

Pathology news

April 2015 – Referral Labs Edition

Your Feedback is Vital to Our Services...

We have developed our specialist testing services over the last twelve years in partnership with our users. Your feedback to us has always been important. Regular presence at the IBMS biennial meeting in Birmingham and ACB Focus meetings have been a key way of meeting users and getting feedback.

As we have incorporated ISO 15189 into our Quality System, we have focussed even more on how we can gain appropriate feedback from users. Ideally, we want systems that allow continuous input of comments on our services. For our CE marked in-house assays, such as TPMT and Thioguanine Nucleotides, we of course already keep feedback logs of all user comments. However, we are keen to have something that is more visible, with which we can actively encourage our users to comment on our NHS specialist services.

Innovation and Feedback Postcard

So, we have invented the 'Innovation & Feedback Postcard'. This is designed for everyone. Copies of the postcard have been sent out with the mailing of this edition of Pathology News and you can also download it from our website. If you would like to feedback to us, be it a suggestion for improving our service or comment on something we do well, we would really appreciate it if you could write it on a postcard and pop it in the post!



Raj and Nadine who are running the Innovation and Feedback Postcard Scheme

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Service Level Agreements Out Now

We are now distributing a Service Level Agreement (SLA) to over 400 centres that refer work to our specialist testing laboratories. This is not only good business practice but also a requirement of ISO 15189 as assessed by UKAS.

The SLA includes reference to this annual *Pathology News* as the source of our pricing. Therefore we won't need to send out a new SLA each year. Rather the annual updated *Pathology News* price list gives the new pricing structure and predicted turn rounds for our specialist tests for the coming year.

See us at...

Focus 2015 and the IBMS Congress

We look forward to meeting many of our referral laboratory users at Focus 2015 in Cardiff, 8-11 June, and the IBMS Biomedical Science Congress in Birmingham, 28-30 September.



Adalimumab Testing

Adalimumab is a synthetic antibody belonging to a group of medicines that are sometimes called 'biological' or 'anti-TNF' drugs or therapies. Adalimumab is an immunosuppressive medicine and helps to suppress overactivity of the immune system by binding to TNF-alpha. This helps to reduce the inflammation and relieve symptoms. Adalimumab is used commonly in rheumatoid arthritis, ankylosing spondylitis, axial spondyloarthritis, psoriatic arthritis, plaque psoriasis, Crohn's disease and ulcerative colitis. It can help to reduce pain and swelling by limiting inflammation.

Detecting Drug Resistance

There has been numerous papers published relating to the efficacy, dosage regimes and therapeutic monitoring of the Adalimumab. The relationship between serum trough levels of anti-TNF α drug and clinical improvement was identified. Within a given

population of patients a significant number have been noted to develop resistance to the drug and show undetectable trough levels of Adalimumab. For these reasons and

with the high cost of this drug serum levels followed antibody measurement in selected samples offers effective patient care.



Ade & Nisha in one of our Pharmacogenomic Laboratories

Sample requirements	Serum or plasma
Sample volume	300ul
Sample transport	First class post
Turn round time	5 days on Adalimumab trough levels 7 days on anti-adalimumab antibodies from the receipt of the sample Electronic results reporting service available.
Sample timing	We currently advise trough levels and Anti-drug antibodies will be reflexed on samples that have sub-therapeutic trough levels.
Cost	£25 Adalimumab levels and £35 for antibody levels

Ethylene Glycol Out of Hours

We have a 24 hour service for ethylene and diethylene glycol in place including, weekends over the last five years despite not having a formal on-call service.

Audit of our results has shown the usefulness of urgent glycol testing, with patients receiving appropriate treatment when the presence of glycol is reported. Our out of hour's service relies on volunteers, including the Head of Department, coming in and undertaking these urgent tests.

"St Elsewheres" YouTube

We have been helping Ian Barnes with a series of YouTube videos which look at the Barnes Pathology Quality Assurance Review. This was published in January 2014 and is a key basis to help drive quality forward. However awareness of the review is surprisingly limited and the series aims to help improve this. The video initiative is designed to have a major impact on Pathology Departments, by raising awareness on the review outcomes as implementation proceeds.



Routine Service for Screening Legal Highs

NPS (Legal highs)

Novel psychotropic drugs (NPS) more commonly known as 'legal highs', are designer drugs that mimic the effect of classic drugs such as amphetamine, cocaine and cannabis. They are sold as research chemicals not for human consumption. They are unclassified so are not covered by the *Misuse of Drugs Act 1971*. These products are currently available to buy on the high street in head shops or online.

Often legal highs are more potent than the classic drugs they are trying to mimic. For example, the latest third generation of synthetic cannabinoids often referred to as 'Blackmamba', 'spice', 'K2' or 'herbal incense' are reported to be 10 to 50 times more potent than cannabis itself.

Challenge for the Laboratory

For the testing laboratory, legal highs present a challenge as they are not detected by most of the conventional methods used to screen for classic drugs of abuse, such as POCT and immunoassay.

To meet this challenge, we have invested in the latest equipment: high resolution mass spectrometry Time of Flight as well as tandem mass spectrometry LC-MS/MS. This new equipment has given us the capability to screen for a wide range of legal highs.

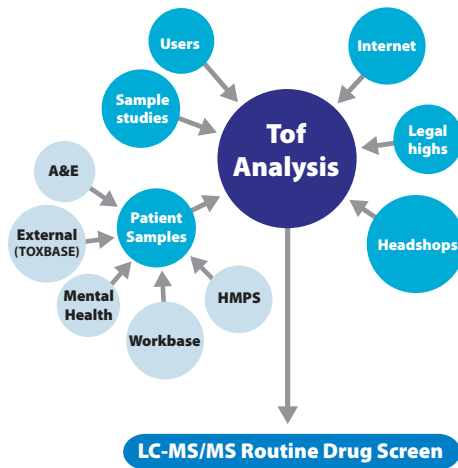
Legal High Vigilance System

Using our new equipment, we have tested legal high products currently on sale to identify the compounds

they contain. Despite claims there are 1,000s of different legal highs available, the majority being retained contain just three different drugs:

- 90% of the powder and pills tested contained either ethylphenidate and/or methiopropamine
- 91% of herbal products contained a third generation synthetic cannabinoid that contains an adamantyl group.

Interestingly 50% of these legal highs also contained traces of Class B drugs. We also detected prescription medication such as methylphenidate (Ritalin) and Viagra.



Routine Screening for Legal Highs

In June 2014, we changed our urine drug screening method to liquid chromatography tandem mass

spectrometry (LC-MS/MS). Our 26-drug panel includes classic drugs of abuse, such as the heroin specific marker 6-MAM, benzoylecgonine a major metabolite of cocaine, but also five legal highs including the three common drugs we identified from testing actual legal high products:

- Mephedrone, also known as 'meow meow', a synthetic cathinone, amphetamine type Class B drug.
- 4-Methylcathinone, also known as 'NRG2', a synthetic cathinone, amphetamine type Class B drug.
- Ethylphenidate, a cocaine mimic
- Methiopropamine (MPA), a metamphetamine analogue
- Adamantyl-type synthetic cannabinoid (NOID) marker. Will detect use of third generation synthetic cannabinoids containing an adamantyl group, including AKB-48, 5F-AKB-48 and STS-235

A recent audit of the last 8 months (July 2014 to Feb 2015) has shown that 3.4% of our total workload of nearly 15,000 urine samples were positive for at least one of these five legal highs. These results are summarised in the table below.

Significantly, the monthly %positive total for legal highs is greater than the %positive total for amphetamine, metamphetamine and ecstasy (MDMA and MDA), and yet none of these legal highs would have been detected if we had used conventional testing.

Drug	July 2014	Aug	Sept	Oct	Nov	Dec	Jan 2015	Feb	Total
Adamantyl-NOID marker	16	41	31	31	37	47	54	39	296
Ethylphenidate	5	9	6	10	10	10	9	6	65
Methiopropamine	5	4	1	5	7	4	5	4	35
Mephedrone	18	11	10	9	4	14	10	13	89
4-MEC	4	2	3	2	2	4	0	1	18
% total legal high positives	2.2	3.9	2.7	2.7	3.1	4.3	4.0	3.7	3.4
%Total amphetamines*	2.4	2.4	1.6	2.1	1.9	2.0	1.2	1.8	1.6



Making a Difference

We are continually developing our expertise in analysis and interpretation of legal highs, which we use to help clinicians managing patients. Currently we have a library of over 300 legal highs that includes classic drug mimics, as well as cultural drugs such as Kratom and Kanna. As well as individual patients, we have helped identify four breakouts of legal high use in secure Mental Health units.

See our SWBH Pathology TV News YouTube Channel for:



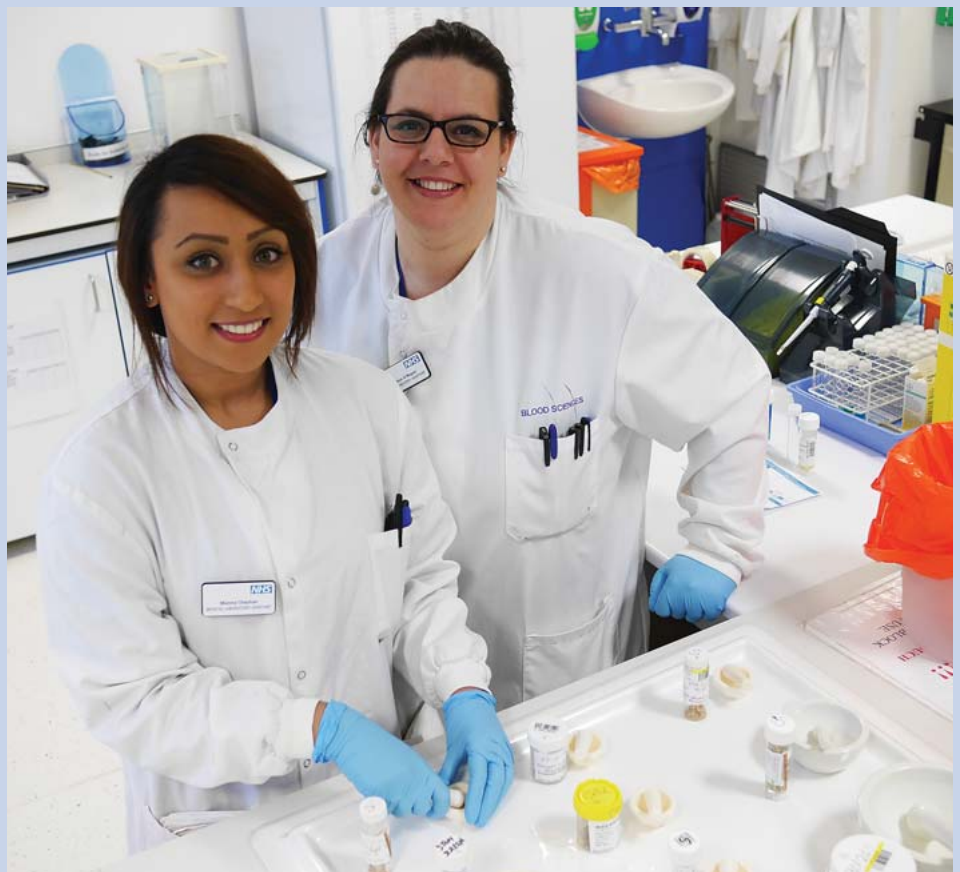
Faecal Calprotectin

Workload audit 2014

We are currently using the Bulhmann Faecal Calprotectin ELISA method with Schebo quick-prep faecal extraction devices. We analyse approximately 1000 samples per month with a turn round time of 3 working days. We analyse faecal IQC material to assess the whole method (CV 8.3%) as well as manufacturer provided IQC (CV low-5.9% and high-6.3%) and participate in external EQA to ensure the quality of the results produced.

Clinical audit 2011-2013

643 requests were received from our Gastroenterology Department over a 24 month period. Of these 196 requests were from patients with known IBD, 94 requests were from patients newly diagnosed with IBD and 353 were from patients diagnosed with IBS. 172 IBS patients and all IBD patients had their diagnosis confirmed by a confirmatory test (either colonoscopy, biopsy, CT or MRI).



Monica & Carrie-Ann in the Stones Laboratory

Table showing Faecal Calprotectin Test Performance Data (at a cut-off of 60ug/g)

Test	(n)	Sensitivity %	Specificity %	PPV	NPV	Diagnostic efficiency
CALPR	265	97	37	0.45	0.96	0.58

Specialist Assays

Prices and turn round targets* offered to NHS Contracts

Biochemistry	Turn round	Cost
ACE	3 days	£15
Bile Acids	1 day	£15
Caeruloplasmin	2 days	£15
Carotenes	5 days	£35
Faecal Calprotectin	3 days	£25
Faecal Elastase	3 days	£35
Fructosamine	1 day	£15
Gilberts Syndrome	3 days	£30
Pro Collagen Type 3 Peptide (P3NP)	7 days	£20
Cholinesterase	within 24 hours	£15
RBC Cholinesterase	within 24 hours	£50
Xanthochromia	2 hours	£35

Pharmacogenomics	Turn round	Cost
Thioguanine Nucleotides	2 days	£27
TPMT Service	1 day	£20
Serum Infliximab	5 days	£25
Anti Infliximab Antibodies	7 days	£35
Adalimumab	5 days	£25
Adalimumab Antibodies	7 days	£35

Fat soluble vitamins	Turn round	Cost
25-hydroxyvitamin D ₂ & D ₃ Serum/Plasma	2-3 days	£10
Vitamin A	2-3 days	£13
Vitamin E	2-3 days	£13

Blood spot analysis	Turn round	Cost
25-hydroxyvitamin D ₂ & D ₃	2-3 days	£16

Stone service	Turn round	Cost
Stone Analysis	5 days	£28
Urine Citrate	5 days	£15
Urine Oxalate	5 days	£15
Urine Stone Screen (calcium, phosphate, citrate, oxalate, magnesium, urate)	5 days	£50

Trace Elements	Turn round	Cost
Aluminium	2-5 days	£25
Arsenic	2-5 days	£25
Cadmium	2-5 days	£25
Chromium	1-2 days	£20
Cobalt	1-2 days	£20
Chromium & Cobalt	1-2 days	£30
Copper (urine)	2-3 days	£20
Lead	2-3 days	£20
Lead HB ZPP	2-3 days	£35
Manganese	2-3 days	£20
Mercury	2-5 days	£25
Nickel	2-5 days	£25
Selenium, Copper & Zinc	1-2 days	£15 ^{ea}
Toxic Metals Screen	1-2 days	£100
Gold	2-3 days	£40
Bromide	2-3 days	£40
Other Metals	2-5 days	£40

Therapeutic drugs	Turn round	Cost
Caffeine	1-2 days	£20
Clozapine & Norclozapine	2-3 days	£20
Lamotrigine	2-3 days	£20
Lithium	1 day	£10
Olanzapine	3 days	£30
Levetiracetam	4 days	£30
Melphalan	4 days	£30

Toxicology	Turn round	Cost
Caffeine & Paraxanthine	1-2 hours	£20
CDT	5 days	£40
Ethanol	1-2 hours	£30
Ethylene/Diethylene Glycol	1-2 hours	£200
	Out of hours:	£400
Methanol (methyl alcohol)	1-2 hours	£100
	Out of hours:	£200
Sulphonyl Urea, Antidiabetic Drug Screen	2-3 hours	£90
Tricyclic Antidepressants (Total) by Immunoassay	1-2 hours	£60
Unknown Drug Screen	2-3 hours	£300
LC-QTOF Screen	1 day	£80
Paraquat	1 day	£90
Diaquat	1 day	£90
Urine Diuretic Screen	1-2 days	£90
Urine Laxative Screen	2-3 days	£90
β-Hydroxy-Butyrate (BHB)	2-3 days	£90
γ-Hydroxy-Butyrate (GHB)	2-3 days	£90
Spiked Drink Screen	1-2 days	£250

Drugs of abuse screen	Turn round	Cost
Saliva Collection Device (pack of 20)		£30
Oral Fluid Reply Paid Kits (pack of 20)		£120
Oral Fluid	1-2 days	£20
Urine	1-2 days	£20

Current drugs of abuse panel includes 26 classic drugs and common legal highs.

Other drugs of abuse screening	Turn round	Cost
Amphetamine ratio (resolution of D, L isomers)	1 day	£40
Barbiturates	1 day	£60
Cannabis Screen	1 day	£7
Screen & Confirmation		£35
LSD	1 day	£20
Other drugs detectable on the LC-QTOF	1 day	£80

Immunology	Turn round	Cost
ISAC (Specific IgE allergen component panel)	14-21 days	£180
Specific IgE single common allergen	3-5 days	£14
Specific IgE single rare allergen	3-5 days	£15
Specific IgE Mixed panel	3-5 days	£15.50
Specific IgE to Mixed Food	3-5 days	£18.50
Specific IgE Bee Venom		

Apim1	3-5 days	£15
Specific IgE Birch, rBetv1	3-5 days	£15
Specific IgE Egg Gald1	3-5 days	£15
Specific IgE Grass – rPhl p7,p12	3-5 days	£15
Specific IgE Hazelnut – Cora1/Cora8	3-5 days	£22
Specific IgE Latex HevB1, B3, B5, B6.01, B6.02, B8	3-5 days	£65
Specific IgE Peanut Arah1,2,3,8, 9	3-5 days	£55
Specific IgE Wasp Vesv5	3-5 days	£15
Specific IgE Wheat Omega5 gliadin	3-5 days	£15
Total IgE	3-5 days	£13
Tryptase	3-5 days	£20
CCP abs	3-5 days	£10
Avian IgG - budgie	3-7 days	£13
Avian IgG - pigeon	3-7 days	£13
Aspergillus IgG	3-7 days	£11
Glomerular Basement Membrane (GBM) abs	3-5 days	£12
Complement C3	1-2 days	£10
Complement C4	1-2 days	£10
Rheumatoid factor	1-2 days	£6
Beta 2 Microglobulin	3-7 days	£7
Tissue Transglutaminase (IgA) abs	2-4 days	£10
Myeloperoxidase (MPO) abs & Proteinase 3 (PR3) abs	3-7 days	£30
Double stranded DNA quantitation abs	1-7 days	£11
IgG/IgM Cardiolipin abs screen	3-7 days	£14
IgG Cardiolipin abs	3-7 days	£6
IgM Cardiolipin abs	3-7 days	£6
ENA Screen	3-7 days	£10
ENA Profile	10-14 days	£22
Thyroid Peroxidase abs (TPO)	3-7 days	£10
Intrinsic Factor abs	3-7 days	£10
HIB abs	10-14 days	£10.50
Tetanus abs	10-14 days	£10.50
Pneumococcal ABS	10-14 days	£13
GAD abs	10-20 days	£16
Anti-nuclear antibodies	1-3 days	£10
Anti-nuclear antibodies titration	1-3 days	£11.50
Mitochondrial abs	3-5 days	£10
Smooth Muscle abs	3-5 days	£10
Gastric Parietal cell abs	3-5 days	£10
Liver Kidney Microsomal abs	3-5 days	£10
Mitochondrial abs quantitation	3-7 days	£15
Smooth Muscle abs quantitation	3-7 days	£15
Endomysial (IgA) abs	3-5 days	£13.50
ANCA abs	1-2 days	£10
Double Stranded dsDNA screen	1-3 days	£7.50
Epidermal abs	3-7 days	£12
Anti-C1INH abs	up to 28 days	£180
T spot	24 hours after sample receipt	£75

*Where days are given these are working days.



Trace Elements Laboratory

Our well-established Trace Elements Laboratory offers a high quality and extensive service for many trace elements measured in clinical practice and occupational settings. We are passionate about providing a complete service with both pre-analytical expertise to deal with for e.g., sample contamination, and post-analytical expertise, to provide results interpretation where appropriate. Next month, we'll have a new state-of-the-art ICPMS (Inductively-Coupled Mass Spectrometer) installed, adding to our two current ICPMS instruments allowing us to further develop our services.

Highlights

- **Copper, zinc and selenium** – analysis is performed on a single specimen and we are able to offer a discount to labs where more than one element is requested together. The assay is performed at least three times per week, leading to fast turnaround times for clinically relevant results.
- **Water aluminium** – we provide a direct service for renal dialysis units or home dialysis patients.
- **Therapeutic drug monitoring for bromide** – a new service introduced this year. Bromide, an old style anti-epileptic, has seen a recent re-emergence, particularly in children with intractable seizures. A trough serum sample is required and it takes 6-8 weeks to reach a steady state.
- **Toxic metal screen** – a semi-quantitative screen of 52



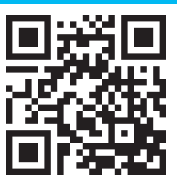
Katie & Mike in our Trace Elements Laboratory

- **elements by ICPMS in blood and urine.** This is often used in cases where there are unexplained symptoms (e.g., neuropathy) or possible exposure to a number of heavy metals. Only relevant, significant findings are reported with interpretative advice where appropriate.
- **Herbal remedies screen** – herbal remedies may contain significant quantities of heavy metals. On occasions this can result in clinical toxicity. In addition to providing reliable analysis in blood or urine, we can report a full metal analysis of the powders/tablets.
- **Occupational monitoring** – we offer an extensive range of elements, including common metals such as chromium, nickel, cadmium and mercury in addition to more specialised elements such

as selenium, antimony, beryllium and tellurium.

- **Esoteric trace elements** – committed to providing a full clinical trace elements service, we offer analysis for very specialised elements, e.g., bismuth, thallium and silver, which although uncommonly encountered, are of paramount importance in some specific cases.

What a Twitter...



Follow us: @Cityassays

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cityassays.org.uk

Our website gives basic details for many of our tests.



This includes:

- Downloadable PDF files of user information leaflets
- Relevant information and background details
- Up to date turn round times

