Killed-Virus Vaccine for HIV/AIDS

Why a proven "product development" approach may be the fastest, most obvious route to an effective vaccine.

The Bottom Line.

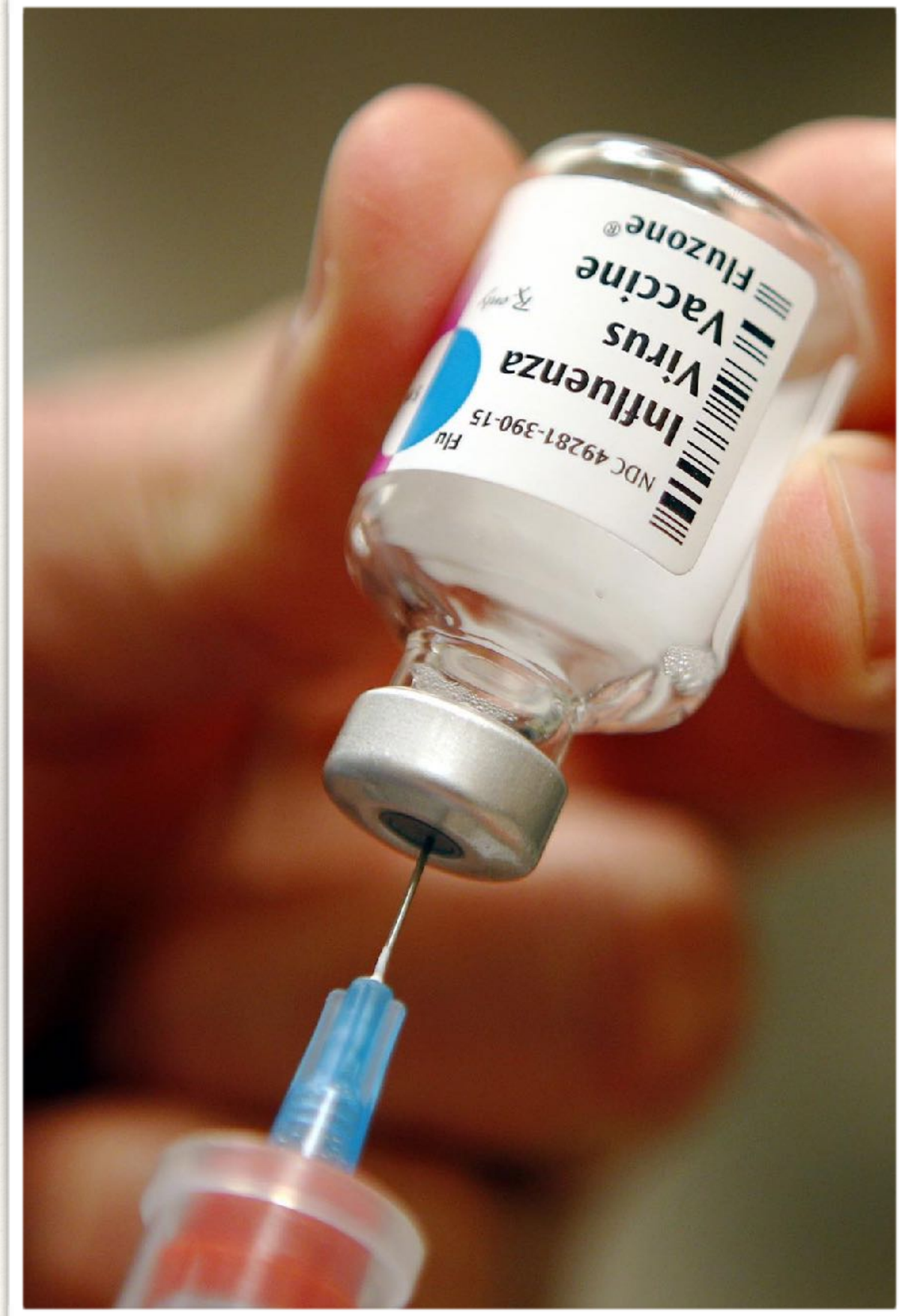
- Opportunity to develop an effective AIDS vaccine by use of well-proven, empirical product development methods.
- Never adequately evaluated by the HIV/AIDS research establishment.
- Very real chance to save tens of millions of lives and hundreds of billions of dollars.
- “Heavy-hitter” medical and science advisors.
- Can be developed in 5-10 years for $50-100M (an order of magnitude cheaper and quicker).
- Requires a bold funder willing to stand up to conventional wisdom.
- Would dramatically change history.

HIV/AIDS crisis

- 80 million infections worldwide to date, including 10 million children, mostly in sub-Saharan Africa
- Still 2 million infections and 1+ million lives lost *every year*

Killed Virus Vaccines

- Well proven, well established, well understood
- Classical, empirical, iterative product development approach
- Examples: Polio (Salk), Hepatitis A, Rabies, Influenza (Flu)
- Clinically-useful outcomes for animal viruses related to HIV in cats (FIV), horses (EIAV), monkeys (SIV)



Engineering-style Product Development

CLASSICAL VACCINE DEVELOPMENT APPROACH:

- Empirical approach using *engineering* principles:
  - Experimental *results* over theory.
  - Start with models drawn from established solutions.
  - Test first the simplest solution that could possibly work.
  - Try multiple options, test, iterate.
  - Build improved solutions incrementally.
  - Obtain useful practical answers promptly — even without unraveling any scientific mysteries.

DOMINANT "BASIC RESEARCH" APPROACH:

- Aimed at "rational design".
- Aimed at innovative vaccines.
- Requires unraveling myriad mysteries of relevant biology, with boundless complexity and woefully incomplete understanding.
- Rational design likely to be decades (and billions of dollars) away.

Simple beats Complex

CLASSICAL KILLED VIRUS APPROACH:

- Choose the virus.
- Grow it.
- Kill it.
- Test it.
- **Iterate on numerous parameters rapidly and inexpensively to identify promising candidates.**

DOMINANT "BASIC RESEARCH" APPROACH:

- Do research on mysteries of interaction between HIV and the body's extraordinarily complex immune system.
- Form hypothesis about a vaccine formulation that might work.
- Spend considerable time and money evaluating that hypothesis in (unreliable) animal models.
- Test for efficacy in humans (6 times in 33 years). It probably fails. Go back to drawing board.

More Specifically…

Iterate on every variable — "thoughtful empiricism"

- Draw upon information accumulated to date about the pathogen & human immunology.
- Evaluate various virus strains and isolates.
- Evaluate various cells to grow them in and grow them.
- Evaluate ways to purify them.
- Evaluate ways to kill them.
- Prove they're dead.
- Formulate candidate vaccine(s) in various ways, with various adjuvants, in various dosages.
- Test in lab animals for absence of acute toxicity and other adverse reactions.
- Compare immunogenicity in human microtrials — various routes of administration, number and timing of doses.
- Tweak the prior choices until you get a promising response.
- Keep doing the above until you typically get a very promising response.
- Advance very promising candidate(s) to large-scale human safety and efficacy trials.

Why not private sector (biotech/pharma)?

Inadequate profit incentives.

- Product development requires a comprehensive R&D effort.
- Greater incentive to invest in R&D aimed at therapeutic drugs.
- Zero incentive for products using non-proprietary public sector technology like killed virus vaccines, with limited potential for patents or profits.

What about public sector (NIH)?

Fully invested in hypothesis-driven research aimed at new understanding.

- Research grants, awards, positions, prestige tied to innovation.
- Attempts to unravel mysteries of extraordinarily complex underlying biology.
- Not in the business of product development, or producing near-term solutions to practical public health problems.
- Academic establishment historically disinterested in old-school product development lacking scientific “novelty.”

Why not Gates or IAVI or other entites?

In practice, they tend to act as extensions of the biomedical research establishment.

- Draw staff and advisors from the biomedical research establishment.
- Subject to conventional wisdom.
- It would require unusual boldness and conviction for one of these entities to depart from dominant paradigms of the biomedical establishment, in the face of “expert opinion.”

Many common (but temporary) objections

- If this was such a great idea it would have been tried already. ..... **You'd think so, but no.**
- This will never work. ..... **Speculative**
- This was tried already and failed. ..... **Not nearly adequately.**

See separate document for more detailed responses

- This can't be done safely. ..... **False — a "red herring".**
- The virus mutates too rapidly. ..... **May not matter.**
- There are too many strains of HIV for this to work. ..... **Speculative.**
- You'll never get sterilizing immunity. ..... **May not be needed.**
- Someone else is already doing that. ..... **Not systematically.**
- First you need proof of principle in animals. ..... **Doubtful.**

Have an expert who has doubts? Ask them to talk to us before any decisions are made.

Research Funding Comparison

Years 2000 - 2016

Genetically-engineered approaches	~ $12 billion
Classical killed-virus approaches	- 0 -

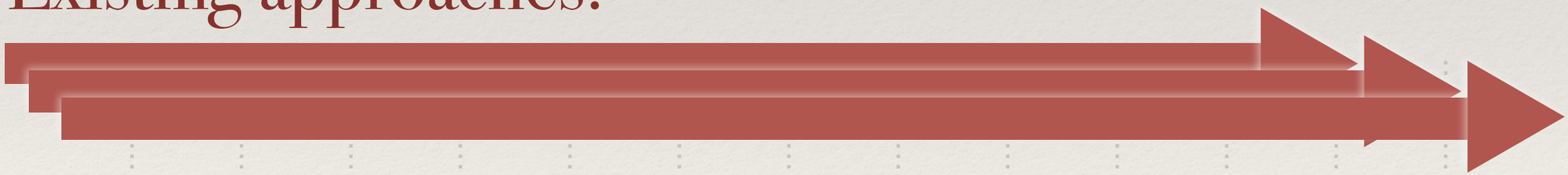
Timeline Comparison

Killed Virus:

3-5 years of candidate vaccine development

3-5 years for testing and global deployment

Existing approaches:



Still may be *decades* away from a usable vaccine. Inherently open-ended.

Cost Comparison

Killed Virus:

$50 million for laboratory research and development

$100-200 million for clinical trials (to be secured later)

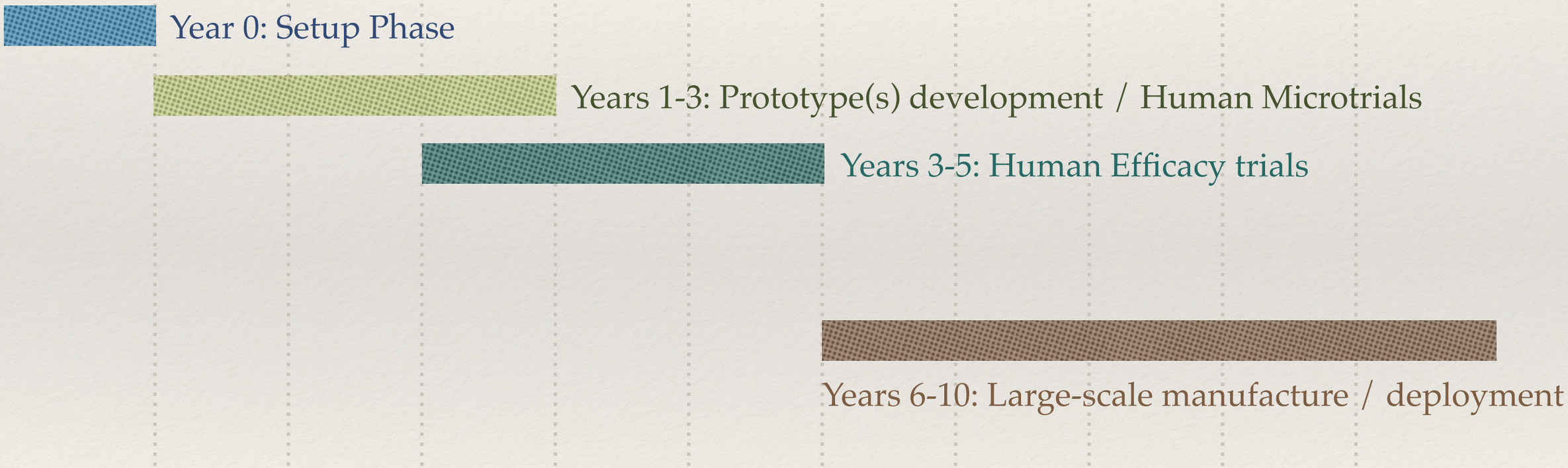
Existing HIV Vaccine R&D:

$900 million *per year*

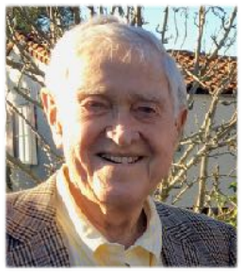
U.S. Federal Budget for HIV/AIDS:

$33 billion *per year* (FY 2016)

Phases and Timeline



Team and Advisors



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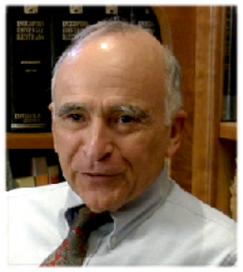

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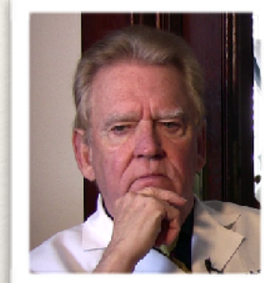
Senior Scientist



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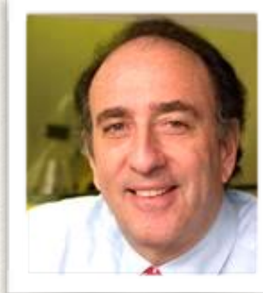

Jay Levy, M.D.
Clinical Advisor

Funding Precedent

Salk's famous killed polio vaccine from 1955

- Vehement opposition by the scientific establishment.

- Basil O'Connor of the March of Dimes funded national trial of Salk's vaccine in a million U.S. school kids despite staunch opposition from the scientific experts of the day.

- Stopped U.S. polio epidemic in its tracks.

- Now used in 100+ countries; 40-50 million doses annually.

- Salk revered by general public but never inducted into the U.S. National Academy of Sciences.

Funder Profile

- AIDS funding entities are unlikely to help — wedded to conventional wisdom.
- Visionary maverick philanthropist needed.
- Willing to pursue common sense solution — even contrary to “expert opinion”.
- Welcomes opportunity to dramatically change the course of history.