NIAID Opportunities Translating to Interventions (NOTIS)

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Abstract

NOTIS began as an interim solution to demonstrate NIAID's enabling role in licensed products in response to growing public and Congressional expectations to demonstrate NIH-enabled outcomes.

As outcomes assessment is not easily supported by the current NIH data infrastructure, a labor intensive manual, retrospective process was developed to document NIAID's role in FDA and USDA licensed products. This process entails: 1) Identify candidate; 2) Retrieve/select data; 3) Validate/update; 4) Archive; 5) Disseminate. The evergreen multiyear NOTIS process has and continues to generate documentation for NIAID's role in 90 plus licensed products housed in the NOTIS repository.

Each product is described by a narrative of NIAID's role in conjunction with key partners. Narrative sections include a product abstract, NIAID's enabling role(s) and public health impact. All narrative statements are supported by documentation. Data sources include NIAID SMEs, review articles, PubMed, Clinicaltrials.gov, USPTO, FDA, USDA, CDC, NIAID internet and commercial/academic websites.

Repository Information can be easily sorted and searched via: 1) Product type (therapeutic/vaccine/diagnostic/other; 2) Disease/organism; 2) Enabling roles (Basic research/Product development/Clinical research-trials/IP support/Material and patent licenses; 3) Commercial partners; 4) Initial approval date; 5) Public health impact.

Once information on a particular product is validated, the long-term goal is to be able to use that information to facilitate NIAID's ability to report on long-term outcomes. This includes: 1) Recognition of NIAID's role(s) in specific products; 2) Tell success stories; 3) Publish white papers; 4) Demonstrate linkage to public health and economic outcomes; 5) Address inevitable "outcomes" requests by Congress.

The NOTIS effort highlights the limitations with the existing data infrastructure and inability to track early stage research across the product development cycle to licensure and public health/economic impacts.

Acknowledgements

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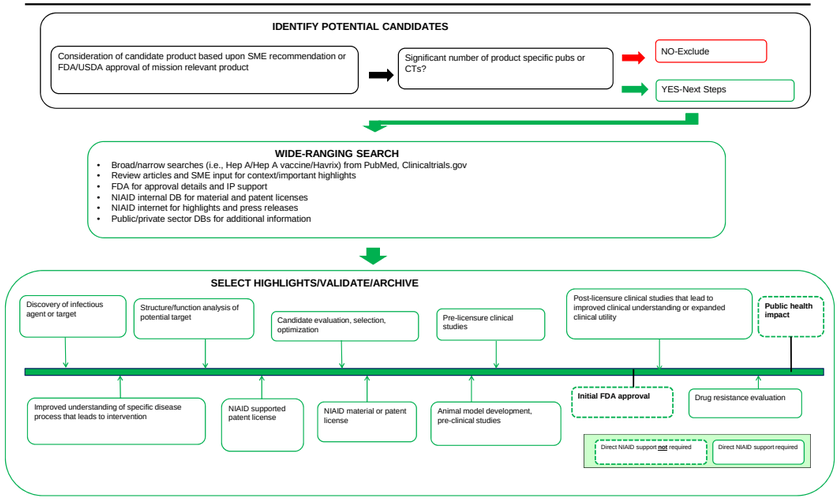
NOTIS: Rationale and Status

- An interim solution to demonstrate NIAID role in licensed products
  - A response to growing public and Congressional expectations to demonstrate NIH-enabled outcomes
  - Outcomes assessment not easily supported by current infrastructure
    - Developed primarily to identify, fund and manage high-quality research
    - Limits ability to track, report and communicate NIH's role in longer term outcomes
- Will facilitate NIAID's ability to report on long-term outcomes
  - Recognition of NIAID's enabling role(s) in specific interventions such as:
    - Did we provide extramural support for any licensed Flumist patent?
  - Tell success stories, publish white papers, peer-reviewed publications
  - Demonstrate linkage to public health and economic impact
  - Address inevitable "outcomes" requests by Congress
- Evergreen knowledge base in a single repository
  - Developed to gather documentation on NIAID's enabling roles pre- and post-licensure
  - Summarized via concise narratives with supporting documentation on 90+ products
  - Supported by easy search and sort functionality
  - Will require SME review/validation tailored for specific outcome reports

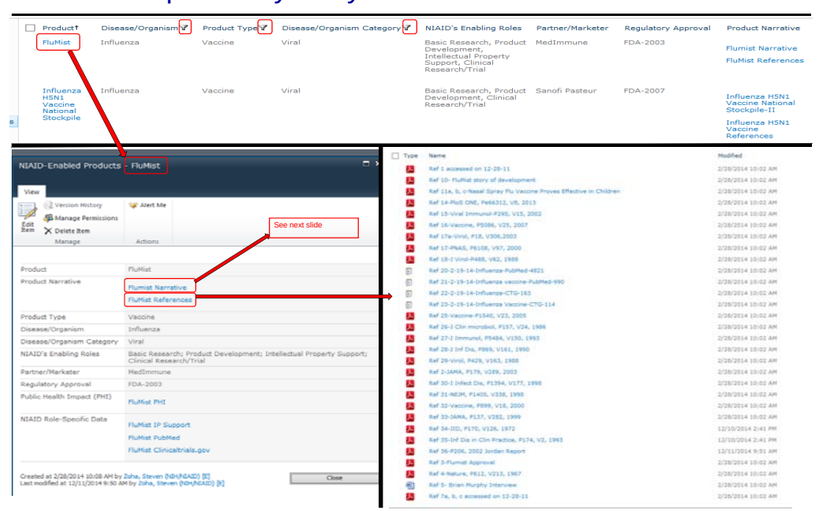
Lessons Learned

- SMEs are needed to validate
- Product list/narratives not intended to be comprehensive/quantitative
  - Variability with definition of "enabling" or "significant"
  - Point "A" - When to start documenting basic research investment
  - Difficult to trace a candidate through companies that dissolved or changed ownership/names
- Data infrastructure issues
  - Developed primarily to identify, fund and manage high-quality research
  - Too much unstructured data in too many non-integrated databases
  - Lack of enforcement/uniform QA for PI data entry into iEDISON
  - Lack of a common identifier(s) through all the baton passes from basic research to licensed product
  - Attribution of grant/funding agency (lack of, data format) in publications, clinicaltrials.gov, FDA submissions, private sector news releases
- Impact of current data infrastructure
  - Outcomes assessment is made unnecessarily labor intensive
  - A practical "non-starter" for holistic, IC-wide approaches to outcomes reporting
  - Labor burden limits scope-NOTIS limited to licensed products and their public health impacts with focus on NIAID/private sector partners
  - Case study analysis time typically exceeds that for urgent outcomes requests

NOTIS Repository: Search and Selection Process-Summary



NOTIS Repository: Layout



NOTIS Repository: Narrative

Influenza Vaccine-FluMist-Narrative (Selected Paragraphs)

Product Abstract

Influenza Virus Vaccine, Live, Intranasal (MedImmune/FluMist), for active immunization for the prevention of disease caused by influenza A and B viruses in healthy children and adolescents, 5-17 years of age, and healthy adults, 18-49 years of age, was approved in 2003[3].

NIAID's Enabling Roles

NIAID supported the development of FluMist through a nearly three-decade research collaboration between Brian Murphy from NIAID Division of Intramural Research-Laboratory of Infectious Diseases (DIR-LID), NIAID Division of Microbiology and Infectious Diseases (DMID), Hunein Maassab from the University of Michigan, Aviron and MedImmune to attenuate influenza viruses for vaccines and conduct clinical trials of vaccine candidates, including the cold-adapted master vaccine strains [(A/Ann Arbor/6/60 (H2N2) and (B/Ann Arbor/1/66)] ultimately used in FluMist by MedImmune[7,8,11,36].

Highlights include:

1) The concept of a cold-adapted influenza virus for use as a live attenuated vaccine was first published (not NIAID supported) by Massaab in 1967[4]; 4) Since 1976, cold-adapted influenza virus vaccines (CAIVs) based upon Maassab's donor strains have been tested in clinical trials conducted by NIAID scientists and others[36]. Dr. Murphy and colleagues studied intranasal installation of CAIV[34] and found that the vaccine was highly protective in adult and pediatric volunteers who were given the vaccine and subsequently challenged with influenza[35];

Intellectual Property Support

In 1995, University of Michigan licensed to Aviron the use of the master vaccine strain A/AA/6/60 *ca* (H2N2)[7a]. In 2002, MedImmune, Inc. acquired FluMist upon purchase of Aviron[7b,8a]. Although NIAID played a vitally important role in the development of FluMist, it has no patent or material licenses associated with FluMist and receives no sales royalties[5,10]. However, NIAID did provide support for US patent[9] 7344722, which is part of the FluMist patent estate.

Public Health Impact

In a recent CDC publication, it was estimated that during a 6-year study period, the number of influenza illnesses averted by vaccination ranged from a low of approximately 1.1 million (95% confidence interval (CI) 0.6–1.7 million) during the 2006–2007 season to a high of 5 million (CI 2.9–8.6 million) during the 2010–2011 season while the number of averted hospitalizations ranged from a low of 7,700 (CI 3,700–14,100) in 2009–2010 to a high of 40,400 (CI 20,800–73,000) in 2010–2011. They concluded that influenza vaccination programs in the US produce a substantial health benefit in terms of averted cases, clinic visits and hospitalizations. The results underscore the potential for additional disease prevention through increased vaccination coverage, particularly among nonelderly adults, and increased vaccine effectiveness, particularly among the elderly[14].