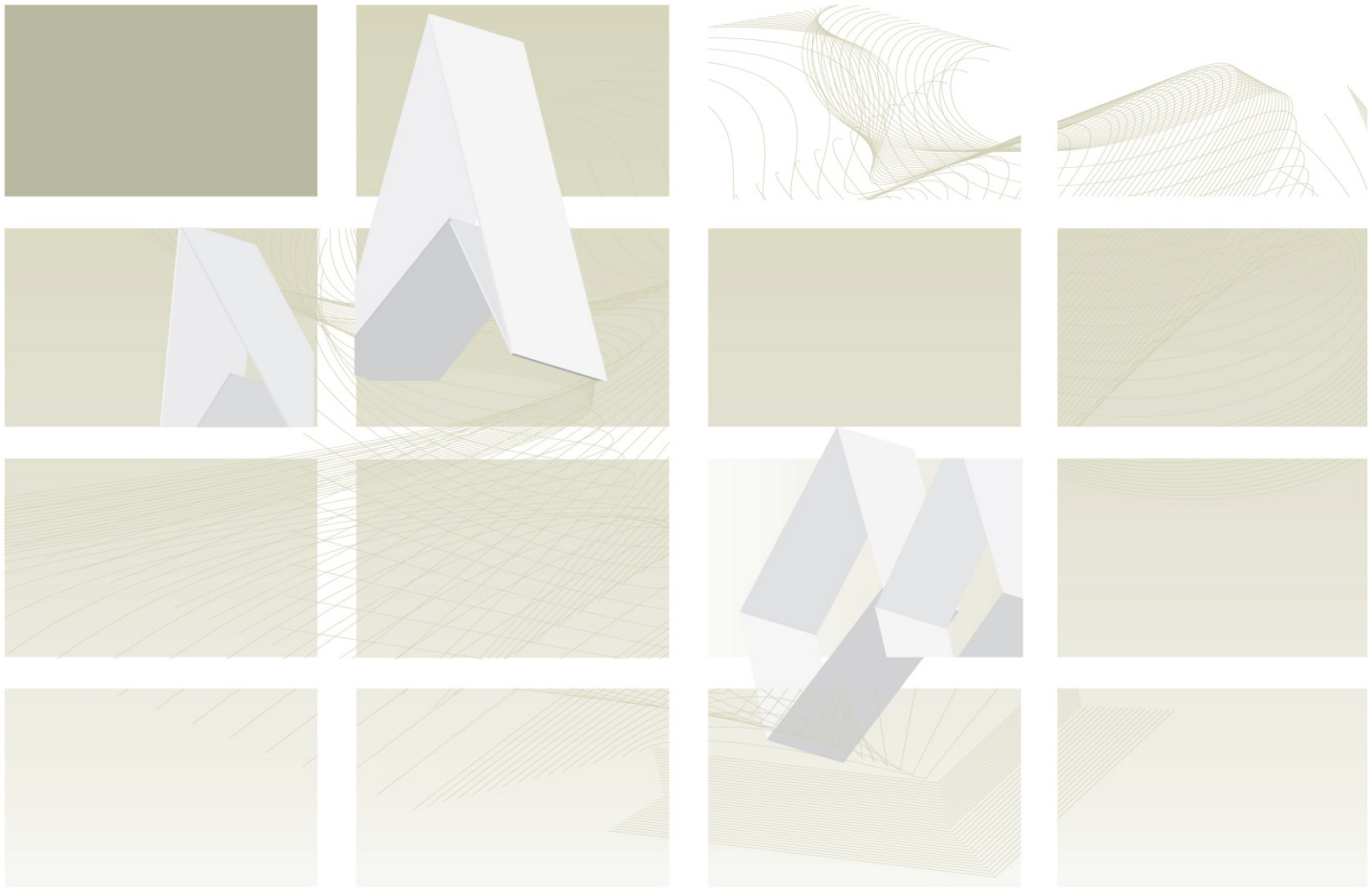
Public Health England

NHS

UK Standards for Microbiology Investigations

Review of users' comments received by
Working group for microbiology standards in clinical virology/serology

V 4 Investigation of hepatitis B infection



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"NICE has renewed accreditation of the process used by **Public Health England (PHE)** to produce **UK Standards for Microbiology Investigations**. The renewed accreditation is valid until **30 June 2021** and applies to guidance produced using the processes described in **UK standards for microbiology investigations (UKSMIs) Development process, S9365', 2016**. The original accreditation term began in **July 2011.**"

Recommendations are listed as ACCEPT/ PARTIAL ACCEPT/DEFER/ NONE or PENDING

Issued by the Standards Unit, Microbiology Services, PHE

RUC | V 4 | Issue no: 1 | Issue date: 07.06.18

First consultation: 16/11/2012 – 08/02/2013

Version of document consulted on: V 4de+

Proposal for changes

Comment number	1		
Date received	04/12/2012	**Lab name**	Microbiology East & North Herts NHS Trust
Section	"Confirmation flowchart by alternative assay - 1st test detected, 2nd test not detected.		
Comment			
In our routine DGH laboratory any discrepant HBsAg result would be sent to the reference laboratory for confirmation and full serological markers (we do not perform confirmatory tests in house). Using Anti-HBc test (assuming it is IgG as it is not stated on the flow chart) on its own would not seem appropriate as early acute HBV cases may be missed if a second sample is not collected as part of patient follow up. If Anti-HBc IgM is indicated this should be made clear on the flow chart.			
Recommended action	**NONE** The flow chart is correct as it stands.		

Comment number	2		
Date received	07/02/2013	**Lab name**	Newcastle
Section	As outlined in each comment		
Comment			
a. Flowchart p14 and note c) p15 We would like to suggest that for HBsAg positive / anti-HBc negative samples a full marker profile would normally be routine rather than optional, and HBV DNA should be optional rather than routine. As suggested in note c) follow-up samples should make the diagnosis in most cases, and could be quicker than HBV DNA, depending on the laboratory. b. Table p16 Row 7. Relating to the above, we are not sure that any lab would perform anti-HBs and HBV DNA in such a case without also performing other markers. Is this row needed? c. Table p16/17 Row 9 is a subset of row 10. It is therefore unclear on what basis these different report comments are being used. Regardless of e-marker status, acute infection or flare of infection are both possible interpretations and should be assessed on clinical history, IgM level. d. Table p17 Rows 10-14: It is unclear why HBV DNA is included in these rows presumably this would not be regarded as essential for testing on the original sample. In most cases this could be done on a further sample sent after specialist referral.			
Recommended action	a. **ACCEPT**		

	The flowchart has been streamlined. b. **NONE** The row is required for completeness. c. **NONE** The row is required for completeness. d. **NONE** The table is designed to cover all eventualities and therefore needs to be present.

Comment number	3		
Date received	14/02/2013	**Lab name**	Public Health Wales
Section	Page 9 and Table		
Comment			
a. Page 9: Inconsistent terminology- we note that you are using detected/not detected for the HBsAg which we are happy with. However, on this page you are using detected/not detected for the HBcAb, while on page 11 you are using positive/negative for the same antibody test. There is also a comment on page 10 in the footnotes stating false reactives, when reactive has not been used at all. b. Page 11: You are referring to the HBV DNA results as positive/negative when we would prefer detected/not detected. In addition, we would not go directly to HBV DNA testing in scenarios where the HBsAG were detected but all other markers (including eAg) were negative. We would telephone to request a further sample to test ASAP (with information about the patient), and if no recent vaccination history would request separate EDTA sample to perform HBV DNA (if the second sample also detected HBsAG). Table: c. 7-We would have a further box as we would not go directly to HBV DNA testing but would perform the e markers and IgM and if negative would request a further sample (and would do so even if we had a negative HBV DNA test) in the report comment section. d. 9 and 10- After the immediate repeat we would request a further sample in 3-6 months (the same as 11/12) in the report comment section. e. 13- Suggest add Refer to hepatologist in the report comment section.			
Recommended action	a. **ACCEPT** The terminology used within the documents has now been defined and standardised. b. **ACCEPT** The UK SMI has been updated. c. **NONE** The table is intended for guidance when all the results		

	have been obtained. d. **ACCEPT** The UK SMI has been updated. e. **ACCEPT** The document has been updated.

Second consultation: 20/08/2015 – 17/09/2015

Version of document consulted on: V 4dzf+

Proposal for changes

Comment number	1		
Date received	20/08/2015	**Lab name**	Public Health Laboratory Bristol
Section	Various (see below)		
Comment			

Title

a. This guideline now includes HBV DNA testing; the title should be revised to avoid uncertainty.

Laboratory diagnosis

b. "Presence of detectable IgM antibody to hepatitis B core antigen (anti-HBc IgM) **or absence of anti-HBc** is used to help determine whether the HBsAg is associated with an acute or a chronic infection."

c. In early acute Hepatitis B, HBsAg, HBeAg and HBV DNA become detectable before development of anti-HBc and anti-HBc IgM.

d. "It is a useful test for validating a positive HBsAg result, and is found together with anti-HBs antibody in past resolved infections." – Change 'validating' to 'corroborating'?

e. A non-specific result is possible due to the low specificity of anti-HBc tests. However past resolved Hepatitis B is also possible as anti-HBs levels decline below detection threshold in a proportion of this group. Use of a second anti-HBc test may be helpful.

f. "Contacts who are HBAg negative, but that are high risk and who are anti-HBc positive should not be vaccinated." Change to "High risk contacts who are HBsAg negative, but anti-HBc positive should not be vaccinated."

g. Branched chain DNA is not an amplification assay.

h. "Detection of HBV DNA is useful in early diagnosis in at risk individuals before HBsAg appears, **in resolving HBV infection status in patients with indeterminate HBsAg results,** and for monitoring viral load during therapy."

i. Abbreviate exposure prone procedures as EPP.

j. Change "If the pre-treatment viral load is between 10^3 and 10^5 geq/mL, the HCW may work whilst taking antiviral therapy provided the HBV DNA level is supressed to below 10^3 geq/mL. If baseline viral load is above 10^5 geq/mL the HCW is ineligible to

perform exposure procedures." to "If the pre-treatment viral load is between 10^3 and 10^5 geq/mL, the HCW may perform EPP whilst taking antiviral therapy provided the HBV DNA level is supressed to below 10^3 geq/mL. If baseline viral load is above10^5 geg/mL the HCW is ineligible to perform EPP." k. Expand ccc DNA: covalently-closed circular (ccc) viral. Public health management l. "Positive anti-HBc IgM results consistent with recent **acute** HBV **infection** should be reported urgently" Hepatitis B reporting for immunocompetent individuals m. Row 7, Hep B DNA column: Change 'not detected' to 'not tested'. n. Row 10, Note column: anti-HBc IgG avidity, clinical presentation and prior evidence of chronic Hepatitis B. o. Row 14, Suggested wording column: The HBe marker pattern is not particularly unusual.	
Recommended action	a. **ACCEPT** Title changed to 'Investigation of hepatitis B infection in the immunocompetent (including pregnant women)'. b. **ACCEPT** Text updated. c. **ACCEPT** Text updated. d. **ACCEPT** Text updated. e. **PARTIAL ACCEPT** Text updated 'decline' replaced with 'may be' as an alternative scenario could be that anti-HBs had not developed. f. **ACCEPT** Text updated. g. **NONE** Branched chain DNA is a signal amplification technique. h. **ACCEPT** Text updated. i. **ACCEPT** Suggested rewording accepted, however text replaced with link to the guidance. j. **PARTIAL ACCEPT** Suggested rewording accepted, however text replaced with link to the guidance.

	k. **ACCEPT** Text updated. l. **PARTIAL ACCEPT** Text updated to 'recent HBV infection'. It was felt that it was not necessary to include 'acute' in the sentence. m. **ACCEPT** Text updated. n. **ACCEPT** Text updated. o. **ACCEPT** Text removed.

Comment number	2		
Date received	21/08/2015	**Lab name**	Scottish National Blood Transfusion Service
Section			
Comment			
Page 9 of 25 Last paragraph refers to HWC and should read HCWs.			
Financial barriers			
No.			
Health benefits			
No.			
Recommended action	**ACCEPT** However, section replaced with link to the guidance.		

Comment number	3		
Date received	01/09/2015	**Lab name**	Newcastle
Section	a. P9 4th paragraph b. P9 final paragraph c. Table line 3		
Comment			
a. P9 4th paragraph, line 5 typo- should read HBsAg. b. P9 final paragraph should this not reflect the change to IU/l?			

c. Table line 3 Isolated anti-HBc. Anti-HBs is not infrequently absent in patients with past HBV infection. An anti-HBc reactive result at good level with confirmation on a second assay should be reported as for those with detectable anti-HBs as 'Consistent with past HBV infection'.	
Financial barriers	
No.	
Recommended action	a. **ACCEPT** Text updated. b. **ACCEPT** Text replaced with link to guidance. c. **ACCEPT** Text updated.

Comment number	4		
Date received	01/09/2015	**Lab name**	Nottingham
Section	Introduction		
Comment			
a. Page 9 para 4 - you refer to HBAg. This is not helpful. I think you mean HBsAg. b. Page 9 para 6 - I have no idea at all why you are bothering to attempt to precis an extensive set of complex guidance on HBV-infected HCWs in this document! In what way does this impact on HBV diagnostic serology? However, if you insist on covering this, then PLEASE get the guidance right!!!!! c. Page 9 para 6 - you refer to HWCs when you mean HCWs. d. Page 9 para 6 - you specify limits of HBV DNA in geq/ml. The Advisory Group on Hepatitis has agreed this should be changed to IU/ml - suggest asking Fortune Ncube when this is going to happen. e. Page 10 1st para. You state DNA levels should be monitored regularly at 3-monthly intervals (on two blood samples, one month apart), followed by yearly monitoring. Quite apart from this being self-evidently ridiculous (how can you monitor 3 monthly on 2 blood samples one month apart??!!??) it is also factually incorrect. Management of HBV-infected HCWs is complicated enough without official guidance such as this making blatantly incorrect statements. You have conflated the guidance on HBV-infected HCWs NOT on antiviral therapy (who require an initial assessment on 2 blood samples taken one month apart, and then annual follow-up) with the guidance on HBV-infected HCWs who ARE on anti-viral therapy (who should be monitored once every 3 months full-stop). You might also bear in mind that this guidance is again being changed, so that the need for 2 initial samples taken one month apart has been dropped - again, Fortune will know the details.			
Evidence			
All published guidance on monitoring of HBV-infected HCWs, both off and on antiviral			

therapy.
Financial barriers
No.
Health benefits
Issuing guidance with incorrect and contradictory statements about monitoring of HBV-infected HCWs is likely to cause several nervous breakdowns amongst occupational health physicians who already find the guidance difficult to follow.

Recommended action	a. **ACCEPT** Text updated. b. **ACCEPT** Text replaced with link to guidance. c. **ACCEPT** Suggested rewording accepted, however section replaced with link to the guidance. d. **ACCEPT** Text replaced with link to guidance. e. **ACCEPT** Text replaced with link to guidance.

Comment number	5		
Date received	03/09/2015	**Lab name**	East Kent Microbiology Service
Section	Hepatitis B		

Comment
No mention of testing/reporting Hepatitis B following recommendations outlined in NSC document below.
Evidence
NHS Infectious Diseases in Pregnancy Screening Programme, Handbook for Laboratories, 2nd edition; UK NSC, October 2012.
Health benefits
No.

Recommended action	**ACCEPT** Text updated and link to the guidance included in the public health management section and report interpretation table.

Comment number	6		
Date received	12/09/2015	**Lab name**	VRD, Colindale
Section	a. Page 9 para 4 b. Page 14: Footnotes relating to Hepatitis B Virus Serology HBsAg confirmation by alternative assay		
Comment			
a. Typo error: there is 's' missing in HBsAg. b. Clarify the terminology anti-HBe antigen test.			
Evidence			
a. Anti-HBs assays use HBsAg bound to solid phase to capture the antibody. Automated assays usually use recombinant antigen as capture antigen and for the labelled probe. In immunocompromised patients anti-HBs may be used to monitor post-vaccination immunity. An initial level of 10 IU/mL is recognised as conferring protection against HBV. Contacts who are HBAg negative, but that are high risk and who are anti-HBc positive should not be vaccinated. b. Consider carrying out HBV DNA PCR if early hepatitis B is likely due to risk factors and raised LFTs with an appropriate pattern are observed. Consider an anti-HBe antigen test.			
Financial barriers			
No.			
Health benefits			
No.			
Recommended action	a. **ACCEPT** Text updated. b. **ACCEPT** Text replaced with anti-HBe antibody. Table of hepatitis B terminology added to the scope of the document.		

Comment number	7		
Date received	18/09/2015	**Lab name**	Public Health Wales
Section	Table: page 18		
Comment			
a. Scenario 7: If you follow the algorithm then you will have tested the IgM and the markers. Change all these to not reactive. Keep the Hep B DNA as not tested. Remove comment on no evidence of viral replication because you have not tested. Put in comment on recent vaccination and send further sample in one week or EDTA			

blood for HBV DNA if no history of vaccination. b. Scenario 9: Change wording of report 'Indicates recent infection with hepatitis B, although a flare in chronic hepatitis B cannot be excluded.' In the notes put in to notify Public Health team. Also put in the notes to review with IgM level and consider core avidity testing. c. Scenario 10: Wording of report in opposition to scenario 9 currently! Suggest to only use this with eAg not reactive in that column. Also suggest that the DNA is probably not known so should state not tested in that column.	
Financial barriers	
No.	
Health benefits	
No.	
Recommended action	a. **PARTIAL ACCEPT** Serology markers have been updated to not reactive. 'No evidence of viral replication' has been removed and a request added to send another sample in 7 days. A comment on recent vaccination and EDTA blood for HBV DNA if no history of vaccination has been added. b. **ACCEPT** Text added to the notes field. c. **ACCEPT** Text updated in line with scenario 9.

Third consultation: 12/06/2017 – 26/06/2017

Version of document consulted on: V 4dzz+

Proposal for changes

Comment number	1		
Date received	13/06/2017	**Lab name**	Northwest London Pathology
Section	Lab diagnosis - HBsAg detection		
Comment			
HBsAg can be detected in plasma shortly after infection: If possible, it would be more useful to provide an indication in days of interval (eg range) between infection and appearance of HBsAg in serum or plasma.			
Evidence			
My understanding is that it can take up to 12 weeks for HBsAg to become detectable.			
Financial barriers			

No.	
Health benefits	
No.	
Recommended action	**NONE** We are not able to give exact timelines as each patient is unique and each assay varies.

Comment number	2		
Date received	14/06/2017	**Lab name**	Dundee
Section	Various		
Comment			
a. Throughout antiHBs should be given as mIU/mL. b. In the section Hep B in pregnancy two links to the green book are given, isn't one enough? c. Neutralisation algorithm: What does 'to investigate' mean? d. Neutralisation algorithm: HBsAg reactive / not confirmed by neut: what other markers do you want done? Shouldn't this go to the HBsAg not detected terminator instead? e. 2nd algorithm footnote c: should does not match the can used in the footnote to previous algorithm. f. I don't think anticore adds much, indeed if the anticore is falsely positive and the patient is denied vaccination couldn't harm be done? g. Table line 10: not tested is given twice under Hep B DNA.			
Recommended action	a. **ACCEPT** This has been replaced throughout the document. b. **ACCEPT** One reference has been deleted. c. **ACCEPT** This has been removed. d. **ACCEPT** A cross reference to the reporting table has been added. e. **ACCEPT** This has been changed. f. **NONE** This is good laboratory practice. g. **ACCEPT**		

	The table has been made consistent.

Comment number	3		
Date received	19/06/2017	**Lab name**	Virology, Hull and East Yorkshire Hospitals Trust
Section	Introduction		
Comment			
a. The European Association for the Study of the Liver has recently changed its recommended nomenclature for the staging of Chronic Hepatitis B infection. Please consider whether to move to this newer nomenclature and to reference the latest EASL document once published. b. In Figure 1, the arrows between the HBeAg Immune Active Phase box and Anti-HBe seroconversion appear to be the wrong way round - ie 90% of persons seroconvert, not sero-revert. The figure of 20-40% if for seroreversion seems rather high. c. There are issues with the formatting of > < and superscripts on pp 10-11.			
Evidence			
EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection (In Press)			
Recommended action	a. **ACCEPT** This has been included in the document. b. **NONE** This has been removed from the document. c. **NONE** This has been removed from the document.		

Comment number	4		
Date received	19/06/2017	**Lab name**	Cardiff
Section	a. Page 10 Algorithm from paper b. Page 18 algorithm c. Page 16 algorithm		
Comment			
a. The 90% and 20-40% arrows are the wrong way round! The 90% should be down and the 20-40% should be up. b. Page 18: Sag by alternative assay: Final box (at bottom), should have HBeAg/HBeAb and not HBcAg.			

c. Page 16: Sag by neutralisation: States 'To investigate' in oblong. This should not be in the reporting box but outside, otherwise the reading of this report comment looks rather strange.	
Financial barriers	
No.	
Health benefits	
No.	
Recommended action	a. **NONE** This section has been removed from the document. b. **NONE** This section has been removed from the document. c. **NONE** This section has been removed from the document.

Comment number	5		
Date received	20/06/2017	**Lab name**	University of Manchester
Section	a. Nomenclature of hepatitis B b. p20 Flowchart 'Hepatitis B antibody testing (confirmed reactive)'		
Comment			
a. 'Hepatitis B surface antigen (also called envelope antigen)': I suggest you remove '(also called envelope antigen)' to avoid any confusion. The term 'envelope antigen' is not widely used for HBsAg, although you do see hepatitis B surface envelope protein sometimes. On the other hand 'envelope antigen' is sometimes used - erroneously - for HBeAg. b. i. Title - Would this not be better as 'Hepatitis B serological profile (confirmed HBsAg positive)'. I can see that you only have antibodies in the flowchart, but HBeAg comes into the confirmatory profile in the boxes and is a very important part, so would prefer not to just say 'antibody' in the title. ii. Typo: Anti Hbe in boxes - please change to anti-HBe iii. Typo: right hand lozenge - 'History' is disembodied from the text - should be '....investigate vaccination history' iv. In the right hand arm a negative total anti-HBc can lead on to a positive anti-HBc IgM. This is not a pattern included in the Table. v. Typo: left hand lozenge - should be 'dependent' rather than 'dependant'.		
Financial barriers			

No.	
Recommended action	a. **ACCEPT** This has been removed from the document. b. i. **NONE** This section has been removed from the document. ii. **NONE** This section has been removed from the document. iii. **NONE** This section has been removed from the document. iv. **NONE** This section has been removed from the document. v. **NONE** This section has been removed from the document.

Comment number	6		
Date received	21/06/2017	**Lab name**	Public Health England
Section			
Comment			
When the lab reports a test result which is positive for Hepatitis B (acute or chronic), the lab comments should include a recommendation to vaccinate sexual and household comments, and also, if a pregnant woman, to give an extra Hepatitis B vaccine to the baby at one month and 12 months of age. Given the vulnerability of babies born to mothers who are Hep B positive and the fact that in London is difficult to achieve 100% completion of the course, every contact counts when it comes to reminding people to get vaccination to protect them against Hep B.			
Evidence			
I am not are of any literature stating that labs including vaccination advice with results leads to increased uptake. However having worked on Section 7a programmes since 2013, I have observed across London that where we optimise reminders of vaccinations at each point of contact, we make it easier for the patient to be vaccinated, thereby leading to increased uptake of immunisations.			
Financial barriers			

No this is a simply additional wording on the test results.	
Health benefits	
No.	
Recommended action	**ACCEPT** This has been amended in the document.

Comment number	7		
Date received	22/06/2017	**Lab name**	Member of the public
Section			
Comment			
I would like you to make a more elaborate mention of PCR done to monitor Viral Load. This can be used to track treatment success/failure.			
Evidence			
A Abe, K Inoue, T Tanaka, J Kato… - Journal of Clinical …, 1999 - Am Soc Microbiol Quantitation of hepatitis B virus genomic DNA by real-time detection PCR Ozaras, R., Tabak, F., Tahan, V. et al. Dig Dis Sci (2008) 53: 2995. doi:10.1007/s10620-008-0263-5 Correlation of Quantitative Assay of HBsAg and HBV DNA Levels During Chronic HBV Treatment			
Recommended action	**NONE** This information is already in the document in the section Inferring Infectivity, sentence 2.		

Comment number	8		
Date received	22/06/2017	**Lab name**	University of Nottingham
Section	Pages 10, 11, 16, 18, 20, 21		
Comment			
a. 3rd bullet point under heading Immune Tolerant phase - from what I can see, the > sign is missing. Likewise on page 11 lines 2 and 5, and < missing from line 11. b. Also on page 10, confusing to use 107-8 IU/ml as this literally reads one hundred and seven to eight. Can you not use superscript? If not, suggest 10^7 - 10^8. c. Page 11, under heading Inactive phase, first bullet point says Anti-HBe. Anti-HBe what? Positive? d. Page 13 - I thought e-antigen spanned pre-core/core trimmed at both ends ie is longer than just precore, but I may be wrong.			

e. Page 16. Follow the algorithm through HBsAg reactive, consider repeat, not reactive, Report HBsAg not detected.' To investigate. Very enigmatic. To investigate what? Should I interpret the fact that 'to investigate' is not within the inverted commas means that this will not go on the report form? If this is meant to be an aide-memoire to the lab that they might like to investigate why they have generated discrepant results, then my suggestion would be to remove the offending words from the box and add them as a footnote. I've studied the algorithms on pages 16 and 18, and at no point can I see that a sample that is HBsAg reactive, confirmed reactive on repeat, and/or confirmed using an alternative assay, is ever actually reported to the clinician!!! Apologies if I've missed that amongst the wealth of arrows all over the pages, but it does seem sensible to me at some stage to report that the patient is HBsAg positive, regardless of everything else going on.

f. Page 20. The heading is Hepatitis B antibody testing (confirmed reactive). Do you mean hepatitis B antibody testing of a sample which is confirmed to be HBsAg reactive (I'm 95% sure you do, but 5% uncertain that you may be referring to some other form of confirmed reactivity)? If so, suggest you remove any doubt by renaming this as Hepatitis B antibody testing of a sample confirmed to be HBsAg reactive.

g. Page 20 - if we go down the route of anti-HBc reactive, core IgM not reactive, why do we not say this is consistent with chronic hepatitis B infection? Is there some subtlety here that I'm missing when you say hepatitis B infection, not of recent onset.

h. Page 20 typo in right hand box on penultimate line History should be history.

i. Page 21, footnote d says HIV and hepatitis C testing should be carried out if hepatitis testing is positive. Firstly, I can't find any reference to a footnote d in the algorithm, so not sure this footnote will come to anyone's attention. Secondly, is there a typo in the phrase if hepatitis testing is positive? Do you mean if HBsAg is positive? Or if either HBsAg or anti-HBc is positive? The phase hepatitis testing is somewhat vague. Thirdly, reading this literally, and with no other prior knowledge, I would interpret that what you are advising is that the lab initiates HIV and hepatitis C testing off its own bat whenever it finds a sample to be hepatitis testing positive . Is that allowable? I thought patient knowledge and consent was necessary for HIV testing. Suggest modifying to HIV .... testing should be discussed with the clinician if hepatitis [XXX] testing is positive.

Evidence

None beyond my own thoughts and prejudices.

Financial barriers

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Recommended action	a. **NONE** This has been removed from the document. b. **NONE** This has been removed from the document. c. **NONE**

	This has been removed from the document. d. **ACCEPT** The document has been amended to cover this. e. **ACCEPT** This has been amended in the document. f. **NONE** This has been removed from the document. g. **NONE** This has been removed from the document. h. **NONE** This has been removed from the document. i. **ACCEPT** This point has been clarified and a reference to EASL 2017 added.

Comment number	9		
Date received	23/06/2017	**Lab name**	Public Health England
Section			
Comment			
Thank you for this useful overview. I am commenting on behalf of the immunisation and hepatitis leads for the SE PHEC. This guidance provides an opportunity to make a simple change to the reporting which has the potential to provide important public health benefits by reminding clinicians about vaccinating contacts and in doing so, to emphasise that PHE is a public health organisation, in which the public health and microbiology departments work closely together. We propose the following changes to the guidance on hepatitis B reporting (the table on pp22-25). Where the test suggests that the patient may have acute or chronic hepatitis B (rows 6, 9, 10 and 11) the following text should be added to the 'suggested wording of report: 'Household and sexual contacts of people with acute or chronic hepatitis B should be tested/vaccinated as soon as possible to prevent acquisition. If a pregnant woman, ensure appropriate treatment of the baby/babies. See https://www.gov.uk/government/publications/hepatitis-b-the-green-book-chapter-18.' (In the consultation draft provided, the landscape pages have been 'shrunk to fit' in 4 portrait format pages if they are to be shrunk anyway, it would make more sense to format the pages in portrait format, so that more of the table can fit on one page). It is sad that such a short time has been made available for consultation. (The document was published on the web site on 12 June with responses required by 17:00 on by 5pm on Monday next week 26th June.) I note that on page 6 it states:'The UK SMI working groups are committed to patient and public involvement in the development of UK SMIs. By involving the public, health professionals, scientists and voluntary organisations the resulting UK SMI will be robust and meet the needs of the user. An opportunity is given to members of the public to contribute to consultations		

through our open access website.' A two-week response time is not sufficient for meaningful consultation.	
Financial barriers	
N/A	
Health benefits	
As above - potential health benefits (preventing secondary cases) could be increased by the changes I suggest.	
Recommended action	**ACCEPT** The wording has been included in the document.

Comment number	10		
Date received	23/06/2017	**Lab name**	Public Health England
Section	p13		
Comment			
I could not find any mention of HBV genotyping in non-outbreak situations. Some experts in the literature suggest HBV genotyping provides information about natural history and therefore prognosis as well as likely response to antiviral treatment. Should this SMI have a line to indicate that HBV genotyping is quite widely available in the UK may be helpful for clinical management of individual patients?			
Evidence			
Please see attached article as an example. Sunbul M. Hepatitis B virus genotypes: global distribution and clinical importance. World J Gastroenterol. 2014 May 14;20(18):5427-34. doi: 10.3748/wjg.v20.i18.5427.			
Financial barriers			
Cost of HBV genotyping in a NHS/PHE reference lab.			
Health benefits			
No.			
Recommended action	**ACCEPT** The Public Health Management section has been amended.		

Comment number	11		
Date received	23/06/2017	**Lab name**	Public Health England
Section	p22-25 Hepatitis B reporting		

Comment
For 'marker combinations' 9 and 10, page 24 , the recommended text should additionally include 'Household and sexual contacts of people with acute hepatitis B should be vaccinated as soon as possible'. For marker combination 11 (chronic HBV infection) 'All household and sexual contacts of people with acute hepatitis B should be vaccinated to prevent acquisition.' Plus ideally 'If a pregnant woman, the baby will need extra Hepatitis B vaccinations at one and 12 months of age.' Phrasing my need refining but basic messages around vaccination of contacts on laboratory reports provide another route to encourage vaccination of contacts which can be challenging.
Evidence
Standards for local surveillance and follow up of hepatitis B and C p 15 paragraph 7.16 states that for Acute Hepatitis B other household members and those exposed to blood or other body fluids of the case can also be offered protection with vaccination Chapter 18 p169 of the green book states that for chronic Hepatitis B cases Sexual partners are most at risk, and they and close household contacts should be vaccinated.

Recommended action	**ACCEPT** The document has been updated.

Comment number	12		
Date received	24/06/2017	**Lab name**	PHE Viral Hepatitis Leads Group
Section	Hepatitis B reporting (p 22 passim)		

Comment
Where a lab report suggests that a patient has acute hepatitis B infection (includes scenarios 9 and 10 on page 24), the recommended lab report text should read: 'Household and sexual contacts of people with acute hepatitis B should be vaccinated as soon as possible. If a pregnant woman, the baby will need an extra Hepatitis B vaccination at one month of age. 'Where a lab report suggests that a patient has chronic hepatitis B infection (includes scenario 11), the recommended lab report text should read: 'All household and sexual contacts of people with chronic hepatitis B should be vaccinated to prevent acquisition. If a pregnant woman, the baby will need an extra Hepatitis B vaccination at one month of age.'
Evidence
The rationale for adding advice on vaccination of contacts to the recommended reporting text is: a. Vaccination of contacts (household and sexual) of people with hepatitis B is not consistently or promptly done. b. Adding this text to reports would raise awareness of the need for these vaccinations. Clinicians do review lab reports; the recommendation will be read by the clinician requesting the test they can then explain this to the case (secondary care) or actually vaccinate contacts (primary care).

c. Only national guidance can get this added to lab reports across the country. HPT staff have lobbied locally for this very change for some time but unfortunately this has not resulted in consistent widespread change.

d. Commissioning changes have meant that laboratories often serve several different trusts and may be outside the NHS and working to a service level agreement (SLA). SLAs would not specify this level of detail, but could refer to the SMI.

e. This is a PHE document. Including the advice that is given in other parts of the organisation demonstrates that all parts of PHE are acting together to minimise unnecessary spread of this costly and preventable infection. This proposal has the strong support of members of the national PHE viral hepatitis leads group - as one among many measures taken by PHE staff across the organisation to prevent household, sexual and mother-to-child spread of Hepatitis B infection. These include letters to GPs about individual patients, promoting GP education about Hepatitis B via an online course, and working with partners across the NHS and PHE to mainstream this advice. The proposed addition is a cost neutral intervention which would encourage labs to update their reporting comments, as well as making it easier to use the commissioning process to achieve this. Inclusion of public health advice in the SMI recommended reporting comments will work synergistically with other initiatives in PHE to reduce avoidable Hepatitis B infections.

Financial barriers
No, this is a cost neutral intervention which is consistent with other areas of PHE work, including Green Book recommendations.
Health benefits
Health benefits from preventing avoidable infection. No harms are anticipated.

Recommended action	**ACCEPT** The document has been updated.

Comment number	13		
Date received	26/06/2017	**Lab name**	NIS PHE Bristol PHL
Section	All		

Comment

The clinical virology team at Bristol PHL discussed V4 draft as a CPD event. It was more functional for us to send the resulting comments back in the form of a tracked edit version in a separate communication; we realize this is not preferred but it was too complex to describe some of the less important points as text in this template for comments. We support the continued production of these helpful documents. We felt it was important to highlight some the more important and wider points using this official form, as below.

Generally- the background scope and introduction information is educational and in part

does help explain the algorithms, but is too long. The nomenclature table, detection threshold recommendations, and the definition of acute and persistent is relevant, much of the rest is not. Inclusion of pathogenesis is a lot of work for the group and is subject to change- in fact the latest EASL guidance is different in some areas to the content in the draft. (Page 13) We think the inclusion of test performance in the context of S/CO and sens with spec should be avoided unless it covers all market assays as a generalization. Algorithms- please clarify that each approach to screening is equally valid. Neutralization algorithm- the inclusion of a 'consider repeat if weakly reactive' unnecessarily complicates the flow and makes it illogical if you do not do a repeat at that stage (reactive box leads to not reactive). We believe that non-neutralizable reactivity is a negative HBsAg result warranting no further action; if it is not, neutralization is redundant. Second assay algorithm- please consider the option of HBV DNA on a first sample that is HBsAg indeterminate in the context of low level reactivity in one assay only and core antibody negative. Our experience is that these are almost never true infection and the rare early acute incidental finding can be excluded with HBV DNA, as the chances of the genotype being missed by NAAT is so low that the NPV of that result combination must be so close to 100% as negligible. Obtaining a further sample is expensive in overall healthcare terms and probably upsetting for the patient. Reporting table- this appears to contain a recommendation in scenario 3 to test for anti-S in all screens for current and past HBV infection if the HBsAg is negative and first line HB core antibody is positive, and if anti-s negative, perform a second core antibody assay. We were uncertain whether this is a recommendation or an advisory note. Our experience is that many people with distant past cleared HBV infection are anti-S negative, meaning the overall costs of adopting this approach need consideration. Can you provide data to support this comment, in an overall healthcare context? Scenario 7 - possible recent infection but public health notification is omitted simply by not testing for HBV DNA. Notification should be recommended. Scenarios 9 and 10- suggest comment includes referral to a specialist. Finally, we were unanimous in preference for reporting tests as positive and negative, not detected and not detected. We believe these are universally understood by service users, whereas not detected and detected are not. We will probably make that comment on every UK SMI reviewed, sorry!	
Evidence	
Peer consensus opinion (three consultant level virologists, one also acts as CCDC, plus one HSST in virology, plus one ST3 virology). Local data.	
Financial barriers	
None.	
Health benefits	
Nothing direct.	
Recommended action	**PARTIAL ACCEPT** Full response to the points raised has been covered in the track

	change document submitted.

Comment number	14		
Date received	26/06/2016	**Lab name**	Member of the public
Section	Investigation of hepatitis B infection		
Comment			
On the whole a good document. It is not clear as to whom the report is directed but for those who don't have expertise it might be helpful to reduce the complexity of the explanation about escaped mutants. In addition, it used to be and probably still is important that those who are found to have a marker indicative of current infection by hepatitis B be asked to provide a second sample for confirmation. This used to be or should still be the case for such blood-borne infections as Hepatitis B, C and HIV.			
Evidence			
There are various reports from the RCPath, RCOG and RCS emphasising the importance of ensuring a second blood test is obtained for a blood-borne infection before a final report is issued.			
Financial barriers			
They are already in existence.			
Health benefits			
No.			
Recommended action	**NONE** The content is already in the document in the reporting table. The Scope and Purpose of the document covers who the documents are written for.		

Comment number	15		
Date received	26/06/2016	**Lab name**	RCPath
Section	a. Introduction b. Hepatitis B in pregnancy		
Comment			
a. Introduction -refer to persistent chronic infection rather than chronic infection. b. Hepatitis B in pregnancy - should indicate that following immunisation high risk babies born to HBsAg positive mothers should be tested for HBsAg at one year. Note: All households and sexual contacts of acute cases should be immunised against hepatitis B as soon as possible.			

Evidence	
Persistent is more accurate description of the circulating HBsAg hBV in pregnancy -Test for infection rather than testing for protective antibody following immunisation.	
Recommended action	a. **NONE** The new EASL guidelines do not refer to persistent chronic. b. **ACCEPT** This has been amended in the document.

Comments received outside of consultation

Comment number	1		
Date received	27/06/2016	**Lab name**	RCPath, retired consulant clinical scientist
Section			
Comment			
My comments are about updating wording, particularly the use of the following: a. Chronic Carrier: the more virologically correct term 'persistent infection' should be used. [this is used correctly on page 13]. b. Vertical transmission: perinatal or mother to baby transmission should be used. c. Bodily fluids! - what's wrong with simple 'body fluids'. d. There is also a reference to a sample to cut of ration of >8 for a core IgM assay - is that appropriate without naming assays?			
Recommended action	a. **NONE** This is not the recommendation of the EASL guidelines b. **ACCEPT** This has been changed in the document. c. **ACCEPT** This has been changed in the document. d. **ACCEPT** This has been removed from the document.		

Respondents indicating they were happy with the contents of the document

Overall number of comments: 7			
Date received	02/09/2015	**Lab name**	Public Health England

Date received	03/09/2015	**Lab name**	Luton & Dunstable University Hospital
Date received	04/09/2015	**Lab name**	Aberdeen Royal Infirmary
Date received	15/06/2017	**Professional body**	British Infection Association
Date received	19/06/2017	**Lab name**	Keith Shuttleworth and Associates Ltd
Date received	27/06/2017	**Professional body**	Institute of Biomedical Science
Date received	28/06/2017	**Professional body**	Society for Applied Microbiology