Gold Np's in Diagnosis
Invitro Diagnosis

Name : Veera CSR, Chittepu

Out line

- Nanodiagnosis is defined as application of nanotechnology to research in Diagnosis.
- Gold particles usage in Diagnosis, which are at commercial level, approved by FDA.
- Current research in this area.
- Companies who made this technology at Point of care level, used in daily life

Functionalization of Au-NPs with biomolecules for clinical diagnostics.

& antibodies for signal enhancement in immunoassays

& carbohydrate functionalization to study specific molecular
Interactions (Carbohydrate functionalized nanoparticles ("glyconanoparticles" have the advantage of increasing the specific interactionsbetween glycans and lectins for biosensing applications)
Under development

& surface functionalization with ligands that can be
tailored for specific protein binding or direct binding of peptides and proteins to the Au-nanoparticle surface

&The specific interaction between biological pairs has also
been widely used,
e.g. biotin–streptavidin and Ni-NTA–histidine tail .

Current on going Research on use of Au Np's

- Fraunhofer IBMT have developed a new integrated biosensor system.= Accurate Diagnosis of prostate cancer using Optoacoustic detection of biologically functionalized gold Nanoparticles. The treatment relies on optoacoustic imaging of gold nanoparticles.
- Use of ELISA technology for liver cancer diagnosis used gold nanoparticles ringed by a charged polymer. coating and an X-ray scatter imaging technique to spot tumor-like masses as small as 5 millimeters earlier it was 5 cm

Researchers at Northwestern University

- an ultrasensitive, automated immunoassay that is capable of detecting serum PSA at concentrations as low as 330 fg/ml—approximately 300 times more sensitive than commercially available immunoassays. Use of Bio-barcode PSA assay. To detect PSA in serial serum samples from 18 patients who had undergone radical prostatectomy for prostate cancer. PSA was detected in 102 (86%) of the 118 serum samples tested using the bio-barcode assay, compared with just 30 (25%) when commercial assays were used.
- UGA researchers use gold nanoparticles to diagnose flu in minutes

Commercial companies by WGC

- Church and Dwight - First response pregnancy kit.
- BBInternational andMerck - detection of food prothegens
- Merck single path assay for presence of salmona , within 20 minutes And duopath assay can be used for salmonella, E.Coli and Campylobacter.
- NanoSphere - Verigene detecting specific biomolecule targets with gold nanoparticles

NanoSphere

Nanosphere develops, manufactures and markets an advanced molecular diagnostic platform, the Verigene System, which enables simple, cost-effective, and highly sensitive nucleic acid (DNA and RNA) and protein testing on a single platform.

- The direct detection of single or multiple nucleic acid targets with single-base pair resolution has diagnostic applications in several clinical areas, including:



- The detection of DNA or RNA targets using nanoparticle probe technology entails:
- Automated nucleic acid extraction and PCR amplification (for some assays) from a clinical sample on the Verigene® Processor *SP*
- Automated transfer of eluted nucleic acids or amplicons into a single-use, proprietary Test Cartridge. The DNA is then cut via a proprietary sonication process, into 300-500 base-pair fragments in order to facilitate hybridization in subsequent steps.
- In the initial hybridization step, the cut genomic DNA (target nucleic acid) is simultaneously hybridized to:
  - Single-stranded DNA capture oligonucleotides arrayed in replicate on a solid support (an array), and
  - Sequence-specific mediator oligonucleotides that detect single-copy DNA regions of each target of interest.
  - A washing step then follows that removes unhybridized gold nanoparticle probes.
- Silver signal amplification is then performed on the gold nanoparticle probes that are hybridized to captured DNA targets of interest.
- There then follows a washing step to remove unreacted signal amplification reagents.
- Qualitative analysis of results (slide reading) can now be performed on the Verigene®Reader.

Respiratory Virus Plus* | N × MyStart by IncrediBar.com ×

ENE RV+ PERFORMANCE VS. CULTURE/DFA AND SEQUENCING (N=1,022)^

	Sensitivity (%)	Specificity (%)
	100	100
	100	100
	100	999
9 H1N1	995	100
	100	100
	99.1[C]	100

e Respiratory Virus Plus Nucleic Acid Test Package Insert.

mples failed sequencing and were excluded from these results.

mple was negative for RSV by RV+ and sequencing, but positive by culture and PCR. This sample is included as a false-negative for RV+.

VERIGENE® RV+ TEST

	Available Test Panels	
	US/FDA-Cleared	Outside US
Influenza A	●	●
Influenza B	●	●
RSV A	●	●
RSV B	●	●
Flu A - 2009 H1N1	●	●
Flu A - H3	●	●
Flu A - H1	●	●
H275Y (oseltamivir resistance)		●
Automation	Sample-to-Result	
Instrumentation	Verigene Reader and Processor *SP*	
Workflow	Random Access	
Pipetting Steps	1	
Hands-On Time	<5 minutes	
Run Time	<2.5 hours	
CLIA Designation	Moderate Complexity	

Show all downl

Gram-positive Blood cultured

Targets	Genus		
	Staphylococcus spp.	●	●
	Streptococcus spp.	●	●
	Micrococcus spp.		●
	Listeria spp.	●	●
	Resistance		
	mecA	●	●
	vanA	●	●
	vanB	●	●
Automation		Sample-to-Result	
Instrumentation		Verigene Reader and Processor *SP*	
Workflow		Random Access	
Sample Type		Positive Blood Culture Bottle†	
Hands-On Time		<5 minutes	
Run Time		2.5 hours	

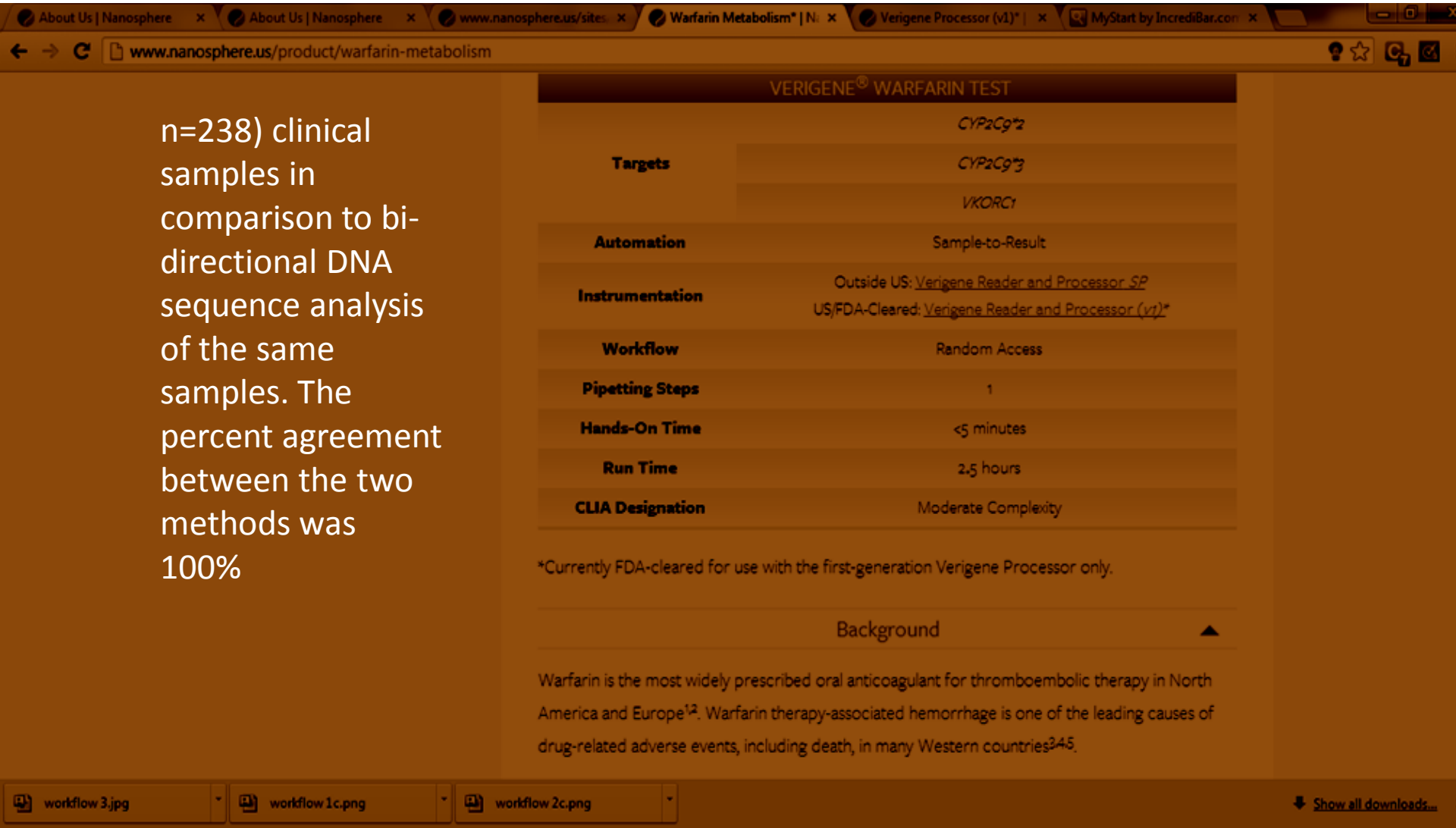
†For use with all adult continuous monitoring blood culture bottles; see BC-GP package insert for details.

Gram Negative Bacteria
FDA not cleared still.

Targets	*Proteus* spp.
	Citrobacter spp.
	Enterobacter spp.
	Resistance
	KPC
	NDM
	CTX-M
	VIM
	IMP
	OXA
Automation	Sample-to-Result
Instrumentation	Verigene Reader and Processor *SP*
Workflow	Random Access
Sample Type	Positive Blood Culture Bottle
Pipetting Steps	1
Hands-On time	<5 minutes
Run Time	<2 hours

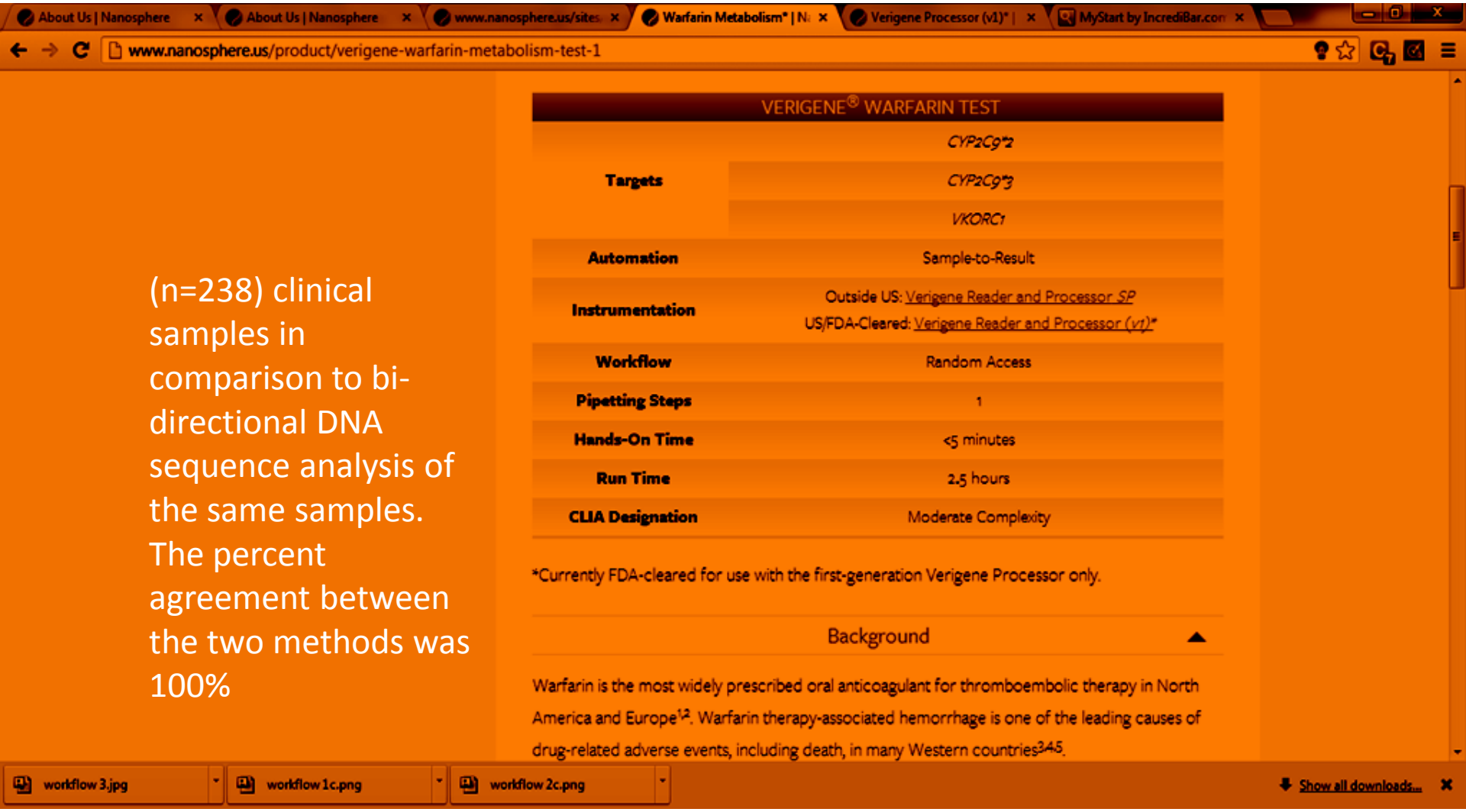
Cardiac Tests
warfarin test

n=238) clinical samples in comparison to bi-directional DNA sequence analysis of the same samples. The percent agreement between the two methods was 100%



Human Genetic Test warferin metabolism

(n=238) clinical samples in comparison to bi-directional DNA sequence analysis of the same samples. The percent agreement between the two methods was 100%



Item	Device	Predicate
Intended Use (Sample type)	Analysis of positive blood culture bottles (unspecified) which contain gram-positive bacteria. Gram positive blood culture Nucleic acid test	Analysis of positive blood cultures using BACTEC Plus™ Aerobic/F and BacT/ALERT FA FAN® Aerobic blood culture bottles, which contain gram-positive bacteria.

Verigene System	Light Cycler Instrument
where nanoparticles are illuminated using a fixedwavelength light source **No Chemical amplification of chemical Signal Single-image sensor** **sample size : 25 µl** **Analysis Time : 2 minutes**	**DNA amplification Via PCR** **Optical detection of stimulated fluorescence.** **Sample Size : 10-20µl** **Analysis Time : Detection occurs at defined intervals during PCR cycle and can be viewed in real-time**

Some Patent : METHOD FOR DETECTING THE PRESENCE OF A TARGET ANALYTE IN A TEST SPOT - and also patent on Nano particle imaging system and method.

FIRST RESPONSE GOLD DIGITAL PREGNANCY TEST

CHURCH & DWIGHT CO., INC.

Regulation Number 862.1155

- early detection of pregnancy by the detection of hCG, a placental hormone in urine. The device detects the presence of hCG in the urine of a pregnant woman by way of a series of immunochemical reactions on a chromatographic strip contained within a plastic housing, which is integral with the digital component that reads and displays the result of the immunochemical reactions on the Display Screen of the device in a manner similar to the predicate device.
- The test is indicated for use from four days before the expected period, that is, five days before the missed period. The intended use is Invitro Diagnostic device intended for detection of hormone presence.
- sensitivity of 18 mIU/ml, accuracy is only 58 percent if test is meant 5 days before, for 100 percent accuracy, we have to wait for biological cycle to reach maximum concentration of harmone.

FIRST RESPONSE EARLY RESULT PREGNANCY TEST (OTC)
CHURCH & DWIGHT CO., INC.
Regulation Number862.1155

- The test result is read in the housing window after the elapse Of 3 minutes. Two pink lines indicate hCG has been detected (pregnant); one pink line indicate not detected.
- DrawBack : The test may detect the pregnancy hormone (hCG), in some cases, as early as 6 days before the missed period (5 days before the expected periodicates no hCG has been detected (not pregnant).

Note : Some pregnant women will not be able to detect hCG in their urine 6 days before the missed period. If you test negative before your missed period, but think you may still be pregnant, you should re-test again a few days after your missed period.

this test detects very low levels of hCG, there is a small chance that this test will give positive results even if you are not pregnant. Chances of this are greater for women nearing age 40 and older.

- Church and Dwight used Gold Nanoparticles to detect hcG hormone, they also use strepdavin, and the only device which can detect low level so f hcG hormone.
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  ABBOTT , Abott advisor one step pregnancy test kit. here in place of gold coated colloidal partciles, colloidal are coated with anti alpha hcG antibody (related to mouse)hormones.

WH Accu Test the sensitivity of the test is 100%, it takes five minutes to read test.

- Recently, some researchers used WBC to test pregnancy(Joseph P. Habboushe, MD Department of Emergency Medicine, New York Hospital–Queens of Cornell University, 56-45 Main St, Queens, NY 11355, USA)
- Regarding patent information, they author has got 3 patents, Authors are **Nazareth, US and Albert Nazareth, Mercerville, NJ US. Here they are using gold nanoparticles** whose sizes are 40-47 nm and 60-75 nm .

Single Path E.Coli O157

Gold labelled Immuno sorbent Assay

PERFORMANCE TESTED AOAC RESEARCH INSTITUTE LICENSE NUMBER 010407

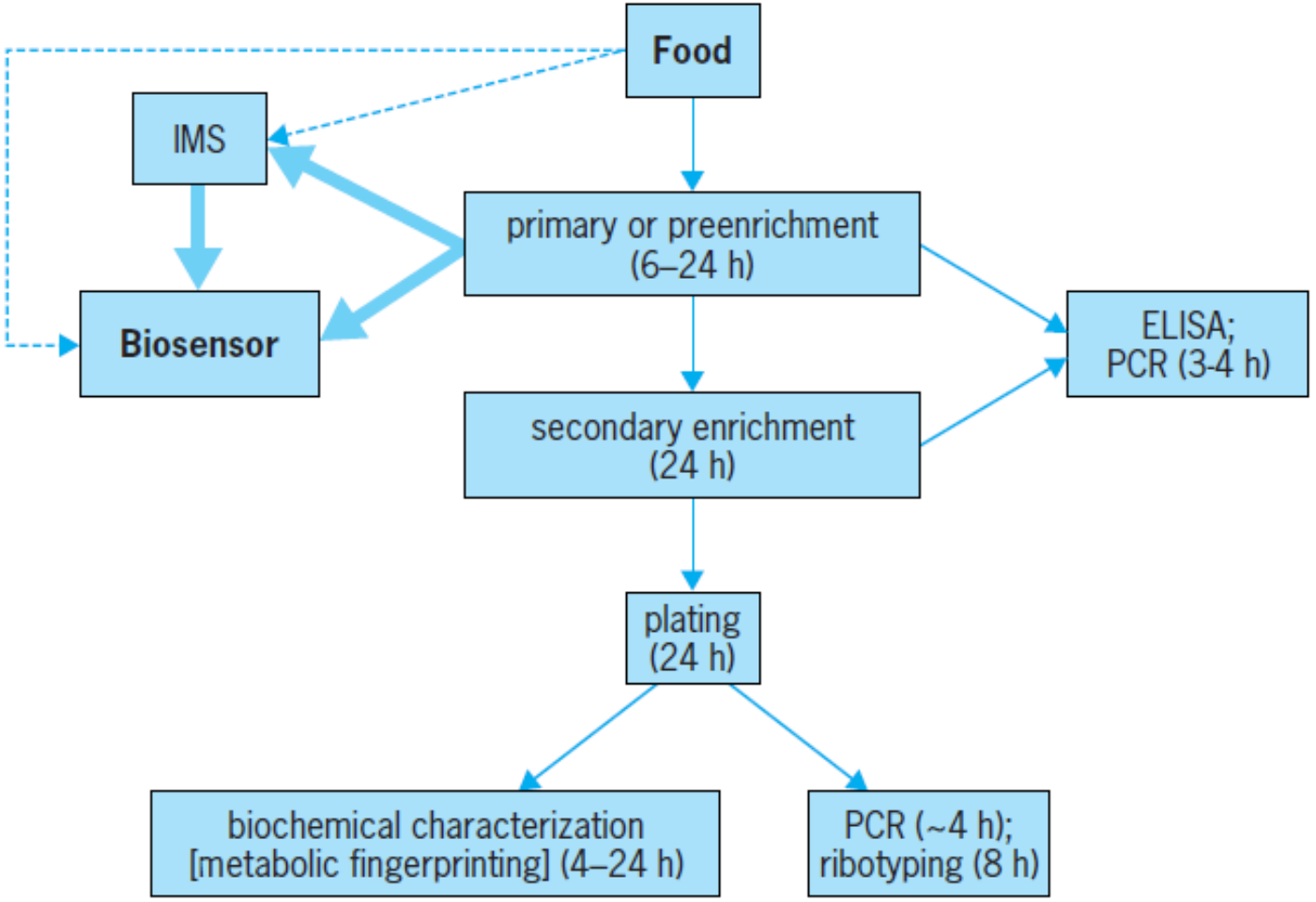
- Used in food analysis laboratories, qualitative detection of E. Coli from a variety of foods
- Immunochromato Graphic rapid Test based on gold labelled anti bodies. Here They get gold labelled particle from BBinternational.
- The test device has Circular sample port, oval Shaped test T, and control window C

The sample is applied to the chromotography paper via sample port. The sample is observed through the pad to the reaction zone containing Gold labelled antibodies specific to Ecoli. Any E. coli antigen present complexes with gold antibody and migrates through the port until it encounters a binding zone in test area T. The Binding zone T contains another anti E coli antibody, which immobilize any E. Coli complex present. Due to gold labelling distinct red line is formed. The rest of the sample migrates to second binding reagent zone within the control Zone C and forms second distinct line

Care must be take when working with samples, culture and media

- Detection limit – 25 gram of sample
- Interferences : no interference of Singlepath E.Coli with food ingredients.
- Sensitivity & Specificity & Efficiency - >99%(according to AOAC trials)
- False negative rate and False positive rate < 1%.
- Problem : No line appears after 20 minutes of the test period., Measure : re run sample again
- AOAC = association of analytical communities
- Duo Path Assay is used to detect salmonella, E.Coli and Campylobacter

Flow diagram showing food brone pathogens How previous method is useful



BioAssayWorks

- BioAssay Works (Ijamsville, Maryland) develops lateral-flow, point-of-care and point-of-use diagnostic tests, with emphasis on assays requiring high sensitivity.
- KIM-1, a whole new dimension in kidney damage detection. Available in ELISA or rapid Rena-strip test format.

BioAssayWorks

***H-Rena-strip*™ and *R-Rena-strip*™ Lateral-Flow Tests** **Fast–test results in just 15 minutes, Reliable–specificity 96%–sensitivity 99%, Easy-to-use–no special training necessary, Semi-quantitative–results can be correlated with color chart, Quantitative results–with reader (sold separately)**	***H-Rena-E*™ and *R-Rena-E*™ ELISA Tests** **• Fast–test results in just 3 hours• Reliable–specificity 100%–sensitivity 100%** **• Quantitative results** **C-FLAT® Counter-Flow Lateral Amplified Test: C-FLAT is a patented lateral-flow immunodiagnostic device**

References

- World Gold Counsil
- FDA
- Corresponding company websites.
- For patents, usa patent database, and company website.

Thank you and Happy X- Mas