

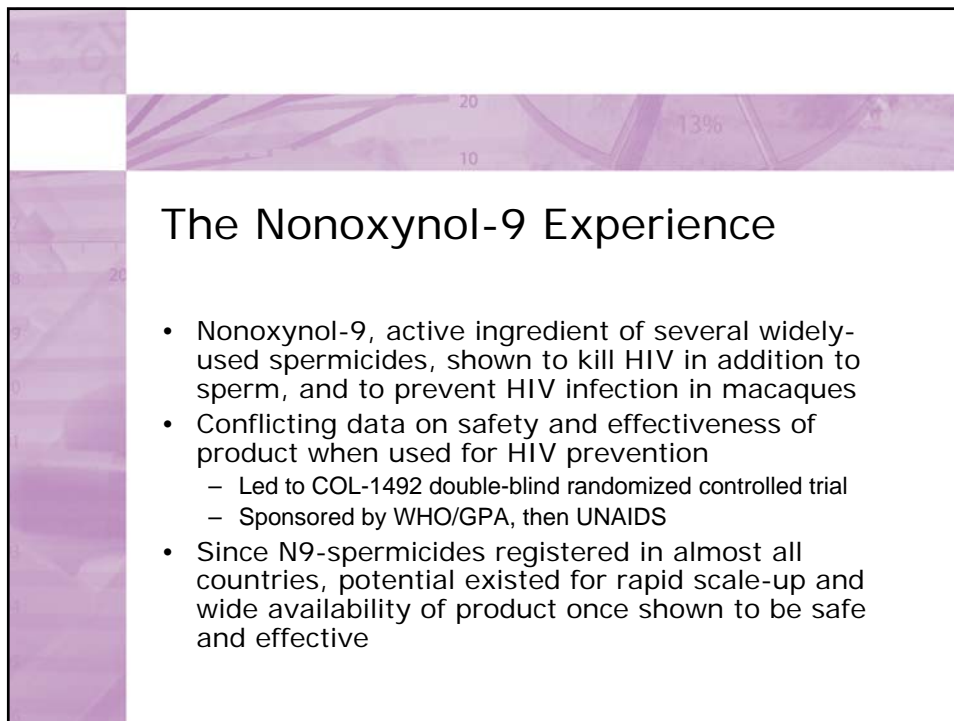
World Health Organization

HIV/AIDS Programme

Strengthening health services to fight HIV/AIDS

Planning for Introduction of Microbicides

Tim Farley  
Controlling Sexually Transmitted Infections,  
Department of Reproductive Health and Research,  
World Health Organization, Geneva



The Nonoxynol-9 Experience

- Nonoxynol-9, active ingredient of several widely-used spermicides, shown to kill HIV in addition to sperm, and to prevent HIV infection in macaques
- Conflicting data on safety and effectiveness of product when used for HIV prevention
  - Led to COL-1492 double-blind randomized controlled trial
  - Sponsored by WHO/GPA, then UNAIDS
- Since N9-spermicides registered in almost all countries, potential existed for rapid scale-up and wide availability of product once shown to be safe and effective

## Plans at Conclusion of N-9 Trial

- Planned scale up of production facilities
  - Off-patent product, distribution networks well established
- Phased expansion of availability according to priorities:
  - Phase III trial participants
  - Communities from which trial participants arose
  - Countries in which trial conducted
- Planned parallel actions in other countries not involved in the research

## New Microbicide Gels

- “Proper” Sequence of Events
  - Completion of study/studies
  - Registration dossier submitted
  - Licensure approval (country of manufacture)
  - Parallel licensure process in high HIV incidence countries
  - Rapid scale-up of production facilities and distribution networks

## New Gels -- post-licensure studies?

- Key questions
  - Patterns of use (frequency, consistency, type of partner)
  - Use with or without condoms
  - Difficulties of use
- Formal adverse event reporting
  - Would be nice, but technically impossible due to nature of product and patterns of use

## Realistic sequence of events

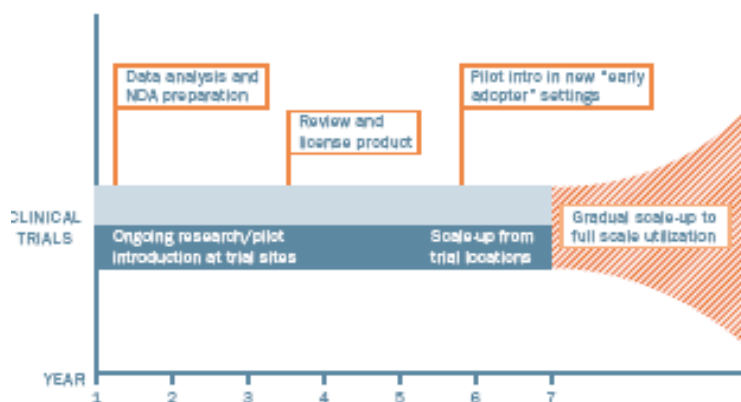
- Registration pathways may not be smooth
  - Possibility that US FDA does not approve product, gives partial endorsement and/or requires additional studies
  - Local NRA might require additional studies on safety and/or acceptability in own population of users
  - Might be several years to complete approval process

## Plan for Introductory Studies

- Need to understand and pilot manufacturing, distribution and introduction of product
- Can be accomplished through phased series of "Introductory Studies" in selected priority populations
- Mechanism to manufacture, export, import and distribute product prior to registration

## Microbicide Development Strategy

TABLE 4 Illustrative product introduction timeline



## Post-Marketing Surveillance of Norplant

- Implantable progestogen-only hormonal contraceptive
  - 5 year duration of action
  - Requires physician insertion and removal
- Licensed in developed countries (UK, USA, ...)
- Research and development of product conducted in both developed and developing countries
- Concerns over safety, acceptability, insertion and removal events
  - particularly in countries with no experience with the method

## PMS Norplant

- Prospective cohort of new users
  - 6,000 index subjects (Norplant initiators)
  - 6,000 controls (sterilisation, IUD initiators)
  - Followed for 5 years, irrespective of changes in contraceptive method
  - China, Bangladesh, Sri Lanka, Chile, Thailand, Indonesia, ...
- No specific endpoints of primary concern
- Provided reassuring information on acceptability and safety
- Important in reassuring regulatory authorities and facilitated registration and introduction



## Microbicide Introduction Studies

- Key issues
  - Acceptability
  - Condom use
  - Patterns of use (frequency, consistency, types of partners, ...)
- Will be difficult since use is not well structured, compared with “provider-dependent” methods
- Must plan for such studies NOW, so that protocols are ready to launch once Phase III trials completed