U.S. FOOD & DRUG ADMINISTRATION

Site Visit Summary
Laboratory of DNA Viruses
Division of Viral Products
OVRR, CBER, FDA

Keith Peden PhD

VRBPAC Meeting
October 10, 2024

History of LDNAV

- Established in 1988
- Andrew Lewis was appointed Laboratory Chief in 1997
- Keith Peden was appointed Laboratory Chief in 2011
- LDNAV was last reviewed in 2018
- While the Lab was set up to review and study DNA viruses as vaccines or vaccine-vectored vaccines, its role has evolved to encompass other viruses and cell-substrate safety issues as priorities change and emergencies arise

Changes in Personnel from Last Site Visit

- Haruhiko Murata, PI, left FDA in June 2021 for a position in industry
- Phil Krause, PI, retired from FDA in November 2022; independent consultant; his personnel were transferred to Keith Peden
- Andrew Lewis, PI, retired in May 2024
- Jason Gorman was recruited as a PI in 2023
- Current LDNAV organization on the next slide

Organization of the Laboratory of DNA Viruses

Laboratory of DNA Viruses

Chief: Keith Peden

Unit of Viral Gene Expression
Jerry Weir, PI

Falko Schmeisser
Clement Meseda
Alonzo Garcia
Vladimir Lugovtsev
Jackeline Soto
Amy Woerner
Cyntia Pedro

Unit of Cell Biology and Molecular Genetics
Keith Peden, PI

Li Sheng-Fowler
Romelda Omeir
Kathryn Phy
Gideon Foseh
Alena Dabrazhynetskaya
Shuang Tang
Amita Patel
Ana Sierra-Honogmann

Unit of Structural Vaccinology
Jason Gorman, PI

Tapan Kanai
Shelby Hodges

Regulatory Responsibilities of LDNAV

- Office of Vaccines Research and Review has responsibility for the regulation of prophylactic vaccines against bacterial and viral diseases
- Division of Viral Products has responsibility for prophylactic vaccines against viral diseases
- Laboratory of DNA Viruses has major responsibility for vaccines:
  - Against diseases caused by DNA viruses
  - DNA viruses as vaccine vectors for other diseases (with other Laboratories in DVP)
  - mRNA vaccines (with other laboratories in DVP)
  - Influenza vaccines
  - COVID-19 vaccines

Regulatory Responsibilities of LDNAV: Types of Vaccines

- Viral vaccines
  - Live-attenuated
  - Inactivated
- Virus-vectored vaccines
- Subunit vaccines
- Recombinant proteins
- Virus-like particles
- DNA vaccines
- mRNA vaccines

Regulatory Responsibilities of LDNAV: Types of Submissions

- Regulation of all stages of development of viral vaccines:
  - Pre-INDs
  - INDs and amendments
  - Master files
  - Biologics license applications (BLAs) and supplements
  - Post marketing commitments
  - Lot-release testing and evaluation

Some Vaccines Recently Licensed: LDNAV involvement

- Herpes zoster vaccine; live, attenuated (2006)
- HPV quadrivalent vaccine; recombinant (2006)
- ACAM 2000 smallpox vaccine; live, attenuated (2007)
- HPV bivalent vaccine; recombinant (2009)
- Adenoviral type 4 and type 7; live (2010)
- Influenza vaccine; inactivated, trivalent, seasonal; MDCK-cell produced (2012)
- HPV 9-valent vaccine; recombinant (2014)
- Shingles vaccine: recombinant gE protein with $AS01_B$ adjuvant, CHO-K1-cell (2017)
- Jynneos (MVA-BN); live, non-replicating smallpox, mpox (2019)
- CHIKV vaccine; live, attenuated (2023)
- COVID-19 vaccines; EUA and approved (2020 – 2024)
- RSV vaccine; mRNA/LNP vaccine (2024)

Examples of How LDNAV Research Program Supports the Public Health Mission of FDA (1)

- Providing guidance to industry on all aspects of vaccine development and manufacturing
- Developing reagents and assays to assist sponsors in pandemic preparedness for pandemic influenza and for COVID-19 (Jerry Weir)
- Exploring the use of pox viruses as vaccine vectors (Jerry Weir)
- Addressing issues associated with vaccine/cell substrate safety (Keith Peden, Andrew Lewis)
  - Addressing issues associated with residual cell-substrate DNA in vaccines
  - Determining whether understanding the mechanism of tumorigenesis assists in estimating risks associated with using tumorigenic cells for vaccine manufacture

Examples of How LDNAV Research Program Supports the Public Health Mission of FDA (2)

- Establishing high-throughput micro-neutralization assays against human pathogenic viruses (Keith Peden)
- Using structural data from cryo-electron microscopy to determine antibody/antigen interactions (Jason Gorman)
  - Examining and defining the humoral immune responses to natural infections and vaccinations at an atomic level with the aim of designing, evaluating, improving, and regulating viral vaccines
  - Detailing the epitopes of protective antibodies, combined with large-scale sequencing data, to aid in predicting potential pitfalls or escape pathways of vaccines
- Allows participation in WHO international collaborative studies to identify binding and neutralizing antibodies for infectious diseases (*e.g.*, influenza virus, ZIKV, LASV, and mpox)

Thank You