News and Updates Regarding UPHS Laboratory Tests
Last Updated: March 18th, 2019

To: Penn Medicine Physicians and Staff

Date: March 12, 2019

From: Malek Kamoun, MD, PhD
Eline Luning Prak, MD, PhD
Joyce Gonzalez, BS, M(ASCP)

Re: **Rheumatoid Factor Assay**

Beginning on March 18. 2019, Penn Medicine Pathology and Laboratory Medicine will change the Rheumatoid Assay Method. This assay will now be performed on The Binding Site's Optilite Turbidimetric analyzer which replaces the Beckman Immage800 Nephelometer.
The cut-off for a positive value in the new assay is 12.5 IU/mL, whereas the old assay had a cut-off value of 30 IU/mL.
Based upon our internal validation process, samples with values between 12.5 and 70 IU/mL exhibited discordance between the Optilite and Immage 800. Samples with values >70 IU/mL were uniformly positive using either assay method.
The order codes and sample type (SST tube) will not change.

For clinical questions related to this change, please contact the Immunology Resident at 215-980-9871. For operational questions related to this change, please contact Joyce Gonzalez at Joyce.Gonzalez@uphs.upenn.edu or 215-662-6023.

TO: UPHS Physicians and Staff
FROM: Department of Pathology and Laboratory Medicine
Division of Precision and Computational Diagnostics (PCD)
Vivianna Van Deerlin, M.D., Ph.D., Director, Molecular Pathology Laboratory
Christopher Watt, M.D., Ph.D., Associate Director, Molecular Pathology Laboratory

DATE: 03/11/2019

SUBJECT: Availability of *BCR-ABL1* quantitative p190 testing

In the middle of March, *BCR-ABL1* quantitative p190 testing will become available from the clinical laboratories at the Hospital of the University of Pennsylvania. This new quantitative test only detects the e1a2 fusion transcript that arises from the minor (p190) breakpoint cluster region. Please note that quantitative testing for the fusion transcripts that arises from the major (p210) breakpoint cluster region (i.e., b2a2 and b3a2 transcripts) will continue to be available as a separately orderable test.

Clinical Significance and Testing Indications
BCR-ABL1 fusion transcript that arises from the minor (p190) breakpoint are predominantly seen in patients with acute lymphoblastic leukemia (ALL); however, the p190 fusion may also be present in a subset of patients with chronic myelogenous leukemia (CML) and even more rarely in acute myeloid leukemia (AML). This quantitative assay is intended for disease monitoring and not for diagnostic purposes.

Results and Reporting:

In comparison to *BCR-ABL1* quantitative p210 studies, there is greater variability in the reporting of *BCR-ABL1* quantitative p190 results. While the majority of laboratories report Normalized Copy Numbers (*e.g.*, *BCR-ABL1* p190 copies/*ABL1* copies), the data are not always reported in the same manner. Some laboratories, including our current reference lab, report a raw ratio (*e.g.*, 0.00096) while others will report the ratio as a percentage (*e.g.*, raw ratio x 100% = 0.096%). To be more consistent with the reporting framework established for *BCR-ABL1* quantitative p210 studies, results from the Hospital of the University of Pennsylvania will be reported as a percent ratio for p190 (*i.e.*, p190 %Ratio). Of note, a standardized reporting scale has not been established for *BCR-ABL1* p190 methods. Furthermore, unlike for p210, a definitive diagnostic reference point and clinically significant milestones (such as the definition of MMR in p210 CML) have not been officially established for p190 measurements. Given this, log reduction values will not be reported for *BCR-ABL1* p190 quantitative studies. Additionally, caution is advised in comparing p190 quantitative results from different laboratories that may report values on a different scale and utilize different testing methodology. For example, the absolute value of a HUP result (reported as p190 %Ratio) will be approximately 25 to 50 times higher than the absolute value of the ARUP result (reported as a raw ratio). Finally, diagnostic samples evaluated by the HUP p190 method will typically to have a result above the upper limit of quantification of the assay (i.e., high positive, above 25%). The linear reportable range for the assay is 25%Ratio to 0.0036%Ratio. Refer to the table below for a summary of the reporting structure:

Overall Result	p190 %Ratio
High Positive, unable to quantify	Above 25
Positive	Value
Low positive, unable to quantify	< 0.0036
Not Detected	Not Detected

Testing Information

Turnaround Time: 7 business days

Acceptable specimen: The recommended sample types are peripheral blood and bone marrow aspirate.

Ordering: The name of the orderable in PennChart is “BCR-ABL1 QUANTITATIVE (P190)” (PxCode CASEP190). The name of the PennChart orderable for BCR-ABL1 qualitative testing with reflex to quantitative testing is “BCR-ABL1 QUAL to QUANT (P210 and P190)” (PxCode C2008460).

Contact Information: Call the Molecular Pathology Laboratory (215-662-6121) weekdays during regular business hours. For information on ordering and specimen requirements, kindly consult the Lab Tests Services Guide

To: Penn Medicine Physicians and Staff

Date: February 13, 2019

From: Malek Kamoun, MD, PhD
Eline Luning Prak, MD, PhD
Joyce Gonzalez, BS, M(ASCP)

Re: SM/RNP assay

Beginning on March 4, 2019, the Immunology laboratory at The Hospital of the University of Pennsylvania will change the anti SM/RNP Assay Method. This assay will now be performed using QUANTA LITE ELISA assays from Inova Diagnostics which replaces the Ouchterlony immunodiffusion method.

Two assays will be performed. A Sm antibody and an RNP/Sm complex assay.

In reporting out the RNP antibodies it will be necessary to take into consideration the contribution of Sm antibodies to the overall reactivity in the assay system. Results from this assay indicate reactivity with the RNP/Sm complex and not necessarily the RNP alone.

Reporting of results will now be a numerical value in Units rather than a positive or negative result. The reference range will be 0-19 Units.

The order codes and sample type (SST tube) will not change.

For clinical questions related to this change, please contact the Immunology Resident at 215-980-9871. For operational questions related to this change, please contact Joyce Gonzalez at Joyce.Gonzalez@uphs.upenn.edu or 215-662-6023.

To: UPHS Physicians and Staff
From: The Division of Precision and Computational Diagnostics (PCD)
Kojo Elenitoba-Johnson, M.D., Director, Center for Personalized Diagnostics
Jennifer Morrissette, Ph.D., Clinical Director, Center for Personalized Diagnostics
Jason Rosenbaum, M.D., Assistant Professor of Clinical Pathology and Laboratory Medicine
Jacquelyn Roth, Ph.D., Assistant Professor of Clinical Pathology and Laboratory Medicine
Date: December 20, 2018

Re: Retirement of BRCA1/BRCA2 site directed mutational testing

The Center for Personalized Diagnostics (CPD) is retiring the germline testing for BRCA1/BRCA2 Ashkenazi Jewish mutation detection testing due to low utilization of the assay. This assay will no longer be orderable in Epic beginning December 20, 2018. Somatic mutation detection for BRCA1 and BRCA2 from tumor tissue remains available on the current 152 gene solid tumor panel.

ALTERNATIVE ORDERING INFORMATION: Consultation with the Cancer Risk Evaluation Program (CREP) can assist with appropriate ordering of germline risk testing and can be initiated by calling (215) 349-9093.

For additional information and questions: Call the Center for Personalized Diagnostics (215-615-3966) weekdays during regular business hours. https://www.pennmedicine.org/departments-and-centers/center-for-personalized-diagnostics

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To: Penn Medicine Physicians and Staff
Date: 12/20/2018
From: Malek Kamoun, MD, PhD

Eline Luning Prak, MD, PhD
Joyce Gonzalez, BS, M(ASCP)

Re: Immunoglobulin Quantitation (IgA, IgG and IgM) assay

The Immunology laboratory was notified by The Binding Site that the IgM reagent for this assay is unavailable until January 7, 2019. Starting December 21, 2018 the test will be temporarily performed at our reference laboratory, ARUP. The methodology used is similar to the Immunology test but the reference ranges are slightly different.

	IMMUNOLOGY RANGE	ARUP RANGE
IgA	50-500 mg/dL	68-408 mg/dL
IgG	650-2000 mg/dL	768-1632 mg/dL
IgM	40-270 mg/dL	35-263 mg/dL

The specimen for this test and the order test code will remain the same.
The expected turnaround time will be 1-2 days.

For clinical questions related to this change, please contact the Immunology Resident at 215-980-9871. For operational questions related to this change, please contact Joyce Gonzalez at Joyce.Gonzalez@uphs.upenn.edu or 215-662-6023.

To: UPHS Physicians and Staff
From: The Division of Precision and Computational Diagnostics (PCD)
Kojo Elenitoba-Johnson, M.D., Director, Center for Personalized Diagnostics
Jennifer Morrissette, Ph.D., Clinical Director, Center for Personalized Diagnostics
Jason Rosenbaum, M.D., Assistant Professor of Clinical Pathology and Laboratory Medicine
Jacquelyn Roth, Ph.D., Assistant Professor of Clinical Pathology and Laboratory Medicine
Date: December 7, 2018
Re: Copy Number Variants (CNVs) in the Solid Tumor Sequencing Panel: Center for Personalized Diagnostics (CPD)

The Center for Personalized Diagnostics (CPD) offers assays designed to detect genomic variants in oncology samples. The CPD is pleased to announce the validation and implementation of a new bioinformatics algorithm for the detection of selected Copy Number Variants (CNVs) on the **Solid Tumor Sequencing Panel**. The new algorithm will be active on all cases processed starting **Monday, December 10, 2018**. The new algorithm offers improved sensitivity over previous versions. To distinguish from prior bioinformatics pipelines, the new version will be designated in the Methodology section of reports as "Halo v1.3."

Copy number gains in the following genes will be reported:

AKT1	*CREBBP*	*GNA11*	*KIT*	*PIK3CA*
AKT3	*CTNNB1*	*GNAQ*	*KRAS*	*RET*
ALK	*DDR2*	*HRAS*	*MAP2K1*	
BRAF	*EGFR*	*IDH1*	*MET*	

BRCA1	*ERBB2*	*IDH2*	*NRAS*
CHEK2	*ESR1*	*KDR*	*PDGFRA*

Copy number losses will not be detected by this assay. Due to the nature of the assay, low-level copy number gains (i.e. polysomy) in many cells cannot be distinguished from high level copy number gain (i.e. amplification) in few cells. For this reason, please note that **CNVs will not be quantified** and **gains in copy number are not necessarily equivalent to gene amplification**. If clinical decision-making depends on the detection of true gene amplification, orthogonal testing is recommended using a methodology that can discriminate individual cells (e.g. fluorescence in situ hybridization [FISH]). Should such testing be clinically warranted, please contact the laboratory for assistance in test selection.

There are no changes in the ability of the assay to identify single-nucleotide variants (SNVs) and small insertions and deletions (indels). There are no changes to the sample requirements, accepted sample types, or ordering procedures for the assay.

Results previously issued from the Solid Tumor Sequencing Panel, v2 can be re-analyzed using the new algorithm by request. To request re-analysis, please enter a new order in APCONS, and use the free-text to indicate "re-analysis of case PD-##-####." Only cases previously successfully processed through the Solid Tumor Sequencing Assay, v2 (analyzed at CPD from approximately October 2016 to present) are eligible for reprocessing.

For additional information and questions: Call the Center for Personalized Diagnostics (215-615-3966) weekdays during regular business hours or visit our website: http://pennmedicine.sitecoreauthoring.uphs.upenn.edu/departments-and-centers/center-for-personalized-diagnostics/gene-panels

To: UPHS Physicians and Staff
From: The Division of Precision and Computational Diagnostics (PCD)
Kojo Elenitoba-Johnson, M.D., Director, Center for Personalized Diagnostics
Jennifer Morrissette, Ph.D., Clinical Director, Center for Personalized Diagnostics
Jason Rosenbaum, M.D., Assistant Professor of Clinical Pathology and Laboratory Medicine
Jacquelyn Roth, Ph.D., Assistant Professor of Clinical Pathology and Laboratory Medicine
Date: October 30, 2018
Re: Lymphoma Panel: Center for Personalized Diagnostics (CPD)

The Center for Personalized Diagnostics (CPD) offers assays designed to detect genomic variants in oncology samples. The CPD is pleased to announce the launch of the **Lymphoma Panel**, detecting single nucleotide variants and small (<25 base pair) insertions and deletions with diagnostic, prognostic and therapeutic utility in lymphomas. This assay can be ordered starting **Wednesday, October 31, 2018**.

This assay will detect critical hotspots in the following genes (underlined genes have full coding sequence coverage):

ATM	***CIITA***	***JAK3***	***PLCG2***	***STAT5B***
B2M	***CREBBP***	***KLF2***	***POT1***	***TCF3***

BIRC3	***CXCR4 (CD184)***	***MAP2K1***	***RHOA***	***TET2***
BRAF	***EGR2***	***MYD88***	***RPS15***	***TNFAIP3***
BTK	***EZH2***	***NFKBIE***	***RRAGC***	***TNFRSF14***
CARD11	***GNA13***	***NOTCH1***	***SF3B1***	***TP53***
CD79A	***ID3***	***NOTCH2***	***SOCS1***	***TRAF3***
CD79B	***IDH2***	***PLCG1***	***STAT3***	***XPO1***

This assay *will not detect* fusion transcripts or copy number alterations. For more details on assay design, please contact the CPD (see below).

Sample requirements: This assay can be used for diagnostic testing on formalin-fixed paraffin embedded (FFPE) tissues (minimum 10% tumor), tissue or fluid in PreservCyt, blood and bone marrow. This assay is agnostic regarding the tissue-type of the specimen.
ORDERING INFORMATION: Special Studies Heme (SPHEME). Choose from "Special Studies" drop down menu (Lymphoma Sequencing Panel). An additional orderable has been created to initiate testing of **both** the lymphoma sequencing panel and the hematological malignancy panel (Lymphoma Sequencing Panel with Hematologic Malignancy Panel).

For additional information and questions: Call the Center for Personalized Diagnostics (215-615-3966) weekdays during regular business hours or visit our website: http://pennmedicine.sitecoreauthoring.uphs.upenn.edu/departments-and-centers/center-for-personalized-diagnostics/gene-panels

TO: UPHS Physicians and Staff

From: Ping Wang, PhD, DABCC, FACB
Director of Clinical Chemistry and Core Laboratory
Department of Pathology and Laboratory Medicine

SUBJECT: Urine creatinine

Effective November 1, 2018, new calibrators will be implemented in urine creatinine testing at HUP, PPMC, and PAH to improve traceability to National Institute of Standards reference materials. This will result in approximately 13.5% decrease in urine creatinine levels across all reported concentrations. If you are tracking urine creatinine concentration for individual patients, or using it to calculate renal clearance, please note that difference at this amplitude is due to lab assay change, and does not reflect pathophysiological changes.

To: UPHS Physicians and Staff
From: The Division of Precision and Computational Diagnostics (PCD)
Vivianna Van Deerlin, M.D., Ph.D., Director, Molecular Pathology Laboratory
Jacquelyn Roth, Ph.D., Molecular Pathology Laboratory

Date: October 29, 2018
Re: **METHOD CHANGE** for Cystic fibrosis transmembrane conductance regulator (*CFTR*) variant analysis

In November 2018, the Molecular Pathology Laboratory will perform *CFTR* variant analysis using an alternative FDA-cleared, next generation sequencing (NGS) methodology (MiSeqDx Cystic Fibrosis 139-Variant Assay), increasing the number of variants detected from the current 23 to a total of 139. This change in methodology is expected to result in increased detection rates of *CFTR* variants in our patient population. The 23 variants recommended for *CFTR* screening by the American College of Medical Genetics and Genomics (ACMG) and the American College of Obstetrics and Gynecology (ACOG) **are included** in the new assay[1,2].

Testing Highlights of the MiSeqDx Cystic Fibrosis 139-Variant Assay:

- Includes 134 cystic fibrosis (CF) disease-associated variants, the p.Arg117His (R117H) variant which is classified as a mutation of varying clinical consequence, the intron 8 PolyTG/PolyT modifying variants, and three benign variants (p.Ile506Val, p.Ile507Val, p.Phe508Cys) conditionally reported only in the context of p.Ile507del (deltaI507) or p.Phe508del (deltaF508) homozygosity.
- The disease-associated variants included have allele frequencies of ≥0.01% in individuals affected with cystic fibrosis.
- The PolyTG/PolyT variant is conditionally reported ONLY in the setting of a p.Arg117His positive result. Phasing of the PolyTG/PolyT and p.Arg117His (i.e., *cis/trans* determination) is not performed by this assay.
- Variants will be reported using the standard Human Genome Variation Society (HGVS) nomenclature. Colloquial variant names can be found at the bottom of the report.

Ordering Information:

- The name of the orderable in PennChart is being changed to "Cystic Fibrosis – CFTR 139 Variant Analysis" (PxCode C2008401).

Acceptable Specimens for *CFTR* Variant Analysis:

- Peripheral blood collected in an EDTA (lavender) tube is the ONLY acceptable specimen Cystic Fibrosis – CFTR 139 Variant Analysis.

For additional information: Call the Molecular Pathology Laboratory (215-662-6121) weekdays during regular business hours.

REFERENCES

1. Watson, *et al*. Cystic fibrosis population carrier screening: 2004 revision of American College of Medical Genetics mutation panel. Genet Med. 6(5):387-91, 2004.
2. Committee on Genetics, American College of Obstetricians and Gynecologists. ACOG Committee Opinion. Number 486, April 2011. Update on carrier screening for cystic fibrosis. Obstet Gynecol. 2011 Apr;117(4):1028-31.

To: Members of UPHS Clinical Staff
From: Leslie M Shaw, PhD and Michael C Milone, MD, PhD
Date: October 15th, 2018

Re: New Pain Management Drug Analysis test procedure

New Pain Management Drug Analysis procedure effective October 22, 2018

The Toxicology laboratory has validated and implemented a new Pain Management Drug Analysis test procedure using liquid chromatography-tandem mass spectrometry (LC-MSMS) that will detect the presence of 44 drugs and metabolites in urine including 11 drugs of abuse, 17 opioids and 16 benzodiazepines (see table below).

This testing procedure replaces and expands upon the current Pain Management tests that includes a combination of urine drug testing using 10 immunoassays(DA10), the Opiate confirmatory testing by

LC-MSMS and additional confirmation testing by GC-MS. The new Pain Management Drug Analysis procedure has a high degree of specificity and sensitivity, for all of the 44 drugs and metabolites and uses a single LC-MSMS test methodology.
Result reporting includes the cutoff concentration values for each of the 44 analytes. The 11 drugs of abuse are reported as qualitative results similar to the current immunoassay-based screening approach. Opioids and benzodiazepines will be reported with quantitative concentration results which should aid in result interpretation. Ethanol testing is done as in the past using a specific alcohol dehydrogenase enzyme assay and the report will include ethanol presence or absence as well as its cutoff value. For many of the analytes, standardized interpretative comments will also be provided.
The enhanced sensitivity of the LC-MSMS methodology provides for lowered cutoff concentrations for most of the 44 analytes as compared to the immunoassay-based cutoffs. These lower detection thresholds may result in changes to typical urine drug screening results for some patients undergoing monitoring when compared with the immunoassay-based screening approach.

EPIC Ordering information:
TEST CODE is DAPM; TEST NAME is DRUG ANALYSIS, PAIN MANAGEMENT
Please feel free to contact us regarding the new Pain Management Drug Analysis testing procedure.

Contact information:

Clinical Chemistry resident: 215-980-9770

Leslie M Shaw
Email: Les.Shaw@uphs.upenn.edu
Cell phone: 267-251-8901

Michael C Milone
Email: Michael.Milone@uphs.upenn.edu
Cell phone: 215-900-4954

Attached: Table of Drug Panel Analytes

The Table below includes the tests for 11 Drugs of Abuse, 17 Opioids & metabolites and 16 Benzodiazepines & metabolites included in the new Pain Management Drug Analysis procedure.

DOA	OPIOIDS		BENZODIAZEPINES	
Benzoylecognine	Buprenorphine	Naloxone	Alprazolam	Desalkylflurazepam
Amphetamine	nor-Buprenorphine	Naltrexone	α-hydroxyalprazolam	2-Hydroxyethylflurazepam
Methamphetamine	Codeine	Oxycodone	7-aminoclonazepam	α-Hydroxytriazolam
MDMA	Dihydrocodeine	Oxymorphone	Chlordiazepoxide	Lorazepam
MDA	Fentanyl	Tapentadol	Clobazam	Midazolam
6-MAM	nor-Fentanyl	N-desmethyltapentadol	Diazepam	α-hydroxymidazolam
Phentermine	Hydrocodone	*cis*-tramadol	nor-Diazepam	Oxazepam

PCP	Morphine	N-desmethyltramadol	Estazolam	Temazepam
THC	Hydromorphone			
Methadone				
EDDP				

To: *Penn Medicine Physicians and Staff*
Date: October 15, 2018
From: Malek Kamoun, MD, PhD
Eline Luning Prak, MD, PhD
Joyce Gonzalez, BS, M(ASCP)

Re: Quantiferon-TB Gold Plus

Beginning on October 15, 2018, Penn Medicine Pathology and Laboratory Medicine will change the Quantiferon-TB Gold Plus reporting format. All four values will now be reported. A qualitative result (Negative, Positive, Indeterminate or Invalid) is based on interpretation of the four values, NIL (medium only), TB1 minus NIL, TB2 minus NIL and MITOGEN (positive control) minus NIL. Reference ranges will remain the same.

For clinical questions related to this change, please contact the Immunology Resident at 215-980-9871. For operational questions related to this change, please contact Joyce Gonzalez at Joyce.Gonzalez@uphs.upenn.edu or 215-662-6023.

Date: October 1st, 2018
Subject: Changes to HUP Total and Allergen-Specific Immunoglobulin E Testing

Dear Colleagues,

We will be changing the performance of our total immunoglobulin E (IgE) and allergen-specific IgE testing on October 1, 2018. These assays are being migrated from the Siemens Immulite platform to Phadia ImmunoCAP.

Total IgE
The total IgE results appear minimally different (new_IgE = old_IgE * 1.1 + 2.5 IU/mL). However, the adult reference range will be changing considerably to 2 – 214 IU/mL from <= 87 IU/mL, based on Martins 2014 study. Based on historical results, this reference range shift will change the fraction of positive tests from approximately 40% down to 25%. Please continue to request total IgE testing using the same order code (IGE TOTAL).

Allergen-specific IgE
The new specific IgE results show reasonable agreement (73% agreement using the >= 0.35 kU/L threshold) with the previous assay's results. The observed level of discordance is expected due to allergen complexity and is consistent with the known differences between platforms. Of note, most discrepancies consist of differences of only a single reference category. The specific IgE interpretive criteria is unchanged.

Specific IgE reference range (kU/L)

< 0.1	Not Detectable
0.1 – 0.34	Very Low (clinical relevance indeterminate)
0.35 – 0.70	Low
0.71 – 3.50	Moderate
3.51 – 17.50	High
>17.5	Very High

Please continue to request each allergen-specific IgE test (see set below) separately using the existing order codes. Note, the "RAST Allergy Default Panel" order will no longer be available.

Fungi and Molds
ALLERGEN, ALTERNARIA ALTERNATA, IGE (Q2706)
ALLERGEN, A. FUMIGATUS, IGE (C9044985)
ALLERGEN, AUREOBASIDIUM PULULANS, IGE (Q6634)
ALLERGEN, CEPHALOSPORIUM / ACREMONIUM KILIENSE, IGE (CEPHALOS)
ALLERGEN, CLADOSPORIUM HERBARUM (HORMODENDRUM), IGE (AHORM)#
ALLERGEN, CURVULARIA LUNATA, IGE (Q11284)
ALLERGEN, EPICOCCUM PURPURASCENS, IGE (AEPICO)
ALLERGEN, FUSARIUM MONILIFORME, IGE (AFUSAR)
ALLERGEN, HELMINTHSPORIUM HALODES, IGE (AHELMI)
ALLERGEN, MUCOR RACEMOSUS, IGE (AMUCOR)
ALLERGEN, PENICILLIUM NOTATUM, IGE (APENO)
ALLERGEN, PHOMA BETAE, IGE (Q6770)
ALLERGEN, RHIZOPUS NIGRICANS, IGE (ARHIZO)

Mites
ALLERGEN, DERMATOPHAGOIDES FARINAE, IGE (ADFAR)
ALLERGEN, D. PTERONYSSINUS, IGE (ADPT)

Trees^
ALLERGEN, ALDER TREE, IGE (Q2502)
ALLERGEN, AMERICAN BEECH TREE, IGE (AABT)
ALLERGEN, BOX ELDER/MAPLE TREE, IGE (Q34927)
ALLERGEN, COTTONWOOD TREE, IGE (Q2514)
ALLERGEN, ELM TREE, IGE (AELM)
ALLERGEN, HICKORY/PECAN TREE, IGE (Q252)
ALLERGEN, OAK TREE, IGE (AOAK)
ALLERGEN, SILVER BIRCH TREE, IGE (ABIRC)
ALLERGEN, SYCAMORE TREE, IGE (ASYC)
ALLERGEN, WALNUT TREE, IGE (AWALT)
ALLERGEN, WHITE ASH, IGE (Q2515)
ALLERGEN, WILLOW TREE, IGE (Q2512)

Animal
ALLERGEN, CAT DANDER, IGE (ACAT)
ALLERGEN, DOG DANDER, IGE (ADOGD)*

Weeds
ALLERGEN, COCKLEBUR, IGE (Q2413)
ALLERGEN, COMMON RAGWEED, IGE (ACOMM)
ALLERGEN, GIANT RAGWEED, IGE (AGIA)
ALLERGEN, ENGLISH PLANTAIN, IGE (AENG)
ALLERGEN, LAMBS QUARTERS, IGE (ALAMB)

Grass
ALLERGEN, JOHNSON GRASS, IGE (Q2310)
ALLERGEN, ORCHARD GRASS COCKSFOOT, IGE (AORC)
ALLERGEN, PERENNIAL RYE GRASS, IGE (Q2305)
ALLERGEN, SWEET VERNAL GRASS, IGE (Q2301)
ALLERGEN, TIMOTHY GRASS, IGE (ATIM)

Insects
ALLERGEN, GERMAN COCKROACH, IGE (ACOCK)

 # Previously named Hormodendrum hordei
^ Sweet Gum Tree allergen testing will now be sent out to our reference laboratory
** Dog Epithelium allergen is no longer offered, because it is strongly correlated with dog dander*

In the second phase of our specific IgE testing transition, we will make available a series of order profiles that include sets of related allergens.

Please contact the Chemistry resident on-call or me directly with any questions or concerns.

Sincerely,

Daniel Herman MD, PhD
Director, Endocrinology Laboratory
Hospital of the University of Pennsylvania
daniel.herman2@uphs.upenn.edu

Date: October 1st, 2018
Subject: Changes to HUP Prolactin, Estradiol, FSH, LH, and DHEA-S testing

Dear Colleagues,

We will be changing the performance of our prolactin, estradiol (E2), follicle stimulating hormone (FSH), luteinizing hormone (LH), and dehydroepiandrosterone sulfate (DHEAS) testing on October 3, 2018. Each assay is being migrated from a Roche immunoassay to a Beckman-Coulter immunoassay. The results and corresponding reference ranges for each assay show minimal to modest changes. See details below.

Please continue to request each of these tests using the same order code. Please contact the HUP Clinical Chemistry resident on-call or me directly with any questions or concerns.

Sincerely,

Daniel Herman MD, PhD
Director, Endocrinology Laboratory
Hospital of the University of Pennsylvania
daniel.herman2@uphs.upenn.edu

DETAILS

Prolactin

Prolactin results within the reference range appear approximately 30% lower (New_Prolactin = Old_Prolactin * 0.7 + 0.5 ng/mL). In a study of 88 clinical orders, all results were concordant relative to the respective reference ranges except for 9 (10%) that were low positive on the old assay and within the reference range of the new assay, of which 2 (2%) appear to be clinically relevant elevations. In addition, the hook effect may still rarely lead to falsely low results that are reported as modestly elevated up to 200 ng/mL. Note that tests with results >200 ng/mL are re-run following 10x dilution. The female reference range is now divided into pre-menopausal and post-menopausal ranges.

Prolactin reference ranges (ng/mL)

Male	2.6 – 13.1
Female, pre-menopausal	3.3 – 26.7
Female, post-menopausal	2.8 – 19.6

Estradiol

Estradiol results <= 100 pg/mL appear approximately 25% lower (New_Estradiol = Old_Estradiol * 0.75 + 0.3 pg/mL). The reference ranges are similarly lower for most patient groups. The new assay reports precise results down to 20 pg/mL.

Estradiol reference ranges (pg/mL)

Male	<= 31.5
Female, Early Follicular Phase	22 – 115
Female, Mid-Follicular Phase	25 - 115
Female, Ovulatory Peak	32.1 – 517
Female, Mid-Luteal Phase	36.5 - 246
Female, Post-Menopausal	<= 25.1

Luteinizing hormone (LH)

LH results appear approximately 20% lower (New_LH = Old_LH * 0.84 – 0.3 mIU/mL). The reference ranges are relatively unchanged.

Luteinizing hormone reference ranges (mIU/mL)

Male	1.2 – 8.6
Female, Mid-Follicular Phase	2.1 – 10.9
Female, Mid-Cycle Peak	19.2 - 103
Female, Mid-Luteal Phase	1.2 – 12.9
Female, Post-Menopausal	10.9 – 58.6

Follicle-stimulating hormone (FSH)

FSH results appear very similar to the old method (New_FSH = Old_FSH * 1.07 + 0.5 mIU/mL). The reference ranges are also relatively unchanged.

Follicle-stimulating hormone reference ranges (mIU/mL)

Male	1.3 – 19.3
Female, Mid-Follicular Phase	3.9 – 8.8
Female, Mid-Cycle Peak	4.5 – 22.5
Female, Mid-Luteal Phase	1.8 – 5.1
Female, Post-Menopausal	16.7 – 113.6

Dehydroepiandrosterone sulfate (DHEAS)

DHEAS results appear similar to that of the old method (New_DHEAS = Old_DHEAS * 0.92 + 13 mcg/dL). The reference ranges are now age-specific, as estimated by the manufacturer.

Dehydroepiandrosterone sulfate reference ranges (mcg/dL)

Age (years)	Male	Female
8 – 21	51 – 321	24 – 537
21 – 30	18 – 391	85 – 690
31 – 40	23 – 266	106 – 464
41 - 50	19 – 231	70 – 495
51 – 60	8 – 188	38 – 313
61 – 70	12 – 133	24 – 244

	>= 71	7 - 177	5 - 253	

Date: October 1st, 2018
Subject: Changes to HUP Tryptase testing

Dear Colleagues,

We will be changing the performance of our blood tryptase testing on October 1, 2018.

Tryptase is released into blood following mast cell activation. Measuring blood tryptase may be useful in the evaluation of patients with possible anaphylaxis or systemic mastocytosis. Following an anaphylactic episode, tryptase levels peak in 15 – 120 minutes and fall with a half-life of approximately 2 hours. In patients with systemic mastocytosis, tryptase concentrations are generally persistently elevated above 20 mcg/L.

Blood tryptase will now be tested in the HUP Endocrinology laboratory, rather than sent out to ARUP reference laboratories. The methodology, Phadia ImmunoCAP, will be unchanged.

Please continue to request this test using the same order code (TRYPTASE). Please contact the HUP Clinical Chemistry resident on-call or me directly any questions or concerns.

Sincerely,

Daniel Herman MD, PhD
Director, Endocrinology Laboratory
Hospital of the University of Pennsylvania
daniel.herman2@uphs.upenn.edu

References:

Schwartz, L. B. (2006). Diagnostic Value of Tryptase in Anaphylaxis and Mastocytosis. *Immunology and Allergy Clinics of North America*, *26*(3), 451–463. http://doi.org/10.1016/j.iac.2006.05.010

TO: UPHS Physicians and Staff

FROM: Department of Pathology and Laboratory Medicine
Ping Wang, Ph.D., DABCC, FACB, Director of Clinical Chemistry and Core Laboratory

SUBJECT: Ultra-sensitive PSA

Effective September 11, ultra-sensitive PSA testing will transition from send-out laboratory ARUP to in-house testing in the Core Laboratory at the Hospital of the University of Pennsylvania.

Ultra-sensitive PSA is used to detect prostate cancer recurrence after radical prostatectomy, and is reported with a lower limit of quantitation of 0.01 ng/mL. This test should not be used for prostate cancer screening, or monitoring of prostate cancer patients before radical prostatectomy. Cutoff of ultra-sensitive PSA to indicate biochemical recurrence has not been well established, and ranges from 0.01 to 0.05 ng/mL in different studies. Interpretation of a detectable ultra-sensitive PSA result should be made in conjunction with other clinicopathologic factors. The test is available in Pennchart as orderable PSA ULTRA SENSITIVE (C9044300).

Please direct any questions related to clinical correlation and interpretation to Dr. Ping Wang (Ping.Wang2@uphs.upenn.edu), or test ordering and reporting to Nichole Rulander (Nichole.Rulander@uphs.upenn.edu). Thank you.

Ping Wang, PhD, DABCC, FACB
Director of Clinical Chemistry and Core Laboratory

PRODUCT UPDATE

July 30th, 2018

Urine Specimen Collection Supplies

The collection cup with a blue lid (shown below) should NOT be sent to the laboratory. This cup has a transfer needle and should be used to transfer the urine into the appropriate container that will be sent to the laboratory.

For Culture:

- BD Culture & Sensitivity KIT (Lawson # 100386)

Grey top tube is sent to the lab. *DO NOT SEND CUP*

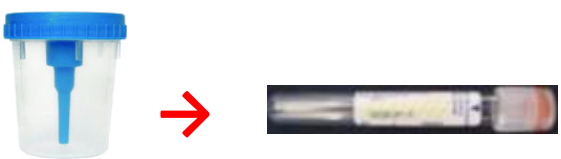
For Urinalysis:

- Collection Cup with Integral Sampling Device (Lawson # 192165)
- Red & Yellow Preservative Tube (Lawson # 204337)

Send red/yellow top tube to the lab. *DO NOT SEND CUP*

Urine chemistry (K, Na, Cl, Ca, Protein, Creatinine, Microalbumin, UN, Osmo, Pregnancy)

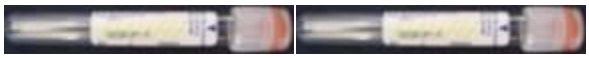
- Collection Cup with Integral Sampling Device (Lawson # 192165)
- Urine Chemistry No Additive Tube (Lawson #192166)



Send clear cap tube to the lab. *DO NOT SEND CUP*

Urine Drug Level (Two Cerner Labels print):

- Two Urine Chemistry No Additive Tubes (Lawson # 192166)



Send clear cap tubes to the lab.

To: Penn Medicine Physicians and Staff
Date: July 26, 2018
From: Irving Nachamkin, DrPH, MPH, FAAM, FIDSA
Director, Division of Laboratory Medicine
Hospital of the University of Pennsylvania

Re: Cytomegalovirus (CMV) by Quantitative PCR from Blood

Cytomegalovirus (CMV) by quantitative PCR on plasma is the preferred test for most clinical indications assessing the presence of CMV DNA in the blood. Please use the PennChart orderable **Cytomegalovirus (CMV), Quantitative PCR** (C3510502) for this testing. Due to the high number of inadvertent orders for qualitative CMV PCR ordered on plasma, the laboratory will automatically perform the quantitative CMV PCR assay on all plasma received for qualitative testing.

Please continue to use the Cytomegalovirus PCR PennChart orderable which is for qualitative testing for all non-plasma and non-BAL testing.

Please contact Client Services at 1-800-PENN-LAB with questions.

Penn Medicine

TO: Intensive Care Nursery (ICN) Physicians and Staff
FROM: Vivianna Van Deerlin, M.D., Ph.D., Director, Molecular Pathology Laboratory
DATE: July 27th, 2018

SUBJECT: HIV-1 Viral Load Testing in Neonates

Neonatal HIV-1 viral load testing will be performed by the Molecular Pathology laboratory at The Hospital of the University of Pennsylvania starting July 30th, 2018. Viral loads are performed using the cobas HIV-1 assay on the cobas 6800 instrument (Roche Diagnostics Corp.). The linear range of this assay is 20 to 10,000,000 copies/mL (log 1.3-7.0) with a limit of detection of 13.2 copies/mL (log 1.1). An acceptable specimen type for this assay is blood collected in an EDTA microtainer tube (i.e. “baby bullet”). HIV-1 viral loads are performed Monday-Friday 8am-8pm.

Ordering Information: Please order HIV-1 Quantitation (Px Code C3510180) in PennChart.

For additional information: Please call the Molecular Pathology Laboratory (215-662-6121) weekdays during regular business hours for additional information.

Penn Medicine
University of Pennsylvania Health System

To: UPHS Physicians and Staff
From: The Division of Precision and Computational Diagnostics (PCD)
Kojo Elenitoba-Johnson, M.D., Director, Center for Personalized Diagnostics
Jennifer Morrissette, Ph.D., Clinical Director, Center for Personalized Diagnostics
Jason Rosenbaum, M.D., Assistant Professor of Clinical Pathology and Laboratory Medicine
Jacquelyn Roth, Ph.D., Assistant Professor of Clinical Pathology and Laboratory Medicine
Date: July 10, 2018
Re: Translocation Panel: Center for Personalized Diagnostics (CPD)

The Center for Personalized Diagnostics (CPD) offers assays designed to detect genomic variants in oncology samples. The CPD is pleased to announce an update to the Fusion Transcript Panel, detecting gene fusions and oncogenic isoforms with diagnostic, prognostic and therapeutic utility in solid tumors. No targets were removed from the original fusion transcript panel; the updated panel is designed to increase utility in neoplasms of the thyroid, and soft tissue tumors. This updated assay continues to provide utility to neoplasms of the lung, brain and prostate and includes targets in *NTRK1*, *NTRK2*, and *NTRK3*, providing therapeutic utility for most types of solid tumors.

This assay will detect known and novel fusions involving common breakpoints in the following genes: (new additions are underlined)

AKT1	*EGFR*[1]	*FOXO1*	*NCOA2*	*PTH*	*TFE3*
ALK	*EML4*	*FUS*	*NRG1*	*RAF1*	*TFG*
AXL	*EPC1*	*GLI1*	*NTRK1*	*RET*	*THADA*
BCOR	*ERBB2*	*HMGA2*	*NTRK2*	*ROS1*	*TMPRSS2*
BRAF	*ERG*	*JAZF1*	*NTRK3*	*SLC5A5*	*USP6*
CALCA	*ESR1*	*KRT20*	*PDGFB*	*SS18*	*YWHAE*
CAMTA1	*EWSR1*	*KRT7*	*PIK3CA*	*STAT6*	
CCNB3	*FGFR1*	*MEAF6*	*PLAG1*	*TAF15*	
CCND1	*FGFR2*	*MET*[2]	*PMS2*	*TCF12*	
CIC	*FGFR3*	*MKL2*	*PPARG*	*TERT*	

[1]In addition to fusions involving *EGFR*, the assay detects aberrant isoforms EGFRvII and EGFRvIII
[2]The assay detects aberrant spliceforms resulting from *MET* exon 14 skipping (MetΔex14)

The assay uses anchored multiplex priming (AMP) and next-generation sequencing (NGS) technology to identify aberrant transcripts from RNA. As such, the Fusion Transcript Panel complements (i.e. *does not replace*) the existing Solid Tumor Sequencing Panel, which identifies single nucleotide variants and small insertions and deletions.

The new Fusion Transcript Panel is meant to expand the coverage and clinical utility of the first version of the panel. This will be offered on samples ordered on or after July 10, 2018.

No changes to other assays are planned at this time. Any future changes to the Fusion Transcript Panel or assays with overlapping coverage will be conveyed separately.

This assay *will not detect* single-nucleotide variants, small insertions and deletions, gene expression alterations, or oncogenic transcripts involving genes or breakpoints not covered by the panel. For more details on assay design, please contact the CPD (see below).

Sample requirements: This assay can be used for diagnostic testing on formalin-fixed paraffin embedded (FFPE) tissues (minimum 10% tumor), and tissue in PreservCyt. This assay is agnostic regarding the tissue-type of the specimen.

ORDERING INFORMATION: Outside AP Consult (APCONS). Choose from "Special Studies" drop down menu.

For additional information and questions: Call the Center for Personalized Diagnostics (215-615-3966) weekdays during regular business hours.

Penn Medicine
University of Pennsylvania Health System

To: Penn Medicine Physicians and Staff
Date: July 9, 2018
From: Malek Kamoun, MD, PhD
Eline Luning Prak, MD, PhD
Joyce Gonzalez, BS, M(ASCP)

Re: Quantiferon-TB Gold Plus

Beginning on July 23, 2018, Penn Medicine Pathology and Laboratory Medicine will change from using the Quantiferon-TB Gold test (QFT-GOLD) to using the Quantiferon-TB Gold Plus test (QFT-Plus). The Quantiferon-TB Gold Plus test utilizes a four-tube format (the NIL, Mitogen, TB1 Antigen and TB2 Antigen).

Compared to its predecessor QFT-GOLD, which contains peptide antigens optimized to stimulate CD4 T cells, QFT-Plus contains new antigens optimized for both CD4 and CD 8 T-cell stimulation in the TB2 tube. Increased interferon gamma levels in the TB2 tube compared to the TB1 tube (which only contains CD4 antigens) are consistent with a CD8+ T cell response. Interferon gamma secretion by TB-specific CD8+ T cells has been associated with recent exposure to TB and with active disease. Testing of CD8+ as well as CD4+ T cell responses improves the sensitivity of latent TB detection. The new formulation of QFT-Plus

has shown good correlation and performance compared to its predecessor with publications on sensitivity, specificity and performance.

Please note that the test results will differ slightly with positive results but the cutoff values will remain the same. There will now be two Tb Antigen quantitation values reported for positive results TB1 (CD4+) and TB2 (CD4+ and CD8+). If either or both tubes have interferon gamma levels exceeding >0.34 IU/mL, the result will be reported as positive.

For clinical questions related to this change, please contact the Immunology Resident at 215-980-9871. For operational questions related to this change, please contact Joyce Gonzalez at Joyce.Gonzalez@uphs.upenn.edu or 215-662-6023.

Penn Medicine
University of Pennsylvania Health System

To: Penn Medicine Physicians and Staff
Date: July 9, 2018
From: Malek Kamoun, MD, PhD
Eline Luning Prak, MD, PhD
Joyce Gonzalez, BS, M(ASCP)

Re: Quantiferon-TB Gold Plus

Beginning on July 23, 2018, Penn Medicine Pathology and Laboratory Medicine will change from the Quantiferon-TB Gold test to the Quantiferon-TB Gold Plus test. This change will require using a four-tube format (the NIL, TB1 Antigen, TB2 Antigen and Mitogen).

If you currently have any of the Quantiferon-TB Gold three tube format left, please dispose of them by July 23, 2018 and replace them with the four-tube Quantiferon-TB Gold Plus format. You can obtain the new four-tube format by contacting the following departments:

Outpatients: Audrey Baylock
215-615-2069
audrey.baylock@uphs.upenn.edu

Inpatients: Immunology Laboratory
(Prior Approval must be obtained by the Immunology Resident 215-980-9871)
215-662-6023

For clinical questions related to this change, please contact the Immunology Resident at 215-980-9871. For operational questions related to this change, please contact Joyce Gonzalez at Joyce.Gonzalez@uphs.upenn.edu or 215-662-6023.

TO: All PCAM Providers

FROM: Department of Pathology and Laboratory Medicine
Ping Wang, Ph.D., DABCC, FACB, Director of Clinical Chemistry and Core Laboratory

SUBJECT: PCAM Chemistry Testing Specimen Type Change

Effective immediately, all plasma samples drawn at PCAM for chemistry testing will be converted to **serum** tubes. Please follow the Cerner label to draw Chemistry samples in **gold-top tubes**. The purpose of the conversion is to ensure accurate results (including LDH) are generated from samples transported through the pneumatic tube system. If *STAT plasma creatinine* results are needed, use orderable *CREATININE (HEMONC) C0250350* in PennChart. Plasma samples drawn at PCAM will be rejected for LDH testing starting July 16, 2018.

Please direct any questions related to clinical correlation and interpretation to Dr. Ping Wang (Ping.Wang2@uphs.upenn.edu), or test ordering and reporting to Nichole Rulander (Nichole.Rulander@uphs.upenn.edu). Thank you.

Ping Wang, PhD, DABCC, FACB
Director of Clinical Chemistry and Core Laboratory

Date: June 5th, 2018
From: Kevin Alby Ph.D. D(ABMM) –Director Clinical Microbiology, Hospital of the University of Pennsylvania

To: All HUP/PPMC Providers

Effective Monday, June 4th, 2018, the Clinical Microbiology Laboratory at the Hospital of the University of Pennsylvania will begin sending urinary *Histoplasma* Antigen to ARUP Laboratories rather than MiraVista Diagnostics. The laboratory already utilizes ARUP for serum *Histoplasma* testing.

There is a new PennChart orderable (HISTOPLASMA AG UR) associated with the new test:

For questions please contact Kevin Alby – Kevin.Alby@uphs.upenn.edu

Department of Pathology and Laboratory Medicine
Hospital *of the* University *of* Pennsylvania
Pennsylvania Hospital
Penn Presbyterian Medical Center

TO: UPHS Physicians and Staff

FROM: Department of Pathology and Laboratory Medicine
Malek Kamoun MD, PhD
Eline Luning Prak MD, PhD

SUBJECT: Anti-Nuclear Antibody (ANA) ordering change

Effective May 16, 2018 there are now two ways to order the Anti-Nuclear Antibody test.

Test code ***ANA*** orders the anti-nuclear antibody screen ONLY.

Test code ***ANA Reflex*** will automatically reflex to dsDNA, C3, C4, RF, SSAB, and SMRNP testing if the ANA result is >/= 1:160. No additional sed rate test order is required.

Penn Chart Orderable

ANA Only:	Anti Nuclear Antibody; C5070018
ANA with Reflex:	Anti Nuclear Antibody Reflex

Please direct any questions related to clinical correlation and interpretation to the Immunology Resident 215-980-9871 or test ordering and reporting to Joyce Gonzalez (Joyce.Gonzalez@uphs.upenn.edu) or 216-662-6023. Thank you.

TO: UPHS Physicians and Staff

FROM: Department of Pathology and Laboratory Medicine
Ping Wang, Ph.D., DABCC, FACB, Director of Clinical Chemistry and Core Laboratory

SUBJECT: ApoA1 and ApoB Specimen Type Change

Effective Monday April 16, 2018, the preferred specimen type for ApoA1 and ApoB is changed to serum.
Please draw a fasting sample in gold-top tube. There is no change in ordering and reporting.

Please direct any questions related to clinical correlation and interpretation to Dr. Ping Wang (Ping.Wang2@uphs.upenn.edu), or test ordering and reporting to Nichole Rulander (Nichole.Rulander@uphs.upenn.edu). Thank you.

Ping Wang, PhD, DABCC, FACB
Director of Clinical Chemistry and Core Laboratory

To: **All Laboratory Users**

Date: **April 4, 2018**

From: **Department of Pathology and Laboratory Medicine, Molecular Pathology Laboratory**

RE: **Collection Tube Change for Infectious Disease Testing in Molecular Pathology**

In an effort to streamline the process for Infectious Disease Testing, the Molecular Pathology Laboratory is changing their collection requirements for selected tests. The blood collection tube will change from a pink 6mL EDTA, to a molecular friendly, pearl white 5mL **PPT™** EDTA tube.

The following tests will be affected:

- Hepatitis B Virus (HBV), Quantitative PCR (C3510220)
- Hepatitis C Virus (HCV), Quantitative PCR (C3510159)
- Human Immunodeficiency Virus 1 (HIV1), Quantitative PCR (C3510180)
- Human immunodeficiency Virus 1 (HIV1), Confirmatory Viral Load (C3510190)
- Hepatitis C Virus Genotype (C3510166)
- Cytomegalovirus (CMV), Quantitative PCR (C3510502)

- BK Virus (BKV), Quantitative PCR (BKVIRUS)
- Epstein Barr Virus (EBV), Quantitative PCR (EBVCASE)

This switch will happen on Monday, April 23, 2018. The new **PPT™** (Plasma Preparation Tube) will be noted on the order label as "white." The Lawson Number for the PPT™ tube is **130554.** Please begin to stock these tubes in your area in preparation of the switch.

****PLEASE NOTE – It is imperative that the PPT™ tube be filled completely. One tube is often utilized for multiple tests ordered at once. In order to avoid QNS samples and a redraw, please ensure that the tube has 5mL of blood before sending to the lab.****

Should you have any questions or require additional information please contact the Molecular Pathology Laboratory at 215.662.6121.

Date: 2/21/2018

Dear Colleagues,

We will be testing anti-Mullerian hormone (AMH) in the HUP Endocrinology laboratory using the Roche Elecsys AMH assay (http://dx.doi.org/10.1016/j.clinbiochem.2015.10.008) effective 02/20/2018. AMH testing can be useful for the evaluation of ovarian function as part of the assessment of menopause, including premature ovarian failure; workup for infertility; and assisted reproductive protocols.

The new method reports results that are slightly lower (Figure 1) than those of the previous testing performed at our reference laboratory (http://ltd.aruplab.com/Tests/Pub/2002656; Ansh picoAMH ELISA). Within the normal physiological range (< 10 ng/mL), results appear to be approximately 15% lower on average (http://dx.doi.org/10.1016/j.fertnstert.2015.06.024). However, very elevated results, in particular those > 15 ng/mL by the previous method, appear to be decreased even further (by as much as 50%). The age-specific reference ranges have been shifted accordingly, per the manufacturer's study (Table 1).

In terms of clinical decision points, patients with an AMH concentration < 0.7 ng/mL frequently have < 3 antral follicles (http://dx.doi.org/10.1016/j.fertnstert.2014.12.093). Women with serum Roche AMH > 2.0 ng/mL may benefit from decreased ovarian stimulation dosing to avoid hyperstimulation (http://dx.doi.org/10.1016/j.fertnstert.2016.10.033; http://dx.doi.org/10.1002/14651858.CD012693.pub2). Women with polycystic ovarian syndrome have approximately 3-fold elevated results (Roche median: 7 ng/mL, 5th percentile: 3 ng/mL) (http://dx.doi.org/10.1016/j.clinbiochem.2015.10.008). For other diagnostic thresholds, we recommend adjusting existing thresholds down ~15%.

Please continue to request this testing using the same order code. Contact me with any questions or concerns.

Sincerely,

Daniel Herman MD, PhD

Director, HUP Endocrinology Laboratory
Daniel.herman2@uphs.upenn.edu

Age (years)	2.5th percentile (ng/mL)	97.5th percentile (ng/mL)
20 - 24	1.22	11.7
25 - 29	0.89	9.85
30 - 34	0.58	8.13
35 - 39	0.15	7.49
40 - 44	0.03	5.47

Table 1: Reference range for healthy women by age (http://dx.doi.org/10.1016/j.clinbiochem.2015.10.008)
Figure 1: Parallel testing using new (HUP Roche AMH) and previous (ARUP Ansh picoAMH) methods on prospective patient specimens and stored, frozen specimens. Deming regression of prospective specimens: New_HUP = 0.86 x Prev_ARUP + 0.05

TO: UPHS Physicians and Staff
FROM: Vivianna Van Deerlin, M.D., Ph.D., Director, Molecular Pathology Laboratory
Christopher Watt, M.D., Ph.D., Associate Director, Molecular Pathology Laboratory
Kevin Alby Ph.D., D(ABMM), Director, Clinical Microbiology Laboratory
DATE: December 18, 2017
SUBJECT: Method Change and Update on Respiratory Pathogen Testing in Molecular Pathology Laboratory

A new FDA-cleared method for molecular testing of respiratory pathogens, the GenMark ePlex Respiratory Pathogen Panel (RPP), is being implemented in the HUP Molecular Pathology Laboratory on December 19th. The RPP detects 15 viral targets and 2 bacterial targets, of which 5 are new compared to the previous in-house RVP method (see below). This method will enable a faster turnaround time for many specimens and includes influenza A subtype information.

Pathogens detected by current and new methods:

New GenMark RPP Assay	Current RVP method
Influenza A (subtype information for:H1,H1-2009,H3)	Influenza A
Influenza B	Influenza B
Respiratory syncytial virus A	Respiratory syncytial virus A
Respiratory syncytial virus B	Respiratory syncytial virus B
Parainfluenza virus 1	Parainfluenza virus 1
Parainfluenza virus 2	Parainfluenza virus 2
Parainfluenza virus 3	Parainfluenza virus 3
Parainfluenza virus 4	
Adenovirus	Adenovirus
Human metapneumovirus	Human metapneumovirus
Coronavirus	
Human rhinovirus/enterovirus	
Mycoplasma pneumonia	
Chlamydia pneumonia	

Ordering Information

- There is no change to how the full respiratory pathogen panel is ordered
- PennChart order name is “Respiratory Virus Molecular Detection.”
- Manual requisitions are also accepted; specify “Respiratory Pathogen Molecular Panel.”
- The HUP Microbiology Lab will continue to offer “Influenza Detection by PCR,” a test which only detects influenza and RSV and is primarily intended for HUP Emergency Department patients who are likely to be admitted and meet appropriate criteria.

Turn-Around-Time

- Approximately 3-4 hours for most NP swab samples received between 8 AM and 5 PM. Samples received after 5 PM will be reported the next day. During the height of flu season testing is performed 7 days per week, and for the remainder of the year, 6 days/week.

Acceptable Specimens for RPP

- Nasopharyngeal (NP) swabs collected in viral transport media (Lawson Number 195443)
- Bronchoalveolar lavage specimens
- Please note that nasal washes, tracheal aspirates and sputums will no longer be accepted

For additional information

- Call the Molecular Pathology Laboratory (215-662-6121) weekdays during regular business hours.

From: Kevin Alby Ph.D. D(ABMM) –Director Clinical Microbiology, HUP
Vivianna Van Deerlin, M.D., Ph.D., Director, Molecular Pathology Lab
To: UPHS Physicians and Staff
Subject: Introduction of Reflexive HCV Antibody Testing

Effective Tuesday December 19th, 2017 the Laboratory at the Hospital University of Pennsylvania will reflex any positive Hepatitis C Antibody Screening Tests to confirmatory viral load testing. There will also be a new test (Hepatitis C Antibody IgM + IgG with Reflex to HCV PCR) to replace the current orderable in PennChart. Hepatitis C Viral Load testing can still be ordered independently of the HCV Antibody screen (Hepatitis C Virus (HCV) Quantitation; C3510159).

For questions please contact Kevin Alby – Kevin.Alby@uphs.upenn.edu

From: Kevin Alby Ph.D. D(ABMM) –Director Clinical Microbiology, Hospital of the University of Pennsylvania
To: HUP ED and PEC Clinicians, Nurses, and Advanced Practitioners

Starting Monday December 18th, 2017 the Microbiology Laboratory at the Hospital University of Pennsylvania will pilot a new initiative to improve the diagnosis and treatment of sexually transmitted infections (STI) of patients presenting to the Emergency Department at HUP. To do so, the Clinical Microbiology Lab will offer rapid molecular testing for Neisseria gonorrhoeae (GC), Chlamydia trachomatis (CT), and Trichomonas vaginalis (TV) via the GeneXpert System, specifically on patients seen in the ED or PEC at HUP. At this time, this pilot program is not available at other locations or entities. Testing will only be performed on unpreserved urine samples sent directly to Microbiology (tube station 03).

Samples submitted using Aptima swabs from any body site will continue to be run according to the standard testing performed at HUP.

There are 2 new PennChart orderables associated with the new testing program:
Procedures
Name: ED CHLAMYDIA & N. GONORRHOEAE; Px Code: EDCTNG; Type: Lab
Name: ED TRICHHOMONAS VAGINALIS; Px Code: EDTV; Type: Lab

Testing will be performed 24/7 with a TAT of 2-2.5 hours between 7a and 10p daily. TAT during off hours will vary depending on staffing and workload in the Microbiology laboratory.
For questions please contact Kevin Alby – Kevin.Alby@uphs.upenn.edu

To: UPHS Physicians and Staff
From: Department of Pathology and Laboratory Medicine
Date: November 9, 2017
Subject: Change to HUP Qualitative Glucose-6-Phosphate Dehydrogenase Testing

Effective November 13, 2017, the qualitative glucose 6-phosphate dehydrogenase (G6PD) test (C2001140) will no longer be available in PennChart, due to unavailability of test reagents. To screen a patient for G6PD deficiency, please order the quantitative G6PD test (GLUC6PD). All future orders for qualitative G6PD (C2001140) will be converted to quantitative GLUC6PD when released. This test is sent out to the reference lab ARUP. ARUP performs the test 7 days a week, with estimated turn-around-time of 2-3 days.

If you have any questions about this change, please contact Dr. Ping Wang (ping.wang2@uphs.upenn.edu), Nichole Rulander (Nichole.Rulander@uphs.upenn.edu) or Lynn Vespasiani (Lynn.Vespasiani@uphs.upenn.edu).

To: Penn Medicine Physicians and Staff
Date: October 12, 2017
From: Megan Lim MD, Ph.D. Director, Division of Hematopathology.
RE: Change to HUP T Cell Immunodeficiency (CD4 MON, CD3 MON), B cell, and NK cell panels

Beginning October 18th, 2017, there will be a change to the T cell immunodeficiency (CD3, CD4, CD8 and CD4:CD8 ratio), B and NK cell subset panels performed in the HUP Flow Cytometry Laboratory. There will be no change to the expected percentage or absolute count results for these subsets but they will now be generated directly from a flow cytometry instrument and will no longer require a simultaneous white blood cell count (CBC) and differential.

Please note that an order for an Immune Deficiency Evaluation (CD4 MON or CD3 MON) will no longer generate an order for a CBC and differential and this testing should be ordered separately if required. A single lavender top tube will now be sufficient for these tests.

Please direct any questions or concerns to the Clinical Flow Cytometry Laboratory at 215-662-6024.

To: Penn Medicine Physicians and Staff
Date: September 22, 2017
From: Irving Nachamkin, DrPH, MPH, D(ABMM), FAAM, FIDSA
Ping Wang, PhD, DABCC
Lynn Vespasiani, BS, MT(ASCP)
Re: 24 Hour Urine Containers, No Preservative

Beginning September 25th, 2017, Penn Medicine Pathology and Laboratory Medicine will no longer be using 24-hour urine jugs containing chemical preservatives. This change is made to simplify 24-hour urine testing sample requirement and decrease burden on nursing and outpatients.
All 24-hour urine jugs will be preservative free. If you currently have any jugs with preservatives, please dispose of them by September 25th and replace them with preservative-free jugs. You can obtain preservative-free jugs by contacting the following departments:

Outpatients:
Audrey Baylock
215-615-2069
audrey.baylock@uphs.upenn.edu

Inpatients:
Place supply order using:
Pennchart Request System
or
Materials Management
215-662-2904

To: UPHS Providers
From: Leslie M Shaw, PhD and Michael C Milone, MD, PhD
Date: July 6, 2017
Re: New sirolimus assay performed in the Toxicology Laboratory at HUP
New sirolimus assay effective July 10, 2017

The Toxicology Laboratory in the Division of Laboratory Medicine has implemented a new liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for measurement of the immunosuppressive drug sirolimus in trough blood samples. The new method replaces the Abbott Architect chemiluminescence immunoassay and provides a method that is free from sirolimus metabolite interference. Blood concentrations of sirolimus measured with the LC-MS/MS reference method are expected to be lower on average compared with concentrations measured by the Abbott Architect immunoassay for this drug. Since metabolism of sirolimus varies from patient to patient, the blood concentration values obtained by the new LC-MS/MS reference method may vary from as <5% to 40% lower when compared to the immunoassay with an overall average of 21% lower concentrations.

The existing therapeutic ranges, 5-8 mg/L for heart transplants and 5-10 mg/L in liver transplant patients, are based on accurate measurement of sirolimus by LC-MS/MS, and will therefore not change.
Please feel free to contact us with any questions regarding this new sirolimus therapeutic drug monitoring test.

Contact information:
Leslie M Shaw, PhD
Email: Les.Shaw@uphs.upenn.edu
Cell phone: 267-251-8901

Michael C Milone, MD, PhD
Email: Michael.Milone@uphs.upenn.edu
Cell phone: 215-900-4954

Memo To: UPHS Physicians and Staff
From: Department of Pathology and Laboratory Medicine, Toxicology Laboratory
Leslie M Shaw, PhD, Director; Michael C Milone, MD, PhD, Associate Director; JoAnn Gardiner, MS, Manager
Date: May 9, 2017
Subject: Change to Glucose-6-Phosphate Dehydrogenase testing in the Wm Pepper Lab at HUP

Effective May 5, 2017, we no longer provide G6PD testing at HUP. It will be a send-out test, performed at our reference laboratory, ARUP (www.aruplab.com). The expected turnaround time is 1-2 days, Sunday – Saturday.
The reference range for the test performed at ARUP is 9.9 – 16.6 U/g Hb. Please note that the reference range values are higher than the 4.7 – 12.3 U/g Hb previously used for the HUP test method due to the difference in temperature employed for each test (37 0C, ARUP and 30 0C, HUP).
The specimen for this test remains the same: 2 mL of whole blood collected in either a green top or lavender top tube. For neonatal specimens, collect two purple or green top bullets. The blood sample should be placed on ice or a cold pack following collection and transported to the Central Receiving Laboratory, 7 Founders Pavilion, for shipment to ARUP.

For any questions please contact us at: 215-662-6575.

Memo To: UPHS Physicians and Staff
From: Department of Pathology and Laboratory Medicine, Endocrinology Laboratory
Date: December 30th, 2016
Subject: Changes to HUP anti-TPO and anti-TG laboratory tests.

We will be changing our anti-Thyroid Peroxidase Antibody (anti-TPO) and anti-Thyroglobulin Antibody (anti-TG) testing effective January 4th, 2017.
Anti-TPO testing will be switching from an ELISA to a more automated and precise Beckman immunoassay. The reference range will be changing from 20 IU/mL – 50 IU/mL (equivocal) and > 50 IU/mL (positive) to >= 9.0 IU/mL (positive). Retesting of 149 specimens showed that the assays are strongly correlated (r = 0.8) and interpretations are 97% concordant. Compared to the old method, the new method interpreted all positive results as positive, but 4 (5%) negative results were found to be positive (range: 9 IU/mL – 13 IU/mL). Of the 8 equivocal results, the new method called 6 (75%) positive.
For anti-TG testing, we have up until now used different immunoassays for autoimmune and thyroid cancer testing. We are consolidating on the Beckman immunoassay platform used for thyroid cancer testing, which is the more precise method. Thus, the anti-TG thyroid cancer testing will be unchanged. The anti-TG autoimmune testing reference range will be changing from 50 IU/mL – 100 IU/mL (equivocal) and > 100 IU/mL (positive) to >= 4.0 IU/mL (positive). Retesting of 113 specimens showed that the assays are well correlated (new_anti-TG = 0.34 * old_anti-TG – 19; R2 = 0.7) and 86% concordant.

Compared to the old method, the new method called 1 (2%) negative result positive and 11 (29%) positive results negative. Based on chart review, the discordant new results were not expected to have changed management. Of the 26 equivocal results, the new method called 4 (15%) positive.

Please continue to request these tests using the same order code. Please contact us with any questions or concerns (215-662-6575).

MEMORANDUM To: All Laboratory Users
From: Department of Pathology and Laboratory Medicine
Date: July 19, 2016
RE: Specimen Collection Tube Improvement

Effective Tuesday July 19, 2016 the Hospital of the University of Pennsylvania Department of Pathology and Laboratory Medicine will adopt smaller volume lavender and blue top collection tubes for blood samples in an effort to support the fight against hospital acquired anemia and reduce the amount of blood taken from patients for laboratory testing. In addition, the blue top tube will convert from glass to plastic for routine coagulation testing mitigating potential breakage and injury from glass containers. Note: Special Coagulation testing will remain unchanged requiring collection in the 4.5 mL blue top glass tube (Lawson # 100391)

Below please find the updated Lawson information:
Lavender:

	Old	**New**
Volume	4.0 mL	2.0 mL
Lawson Number	100396	209016

Blue:

	Old	**New**
Volume	4.5 mL	2.7 mL
Lawson Number	100391	209018

We have attached a tip sheet refresher for sample collection. Should you have any questions or require any additional information please contact PENNLAB Client Services at 215.662.4808 or 1-800-PENNLAB.

Date: 5/6/16
Memo to Medical and Housestaff
From: Irving Nachamkin, DrPH, MPH, Laboratory Director, Division of Laboratory Medicine
Re: Reporting of Reference Ranges for INR

In a review our of laboratory reports, it came to my attention that reference ranges for INR were not being reported and is a requirement for all laboratory tests. Moving forward, you will now see PT/INR results reported with the following information:

Procedure		**Ref Range**	**Units**
PT	result	11.2-13.5	seconds
INR	result	0.9 – 1.1	

Prothrombin Time/INR: Result of the Prothrombin time is reported in seconds and is converted to the international normalized ratio (INR). The INR is a calculation based on the result of the prothrombin time and serves to standardize results from different laboratories and the variable response to different thromboplastin reagents. Recommended therapeutic warfarin range is patient specific and is determined by the physician/provider.

DATE: February 23, 2016
TO: UPHS Physicians and Staff
FROM: Hospital of the University of Pennsylvania
Vivianna Van Deerlin, M.D., Ph.D., Director, Molecular Pathology Laboratory
Christopher Watt, M.D., Ph.D., Associate Director, Molecular Pathology Laboratory

Kevin Alby, Ph.D., D(ABMM), Assistant Director, Clinical Microbiology
SUBJECT: HCV genotyping method change

As of February 23rd, 2016, hepatitis C virus (HCV) genotyping will be performed using the eSensor® HCVg Direct Test (GenMark Diagnostics, Inc.). This qualitative in vitro test uses reverse transcription polymerase chain reaction (RT-PCR), nucleic acid hybridization, and electrochemical analysis for the detection of 8 prevalent HCV type/subtypes (1a, 1b, 2, 2a/c, 2b, 3, 4, 5, and 6). In addition to an overall improvement in laboratory workflow, this new method has an improved ability to subtype HCV genotype 1 as compared to the prior method (see clinical significance and assay limitations for additional details).
CLINICAL SIGNIFICANCE: HCV is a heterogeneous virus that is classified by phylogenetic analysis into seven genotypes, each with 1 or more subtypes. In the United States, HCV genotypes 1 and 2 are the most common with genotype 1 being the most prevalent (approximately 75% of all HCV cases). Direct-acting antiviral (DAA) agents such as protease inhibitors, viral subunit NS5A inhibitors, and viral RNA polymerase inhibitors are among the therapies used to treat HCV infection. Drug selection and treatment duration are typically based on HCV genotype information. Outside of subtypes 'a' and 'b' for HCV genotype 1, the clinical utility of subtype information for HCV genotypes is limited.

ASSAY LIMITATIONS: This assay may have difficulty:

- Distinguishing some HCV subtypes
- Genotyping samples with an HCV viral load < 1,000 IU/mL
- Genotyping mixed infections, especially if one of the HCV genotypes in the sample is much more predominant than the other(s)
- Detecting HCV genotype 4f due to cross-reactivity between signal probes for HCV genotype 1b

TESTING INFORMATION:
Turnaround Time: 1-5 business days
Acceptable Specimen: Plasma (preferred) or Serum
Ordering: Hepatitis C Virus Genotype (Includes HCV Quantitative Viral Load), EPIC or Sunrise
Possible Results: The following HCV genotypes will be reported:

- 1, 1a, 1b, 2, 2b, 2a/c, 3, 4, 5, or 6

The following mixed infections will be reported:

- 1a/1b, 1a/2b, 1b/2b, 1/2, 1a/2a/c, 1b/2a/c, 1/2a/c, 1a/3, 1b/3, 1/4

CONTACTS FOR MORE INFORMATION:
Laboratory Main Number: 215-662-6121
Molecular Pathology Service Pager: 215-980-9868

Date: November 18, 2015
To: All Medical Staff, House Staff, and Nursing Leadership
From: Jennifer Morrissette, Ph.D.
Clinical Director, Center for Personalized Diagnostics
Kojo Elenitoba-Johnson, MD
Director, Center for Personalized Diagnostics
Katherine Nathanson, MD
Chief Oncogenomics Physician, ACC
Re: Next generation sequencing for somatic mutations in BRCA1, BRCA2 and ESR1

The clinical laboratory of the Center for Personalized Diagnostics is now offering mutation testing for mutations in BRCA1, BRCA2 and Estrogen Receptor1 (ESR1) on tumor samples, using massively parallel sequencing technology.
This panel can be ordered in the same way that other next generation sequencing panels from the CPD are ordered, using APCONS in EPIC or through paper requisition. Triage will be performed through the Molecular Anatomic Pathology (MAP)

service (Dr. Leslie Litzky, Director). This test has been validated for somatic (tumor) mutation detection only and a minimum of 10% tumor cells in the submitted sample is necessary for detection of alterations. ESR1 amplifications should be detectable, dependent on the percent of submitted tissue. This assay is validated for analysis of fixed paraffin-embedded tissue samples.
Please contact the CPD clinical laboratory if you need additional information regarding test ordering or materials necessary to conduct the assay. Questions regarding the test should be referred to David Lieberman (215-349-8416) or Jennifer Morrissette (215-898-8066/5578).

Date: May 11, 2015
To: UPHS Faculty and Resident Physicians
From: Larry Kricka, DPhil, FACB, CChem FRSC, FRCPath,
Interim Director, Endocrinology Laboratory
Irving Nachamkin, DrPH, MPH, Director, Division of Laboratory Medicine
Subject: Updated reference ranges for serum estradiol

A new and improved method for serum estradiol will be implemented on Monday, May 18th. The new method shows reduced cross-reactivity, and has improved traceability to the ID-GC/MS reference method. This highly sensitive method has a limit of quantitation (LoQ; concentration that results in a CV=20%) of 25 pg/mL, (lower than the current limit of the reportable range 30 pg/mL).
Compared to the method currently in use, the new formulation shows a 10-15% negative bias. Therefore, implementation of this improved method will necessitate an update to our reference ranges as follows:

Adult Male 27.1 - 52.2 pg/mL

Adult Female
Follicular phase 26.7 - 156 pg/mL
Ovulation phase 48.1 - 314 pg/mL
Luteal phase 33.1 - 298 pg/mL
Postmenopause <49.9 pg/mL

Healthy pregnant women
1st trimester 154 - 3065 pg/mL
2nd trimester 1561 - 18,950 pg/mL
3rd trimester 10,030 - >30,000 pg/mL

To: UPHS Physicians and Staff
From: Michael Husson MD, Pathology and Laboratory Medicine
Date: April 21, 2015
Re: Anion Gap Reporting

Effective immediately the anion gap will be reported with electrolyte results.
The reference range is 3-12 (established on the Beckman testing platform used by all UPHS labs).
The following comment will be attached to the result:
With hypoalbuminemia, anion gap correction is suggested using Na - (Cl+CO2) + 2.5*(4 - Albumin). The lab reports Na - (Cl+CO2).
For general questions, please contact: michael.husson@uphs.upenn.edu

From: Amy Behrman, MD – Medical Director, Occupational Medicine, HUP
Kevin Alby Ph.D., D(ABMM) – Assistant Director, Clinical Microbiology, HUP
To: UPHS Housestaff, Providers, and Clinical Faculty, CPUP and CCA Practices
Re: Changes in Source Patient/Occupational Exposure Testing at HUP

Effective Monday March 23rd, 2015, the clinical laboratory at HUP will offer new source patient testing in cases of occupational exposure. This testing will include HBsAg testing, HCV Ab testing, and 4th generation HIV testing* 24 hours/day. Exposed HCWs at HUP will still need to report the injury using the online portal found on the Intranet homepage, however the testing on the source patient should now be ordered electronically rather than with a paper requisition. After

obtaining consent for HIV testing, source patient testing can now be ordered in both SCM and Epic using the test "Occupational Exposure Profile" OCCEXP. Send a single labeled gold top tube to Central Receiving (tube station 01 or 02). Again, this change is for occupational exposures at HUP; other entities will continue their standard practices.

Please contact the Occupational Medicine Case Manager (at 662-2358 or 662-4047 or occhealth@uphs.upenn.edu) or Dr. Kevin Alby for laboratory related issues (662-6652; kevin.alby@uphs.upenn.edu) if you have any questions about these changes.

*Fourth generation HIV testing includes HIV Ab and p24 antigen for increased sensitivity to early infection

Legionella PCR replaces culture

Effective 2/16/2015 the HUP Clinical Microbiology Laboratory will perform real time PCR instead of culture for the detection of Legionella spp. in lower respiratory tract specimens. This PCR assay will replace conventional culture for these specimen types, so that if culture is ordered PCR will be performed instead.

All PCR-positive specimens will be cultured for quality assurance and public health purposes. Tissue specimens and specimens not obtained from the respiratory tract, which represent less than 1% of our current culture requests, will continue to be cultured. Urinary antigen testing for L. pneumophila serogroup 1 will also remain available.

The Legionella spp. real time PCR assay is 100% sensitive and specific when tested against Legionella spp. culture-positive and culture-negative respiratory tract specimens. The analytical sensitivity of the assay (ability to detect bacteria in seeded specimens) is about 100 times that of culture. Both Legionella spp. and L. pneumophila are targeted in different reactions, allowing the identification and reporting of both L. pneumophila and non-L. pneumophila Legionella spp. infections. In clinical studies of this and similar PCR tests, PCR has been about 15 to 30% more sensitive than that of culture or urine antigen testing. Although data are limited, the PCR test has remained positive after the start of antibiotic therapy for Legionnaires' disease, and after cultures become negative, for up to a week. Neither this test nor culture should be used as test of cure.

Five extremely rarely isolated Legionella spp. are not detected by the PCR assay, only one of which has been reported to cause human infection; there is a single case report of one of the fived undetected species causing Legionnaires' disease in a severely immunocompromised patient. No HUP patient has had known infection caused by these extremely rare species over the last 30 years, despite the aggressive use of culture diagnosis. On request and consultation, culture will be set up if the patient is severely immunocompromised and the PCR test is negative.

The PCR assay will be performed up to three times weekly, depending on demand, with results available on the same day that the assay is performed. The SCM and EPIC order code names are "Legionella ID by PCR" and "Legionella Detection by PCR", respectively. This test should only be ordered for patients with pneumonia. It is not a useful tool to determine the cause of fever without pneumonia. Since the majority (~70%) of cases of Legionnaires' disease at HUP are still detected by urine antigen testing, both urine antigen testing and PCR of respiratory tract specimens should be requested. Please direct questions about ordering the test to the Clinical Microbiology Laboratory, 662-3406.

Questions regarding assay performance and interpretation should be directed to Paul Edelstein, M.D., 662-6651.

To: UPHS Physicians and Staff
From: Michael Husson MD, Dr L J Kricka, DPhil, Franz Fogt MD,
Date: December 15, 2014
Re: Body fluid total protein sensitivity = 0.5 g/dL

The clinical laboratories at HUP, PPMC and PAH will have improved sensitivity of body fluid total protein reporting.
Lowest reportable values will decrease from 3.0 g/dL to 0.5 g/dL.
Improved sensitivity of total protein measurement will aid in the evaluation of pleural and peritoneal effusions associated with very low total protein levels.
The change in sensitivity will be implemented during the week of Dec 15th at all three entities.

From: Stephen Master, MD, PhD, Director, Endocrinology Laboratory
David Cardamone – Manager, Endocrinology Laboratory
To: HUP, PPMC Housestaff and Clinical Faculty, CPUP and CCA Practices
Re: Change in AFP MoM cut-off
Effective date: November 17, 2014

In consultation with Maternal Fetal Medicine and Genetics, the endocrinology laboratory will change the second trimester AFP multiple of the median (MoM) cut-off for Neural Tube Defects from 2.0 to 2.5.
<2.5 will be reported as screen negative and AFP MoMs = 2.5 (singleton, non-diabetic) will be reported as screen positive. The new cut-off is in alignment with published recommendations.

Please contact David Cardamone (215-662-3420 or david.cardamone@uphs.upenn.edu) if you have any questions about these changes.

To: UPHS Physicians and Staff
From: Vivianna Van Deerlin, M.D., Ph.D., Director, Molecular Pathology Lab
Christopher Watt, M.D., Ph.D., Associate Director, Molecular Pathology Lab
Kevin Alby, Ph.D., Assistant Director, Microbiology Laboratory
Date: November 11, 2014
Re: Method change for Hepatitis C viral load testing

On November 12, 2014 version 2.0 of the COBAS AmpliPrep/COBAS TaqMan HCV Test (Roche Diagnostics Systems, Inc.) will be implemented in the Molecular Pathology Laboratory. In contrast to the current version of the test, version 2.0 uses two detection probes in combination with one forward and two reverse primers in the 5' non-translated region (NTR) of the viral genome (see figure). This design adds redundancy and improved mismatch tolerance for accurate and specific quantification of HCV RNA from a wide range of HCV isolates including those with high sequence heterogeneity, for example as a result of potential polymorphisms that may occur in the genome of constantly evolving virus. Although the correlation between version 2.0 and the previous method is good, viral loads using version 2.0 may be higher due to an improved viral quantification method and thus may not represent a clinical increase in viral load. Both the current and new methods detect and quantify HCV RNA genotypes 1 to 6. Finally, this new methodology expands the upper and lower limits of quantification (see table).
Table: Performance characteristics of COBAS TaqMan HCV v2.0
COBAS HCV v2.0
Current COBAS method
Limit of detection 15 IU/mL
18 IU/mL
Linear range 15 to 100,000,000 IU/mL
43 to 69,000,000 IU/mL
There is no change in test code, specimen type, or testing schedule. Additional information on ordering this test can be found in the laboratory services test guide: https://www.testmenu.com/HUP/Tests/333110
For additional information please contact the laboratory at 215-662-6121

November 5, 2014
From: Stephen Master, MD, PhD, Director, Endocrinology Laboratory
David Cardamone – Manager, Endocrinology Laboratory
To: HUP, PPMC Housestaff and Clinical Faculty, CPUP and CCA Practices
Re: Changes in Tumor Marker testing

Effective November 04, 2014 , the laboratory has switched from performing CA 125 and CA 15.3 tumor markers from the Ortho 3600 platform to the Roche Elecsys platform. The new platform provides improved low-end precision. The laboratory has therefore changed the lower reporting limit for CA 125 from 7 U/mL to 1 U/mL.
Tumor marker values on different platforms are not directly comparable, and, the health care provider may ask for a rebaseline with the previous method for up to 6 months for comparison purposes.
Method validations showed an approx. average bias of the following:

CA 15.3 (noted as average % bias): 2% (range:1-30 U/mL); -10% (range:30 – 100 U/mL); -17% (range:>100)

CA 125 (noted as average % bias): 25% (range:1-30 U/mL); 6% (range:30 – 100 U/mL); -2% (range:>100)

Please contact David Cardamone (349-5031; David.Cardamone@uphs.upenn.edu) if you have any questions about these changes.

October 23, 2014
From: Kevin Alby Ph.D., D(ABMM) – Assistant Director, Clinical Microbiology
David Cardamone – Manager, Endocrinology Laboratory
To: HUP, PPMC Housestaff and Clinical Faculty, CPUP and CCA Practices
Re: Changes in Hepatitis A Testing

Effective Tuesday October 21st, the laboratory will switch from performing Hepatitis A Total Antibody (EPIC Code: HAVTOTAL) to a Hepatitis A IgG specific antibody (EPIC Code: HEPAIGG). The laboratory will continue to offer Hepatitis A IgM specific antibody (EPIC Code: C3510110) testing for acute infection. The switch allows for better determination of recent vs past infection as the presence of an IgG antibody can be detected even in cases where an IgM antibody is present. This distinction cannot be made using a Hepatitis A total antibody test.

Please contact David Cardamone (349-5031; David.Cardamone@uphs.upenn.edu) if you have any questions about these changes.

June 4, 2014
From: Michael Husson, MD, Laboratory Director, HUP Core Lab and PAH Chemistry Lab
Franz Fogt, MD, PPMC Laboratory Director
To: HUP, PPMC, PAH Housestaff and Clinical Faculty, CPUP and CCA Practices
Re: Change in laboratory reference and critical ranges effective June 4, 2014

On June 4 the labs at HUP, PPMC and PAH will transition to new AU analyzers that perform general chemistry, TDM and urine drug screen tests.
Due to different methods for albumin, amylase and lipase measurement, there will be slight changes in the reference ranges for these three tests.
Amylase and lipase values are lower in general with the new analyzer, but the difference is most apparent in higher range values.
Additionally, PAH will experience minor changes in several other reference ranges related to the lab's goal of aligning ranges at HUP, PPMC and PAH.
Further alignment in ranges for some other tests will be coming and announced separately.
Finally, some critical value limits will change at PAH as part of this standardization of laboratory reporting.
All of the changes effective June 4 are documented below.

Changes in reference ranges affecting HUP, PPMC, and PAH:
Amylase U/L
All 29-103
--- Current values below in parentheses ---
(All 28-100 UPHS)

Lipase U/L
All 11-82
--- Current values below in parentheses ---
(All 22-51 UPHS)

Albumin g/dL
All 3.5-5.1
--- Current values below in parentheses ---
(All 3.4-4.8 HUP/PPMC)
(<1 yr 2.8-4.4 PAH)
(1-10 yr 3.1-4.8 PAH)
(>10 yr 3.4-4.8 PAH)

Changes in reference ranges affecting PAH only:

Acetaminophen therapeutic range ug/mL
All 2-15

--- Current values below in parentheses ---
(All 10-30 PAH)

Bilirubin Total mg/dL
<1 mo 0-11.6
1 mo-18 yr 0-1.9
>18 yr 0.3-1.2
--- Current values below in parentheses ---
(<1 mo 0-12 PAH)
(>1 mo 0.2-1.2 PAH)

Bilirubin Direct mg/dL
<1 Wk 0-0.9
>1 Wk 0.1-0.5
--- Current values below in parentheses ---
(All 0-0.2 PAH)

Calcium Total mg/dL
All 8.9-10.3
--- Current values below in parentheses ---
(All 8.6-10.3 PAH)

Carbamazepine mg/L
All 6-12
--- Current values below in parentheses ---
(All 4-12 PAH)

Chloride mmol/L
<1 mo 99-116
>1 mo 101-111
--- Current values below in parentheses ---
(All 98-107 PAH)

Cholesterol mg/dL
All 100-200
--- Current values below in parentheses ---
(All 100-199 PAH)

Carbon Dioxide mmol/L
<1 yr 15-28
>1 yr 22-32
--- Current values below in parentheses ---
(<1 mo 20-27 PAH)
(>1 mo 22-32 PAH)

Creatine Kinase U/L
All 49-397 M
All 38-234 F
--- Current values below in parentheses ---
(All 38-174 M PAH)
(All 26-140 F PAH)

Creatinine mg/dL
0-1 mo 0.3-0.8 M
>1 mo 0.64-1.27 M
0-1 mo 0.3-0.8 F

>1 mo 0.44-1.03 F
--- Current values below in parentheses ---
(All 0.7-1.3 M PAH)
(All 0.6-1.1 F PAH)

LDH U/L
All 98-192
--- Current values below in parentheses ---
(All 100-190 PAH)

Magnesium mg/dL
All 1.8-2.5
--- Current values below in parentheses ---
(All 1.7-2.5 PAH)

Phosphorus mg/dL
<3 mo 4.5-8.1
3 mo-1 yr 3.8-6.2
1-5 yr 3.4-5.9
5-10 yr 2.9-5.9
10-15 yr 3.3-6.2
15-18 yr 2.7-4.9
>18 yr 2.4-4.7
--- Current values below in parentheses ---
(0-3 mo 4.5-8.1 PAH)
(3-12 mo 3.8-6.2 PAH)
(>1 yr 2.4-4.7 PAH)

Potassium mmol/L
<1 yr 4-6.2
>1 yr 3.6-5.1
--- Current values below in parentheses ---
(<1 mo 3.5-5.1 PAH)
(>1 mo 3.5-5.1 PAH)

Salicylate mmol/L
All 25-35
--- Current values below in parentheses ---
(All 0-29.9 PAH)

Sodium mmol/L
<1 mo 131-143
>1 mo 136-144
--- Current values below in parentheses ---
(<1 mo 136-145 PAH)
(>1 mo 136-145 PAH)

Theophylline mg/L
<1 yr 5-10
>1 yr 10-20
--- Current values below in parentheses ---
(All 8-20 PAH)

Protein Total g/dL
All 6.1-7.9
--- Current values below in parentheses ---

(All 6-8 PAH)

Triglycerides mg/dL
All 25-150
--- Current values below in parentheses ---
(All 30-149 PAH)

Uric Acid mg/dL
All 4.8-8.7 M
All 2.6-8 F
--- Current values below in parentheses ---
(All 4.4-7.6 M PAH)
(All 2.3-6.6 F PAH)

Vancomycin Trough mg/L
All 5-20
--- Current values below in parentheses ---
(All 10-20 PAH)

Critical value changes affecting PAH only:

Carbamazepine Level
Critical high >15 change to >12

Bicarbonate
ICN neonates
Critical low <19 change to <13
Critical high 28 eliminated

Creatinine
ICN neonates
Critical high >=2.0

Glucose
ICN neonates
Critical high >500 change to >400

Magnesium
Critical high >=8.0 change to >=3.5

Phosphorus
ICN neonates
Critical low <1.0 change to <1.7
Critcial high >=30
Adults
Critical low 0.9 change to 1.0
Critcial high >=30

Salicylate level
Critcial high >30 change to >40

Sodium
Adults
Critical low <=120 change to <=115
Critical high >=160 change to >=165

Theophylline
Critical high >25 change to >20

Valproic Acid Level
Critical high >150 change to >200

Vancomycin Trough
Critical high >20 change to >25

November 25, 2013
Discontinuation of Caspofungin Susceptibility Testing of Yeasts and Change to a New Test Platform

Effective immediately, the Clinical Microbiology Laboratory will stop performing and reporting caspofungin susceptibility testing of Candida spp. This is because of the results of a newly published international study that showed that caspofungin susceptibility testing is unreliable and imprecise for technical reasons that are not understood (pubmed 24018263). This unreliability does not extend to micafungin or anidulafungin susceptibility testing. The international group of authors who are respected authorities on yeast susceptibility testing recommended that caspofungin testing not be performed, and that either micafungin or anidulafungin be tested instead if susceptibility testing is required. Unfortunately there are no commercial sources of susceptibility panels containing either of these echinocandins, and a research use only Etest has major performance issues. We will send C. glabrata isolates to a reference laboratory for micafungin susceptibility testing (a good marker of echinocandin susceptibility) on request when one of the following conditions is met:

- Persistent C glabrata fungemia while a patient is receiving caspofungin, despite adequate source control
- C glabrata endovascular infection such as endocarditis, infection of a vascular graft or pacemaker lead
- C glabrata osteomyelitis

Caspofungin resistance of yeasts other than C glabrata is extremely rare, hence the restriction to C glabrata infections only. We will also be moving fluconazole and voriconazole susceptibility testing to the Vitek from a manual microbroth dilution panel, after extensive validation of the Vitek panel. This will result in much faster turn-around-times, as we can set these up on weekends and daily as needed. Vitek testing will begin in December.

Paul H. Edelstein, M.D
Director Clinical Microbiology, Hosp Univ Pennsylvania
Professor Pathology & Laboratory Medicine, Perelman School of Medicine, Univ of Pennsylvania
4 Gates
3400 Spruce St.
Philadelphia, PA 19104-4283
215.662.6656

To: UPHS Physicians and Staff
From: Vivianna Van Deerlin, M.D., Ph.D., Director, Molecular Pathology Laboratory
Christopher Watt, M.D., Ph.D., Associate Director, Molecular Pathology Laboratory
Paul H. Edelstein, M.D., Director, Clinical Microbiology Laboratory
Kevin Alby, Ph.D., Assistant Director, Clinical Microbiology Laboratory
Date: November 15, 2013
Re: Method Change for Quantitative Cytomegalovirus (CMV) testing

On November 19th, 2013 the Molecular Pathology Laboratory will implement the COBAS AmpliPrep/COBAS TaqMan CMV Test (Roche Diagnostics Corp) for quantitative measurement of CMV DNA in both plasma and bronchoalveolar lavage (BAL) specimens. This will replace the current artus CMV Assay (Qiagen). This methodology change will impact testing and reporting in the following ways:

- CMV testing will now be performed every weekday with an expected turnaround time of 1-3 days.
- CMV titer results will now be reported in international units (IU)/mL and log IU/mL as opposed to copies/mL and log copies/mL.

- The linear dynamic range of the assay is between 137 and 9,100,000 IU/mL (2.1- 7.0 log IU/mL). CMV titers below 137 IU/mL but above the lower limit of detection of the assay (~91 IU/mL) can be detected but not quantified.
- To improve clarity and interpretation, CMV result categories have been updated. A description of possible result categories from the COBAS TaqMan CMV test is presented in the table below.

Description of Possible Results	IU/mL	Log IU/mL
CMV DNA not detected at the level of sensitivity of the assay	Not detected	-
CMV DNA detected at a low level that is below the dynamic range of the assay so it cannot be quantified	< 137 IU/mL	< 2.1 log IU/mL
CMV DNA detected in the dynamic range of assay	137 - 9,100,000 IU/mL	2.1 - 7.0 log IU/mL
CMV DNA detected at a high level that is above the dynamic range of the assay so it cannot be quantified	> 9,100,000 IU/mL	> 7.0 log IU/mL

NOTE: For BAL specimens, changes in CMV titers between tests do not necessarily indicate a change in CMV viral load in the lung due to sampling and dilution effects that can occur during specimen collection.

METHOD COMPARISON
Studies comparing the new COBAS TaqMan CMV test with the preceding quantitative CMV method (Qiagen) demonstrated comparable sensitivity and good correlation (r2=0.89 and slope=1.02) between the two methods across a wide range of CMV titers. When comparing log copies/mL (Qiagen) to log IU/mL (COBAS), measurements on the new COBAS TaqMan CMV test are typical 0.2 logs lower than the Qiagen method (95% limit of agreement of approximately +/- 0.6 log). When comparing on the linear scale, one Qiagen copy/mL is on average 0.62 IU/mL. Please note that this relationship between copies/mL (Qiagen) and IU/mL (COBAS) cannot be extended to CMV results from outside laboratories reporting in copies/mL.

TESTING INFORMATION
Ordering and specimen requirements remain unchanged.

CONTACTS FOR MORE INFORMATION:
For information on ordering and specimen requirements, kindly consult the Lab Tests Services Guide
For additional information about testing or the transition to the international units please contact the lab.
Laboratory main number: 215-662-6121
Molecular Pathology service pager: 215-980-9868

Date: 11/13/13
From the Clinical Microbiology Laboratory, Division of Laboratory Medicine, Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania
Laurel Glaser, MD PhD, Clinical Microbiology Fellow
Paul Edelstein, MD, Director, Clinical Microbiology Laboratory
Re: Detection of Cryptococcal Antigen in Serum and CSF samples

Effective 12/2/2013, the Clinical Microbiology Laboratory will change its method for detecting Cryptococcus neoformans and C. gattii antigen in serum and CSF. The CrAg Lateral Flow Assay (Immuno-Mycologies, Inc.) will replace the current Cryptococcus latex agglutination assay for initial sample testing. The newer assay is slightly more sensitive than the latex agglutination assay, does not suffer from false-positive reactions from rheumatoid-like factors, and is much easier to perform in the laboratory. The CrAg will be used as a qualitative screening test. All test-positive specimens will be retested with the latex agglutination assay so that an antigen titer can be determined. The sample requirements and order codes remain unchanged. Because the newer assay does not require specimen pretreatment and is easier to perform, it will be performed on both day and evening shifts, and on weekends. If time allows, the testing will also be performed on the late night shift as well (midnight to 8AM). Since the new test does not suffer from false-positive results due to non-specific blood and CSF proteins, a positive test can be regarded as a true positive without the need for quantification of the antigen titer, therefore, the titration of positive specimens is only done on the day shift, Monday thru Friday.

As with the latex test, rare false negative results are possible due to very high levels of cryptococcal antigen (prozone effect); please alert the laboratory if you suspect such a circumstance. Since hemolyzed blood can interfere with test performance, hemolyzed blood specimens cannot be tested with this test. It is unknown if the new test cross-reacts with the latex agglutination cross-reactive microorganisms (Capnocytophaga canimorsus, Rothia spp., Trichosporon spp.) or hydroxyethyl starch. While the CrAg assay does not react with Aspergillus spp. antigens, some galactomannan-positive specimens were positive in clinical trials; whether this was due to cryptococcal disease or to cross-reactions of the CrAg test with unknown non-cryptococcal fungal antigens is not known. Since the CrAg assay can be more sensitive than the latex agglutination assay, a patient specimen may rarely be positive in the qualitative test and have an undetectable titer by the latex agglutination assay. Multiple published studies have evaluated the CrAg test in comparison to other available methods and show excellent (>98%) agreement. In our internal validation, there was 100% agreement between the new lateral flow assay and the previous latex agglutination assay for banked positive serums and CSFs. In addition serums and CSFs spiked with purified CrAg were 99% positive.
As a reminder, the sensitivity of any cryptococcal antigen test is not 100%. In addition to submission of several high volume CSF specimens for fungal culture at least two additional cryptococcal antigen tests of CSF may be indicated in patients with suspected cryptococcal meningitis and a single negative CSF cryptococcal antigen test.
Please call the laboratory supervisor, Jill Wadlin, 215-662-6657 for questions about this assay.

To: All clinicians at PennMedicine
From: Michael Husson, MD, William Pepper Laboratory, Hospital of the University of Pennsylvania
Subject: Correct order names for common CSF test requests
Date: Aug 13, 2013

The lab occasionally receives CSF samples with incorrect orders due to confusion with body fluid test names. Please be aware that CSF samples have their own specific test names which should be chosen in Epic or Sunrise.
The correct common test names for CSF samples are the following:

EPIC
Cell count CSF#1
Cell count CSF tube #4
Spinal fluid glucose
Spinal fluid protein
CSF lactate dehydrogenase
Cerebrospinal Fluid Culture
Cryptococcal Antigen

SCM
Cell Count CSF Number 1
Cell Count CSF Number 4
Glucose, CSF
Protein, CSF
CSF LDH
CSF Culture & Gram Stain
Cryptococcal Antigen

If there are any questions, please do not hesitate to contact Client Services at 215-662-4808 or 1-800-PENN-LAB.
Thanks very much for your attention to these ordering details.

TO: UPHS Physicians and Staff
FROM: Hospital of the University of Pennsylvania
John Brooks, Interim Director of Anatomic Pathology, for the entire Cytopathology and Molecular Pathology faculty and laboratory team
DATE: January 21, 2013
SUBJECT: Position Statement on HPV testing & SurePath

A recent USA Today article raised concerns about HPV testing using SurePath GYN cytology specimens. We thought it best to explain what we do, so that you may be in a better position to answer questions from your patients if they call about this

matter.

Position Paper
UPHS Pathology-Cytopathology Does Not Use Hybrid Capture Test for HPV

Concerns have arisen around the potential for false negative HPV tests when using the Hybrid Capture II (HCII) HPV testing method on SurePath cytology specimens, a procedure which is not FDA approved. UPHS does not use the HCII method for HPV testing. Instead, HPV testing has been performed in HUP's Molecular Pathology Laboratory since 2008 using the more robust Hologic Cervista® HPV HR test, which includes an internal control for DNA preservation that is not available with the HCII method. The Hologic test gives excellent results: 97% of samples are resulted as positive or negative, and only 3% of samples are found to have an inadequate amount of DNA; in those cases a new sample is requested. We have high confidence in the Hologic Cervista® HPV HR test results.

Concerning our collection system, the use of SurePath has been under review since the issuance of the Technical Bulletin by its manufacturer (Becton Dickinson), with the likelihood of switching to the ThinPrep collection system within the next few months, for some or all samples depending upon the preference of clinicians offices both within our system and our expanding outreach practice.

Summary: 1) our patients are not tested for HPV by the recently reported problematic HCII method; 2) we use a more robust testing method (Cervista® HPV HR by Hologic); and 3) our highest priority is providing the highest quality care to all our patients and we have a high level of confidence that we are doing that with our testing methodology.

To: Members of UPHS Clinical Staff
From: Robert Metheny
Date: October 29, 2012
The send out/reference lab tests are suspended until Wednesday October 31, 2012.

To: Members of UPHS Clinical Staff
From: Leslie M Shaw, PhD, Director, Toxicology Laboratory, and Michael C Milone, MD, PhD, Associate Director
CC: Irving Nachamkin, DrPH, MPH, Director, Laboratory Medicine
Date: August 6, 2012
Re: Modified reporting for opiates and amphetamines in urine drug screen testing

Effective Tuesday, August 7, 2012, urine drug screen reports will be modified to include separate reporting of oxycodone and MDMA (ecstasy) test results in addition to the opiate and amphetamine screening results currently reported. There is NO change to the immunoassay screening or gas chromatography confirmatory testing procedures used by the laboratory. This is only a modification in reporting of the drug screen testing results. As before, when a specimen is positive in the immunoassay screening test for either of these drug classes, these results will be confirmed by gas chromatography with mass spectrometry detection and reported separately.
The laboratory has been performing separate opiate and oxycodone screening assays for several years. These results were previously reported as positive under the single opiate result if either screening test was positive. Considerable cross-reactivity occurs with opioid drugs in these assays so a positive result is possible with many of these drugs in both assays, especially at higher drug concentrations. Confirmatory testing is necessary to definitively identify the opioid drugs detected by these screening assays. The separate oxycodone assay (which is also better at detecting oxymorphone) was included in the current screening approach to avoid missing lower levels of these drugs, which are currently widely prescribed and misused. A similar testing and reporting approach was used for amphetamine and MDMA testing to avoid missing these less commonly encountered, but important stimulants. Caveats similar those in opioid screening exist, and confirmatory testing is necessary to identify drugs in this class.
Please feel free to contact the on-call laboratory medicine resident with any questions regarding this change in reporting or other questions related to the drug testing program.

May 7, 2012

Canceled Lab status displayed in Sunrise: Enterprise wide launch 5/10/2012

The SCM lab results section will now indicate when a lab has been canceled by the performing department. This will be

indicated by displaying CAN on the results screen and when clicked, the reason for the cancellation will be shown. In addition, canceled labs will display as "AA" on sign out documents and progress notes.

To: UPHS Physicians and Staff
From: Vivianna Van Deerlin, M.D., Ph.D. Director, Molecular Pathology Laboratory
Christopher Watt, M.D., Ph.D. Associate Director, Molecular Pathology Laboratory
Cindy McGrath, M.D., Clinical Associate Professor, Cytopathology, GYN QA InCharge
Date: March 9, 2012
Re: HPV high risk testing on gynecologic specimens without cytology examination

Human papillomavirus high risk testing is now available for order directly on gynecological specimens (Surepath Liquid-based specimens only at this time) without concomitant cytological evaluation. Until now HPV high risk testing was only available in conjunction with a cytological examination (Pap test).
CLINICAL SIGNIFICANCE: High-risk HPV is a causative agent of cervical cancer. High-risk HPV DNA testing is used in patients with a cervical cytology result of atypical squamous cells of undetermined significance (ASC-US) to determine the need for referral to colposcopy. It can also be utilized to determine clinical management and colposcopy referral in postmenopausal patients with low grade squamous intraepithelial lesion (LSIL) cervical cytology results. In addition, in women 30 years and older HPV DNA testing results can be used along with cervical cytology to adjunctively screen to assess the presence or absence of high-risk HPV types. Limited evidence suggests that high-risk HPV DNA testing can be used as a primary screening tool when combined with cytology follow up testing in high-risk HPV positive patients.

HOW TO ORDER THE TEST IN EPIC
The Epic code for the HPV high risk only test without cytopathology evaluation is:
"Gyn HPV High Risk Only" (PAP04)
If a cytopathology (Pap) is desired, then the following original Epic orders should be used:
PAP with HPV Regardless (PAP01)
PAP with HPV Reflex for ASCUS or LSIL in PMP (PAP02)

TESTING INFORMATION
Sample type: SurePath liquid-based gynecologic specimen. These specimens should be sent to HUP with the regular PAP order deliveries.
Turn-around Time: 7-10 working days
Method: The presence of high-risk HPV was assessed using the Cervista HPV HR IVD assay which utilizes Invader signal amplification technology. The assay detects, but does not specifically identify, 14 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) in 3 probe pools based on phylogenetic relatedness.
Additional information: Call the Molecular Pathology lab weekdays during regular business hours (215-662-6121).

REPORTING
The reported result categories of the HPV high risk test are:
Not Detected: a negative result; high-risk HPV was not detected at the level of sensitivity of the assay
Detected: high-risk HPV was detected
Low DNA: The level of genomic DNA in the sample was too low to definitively assess the presence or absence of HPV; a new specimen should be submitted for analysis, if clinically indicated.
Equivocal: The result is equivocal; either due to a low level of HPV or high background signal; a new specimen should be submitted for analysis, if clinically indicated.
Inconclusive: a technical problem prevented testing or interpretation

TO: UPHS Clinical Faculty and Staff
FROM: Leslie M Shaw, PhD, Director, Toxicology Laboratory
Michael C Milone, MD, PhD, Associate Director, Toxicology Laboratory
DATE: March 5, 2012
SUBJECT: Discontinuation of fetal lung maturity testing

Effective March 1, 2012, the Toxicology laboratory no longer provides fetal lung maturity testing at HUP. The current assay, manufactured by Abbott Diagnostics, is no longer available. Furthermore, a recent review of the literature suggests that there is limited clinical utility for fetal lung maturity testing for a number of reasons including:

1. At >36 to <39 weeks, the majority of lung maturity tests will provide a positive result and even for those that are negative the probability of respiratory morbidity is very low.
2. Even with positive lung maturity test results, neonates born >36 to <39 weeks suffer from higher rates of complications than infants born at or beyond 39 weeks.
3. Amniocentesis at >36 to <39 weeks does not help differentiate pregnancies at high or low risk for neonatal.

Based on these findings and the lack of the fetal lung maturity testing assay at HUP, our colleagues in Maternal Fetal Medicine developed guidelines for scheduling elective cesarean deliveries without an amniocentesis for fetal lung maturity testing based on indication and gestational age. Please contact Dr. Sam Parry(parry@mail.med.upenn.edu) for a copy of these guidelines.

If there are any questions regarding the laboratory testing for fetal lung maturity please contact us:

Leslie M Shaw, PhD
Les.Shaw@uphs.upenn.edu

Michael C Milone, MD, PhD
Michael.Milone@uphs.upenn.edu

TO: UPHS Physicians and Staff

FROM: Molecular Pathology Laboratory, 7 Maloney
Hospital of the University of Pennsylvania
Vivianna Van Deerlin, M.D., Ph.D., Director
Christopher Watt, M.D., Ph.D., Associate Director

DATE: December 2, 2011

SUBJECT: Expanded BRAF mutation analysis

BRAF mutation analysis by pyrosequencing in the HUP Molecular Pathology Laboratory has been modified to detect an expanded set of mutations in codon 600 beyond the common V600E mutation the assay was originally designed to detect. Mutations detected include but are not limited to: V600E, V600K and V600R.

CLINICAL SIGNIFICANCE:

BRAF codon 600 mutations are seen in a variety of tumors, including melanoma, colorectal carcinoma, thyroid carcinoma, ovarian carcinoma, non-small cell lung cancer and hairy cell leukemia. Although the clinical utility of the test varies depending upon the clinical indication, BRAF codon 600 mutations may have diagnostic, predicative or prognostic significance.

ASSAY LIMITATIONS:

This assay is designed to detect the three most common BRAF mutations in codon 600 including V600E (c.1799T>A), V600K (c.1798_1799GT>AA) and V600R (c.1798_1799GT>AG). While these three mutations represent approximately 98% of reported BRAF abnormalities in codon 600, other rare BRAF mutations may be detectable by this pyrosequencing assay including K601E (c.1801A>G). However, these alternate rare mutations may not be reliably detected or distinguished from the three common mutations if the percent of mutation containing cells in the specimen is low. The limit of detection of this assay is approximately 10% as determined by admixture of DNA from a cell line containing the V600E (c.1799T>A) mutation with DNA lacking the mutation.

TESTING INFORMATION

Acceptable Specimens: Paraffin-embedded tumor tissue, fine needle aspirations
Note: All requests will be reviewed by an anatomic pathologist to determine adequacy of available material for testing.
Turn-around time: 10-15 business days
Ordering: If unfamiliar with the process for requesting testing on solid tumors, please contact the Molecular Pathology Laboratory weekdays during regular business hours (215-662-6121) for details on ordering.

To: UPHS Physicians and Staff
From: Molecular Pathology Laboratory
Vivianna Van Deerlin, M.D., Ph.D., Director
Christopher Watt, M.D., Ph.D., Associate Director
Re: Change in method for HIV viral load testing

On August 15th, 2011 the Molecular Pathology Lab will implement the COBAS AmpliPrep/COBAS TaqMan HIV-1 Test, version 2.0 ("TaqMan", Roche Diagnostics Corp) for HIV-1 viral load testing. This will replace the current Versant HIV-1 RNA 3.0 Assay ("bDNA", Siemens Diagnostics). The TaqMan assay is an FDA-cleared (IVD) test for the quantification of HIV-1 RNA in human plasma over the range of 20 - 10,000,000 copies (cp)/mL. Benefits of the new assay include higher sensitivity and specificity, extended linear range, dual target region design, and a workflow that will enable faster turn-around-time than the current method. A dual-target approach addresses the risk of mutational escape by co-amplification of two target regions of HIV-1 (long terminal repeat and gag regions).

COMPARISON BETWEEN OLD AND NEW METHODS

Quantitative correlation: Quantitative results between the old and new assays are well correlated, however when comparing the cp/mL values directly the TaqMan results are approximately 2X (0.3 log cp/mL) higher than the bDNA results (95% confidence intervals: 1.3X-3.1X or 0.12 – 0.49 log cp/mL). However, when the two assay's results are converted to International Units (IU)/mL the difference between them is essentially eliminated.

- One copy of HIV-1 RNA in TaqMan assay = 1.7 IU based on the WHO 1st Int'l Standard for HIV-1 RNA.
- One copy of HIV-1 RNA in bDNA assay = 3.28 IU.
- By convention, the HIV-1 viral load is still reported in cp/mL and log cp/mL (rather than IU).
- For approx comparison to old bDNA results divide the new TaqMan results by 2 or subtract 0.3 log.

Linear range: The linear range of the new TaqMan assay is 20 - 10,000,000 cp/mL compared with 75 – 500,000 cp/mL for the bDNA assay. Quantitative results will be reported over the linear range.

Negative result: Whereas the lowest result reportable with the bDNA assay is "<75 cp/mL", a 0 (zero) result is reported with the TaqMan assay if HIV-1 RNA is not detected.

Sensitivity: The TaqMan assay (limit of detection (LOD) = 20 cp/mL) is more sensitive than the bDNA method (LOD = 75 cp/mL). If HIV-1 RNA is detected below the TaqMan LOD, it will be reported as <20 cp/mL, otherwise the numerical viral load will be reported. In our validation with parallel testing for samples which were <75 cp/mL by bDNA the concordance between the two methods was about 95% after correcting for the IU conversion (see above for details). Whereas about 5% of samples had a viral load greater than the corresponding bDNA result, most of these slightly higher viral loads (range 145 to 350 cp/mL) were seen in patients who had a historical viral load of 4.0 log or higher within 2 months of the sample tested.

Specificity: Although very rare false positives (all at low viral loads near or below the limit of detection) were reported during clinical trials by the manufacturer, the specificity of the TaqMan assay is nearly 100%.

Viral subtypes detected: The TaqMan assay quantifies all major subtypes of HIV-1 group M and HIV-1 group O, whereas the bDNA assay only quantifies HIV-1 Group M subtypes A-G.

Interpretation of changes: As with the bDNA assay, changes of less than 0.5 log (3-fold) may be within the analytical variability of the assay or the biological variation of the HIV viral load.

Turn-around-time (TAT): Assay will be performed twice weekly for a TAT of at most 5-7 days.

Sample type: No change; HIV viral load testing is performed on plasma from a lavender top (EDTA) tube.

Use as a diagnostic test: Although patients in the acute phase of HIV infection would be expected to have a high viral load, neither the old nor the new assay is FDA cleared for use as a diagnostic test to confirm the presence of HIV-1 infection. If diagnostic molecular HIV testing is needed a send-out test can be arranged. Please call the laboratory for more information.

If you have questions regarding this change in method please contact the Molecular Pathology laboratory weekdays during regular business hours at 215-662-6121.

TO: UPHS Physicians and Staff

FROM: Molecular Pathology Laboratory, 7 Maloney
Hospital of the University of Pennsylvania
Vivianna Van Deerlin, M.D., Ph.D., Director
Christopher Watt, M.D., Ph.D., Associate Director

DATE: July 27, 2011

SUBJECT: In-house availability of KRAS mutation analysis

Testing for the seven most common mutations in codons 12 and 13 of KRAS by multiplex PCR is now available in the Hospital of the University of Pennsylvania Molecular Pathology Laboratory.

CLINICAL SIGNIFICANCE:
KRAS mutations are seen in a wide variety of malignancies including colorectal cancer and non-small cell lung cancer. The presence of a KRAS mutation in tumor cells is associated with resistance to therapies targeting the EGFR pathway. In certain malignancies, such as non-small cell lung cancer, KRAS mutations have also been associated with a poor prognosis.

ASSAY LIMITATIONS:
The assay is designed to detect the seven most common KRAS mutations in codons 12 and 13. While this panel of seven mutations comprises the vast majority of the mutations seen in colorectal cancer and non-small cell lung cancer, other less common mutations have been described that are not detected by this assay. This assay can detect approximately 5% mutant cell DNA admixed with DNA lacking a KRAS mutation.

TESTING INFORMATION

Acceptable Specimen: Paraffin-embedded tumor tissue

Note: All requests will be reviewed by an anatomic pathologist to determine adequacy of available material for testing

Turnaround time: 10-15 business days

Ordering: If unfamiliar with the process for requesting testing on solid tumors, please contact the Molecular Pathology Laboratory weekdays during regular business hours (215-662-6121) for details on ordering.

To: Clinical Faculty
From: Malek Kamoun, MD, PhD
Director, Immunology Laboratory
Re: Anti-N-methyl-D-aspartate Receptor (NMDAR) Antibody Assay

Beginning 7/11/11, the anti-NMDAR antibody assay will be available for clinical use in the HUP Clinical Immunology Laboratory.
The test is an indirect immunofluorescence assay developed commercially in collaboration with Dr. Josep Dalmau, the leading expert in NMDAR antibody associated encephalitis.

The preferred specimen for testing is CSF but serum samples will also be accepted. Ideally, a serum specimen should accompany the CSF. The test codes for these assays are NMDAR C (CSF) and NMDAR S (serum).
An initial screening test will be performed on neat CSF (or a 1:40 dilution of serum if CSF has not been provided). The result will be reported positive, indeterminate or negative (<1:40).
If the CSF or serum screening test is positive for anti-NMDAR antibodies, a titration will be performed on the serum specimen. CSF titration cannot be reported at this time as the commercial kit in use is FDA approved only for serum titration. However, once sufficient data are collected for appropriate validation, CSF titration will also be offered.
Please refer questions regarding this testing to Anne Crivaro, PhD., Technical Manager of Immunology at (215)662-6023 or Dr. Malek Kamoun, MD, PhD., Director of Immunology at (215)614-1902.

To: UPHS Physicians and Staff
From: Vivianna Van Deerlin, M.D., Ph.D., Director and Christopher Watt, M.D., Ph.D.,
Associate Director, Molecular Pathology Laboratory
Date: April 18, 2011
Re: In house availability of quantitative BK virus testing

BK virus quantification by real-time PCR is now available in the HUP Molecular Pathology lab. The linear reportable range of the assay is between 325 -100 million copies/mL (2.5-8.0 log copies/mL). Reports will include a qualitative result assessment, a copy number/mL, and log copy number/mL. Each possible result is summarized in table in the following PDF file...
http://labweb.uphs.upenn.edu/web/clinical/Rolodex/BKNewMethodLetter41411.pdf

COMPARISON TO SEND OUT METHOD (ARUP laboratories)
The correlation between the HUP method (artus, Qiagen) and the previous send-out method at ARUP laboratories (Nanogen) is very good; however there is a bias of about 1 log copies/mL, with the ARUP results higher than the HUP method by 1 log. This bias arises from differences in the controls used to define the copy number of BK virus since there is as of yet no international standard available. For BK genotype IV, which is very rare, we have observed no significant bias between ARUP results and the HUP assay indicating that the ARUP method underquantifies the BK viral load for this genotype which has been reported in the literature (Hoffman, N.G. et al, J Clin Microbiol 46(8): 2671-2680). Re-baselining can be performed, but only upon request and only for patients in which BK virus was detected and quantifiable in the most recent sample tested at ARUP.
Approx conversion for majority of patients: 10 ARUP BK copies/mL = 1 HUP BK copies/mL

CLINICAL SIGNIFICANCE AND RECOMMENDATIONS
Because of the known variability between different quantitative BK assays, we recommend that patients be monitored over time in the same laboratory. This is most important when BK virus is present and quantified. Additionally, because of the variability of BK viral loads between methods/laboratories a specific copy number cut-off for making the diagnosis of BK virus nephropathy (BKVN) from the literature is difficult to apply. However, based on a review of renal biopsy results at HUP and corresponding BK viral load results (taking into account the anticipated bias) a viral load with the in-house assay greater than 10,000 copies/mL does appear to correlate with biopsy-proven BKVN. In order to continue to refine these correlations, it is very important to obtain a BK viral load assessment in conjunction with all renal biopsies.

CROSS-REACTIVITY INFORMATION
There is no cross-reactivity with the JC virus at viral loads <7.5 log (copies/mL). However, extremely high JC viral loads may falsely appear to have a copy number of BK below the limit of quantification. Therefore, JC virus infection should be considered if the BK viral load is very low and this does not fit with the clinical impression.

TESTING AND ORDERING INFORMATION
The sample for BK viral load testing is plasma from a lavender top (EDTA) tube. BK virus testing will be performed approximately twice per week and the turn-around-time will be ~4 business days. The new test name in Epic and Sunrise is: BK virus - Quantitation PCR. For more information please contact the Molecular Pathology lab weekdays during regular business hours (215-662-6121).

New vitamin D test procedure effective March 9, 2011

The Toxicology Laboratory has implemented a new sensitive and specific liquid chromatography-tandem mass spectrometry (LC-MS/MS) procedure for measurement of 25-hydroxy vitamin D. This new test method, replaces the ARUP reference laboratory Vitamin D 25-OH immunoassay procedure which measures the sum of 25-hydroxy vitamin D3 and 25-hydroxy vitamin D2.
The new LC-MS/MS Vitamin D25-0H method specifically measures 25-hydroxy vitamin D3 and 25-hydroxy vitamin D2 reliably to a sensitivity of 5 ng/mL. The total Vitamin D 25-OH which is the sum of 25-OH vitamin D3 and 25-OH vitamin D2 will also be reported. As part of the validation of this new method we have done comparison studies with two other laboratories using the mass spectrometry method with excellent correlation results and sensitivity limits. The accuracy of our procedure is based on the NIST standard reference preparations of the 25-hydroxy metabolites of vitamin D2 and D3. Please note that when a 25-OH vitamin D2 or D3 concentration is below our analytical sensitivity limit of 5 ng/mL the reporting system reports this result as a value of 0 ng/mL, however the actual concentration may range anywhere from 0 to the cutoff

value of 5 ng/mL.
Vitamin D25-OH is the recommended test procedure for diagnosing Vitamin D deficiency. The generally accepted threshold serum total Vitamin D 25-OH for the diagnosis of deficiency is less than 20 ng/mL. The new LC-MS/MS procedure permits not only diagnosis of Vitamin D deficiency but assessment of vitamin D supplementation.
In relatively rare circumstances (e.g. in patients with renal failure) testing is warranted for 1,25-OH vitamin D, the active metabolite of Vitamin D 25-OH produced by the kidney. For the rare circumstances where further evaluation of Vitamin D status in a patient requires testing for 1,25 OH vitamin D, a separate sample should be collected and ordered only for 1,25 OH VitD. The request for this test will be sent to the ARUP reference laboratory for measurement by a radioimmunoassay procedure.
Please feel free to contact us with any questions regarding this new vitamin 0 test procedure.

Contact information:
Leslie M Shaw, PhD
Email: Les.Shaw@uphs.upenn.edu
Cell phone: 267-251-8901

Michael Milone, MD, PhD
Email: MichaeI.Milone@uphs.upenn.edu
Cell phone: 215-900-4954

Date: January 21, 2011
Subject: Pediatric Alkaline Phosphatase Reference Ranges
From: Michael Husson, MD, Medical Director of Core Laboratory, Hospital of the University of Pennsylvania
To: All outpatient physicians and practices

Effective Jan 18, 2011, pediatric reference ranges for alkaline phosphatase have been instituted, replacing the single range used for children and adults. Alkaline phosphatase is normally higher in children and adolescents as a marker of normal bone growth. Health care providers ordering and interpreting alkaline phosphatase results from patients 16 years and younger will now see results with appropriate age based reference range values.

Alkaline phosphatase, IU/L

age (yrs)	range
0-5	60-321
5-10	118-360
10-12	103-373
12-14	83-382
14-16	67-372
>16	38-126

To: UPHS Physicians and Staff
From: Paul H. Edelstein, MD, Director, Clinical Microbiology Laboratory

Date: 12/10/10
Subject: Change in Confirmatory Test for Clostridium difficile toxin and Elimination of C. difficile Toxin Duplicate Testing

Effective December 13th, 2010, the Clinical Microbiology Laboratory will change its approach to the detection of C. difficile in stool samples by using a molecular amplification confirmatory assay as well as no longer accepting repeat samples for testing if a single sample has a negative C. difficile screen result.
The current laboratory algorithm for C. difficile testing is to screen specimens with a sensitive (90- 100% in most studies), but non-specific (positive predictive value ~50%), test for C. difficile antigen ("GDH") in combination with specific but

insensitive (~80% negative predictive value) immunoassays for C. difficile toxins A and B. Samples that are antigen positive and toxin positive are reported as positive for C. difficile toxin. A small proportion of samples submitted to the laboratory (12%) give a positive antigen result, but test negative with the toxin immunoassay. Currently, we further test these samples with a cell culture cytotoxin neutralization assay, which takes several days to perform and is less sensitive than newer molecular based confirmatory assays (~70%).

A "LAMP" (loop mediated isothermal molecular amplification) assay for C. difficile toxin (both A and B) will replace the cell culture cytotoxin neutralization test. This test will be performed daily, with results available on the same day of the run. Clinical trials show that this assay is more sensitive than cell culture cytotoxin neutralization testing, and almost as sensitive (97%) as the C. difficile culture gold standard reference method. Thus we expect that this change in methodology will decrease the false-negative rate for C. difficile toxin testing, and also greatly speed results. The GDH antigen assay/toxin immunoassay will continue to be used to screen stool specimens. The change will be that the LAMP assay will be used to test GDH-positive, but immunoassay-negative specimens, instead of cell culture cytotoxin neutralization testing.

Concurrent with the change to a molecular assay, and partly because of it, the laboratory will no longer routinely accept 2nd specimens for testing within a three week period if the 1st specimen was GDH antigen negative. The current laboratory policy allows testing of two specimens before implementation of this limit on further testing. The change from testing one rather than two specimens per episode is based on an analysis of four months of data, which showed that of the 305 duplicate specimens tested within 48 hrs of an earlier negative specimen (GDH negative or GDH positive but cell culture cytotoxin neutralization-negative), only five (1.6%) were positive in a second test, three of which would be expected to be positive with the LAMP assay. Thus the incremental yield with repeat testing would be around 0.6% when the LAMP assay is in use, and so low as to not justify routine duplicate testing. In clinical situations where the pre-test probability of C. difficile disease is very high, or there is a new episode of diarrhea, and the first test is negative, then the laboratory will accept a second specimen for testing, after consultation with a pathology resident. In rare cases, even the most sensitive C. difficile assay may be negative repeatedly, mandating empiric therapy when the pre-test probability is very high.

Please direct any questions on this new policy to the laboratory supervisor, Jill Wadlin 662-6657.

To: UPHS Physicians and Staff
From: Paul H. Edelstein, MD, Director, Clinical Microbiology Laboratory
Date: 11/30/10

The following is a revised policy for adequate Cerebrospinal Fluid (CSF) volumes received for testing in the Microbiology Laboratory at the Hospital of the University of Pennsylvania, effective 11/30/2010. Optimal sensitivity for bacterial and fungal culture requires centrifugation of the sample, whereas molecular testing (polymerase chain reaction or PCR) requires an un-spun sample. Therefore adequate volume is required for multiple tests, especially since optimal test performance requires different laboratory manipulations and storage conditions. To avoid problems it is best to submit a large volume CSF (8-10 ml) specimen if you anticipate ordering multiple tests on the spinal fluid. Of note, about 2 ml is required for cell count, protein and glucose studies, so you need not submit more than 2 ml of CSF in the tubes destined for these studies.

Minimum sample volumes:
Bacterial and fungal culture: 2 mls CSF total required.

- Lower volumes will still be processed, but may have reduced sensitivity.
- For optimal fungal culture, additional volume (5-10 ml) is recommended. Please denote this ("large volume culture for fungi") on the request so that we know whether the excess CSF should be used for fungal culture or for saving for possible PCR testing.
- If a specimen of ? 2mls is negative for fungus, submitting a second specimen with larger volume specimen is recommended.

Mycobacterial culture: = 5mls CSF required.

- Only performed on AIDS patients or by special (phone) request
- Lower volumes will not be processed for either culture or AFB smear because of unacceptable yield.
- If mycobacterial culture is requested CSF is held at elevated temperatures while awaiting special phone request, or clarification that the patient has AIDS. While this storage method will enhance yield for mycobacteria, it invalidates the specimen for molecular studies. Since mycobacterial meningitis is very rare in our patient population (<1 positive per year), do not request this test routinely, as it will eliminate the possibility of using the CSF for an alternative test. If a large volume CSF is sent for mycobacterial culture please denote this on the request ("large volume culture for mycobacteria") so that we know whether the excess CSF should be used for mycobacterial culture or for saving for possible PCR testing.

Molecular testing: 1 ml CSF required; each additional test requires 0.7 ml.

- This is in addition to the volume required for culture. These specimens are stored frozen unspun and can not be used for culture tests. The molecular assays have been validated only with unspun CSF and the effect of testing centrifuged CSF is not known. Please note that add-on testing from specimens submitted for other studies (TB, bacteria, fungal, etc.) is not possible because these studies require handling and storage that could degrade nucleic acids.

Procedure for specimens with inadequate volume (=2 ml):

- Specimen will be centrifuged in its entirety for culture.
- Culture will take priority over molecular tests.
- The resulting acellular supernatant will be kept frozen and may be used for cryptococcal antigen testing, and CSF antibody tests, including for West Nile virus testing.

During the Molecular test request review process, the adequacy of the sample will be addressed by the Microbiology resident. If the test request is reasonable but the sample volume is inadequate, the clinician can request testing on the CSF supernatant, albeit at the possible risk of decreased, but unknown, test sensitivity, or arrange to submit an additional sample.

Examples of proper CSF volumes to ensure adequate test sensitivity

Tests requested	Submit
routine bacterial culture and HSV PCR	3 ml minimum
routine bacterial culture and HSV and VZV PCR	4 ml minimum
routine bacterial culture and four PCR tests	5 ml minimum
routine bacterial and fungal culture, TB, and two PCR tests	9 ml minimum
routine bacterial culture, with enhanced yield for fungal culture	7 ml minimum
routine bacterial culture	2 ml minimum

Examples of how the lab will handle CSF

Tests requested	Volume submitted#	Use of CSF	Residual volume available for :
routine bacterial culture and HSV PCR	5 ml	2 ml –bacterial culture 1 ml – HSV PCR* 2 ml stored frozen unspun for additional molecular tests for 2 weeks	less then or = 2 additional molec. tests
routine bacterial culture and HSV PCR	3.5 ml	2 ml –bacterial culture 1 ml – HSV PCR* 0.5 ml stored frozen unspun for additional molecular tests for 2 weeks	0 additional molec tests (no tests possible with this volume)
routine bacterial and fungal culture, TB, and two PCR tests	8.5 ml	2 ml – bacterial/fungal culture 5 ml – TB culture** 1 ml – One molec test only – which one will be clarified in a call*	0 additional molec tests (no tests possible with this volume)
routine bacterial and fungal culture, TB, and two PCR tests	10 ml	2 ml –bacterial/fungal culture 5 ml – TB culture 1.7 ml – 2 PCR tests* 1.3 ml stored frozen unspun for additional molecular tests for 2 weeks	1 additional molec test
routine bacterial and fungal culture, HSV PCR	1 ml	1 ml bacterial/fungal culture*** no molecular tests can be performed with this volume	0 additional tests

Unless specifically noted on the lab request, it will be assumed that any excess CSF will be frozen for possible future PCR

testing, and not for mycobacterial or fungal culture.
* Pending review with Microbiology resident
** Performed only with telephonic request
***Submitted volume may result in suboptimal test sensitivity

If you have questions about this new policy, please contact the microbiology laboratory supervisor, Jill Wadlin, at 662-3406 or Jill.Wadlin@uphs.upenn.edu

To: UPHS Physicians and Staff
From: Vivianna Van Deerlin, M.D., Ph.D. and Christopher Watt, M.D., Ph.D.
Director and Associate Director, Molecular Pathology Laboratory
Date: October 27, 2010
Re: Change in method and reporting for HBV viral load testing

As of November 3, 2010 the Molecular Pathology Lab will implement the COBAS Taqman HBV Test (Roche Diagnostics Systems, Inc.) for HBV viral load testing. This will replace the current Siemens Versant ® bDNA signal amplification assay. The new method uses real-time PCR with TaqMan reagents to quantify HBV DNA. The assay will be run as a modified in vitro diagnostic (modified FDA approved) assay. This new assay will improve the analytic sensitivity for detection of HBV DNA (i.e. a lower limit of detection), will extend the range over which HBV can be accurately quantified and will improve turn-around-time.

CHANGE IN REPORTING UNITS ß IMPORTANT PLEASE READ
Results will now be reported in international units per milliliter (IU/mL) rather than copies/mL. Results will also be reported as Log (IU/mL). The conversion factor between IU/mL and copies/mL is: 5.82 copies/mL = 1 IU/mL.

To convert an existing # copies/ml? to # copies IU/ml:

Divide the copies/mL value by 5.82 (e.g., 10,000 copies/mL ÷ 5.82 = ~1718 IU/mL)

To convert an existing ?log scale copies/mL? to ?log scale IU/mL?:

Subtract 0.8 from the log scale copies/ml result (e.g., 4 log (copies/mL) ? 0.8 = ~3.2 log (IU/mL))

REPORTABLE VALUES

- Between values of 29 IU/mL and 110,000,000 IU/mL the raw value and Log (IU/mL) are reported.
- Values below 29 IU/mL (i.e. low positive and unable to quantify) reported as <29 IU/mL.
- Values greater than 110,000,000 IU/mL (i.e. above the upper limit of quantification) reported as>110,000,000 IU/mL.
- Zero ?0? copies reported if HBV DNA is not detected.
- Inconclusive reported if internal control fails to amplify indicating possible inhibitor or poor sample quality.

COMPARISON BETWEEN OLD AND NEW METHODS

Direct parallel testing was performed; the results of the old and new assays are well correlated and the results are NOT statistically different between the two methods. No re-baselining is required. However, there are a few key differences: the reporting units are different (see above), the new method has a lower limit of detection (more sensitive) and an extended linear range (see table below for details). The limit of detection for the new method ranges between 4-10 IU/mL depending on HBV subtype. As noted below, samples above the limit of detection, but below the lower limit of quantification will be reported as <29 IU/mL.

	New Method COBAS TaqMan	Old Method BAYER bDNA	Old Method Converted to IU/mL
Lower limit of quantification	29 IU/mL	2000 copies/mL	~344 IU/mL

Linear Range	29–1.1 x 10^8 IU/mL	2000–1x10^8 copies/mL	344 – 1.7 x 10^7 IU/mL
Upper limit of quantification	1.1 x 10^8 IU/mL	1 x 10^8 copies/mL	1.7 x 10^7 IU/mL

CLINICAL SIGNIFICANCE: HBV DNA levels are used to guide therapy for chronic hepatitis B and cirrhosis. Guidelines for the interpretation of HBV DNA levels, updated in 2009, are available from the American Association for the Study of Liver Diseases (www.aasld.org <http://www.aasld.org>); practice guidelines are available at the following address: http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20Practice%20Guidelines/Chronic_Hep_B_Update_2009%208_24_2009.pdf <http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20Practice%20Guidelines/Chronic_Hep_B_Update_2009%208_24_2009.pdf>

TESTING INFORMATION
The preferred sample for HBV viral load testing is still plasma from a lavender top (EDTA) tube. Serum is also an acceptable sample. The turn-around-time for HBV viral load testing will be approximately 5-10 business days.
If you have question or concerns regarding the change in method for HBV viral load testing please contact the molecular pathology laboratory weekdays during regular business hours (215-662-6121).

To: UPHS Physicians and Staff
From: Vivianna Van Deerlin, M.D., Ph.D.
Director, Molecular Pathology Laboratory
Christopher Watt, M.D., Ph.D.
Associate Director, Molecular Pathology Laboratory
Date: September 28, 2010
Re: Cystic fibrosis carrier screening changes

Cystic fibrosis (CF) carrier screening is now being performed in the Molecular Pathology Laboratory using the FDA approved eSensor® CF Genotyping Test (GenMarkDx). The panel of cystic fibrosis transmembrane regulator (CFTR) gene mutations detected HAS NOT changed and includes the 23 CFTR mutations recommended for screening by the American College of OB/GYN (ACOG) and the American College of Medical Genetics (ACMG). Reflex testing for the poly T tract polymorphism (5T-7T-9T) is performed and reported automatically if the R117H mutation is detected.

CHANGES IN RISK ASSESSMENT:
The sensitivity of the CF screening test and the carrier risk vary among different ethnic groups. A negative CF carrier test lowers the risk that an individual is a carrier of a CFTR mutation, but does not completely eliminate the risk. The reduction in carrier risk is dependent on the carrier rate and the detection rate of the test in each ethnic group. The carrier risks and detection rates are determined by population data which are occasionally revised to reflect new information. The original recommendations for post-test risk assessment and ethnic categories which we have been using were revised in 2005 by ACOG and ACMG (see references). We will be adopting the revised recommendations as of October 1, 2010 for all new CF carrier test reports. The new risk assessment data table is shown below. Importantly, the risk assessments shown below are based on the assumption that there is no family history of CF.

		Estimated Carrier Risk	
	Detection Rate	Before Testing	With Negative Test
Ashkenazi Jewish	94%	1/24	~1 in 380
Non-Hispanic Caucasian	88%	1/25	~1 in 200
Hispanic Caucasian	72%	1/58	~1 in 200
African American	64%	1/61	~1 in 170
Asian American	49%	1/94	~1 in 180

If you have question or concerns regarding these changes, please contact either the Molecular Pathology Laboratory (215-662-6121) or the molecular pathology resident/fellow (215-980-9878) during normal working hours on weekdays.

REFERENCES

1) American College of Medical Genetics Technical Standards and Guidelines for CFTR Mutation Testing 2006 edition http://www.acmg.net/Pages/ACMG_Activities/stds-2002/cf.htm

2) Committee on Genetics, American College of Obstetricians and Gynecologists. ACOG Committee Opinion. Number 325, December 2005. Update on carrier screening for cystic fibrosis. Obstet Gynecol. 2005;106:1465-1468.

To: Clinical Staff of the Hospital of the University of Pennsylvania, CPUP and CCA
Subject: New coagulation instruments at HUP
From: Michael Husson, MD, Director of Automation Laboratory Medicine
Date: August 30, 2010

Effective August 31, 2010, new instruments are performing routine coagulation testing at HUP, using a different methodology. There will be minimal change in the reference ranges (see below), and no change in INR values. PTT results compared from patients on heparin showed a mean difference of about 3 seconds longer with the new instruments. Ongoing laboratory evaluation of heparin response curves will continue.

If any unusual concerns arise after the transition, please let me know.

Reference ranges follow:

PT
10.8 - 13.3 old instruments
10.3 - 13.1 new instruments

PTT
21.0 - 32.5 old instruments
20.8 - 34.4 new instruments

Best regards,
Michael

Michael Husson, MD
Department of Pathology & Laboratory Medicine
Director of Automation Laboratory Medicine
Hospital of the University of Pennsylvania
email: Michael.Husson@uphs.upenn.edu

DATE: July 23,2010
TO: Medical Staff: CPUP
Hospital of the University of Pennsylvania
Presbyterian Medical Center
Penn Medicine at Radnor
CCA Practices
FROM: Stephen R. Master, MD, PhD
Medical Director, Endocrinology Laboratory
SUBJECT: Change in Methodology for Insulin, C-Peptide, and Ca 19-9.

The Endocrinology Laboratory is pleased to announce that as of July 26, 2010 we will be changing methodologies for the 3 analytes listed above. For Insulin and C-peptide we are changing from the Siemens Immulite to Roche Elecsys instrumentation. We are bringing Ca 19-9 in-house on a Roche analyzer; however this is the same method which is used by

our reference laboratory.
The principal motivation for changing insulin and C-peptide is to improve the precision and low-end sensitivities of the assays. The method correlations for both assays are acceptable; however, the reference ranges for these analytes will change slightly. The new reference ranges are given at the end of this memo.
Since Ca 19-9 will be the same method used by our reference laboratory, the method correlation is excellent, and the reference range remains unchanged. Rebaselining will not be offered for this tumor marker, since a new result should be directly comparable to any previous result for patients who are being longitudinally monitored.
If you have any questions or concerns about any of these assays please call:
Marilyn Senior, Ph.D., Technical Manager Endocrinology Laboratory 215-349-5031 or Stephen R. Master, MD, PhD, Medical Director Endocrinology Laboratory at 215-620-7354.

The new reference ranges for these analytes are given below:

Analyte	Age Range	Male	Female
Insulin, fasting	Adult	2.6-25 mIU/L	2.6-25 mIU/L
C-Peptide, fasting	Adult	1.1-4.4 ng/mL	1.1-4.4 ng/mL
Ca 19-9	Adult	<35 IU/mL	<35 IU/mL

The correlations between our former assays (Siemens Immulite insulin and C-peptide, reference laboratory Ca 19-9) and the in-house Roche assays are as follows:

	n	Slope	Intercept	r	Lower Reporting Limit
Ca 19-9	30	1.095	19	0.9995	1 IU/mL
Insulin	88	1.478	-4.3	0.7799	1 mIU/L
C-peptide	75	0.962	0.472	0.9891	0.1 ng/mL

Of note, the most recent College of American Pathologist proficiency survey shows that ~20% of surveyed labs utilize the Roche Insulin assay.

DATE: June 14, 2010
TO: Medical Staff: CPUP
Hospital of the University of Pennsylvania
Presbyterian Medical Center
Penn Medicine at Radnor
CCA Practices
FROM: Stephen R. Master, MD, PhD
Medical Director, Endocrinology Laboratory
SUBJECT: Temporary Change in Methodology for Hepatitis B Surface Antibody

Due to a temporary interruption in the availability of functional reagents for Hepatitis B surface Antibody for the instrumentation at the Hospital of the University of Pennsylvania, we will be sending these specimens to Pennsylvania Hospital until further notice. The procedure for ordering and viewing results will remain unchanged; however, as the assay at PAH is qualitative, we will report only the qualitative interpretation for the duration of the problem. A quantitative result will be provided on special request by calling 215-349-5031. Quantitative results are not needed to ascertain immunity, but may be helpful in post-exposure assessments and to confirm the immune response to vaccination.
If you have any questions or concerns about any of these assays please call:
Marilyn Senior, Ph.D., Technical Manager Endocrinology Laboratory 215-349-5031 or Stephen R. Master, MD, PhD, Medical Director Endocrinology Laboratory at 215-620-7354.

Date: May 3, 2010
Dear Colleagues,

Beginning May 6, 2010, the Clinical Microbiology Laboratory will switch methods for MRSA screening. After careful analysis, the PCR method used for detecting MRSA in nasal swab specimens has not been cost effective and we will switch to an enhanced culture screening method. This new method uses a specific culture medium for detecting MRSA in nasal swabs and definitive results will be available within 24 hours after the sample is received in the laboratory. You may continue to use

the normal swabs for MRSA testing and ESwab system when it becomes available on your floor/clinic area.
Although there will be a slightly longer turn around time for obtaining results (same day vs next day), the MRSA culture results will be definitive and will not require any confirmatory tests as are currently performed in the laboratory. Should you have any questions about sample collection or testing questions, please feel free to speak to one of the laboratory directors or supervisors.

Thank you,

Irving Nachamkin, Dr.P.H., M.P.H.
Professor and Interim Vice-Chair
Division of Laboratory Medicine
Associate Director, Clinical Microbiology Laboratory
Department of Pathology and Laboratory Medicine

From: Doug Cines, MD, Director, Coagulation Laboratory
To: Attending Medical and House Staff, HUP, PPMC, CPUP, CCA Practices, Penn Medicine-Radnor
Date: Friday, April 16, 2010
Subject: von Willebrand factor results will no longer include ABO-specific reference ranges

The Hospital of the University of Pennsylvania will discontinue the use of ABO typing for the interpretation of the von Willebrand Panel effective April 19, 2010.
Guidelines published by the National Institutes of Health/NHLBI for the diagnosis of von Willebrand Disease (VWD) indicate that the ABO blood group should not be incorporated into the diagnostic criteria for VWD. Result interpretation provided by the Coagulation Laboratory at the Hospital of the University of Pennsylvania will be based on our laboratory-established reference ranges for VWF Ristocetin Cofactor Activity and VWF Antigen and no longer include the ABO-specific reference values.

New Reference Ranges:

VWF Ristocetin Cofactor Activity 50-160%

VWF Antigen 50-160%

Please call the Special Coagulation Laboratory at 662-3447 with any questions or concerns.

To: UPHS Physicians and Staff
From: Vivianna Van Deerlin, M.D., Ph.D.
Director, Molecular Pathology Laboratory
Date: January 25, 2010
Re: Change in method for HCV viral load testing

As of February 1, 2010 the Molecular Pathology Lab will implement the FDA-approved COBAS Ampliprep/COBAS Taqman HCV Test (Roche Diagnostics Systems, Inc.) for HCV viral load testing. The new assay, like the current one, uses real-time reverse transcription PCR with TaqMan reagents to quantify HCV RNA. This method change was mandated by Roche in response to FDA Approval of its COBAS Ampliprep assay for HCV which replaced its previous Analyte Specific Reagent (ASR) version of the assay.

What you should know about the new HCV method

- FDA-approved method [previous: ASR using same technology validated by lab]
- Direct parallel testing confirms that the results of the old and new assays are well correlated and the results are NOT statistically different between the two methods. No re-baselining will be necessary.
- The new assay is still highly sensitive and specific for HCV and as such can be used for diagnostic testing in addition to determining HCV viral loads.
- Linear range: 43 and 69,000,000 International Units/mL (IU/mL) [previous: 50-10,000,000 IU/mL]

- Analytic sensitivity: 18 IU/mL [previous: 25 IU/mL]
- Reportable values:
  - Between values of 43 IU/mL and 69,000,000 IU/mL the raw value and Log(IU/mL) will be reported.
  - Values below 43 IU/mL will be reported as <43 IU/mL.
  - Values greater than 69,000,000 IU/mL will be reported as >69,000,000 IU/mL.
  - Zero 0 copies will be reported if HCV RNA is not detected.
  - Inconclusive will be reported if the internal control fails to amplify indicating a possible inhibitor or poor sample quality.
  - Indeterminate results will NO LONGER be routinely reported for values below the level of analytic sensitivity of the assay except in rare circumstances if necessary.
  - HCV viral load testing will continue to be performed approximately 2 times per week and turn-around time will remain unchanged.

If you have question or concerns regarding the change in method for HCV viral load testing, please contact either the molecular pathology laboratory (215-662-6121) or the molecular pathology resident/fellow (215-980-9878) during normal working hours on weekdays.