Irish Guideline for the Investigation of Blood Culture Samples

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Update September 2021
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Report to ISCM executive committee.

Effective date.

October 2021

Document History

Amendment: Version 2 - September 2019
Amendment Location: Page 5, Scope "It is accepted that aspects of this guideline will be enhanced or replaced by the introduction of molecular techniques.".
Amendment: Version 3 - September 2021. Interim measure pending full review.
Amendment: Version 3 - October 2021
Amendment locations:
Page 2, Summary of recommendations - analytical stage.
Page 5, Scope.
Page 6, Analytical stage
Page 8, Table 1 - analytical stage

Document Reference Number: CDI015/2021. Version 3

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Executive Summary

The detection of microorganisms in blood using automated blood culture systems continues to be the gold standard in bloodstream infection (BSI) diagnosis. The clinical utility of blood cultures is widely accepted. The detection of significant organisms in blood is helpful in directing further investigations as to the source of an infection. Furthermore, blood culture identification and susceptibility results allow for the rationalisation of antimicrobial therapy to target the organism(s) isolated, and optimise treatment thus reducing the emergence of antimicrobial resistance.[1]

Timeliness in the handling, processing and reporting of blood culture samples by the microbiology laboratory is of great importance in the provision of a quality service to users, and to guide effective management of the patient with BSI.[2] The aim of this guideline is to recommend the optimal turnaround times (TATs) for the handling, processing, and reporting of blood culture samples which reflect the clinical needs of the patient.[3]

Summary of Recommendations (See Table 1)

Pre-analytical stage

It is recommended that blood culture bottles are transported and loaded as soon as possible, and ideally within 4 hours from the time the sample is taken.

Analytical stage

Once noted to have a positive reading, the blood culture bottle should be sub-cultured without delay to the appropriate media (with or without direct susceptibility testing), as per local policy.

In recognition of the growing availability of molecular technologies within Irish laboratories when a blood culture flags positive either Gram stain or molecular identification of organisms can occur. Each laboratory must have a clear process/ SOP on how to deal with unusual or unexpected results from molecular identification (including possible false negative results) - these can include confirmatory gram staining and/or referring to reference laboratory.

It is recommended that the Gram stain/application of a commercial system for molecular identification of organisms of a positive blood culture should be performed, in line with local laboratory risk assessment, by a scientist equipped with the skills for Gram stain interpretation. There is no international evidence based consensus on TAT for Gram stains.[4, 5]

The *clinical significance* of the Gram stain/ molecular identification result is interpreted by the doctor to whom the result is communicated. A TAT of 24-48 hours is recommended for isolate identification, from the time a pure and adequate growth of the isolate is available for further testing.

A specific TAT is not recommended for direct susceptibility results.

A TAT of 24-48 hours is recommended for susceptibility results, from the availability of a pure and adequate growth of the isolate for susceptibility testing.

Post-analytical stage

Results of microscopy should be communicated in line with local risk assessment to the physician or other clinical personnel responsible for patient care. There is no evidence-based consensus within the international literature for TAT for performing and communicating Gram stain results.[4,5]

Preliminary positive reports pertaining to isolate identification should be reported verbally or electronically on the same working day the information becomes available.

If the preliminary identification of the organism suggests that a change in antimicrobial therapy may be warranted, the result should be communicated promptly to the clinician or other healthcare personnel responsible for the patient.

Preliminary negative results should be reported at 48 hours (or as per local agreement).

Final written or computer-generated reports should be issued after five days of incubation for standard negative blood culture investigations.

Direct antimicrobial susceptibility results should be interpreted by the Consultant microbiologist and are not formally reported, given the lack of standardisation possible.

Final susceptibility results should be reported verbally and / or electronically on the same day as the results are confirmed by the laboratory. If final susceptibility results suggest that a change in antimicrobial therapy may be warranted, they should be communicated promptly to the clinician or other healthcare personnel responsible for the patient.

Introduction

The detection of microorganisms in blood using automated blood culture systems continues to be the gold standard in bloodstream infection (BSI) diagnosis. Techniques which allow for the direct detection of microorganisms in blood are not routinely used in Irish laboratories. BSIs are common in Irish communities and hospitals. In 2013, over three and a half thousand *Escherichia coli* and *Staphylococcus aureus* bloodstream isolates were reported by Irish laboratories to the European Antimicrobial Resistance Surveillance Network (EARSNet).[6] The clinical utility of blood cultures is widely accepted. Positive blood culture results are an integral part of diagnostic algorithms such as the Duke criteria for endocarditis.[7] The detection of significant organisms in blood is helpful in directing further investigations as to the source of an infection. Blood culture identification and susceptibility results allow for the rationalisation of antimicrobial therapy to target the organism(s) isolated. Narrowing the spectrum of antimicrobial therapy reduces the emergence of antimicrobial resistance, as well as minimising hospital costs.[1,8] Equally, sterile blood culture results are useful in the assessment of any patient with a febrile illness.

Rationale

Timeliness in the handling, processing and reporting of blood culture samples by the microbiology laboratory is of great importance in the provision of a quality service to users, and to guide effective management of the patient with BSI.[2] The overall mortality associated with true BSI is 17.5%. Mortality is higher if the BSI is acquired in hospital (20.3%) or if the causative organisms are fungi (35.8%). BSI mortality also increases with age and other predisposing factors such as renal failure.[9] Extended-spectrum beta-lactamase- producing *Escherichia coli* and *Klebsiella pneumoniae* bloodstream isolates have become increasingly prevalent in Ireland.[6] The emergence of these resistant organisms in hospitals and communities compromises the success of commonly used antimicrobials and adds to the need for their earliest detection by the laboratory. Therefore, blood cultures are recognised as important samples.

Aim

The aim of this guideline is to recommend the optimal TATs for the handling, processing, and reporting of blood culture samples which reflect the clinical needs of the patient.[3]

Guideline Development Group & Methodology

Under the auspices of the National Clinical Programme for Pathology (NCPP) Laboratory Handbook subcommittee, an Irish Society of Clinical Microbiologists (ISCM) Blood Culture Guideline Development Group was convened. The purpose of this group was to devise an Irish guideline on the handling, processing and reporting of blood cultures. The Guideline Development Group consisted of seven members, including five clinical microbiologists and a representative from each of the Academy of Clinical Science and Laboratory Medicine (ACSLM) and the Royal College of Physicians Clinical Microbiology Specialist Training Programme. The 2017 revision group included all members of the previous subgroup with the exception of Dr. P . Stapleton. Additional members included in this review are listed at the front of this document and served to broaden the expertise of the group. A 2021 interim update was performed by Dr. Susanna Frost, consultant Microbiologist, with the support of the executive team of the Irish Society of Clinical Microbiologists (ISCM). A subsequent 2021 formal revision was performed by Dr. Suanana Frost (representing ISCM) and Dr. Richard Drew (representing the Irish Meningitis and Sepsis reference laboratory).

Accredited Irish laboratories are compliant with the ISO 15189 standard.3This document was the core reference for the group. To this end, the guidance followed the recommendations of Section 5.5.1 of the ISO 15189 document according to the following statement: ''Preferred procedures are those specified in the instructions for use of in vitro medical devices or those that have been published in established authoritative textbooks, peer-reviewed texts or journals, or in international consensus standards or guidelines, or national or regional regulations.3

The Health Protection Agency UK Standard for Microbiology Investigations (SMI), "Investigation of Blood Cultures (for organisms other than Mycobacterium species)," was available to the group.10This document and its references were reviewed in detail. As a result of this review, the group conducted a wider literature search, the references for which are cited in the text.

Review Process

The consultation process involved distribution of the guidance, as agreed by the Guideline Development Group, to clinical microbiologists and clinical microbiology scientists via the ISCM and ACSLM, respectively. Submissions made during the consultation process were reviewed and the relevant changes were incorporated into the final document submitted to the NCPP Clinical Advisory Group initially in 2015. This guidance will be reviewed every three years. Interim guidance will be issued in the intervening period, if necessary. Similar consultation has been employed for the 2017 revision.

Definitions

Infection is defined as a pathological process caused by invasion of normally sterile tissue or fluid (e.g. blood) or body cavity by pathogenic or potentially pathogenic micro-organisms. It is important to point out that frequently, infection is strongly suspected without being microbiologically confirmed.[11]

Bloodstream infections are caused by the entry of micro-organisms into the blood. BSIs may be primary or secondary in origin and transient, intermittent or continuous in nature.[12] Detailed case definitions can be found at *http://www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef_current.pdf*.

Sepsis is the clinical syndrome defined by the presence of both infection and the systemic inflammatory response syndrome (SIRS). However, since infection cannot always be microbiologically confirmed, the diagnostic criteria are infection, suspected or confirmed and the presence of any two or more of the modified SIRS criteria.[11]

Laboratory Risk Assessment

It is recommended that each laboratory should perform a clinical risk assessment to determine their own TATs for blood culture results

Factors for consideration include:-

i. Hospital setting and patient population.
ii. The timeline for processing a positive blood culture with regard to detection, subculture, Gram stain or molecular identification process, organism/s identification and susceptibility testing.
iii. Timeline for communication of results to clinical teams.
iv. Consultation with clinicians to ensure satisfaction with service.

Audit of the blood culture process and agreed time lines is recommended. Document agreed time lines within the laboratory handbook**.**

Caveats considered by the ISCM Blood Culture sub-group in the formulation of the guideline

Evaluation of the usefulness and limitations of blood culture results, particularly in the setting of the ongoing management of sepsis, led to the following conclusions which influenced the recommendations of this guideline:

Owing to time taken for current conventional methods to detect organism growth in blood, culture results do not facilitate the initial management of the septic patient. In this time-dependent critical situation the kernel of effective management is early recognition of sepsis, escalation of care as appropriate and prompt initiation of bundles of care such as the 'Sepsis Six', one element of which involves the taking of blood cultures. The Guideline Development Group recommends that patients with sepsis should be managed as outlined in the National Clinical Guideline.[11]

It was noted by the group that the recognition of sepsis has been greatly facilitated by institution of the National Early Warning Score (NEWS) tool, which is now in use in most acute hospitals in Ireland .[11,13]

Although the usefulness of blood culture results should not be under-estimated; timely appropriate empiric antimicrobial therapy and source control are the cornerstones of sepsis management as outlined in the National Clinical Guideline.[11] 'Awaiting' culture results is not appropriate in this context.

The institution of appropriate broad-spectrum antimicrobial therapy has been shown to reduce mortality in the setting of sepsis.[14].Therefore, it was noted by the group that the availability to clinicians of up-to-date empiric antimicrobial guidelines, which take national and local microbiological data into account, is essential. Timeliness in the initiation of antimicrobial therapy was also noted to be a critical component of sepsis management. Prompt administration of antimicrobials particularly within the first hour of recognition of sepsis leads to increased patient survival.[15].It is essential that an expert in infection is available at all times to provide advice on the management of the patient with sepsis.

The group recognised that the clinical utility of positive blood culture results is negatively affected by contamination with skin-type or environmental flora. Up to 50% of positive blood culture results represent pseudobacteraemia rather than true BSI.1In one study, only 12.4% of coagulase-negative staphylococcal (CoNS) isolates were found to be clinically significant.9In the initial stages these results can be harmful, particularly in the out-of-hours setting when the patients' clinical team are not available to make an informed decision regarding appropriate further action. This may lead to the initiation of unnecessary antimicrobial therapy and investigations, as well as lengthier hospital stays and costs. Efforts to reduce blood culture contamination rates in excess of 3% should be a consideration for the quality-improvement process in Irish microbiology departments in conjunction with their relevant clinical directorates or units.[16]

Where specific TATs are recommended in this document, they represent the optimal TAT for that process as agreed by the Guideline Development Group. The group recognises that there are differences in microbiology services in Ireland with regard to the funding and resources available to them. Implementation of this guidance may require augmentation of personnel and other resources. These resources may not be available in the short to medium term. Therefore, audit and risk assessment should form part of the implementation of this guideline, to ensure the timeliness and clinical utility of blood culture results in the context of patient safety.

Scope

Standard operating procedures relating to microscopy, culture, choice of media, incubation conditions, identification, susceptibility testing, patient selection and venesection method are found elsewhere.[17,18]The document does not describe the detection of viruses, parasites or Mycobacterium species, the processing of post-mortem blood cultures or the significance of individual organisms. It was previously accepted that aspects of this guideline will be enhanced or replaced by the introduction of molecular techniques, this 2021 interim revision reflects the more widespread availability and introduction of commercial molecular diagnostic tools.

Unless otherwise stated, the document refers to commercial, automated, continuous monitoring blood culture systems as the instrument for detection of microbial growth and commercial CE marked molecular systems. Individual instruments are not critically appraised. Manual or semi-automated blood culture processes are not considered in this document.

Type of specimen

Blood.

Please refer to local laboratory policy for the investigation of fluids from normally sterile sites.

Recommendations

A. Pre-analytical stage

The pre-analytical stage involves the time from collection of blood culture samples to the loading of blood culture bottles onto the analyser.

Recommended Loading Time (LT) for Blood Culture samples.

It is recommended that blood culture bottles are loaded as soon as possible, and ideally within 4 hours from the time the sample is taken. Urgent transport of blood culture bottles from clinical wards/departments to the Microbiology Laboratory is essential. An awareness of the impact of delays in transport by clinical teams and hospital porters should be emphasised.

Prompt incubation of blood culture bottles leads to reduced time to detection of positive growth (TTD).[19,20] Conversely, delays in the loading of blood cultures can result in false negative results.[18] Whilst a LT of 4 hours or less has been shown to be achievable,[21] it must be noted that factors such as internal and external transport facilities and out-of-hours staffing levels can have a significant impact on LT. Therefore, out-of-hours arrangements should be in place to facilitate the timely loading of blood culture bottles. This may involve setting up local transport arrangements between satellite hospitals or laboratories and the recipient laboratory, and / or the training of non-microbiological staff to load the bottles onto the instrument out-of-hours. A ≤ 4 hours TAT for the loading of blood culture bottles was considered to be the optimal TAT by the group. It is recommended that the LT is audited. Healthcare workers should be encouraged to document the time of venesection in order to facilitate this process. Factors identified by the audit process which result in systematic delays in the transport or loading of blood culture bottles should prompt remedial actions. Local risk assessment and audit may identify LTs outside of the range recommended here, which may also allow for the timely and successful recovery of microorganisms.

B. Analytical stage

The analytical stage involves monitoring for microbial growth by the analyser and the subsequent generation of microscopy, identification and susceptibility results from positive blood culture samples.

Recommended TAT for Sub-culture and Gram Stain of Positive Blood Culture samples

Once noted to have a positive reading, the blood culture bottle should be sub-cultured without delay to the appropriate media (with or without direct susceptibility testing) as per local policy.

As before, when a blood culture flags positive either Gram stain and / or rapid molecular tests for organism identification may be performed.

It is recommended that the Gram stain/molecular identification testing of a positive blood culture should be performed in line with local laboratory risk assessment, by a scientist equipped with the skills for performing and interpreting the test. The clinical significance of the result is interpreted by the doctor to whom the result is communicated.

The availability of a microbial isolate for further testing is essential to guide optimal management of the patient. It is recommended that once the blood culture bottle is noted to have flagged with a positive growth, the bottle should be sub-cultured to the appropriate media, (according to local policy) without delay. The decision to include direct susceptibility testing at this stage should be guided by the local laboratory risk assessment.

Gram stain results can result in more rational, cost- effective treatment, reduced length of stay (LOS),[6,20] and facilitate the earlier identification of patients on inadequate or inappropriate antimicrobial therapy. The application of molecular methods to positive blood cultures show similar benefits within a shorter time frame.[21-25]

A specific TAT has not been suggested for Gram staining/ molecular identification of positive blood cultures, as there is insufficient evidence to recommend a specific TAT. Gram stain interpretation is an important skill requiring extensive training and experience and should only be performed by those individuals competent to deliver consistent accurate results.

Inaccurately reported Gram stain results can lead to sub-optimal and inappropriate therapy and represents a patient safety issue.[2] Equally, the reporting of a Gram stain result from a contaminated blood culture, or one that is not in keeping with the culture the following day, has similar adverse consequences.[23] This scenario is further exacerbated if the Gram stain report is inappropriately interpreted by staff who may not be familiar with the patient. Therefore, careful consideration should be used in deciding to whom Gram stain interpretation is entrusted[2]. Efforts should also be made to reduce blood culture contamination rates.[16,23] Local risk assessment or audit is recommended to ensure TATs for Gram stain interpretation and reporting meet the clinical needs of the patient.[3] This may be aided by liaison with laboratory users, which in turn may lead to locally agreed TATs.[3]

Recommended TAT for Isolate Identification

A TAT of 24-48 hours is recommended, from the time a pure and adequate growth of the isolate is available for further testing.

Recommended TAT for Direct Susceptibility Results

It was agreed by the group that direct susceptibility results can be useful for microbiologists in directing early antimicrobial therapy. However, as the direct susceptibility testing method is not a standardised process, a specific TAT is not recommended.

Recommended TAT for Final Susceptibility Results

The recommended TAT for final susceptibility results is 24-48 hours from the availability of a pure and adequate growth of the isolate for susceptibility testing.

C. Post-analytical stage

The post-analytical stage involves the reporting and communication of microscopy and culture results. A medical microbiologist should be available to provide further advice on blood culture results that have been communicated, if required.

Recommended Reporting Procedure for Microscopy Results

Results of microscopy should be communicated in line with local risk assessment by the laboratory to the physician or other clinical personnel responsible for patient care. [10]

Requestors have a responsibility to ensure contact details are clear when ordering the test.[24] The laboratory, in conjunction with its users, should establish, define and document local protocols for the effective and standardised communication of results. Criteria to be followed on receipt of such communications should also be considered.[24] Written or computer-generated reports should follow preliminary / verbal reports as soon as practicable.

Recommended Reporting Procedure for Culture Results

Preliminary positive reports pertaining to isolate identification should be reported verbally or electronically on the same working day the information becomes available. If the preliminary identification of the organism suggests that a change in antimicrobial therapy may be warranted, the result should be communicated promptly (within a two-hour period) to the clinician or other healthcare personnel responsible for the patient. If appropriate, it should be stated that a further report will be issued. Final written or computer-generated reports should follow preliminary / verbal reports on the same day as confirmation, where possible.[10]

Preliminary negative results should be reported at 48 hours from collection (or as per local agreement).[10] Ideally preliminary negative results should be generated automatically to closely reflect the true incubation time.

Final written or computer-generated reports should be issued after five days of incubation for standard negative blood culture investigations. Cultures requiring extended incubation or reference laboratory testing may require a greater period of time before generation of a final report.

Recommended Reporting Procedure for Antimicrobial Susceptibility Results
Direct Susceptibility Results.
As direct susceptibility testing is not a standardised process, these results should be relayed to the clinical team according to local policy and under the direction of the microbiologist interpreting the results.

Final Susceptibility Results
Final susceptibility results should be reported verbally and / or electronically on the same day as the results are confirmed by the laboratory. If final susceptibility results suggest that a change in antimicrobial therapy is warranted, they should be communicated promptly (within a two-hour period) to the clinician or other healthcare personnel responsible for the patient. Owing to the slow-growing nature of certain organisms, a longer incubation period may be required before susceptibility results can be correctly interpreted and reported.

Notification to the Health Protection Surveillance Centre (HPSC)

The Infectious Diseases Regulations 1981 (and subsequent amendments) require diagnostic laboratories to notify the Medical Officer of Health (MOH) / Director of Public Health (DPH) of certain *diseases*. Immediate preliminary notification is required for a *sub-set of notifiable diseases*. Notifications may be made in writing, by email or by telephone to the MOH / DPH. A comprehensive list of causative agents notifiable to the HPSC under the *Infectious Diseases (Amendment) Regulations 2011 (S.I. No. 452 of 2011)* is available at: *http://www.hpsc.ie/NotifiableDiseases/ListofNotifiableDiseases/File,678,en.pdf*.

Table 1 Summary of Recommendations for Investigation of Blood Culture Samples		
Investigative Stage	**Test/Process**	**Recommended TAT or Reporting Procedure**
	Pre-Analytical	
Collection, transport and loading of samples	TAT for collection to loading	≤ 4 hours
	Analytical	
From Flagging Positive to Microscopy & from availability of an isolate for identification and susceptibility results	Sub-culture	Once a positive flag is noted sub-culture without delay
	Gram stain/rapid molecular identification	In line with local laboratory risk assessment, by a scientist with the skills for Gram stain interpretation.
	Identification	24-48 hours
	Susceptibility testing	24-48 hours
	Post –Analytical	
Negative report (from receipt in lab to negative reporting)	Preliminary Negative Report	48 hours (or as per local policy)
	Final Negative Report	After five days of incubation (greater if extended incubation applied)
Positive report (from positive flag to positive reporting)	Positive Microscopy Report	≤ 2 hours (from the time the result is available for reporting)
	Preliminary Identification Report (e.g. *S.aureus-'presumptive')*	Report as soon as possible, ≤ 2 hours if result suggests a change in therapy may be warranted
	Direct susceptibility results	As per local policy/directed by microbiologist
	Final identification and susceptibility Results	Report the same day as confirmation of results ≤ 2 hours if results suggest a change in therapy warranted

References

1. Fitzpatrick F, Turley M, Humphreys H, Smyth E. An after-hours clinical liaison blood culture service-is it worth it? Clin Microbiol Infect.2004;10:917-921.

2. Uehara Y, Yagoshi M, Tanimichi Y, Yamada H, Shimoguchi K, Yamamoto S et al. Impact of Reporting Gram Stain Results from Blood Culture Bottles on the Selection of Antimicrobial Agents. Am J Clin Pathol. 2009;132(1):18- 25.

3. ISO 15189:2012(en) available at: *https://www.iso.org/obp/ui/#iso:std:iso:15189:ed-3:v2:en*.

4. C.Fitzgerald, P. Stapleton, E.Phelan, P.Mulhare, B.Carey, M.Hickey, B.Lynch, M.Doyle. Rapid Identification and antimicrobial susceptibility testing of positive blood cultures using MADLI-TOF MS and a modification of the standardised disc diffusion test: a pilot study. BMJ J. Clin Pathol 2016;**69**:1025-1032. Doi:10.1 1136/jclinpath- 2015-203436.

5. Manjula Meda, James Clayton, Reela Varghese, Jayakeerthi Rangaiah, Clive Grundy et al. What are the critical steps in processing blood cultures? A prospective audit evaluating current practice of reporting blood cultures in a centralised laboratory serving secondary care hospitals. BMJ J. Clin Pathol 2017;**70**:361-366. Doi:10. 1136/jclinpath-2016-204091.

6. EARS-Net Report, Quarter 4 2013. March 2014. Available at: *http://www.hpsc.ie/A-Z/ MicrobiologyAntimicrobialResistance/EuropeanAntimicrobialResistanceSurveillanceSystemEARSS / EARSSSurveillanceReports/2013Reports/File,14572,en.pdf*.

7. Durack DT, Lukes AS, Bright DK. Duke Endocarditis Service. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Am J Med 1994;96:200-9.

8. Cunney RJ, McNamara EB, Alansari N, Loo B, Smyth EG. The impact of blood culture reporting and clinical liaison on the empiric treatment of bacteraemia. J Clin Pathol .1997;50(12):1010-1012.

9. Weinstein MP, Towns ML, Quartey SM, Mirret LG et al. The Clinical Significance of Positive Blood Cultures in the 1990s: A Prospective Comprehensive Evaluation of the Microbiology, Epidemiology, And Outcome of Bacteremia and Fungemia in Adults. Clin Infect Dis 1997;24:584-602.

10. The Health Protection Agency UK Standard for Microbiology Investigations. Investigation of Blood Cultures (for organisms other than Mycobacterium species). Bacteriology B 37(7):1-47.

11. Sepsis Management. National Clinical Guideline no. 6. ISSN 2009-6259. Available at: *http://hse.ie/eng/ about/Who/clinical/natclinprog/sepsis/sepsis6.pdf* accessed December 2014.

12. CDC/NHSN Surveillance Definitions for Specific Types of Infections. Available at: *http://www.cdc.gov/ nhsn/PDFs/pscManual/17pscNosInfDef_current.pdf* accessed December 2014.

13. Clinical Practice Guideline. The Irish Maternity Early Warning System (IMEWS) available at: *http://www.hse. ie/eng/about/Who/clinical/natclinprog/obsandgynaeprogramme/imews/* accessed January 2015.

14. Leibovici L, Drucker M, Konigsberger H et al. Septic shock in bacteremic patients: risk factors, features and prognosis. Scand J Infect Dis. 1997;29:71-71.

15. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34(6):1589–1596.

16. Snyder SR, Favoretto SM, Baetz RA, Derzon JH, Madison BM, Mass D, Shaw CS, Layfield CD et al. Effectiveness of Practices to reduce Blood Culture Contamination: A Laboratory Medicine Best Practices systematic review and meta-analysis. Clin Biochem. 2012;45:999–1011.

17. Public Health England. Standards for Microbiology Investigations (SMI). Available at: *https://www.gov.uk/ government/collections/standards-for-microbiology-investigations-smi* accessed January 2015.

18. *Saving Lives – Taking blood cultures. A summary of best practice.* London, 2007.

19. Kerremans. Van der Bij AK, Goessens W, Verbrug HA, Vos MC. Immediate Incubation of Blood Cultures Outside Routine Laboratory Hours of Operation Accelerates Antibiotic Switching. J Clin Microbiol. 2009.47(11) 3520-3.

20. Sautter RL, Bills AR, Lang DL, Ruschell G, Heiter BJ, Bourbeau PP. Effects of Delayed-Entry Conditions on the Recovery and Detection of Microorganisms from BacT/ALERT and BACTEC Blood Culture Bottles J Clin Microbiol. 2006;44(4):1245-1249.

21. Bengtsson J, Wahl M, Larsson P. Assessment of the BacT/Alert blood culture system: rapid bacteraemia diagnosis with loading throughout the 24 h. Clin Microbiol Infect. 1998;4(1):33-37.

22. Beekman SE, Diekema DJ, Chapin KC, Doern GV. Effects of rapid detection of bloodstream infections on length of hospitalisation and hospital charges. J Clin Microbiol. 2003;41(7):3119-3125.

23. Huang AM, Newton D, Kunapuli A, et al. Impact of rapid organism identification via matrix-assisted laser desorption/ionization time-of-flight combined with antimicrobial stewardship team intervention in adult patients with bacteremia and candidemia. Clin Infect Dis. 2013;57:1237–1245.

24. Gaydos CA, Quinn TC, Willis D, Weissfeld A, Hook EW, Martin DH, Ferrero DV, Schachter J. 2003. Performance of the APTIMA Combo 2 assay for detection of Chlamydia trachomatis and Neisseria gonorrhoeae in female urine and endocervical swab specimens. J. Clin. Microbiol. 41:304–309. 10.1128

25. Ray STJ, Drew RJ, Hardiman F, Pizer B, Riordan A. Rapid Identification of Microorganisms by FilmArray Blood Culture Identification Panel Improves Clinical Management in Children, The Pediatric Infectious Disease Journal: May 2016;35(5): 134-138

26. Hall KK, Lyman JA. Updated Review of Blood Culture Contamination. Clin Microbiol Rev. 2006;19(4):788802.

27. Key Performance Indicators in Pathology. Recommendations from the Royal College of Pathologists. Available at: *www.rcpath.org/Resources/RCPath/Migrated%20Resources/Documents/K/key_ performance_indicators_in_pathology_3_2.pdf* accessed August 2014.