Frederick National Laboratory
for Cancer Research

FNLCR Operational Update

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The Frederick National Laboratory is a federally funded research and development center operated by SAIC-Frederick, Inc., for the National Cancer Institute

DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Cancer Institute

Topics

Frederick National Laboratory for Cancer Research

- **Follow up from September FNLAC meeting topics**
  - Ebola Response
  - Partnering
  - National Programs

- **Implementation of FFRDC Best Practice**
  - User Facility
  - Strengthen Ties to Local Universities
  - Culture an ‘Intrapreneurial” Mindset – Lab-Directed R&D Fund

FNLCR Support of Ebola Outbreak Response

Manufacture of Chimpanzee Adenovirus Ebola Vaccine Drug Product

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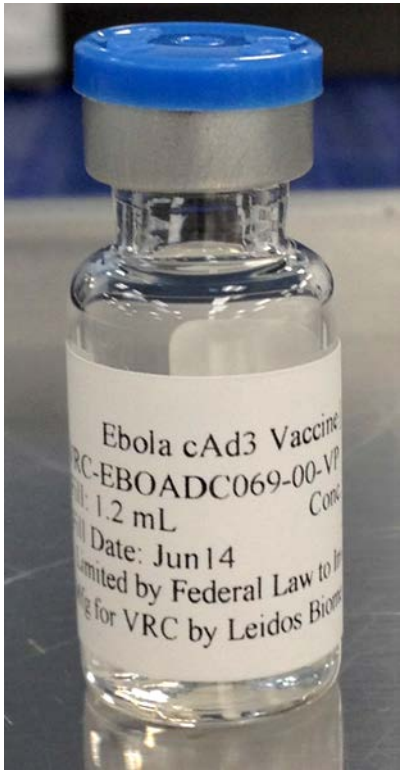
- **Vaccine Clinical Materials Program**
  - Completed manufacture of ~6000 vials of chimpanzee adenovirus vector vaccines – formulation, fill, and finish
    - The vaccine candidate was developed by the VRC in collaboration with Okairos, a European biotech recently acquired by GSK
    - 5 manufacturing runs from September to December
  - All vials were shipped to clinical sites or distribution centers as directed by NIAID
  - No additional Ebola vaccine manufacturing is anticipated in the forseeable future
- **Based on positive results of Phase I trials, NIAID is continuing with plans for larger efficacy trials in West Africa**



http://www.niaid.nih.gov/news/QA/Pages/EbolaVaxResultsQA.aspx

FNLCR Support of Ebola Outbreak Response
Support of Vaccine Clinical Trials

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Clinical Monitoring Research Program

- **Establish required infrastructure and operational centers to conduct NIAID-sponsored clinical vaccine trial in Monrovia, Liberia**

- Operational planning and project management
- Clinical trials management, regulatory and pharmacovigilance support
- Renovation of laboratory and clinical facilities in Monrovia
- Staffing of operations center in Monrovia
- Procurement - supplies, equipment, subcontracts, logistics
- Team leads for the NIAID Ebola Working Group (lab and operations)

STATUS : PREVAIL Phase 2/3 trial opened Feb 2, 2015

http://www.niaid.nih.gov/news/newsreleases/2015/Pages/PREVAIL.aspx

FNLCR Partnering Update
Approvals since last update

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- **2 new cCRADAs signed**

FNL LEAD	Partner	Subject	Duration
CRTP (Nissley)	**UCSF**	RAS Biology, Reagent, Cell Line Development and Validation	5 yrs
NCL (McNeil)	**AstraZeneca**	Nanomicelle Formulations of pharmaceuticals for delivery to solid tumors	2 yrs

- **24 Technical Service Agreements signed**
  - Total value - $1,033,145

Partnering Update

Pipeline cCRADAs with approved Concept Approval Form

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FNL LEAD	Partner	Subject	Duration
CRTP (Stephen)	**Local University**	Structural characterization of KRAS 4b hypervariable region interactions using NMR	3 yrs
NCL (Stern)	**Pharma**	Novel method to evaluate bioequivalence of nanomedicines	1 yr
BSP (Carrington)	**Major University**	Visiting Professorship	1 yr
CRTP (Holderfield)	**Top 20 Pharma**	KRAS-CRAF inhibitor screen	1 yr
ACVP (Lifson)	**Top 10 Pharma**	NHP model of targeting residual virus in individuals on suppressive antiretroviral drug treatment	1 yr
ACVP (Estes)	**Major University**	Impact of combination antiretroviral treatment and CD4+ cell depletion on the SIV reservoir in macaques	1 yr
NCL (McNeil)	**Top 20 Pharma**	Nanotech formulation of regulatory inhibitor	1 yr

NEW

National Program Implementation
AIDS and Cancer Virus Program

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- **Proposed that the ACVP acquire a new primate facility to :**
  - Enable return of current primate housing to the Center for Cancer Research
  - Accommodate anticipated cCRADA demand from academia and pharma for new AIDS primate models

- **Options being explored include existing Federal facilities, Contract Research Organizations, and leased space**

- **Key topics include :**
  - Optimizing use of existing facilities
  - Cost of fit-out and operation
  - “Buyer of last resort” if cCRADA’s do not materialize in a timely fashion
  - Early lease termination costs

National Program Implementation
Nanotechnology Characterization Laboratory

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The evolution of nanomedicine in the 10 years since the formation of the NCL creates new opportunities

NCL Nanotechnology Characterization Laboratory

Continue to Provide Assay Cascade Resource

- Provides "pharmaceutical mentorship" for materials scientists and engineers

Reformulation & cGMP

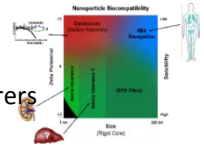
- Collaborations with Pharma, CMOs & industry consortia

Non-oncology Nanomedicines

- Infectious disease, cardiovascular, etc.

Metrology & New Methods

- Working with instrument manufacturers



Basic Research & Grand Challenges

- Immunotox
- Active targeting

Informing Regulatory

- Equivalence testing for nanosimilars
- Addressing FDA's scientific questions
- NBCDs

FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Transnational Collaboration

A detailed proposal to exploit these opportunities will be presented by Dr. Scott McNeil later in the day

Topics

Frederick National Laboratory for Cancer Research

- **Follow up from September FNLAC meeting topics**
  - Ebola Response
  - Partnering
  - National Programs

- **Implementation of FFRDC Best Practice**
  - User Facility
  - Strengthen Ties to Local Universities
  - Culture an ‘Intrapreneurial” Mindset – Lab-Directed R&D Fund

Key Opportunities illuminated by DOE Labs
Opinions will vary……

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1. **Identify a suitable "User Facility" capability that will draw a continuous flow of external scientists to FNLCR**
2. **Strengthen ties to local universities**
   - U. MD and Johns Hopkins University
3. **Culture an "intrapreneurial" mindset**
   - "Intrapreneur" – provide freedom and financial support to create exploratory new programs
   - "Venture" funding of exploratory projects is required to get them started, then transition to other funding sources
     - DOE Labs use Laboratory Directed R & D (LDRD) fund as the primary vehicle

Today's "National Molecular Microscopy Laboratory" presentation by Dr. S. Subramaniam addresses the first opportunity…

Strengthening Ties to Local Universities

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- **Potential benefits of stronger academic ties are apparent**
  - Joint appointments, new perspectives, reciprocal training, etc
- **FNLCR does not currently have a strategic research relationship with any local research institution**
  - Individual laboratories build collaborations based on expertise and mutual interest at the national level
  - The Visiting Scientist Program has not generated a robust flow of prominent scientists interested in coming to work at FNLCR
  - ~ Two dozen postdocs in FNLCR laboratories
- **How to implement, and with whom?**
  - Physical co-location akin to “Berkeley” not feasible – more of a “Sandia” or “Oak Ridge” model
  - RAS program Spokes and RAS Community - not regional, but provides a compelling draw
  - Frederick Regional Higher Education initiative with University System of MD & Johns Hopkins
    - Fulfills a regional need for creating local Higher Education (post-baccalaureate) opportunities
    - Supported by MD General Assembly

Strengthening Ties to Local Universities
University of Maryland

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- **There are ongoing tactical scientific collaborations**
- **Our first recent attempt to build a strategic university relationship**

- **Meetings in 2013 and 2014 led to Dr. Patrick O'Shea (Vice President and Chief Research Officer) joining the Leidos Biomed Board of Directors**
  - Sustained interaction provides more insight into areas of mutual collaborative interest

http://www.research.umd.edu/about/staff/oshea

Strengthening Ties to Local Universities
Johns Hopkins University

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- **There are ongoing tactical scientific collaborations but no strategic effort**

  - **Dr. Varmus hosted a visit by Johns Hopkins University leadership to FNLCR in October**
    - Included Medical School, Cancer Center, Advanced Physics Lab, and administrative leadership
    - FNLCR leadership provided an overview of some of our key programs, including RAS, biomarker and clinical support areas, and partnering
  - **Follow up**
    - Leidos Biomed has committed funding to a joint scientific symposium this spring to build scientist-to-scientist contacts
    - Ongoing discussions with leadership between JHU, Leidos Biomed, and NCI on the type of strategic relationships which could emerge

Strengthening Ties to Local Universities
Aligning with the Frederick Community

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The Frederick Major Employers Group identified the creation of a Higher Education Center as a top priority

- **In 2013, the Maryland Legislature approved the formation of an Advisory Board and funded a "needs assessment"**

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FREDERICK COUNTY, MARYLAND 1748

Needs Assessment Conclusions :

- **There is a significant need for expanded educational opportunities in Frederick, especially at the post-baccalaureate level**
  - Biological sciences, Bioinformatics, Allied Health, Engineering, Cyber
- **Local biological science expertise and infrastructure (FNLCR, BNBI, Medimmune / Astra Zeneca, Lonza, etc) can be both an asset and a customer for the Center**
- **Local academic institutions (Mt. Saint Mary's, Frederick Community College, Hood College) should be partners, and not competitors**
- ***The national reputation of the degree-granting institution is important***
  - *U. MD, Johns Hopkins*

Strengthening Ties to Local Universities
Frederick CREST- Advisory Board Activities

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- **Vision for the Frederick CREST (Center for Research and Education in Science and Technology) :** a collaborative educational and research hub in Frederick County between regional businesses and educational institutions designed to enhance economic development and job creation.
- **Drafted an operating plan consisting of an Operational Board, with a permanent Center Director and Educational Advisory Board underneath**
- **Created a draft Maryland legislative bill (HB37 / SB25) to transition to operating status and enable access to state funding**
- **Initiated contacts with U. MD and Johns Hopkins University to discuss how they could participate in the Frederick CREST**

The FNLCR and Frederick community efforts to strengthen ties with local research universities are synergistic

Culture an "Intrapreneurial" Mindset

Intrapreneurial science enabled by academic mindset and "ownership" of the project

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- **Virtually *all* significant new projects at the 3 DOE labs visited started with LDRD, funded by the Congressionally-enabled "tax" on all funding**
  - Varying levels of government involvement in project approval in different Labs
- **FNLCR does not have LDRD, but modest "Venture Funding" did exist**
  - "Technology development" funding from Office of Scientific Operations (OSO) solicited and funded Contractor-originated research proposals within the (now pivoted) Advance Technology Program – up to $3M / year
  - Leidos (corporate parent to Leidos Biomed) allows Laboratory Director to retain a portion of earned award fee to fund discretionary one-time or short-term research activities ($0.2 to $0.4 M / year)
- **Based on DOE Lab experience, a vibrant intrapreneurial scientific culture requires robust "venture" funding of pilot projects**

Lab-Directed R&D fund at FNLCR

A Cornerstone of DOE FFRDC Success

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- **"Pseudo-LDRD" - Funding from NCI's Office of the Director, rather than an "overhead" charge on all contract funding**

- **LDRD Fund Objectives**
  - Enhance the innovation, creativity, originality, and quality of its research activities
  - Facilitate collaborations within FNLCR
  - Engage local universities to encourage collaboration and strategic interactions
  - Enable demonstration of exploratory "proof of concept" projects which will lead to durable funding through contract or grant mechanisms

- **The Laboratory Director of FNLCR is responsible for the overall execution and management performance of the LDRD program**

Lab-Directed R&D fund at FNLCR
Proposal Creation

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- **Create a "Technical Fellows Team" to define a strategic focus for the initial Request for Proposals**
  - Subject to approval by Laboratory Director and NCI Office of Director
- **Open solicitation of proposals in the strategic focus areas from FNLCR scientists**
  - 3-page maximum
  - Firm fixed budget
  - Includes plan for mitigation of impact on other contract deliverables, if funded
  - 1 year, renewable upon review and approval
  - Not intended to :
    - Substitute or increase funding for any tasks for which a limitation has been established by Congress or which have been funded by NIH or any other users of FNLCR
    - Require additional funds for completion of project
    - Fund construction design beyond preliminary phase
    - Fund general capital expenditures apart from what is required for the project

Lab-Directed R&D fund at FNLCR
Proposal Pathway

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- **Proposals will be reviewed and prioritized within each directorate**
- **The Technical Fellows Team will convene a review panel consisting of themselves and external scientific reviewers, including participants from U. MD and JHU, to evaluate the proposals**
  - Review based on written proposal, directorate prioritization, and brief verbal presentations for each proposal
- **The review panel will score all proposals and provide the information to the Laboratory Director**
- **The Laboratory Director will decide which proposals to fund, based on priorities and available budget**
  - Follow up discussions may be required
- **The Laboratory Director will provide the approved proposal list, budget, and impact mitigation plans to NCI's Office of the Director**

Lab-Directed R&D fund at FNLCR
Project execution

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- **Program updates at 6 months**
- **Project review after 1 year or at expenditure of budgeted funds**
  - Each project will submit a brief (5 page max) description of what was accomplished, what remains to be done, and next steps (if any) at the end of the funding year
  - Options : Terminate program or renew with additional funding (through normal proposal process)
- **Laboratory Director will report on LDRD accomplishments annually to NCI's Office of the Director and the Frederick National Laboratory Advisory Committee**

Open issues

- **Establishing robust processes**
  - Build off of cCRADA efforts
- **Staffing LDRD efforts without impacting deliverables for other NIH programs**
- **Funding access and amounts**

Lab-Directed R&D Proposals at FNLCR

Reviewed annually by NCI & FNLAC

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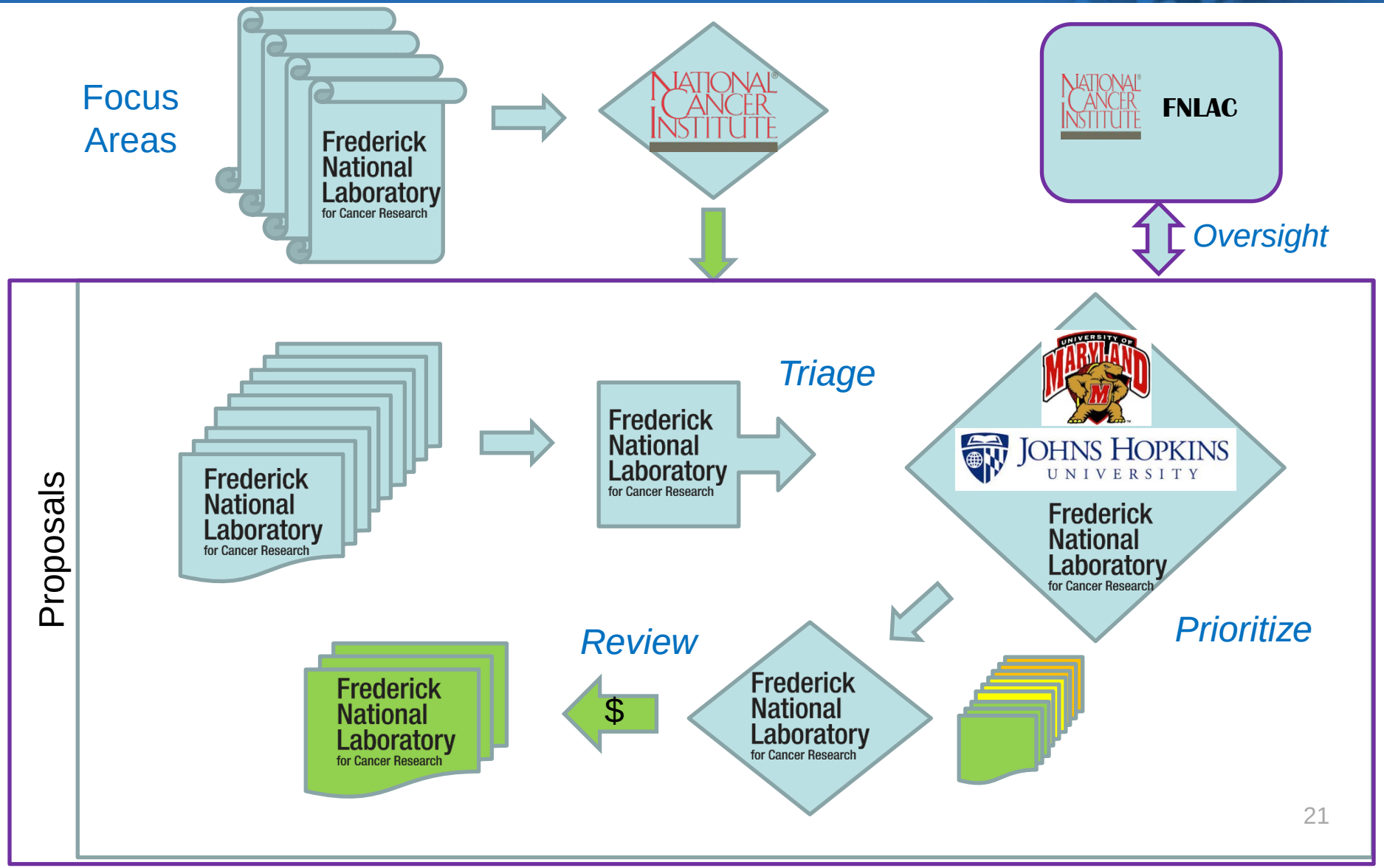

Conclusions

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- **Two key elements of FFRDC "Best Practice" are being pursued**
  - Building relationships with local research universities has emerged is a top priority for both FNLCR and the Frederick community
  - We have developed a plan to initiate "Lab-directed R & D" funding to seed new programs at FNLCR

Does the FNLAC support these efforts?