current school tax system. We agree with the ACD report that consideration should be given to alternate funding models such as funding the CC from the NIH management fund outside of the IRP, with appropriate adjustment to the IRP budgets to offset the costs. Such consideration should not be rushed and should have input from Clinical Directors and other key intramural stakeholders. In addition, we suggest that the process begun in 2015 to assess CC departments with a group consisting of key IC-based stakeholders working with CC representatives continue under the new governance structure of the CC. New funds should be added to the appropriate budgets to fund the Compliance Office, the CPC and its committees, and the PDS remediation beginning this fiscal year.

6. **Chief Executive Officer (CEO).** We suggest that the CEO of the CC be a physician with extensive experience in conducting clinical research including clinical trials amongst other attributes and that members of the MEC be involved in the selection process.