HIV Rapids

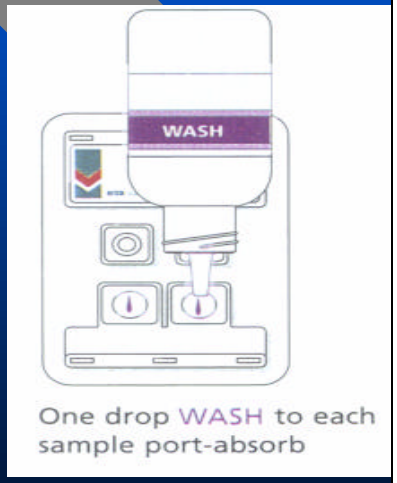
Trinity Biotech Plc

Sept 2001

Marie Mc Carthy

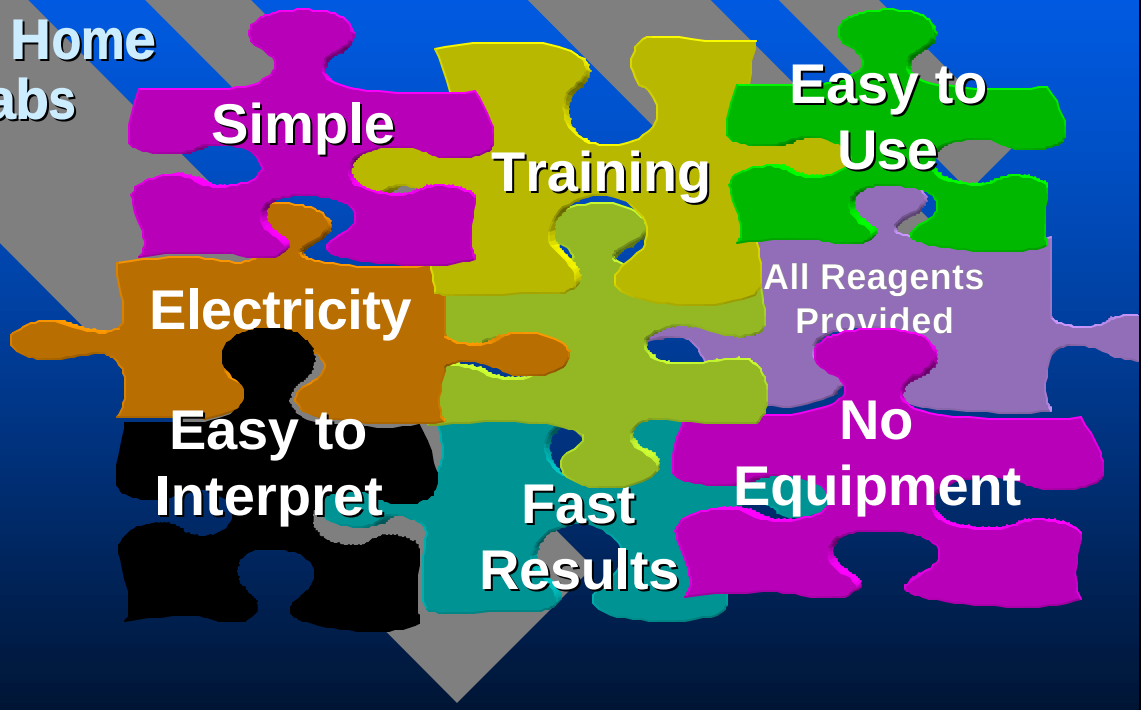
Trinity Biotech Rapids History

- Capillus™:
- SeroCard HIV
- Uni-Gold™ rapid tests



What is a rapid Test and Why use rapid Tests??

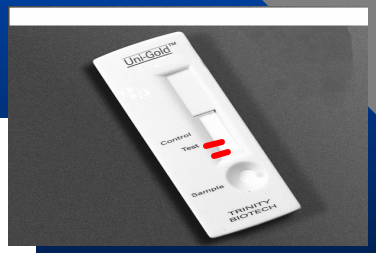
- One-Step Technology
- Self-Contained test
- Aimed at POC, Home testing, small labs
- Speed
- Easy to use
- Limited Testing Facilities
- Out of Hours Testing



Uni-Gold™ Rapid Tests

Hormone

- hCG
  - Cassette
  - Stick



Infectious Diseases

- HIV
  - Capillus
  - SeroCard
- H pylori
- HBsAg
- Strep A
- Malaria

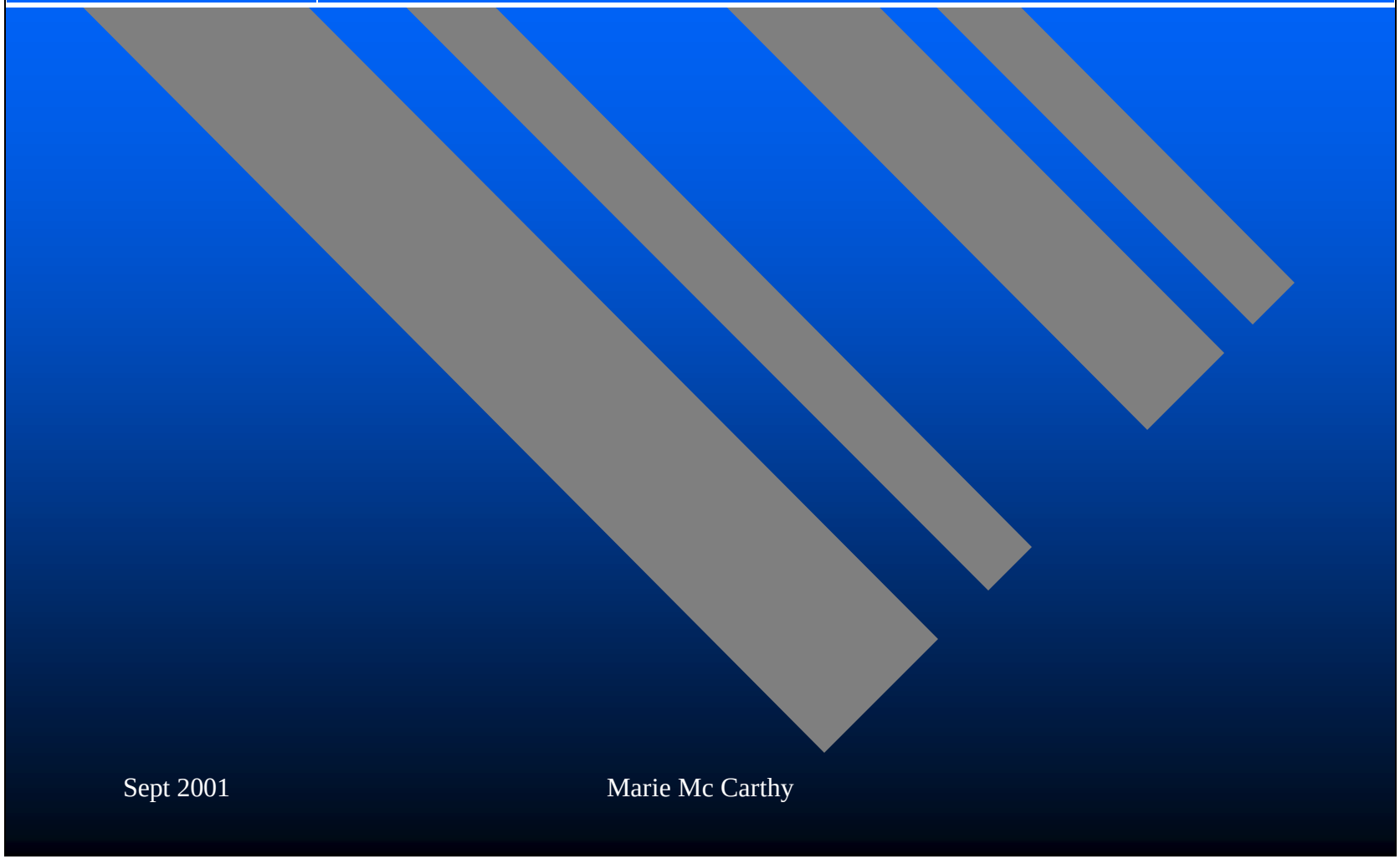
HIV Rapids

- Diagnostic Applications
- Capillus HIV 1/ HIV 2
- SeroCard HIV
- Uni-Gold™ HIV
- Selling HIV rapid tests

HIV the Beginning

Twenty years ago, on June 5th 1981 the CDC Flagship publications Morbidity and Mortality Weekly report (MMWR) reported 5 cases of Pneumocytis carinii pneumonia affecting young gay men in Los Angles!

1926-1946	Some scientists believe HIV spread to humans from monkeys



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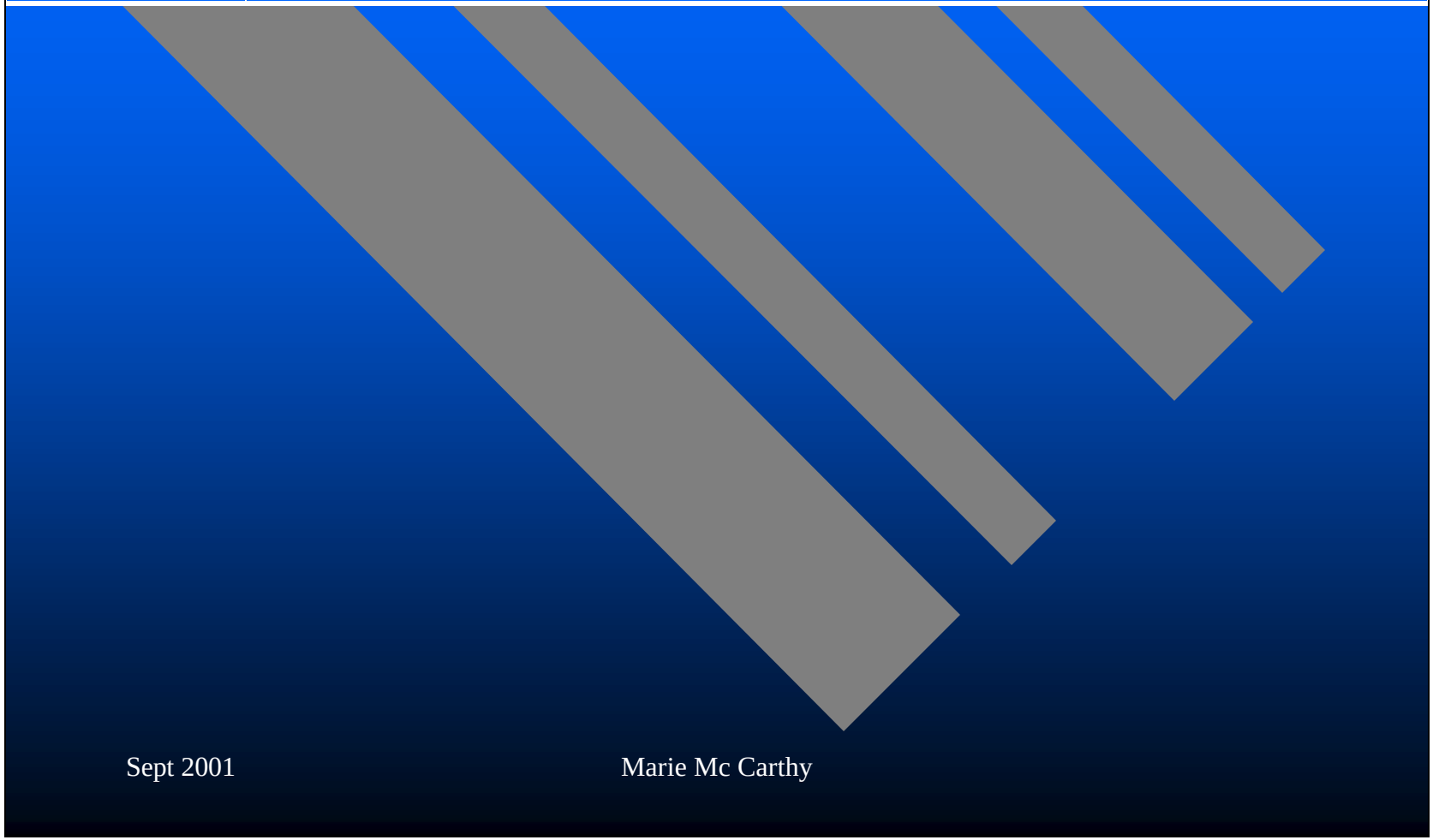

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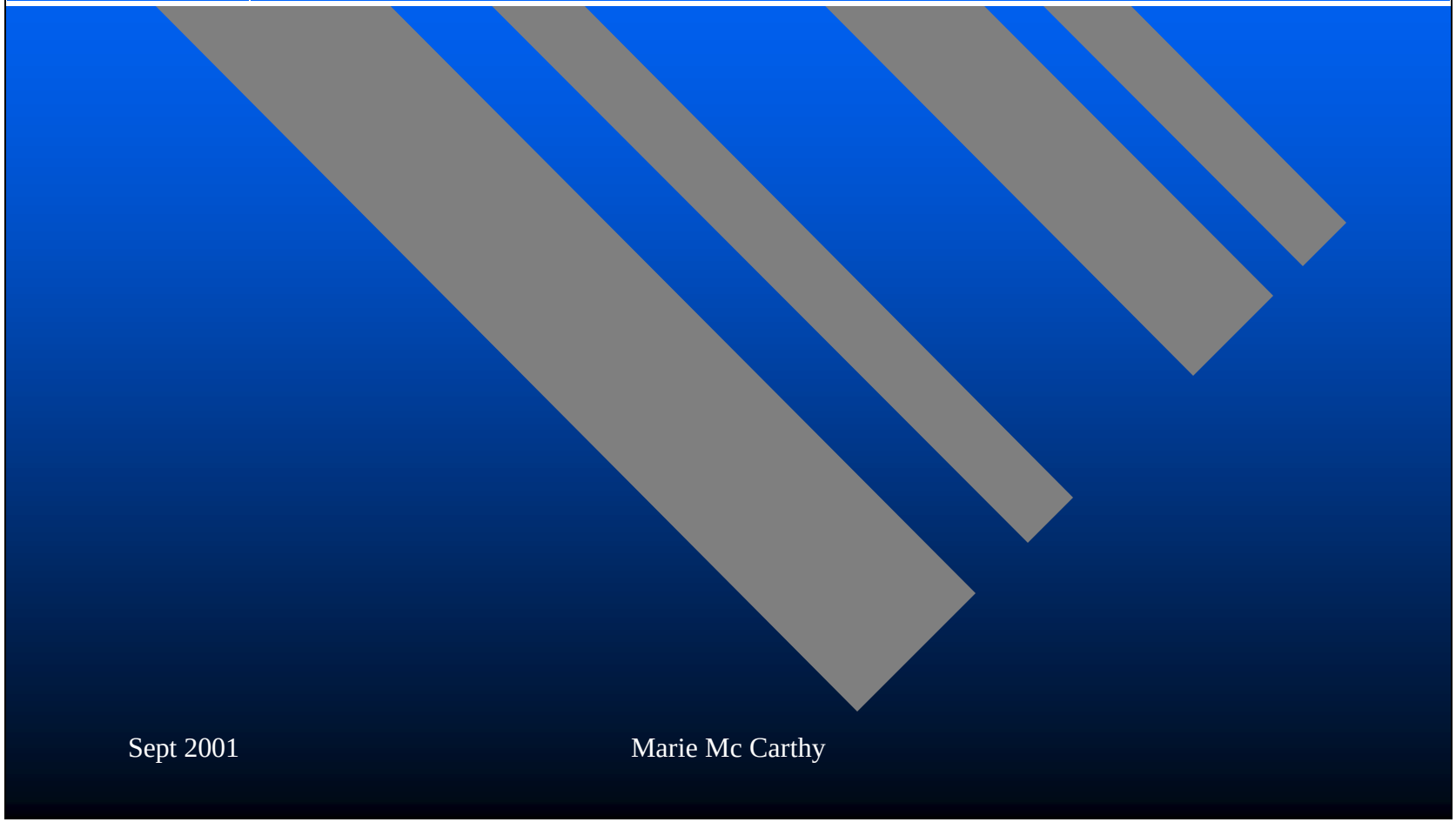
1978	Gay men in US and Sweden



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1989	**First kit to detect HIV-1 antigens**

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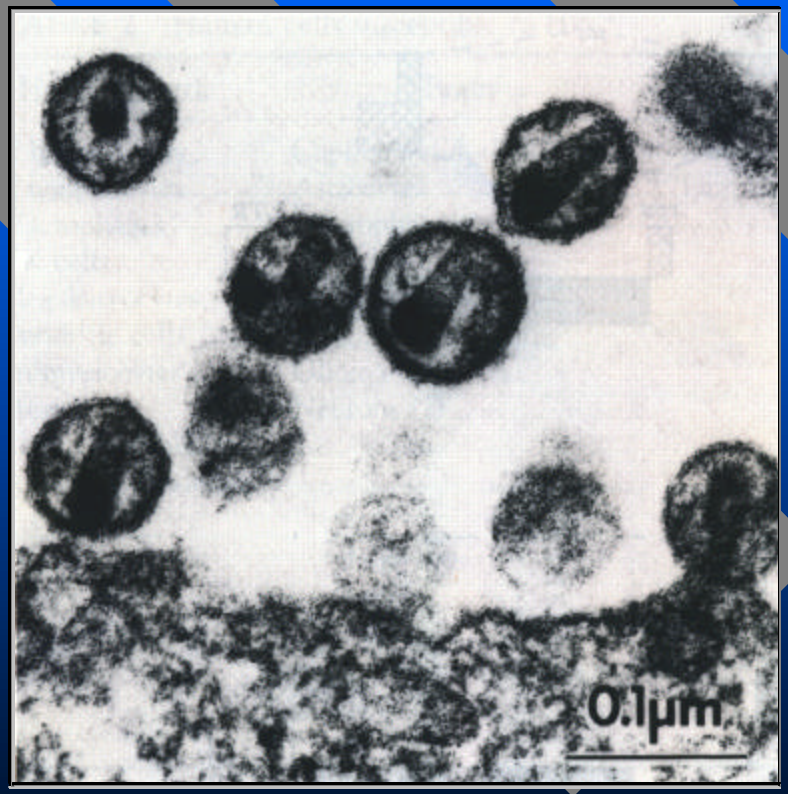
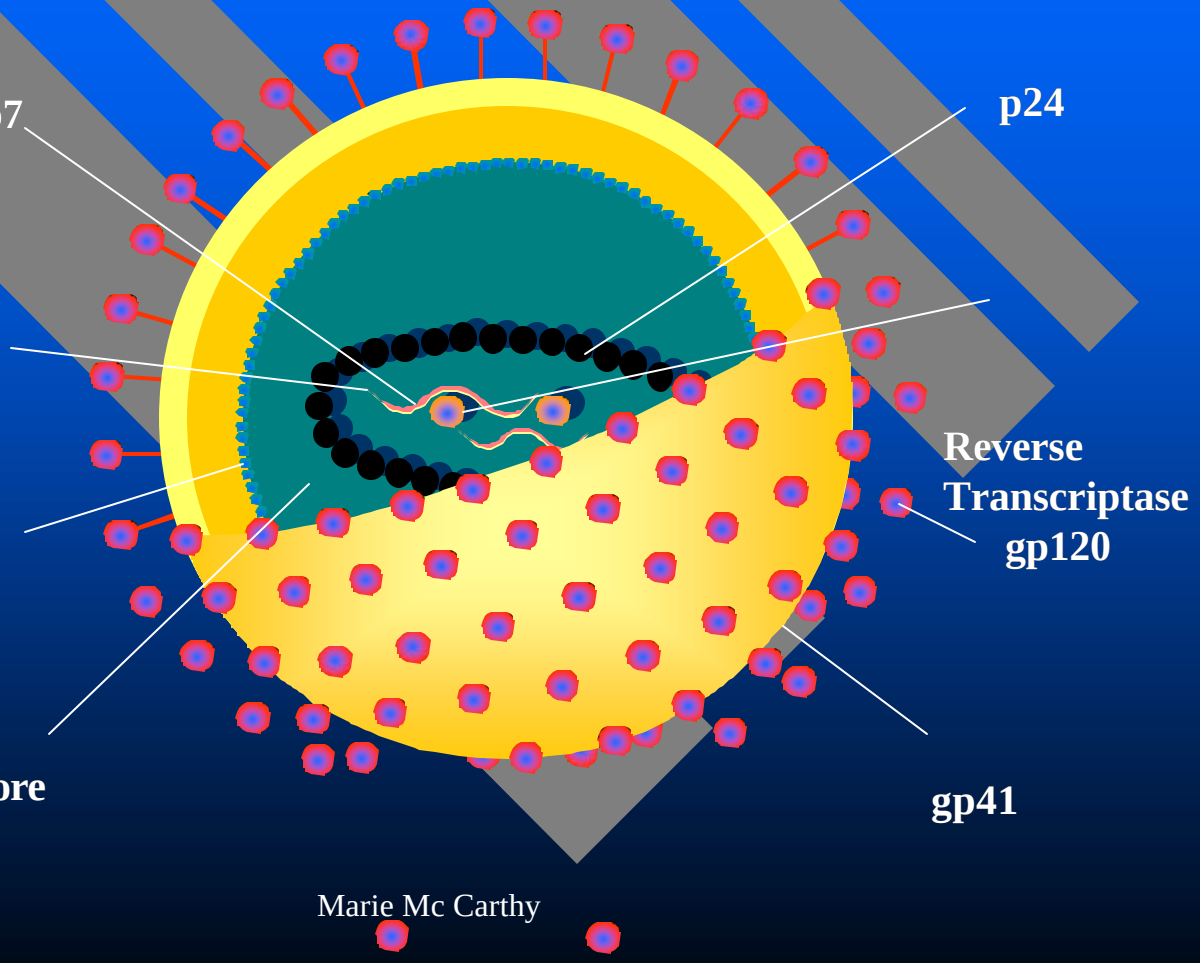
1991	10 million have HIV worldwide- 1million of whom are in the US.

HIV Overview



The HIV virus was discovered in 1984 and identified as the causative agent of AIDS.

HIV Overview

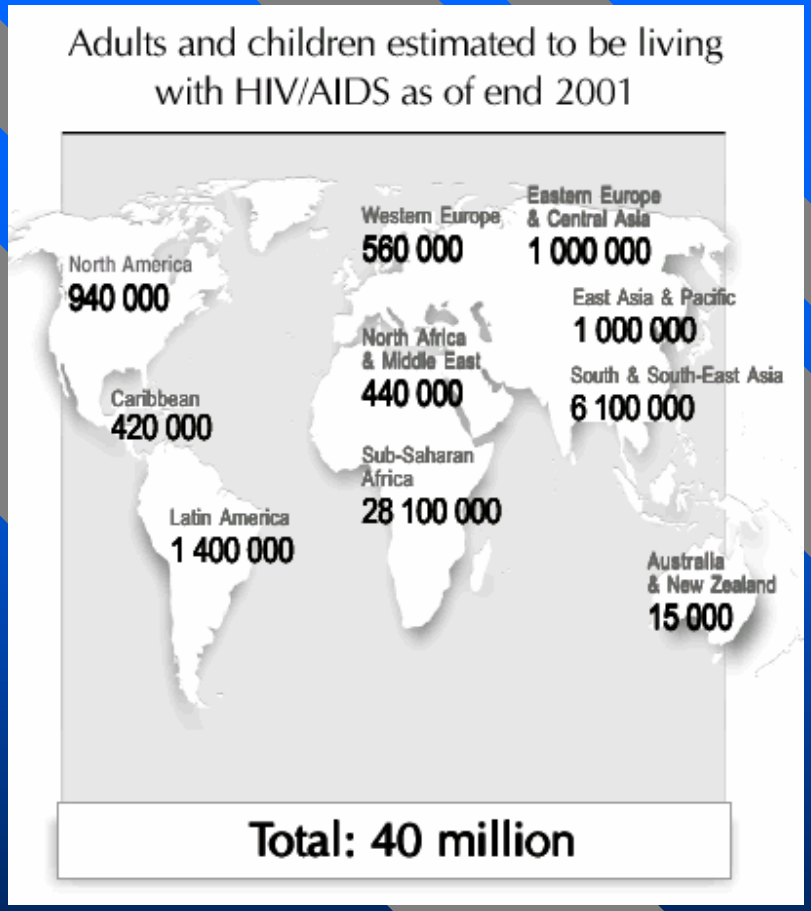


Understanding the make up of the virus was the key to developing tests to confirm exposure to the virus.

HIV Overview

- Since the 80's HIV has infected more than 60 million people with 3.0 million d 01.
- 4th leading cause o
- Over 95% of a c n the developing world. Young adults a women.
- In the year 2000, in Africa, there were 200,000 deaths due to war. There were 2,000,000 due to AIDS!

Trinity biotech



1/3 of those currently living with HIV/AIDS are aged 15-24.

Most of them do not know they carry the virus!

Sub-Saharan Africa

2.3 M African People died of AIDS in 2001
2.4 M new infections in 2001
28.1m Africans live with the virus
Prevalence rate among pregnant women varies from 30%-43%
However in Uganda prevalence among adults continues to fall.

Uganda

First African country to have subdued a major HIV/AIDS epidemic:

Prevalence in pregnant women has fallen for 8 years in a row:

29.5% in 1992

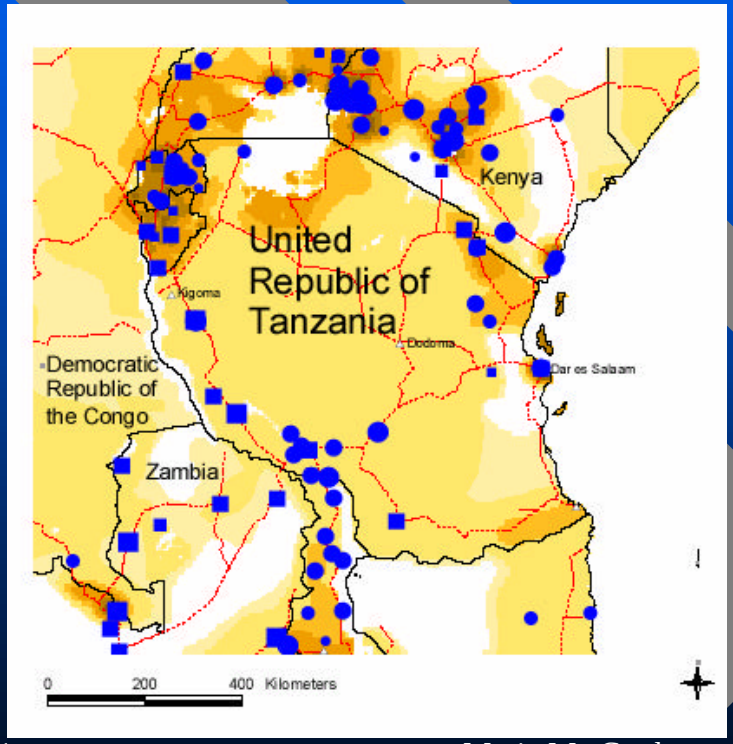
to

11.25% in 2000

Uganda

- Information.
- Education.
- Communication.
- Decentralized programmes that reach down to village level.

United Republic of Tanzania Epidemiological Facts on HIV/AIDS



SENTINEL SURVEILLANCE IN PREGNANT WOMEN

Percent seropositive

1999 - 01	1996 - 98	
		0 - 0.9
		1 - 4.9
		5 - 9.9
		10 - 19.9
		+20
△		Major cities
		Main roads

Population density (pers./sq.km)

0 - 10
10 - 50
50 - 100
100 - 250
250 - 500
500 - 750
750 and more

United Republic of Tanzania Epidemiological Facts

Population 35,965,000	Estimated Number living with AIDs
Adults and Children	1,500,000
Adults (15-49)	1,300,00
Women (15-49)	750,000
Children (0-15)	170,000

Adult Rate 7.8%

United Republic of Tanzania Epidemiological Facts

Estimated number of Deaths	140,000
Estimated number of living Orphans	810,000

*Statistics 2001

Tanzania

40% of adolescent girls in Tanzania harbour serious misconceptions about how the virus is transmitted.

50% of Adult Tanzanian women know where they can be tested for HIV and only 6% have been.

Uganda

- Information
- Education
- Communication
- Decentralized programmes that reach down to village level.

Diagnosis of HIV

Antibody tests:

EIA; Indirect antibody sandwich, antigen sandwich

Western Blot; indirect antibody

Rapid tests; indirect antibody sandwich, antigen sandwich

Antigen tests:

EIA P24 tests

4th Generation:

Combi tests (EIA detecting antibody and antigen)

Diagnosis of HIV

Screening and confirmatory algorithms

EIA screen, western blot confirmation.

Multiple EIAs – screen and confirm

Multiple rapid tests- screen and confirm

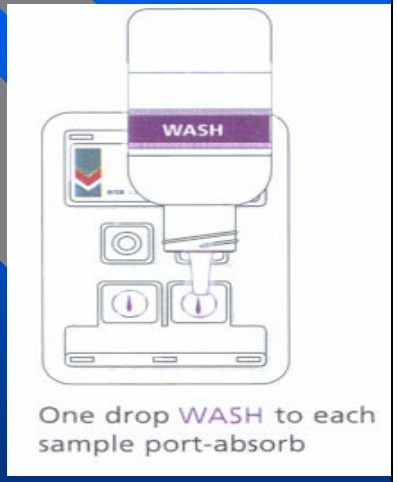
WHO and CDC have recommended and set guidelines for the use of HIV rapid tests in screening and confirmatory algorithms.

Trinity Biotech
HIV rapid Tests

Capillus™ HIV1/HIV2

SeroCard™ HIV1/HIV2

Uni-Gold™ HIV1/HIV2



Involved in the manufacture and sales of HIV rapid tests for over 10 years

Tests are used by WHO, CDC and on a number of programmes in Africa, India and in the developing world.

Trinity Biotech HIV Tests

- Simple
- Easy to use
- Ease to interpret
- All of the reagents are supplied
- Immediacy of Results
- Newer tests one step and
- Do not require refrigeration

Can be used to:

- Reduced Spread of Disease
- Immediate intervention and reduced loss to follow up
- Effective counselling

Capillus™
HIV 1/ HIV 2

Simple

Rapid assay

Easy to use

Whole Blood

Serum

Plasma

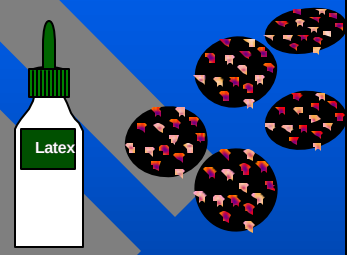
Capillus™ HIV 1/ HIV 2

3 Main Components

Recombinant HIV coated latex particles:

HIV-1: Recombinant HIV 1 *env* protein representing: gp 120 and gp 41.

HIV-2: Recombinant HIV 2 protein representing: gp 120 and gp 34.

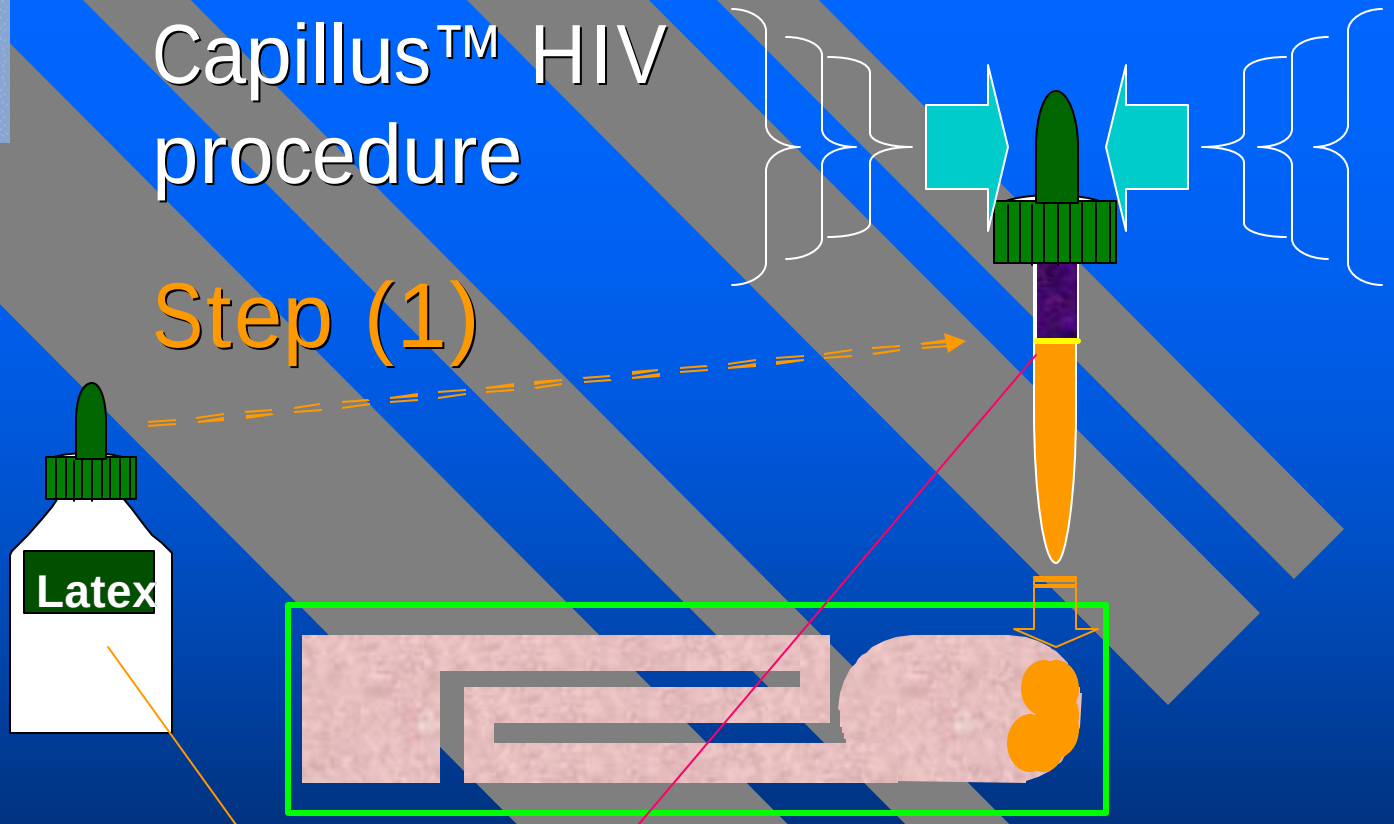


Patented Capillary Slide

Positive and negative controls

Capillus™ HIV procedure

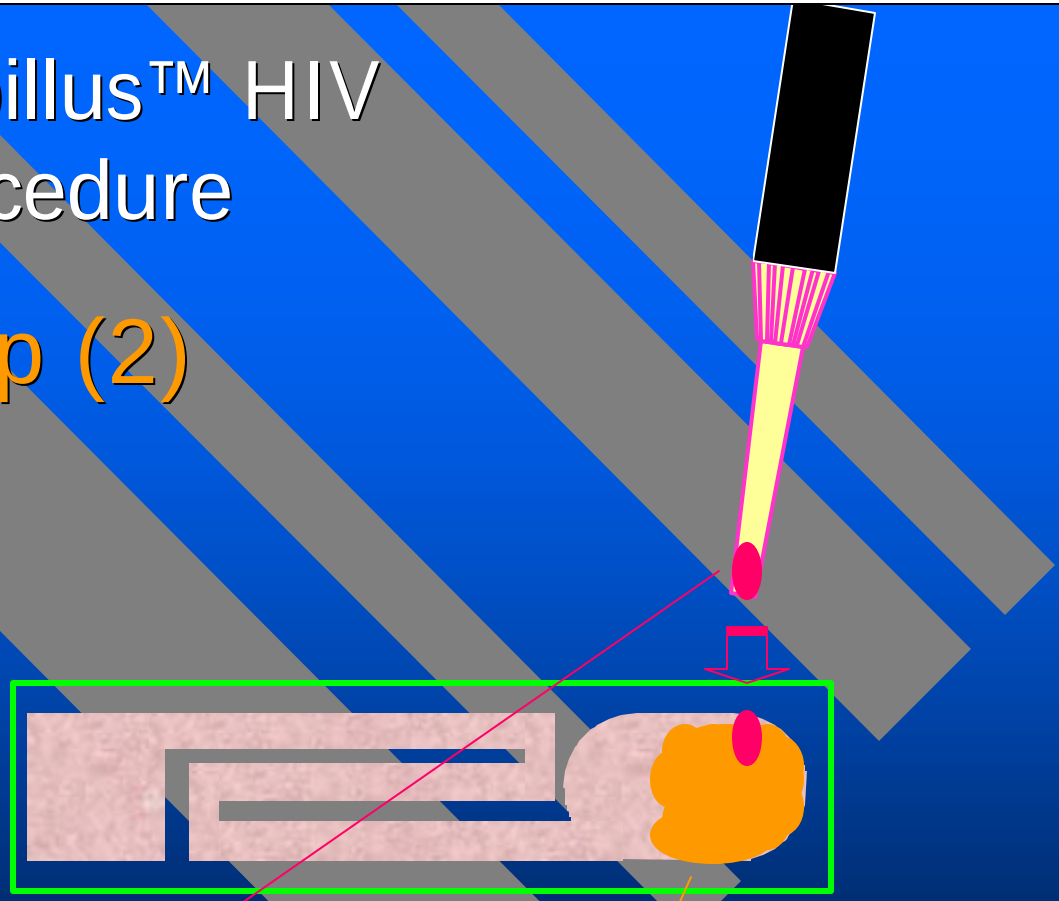
Step (1)



Mix latex thoroughly, draw up to the graduation on the dropper and dispense onto the top edge of the mixing well.

Capillus™ HIV Procedure

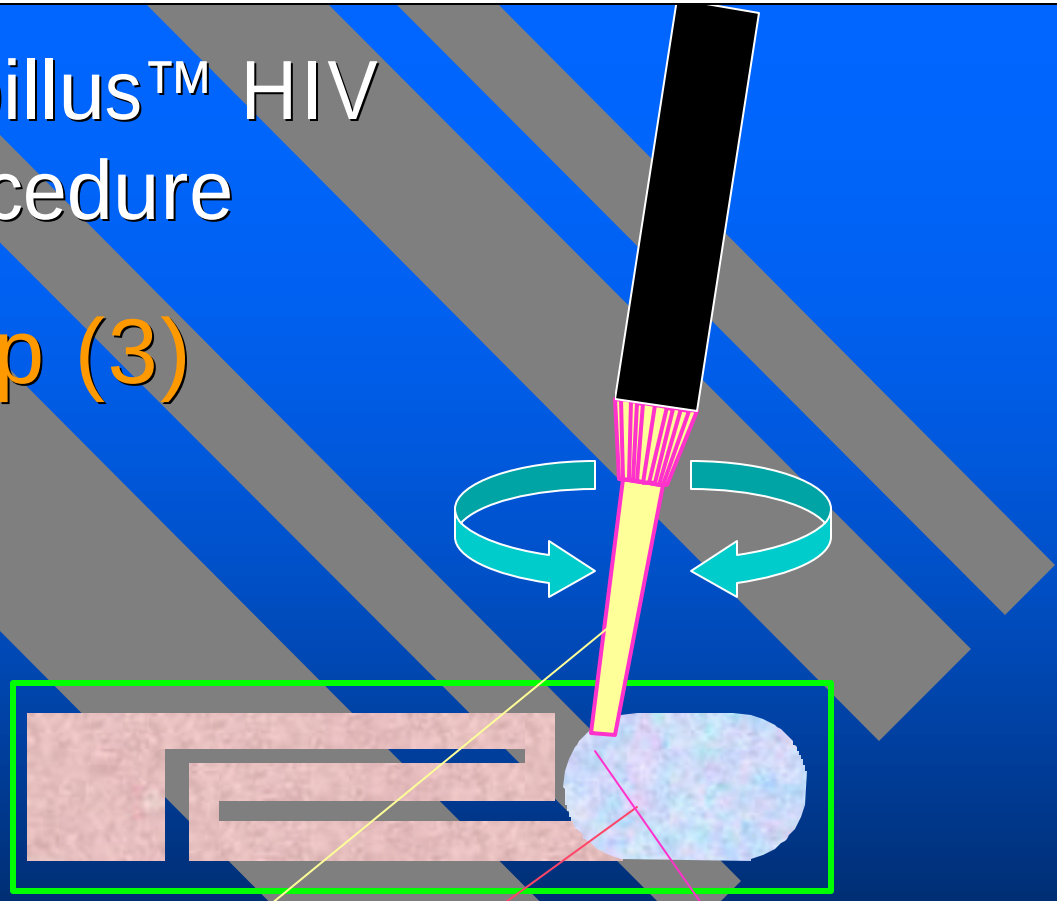
Step (2)



Using the pipette and tip supplied, dispense the sample directly into the latex solution.

Capillus™ HIV procedure

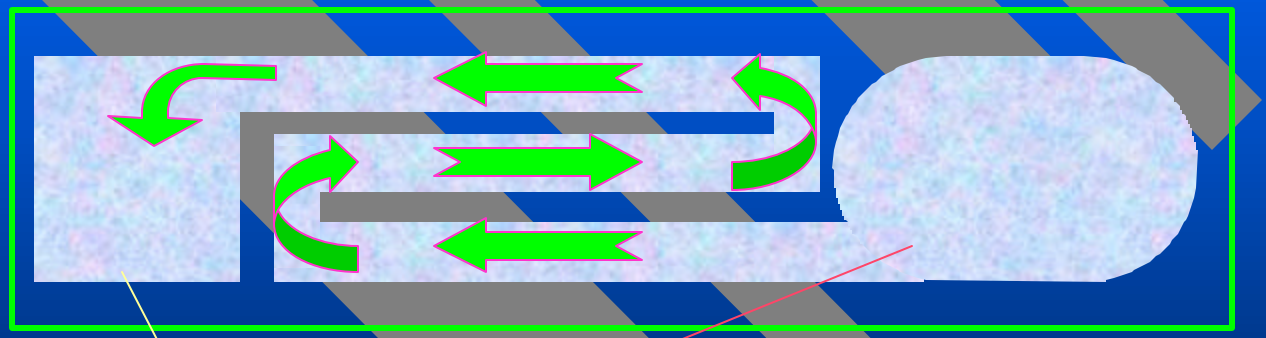
Step (3)



Use the pipette tip to move the well mixed sample and latex solution to the opening of the channel until the capillary flow begins.

Capillus™ HIV procedure

Step (4)



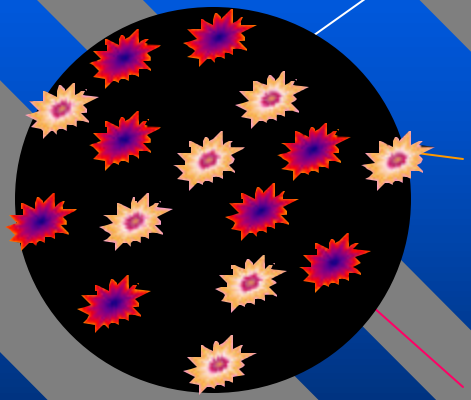
Allow the latex mixture to flow through the entire capillary channel and into the viewing window before interpreting the result. This will require approximately 3 - 7 minutes.

Capillus™ HIV-1/HIV-2
Principle of Reaction (1)

Anti-HIV antibodies

HIV-1 IgG

HIV-1 IgM



Polystyrene latex bead

HIV-1 recombinant polypeptides

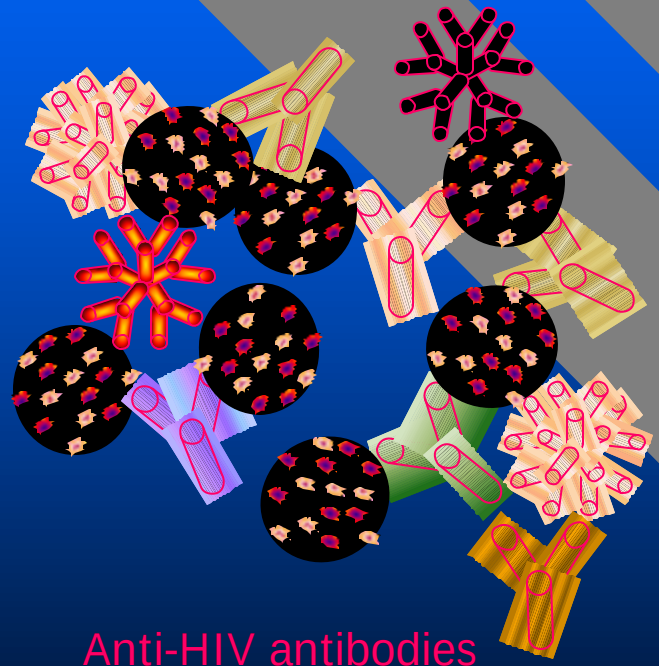
HIV-2 recombinant polypeptides

HIV-2 IgG

HIV-2 IgM

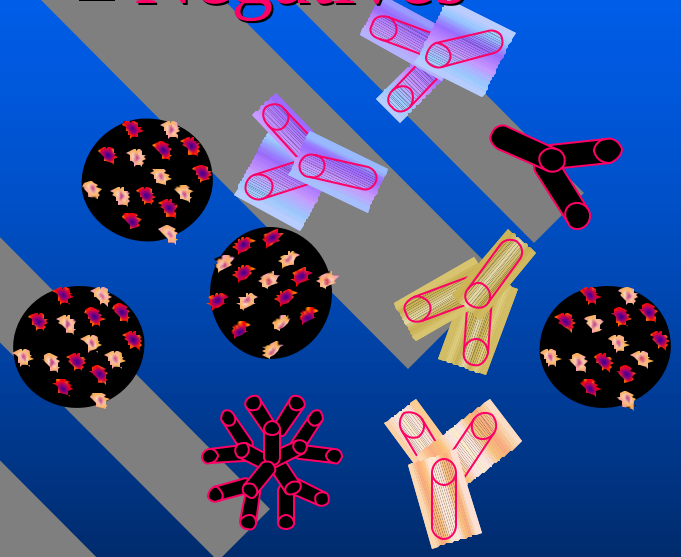
Capillus™ HIV-1/HIV-2
Principle of Reaction

- Positive



Anti-HIV antibodies bind to the antigen coated latex particles.

- Negatives



No anti-HIV antibodies are present to bind to the specific antigens on the latex partcles.

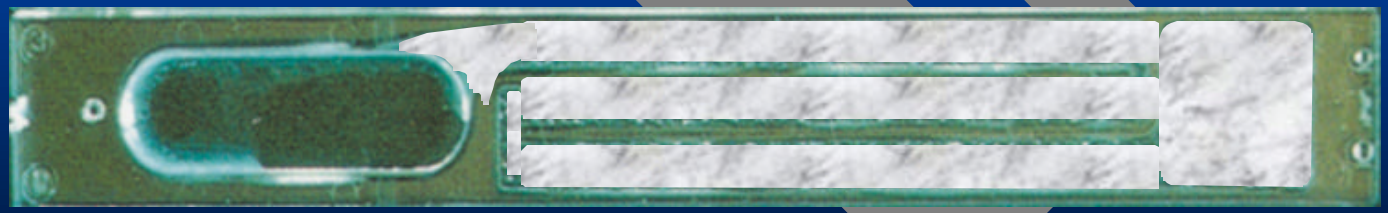
Capillus™ HIV-1/HIV-2

Positive

Observe viewing window.

Latex aggregation should be considered as initially reactive.

Negative



Capillus™ HIV1/ HIV 2

Capillus has been independently evaluated by organizations such as:

- WHO
- PHLS
- CDC
- SABTS
- ORSTROM
- Swedish Institute for Infectious Disease Control

Capillus™HIV1/ HIV2

Field Data

Leads the field as:

(1) Test of choice in the many new programs that effectively utilize rapid tests to determine serostatus and respond accordingly.

(2) A test of choice of the World Health Organization.

(3) In hospitals, clinics and counseling centers throughout the developing world

Capillus™ Trial Data Summary

Site	Total Samples	Sensitivity	Specificity
Swedish Inst.	245	100	99.2
Orstrom, Nigeria	2300	100	99.9
Ndola, Zimbabwe	212	100	100
CDC	756	100	100
PHLS	664	100	99.7
UVRL, Entebbe	211	100	99.3
UVRL, Entebbe	2135	99.6	99.8
SAIMR	188	100	100
WHO, Antwerp	600	100	99.6
Swedish Inst.			
Phase 1	1110	100	99.8
Phase 2	1501	98.3	99.2

Capillus™ HIV

Sensitivity: = 99.8%

Specificity: = 99.5%

Capillus™ Performance

Publications: *WHO, Operational Characteristics of Commercially available assays to determine antibodies to HIV-1 and/or HIV-2 in Human Sera*

Sensitivity: 100%

Specificity : 98.8%

Inter-reader variability %: 0

Ease of Performance: Very easy

Suitability for use in small labs: *Very Suitable*

WHO Report

- Ease of Performance:

  Need to Prepare: Antigen, Substrate, Wash solution, conjugate, predilution of sample.

  Stability after opening.

  Items needed but not provided in kit.

Capillus™ : 20/20

WHO

Suitability for use in small labs:

Sensitivity:

Specificity:

Incubation Temp:

Shelf-Life:

Storage Temp:

Price:

Ease of performance:

Rapidity of Performance:

Washer/Agitator

Reading:

Capillus™ Scored 25/30

Capillus™ Performance

Publications: Journal of Virological Methods Feb 02

Swedish Institute for infectious Disease control

With

Dept of Microbiology and Immunology, Muhimbili University College of Health Services Dar es Salaam

Objectives: *Alternative confirmatory strategies for detection of Antibodies to HIV EIAs in laboratories of limited resources.*

1412 fresh Serum.

3 rapid tests.

Results: *Specificity of Capillus™ was best at 98.7%*

Testing Algorithm of Choice: *Use of Capillus™ followed by SeroCard™ which gave a specificity of 99.9%.*

Capillus™ Performance

Publication: Journal of Clinical Microbiology. Apr 2002

Department of Clinical Virology and Clinical Microbiology Tamil Nadu India.

Objective: *Evaluate performance of Capillus™ on Hospital samples compared with EIA's.*

There is significant need for simple tests for use in voluntary counselling and testing for HIV prevention measures.

EIA's are sensitive but require the necessary infrastructure, trained personnel and batch testing.

6655 samples were tested between 1998 and 2001

Results: ***Capillus™ had a sensitivity of 99% and a Specificity of 98.9%***

Recommendation:"This test can safely be used for voluntary counselling and testing in India"

Capillus™ Performance

Publication: International Journal of STD and AIDS 1998.

CDC Atlanta and Aids Information Centre Uganda.

Summary: On site HIV testing with same day results may improve services and increase the number of clients who learn their serostatus in developing.

Conducted Field trial using Capillus™ compared to standard EIA testing Algorithm.

Results: Sensitivity: 99.6%. Specificity: 98.8%

Results were returned to Clients in less than an hour.

27% increase in proportion of clients who learned their serostatus and received counselling.

Conclusion: Capillus™ was a simple rapid HIV test that could be accurately performed on-site within the timeframe of a clinic visit, increasing the number of clients who learn their serostatus and receive post-test counselling.

Capillus™ HIV 1/HIV 2 Summary:

- 5 minute test time
- Sensitivity>99%
- Specificity >99%
- WHO Approved
- All Reagents supplied
- No Equipment required
- Mid-Level Training
- Low Cost per test

Capillus™ HIV 1/2 Summary

Ideal for:

- At risk Pregnant Women
- Occupational exposure
- Small labs with Limited facilities
- Out of Hours testing
- VCT
- Situations where there is no:

electricity, laboratory equipment, trained personnel, refrigeration.

SeroCard HIV

- Simple,
- Rapid
- Easy to use
- Serum, plasma,Whole Blood.

SeroCard HIV is a lateral flow, membrane based EIA which yields results in 8 minutes.

SeroCard™ HIV

There is field data available through these evaluations from many different countries including:

- Uganda
- Kenya
- Tanzania
- Senegal
- Mexico
- Peru

SeroCard™ HIV Trial Data Summary

Site	Total Samples	Sensitivity	Specificity
WHO 1	394	100	99.0
WHO 2	595	100	98.1
UCD	413	100	100
Liverpool	200	100	100
Senegal	247	99.1	98.48
Tanzania	56	100	100
Cork	550	---	100
Italy	837	---	100
VRL,Ire	238	100	100
Mexico	348	100	100
Peru	51	100	---
USA	568	100	100
Uganda	383	99.5	93.8

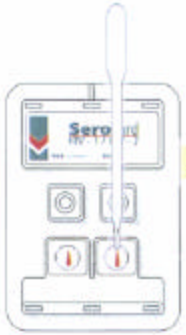
Sept 2001

SeroCard™ HIV

- Simple 8 step assay'
- No sample pretreatent.
- Results in 8 minutes.
- HIV antibodies, if present, are captured by synthetic peptides immobilised on a membrane:
  - HIV 1 *env* protein representing gp 120 and gp 41.
  - HIV 2, representing gp 120 and gp 34.
- Anti human conjugate binds specifically to the patient antibody

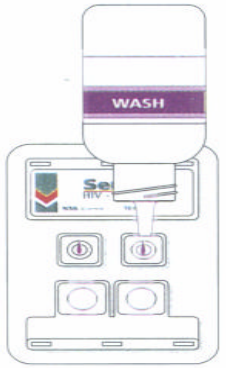
SeroCard™ HIV
Assay Procedure

One drop WASH to each sample port-absorb

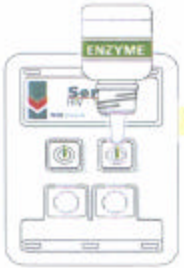


One drop sample to each sample port-absorb
INCUBATE: 30 SECONDS

One drop WASH on each sample port-absorb
INCUBATE: 30 SECONDS



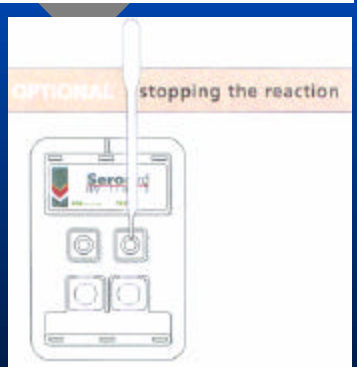
One drop WASH on each reaction port-absorb



One drop ENZYME on each reaction port-absorb
INCUBATE: 1 MINUTE

Four drops WASH on each reaction port
Allow each drop to absorb before adding a subsequent drop

Two drops SUBSTRATE on each reaction port
INCUBATE: READ AFTER 5 MIN



One drop 3N HCl to each reaction port.
Allow to absorb
RESULT STABLE FOR UP TO 12 HOURS

SeroCard™ HIV Summary

- 8 Minute test time
- Sensitivity>99%
- Specificity >99%
- WHO Approved
- No Equipment necessary
- All reagents supplied
- Mid-level Training
- Low const per test

Uni-Gold™ HIV

UNI-GOLD™ HIV

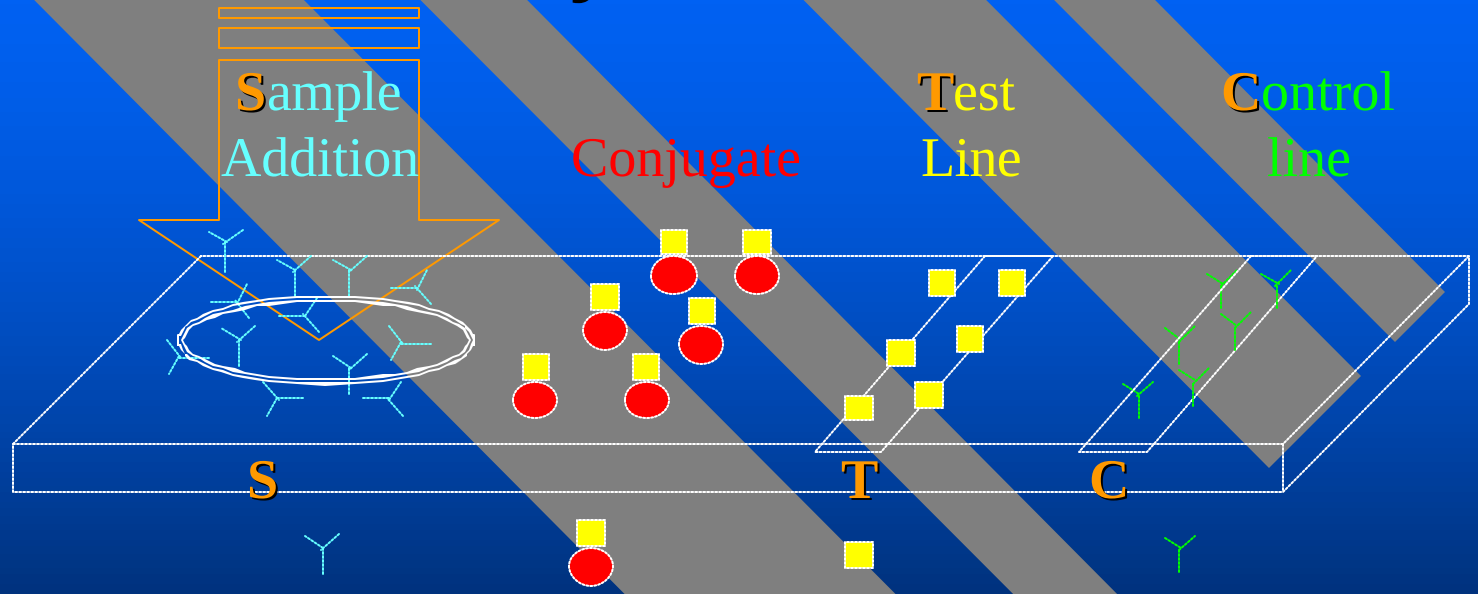
- Simple test
- Easy to use
- Results in 10 Minutes
- Single Step test
- One Reagent
- All Reagents supplied
- No Equipment necessary
- Low Skill required
- No Refrigeration requires
- Low Cost

Uni-Gold™ HIV1/2 Assay Procedure

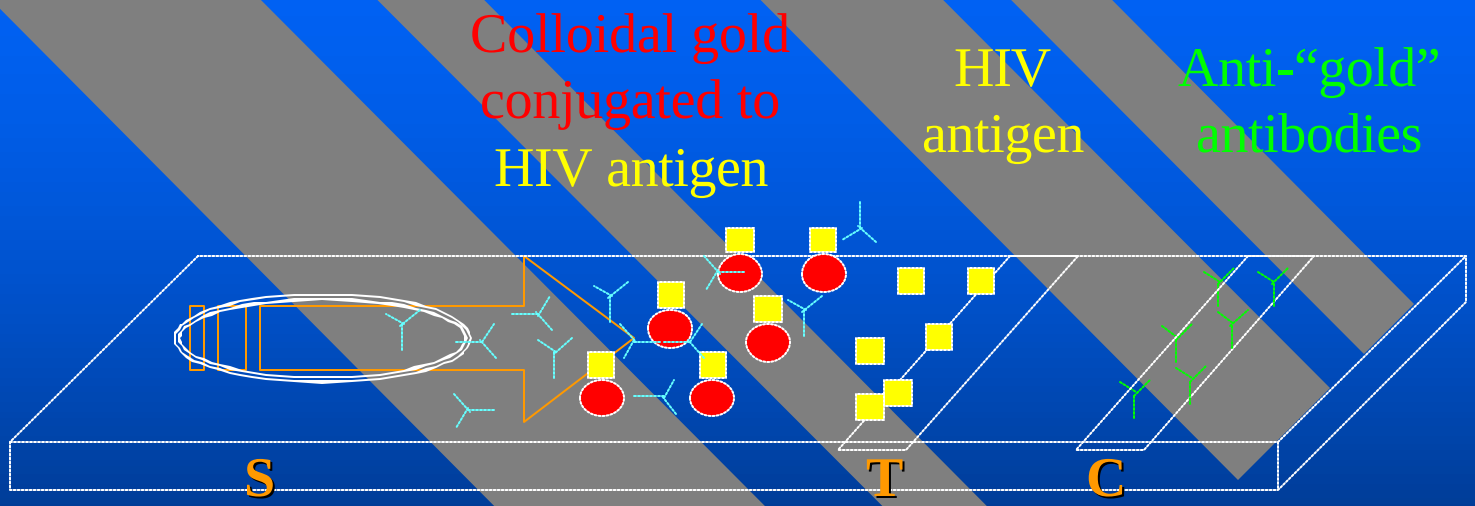
Sept 2001

Marie Mc Carthy

Uni-Gold™ HIV1/2 Assay Procedure

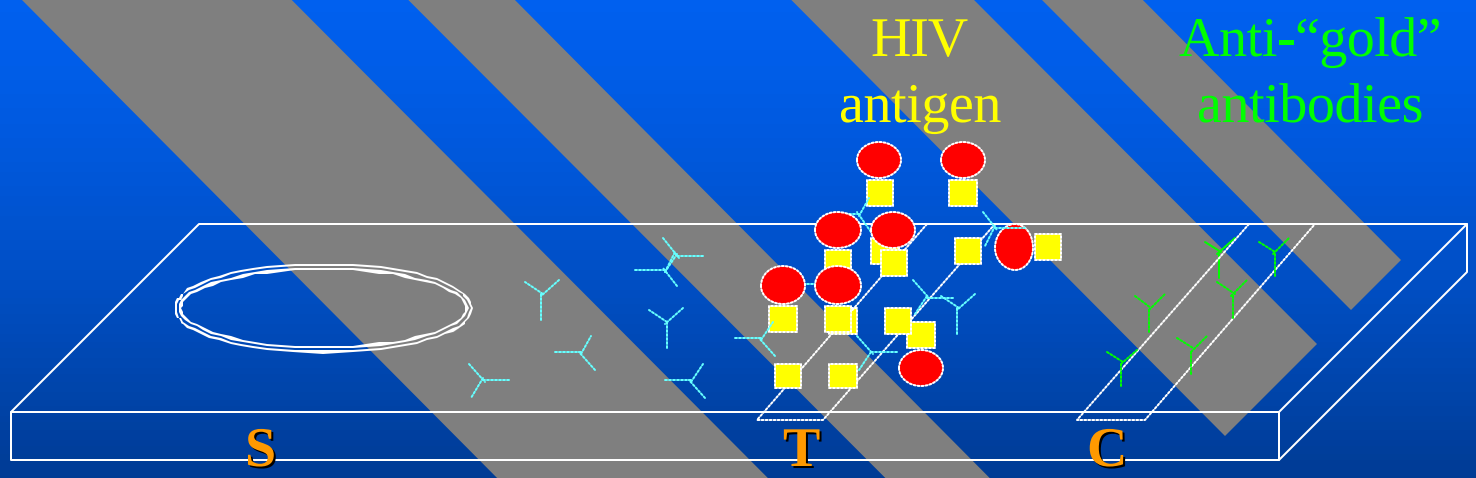


Uni-Gold™ HIV1/2 Assay Procedure



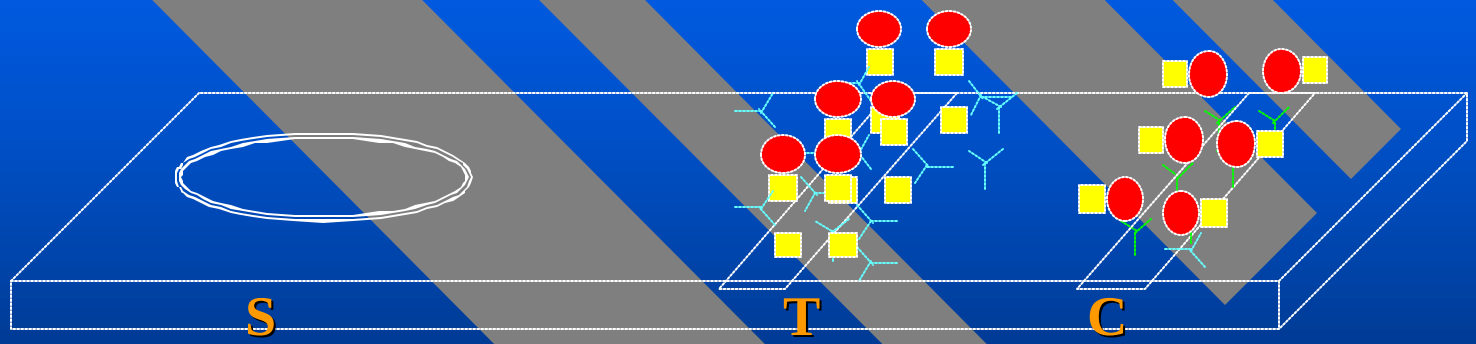
HIV antibodies *(if present)* migrate along the membrane and bind to the HIV antigen that is conjugated to the colloidal gold particles.

Uni-Gold™ HIV1/2 Assay Procedure



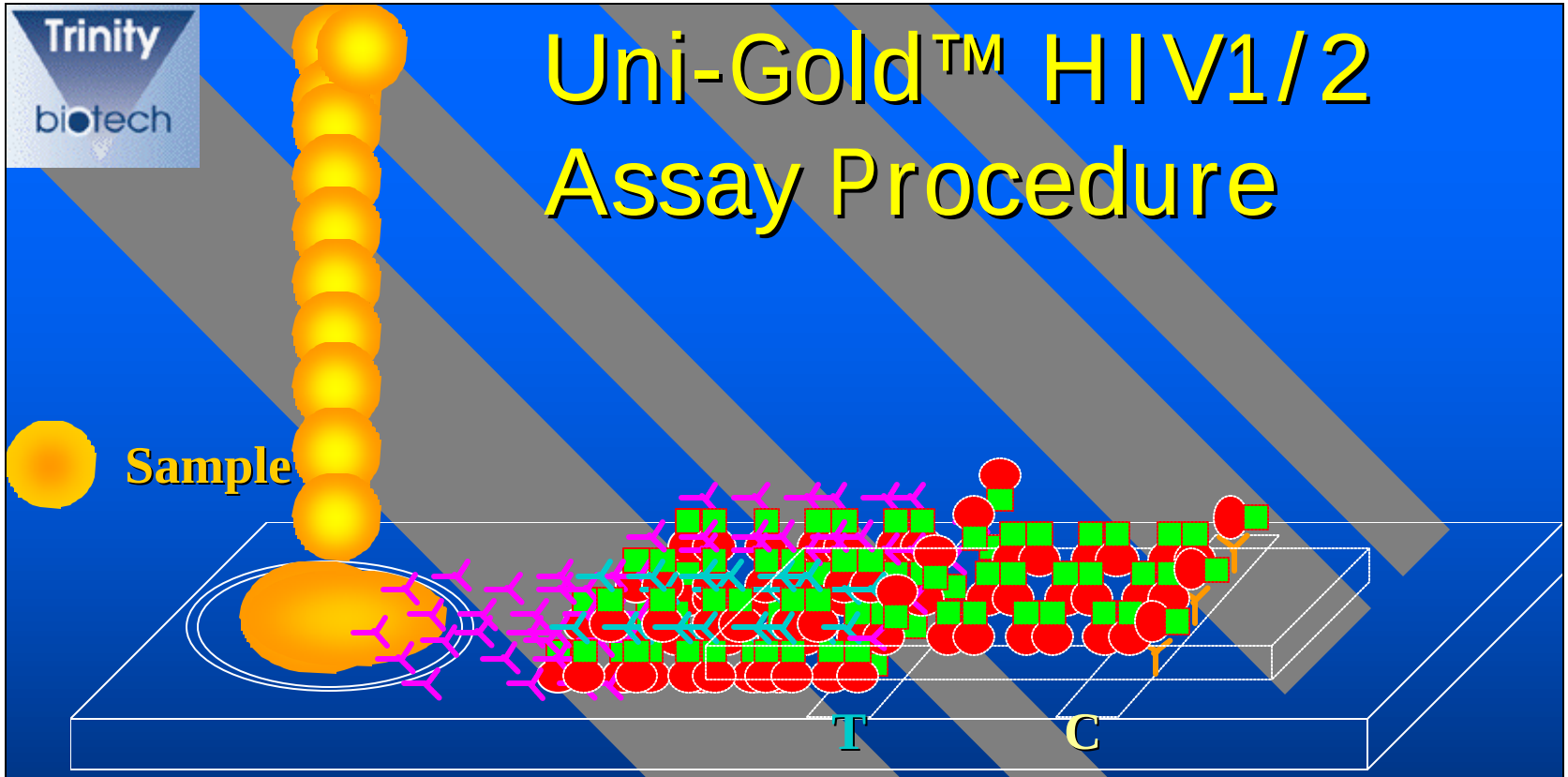
•The HIV antibody/ HIV antigen gold complex migrates along the membrane where the HIV antibodies also bind to the immobilised HIV antigen at the Test line forming a visible red band.

Uni-Gold™ HIV1/2 Assay Procedure



- The anti-"gold" antibodies immobilised at the **C**ontrol line bind to any unbound colloidal gold particles forming a visible red band.
- This **C**ontrol line should **ALWAYS** appear to indicate that the test has performed correctly.

Uni-Gold™ HIV1/2 Assay Procedure



Colloidal gold conjugated to antigen

HIV antigen

Anti-HIV antibody

Anti-"Gold" antibody

T Test Line

C Control Line

Uni-Gold™ HIV1/2 Assay Procedure

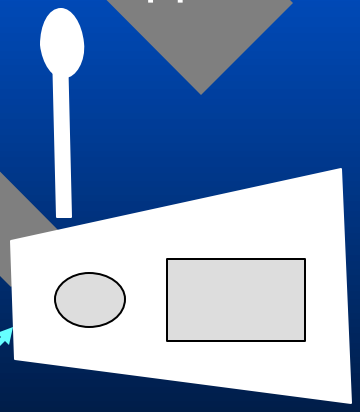
- Uni-Gold™ Devices can be stored from 2-27°C.
- Pipettes, wash and devices are supplied in the Uni-Gold™ HIV kit
- Serum, Plasma and Whole Blood (finger stick and venous blood) can be used
- Package Insert must be read prior to commencing testing
- GLP must be followed during sample handling, and disposal
- Uni-Gold™ HIV 1/2 devices must not be used past the expiry date

Uni-Gold™ HIV 1/2 Assay Procedure

Step 1: Removed required number of devices and pipettes. (If stored at 2-8°C allow devices to come to room temperature).

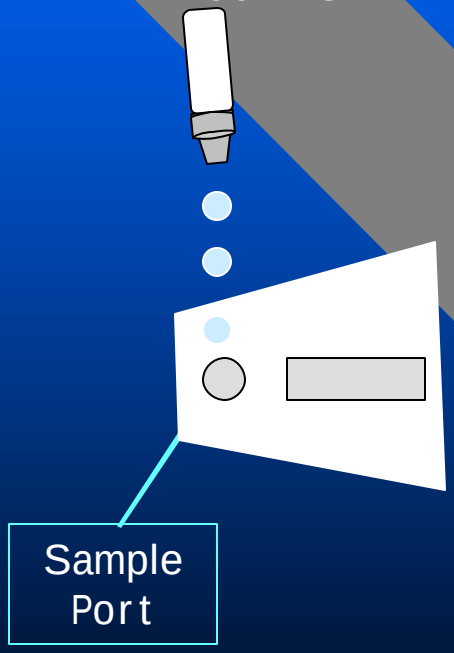
Step 2: Add 2 drops of sample to the sample port in the device using the pipette supplied

Buffer Pipette Uni-Gold™ HIV device

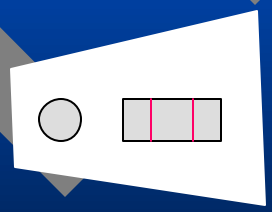


Uni-Gold™ HIV 1/2 Assay Procedure

Step 3: Add 3 drops of wash buffer

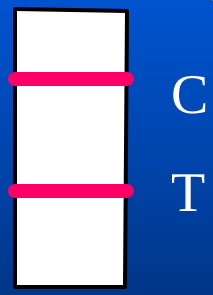


Step 4: Read the result at 10 minutes. The results are stable for an additional 10 minutes (20 minutes in total from the addition of the sample)



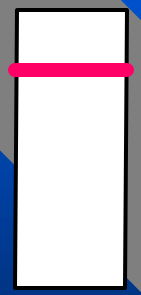
Uni-Gold™ HIV 1/2 Assay Procedure

Interpretation



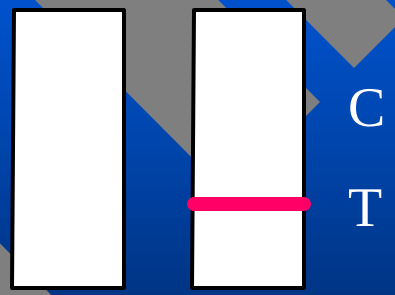
Positive:

Red line in both the control and test regions.



Negative:

Red line in the control region only.



Indeterminate:

Red line does not appear in the control region. Sample must be run again on a fresh device.

Uni-Gold™ HIV 1/2 Performance

Uni-Gold™ HIV 1/2 has been evaluated by the following groups:

WHO

CAREC

NIH

Institute	Sensitivity	Specificity	No of Specimens	Predicative values
WHO	100%	100%	250 80 positive whole blood 170 negative Whole Blood	PPV 100% NPV 100%
CAREC Caribbean Epidemiology Centre	100%	99.7%	471 102 HIV positive fresh Sera 369 HIV negative fresh Sera 100 HIV positive frozen Plasma	PPV 99% NPV 100%
NIV National Institute for Virology	100%	100%	150 75 positive serum, plasma, whole blood 75 negative serum, plasma, whole blood	Not reported

Uni-Gold™ HIV Summary

- One Step.
- Easy to use.
- Room Temperature Storage.
- No equipment necessary
- Proved reliability.
- Independently evaluated.

Uni-Gold™ HIV Summary

Ideal for:

- At risk Pregnant Women
- Occupational exposure
- Small labs with Limited facilities
- Out of Hours testing
- VCT
- Situations where there is no:

electricity, laboratory equipment, trained personnel, refrigeration.

HIV rapids

Trinity Biotech plc

Thank You!