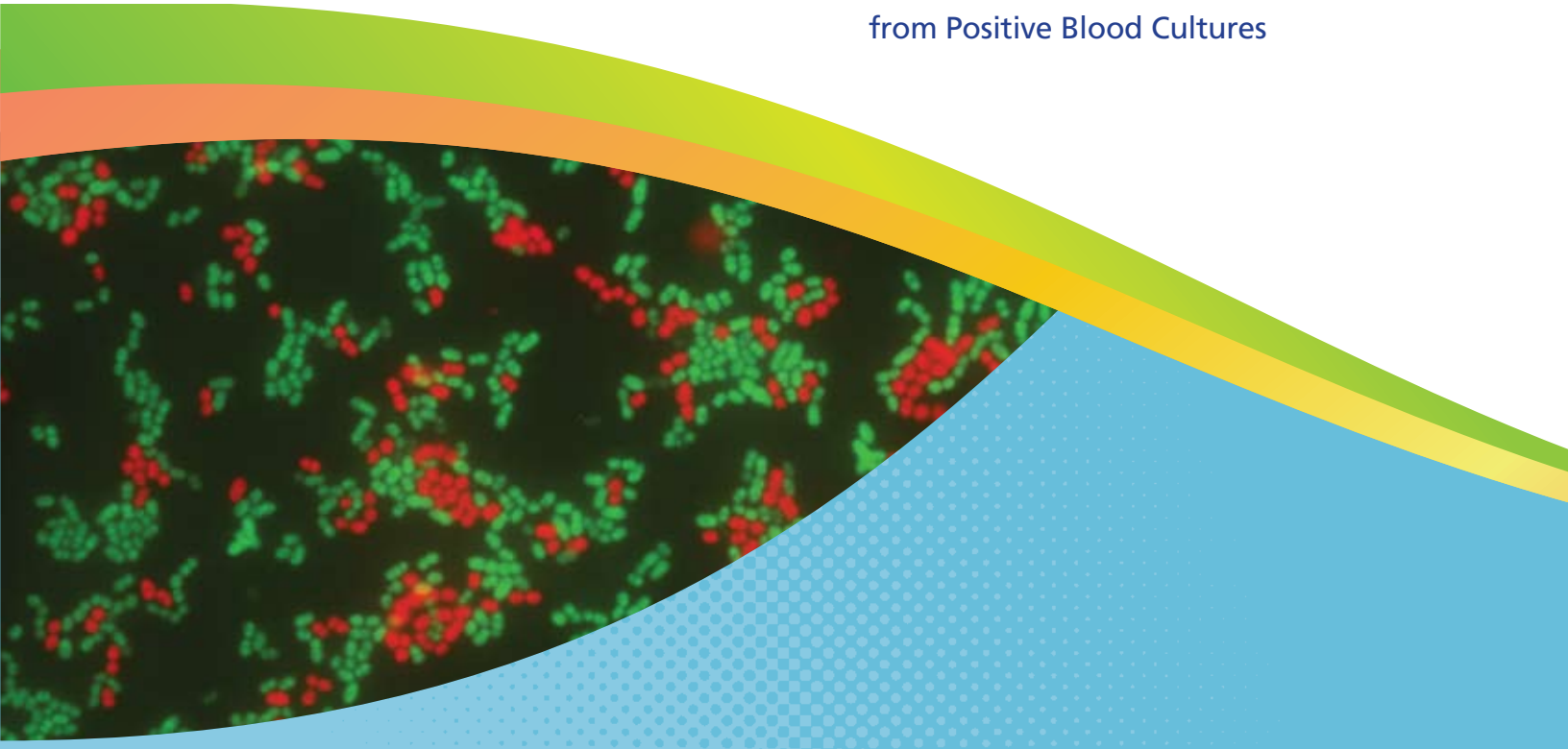
PNA FISH®
Enterococcus sp.

90 Min. Identification of *E. faecalis, E. faecium* and Other Enterococci from Positive Blood Cultures



Ampicillin and Vancomycin Resistant *E. faecium*

AdvanDx

"PNA FISH identified *E. faecium* a median 2.3 days earlier and was associated with statistically significant reductions in the time to initiating effective therapy and decreased 30-day mortality." Forrest et al. Antimicrob Agents Chemother. 2008 Oct; 52(10): 3558-63

Accuracy You Can Trust

PNA FISH Reliability: Sensitive and Specific

PNA FISH tests have been validated on all major blood culture systems and compared to identification results obtained via conventional, phenotypic identification methods. Refer to the package insert for complete performance data.

E. faecalis/OE PNA FISH® (KT003)

		Conventional Identification			
		E. faecalis	Other Enterococci*	Other Species†	Total
PNA FISH®	*E. faecalis*	41	0	0	41
	Other Enterococci	0	33	0	33
	Negative	0	0	78	78
	Total	41	33	78	152

Sensitivity *E. faecalis*: 100%

Sensitivity OE: 100%

Specificity: 100%

PPV *E. faecalis*: 100%

PPV OE: 100%

NPV: 100%

*_E. faecium_ (27), _E. casseliflavus_ (2), _E. gallinarum_ (2), Other _Enterococcus_ spp. (2)
†_Streptococcus_ spp. (75), _Abiotrophia_ spp. (3)

For more information visit www.PNA-FISH.com

The Challenge

Appropriate Therapy for Antibiotic Coverage for *E. faecium* Bloodstream Infections

Enterococcus species are the fourth most common cause of hospital-acquired bacteremia in the US and the fifth most common in Europe.[1] Although the vast majority of these infections can be linked to two causative pathogens, *Enterococcus faecalis* and *Enterococcus faecium*, treatment decisions are difficult as each species exhibits differing antibiotic resistance profiles.

While *E. faecalis* is generally susceptible to ampicillin, infections with other enterococci, mainly *E. faecium*, are often resistant to ampicillin or vancomycin or both. Since conventional identification methods can take up to 3 days or longer, patients with *E. faecium* bloodstream infections often receive inappropriate antimicrobial therapy[2,3] for days leading to higher mortality and significant extra hospital costs.[4]

The challenge for clinicians is how to ensure early, appropriate therapy for patients with *E. faecium* infections.

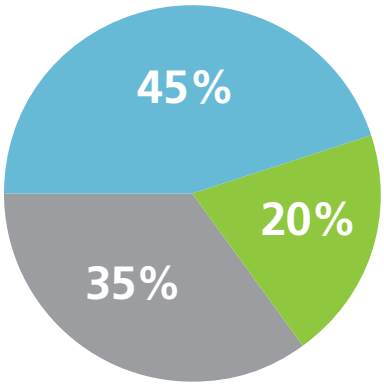
GPCPC-Positive Blood Cultures: Species Distribution[5]

E. faecalis (45%)

- 45% of GPCPC-Positive Blood Cultures
- Usually susceptible to ampicillin, rarely VRE
- Often unnecessarily treated with broad-spectrum antibiotics such as vancomycin

Streptococcus Species (35%)

- 35% of GPCPC-Positive Blood Cultures
- Generally susceptible to ceftriaxone and/or vancomycin[5]



E. faecium & Other Enterococci (20%)

- 20% of GPCPC-Positive Blood Cultures
- Often resistance to both ampicillin and vancomycin
- Primary causative pathogen of VRE bacteremia
- Up to 80% of patients with *E. faecium* bloodstream infections receive ineffective therapy[6]
- Associated with increased mortality, longer hospital stays and higher health care cost[4]

GPCPC= Gram positive cocci in pairs and chains

The Dilemma

Enterococci & Streptococci in Positive Blood Cultures: Ampicillin and Vancomycin Resistance

Gram Stain: *E. faecalis, E. faecium* and Other Enterococci or Streptococci?

- **Cannot distinguish *E. faecalis*** from ***E. faecium*** & other enterococci in Gram stain.
- **Dilemma:** Does the enterococci in the positive blood culture represent **vancomycin (VRE)** or **ampicillin resistant *E. faecium***, **ampicillin sensitive *E. faecalis*** or streptococci?
- When to **escalate therapy for *E. faecium*?**

Culture: Identification in 2-3 days.

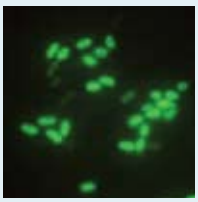
- **Conventional culture** and phenotypic identification can take an additional **2-3 days**.
- **Dilemma: Clinicians can't wait** an additional 2-3 days to prescribe the appropriate antimicrobial to cover for ampicillin and vancomycin resistant *E. faecium.*

The Solution

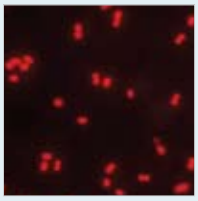
90 Minutes Identification and Differentiation of *E. faecalis* from *E. faecium* and Other Enterococci

Gram Stain

PNA FISH®: Identification Directly from Positive Blood Cultures



E. faecalis



E. faecium and Other Enterococci (OE)

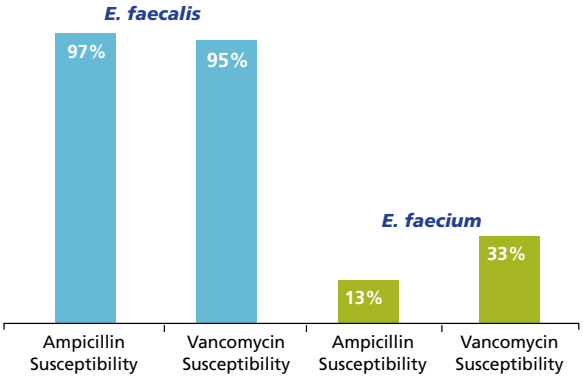
- **90 minutes, molecular identification** and differentiation of *E. faecalis* (green) from *E. faecium* & other enterococci (red), directly from positive blood cultures.
- Results **2-3 days earlier** than conventional methods.
- Ensure early, aggressive and **effective therapy for patients** with ***E. faecium* infections.**
- **Reduce mortality** for *E. faecium* bloodstream infections.
- **Avoid unnecessary use of broad-spectrum antimicrobials** (e.g. vancomycin, linezolid) for *E. faecalis.*

Proven Clinical Benefits

Use of PNA FISH to rapidly identify *Enterococcus* species from positive blood cultures has been shown to significantly improve therapy decisions and patient outcomes.

Differing Susceptibility to Ampicillin and Vancomycin for *E. faecalis* and *E. faecium*

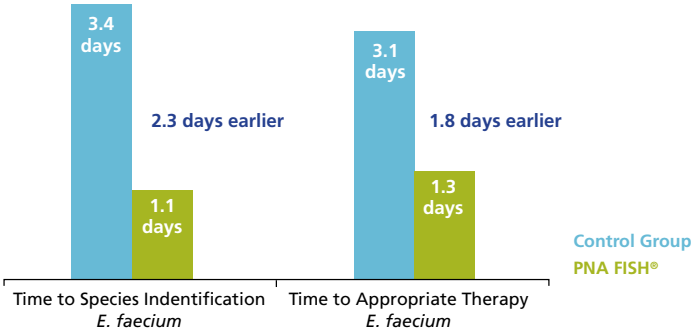
Summary of data collected from 268 hospitals in the United States on 14,430 GPCPC-positive blood cultures[5]



- ***E. faecalis*: 97% susceptible to ampicillin and 95% susceptible to vancomycin**
- ***E. faecium*: 13% susceptible to ampicillin and 33% susceptible to vancomycin**

Reduce Time to Appropriate Therapy

Quasi-experimental study of 224 patients (129 pre-intervention, 95 post-intervention) with *E. faecalis* and *E. faecium* positive blood cultures performed at the University of Maryland Medical Center (Baltimore, MD)[6]

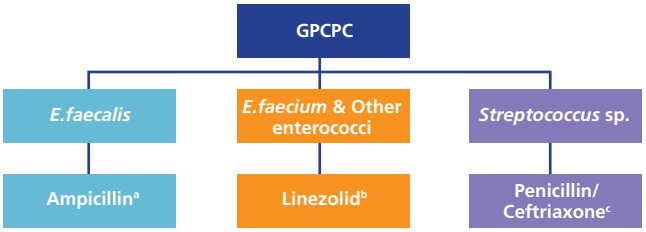


- **Initial empiric antimicrobial therapy was inadequate for 82% of *E. faecium* patients in the Control Group and 87% in the PNA FISH group**
- **Reduced time to species identification for *E. faecium* by 2.3 days**
- **Reduced time to appropriate therapy for *E. faecium* by 1.8 days**

Reduce Mortality for *E. faecium* Bloodstream Infections

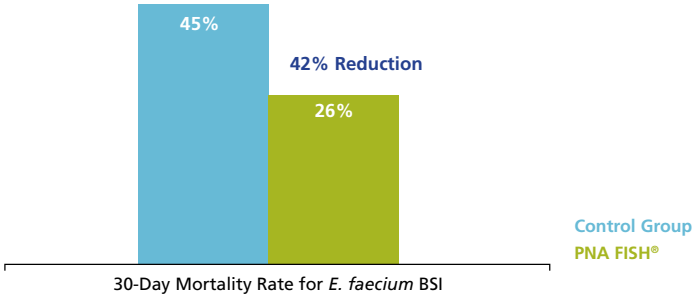
University of Maryland Medical Center Study[6]

Antimicrobial Treatment Alogrithm for PNA FISH results



a. vancomycin could be substituted for patients allergic to penicillin
b. high-dose daptomycin could be substituted if a patient is unable to take linezolid
c. vancomycin could be added with febrile neutropenia or suspected meningitis

Reduction in 30-Day Mortality



Bloodstream Infections and Positive Blood Cultures:

PNA FISH® tests provide rapid identification results for 95-99% of positive blood cultures.

Improving Care and Outcomes

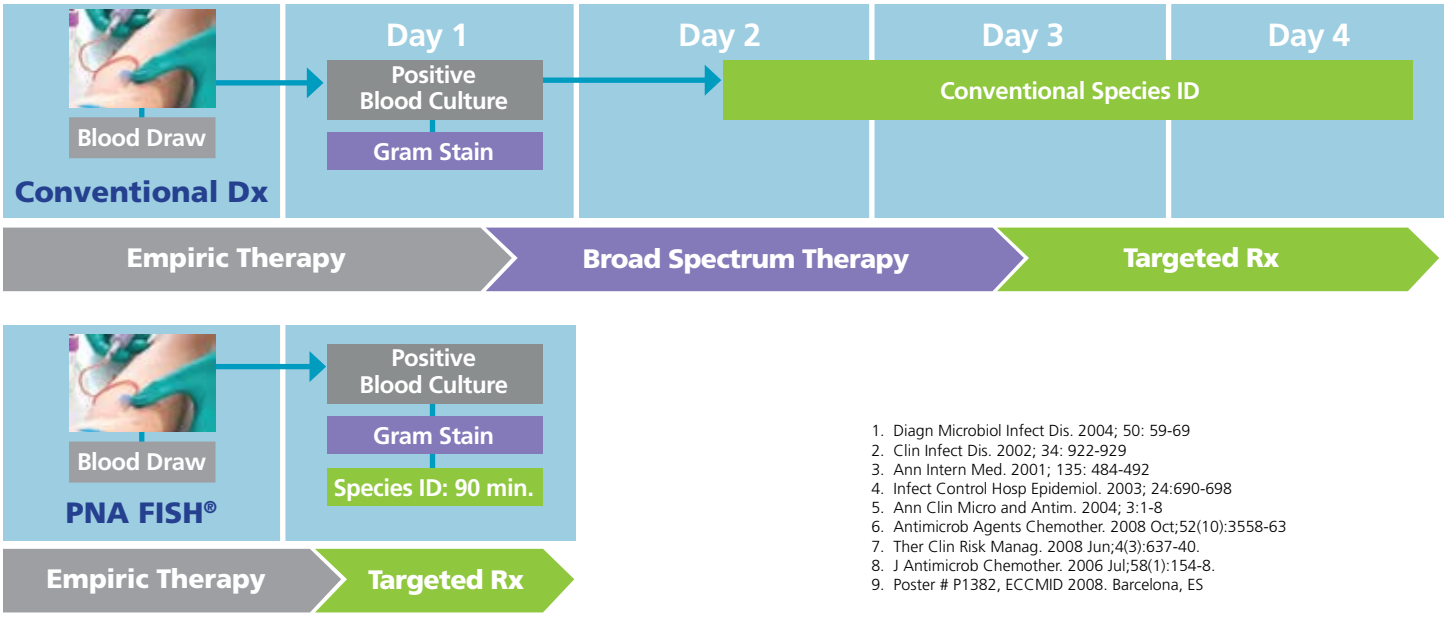
Rapid identification of bloodstream pathogens with PNA FISH can help physicians improve antimicrobial selection and has been shown to:

- **Reduce mortality rates** for *S. aureus* bacteremia[7]
- **Reduce unnecessary vancomycin** use, LOS and costs due to blood culture contamination[8]
- **Improve time to appropriate therapy** for *E. faecium* bacteremia by 1.8 days[6]
- **Reduce mortality rates** for *E. faecium* bacteremia[6]
- **Improve antifungal selection** for candidemia[9]

Species Distribution in Positive Blood Cultures

Gram Stain - Dilemma	Species	% of Group
GPCC (55%) Infection vs. Contamination	*S. aureus* Coagulase-Negative Staph	25% 75%
GPCPC (15%) Ampicillin and Vancomycin Resistance	*E. faecalis* *E. faecium* *Streptococcus* sp.	40% 25% 35%
GNR (20%) *P. aeruginosa* vs. non-*P. aeruginosa*	*E. coli* *K. pneumoniae* *P. aeruginosa* Other GNRs	35% 20% 15% 30%
Yeast (5%) Echinocandin vs. Fluconazole	*C. albicans* *C. glabrata* *C. parapsilosis* Other *Candida* sp.	50% 20% 15% 15%
Other (5%)		

PNA FISH® vs. Conventional Dx (90 Min. vs. 1-3 Days)



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2. Clin Infect Dis. 2002; 34: 922-929
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5. Ann Clin Micro and Antim. 2004; 3:1-8
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