Supplementary Figures and Tables

hostDx SEPSIS

Patient Report

Ordering and patient demographics info

Test Result and Interpretation

Bacterial Infection:	B4	Bacterial infection **very unlikely**
Viral Infection:	V22	Viral infection **possible**
Infection Severity:	S8	30-day mortality **very unlikely**

Likelihood Ratios

Test description and intended use statement

HostDx™ Sepsis is a gene expression profiling assay that quantifies relative expression of host response genes from whole blood collected in the PAXgene Blood RNA tube that generates three scores that fall within discrete interpretation bands for the likelihoods of bacterial infection, viral infection, and composite disease progression and 28-day mortality.

The test is intended to be used at the time of suspicion for acute infection to assess the risk of bacterial and/or viral etiologies, and to act as an aid in guiding antimicrobial treatment decisions and in the risk assessment of disease progression and 28-day in-hospital mortality in conjunction with clinical assessment and laboratory findings.

Additional performance characteristics (label requirements)

Inflammatix

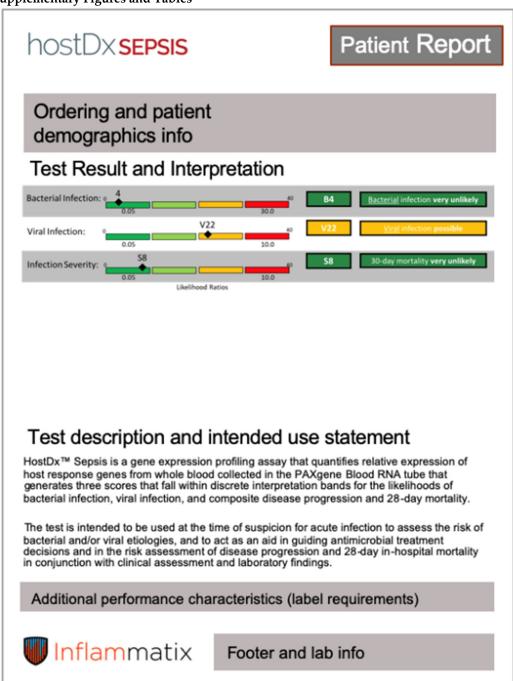Footer and lab info

Suppl. Figure 1: Proposed patient report for InSep as presented to the advisory board. Horizontal representation of test result and interpretation. Adoption of a new test in the emergency room setting can only be successful if the required performance criteria are met (see below) and if the result readout (patient report) is easy to understand and actionable. The advisors agreed that presenting

the test results including the interpretation would be suitable as a patient report. Advisors appreciated the concept of having three distinct results (scores) presented. While it may complicate decision making compared to the current standard of care, it also yields novel opportunity such as a low bacterial/high viral score which in current diagnostic tests cannot be achieved. To make the test results immediately available to physicians in the EHR, simplified reports such as a combination of numbers and letters would be required; the report could however be visualized as a pdf in an EHR with uncertain level of usage by providers in a busy ER setting. To ensure that providers actually act upon the results presented the report must be compatible with EHR inclusion. The proposed reports were considered optically pleasing but could easily be misinterpreted since providers are used to looking at the color scales but not the scores. Therefore, providing results in words (e.g., likely, unlikely, indeterminate) would be a preferred simplification. Advisors also pointed towards the need for education on test performance and actionable results in addition to simplicity to ensure appropriate actions. Advisors also discussed the need to have sensitivity and specificity shown in the patient report. While having this information available is important, it will most likely not be used in the ED.

Supplementary Table S1: Modelled results for InSep results at a fixed prevalence of 50% with varying likelihood ratios of (A) 10, (B) 7.5, and (C) 5 for the very likely (rule-in) interpretation band.

(A)

	Neg	Pos	LR	% in band	NPV	PPV	Sens	Spec
Prevalence = 50%, LR low = 0.05, LR high = 10								
Very likely	28	281	**10.0**	**31%**	**68%**	**91%**	**56%**	**94%**
Possible	73	151	**2.07**	**22%**	**55%**	**68%**	**30%**	**86%**
Unlikely	218	59	0.27	28%	79%	61%	88%	44%
Very unlikely	181	9	0.05	19%	95%	61%	98%	36%

(B)

	Neg	Pos	LR	% in band	NPV	PPV	Sens	Spec
Prevalence = 50%, LR low = 0.05, LR high = 7.5								
Very likely	47	351	**7.49**	**40%**	**75%**	**88%**	**70%**	**91%**
Possible	68	91	**1.33**	**16%**	**51%**	**57%**	**18%**	**86%**
Unlikely	204	49	0.24	25%	81%	60%	90%	41%
Very unlikely	181	9	0.05	19%	95%	61%	98%	36%

(C)

	Neg	Pos	LR	% in band	NPV	PPV	Sens	Spec
Prevalence = 50%, LR low = 0.05, LR high = 5								
Very likely	83	415	**5.0**	**50%**	**83%**	**83%**	**83%**	**83%**
Possible	59	41	**0.7**	**10%**	**59%**	**51%**	**92%**	**12%**
Unlikely	177	35	0.19	21%	84%	59%	93%	35%
Very unlikely	181	9	0.05	19%	95%	61%	98%	36%

Supplementary Table S2: Modelled InSep results at a fixed prevalence of 50% with varying likelihood ratios of (A) 0.05, (B) 0.075, (C) 0.1, and (D) 0.15 for the very unlikely (rule-out) interpretation band.

(A)

Prevalence = 50%, LR low = 0.05, LR high = 5							
	Neg	**Pos**	**LR**	**% in band**	**NPV**	**PPV**	**Sens**	**Spec**
Very likely	83	415	**5.0**	**50%**	**83%**	**83%**	**83%**	**83%**
Possible	59	41	**0.70**	**10%**	**59%**	**51%**	**92%**	**12%**
Unlikely	177	35	0.19	21%	84%	59%	93%	35%
Very unlikely	181	9	0.05	19%	95%	61%	98%	36%

(**B**)

Prevalence = 50%, LR low = 0.05, LR high = 5							
	Neg	**Pos**	**LR**	**% in band**	**NPV**	**PPV**	**Sens**	**Spec**
Very likely	83	415	**5.0**	**50%**	**83%**	**83%**	**83%**	**83%**
Possible	59	41	**0.70**	**10%**	**59%**	**51%**	**92%**	**12%**
Unlikely	177	35	0.19	21%	84%	59%	93%	35%
Very unlikely	181	9	0.05	19%	95%	61%	98%	36%

(C)

Prevalence = 20%, **LR low = 0.1**, LR high = 10							
	Neg	**Pos**	**LR**	**% in band**	**NPV**	**PPV**	**Sens**	**Spec**
Very likely	45	112	10.0	16%	90%	71%	56%	94%
Possible	115	60	2.08	18%	83%	34%	30%	86%
Unlikely	115	14	**0.49**	**13%**	**89%**	**21%**	**93%**	**14%**
Very unlikely	524	13	**0.1**	**54%**	**98%**	**40%**	**93%**	**66%**

(D)

Prevalence = 20%, LR low = 0.15, LR high = 10							
	Neg	**Pos**	**LR**	**% in band**	**NPV**	**PPV**	**Sens**	**Spec**
Very likely	45	112	10.0	16%	90%	71%	56%	94%
Possible	70	48	2.73	12%	83%	41%	24%	91%
Unlikely	70	17	**0.95**	**9%**	**80%**	**19%**	**8%**	**91%**
Very unlikely	616	23	**0.15**	**64%**	**96%**	**49%**	**89%**	**77%**

Supplementary Table 3: Modelled InSep results at a fixed prevalence of 20% with varying likelihood ratios of (A) 10, (B) 7.5, and (C) 5 for the very likely (rule-in) interpretation band.

(A)

Prevalence = 20%, LR low = 0.05, LR high = 10							
	Neg	**Pos**	**LR**	**% in band**	**NPV**	**PPV**	**Sens**	**Spec**
Very likely	45	112	**10.0**	**16%**	**90%**	**71%**	**56%**	**94%**
Possible	116	60	**2.07**	**18%**	**83%**	**34%**	**30%**	**86%**
Unlikely	349	24	0.27	37%	94%	28%	88%	44%
Very unlikely	290	4	0.05	29%	99%	28%	98%	36%

(B)

	Neg	Pos	LR	% in band	NPV	PPV	Sens	Spec
Prevalence = 20%, LR low = 0.05, LR high = 7.5								
Very likely	75	141	**7.49**	**22%**	**92%**	**65%**	**70%**	**91%**
Possible	109	36	**1.33**	**15%**	**81%**	**25%**	**18%**	**86%**
Unlikely	326	20	0.24	35%	94%	28%	90%	41%
Very unlikely	290	4	0.05	29%	99%	28%	98%	36%

(C)

	Neg	Pos	LR	% in band	NPV	PPV	Sens	Spec
Prevalence = 20%, LR low = 0.05, LR high = 5								
Very likely	133	166	**5.0**	**30%**	**95%**	**56%**	**83%**	**83%**
Possible	94	17	**0.7**	**11%**	**85%**	**21%**	**92%**	**12%**
Unlikely	283	14	0.19	30%	95%	27%	93%	35%
Very unlikely	290	4	0.05	29%	99%	28%	98%	36%