

HSL – Advanced Diagnostics

Service User Guide – 2023/24

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GENERAL INFORMATION

INTRODUCTION

HSL Advanced Diagnostics (HSL-AD) is wholly owned and managed by Health Services Laboratories (HSL). HSL-AD and its team of 38 scientific and administration staff provide a leading service for immunohistochemistry, *in-situ* hybridization and molecular pathology services nationally and internationally. HSL-AD is also supported by a team of specialist Consultant Histopathologists.

In 2022, we performed 275,000 immunohistochemistry and 8,500 fluorescent in situ hybridization tests for a whole spectrum of diseases. Full details of our service can be found at <http://www.hsl-ad.com/>.

In 2023, we are expanding our offering of referral testing to include special stains. The laboratory service has a comprehensive test repertoire. Most stains are carried out using the Agilent Artisan, with the remainder performed manually.

ACCREDITATION

HSL-AD is accredited by UKAS under the ISO15189:2012 standards. Our UKAS customer number is 9007 and our full scope of accreditation can be viewed at the UKAS website using the following link: [HSL-AD Scope of Accreditation](#).

Referral for special stains are received and managed by the HSL-AD laboratory, and then stained at our sister histology laboratory at 60 Whitfield Street. Staining for these tests falls under the UKAS customer number 9706 and the scope of accreditation for that service can be viewed at the UKAS website using the following link: [HSL Cell Path Scope of Accreditation](#).

<u>SERVICE AVAILABILITY</u>	<u>LABORATORY CONTACT DETAILS</u>
Routine working hours for the laboratories are: Monday – Friday: 07:30 – 19:00 Our Specimen Reception Team is available for telephone queries from 09:30 – 18:00 No weekend work or on-call services available	HSL-Advanced Diagnostics Ground Floor, 60 Whitfield Street London W1T 4EU TEL: +44 (0)203 912 0280 EMAIL: AD@hslpathology.com

TESTS

HSL-AD has a large repertoire of IHC and ISH tests. If there are any markers not currently listed on our website, please contact the laboratory to enquire. We monitor all requests received into the laboratory and ensure that we have the broadest repertoire of antibodies and probes to supplement your diagnostics workflow. All referring laboratories will be contacted directly if any requested tests are not currently stocked by HSL-AD.

Clinical antibodies: http://www.hsl-ad.com/ihc/clinical_antibodies

Research antibodies: http://www.hsl-ad.com/ihc/research_antibodies

Clinical ISH probes: http://www.hsl-ad.com/ish/clinical_probes

Research ISH probes: http://www.hsl-ad.com/ish/research_probes

IMMUNOHISTOCHEMISTRY, IN-SITU HYBRIDISATION & SPECIAL STAIN REQUESTS

Copies of request forms can be downloaded from:

http://www.hsl-ad.com/ihc/ihc_and_ish_request_forms/

For 2023, the HSL-AD service has amalgamated all request forms into two separate forms.

- General: Test Request Form (IHC/ISH/Molecular/Special Stains for stain and return).
- Reported: Reported IHC/FISH/Molecular Profiling request form for staining/processing and specific report generation at HSL-AD.

These have been trialed as various referring laboratories, but any further feedback will be most welcomed. This improvement follows comments raised following our customer surveys, coupled with a much more complex availability of reported IHC carried out at the HSL-AD service, especially around PD-L1 testing. Reporting proformas released from the laboratory will also be generated on request (in lab) and represent the most up to date information associated with each individual test indication reported.

Please complete all request forms in full. In particular **three points** of patient identification are required. Ensure that the slide/block and request form information match.

Patient identification required:

1. Surname
2. Date of Birth
3. Referring hospital laboratory/surgical number and block ID

The referring hospital/laboratory accepts responsibility for errors caused due to insufficient patient identification provided for diagnostic tests.

For all interpretation requests we use the specific reported IHC/FISH/Molecular request forms. Please select the appropriate form and complete all details. These can be found by using the above link.

SAMPLE REQUIREMENTS AND TRANSPORT

IHC (stain and return only): For stain and return IHC requests, we require sections cut at 3-4µm placed on positively charged IHC slides. Please provide an appropriate number of unstained sections to cover the number of requests per case plus an additional 2-4 sections for repeat staining that may be required.

Special Stain (stain and return): For special stains, the vast majority of sections can be cut at 3µm onto positively charged IHC slides. Please provide an appropriate number of unstained sections to cover the number of requests per case. See the table below for slide requirements for Reticulin stain.

IHC and FISH for interpretation: For all interpretative requests, we require an appropriate number of unstained sections plus an additional 2 unstained sections for repeat/reflex testing that may be required.

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We recommend SuperFrost Plus, Leica Bond Plus slides for all IHC staining. Please note that the use of X-tra® Slides from any manufacturer is not suitable for FISH testing and not recommended for some automated IHC testing platforms.

IHC/CISH	No of slides required	Section thickness	Additional material required	Slide type
Stain & Return IHC/ISH	No of tests + 1 USS per 4 IHC (max 4 USS)	3µm	N/A	SuperFrost Plus, Leica Bond Plus RECOMMENDED
Breast Her-2	4	3µm	Any relevant markers, such as p63 or SMM	
Gastric Her-2	4	3µm	H&E	
NSCLC IHC Panel (ALK, ROS1, PD-L1)	7	3µm	H&E	
ALK	3	3µm	N/A	
ROS1	3	3µm	N/A	
PD-L1 (22C3)	3	3µm	N/A	
PD-L1 (28-8)	3	3µm	N/A	
PD-L1 (SP142)	3	3µm	N/A	
EGFR (3C6)	2	3µm	N/A	
Mismatch Repair (MMR, HNPCC)	6	3µm	N/A	
p16	3	3µm	N/A	

FISH	Test Type	No of slides required	Section thickness	Additional material required	Slide type
HER2 (ERBB2)	Amplification	3	3-4µm	H&E, Her-2 IHC & any relevant markers	SuperFrost Plus, Leica Bond Plus ESSENTIAL
MYC	Amplification	3	3-4µm		
NSCLC FISH ALK, NTRK1-3, RET, ROS1	Rearrangement	No of tests + 2	5µm	H&E, ALK, pan-Trk & ROS1 IHC (if tested)	
Lymphoma* BCL2, BCL6, CCND1, IGH, IRF4, MALT1, MYC	Rearrangement	No of tests + 4	2-3µm	H&E PLUS Any relevant markers	
*Lymphoma DLBCL / ?HG B-Cell Lymphoma	*All requests will automatically be processed for BCL2, BCL6, MYC, MYC::IGH FISH. Subsequent FISH testing for IGK, IGL, MYC::BCL6 and/or BCL2::IGH may be required to provide a complete diagnostic profile.				
Lymphoma CCND1, CCND1::IGH	Rearrangement	4	2-3µm	H&E PLUS Any relevant markers	
Liposarcoma CDK4, MDM2	Amplification	No of tests + 2	3-4µm	H&E	
DDIT3, ETV6*, EWSR1, MAML2, MYB, NUTM, TFE3	Rearrangement	No of tests + 2 *ETV6 & NTRK3	5µm	H&E	
FGFR1, FGFR2, MET	Amplification	No of tests + 2	3-4µm	H&E	
FGFR2	Rearrangement	No of tests + 2	5µm	H&E	
NTRK1, 2, 3	Rearrangement	No of tests + 2	5µm	H&E	
PDGFB	Rearrangement	No of tests + 2	3µm	H&E	
Melanoma	Copy number alterations	No of tests + 3	3-4µm	H&E	

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Stain and Return Special Stains	No of slides required	Section thickness	Additional material required	Slide type
General Special Stains All other silver stains except Retic	No of tests	3µm	N/A	SuperFrost Plus, Leica Bond Plus, Routine Non-adhesive slide
Congo Red	2	6-7µm	N/A	RECOMMENDED
Silver stain: Retic	2	5µm	N/A	SuperFrost Plus, Leica Bond Plus ESSENTIAL

Molecular	No of slides required	Additional material required
HPV Genotyping	Tissue Block Only	H&E
Veracyte Prosigna	Tumour Resection Block Only	ESSENTIAL: Patient should be ER Positive & HER2 Negative, with accompanying full pathology report, to include biopsy, lymph node and excision specimens

Slide Requirements for staining carried out by HSL-AD

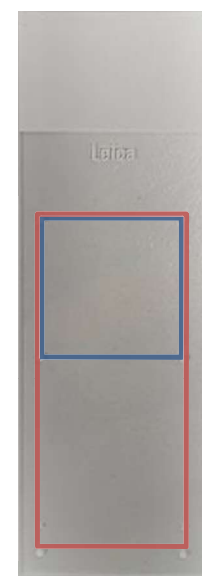
Cutting of tissue sections to be referred to HSL-AD for IHC or FISH testing:

All sections cut for IHC or FISH testing require special precautions for optimal performance and quality of staining procedures.

- Sections should be cut onto the recommended slide type.

Tissue Placement (All Routine Stain & Return IHC, MMR)

- Section placement should not be excessively high. HSL-AD primarily uses the Leica Bond III platform for IHC staining and the staining area does not cover the entire surface area of the slide.
 - (Please see life sized photograph of a Leica Bond PLUS slide for reference, this can be printed and laminated to use as a template in your microtomy area).
- Sections from biopsies and small pieces of tissue should be placed in the area within the blue box.
- Sections from resections and larger/multiple pieces of tissue should be placed in the area covered by the red box.
- Placement of tissue in this way is applicable for all slide types.
- It is very important that the lesion of interest from mega blocks is placed on the test slides appropriately.



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Tissue Placement (Her-2, ALK, ROS1, p16, All PD-L1 and All FISH Tests)

- These IHC tests are primarily performed on the Roche/Ventana and Agilent/Dako platforms.
- Section placement should be in the top third of the slide.
- Sections from resections and larger/multiple pieces of tissue should be placed as required, leaving some free space towards the bottom of the slide.



Virology / Bacteriology IHC Requests

- Cut a ribbon of 3 sections on each slide referred for the these tests e.g. CMV, *H. pylori*, *T. pallidum* [Syphilis] and VZV.



Slide Drying / Baking

- Once cut, all sections for IHC and FISH should be left to dry naturally or in a slide rack above a gentle heat source in an upright position for 30 minutes to 1 hour. Ensure that there is no remaining water underneath the section before baking. The use of slides recommended in this user guide are selected to optimize the drying process, reduce the time required and significantly reduce the number of repeat tests we perform.
- All sections for IHC or FISH should be placed in a temperature controlled oven at 60°C for 1 hour or at 37°C overnight.
- Sections should not be hot-plated using direct heat on the slide, as this may cause poor tissue adherence and unreliable IHC/FISH staining quality.
- The use of X-tra® Slides from any manufacturer is not suitable for FISH testing.
- If slide identification at the referring laboratory is done through printed labels, the maximum height of these labels must not exceed 22mm. If this is not possible, slides hand written with pencil are preferable.

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- This is critical as HSL-AD primarily uses a range of staining platforms. IHC/CISH staining on these have been calibrated and validated for a specific slide surface area. Furthermore, labels extending down onto the slide staining area may exert a hydrophobic effect on the reagents applied.
- Any deviations to these instructions may lead to compromised staining quality.

Packaging and Sending of slides/blocks to HSL-AD

- All slides sent to us must be securely packaged in slide mailer boxes with lids taped down.
- Where possible, tape the slide boxes together to minimise movement inside the package.
- Blocks and slides must be thoroughly secured in protective material before sending i.e. blocks and slides should not be placed loose in any transport container (box) when accompanying other material.
- A new padded envelope should be used for all specimens. The reuse of envelopes is not advised as these may open during transport.
- Ensure all material (forms, slides and blocks) is in the package before sealing. (**Confirm that three points of identification are present**).
- Material receipt forms sent to HSL-AD must state the material sent i.e. block and slide numbers.
- Please ensure the correct address label is on the envelope.

Packaging and returning of slides/blocks to requestor

- All slides (slide mailer boxes) and blocks (secured in protective material) are sent out in securely padded envelope via Royal Mail or courier.
- As standard, all cases are returned to referring laboratories using 1st class postage through the Royal Mail. Tissue blocks are tracked via the Royal Mail signed for service.
- If you would like to arrange a courier or want us to arrange one please contact us directly.

REJECTION CRITERIA

Requesting laboratories will be notified where samples are unsuitable for testing. Changes to the request form or new tissue section may be requested and testing will commence once the issue has been corrected. Patient material and requests will be returned to sites for correction if no communication to resolve is received.

The following issues will result in specimen rejection:

- **Request Forms:**
 - Illegible request (all request forms are designed as editable pdf documents, we recommend that requesting laboratories complete forms electronically).
 - Test(s) required not stated.
 - Requesting laboratory not stated.
 - Requesting laboratory/surgical slide/block number not stated.
- **Slides/Blocks:**
 - Number mismatch between slide/block and request form
 - Slides/blocks without information.
 - Insufficient material received or slides broken in transit.

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- **Clinical Trials:**

- Inclusive of above, all requests for work coming through the laboratory as part of an organised clinical trial must have all information points completed and correct. All identifiable patient information must be anonymised (unless such information forms part of the trial process, e.g. DOB). Cases with incorrect or no information will be rejected. All corrections to request forms or data should be corrected with a single line through the incorrect information, be signed and dated. Where appropriate, an explanation of the nature of the correction should be stated.

RESULTS

RESULTS INTERPRETATION

Any request with interpretation will be done by the appropriate specialist Consultant Histopathologist or Biomedical Scientist team depending on the test requested.

CLINICAL & SCIENTIFIC ADVICE

Customers are encouraged to contact the laboratory with any queries about the testing service we provide. All requests should be either telephoned directly or emailed to AD@hslpathology.com. The laboratory will liaise with our consultant colleagues where their clinical input is required.

RESULTS AVAILABILITY

Reports are returned by email to the requesting hospitals only.

HSL use encrypted email for the secure transmission of patient results and information as required.

Where results are unexpected, require explanation or may require urgent intervention we will endeavour to contact the requestor.

DOWNTIME

Rarely there are times where instrument downtime may result in delay of slides being processed and returned. This occurrence is very rare and all major engineering tasks required for our IHC instruments and department are carried out during weekend periods. In the event of this, all customers will be contacted directly and will be informed of any situation with expected turnaround times.

COMPLAINTS

HSL-AD makes every effort to provide the best service to users and to maintain a high standard of quality at all times. However, mistakes do occur and we are happy to receive any comments and to try to resolve any complaints. If you feel that the service we have provided is not up to an excellent standard then please contact our Head of Department, Quality Manager or a member of our Senior BMS team. Non-conformance reports are provided to affected customers upon request.

TERMS AND CONDITIONS

Each individual test request is considered as an agreement between HSL-AD and the referring laboratory to perform all available tests requested.

Service level agreements are available for all referring laboratories/customers, please enquire for further information. For all requests not covered by SLA, the terms and conditions of our generic SLA will apply as outlined in our website: http://www.hsl-ad.com/terms_and_conditions/

PATIENT CONFIDENTIALITY

Patient confidentiality is of the upmost importance to HSL-AD. All staff that come into contact with any confidential information are bound by the laws of the Data Protection Act 2018 (GDPR) and Human Rights Act 1998. The laboratory's privacy policy can be found at http://www.hsl-ad.com/privacy_statement/

The Laboratory also complies with Modern Slavery and Human Trafficking Statement under Section 54 of the UK Modern Slavery Act 2015.

TURNAROUND TIME & EQA

HSL-AD is always looking at ways to improve the TAT without compromising diagnostic accuracy and patient safety. TATs are closely monitored by the laboratory management on a regular basis and this information is available to service users upon request.

Please note stated turnaround times are in working days and are dependent on the following factors

- Day of receipt of tissue block or pre-cut slides.
- Test with or without interpretation.
- Arrival time in laboratory (all FISH requests must arrive in the laboratory by 12:00 for TAT calculation to begin on that day, otherwise it will begin from the following working day).
- Courier or standard post (please send by at least 1st Class Royal Mail or Special Delivery).
- Stated TATs are based on receipt of sample in lab to sample/result leaving the HSL-AD Laboratory and do not include postal/courier delivery times to and from the lab. All requests involving interpretation are sent by encrypted email.

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Test	TAT (working days)	EQA Scheme / Alternative QA	2022 EQA
Routine IHC & ISH (FFPE)	24-48 hours	UKNEQAS ICC & ISH (General, Lymphoma, GIST, Breast, Neuropathology)	Good
Routine IHC (Cytology)	24-48 hours	UKNEQAS ICC & ISH (Cytology)	Good
HER2 IHC + Interpretation	72 hours	UKNEQAS ICC & ISH (Breast & Gastric)	Good
ALK IHC + Interpretation	72 hours	UKNEQAS ICC & ISH (ALK)	Good
ROS1 IHC + Interpretation	72 hours	UKNEQAS ICC & ISH (ROS1)	Good
PD-L1 22C3 + Interpretation	5 days	UKNEQAS ICC & ISH (PD-L1)	Good
PD-L1 28-8 + Interpretation	5 days	Alternative QA method	Good
PD-L1 SP142 + Interpretation	5 days	UKNEQAS ICC & ISH (PD-L1 SP142 pilot)	Good
Mismatch repair (MMR) IHC + Interpretation	7 days	UKNEQAS ICC & ISH (MMR)	Good
p16 IHC + Interpretation	72 hours	UKNEQAS ICC & ISH (General)	Good
HPV Genotyping + Interpretation	10 days	GENQA FFPE DNA Extraction Alternative QA method	Good
HER2 FISH + Interpretation	5 days	UKNEQAS ICC & ISH (Breast HER2 ISH)	Good
ALK, ROS1, RET FISH + Interpretation	10 days	UKNEQAS ICC & ISH, Alternative QA method	Good
NTRK1, 2, 3 FISH + Interpretation	10 days	GENQA	Good
MDM2, CDK4 FISH + Interpretation	10 days	Alternative QA method	Good
Lymphoma FISH + Interpretation	10 days	GENQA Alternative QA method	Good
Melanoma FISH + Interpretation	10 days	Alternative QA method	Good
All other FISH (Amplification) EGFR, FGFR1, FGFR2, MET, MYC	10 days	Alternative QA method	Good
All other FISH (Translocation) DDIT3, ETV6, EWSR1, FGFR2, MAML2, MYB, NUTM, PDGFB, TFE3	10 days	Alternative QA method	Good
Veracyte Prosigna	10 days	Alternative QA Method	Good

CONTACT DETAILS

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