



Pathologynews

partnership

Updated Handbook Edition – July 2014



Clinical Science Making a Difference for BSMHFT Patients

Over the last five years we have put considerable emphasis on taking forward new relevant testing to ensure that clinical science can make a difference to our patients and this is a continuum which is seeing considerable benefit from our team approach across our organisations.

We are seeing an explosion in use of the new so called 'legal high' drugs across the UK including the Midlands. These products are being openly sold across our locality in 'head shops' and are also widely available on the internet. There are reports of many hospital admissions due to legal high intoxication. We

are involved in a major campaign to raise public awareness of the dangers of these products. This has included items on local TV and radio. We have also helped with the production of a video warning of the problems with legal highs which is being shown at music festivals around the country this summer - see www.legalhighgameover.com to view.

New Legal High Tests

We have pioneered new drugs of abuse methods to help keep up with all the new substances being used. Our test panel for oral fluid and urine currently includes 25 drugs and metabolites. We have now established a novel marker for

a major class of the cannabinoids and during the R&D phase of this work we have been seeing up to 10% of samples from BSMHFT positive for the drug class containing the substances AKB-48 and 5F-AKB-48. These cannabinoids are currently found in a majority of herbal cannabis lookalike products and we have even found positive samples in a new born baby and mother.

Correct Data on Requests is Key...

We monitor the work that comes in every day and feed back to you when details on forms and samples are incomplete. We have found it hard to improve on an error rate of around 5% in the last year or so. We know that it is full electronic test ordering and result reporting that ultimately gives us the most efficient services and as a first step we are currently working with BSMHFT IT department to introduce a full results reporting system via the RIO system.



BBC Midlands Today filming for a recent item on new our methods for legal highs

Please note:
The technical data in this handbook replaces the edition published in October 2012. Please destroy the previous edition and replace with this one.



Our New Clinical Toxicology Service

Over the last three years our Toxicology Laboratory R&D focus has been to create a relevant service suitable for the modern clinical situations presented to us.

We have invested over £1 million in new equipment and have a new team of scientific staff excitingly taking our services forward. Our state of the art techniques are now available routinely to other laboratories with key developments being:

- Moving away from immunoassay
- Simplifying our approach
- Providing clinically robust information, and overall cost reduction for users
- Ability to detect the many new drugs of abuse being used in the UK
- New techniques for our 'unknown drug screen' service.

Drivers for Change

Historically there have been major disadvantages to using immunoassay for drugs of abuse screening including:

- Poor sensitivity with false negatives
- Lack of specificity with false positives
- Identifying drug classes rather than individual drugs, for example: reporting 'opiates' rather than codeine, morphine, dihydrocodeine, 6-monacetylmorphine (heroin use specific marker) separately can be very misleading. Clinicians trying to interpret such results can experience patient-doctor disputes.

Immunoassay testing best practice is to confirm positive screen results with sensitive and specific methods such as Capillary GC or LC-MS/MS.

However, this delays turn round of results and has a high cost so in practice many laboratories try to 'get away' without any confirmation. Previously we charged an additional £26 on top of the cost of the initial immunoassay screens for every confirmation we performed. Now, by our new techniques the total price for the 'Screen and Confirmation' is just £20.

Goodbye Immunoassay!

Our routine LC-MS/MS oral fluid drug screening service commenced in September 2012. This service has given us considerable experience of LC-MS/MS as a first line approach. In January 2014 we switched our high throughput urine drug screening service from immunoassay to LC-MS/MS. Both urine and oral fluid services now look for the same 26 drugs and metabolites, with this repertoire trying to reflect the most common substances misused in the UK population. The flexibility to alter the repertoire as fashions in substance misuse change is of course fundamental to this service.

Right Result First Time

Our new drugs of abuse services use LC-MS/MS on every sample. Positive cut-off thresholds are much lower

than immunological methods and we detect and report individual drugs rather than drug class.

- Multiple reaction monitoring (MRM) for every drug
- Monitoring 2 MRM (Quantifier and Qualifier) reactions
- Calculation of drug specific target Quantifier/Qualifier ratios
- Drug specific retention times
- Inclusion of deuterated standards to correct for ion suppression or enhancement

Our new service eliminates the need for separate screen and confirmation, making testing much cheaper. We use the same method for every sample and even if you just request confirmation of a cocaine positive result we still report all 26 drug results to you. You need to understand that often we uncover poor quality results by immunoassay when we analyse samples that have been previously screened locally. Our target turnaround is <48 working hours on receipt and for urgent samples <3 hours.

Street Highs

An increasing problem has been the rise of 'street high' use in the UK.



Dr Loretta Ford, who heads up our Toxicology Laboratory assisted by Meenal Chauhan on the LC-QTOF analyser





SWBH staff talking at a recent event on substance misuse at George Eliot Hospital, Nuneaton

These designer drugs, which mimic the effects of classic drugs of abuse, are readily available in 'head shops' and on the internet. They are not detected by most immunological techniques and there is growing concern about the lack of specific testing in the UK.

We are the first NHS laboratory to routinely screen for street highs such as mephedrone (meow, meow, MCAT) on every sample you send to us.

Cannabis

Currently we still analyse cannabis separately by immunoassay and the cost of a cannabis screen is just £7. We are working on a new LC-MS/MS method which will include the new synthetic cannabinoids that are now being sold and used throughout the UK.

New LC-QTOF Service

For unknown toxicology screening we now use LC-QTOF (time of flight) as our primary technique. This 'exact mass' analyser measures to 3 decimal places (<1 mDa). Our LC-QTOF drug library has been created using exact mass of the compound (precursor), the fragment ion data and the specific drug retention time, giving great specificity. We look for over 1,200 drugs and metabolites and are constantly adding to this repertoire as new drugs are found in patient samples.

We can analyse liquids, powders and pills by LC-QTOF which lends it to multiple clinical questions. Now we have two approaches to 'unknown drug' screens:

- **LC-QTOF screen: A one off analysis for any sample, costing £80**
- **Full unknown toxicology screen at £300**

LC-QTOF Screen

Interestingly, our users are creating their own clinical services using our LC-QTOF service – examples include:

Checking Drug Compliance:

Investigation of resistant hypertension by screening for multiple drugs. There are over 50 antihypertensive drugs in the LC-QTOF library.

'Street High' Investigation: Street high use is both fashionable and fast moving, with new drugs emerging all the time. One of the challenges with street highs is to identify not only parent drugs but more importantly metabolites. Often commercial products contain a number of different active chemicals. Our LC-QTOF library includes over 60 new legal highs and is growing by the week.

Unusual Requests: LC-QTOF is also useful for testing those strange requests laboratories receive now and again, and don't know what to do with. Some recent examples are shown in the Q& A box below.

Full Unknown Toxicology Screen

Unknown toxicology screens represent a lot of work on our specialist equipment. This service comprises:

- **LC-MS/MS drug screen**
- **Cannabis; alcohol; barbiturates and LC-QTOF screen**

Results can be diagnostic, for example identifying antipsychotic drug use in a safe-guarding child case, where the patient had multiple previous hospital admissions without detecting the underlying problem.

We have the option to quantitate certain drugs in individual cases. Our goal is to report preliminary results the same working day. We work closely with duty biochemists and clinicians during an investigation as often further clinical details are needed as the laboratory studies proceed.

Transport

The transport system is designed on a hub and spoke principle. The pathology service will collect from the hubs as shown in the table.

Hub Locations	Time
Barberry Centre	AM & PM
Northcroft	AM & PM
Reaside	PM
Solihull	PM
Zinnia	AM & PM

Additional collections: Harry Watton House, Tues PM; Newbridge Mon, Tues & Wed PM.

Substance Misuse Sites

Appropriate daily collections fitting in with service requirements.

Samples transport to the Hub

This is provided by BSMHFT transport staff. Order your collection by phoning the following Numbers:

Sites Serviced by AMEY Porters: call the AMEY Help Desk on Extension 6200 internal, or tel. 01628 818564 on an outside line.

All other sites: extension 2005 internal, or tel. 0121 301 2002 on an external line

Postal address

Pathology Department, SWBH NHS Trust, City Hospital, Dudley Road, Birmingham B18 7QH

Don't forget to note the Transport Log Event Number you are given on the space provided on your request form. This will assist sample tracking.



Common Adult Reference Intervals

Our printed results should have the relevant reference intervals printed alongside them. Some ranges are age and sex dependent so it is important not to apply ranges from one patient report to another.

Biochemistry Results

ANALYTE	REFERENCE INTERVAL	UNITS
U&E		
Sodium	133 - 146	mmol/L
Potassium	3.5 - 5.3	mmol/L
Urea	2.5 - 7.8	mmol/L
eGFR	>90	mL/min

Liver Function		
Albumin	35 - 50	g/L
Bilirubin	< 21	umol/L
Alkaline phosphatase (adult)	20-130	U/L
Alanine amino transferase	< 41	U/L
GGT (male)	< 64	U/L
GGT (female)	< 45	U/L

Lipids		
Cholesterol	2.5 - 5.0	mmol/L
HDL-Cholesterol (male)	>1.0	mmol/L
HDL-Cholesterol (female)	>1.2	mmol/L
Triglycerides (fasting)	< 2.3	mmol/L
Glucose (fasting)	3.6 - 6.0	mmol/L
Adjusted Calcium	2.2 - 2.6	mmol/L

Haematology

ANALYTE	REFERENCE INTERVAL	UNITS
Full blood count		
Haemoglobin Hb (male)	125 - 180	g/L
Haemoglobin Hb (female)	115 - 160	g/L
WBC	4.0 - 11.0	x10 ⁹ /L
Platelets	150 - 450	x10 ⁹ /L
MCV	79 - 99	fl
HCT (PCV) (Male)	38 - 54	L/L
HCT (PCV) (Female)	30 - 50	L/L
MCH	27.0 - 34.5	pg
Neutrophils	1.7 - 7.5	x10 ⁹ /L
Lymphocytes	1.0 - 4.5	x10 ⁹ /L
Monocytes	0.2 - 0.8	x10 ⁹ /L
Eosinophils	0.0 - 0.5	x10 ⁹ /L
Basophils	0.0 - 0.1	x10 ⁹ /L
Reticulocytes	No reference range quoted	
ESR	Gender/age dependent	

Coagulation		
PT	11.8 - 17.4	Seconds
INR	0.85 - 1.25	(ratio)
APTT	23.2 - 40.2	Seconds
APTT ratio	0.75 - 1.30	(ratio)

Haematinics		
Vitamin B12	251 - 883	ng/L
Folate	3.1 - 20.0	ug/L

Ferritin (Males)	25 - 380	ug/L
Ferritin (Females child bearing age)	10 - 300	ug/L

Therapeutic Drug Monitoring

ANALYTE	REFERENCE INTERVAL	UNITS
Clozapine		
Non-compliance, suboptimal dose	< 350	µg/L
Maximum drug efficacy (Trough plasma Clozapine concentration taken pre-dose or minimum 12 hours post-dose)	350 - 600	µg/L
Increased risk of side effects	> 600	µg/L

Lamotrigine		
Therapeutic range (epilepsy) (Trough plasma Lamotrigine concentration taken pre-dose or minimum 6 hours post-dose)	1 - 4	mg/L

Quetiapine		
Recommended range for efficacy (Trough specimen taken pre-dose or minimum 12 hours post-dose)	50 - 200	µg/L

Olanzapine		
Maximum drug efficacy	20 - 40	µg/L
Risk of severe toxicity at levels greater than 100 µg/L (provided trough specimen taken pre-dose or minimum of 12 hours post dose)		

Others		
Carbamazepine	4 - 12	mg/L
Phenobarbitone	10 - 40	mg/L
Phenytoin	5 - 20	mg/L
Lithium	0.4 - 1.0	mmol/L

Microbiology Results

Bacteriology results

Presented as:

- Negative
- No significant growth
- Indicate the presence of an organism causing infection

Use of antibiotics

In the case of a pathogen being present, appropriate antibiotics are reported as:

- Susceptible (can be used for treatment)
- Resistant (cannot be used for treatment)

If necessary a comment will be made by the Medical Microbiologist.

Serology/Virology results

Reported as:

- Positive
- Negative

If necessary appropriate comments are also given.



Facing the 'Legal High' Challenge

'Legal highs' are a major clinical problem, with products retailed throughout the UK. Patient presentations include reduced consciousness, heart problems, seizures and psychotic episodes.

- Seen in 2.5- 10% of samples from substance misuse clinics, depending on location.
- Our new markers cover compounds found in current 'head shop' products.

Drugs of Abuse Service

- Urine or oral fluid
- Panel of 25 tests (see below)
- Overcomes false positive/negative results and high cost of immunoassay screening
- Turn round: 1 working day

LC-QTOF Screen

- Looks for over 1,200 drugs and metabolites in urine
- Includes over 60 legal highs with more being added
- Service includes detailed clinical interpretation
- Turn round: 1 working day

New Test Panel from 1 July 2014

- Identical repertoire for urine and oral fluid
- Legal high markers are best detected and interpreted in urine samples where we have most experience

Opiates: Morphine, Codeine, DHC, 6-MAM

Opioids: Thebaine, Methadone, EDDP, Buprenorphine, Norbuprenorphine

Cocaine: Cocaine / Benzoyllecgonine

Benzodiazapines: Diazepam, Nordiazepam, Oxazepam, Temazepam

Amfetamines: Amfetamine, Metamfetamine, MDMA, MDA, Mephedrone,¹ 4-MEC¹

'Legal Highs': Adamantyl marker² (AKB-48, 5F-AKB-48 & STS-135), Ethylphenidate,³ MPA³

Other drugs: Ketamine, Tramadol

1: Originally a 'legal high' now Class B. 2: Predominant compounds in current smoking products.

3: Major drugs in current powders and pills.



Further info: info@cityassays.org.uk • www.cityassays.org.uk • 0121 507 4138

Address for samples: Clinical Biochemistry, City Hospital, Dudley Road, Birmingham B18 7QH

Coming soon: Serology Screening Blood Spot Service

Using the SWBH patented blood spot device we are working on new tests for serology screening for blood borne viruses such as hepatitis and HIV testing. We are working to ensure that methods are robust and give the same level of sensitivity and specificity as more conventional testing based on venous samples. We hope to have this service fully in place by September 2014.



Electronic Requesting Made Simple

- From the patient's **Case Record** screen, select **Investigations > Order Forms**
- Click **Create New**
- Fill out the form and click **Save**
- Return to the **Case Record** screen
- Select **Clinical Documentation > Editable Letters**
- Choose a letter type of **Pathology Laboratory Test Request Form** and click **Create**
- Print the form and then upload it to RiO
- **DO NOT** go directly to the Editable Letter without first filling in the RiO form

The use of electronic test request forms sent in a bag with the specimen reduces the potential for errors and interpreting handwriting which can be problematic at times. It also saves us money and ultimately provides a safer service. It is helpful to include telephone numbers of requesting clinicians for urgent anomalies to be reported back where necessary.

Contact Points

Project management

Laboratory	Andrew Whiles andrew.whiles@nhs.net Tel: 0121 507 4276
BSMHFT	Sue Coffee sue.coffee@bsmhft.nhs.uk Tel: 0121 301 1048

Biochemistry

Head of Department	Dr Jonathan Berg jonathanberg@nhs.net Tel: 0121 507 5353
Departmental Manager	Simon Brown simon.brown8@nhs.net Tel: 0121 507 3930
Clinical Scientist in Charge of Toxicology	Dr Loretta Ford loretta.ford@nhs.net Tel: 0121 507 6026
Responsible Manager in Toxicology	Vanessa Lane vanessalane@nhs.net Tel: 0121 507 6027

Haematology

Head of Department	Dr Shivan Pancham shivan.pancham@nhs.net Tel: 0121 507 5358
Departmental Manager	Jackie Martin jackie.martin2@nhs.net Tel : 0121 507 5363

Microbiology

Head of Department	Dr Natasha Ratnaraja natasha.ratnaraja@nhs.net Tel : 0121 507 4824
Departmental Manager	Padma Patel padmavati.patel@nhs.net Tel: 0121 507 5906

Immunology

Head of Department	Dr Sadia Noorani sadia.noorani@nhs.net Tel : 0121 507 4250
Departmental Manager	Helen Sandy helen.sandy@nhs.net Tel: 0121 507 4606

Call Centres for results and advice

Biochemistry & Haematology	Tel: 0121 507 5162
Toxicology	Tel: 0121 507 4134
Microbiology	Tel: 0121 507 4261

Ordering Pathology Consumables

Consumables include:

- Request forms
- Sample tubes and phlebotomy consumables
- Collection bottles for urine drug screening

Debbie Goldthorpe or Deljit Hayre
Tel: 0121 507 4135



Deljit Hayre and Debbie Goldthorpe who are at the end of the phone to send you out Pathology supplies.