



GenomEra test for rapid detection of *Staphylococcus aureus* and MRSA in blood culture

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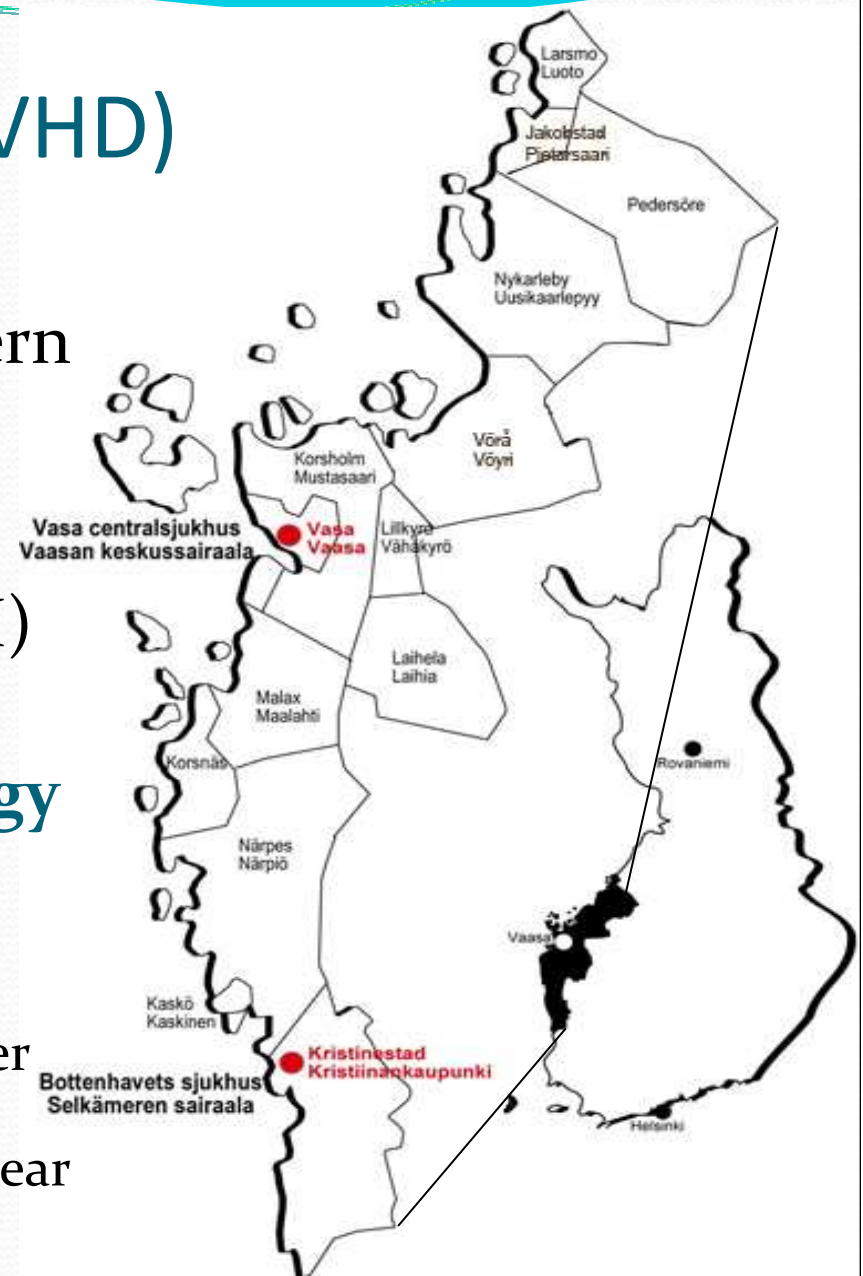
Italy, Padenghe sul Garda
March 2013

Vaasa Hospital District (VHD)

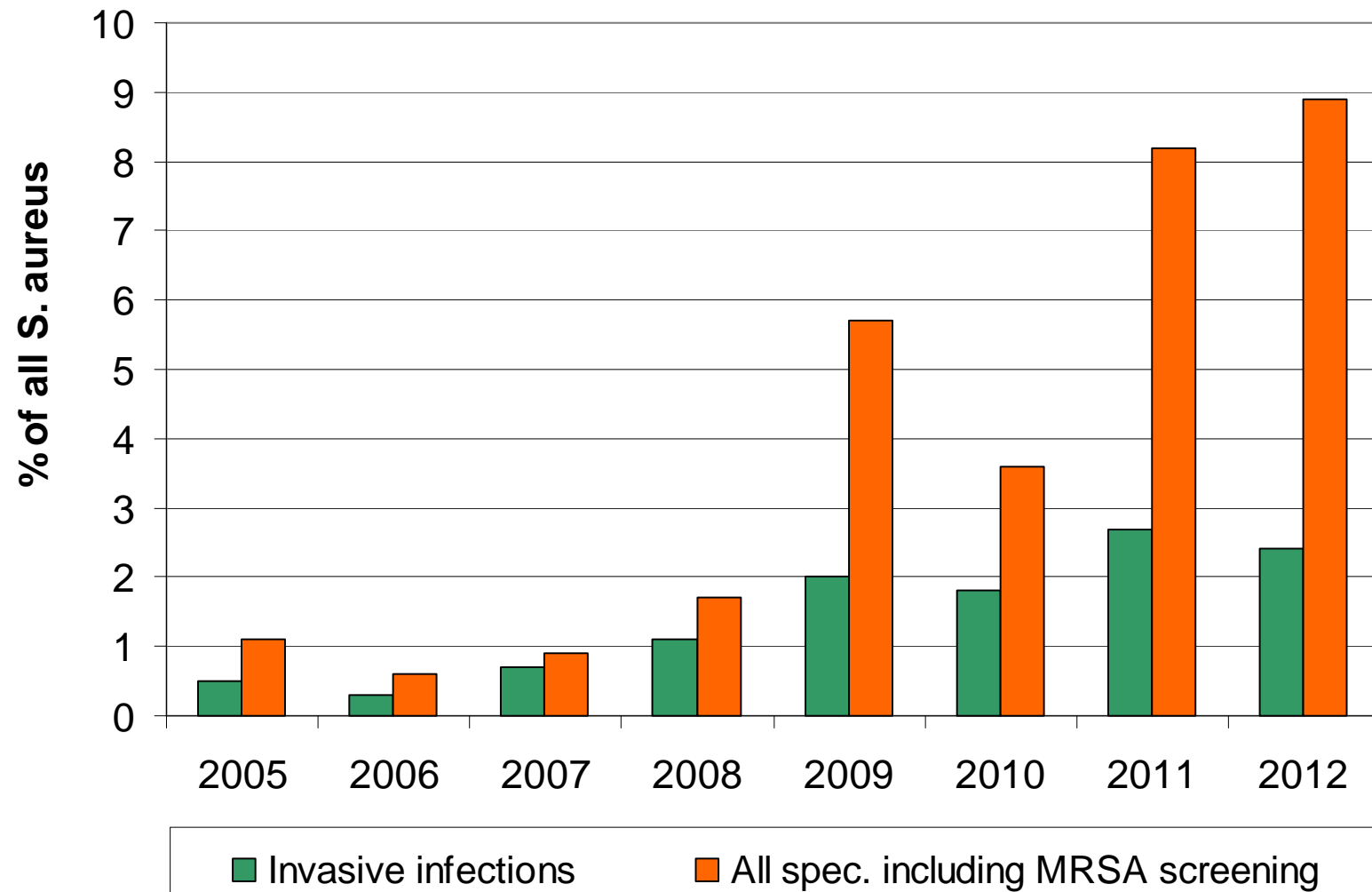
- Locates on the coast in western Finland
- Population ~170 000
- Vaasa Central Hospital (VCH)

Dept. of Clinical Microbiology

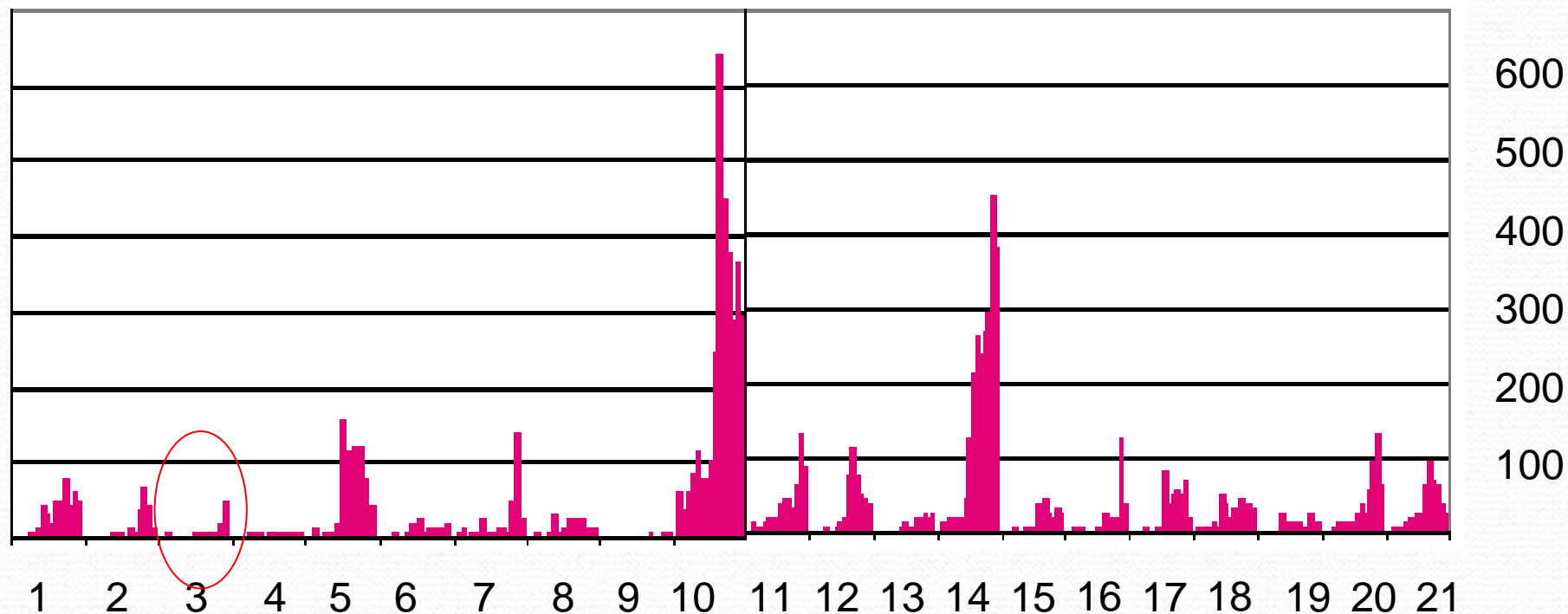
- Microbiological samples per year ~80 000
 - MRSA screening samples ~5000 per year
 - Blood culture samples ~7500 per year



MRSA in VHD 2005-2012



MRSA (new cases) in Finland 1995-2009



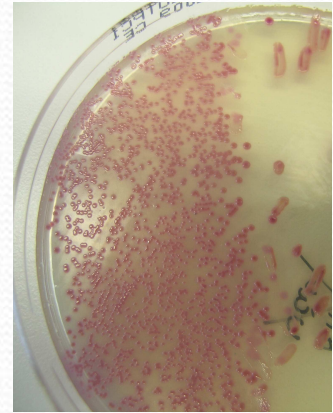
1=K-Sshp, 2=E-Pshp, 3=Vaasan shp, 4=K-Pshp, 5=P-Pshp, 6=Kainuun shp, 7=L-Pshp, 8=Lapin shp, 9=Ahvenanmaa, **10=HUS**, 11=V-Sshp, 12=Satakunnan shp, 13=K-Hshp, **14=Pshp**, 15=P-Hshp, 16=Kymenlaakson shp, 17=E-Kshp, 18=El-Sshp, 19=I-Sshp, 20=P-Kshp, 21=P-Sshp

Methicillin resistant *S. aureus* (MRSA) in VHD

- Circulating strains diverse (10 different genotypes)
 - Several small outbreaks in the area
 - Incidence increasing
- Low level oxacillin / ceftazidime resistance among MRSA isolates (oxacillin MIC < 4 mg/L)
 - Difficulties in phenotypic detection
- Also borderline resistant (oxacillin MIC ~2–4 mg/L) BORSA isolates in the region

Screening of MRSA in VCH

- Combined selective and enrichment culture
 - Incubation at minimum 18h
- Phenotypic confirmation of possible MRSA
 - Additional 18h
- Difficulties differentiating low level oxacillin / cefoxitin resistant MRSA isolates from BORSA strains
- Reliable MRSA confirmation only by detecting the *S. aureus* specific and *mecA* genes
- However, no PCR facilities (no space)
 - Confirmation extremely slow (2–5 days)

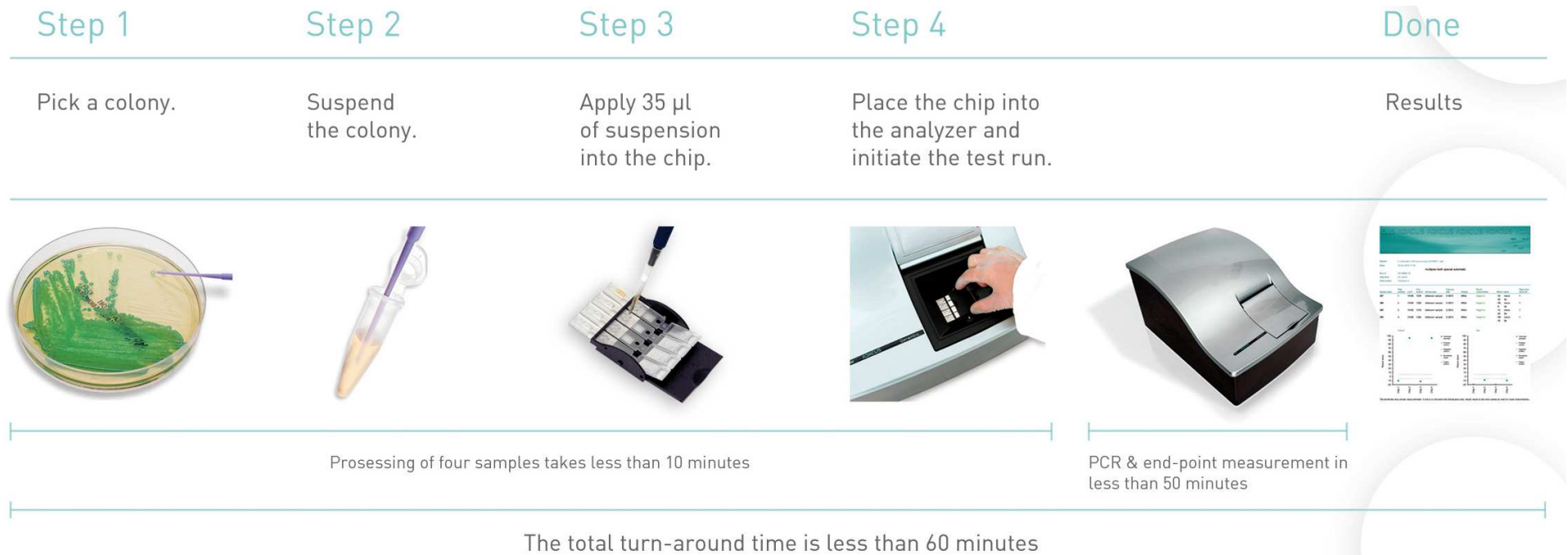


Evaluation of GenomEra, a new automated PCR system



- Participated in an evaluation project of a new PCR assay for MRSA confirmation
 - GenomEra MRSA/SA Diagnose test
 - Minimal preparation requirements of samples, easy-to-use run protocol, safe to handle and dispose
- Closed system, no requirements for separate PCR facilities
 - Simultaneous detection of *S. aureus* specific and *mecA* genes, analyses 1–4 samples in 50 minutes





- First a performance study with known MRSA and non-MRSA isolates
- Assay runs from different isolates on different agar plates

- Second a suitability study for routine use
- In combination with preliminary screening with selective agar plates

Results of the evaluation

Hirvonen et al. Rapid confirmation of suspected methicillin-resistant *Staphylococcus aureus* colonies on chromogenic agars by a new commercial PCR assay, the GenomEra MRSA/SA Diagnose. **Eur J Clin Microbiol Infect Dis** 2012 31(8):1961-1968.

Study included:

- 304 MRSA isolates (68 different *spa* types)
- 146 non-MRSA staphylococci
- Assay sensitivity and specificity for MRSA confirmation 100%
- 4 samples within 50 minutes (32 / 8h workday)
- Combined screening practise permitted MRSA detection and confirmation within 24 h

Improvements in MRSA detection

- Significant improvement in speed
 - Confirmation of suspected MRSA growth within 50 minutes
 - **Confirmation of MRSA colonization within 24 h**
- Laboratory costs remained stable
 - No need for routinely used biochemical confirmatory tests, due to the reliable detection of *S. aureus* and *mecA*
 - Decreased hands-on time and faster result interpretation
- No extra space requirements
- **High interest to get a similar test for the urgent sepsis patients**

Use of GenomEra in rapid detection of MRSA and MSSA in blood cultures

S. aureus bacteremias

- *S. aureus* is the second most common cause of bacteremia in Finland (SIRO materials)
- High morbidity and mortality rates
- MRSA proportion ~4%





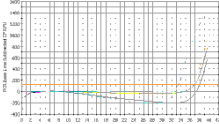
Bacteremias caused by other staphylococci

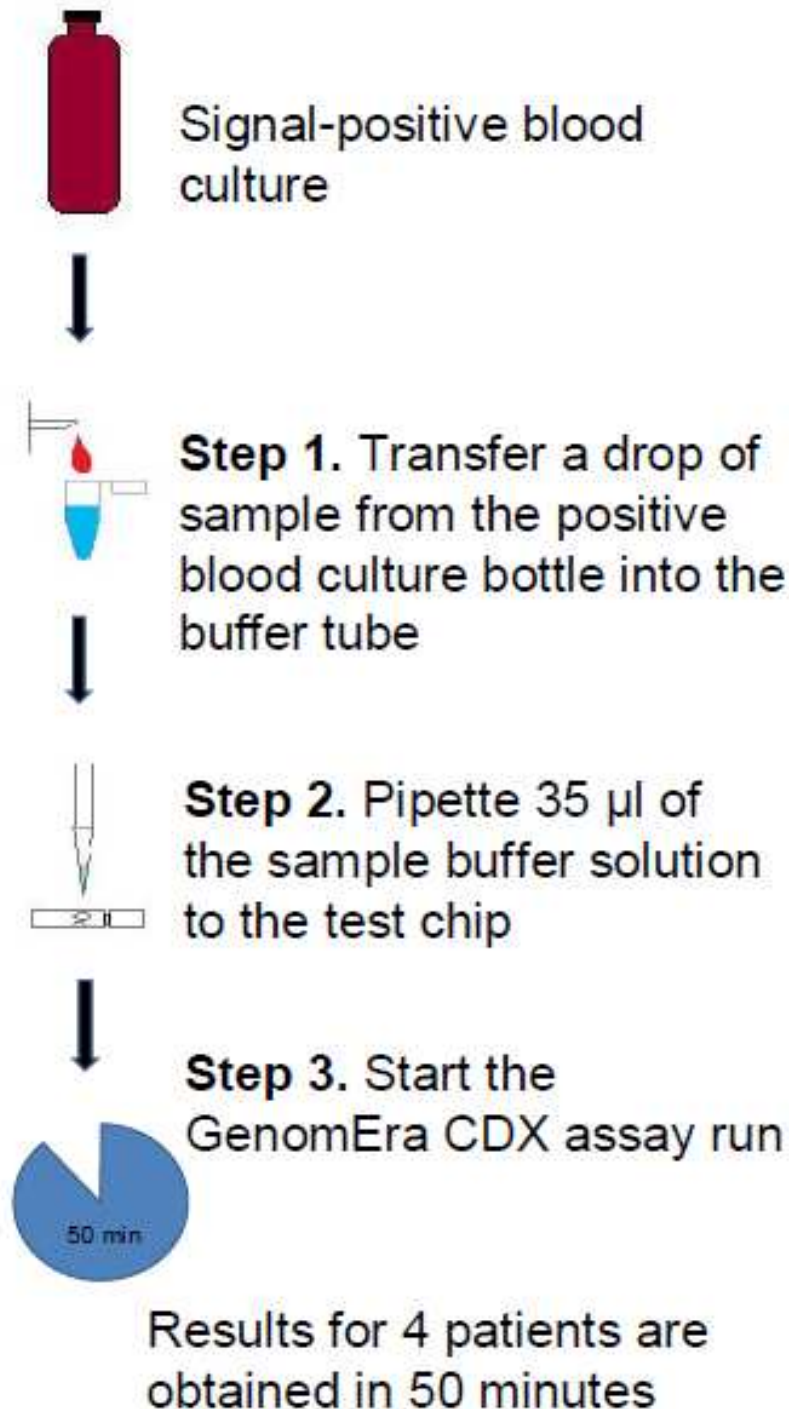
- Most common cause
- MR proportion ~50%



Routine methods

- After positive signal from blood culture automate
 - Gram-staining and microscopy (~10 - 20 minutes)
- If gram positive cocci in clusters
 - Biochemical tests, susceptibility testing and basic cultures (hands-on time ~10 – 30 minutes, **total turn-around time 16 – 24 hours**)
- If any problems with any of the tests
 - Additional testing (hands-on time ~10 – 30 minutes, total turn-around time 16 – 24 hours)

Total time to results after positive signal ~1 -2 days				
1. Subculture	2. Agglutination test	3. Susceptibility testing	4. Colorimetric test	5. Genetic PCR
				



BC diagnostics with GenomEra assay

- **After positive signal from blood culture automate**
 - Gram-staining and microscopy (~10 - 20 min.)
- **If gram positive cocci in clusters**
 - GenomEra MRSA/SA assay, (hands-on time ~1 minute, total turn-around time 50 minutes)
 - Susceptibility testing and basic cultures (hands-on time ~10 – 20 minutes, total turn-around time 16 – 24 hours)
- **Total time to MSSA, MRSA and MRCoNS detection after positive signal ~1 h**

Rapid detection of MRSA and MSSA in blood cultures

Hirvonen et al. One-step sample preparation of positive blood cultures for the direct detection of methicillin-sensitive and resistant *Staphylococcus aureus* and methicillin-resistant coagulase-negative staphylococci within one hour using the automated GenomEra CDX™ PCR system. **Eur J Clin Microbiol Inf Dis** 2012 31(10):2835-2842

Study included:

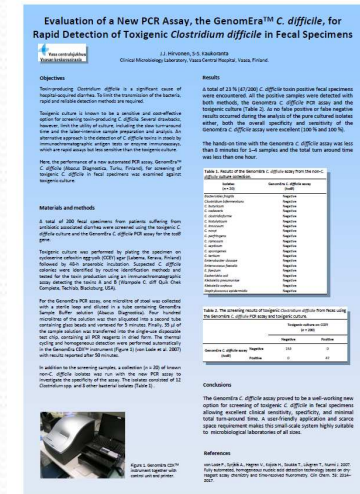
- 725 positive blood culture samples
 - 419 grampositive cocci in clusters
 - (159 MSSA, 9 MRSA ja 133 MRCoNS)
 - 316 other microbes
- 24 negative blood culture samples
- Sensitivity: 99.4% (MSSA), 100.0% (MRSA) and 99.3% (MRCoNS)
- Specificity: 99.8%



Next GenomEra tests in routine and evaluation in VCH?

Direct molecular screening of toxigenic *Clostridium difficile*

- GenomEra *C. difficile* evaluation poster at ECCMID 2013
- Fecal specimens screened with GenomEra
- Results compared to toxigenic culture
 - Simple sample preparation and rapid target detection when using GenomEra (50 min assay run, total turn around time < 1 h)
 - Toxigenic culture requires 2 d enrichment and more laborious sample analysis



	Positive	Negative
Total samples (n=200)	47	153
	Sensitivity	Specificity
	100.0%	100.0%

Direct MRSA swab screening evaluation

- Ongoing evaluations to change existing practices
 - Sensitivity of high importance
- Excellent NPV
- Cost efficiency important
 - Isolation day costs vs. total test costs



The near future blood culture and other evaluations?

- *Streptococcus pneumoniae*
- *Streptococcus agalactiae* (GBS)
- *E. coli* vs. other species
- VAN A & B
- CTX-M
- KPC
- NDM
- VIM



Thank you