National Institute of Allergy and Infectious Diseases

Forging New Partnerships to Advance Pediatric Formulations Development: An Overview of NIH Resources Spanning the Formulation Development Lifecycle

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February 29, 2024

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What are the Goals of This Presentation?

- Describe the mission of the U.S. National Institutes of Health (NIH) and available NIH resources to advance pediatric formulations
- Demonstrate our intention to use these resources to support advancement of new age-appropriate formulations
- **Highlight the opportunity to use these resources to develop new models and fill key gaps that limit formulation development**

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PQRI Workshop: Model-Informed Drug Development (MIDD) Approaches in Pediatric Formulation Development

Who is NIH and What Do We Do?

- The National Institutes of Health (NIH) is one of the world's foremost medical research centers.
- 168 NIH-supported scientists from around the world have been sole or shared recipients of 99 Nobel Prizes for their groundbreaking achievements in Physiology or Medicine, Chemistry, Physics, and Economic Sciences.
- NIH is one of 11 agencies in the Department of Health and Human Services and the federal focal point for health research in the United States.
- NIH is organized into 27 Institutes and Centers with the following goals:
  - Foster fundamental creative discoveries, innovative research strategies, and their applications as a basis to advance significantly the capacity to protect and improve health
  - Develop, maintain, and renew scientific human and physical resources that will assure the capability to prevent disease
  - Expand the knowledge base in medical and associated sciences in order to enhance the economic well-being and ensure a continued high return on the public investment in research

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Multiple NIH Agencies are Interested in Development of Pediatric Formulations

NIH National Institute of Allergy and Infectious Diseases

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

NIH National Institute on Deafness and Other Communication Disorders

National Institute of Allergy and Infectious Diseases (NIAID):

- Development of long-acting or extended-release antiretroviral products for HIV treatment and prevention in infants, children, and adolescents
- Contract and other resources to support the development and advancement of age-appropriate formulations for HIV and associated co-morbidities such as tuberculosis

National Institute of Child Health and Human Development (NICHD):

- Development of appropriate pediatric formulations and pediatric drug delivery systems
- An understanding of the scientific, technical, and regulatory barriers for the development of pediatric formulation
- Taste, smell, and flavor research in infants and children
- Use and application of new drug delivery systems in pediatrics

National Institute on Deafness and Other Communication Disorders (NIDCD):

- Studies of the chemical senses—taste, smell, and chemesthesis (chemically provoked irritation) -- to enhance our understanding of how individuals communicate with their environment
- Research on the development of bitter-taste blockers to identify compounds that can mask the bitter taste of essential medications, especially for young children.

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New NIAID Contract: Resources to Advance Pediatrics and HIV Prevention Science (*RAPPS)

- Purpose

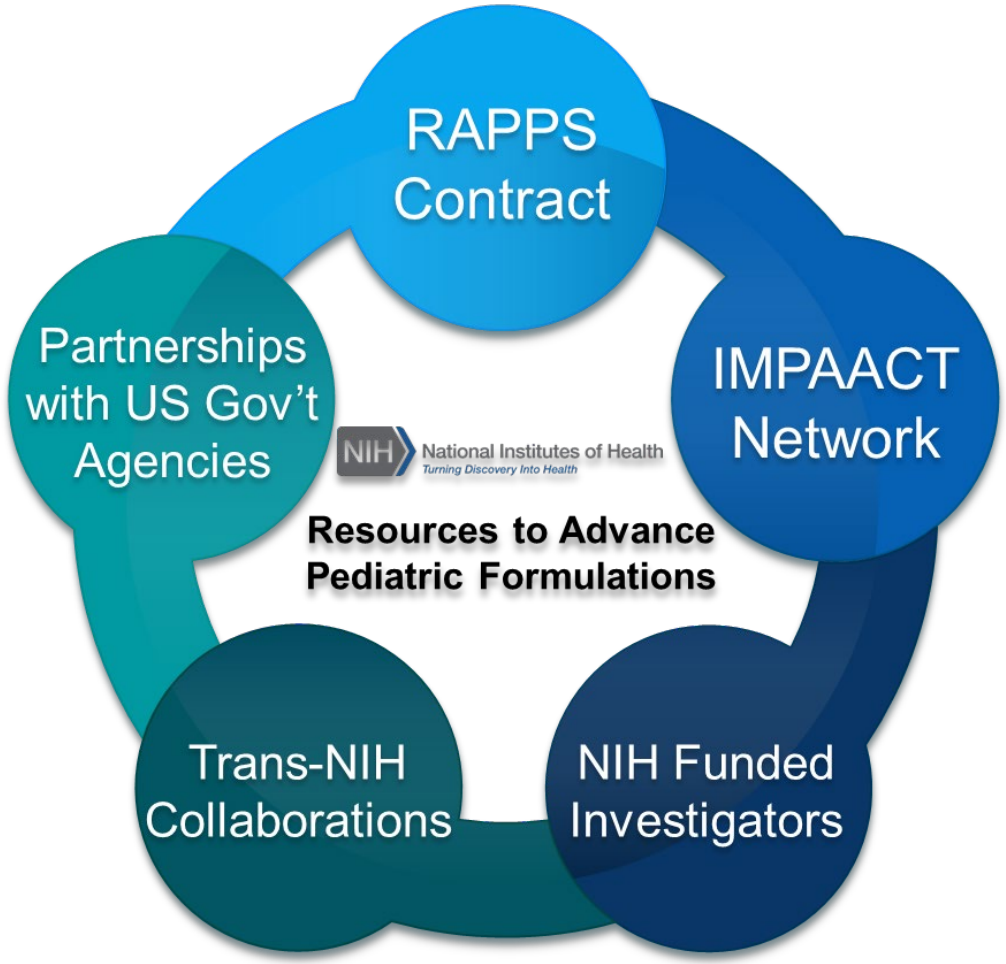
- To provide drug development resources to support advancement of the next generation of HIV biomedical prevention products and **HIV treatment and prevention strategies in maternal (pregnant or breastfeeding women) and pediatric populations**

- Objectives of the Program

- Advancement of promising next generation non-vaccine HIV biomedical prevention products into human clinical testing
- Expansion of user preference studies to better understand desire/choice and how best to engage women and men in HIV treatment or prevention
  - Emphasis on adolescent girls and young women (AGYW) ages 14-25 years old
  - **Potential for studies in caregivers of pediatric populations**
- Provision of gap-filling resources to support **HIV treatment and prevention strategies in maternal and pediatric/adolescent populations**
  - **Includes age-appropriate formulations and co-infections/co-morbidities**
  - **Includes treatment/prevention strategies in newborns/infants**

*April 2023 – April 2030

Why Partner with NIAID to Develop Pediatric Formulations?



- The RAPPS contract can provide resources to develop a pediatric formulation, including cGMP manufacture for early clinical testing
- The NIAID International Maternal Pediatric Adolescent AIDS Clinical Trial Network (IMPAACT) can provide support for clinical testing of a pediatric formulation
- NIH-funded investigators have developed novel drug delivery systems that could be considered with the right drug as a potential pediatric formulation
- NIAID can leverage our partnerships with other NIH institutes or other U.S. agencies to facilitate advancement of pediatric formulations
- **NIAID resources can be used to develop new models and fill key gaps that limit formulation development**

NIAID Contracts Have Supported Formulation Development for the Evolving Landscape of Non-Vaccine HIV Prevention

- Over the past 12 years, NIAID contracts have supported the development of 12 product IND's – leading to the activation of multiple clinical trials.
- Supported formulation types have included topical gels, films, intravaginal rings (IVR's), a long-acting injectable, and an implant.
- As products have evolved from early topical microbicides to more advanced sustained-release formulations, our contracts have adapted to support the ongoing needs of product developers.

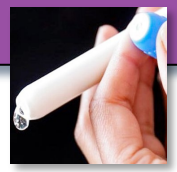
FDA Approval – July 2012

Truvada (FTC/TDF) pill

FDA Approval – December 2021

Cabotegravir injection

2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020

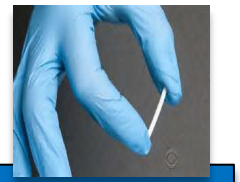


***Tenofovir gel**

*Development stopped due to adherence issues

Dapivirine IVR

SAHPRA Approval – March 2022
(South Africa)



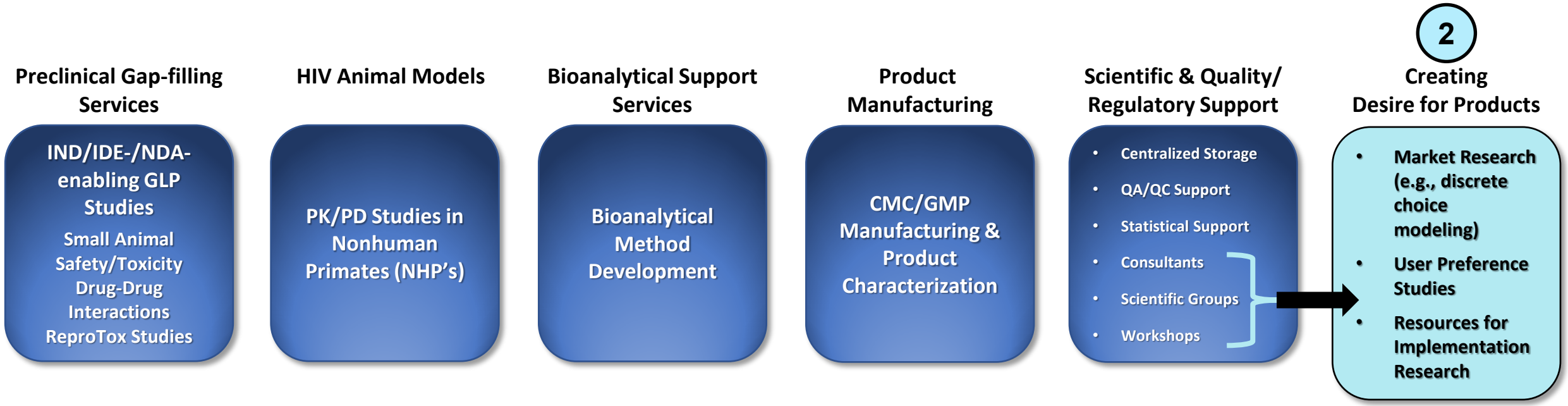
New Technologies – Injectable Depots & Implants

Topical/Coitally Dependent → **Systemic/Sustained Release**

How Can the RAPPS Contract Be Used to Support Pediatric Formulation Development?

1. RAPPS contract resources will be based on those in a current DAIDS contract but expanded to include HIV treatment and prevention strategies/age-appropriate formulations in maternal and pediatric populations

2. RAPPS contract will include greater emphasis on use of contract resources to better understand desire/choice and how best to engage women and men in HIV treatment and prevention (e.g., caregivers for infants and adolescents)

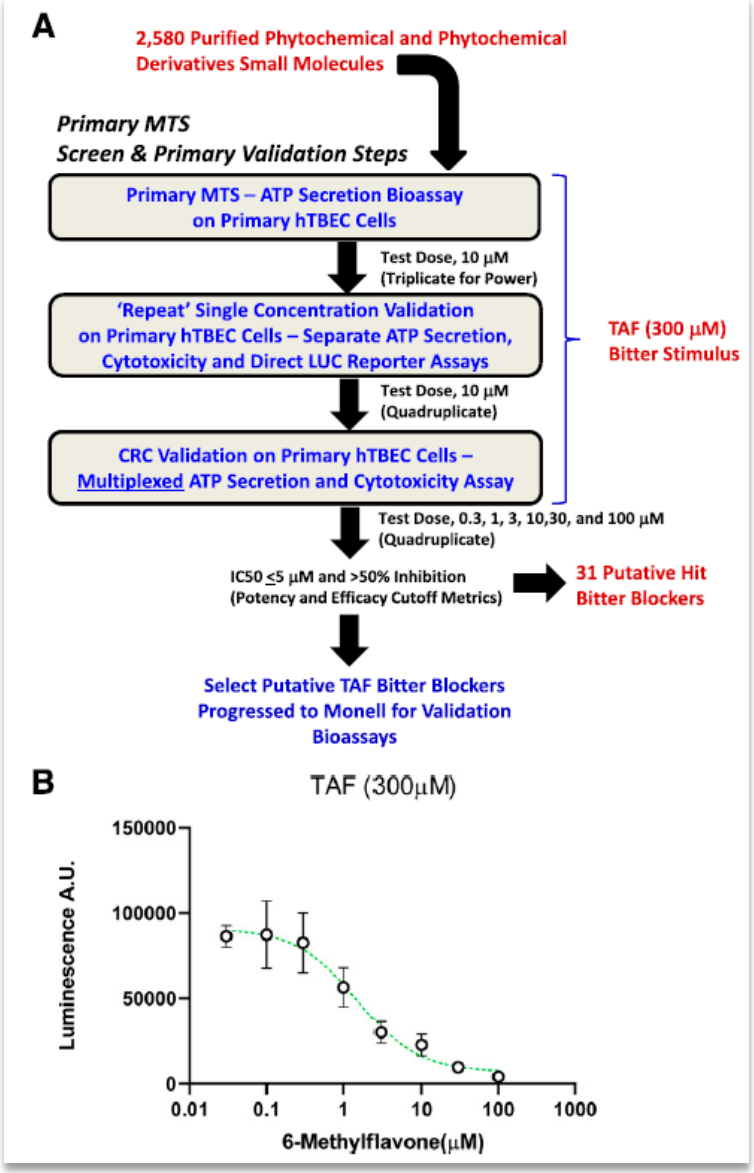


1. The resources available in these key task areas will allow expansion of the contract to support the range of preclinical activities that are necessary to develop age-appropriate formulations.

How Will NIH Leverage Resources to Support Pediatric Formulations?

- Current plans are to start with a focused set of projects as "proof of concept" to demonstrate success with available funds
  - ✓ Includes bitter blockers and development of an oral film formulation of Rifapentine
  - ✓ Expansion of an excipient database
- As the contract activities evolve over the next 6 years, NIH will assess available resources and bandwidth to determine if additional pediatric formulations can be supported
- **NIH resources can also be used to support drug-agnostic, platform-building technologies and models that can be applied across API's and diseases**

Development of Bitter Blockers for HIV & TB Drugs



- Monell Chemical Synthesis Centers has developed a cell-based primary human taste cell–based screening led to identify suppressors of drug-induced bitterness
- This group has identified 6-methylflavone as a blocker of TAF-induced bitterness
- Two NIH projects are proposed as next steps toward a "universal" bitter blocker for HIV/TB drugs
  - Project 1:
    - ✓ Identify bitter receptors activated by API's (HIV & TB)
    - ✓ Identify compounds to block activation of bitter receptors
  - Project 2:
    - ✓ Sensory testing of bitter blockers for TAF
    - ✓ Sensory profiling for 8 API's for HIV and TB

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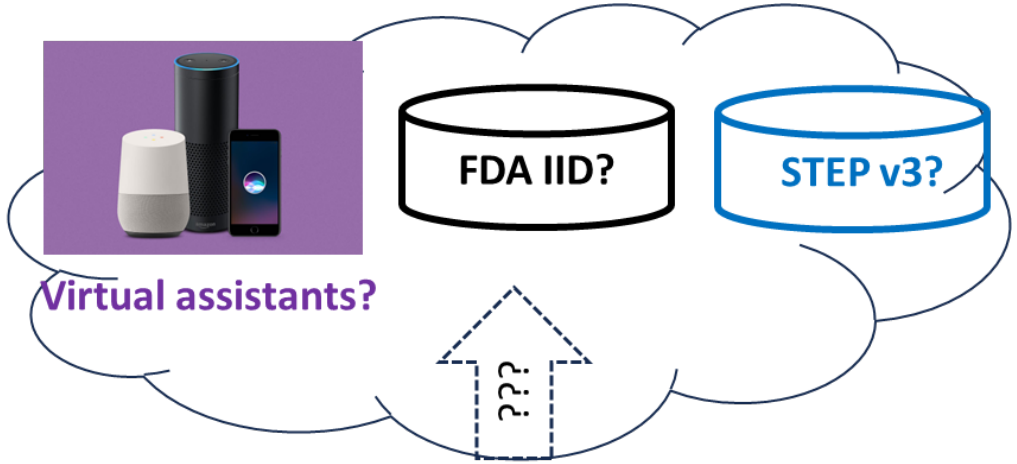
Concept for NIH Partnership with STEP Database Team

https://step-db.ucl.ac.uk/eupfi/appDirectLink.do?appFlag=login



NIH

STEP v2

EuPFI
European Paediatric Formulation Initiative

Proposed Collaboration EuPFI & NIH (US)

Enhancement AI/ML?

STEP

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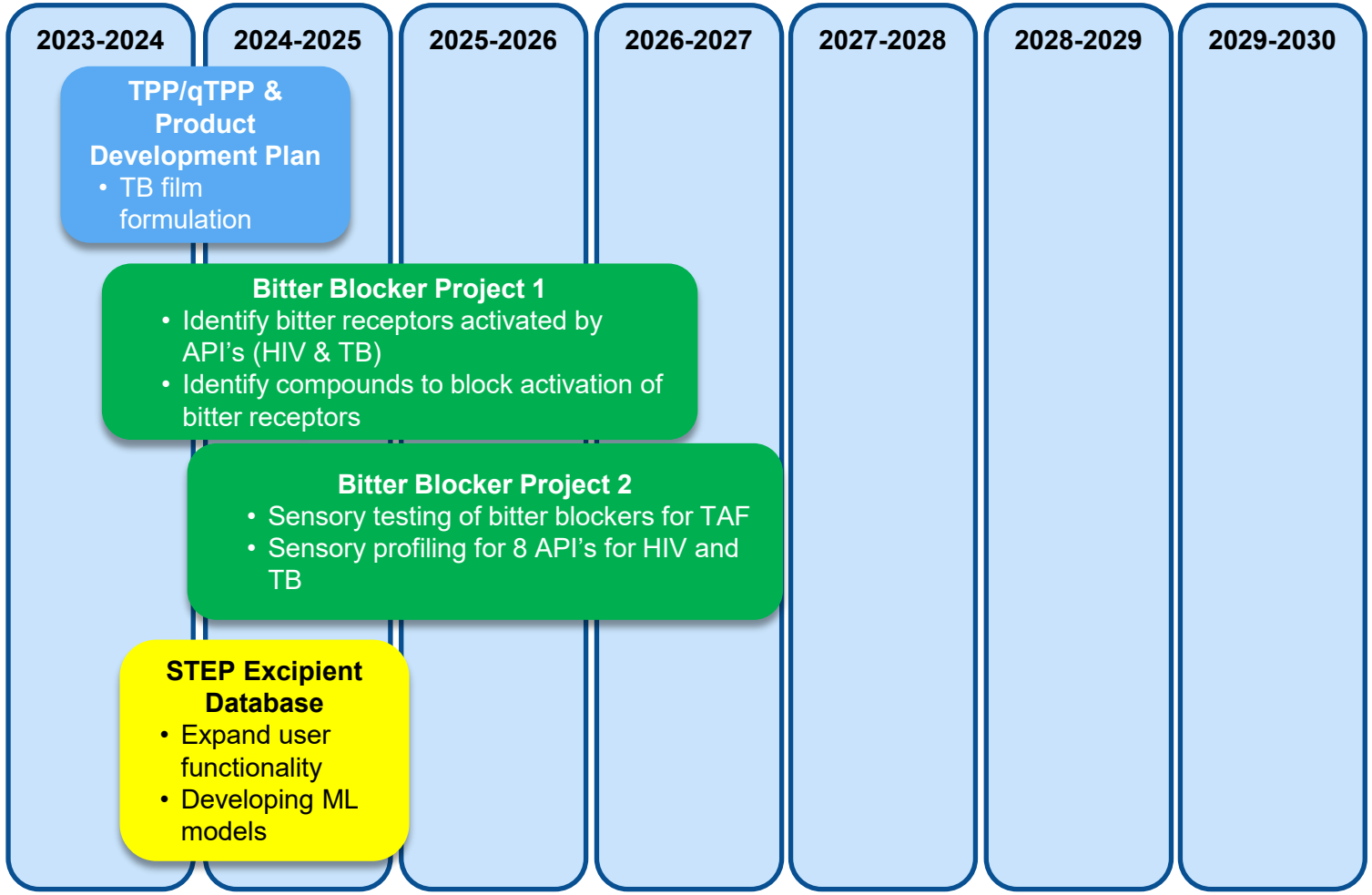
NIH RAPPS[1] Contract: Planned Projects and Timelines

Anticipated Start Dates[2]	
Q3 2023	
Q4 2023	
Q1 2024	



- [1]Resources to Advance Pediatrics and HIV Prevention Science (RAPPS); period of performance from July 2023 – July 2030
- [2]Actual start dates will be available once federal funds are obligated to the projects.

NIH RAPPS[1] Contract: Planned Projects and Timelines

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NIH RAPPS[1] Contract: Planned Projects and Timelines

2023-2024 | 2024-2025 | 2025-2026 | 2026-2027 | 2027-2028 | 2028-2029 | 2029-2030

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CONTACT US

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How Do You Learn More about These Resources?

- Link to contract webpage (QR Code):

- NIAID Program Contact for more information:

  Dr. Kristen Porter, Ph.D.
  Email: kristen.porter@nih.gov

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Research › Resources for Researchers

Resources to Advance Pediatrics and HIV Prevention Science (RAPPS)

NIAID maintains contracts to support the development of emerging HIV therapeutics, vaccines, and non-vaccine biomedical prevention (nBP) candidates. As promising adult and pediatric formulations emerge for the treatment and prevention of HIV and co-infections, there is a critical need to move these candidates rapidly and efficiently into clinical testing.

The services under these contracts are provided on a case-by-case basis and are designed to assist product developers (i.e., Sponsors) in filling key gaps in their product development pathway. These services have enabled the acquisition of preclinical data, development of essential methods, manufacture and characterization of products, fulfillment of regulatory requirements, and completion of studies necessary to advance these products into clinical trials. These contract services have also helped Sponsors obtain critical data and materials to attract additional funding and identify prospective partnerships.

Main Areas of Focus

- To fill specific gaps in a Sponsor's product development plan that are delaying advancement of an HIV prevention drug formulation or strategy into clinical testing and to product licensure
- To support preclinical/nonclinical activities for the development of drug formulations to treat and prevent HIV and co-infections in pediatric populations
- To address critical issues blocking advancement of a drug formulation or drug delivery system (e.g., *in vivo* delivery system optimization/verification, dose selection, drug metabolism and transport, pharmacokinetic (PK)/pharmacodynamic (PD) relationships, physiologically based PK modeling, etc.)

Identifying Partners & Relevant Stakeholders

Past Partners
(HIV Prevention)

MTN microbicide trials network

ALLIANCE FOR MICROBICIDE DEVELOPMENT

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

CONRAD
Leaders in Reproductive Health and HIV Prevention

POPULATION COUNCIL
Ideas. Evidence. Impact.

ViiV Healthcare

USAID FROM THE AMERICAN PEOPLE

CDC

Leveraging Relationships

Identifying Opportunities

Current Partners
(Pediatric Formulations)

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

EuPFi

GAP·f
Global Accelerator for Paediatric formulations
WHO Hosted Network

IQ INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

CLINTON HEALTH ACCESS INITIATIVE

FDA

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