Point-of-Care Diagnostics: Strategies and Implementation

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Rapid diagnostics and PoC

- What is “PoC”?
  - Infectious diagnostic testing performed outside the clinical microbiology laboratory

The challenge

- More patients requiring contact isolation
- MRSA, VRE, CPE, *C. difficile*, Flu, RSV, Noro
- Expensive logistics – inferior patient management
- Fast TAT at Clinical Microbiology is not fast enough

The solution

- near patient testing (PoC)

- Skipping logistics delay – reduction of total turn-around-time
- Fast impact on patient management (e.g. contact isolation)
- Fast impact on patient treatment (e.g. no antibiotics for Flu or RSV positive patients)

PoC testing

- barriers (as seen from Clinical Microbiology)

- A variety of platforms with different performance
- Risk of LIS loss of data
- No control over test indication and interpretation
- Risk of misuse of antimicrobials
- PoC will be more expensive than test in central lab

PoC testing

- threats (against Clinical Microbiology)

- Widespread clinical perception of “unmet need”
- Molecular PoC as good as centralized tests
- Mature technology (low complexity)
- Aggressive marketing

- Will be implemented with or without Clinical Microbiology
- “If you are not at the table, you are on the menu” (D. Wolk)

PoC testing
- the strategy

- Integration of PoC testing in Clinical Microbiology
  - Ensures testing quality
  - Ensures data capture – 2-way communication with LIS
- Clinical Microbiology responsible for:
  - Platform verification
  - Menu verification
  - Guidelines for test indication and interpretation
  - Education
  - QC
  - Real-time support

PoC in Clinical Microbiology

- Guidelines

- Local
- Regional
- National

PoC in Clinical Microbiology

- Danish National Guidelines, December 2017

To avoid the negative consequences of an uncoordinated and unstructured implementation of PoC infectious disease testing,
the Danish Society for Clinical Microbiology recommends that

a local or regional PoC committee is established in collaboration with the local Department of Clinical Microbiology to evaluate individual business cases as well as the optimal placement of PoC instrument(s) and selection of personnel to perform the PoC assays in the local context.

Due to the quality and safety of patient treatment, it is crucial to ensure that infectious disease diagnostics assays performed outside the geography of the Department of Clinical Microbiology are performed according to the guidelines and Standard Operating Procedures of the Department of Clinical Microbiology. To ensure this, **the Danish Society for Clinical Microbiology recommends that it is the responsibility of the Department of Clinical Microbiology to:**

verify PoC assays before implementation in routine diagnostics
select optimal PoC platform(s) in collaboration with local users
select PoC assay menu(s) following local or regional evaluation of clinical relevance in collaboration with local users
define local test indications
ensure correct test reporting according to local guidelines and ensure local guidelines for interpretation of test results
ensure adequate training as well as regular evaluation of local personnel performing the PoC assays
ensure electronic communication between the local PoC platform and the Department of Clinical Microbiology Laboratory Information System
ensure that Standard Operating Procedures for handling of errors and failures are in place
ensure quality control procedures and participation in relevant external quality control programs

PoC testing
- geography

- PoC “version”
  - Version 1:
    - a) In-hospital, in-lab (e.g. Biochemistry 24/7)
    - b) In-hospital, outside lab (e.g. ER, ICU, Pediatrics)
  - Version 2:
    - a) Outside hospital, in-healthcare facility (e.g. GP)
    - b) Outside hospital, outside healthcare (e.g. field-use, military)
  - Version 3:
    - Home testing

PoC testing
- menu

- Menu selection
  - Version 1: Contact isolation tests
  - Version 2: E.g. Respiratory, STD
  - Version 3: E.g. STD, Travel fever

PoC Implementation in Denmark

- Current Status

- First wave of implementation
- Contact isolation assays (Flu and RSV)

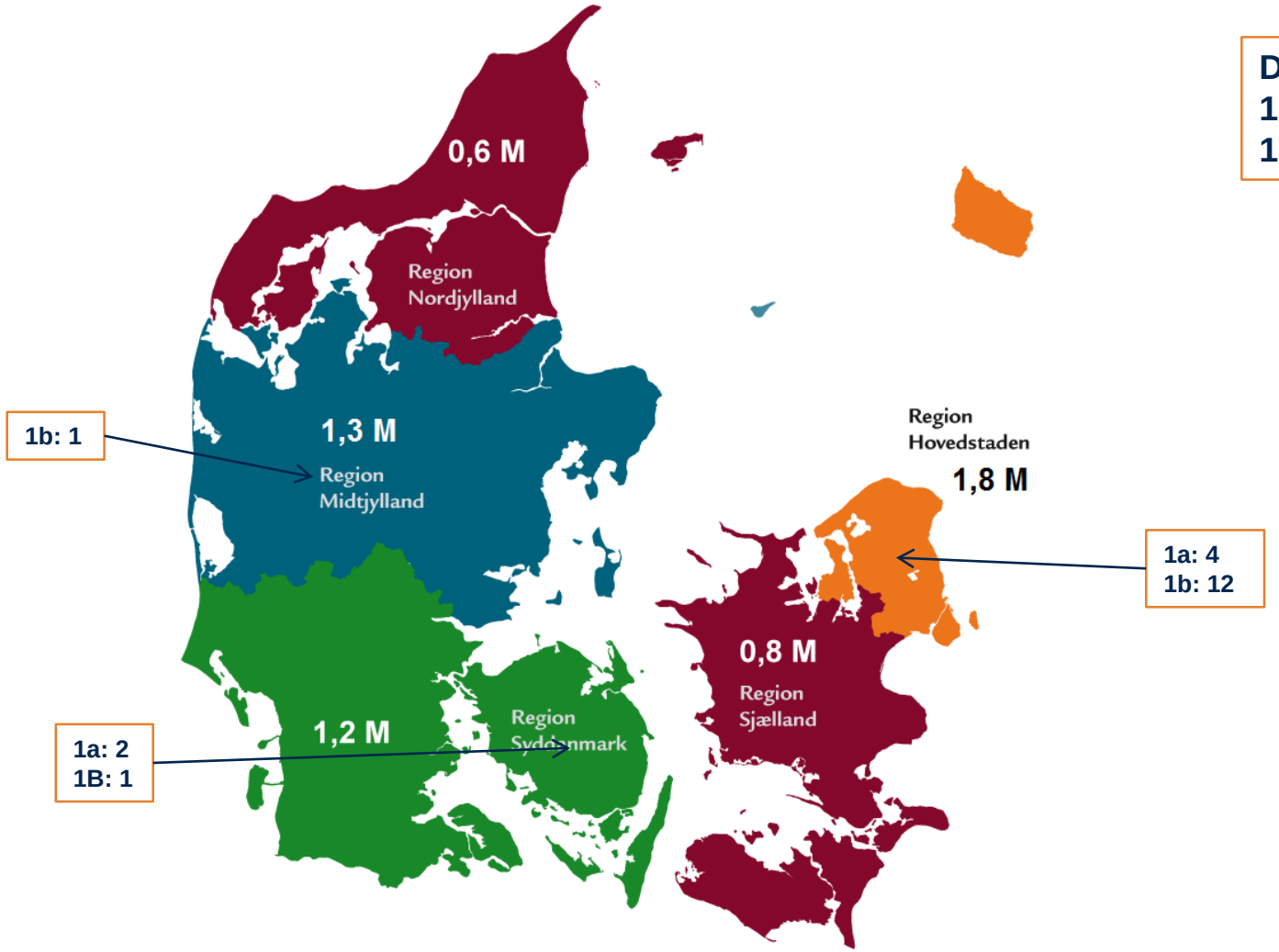
PoC Implementation in Denmark

- First Platform

Flu A/B, Flu A/B+RSV, MRSA, C. diff, Strep A; 15-30 min

PoC Implementation in Denmark

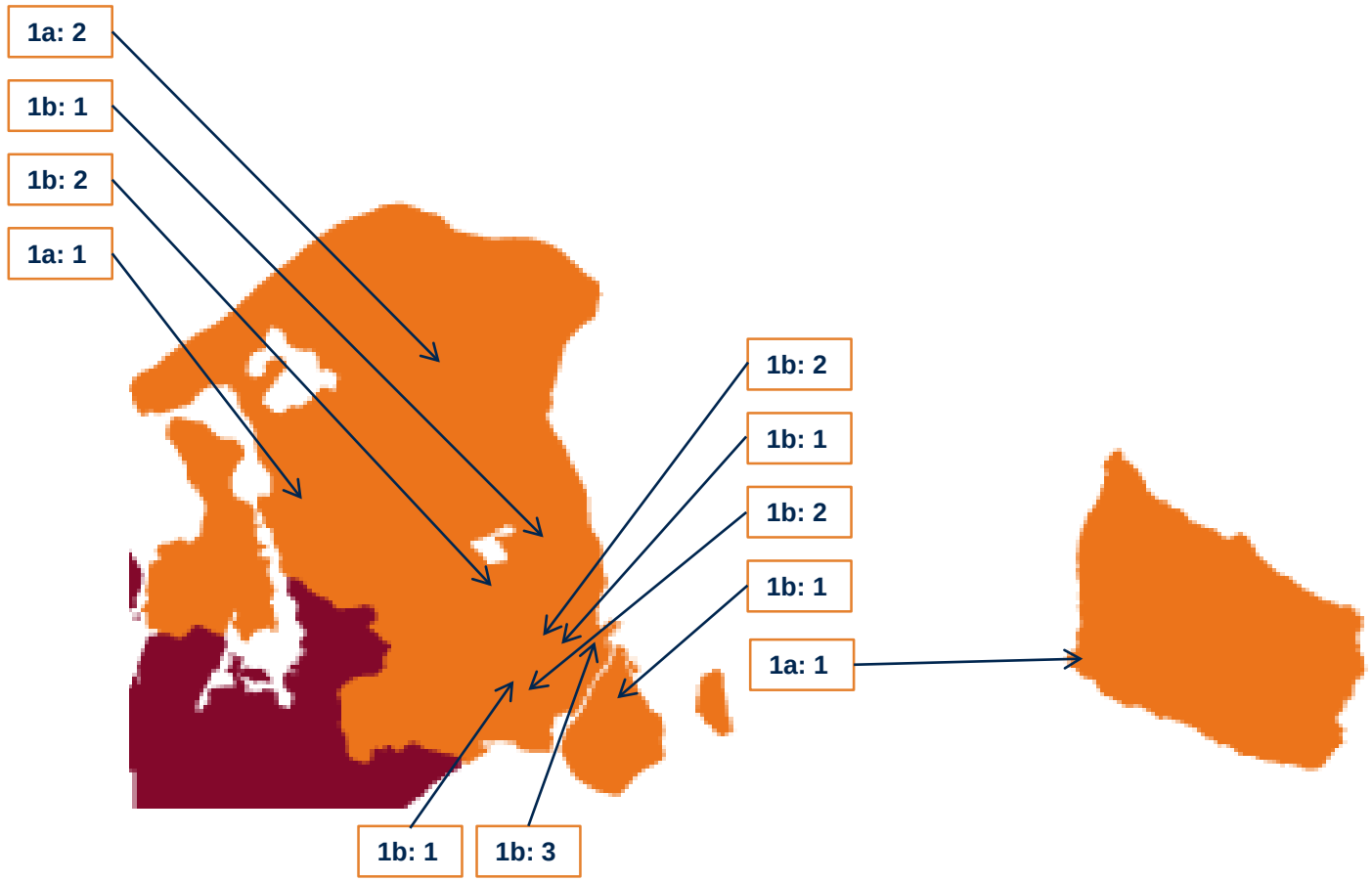
- Current Status



Denmark:
1a: 6
1b: 14

PoC Implementation in Denmark

- Current Status / Capital Region



PoC Implementation in Denmark

- The First Season (01.01-31.07.2018)

- 619 patient samples analyzed on Roche Liat.
- Samples to be sent to State Serum Institute as part of National surveillance. 73% (still counting) have been reflex tested.

PoC Implementation

- The Next Steps

Syndromic Testing

- Respiratory Testing
- Meningitis/encephalitis Testing
- Gastro Testing

Stat-Dx DiagCORE

Up to 48-plex RT-PCT, 21-plex Respiratory Panel 2, 69 min

Stat-Dx DiagCORE

Single pipetting step – loading 300 µL

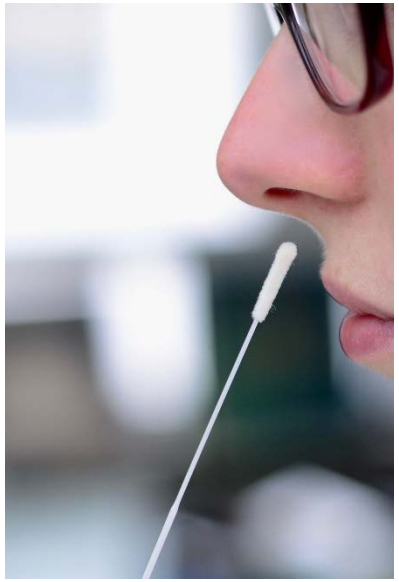
Stat-Dx DiagCORE

Scan cartridge and sample ID and load

Stat-Dx DiagCORE

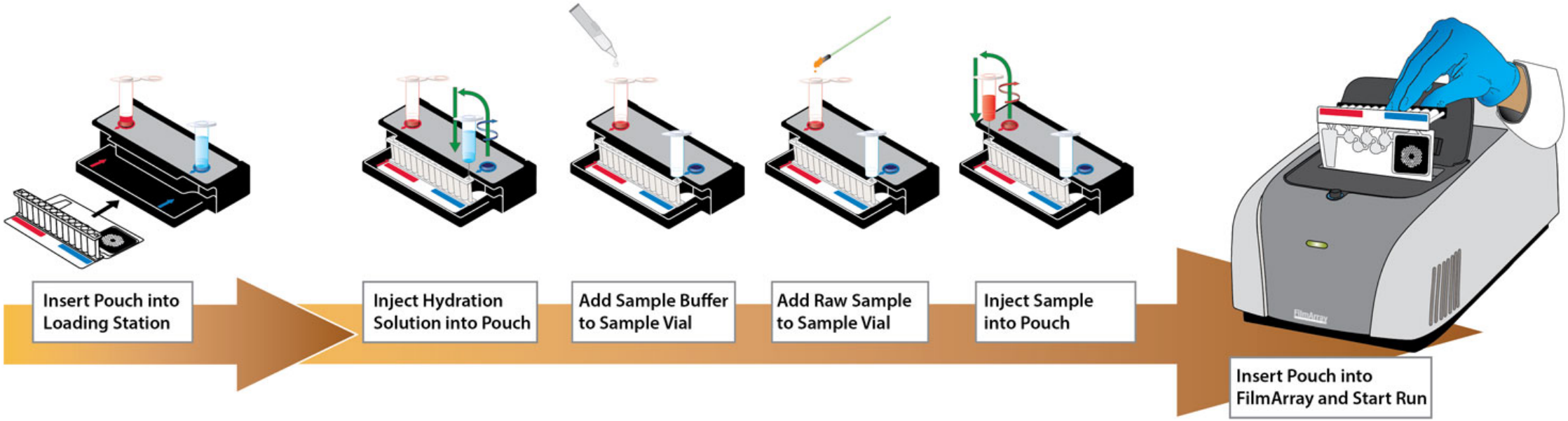
- Dry Swab

- ”Swab’n’go” – no need for transport media



GenMark ePlex

BioFire Film Array



BioFire Film Array

BioFire Film Array

- Meningitis Panel

Journal of Clinical Microbiology

Multicenter Evaluation of BioFire FilmArray Meningitis/Encephalitis Panel for Detection of Bacteria, Viruses, and Yeast in Cerebrospinal Fluid Specimens

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Rapid diagnosis and treatment of infectious meningitis and encephalitis are critical to minimize morbidity and mortality. Comprehensive testing of cerebrospinal fluid (CSF) often includes Gram stain, culture, antigen detection, and molecular methods, paired with chemical and cellular analyses. These methods may lack sensitivity or specificity, can take several days, and require significant volume for complete analysis. The FilmArray Meningitis/Encephalitis (ME) Panel is a multiplexed *in vitro* diagnostic test for the simultaneous, rapid (~1-h) detection of 14 pathogens directly from CSF specimens: *Escherichia coli* K1, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, cytomegalovirus, enterovirus, herpes simplex virus 1 and 2, human herpesvirus 6, human parechovirus, varicella-zoster virus, and *Cryptococcus neoformans*/*Cryptococcus gattii*. We describe a multicenter evaluation of 1,560 prospectively collected CSF specimens with performance compared to culture (bacterial analytes) and PCR (all other analytes). The FilmArray ME Panel demonstrated a sensitivity or positive percentage of agreement of 100% for 9 of 14 analytes. Enterovirus and human herpesvirus type 6 had agreements of 95.7% and 85.7%, and *L. monocytogenes* and *N. meningitidis* were not observed in the study. For *S. agalactiae*, there was a single false-positive and false-negative result each, for a sensitivity and specificity of 0 and 99.9%, respectively. The specificity or negative percentage of agreement was 99.2% or greater for all other analytes. The FilmArray ME Panel is a sensitive and specific test to aid in diagnosis of ME. With use of this comprehensive and rapid test, improved patient outcomes and antimicrobial stewardship are anticipated.

Infectious meningitis and encephalitis are clinical conditions that can have very serious consequences. The morbidity and mortality of these infections can be high, particularly with bacterial meningitis, which can be rapidly life threatening, and the best outcomes are achieved with rapid initiation of the appropriate antimicrobial therapy (1). Those surviving infection may have significant long-term sequelae, such as loss of limbs, problems with vision and hearing, seizures, and cognitive deficits (2). In addition, the costs associated with these infections are significant, both in the short term related to hospitalization and treatment and in the long-term related to lost contributions to society (3, 4).

In the United States, there are approximately 4,100 cases of bacterial meningitis, including 500 deaths, every year (5). The most common pathogens of acute infections are *Streptococcus pneumoniae*, *Streptococcus agalactiae* (group B *Streptococcus*), *Neisseria meningitidis*, *Haemophilus influenzae*, *Escherichia coli* (particularly the K1 serotype), and *Listeria monocytogenes*, which together account for over 80% of infections. Viruses are the major cause of aseptic meningitis, a relatively common and often benign infection, with up to 85% being caused by non-polio enteroviruses (EV). Viral meningitis is more common than bacterial meningitis and often is much less severe. There are approximately 20,000 encephalitis-related hospitalizations per year in the United States, with an average of 1,400 deaths per year (6, 7). There is a vast array of pathogens that cause encephalitis, the majority of which are viruses. A number of noninfectious processes can also cause encephalitis, and the etiology remains unknown in up to 70% of cases (7).

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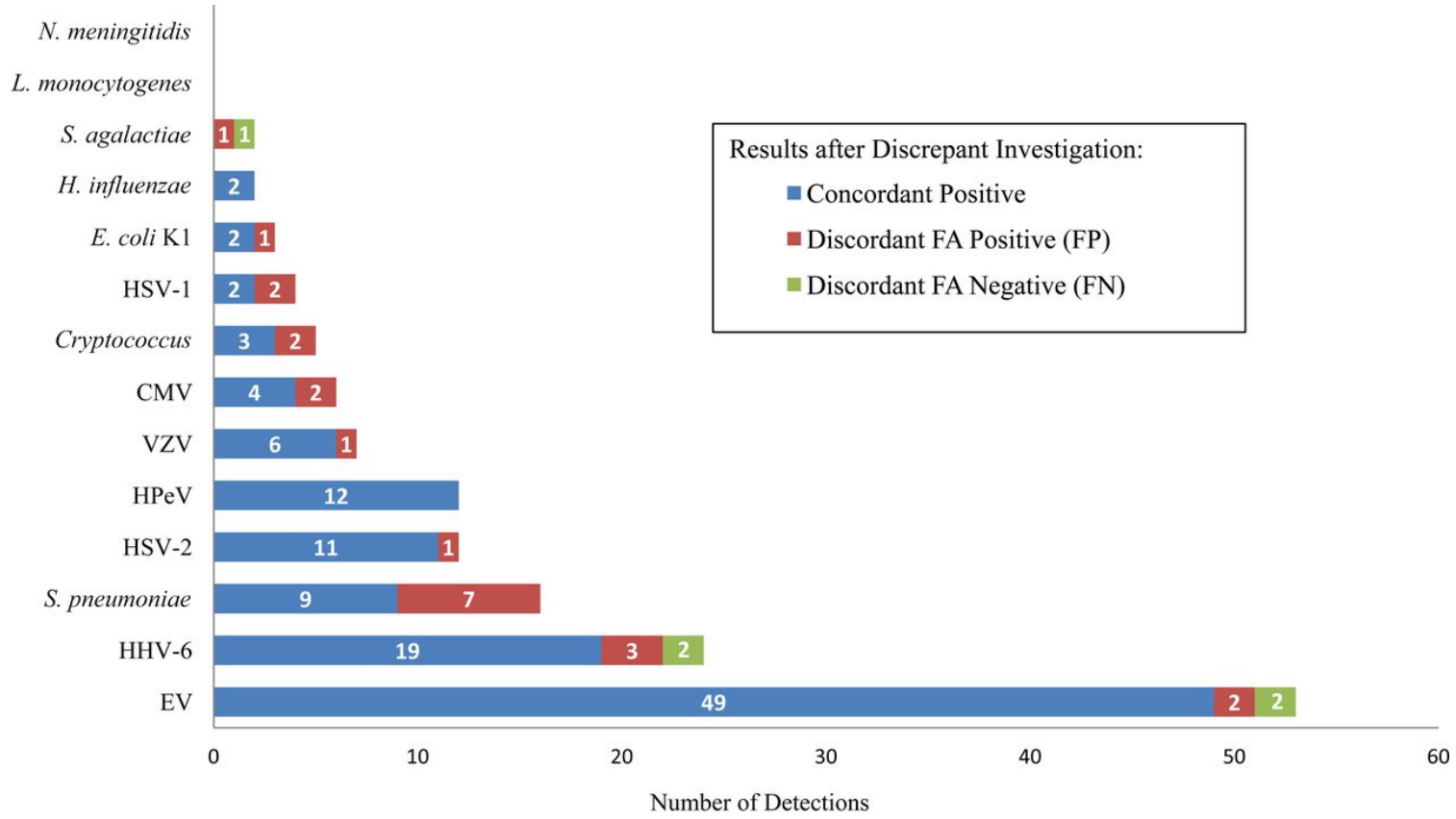
BioFire Film Array

- Meningitis Panel



PoC Implementation in Denmark

- The Future

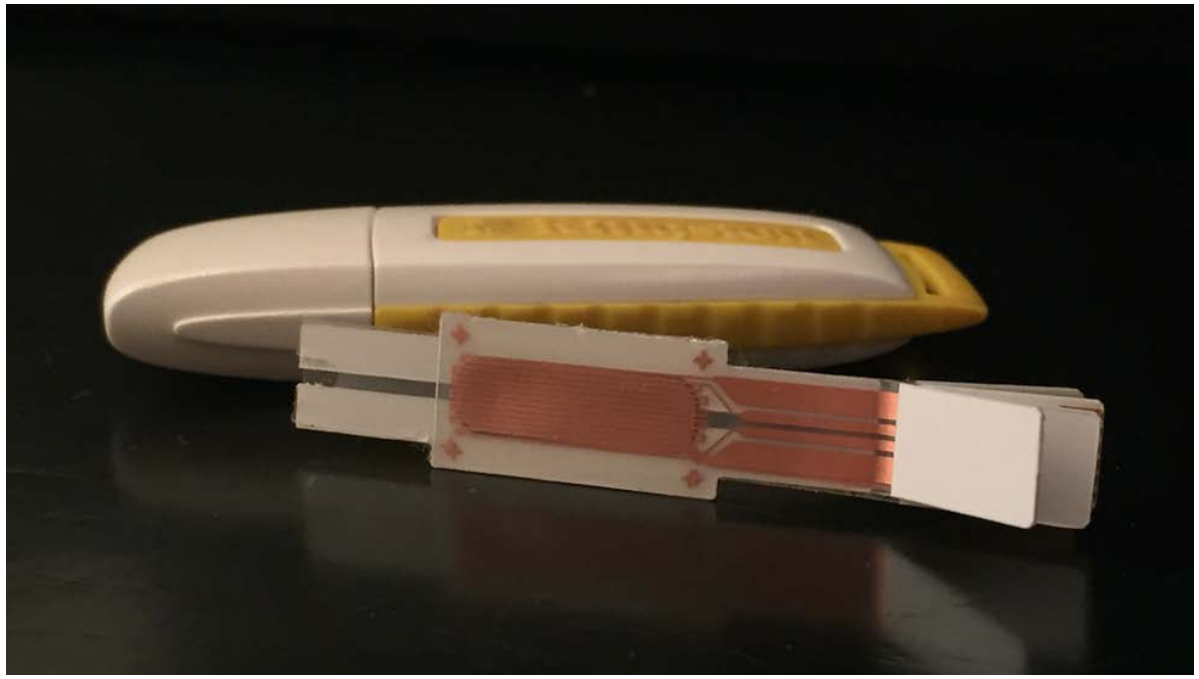
- Sepsis Testing
- Home Testing

Faster ID

- direct from blood molecular sepsis diagnostics

PoC testing

- Home Testing



Conclusion

- **Point-of-Care has arrived**
- **May offer maximum impact on patient management**
- **Will change clinical microbiology**
- **And it is all about strategy**