

# Advocates' Primer: Understanding Bioequivalence and Pharmacokinetic Studies in Next-Generation HIV Prevention Products



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*Case Studies of Once-Yearly Injectable LEN and Four-Monthly Injectable CAB*

## Background: A New Chapter in HIV Prevention Research

The HIV prevention landscape is rapidly evolving, with next-generation PrEP options offering greater convenience and potential public health impact. As a result, HIV prevention research is evolving. Research is shifting from large, multi-year efficacy trials of new products to pharmacokinetic (PK) and bioequivalence (BE) studies that assess whether new formulations perform in the body similarly to a proven product.

This expansion of approaches is critical for advocates to understand, as it affects:

- How quickly products reach communities
- Where studies are conducted
- Who participates
- What questions communities should be asking
- How pricing and access negotiations unfold

## Next-Generation Formulations

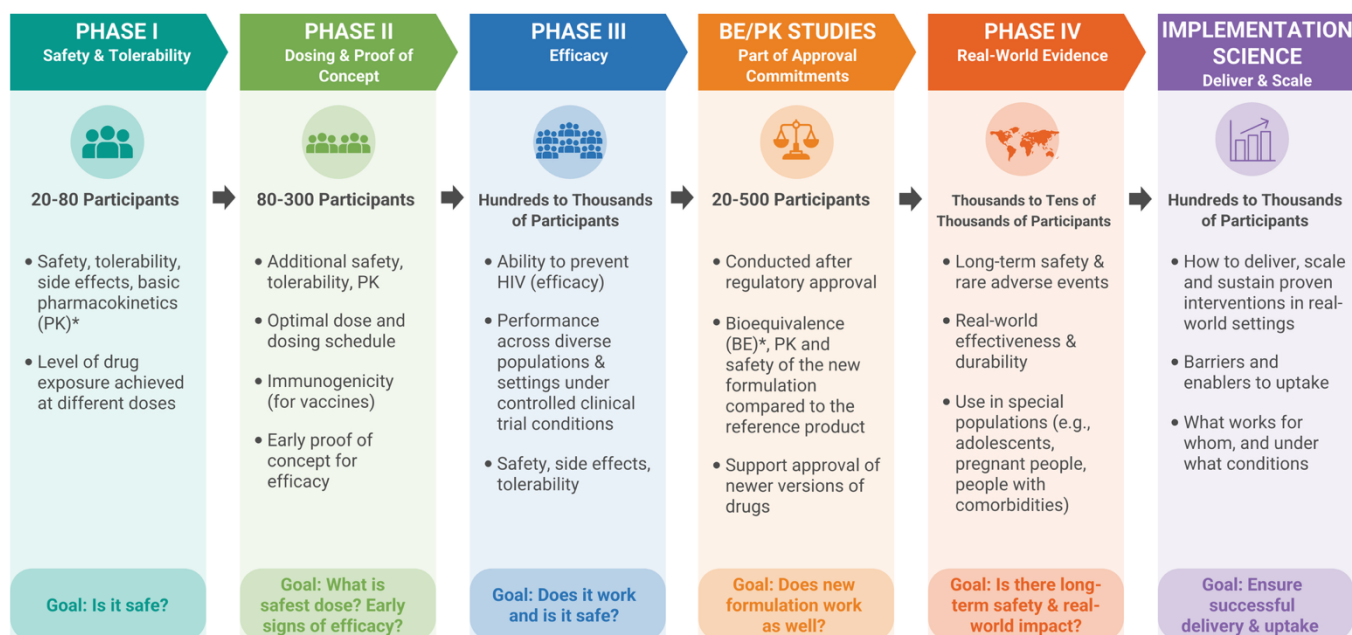
Twice-yearly injectable [Lenacapavir \(LEN\)](#) is at the forefront of this shift in HIV prevention research. Its extended dosing interval has the potential to improve adherence, expand choice, and reshape how HIV prevention is delivered. Building on this progress, Gilead Sciences is now studying a once-yearly injectable LEN formulation that could reduce dosing to a single injection per year (following a loading dose), with a potential to further simplify delivery and transform HIV prevention programs.

Injectable [Cabotegravir \(CAB\)](#) is also helping drive this transition. Following the currently approved two-monthly injectable formulation, ViiV Healthcare is now evaluating a longer-acting four-monthly injectable option using PK-based approaches rather than traditional efficacy trials. This investigational formulation could reduce the number of clinic visits required each year and reflects a broader shift towards faster development pathways for next-generation HIV prevention tools.

## Understanding the HIV Prevention Product Development Pathway

Understanding how HIV prevention products move from early research to real-world use is essential for meaningful engagement and advocacy. The pathway below provides a simplified overview of the traditional drug development process – from Phase 1 safety studies through regulatory approval and post-licensure monitoring. It also highlights where new approaches, such as PK and BE studies, fit within the evolving HIV prevention research landscape.

## Understanding the HIV Prevention Product Development Pathway



\* PK studies measure how a drug is absorbed, distributed, metabolized and eliminated by the body; BE studies determine whether products deliver the same amount of drug at a similar rate






### What Are PK and BE Studies?

Once a product has been shown to prevent HIV effectively, an important next question is whether new formulations of that product perform similarly in the body. This is where PK and BE studies become essential. Studies such as the [PURPOSE 365 study](#) for once-yearly LEN and ViiV Healthcare's [Phase IIb PK study](#) for a four-monthly CAB formulation are examples of how HIV prevention research is evolving toward PK-driven development pathways. Rather than re-establishing whether a drug works to prevent HIV, these studies are designed to determine whether new, longer-acting formulations achieve drug levels comparable to, or supportive of, concentrations already associated with HIV protection.

This approach differs from traditional efficacy trials, which measure whether a product prevents HIV by comparing HIV incidence between study groups or against an expected background incidence. Efficacy trials are typically large, expensive and time intensive. PK and BE studies, by contrast, build on existing efficacy evidence and focus instead on how the drug behaves in the body. This creates a faster and more streamlined pathway for next-generation HIV prevention products, with the potential to accelerate development, regulatory review and access. At the same time, it also reshapes the advocacy landscape, requiring advocates to engage with new types of evidence, understand what PK and BE studies can and cannot show and proactively influence conversations around affordability, equitable access, regulatory readiness and rollout planning before products reach communities.

## Pharmacokinetic (PK) Studies


Examine how a drug moves through the body

-  How quickly does the drug enter the bloodstream?
-  How long does it stay in the body?
-  Does it reach levels associated with HIV protection?
-  How long can protection potentially last between doses?
-  What happens if someone delays or misses a dose?


Especially important for long-acting HIV prevention products, because they help determine whether drug levels are high enough, in the right places, for long enough to support prevention

## Bioequivalence (BE) Studies

Compare a new formulation with an approved product

-  Does the new product produce similar drug levels to the product we already know works?



-  If the answer is yes, regulators may be able to approve the new formulation without requiring another large efficacy trial

## Case Study: The PURPOSE-365 Once-Yearly LEN Study

### What It Is

The [PURPOSE 365](#) study is a PK and BE study launched in July 2025 to support regulatory submission for a once-yearly injectable lenacapavir (LEN) formulation. It builds on the evidence from earlier lenacapavir for PrEP studies (PURPOSE 1 & 2) and is focused on whether a longer-acting formulation can maintain drug levels that support prevention over a one-year dosing interval.

### Why It Matters

- The study does not evaluate HIV incidence. PURPOSE 365 is not designed to measure HIV infections, compare against placebo/background incidence, or re-prove prevention efficacy.
- Instead, it monitors LEN blood levels over time – including whether the once-yearly formulation achieves drug concentrations comparable to the proven six-monthly version.
- Because LEN's efficacy as PrEP has already been established and confirmed through large Phase 3 trials (PURPOSE 1 and PURPOSE 2), regulators can accept BE/PK evidence as a basis for approval of new formulations.
- This approach can shorten development timelines, reduce costs, and avoid repeating large-scale efficacy trials for each formulation change.

This represents a regulatory shift toward using existing efficacy data plus BE/PK evidence – a trend that both expedites development and underscores the need for advocates to understand new endpoints and their implications for access.

## Case Study: ViiV Healthcare Phase IIb Four-Monthly CAB Study

### What It Is

The [Phase 2b PK study](#) of injectable CAB is designed to evaluate an extended-duration, four-monthly injectable formulation for HIV PrEP. Unlike the currently approved two-monthly CAB regimen, this new formulation aims to reduce the number of clinic visits and injections needed each year. In some settings, an oral lead-in may be used to assess tolerability before transitioning to long-acting injections.

### Why It Matters

- This study is not intended to measure HIV infections, compare against placebo/background incidence, or re-establish efficacy.
- The study monitors CAB concentrations in the blood to ensure that the four-monthly formulation maintains levels above the protective threshold, comparable to the approved two-monthly regimen.
- Because CAB's efficacy for PrEP has already been demonstrated in HPTN 083 and HPTN 084 Phase 3 trials, PK data showing consistent drug levels are sufficient for regulators to consider approval of the new formulation.
- Using PK evidence allows for shorter development timelines, reduced costs, and avoids repeating large-scale efficacy trials for each formulation change.

The study is designed to confirm that the four-monthly CAB formulation achieves protective drug concentrations over each dosing interval, supporting the same level of HIV prevention as the two-monthly version.

## Why These Studies Matter for Advocates

PK and BE studies can help move promising products faster, but speed alone is not enough. Advocates should ensure that streamlined research pathways do not bypass the questions communities care about most:

- Faster timelines require earlier advocacy: PK and BE studies are often shorter than large efficacy trials. This means countries may need to prepare for policy review, regulatory engagement, guideline updates, and rollout planning much earlier.
- Lower development costs should support fair pricing: If developers save money by avoiding repeated large efficacy trials, advocates should ask how those savings will translate into affordable pricing and sustainable public-sector access.
- Community engagement remains essential: Even when a study is not measuring HIV incidence, communities still need clear information about the study purpose, product profile, safety, access pathways, and implications for rollout.
- Equity must be planned from the beginning: PK and BE studies may be conducted in fewer sites or in higher-resource settings. Advocates must push for early access planning for high-burden and high-incidence communities, including adolescent girls and young women, key populations, gender-diverse communities, and others often left behind.

- Implementation questions remain central: A product can work biologically and still fail programmatically. Delivery models, provider training, supply chains, demand creation, monitoring, and user support will determine whether people can actually access and use new options.

## Advocacy Priorities for BE/PK Studies in HIV Prevention

BE and PK studies can accelerate the availability of innovative HIV prevention options. Because these studies focus on demonstrating equivalent drug levels or optimized dosing, rather than re-proving efficacy, they follow a faster regulatory pathway. However, this speed does not reduce the need for advocacy to ensure community engagement, equity, affordability, and meaningful rollout. Drawing on lessons from the [Dual Prevention Pill \(DPP\)](#), advocates can use the PK/BE pathway to push for faster, fairer, and more accountable product introduction.

### Priority actions include:

- Build community literacy on what PK and BE studies are, what they can show, and what they cannot show
- Ask sponsors for regular, accessible updates on study design, timelines, and expected regulatory pathways
- Push for early engagement with regulators, Ministries of Health, guideline bodies, and community networks
- Demand pricing transparency and affordability, especially where development costs are lower
- Advocate for access plans that prioritize communities with the greatest prevention needs
- Ensure rollout planning includes differentiated delivery models, such as clinics, community-based services, pharmacies, mobile services, and other user-centered options
- Monitor whether community concerns, safety, access, and equity are being tracked after approval

As BE and PK studies like PURPOSE 365 and the four-monthly CAB studies demonstrate, HIV prevention research is entering a new era; shifting from proving efficacy to optimizing dosing, delivery, and real-world impact. For advocates, this moment calls for translating scientific progress into tangible benefits by ensuring equity and affordability, community-driven planning, and accessible, acceptable delivery models. Advocates hold a critical role in claiming this moment – turning innovation into access, choice, and protection for all who need it, and ensuring that no one is left behind as the promise of longer-acting HIV prevention becomes reality.

This guide was created by AVAC. AVAC is an international non-profit organization that leverages its independent voice and global partnerships to accelerate ethical development and equitable delivery of effective HIV prevention options, as part of a comprehensive and integrated pathway to global health equity. Find more at [www.avac.org](http://www.avac.org) and [www.prepwatch.org](http://www.prepwatch.org).