RDL Reference Laboratory 10755 Venice Blvd., Los Angeles, CA 90034
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June 1, 2017

Client Letter Test Update—June 2017

Dear Colleague:

Beginning June 19th 2017, RDL will be expanding and upgrading our Lupus Anticoagulant (LAC) testing to a more accurate and comprehensive LAC panel.

In accordance with the most recent ISTH/SSC guidelines [(1)], RDL's LAC testing will now consist of 4 initial screens: Prothrombin Time (PT), Thrombin Time (TT), LAC-dRVVT and LAC-PTT-LA. Confirmatory testing is done for positive results. As per the guidelines, all results will include a physician interpretation. PT and TT testing is important for being able to identify patients on oral anticoagulants that would otherwise cause false positive LAC results.

Unfortunately, we all have experienced a high variability in the performance of LAC testing among clinical laboratories. The rates of false-positive and false-negative results remain unacceptably high[(1)]. In addition, the wide use of direct oral anticoagulant agents (DOACs) complicates the issue; both the direct thrombin inhibitors (Pradaxa®, Argatroban) and the direct Xa inhibitors (Xarelto®, Eliquis®) cause a false positive LAC result [(2)].

The LAC assay continues to be critical in diagnosing Antiphospholipid Antibody Syndrome (APS) and/or SLE; it is also extremely important in predicting clinical complications and outcomes. Among all the tests used to measure the presence of antiphospholipid (aPL) antibodies, the presence of LAC is the strongest risk factor for thromboembolic events [(3)]. This risk is increased when LAC is present along with anti-B2GPI [(4)]. The occurrence of a thrombotic event is associated with higher mortality in patients that are positive for LAC [(5)].

In aPL-associated pregnancies, LAC is the primary predictor of adverse outcomes after 12 weeks gestation [(6)].

To be able to offer our clients the highest quality and the most accurate up-to-date testing, RDL has changed platforms to the industry's premier coagulation instrument (Stago), as well as enlisted the expertise of consultants with over 30 years of coagulation experience.

Moreover, in order for us to provide the most accurate interpretation of the LAC result, an order-form requesting details of the patient's history and medications should be completed by the ordering physician.

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We are excited to offer the highest quality LAC testing to our clients, thus greatly reducing the frequency of false positive and false negative results.

We hope you find this update letter informative and helpful.

Please feel free to contact us with any questions or comments at 800-338-1918 or info@rdlinc.com.

Best Regards,

Dmitry Karayev, M.D., F.A.C.R.
Medical Director

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DISCONTINUED TESTS

The following PANELS will be DISCONTINUED and REPLACED by new panels effective June 19, 2017:

OLD Code	NEW Code	Panel Name
116	3002	Lupus Anticoagulant
1811	3003	Antiphospholipid Ab Panel I
1850	3004	Antiphospholipid Ab Panel II
1277	3005	Implant Failure Panel
1789	3006	Recurrent Pregnancy Loss Panel
Note: Any orders received after June 1st with the old code will automatically be changed to the NEW Code		

NEW TESTS

The following tests will now be available effective June 19, 2017

Order Code	Name	Type
3002	Lupus Anticoagulant (LAC)	Panel
3003	Antiphospholipid Ab Panel I	Panel
3004	Antiphospholipid Ab Panel II	Panel
3005	Implant Failure Panel	Panel
3006	Recurrent Pregnancy Loss Panel	Panel

[3002] Lupus Anticoagulant (LAC)

Clinical Utility	The LAC assay continues to be critical in diagnosing APS and/or SLE and is also extremely important in predicting clinical complications and patient outcomes. Among all of the tests used to measure the presence of antiphospholipid (aPL) antibodies, the presence of LAC is the strongest risk factor for thromboembolic events [(3)]. This risk is increased when LAC is present along with anti-B2GPI [(4)]. The occurrence of a thrombotic event is associated with higher mortality in patients that are positive for LAC [(5)]. In aPL-associated pregnancies, LAC is the primary predictor of adverse outcomes after 12 weeks gestation [(6)]. ***References available upon request.***
Specimen Req.	(2) 4.0 mL FROZEN Plasma Citrated
Special Collection Instructions:	Collect samples in 2 sodium citrated tubes (light blue) and ensure that tubes are filled appropriately to obtain proper blood to anticoagulant ratio. Mix samples immediately by gently inverting tubes at least 10 times or use by using a tube rocker. Check for fibrin clots using wooden applicator sticks (**CLOTTED** specimen is not acceptable). **Centrifugation:** Plasma should be as platelet-free as possible. Centrifuge samples within 20 minutes of collection for 15 minutes at 2000-2500 g. Pipette plasma from the light blue vial to a 2 plastic vials **(at least 1.0 ml of plasma each vial)** and repeat the centrifugation process. The platelet count after the second centrifugation should be less than 10,000 mcl. Affix or mark all vials with "citrated plasma" label. ***Freeze immediately and ship on dry ice.***

	Note: The specimen must arrive at the laboratory frozen, if shipping via third party courier ensure that there is sufficient dry ice and samples will not thaw prior to arriving at the laboratory. If samples are being picked up by the local courier, ensure that they are kept frozen by informing the courier that these are FROZEN samples.
Methodology	Clot Detection (CD)
Setup/TAT	Tues. & Thurs. / 3 – 5 days
CPT Code :	85613, 85610, 85730, 85670, 85597, 85598, 80500

Reference Range:

Test	Method	Reference Range
LAC - dRVVT Screen	CD	< 1.2 ratio
LAC - Prothrombin Time (PT)	CD	12.5 – 14.6 seconds
LAC - PTT LA	CD	33 - 44 seconds
LAC - Thrombin Time (TT)	CD	< 21 seconds
LAC - dRVVT Confirm	CD	< 1.2 ratio
LAC - Normalized Ratio	CD	< 1.2 ratio
LAC- Hexagonal Phase	CD	<10 seconds
Interpretation		

[3003] Antiphospholipid Ab Panel I

Clinical Utility	APA Panel I is designed to satisfy the 2006 APS revised classification criteria [13], as well as the APA portion of the 2012 SLICC classification criteria for SLE [14]. References available upon request.
Specimen Req.	3 mL Serum & (2) 4.0 mL FROZEN Plasma Citrated
Methodology	IFA, EIA, Turb, CD
Setup/TAT	3 – 5 days
CPT Code :	86146 X3, 86147 X3, 85613, 85610, 85730, 85670, 85597, 85598, 80500

Reference Range:

Test	Method	Reference Range
Anticardiolipin Ab, IgG (EIA)	EIA	< 15.0 GPL
Anticardiolipin Ab, IgA (EIA)	EIA	< 15.0 APL
Anticardiolipin Ab, IgM (EIA)	EIA	< 12.5 MPL
Anti-Beta-2 Glycoprotein Ab, IgG (EIA)	EIA	< 20 EU
Anti-Beta-2 Glycoprotein Ab, IgA (EIA)	EIA	< 20 EU
Anti-Beta-2 Glycoprotein Ab, IgM (EIA)	EIA	< 20 EU
LAC - dRVVT Screen	CD	< 1.2 ratio
LAC - Prothrombin Time (PT)	CD	12.5 – 14.6 seconds
LAC - PTT LA	CD	33 - 44 seconds
LAC - Thrombin Time (TT)	CD	< 21 seconds
LAC - dRVVT Confirm	CD	< 1.2 ratio
LAC - Normalized Ratio	CD	< 1.2 ratio
LAC- Hexagonal Phase	CD	<10 seconds
Interpretation		

[3004] Antiphospholipid Ab Panel II

Clinical Utility	APA Panel II combines panel I with “non-criteria” anti-phospholipid antibodies which have important clinical utility. References available upon request.
Specimen Req.	3 mL Serum & (2) 4.0 mL FROZEN Plasma Citrated
Methodology	IFA, EIA, FLOC, Turb, CLIA, CD
Setup/TAT	3 – 5 days

CPT Code :	86592, 86146 X3, 86147 X3, 86148 X3, 83520 X2, 85613, 85730, 85670, 85610, 85597, 85598
Reference Range:	

Test	Method	Reference Range
Anticardiolipin Ab, IgG (EIA)	EIA	< 15.0 GPL
Anticardiolipin Ab, IgA (EIA)	EIA	< 15.0 APL
Anticardiolipin Ab, IgM (EIA)	EIA	< 12.5 MPL
Anti-Beta-2 Glycoprotein Ab, IgG (EIA)	EIA	< 20 EU
Anti-Beta-2 Glycoprotein Ab, IgA (EIA)	EIA	< 20 EU
Anti-Beta-2 Glycoprotein Ab, IgM (EIA)	EIA	< 20 EU
Phosphatidylserine Ab, IgG (EIA)	EIA	< 11 GPS U/mL
Phosphatidylserine Ab, IgA (EIA)	EIA	< 20 APS U/mL
Phosphatidylserine Ab, IgM (EIA)	EIA	< 25 MPS U/mL
Anti-PS/PT Ab IgG	EIA	< 30.0 Units
Anti-PS/PT Ab IgM	EIA	< 30.0 Units
RPR	FLOC	Negative
LAC - dRVVT Screen	CD	< 1.2 ratio
LAC - Prothrombin Time (PT)	CD	12.5 – 14.6 seconds
LAC - PTT LA	CD	33 - 44 seconds
LAC - Thrombin Time (TT)	CD	< 21 seconds
LAC - dRVVT Confirm	CD	< 1.2 ratio
LAC - Normalized Ratio	CD	< 1.2 ratio
LAC- Hexagonal Phase	CD	<10 seconds
Interpretation		

[3005] Implant Failure Panel

Clinical Utility	Explores antibodies associated with implantation failure in patients undergoing in vitro fertilization. References available upon request.
Specimen Req.	3 mL Serum & (2) 4.0 mL FROZEN Plasma Citrated
Methodology	IFA, EIA, Turb, CLIA, CD
Setup/TAT	3 – 5 days
CPT Code :	86256, 86146 X3, 86039, 86431, 86038, 86147 X3, 86800, 86376, 86148 X3, 85613, 85730, 85670, 85610, 85597, 85598
Reference Range:	

Test	Method	Reference Range
Anticardiolipin Ab, IgG (EIA)	EIA	< 15.0 GPL
Anticardiolipin Ab, IgA (EIA)	EIA	< 15.0 APL
Anticardiolipin Ab, IgM (EIA)	EIA	< 12.5 MPL
Anti-Beta-2 Glycoprotein Ab, IgG (EIA)	EIA	< 20 EU
Anti-Beta-2 Glycoprotein Ab, IgA (EIA)	EIA	< 20 EU
Anti-Beta-2 Glycoprotein Ab, IgM (EIA)	EIA	< 20 EU
Phosphatidylserine Ab, IgG (EIA)	EIA	< 11 GPS U/mL
Phosphatidylserine Ab, IgA (EIA)	EIA	< 20 APS U/mL
Phosphatidylserine Ab, IgM (EIA)	EIA	< 25 MPS U/mL
Anti-Nuclear Ab (IFA)	IFA	Negative
ANA Titer	IFA	<1.40
ANA Pattern	IFA	No Pattern
Rheumatoid Factor (Turb)	Turb	< 15 IU/mL
Anti-Ovary Ab (IFA)	IFA	<1.4

	Anti-Thyroglobulin Ab	CLIA	< 4.1 IU/mL
	Anti-TPO Ab	CLIA	< 5.6 IU/mL
	LAC - dRVVT Screen	CD	< 1.2 ratio
	LAC - Prothrombin Time (PT)	CD	12.5 – 14.6 seconds
	LAC - PTT LA	CD	33 - 44 seconds
	LAC - Thrombin Time (TT)	CD	< 21 seconds
	LAC - dRVVT Confirm	CD	< 1.2 ratio
	LAC - Normalized Ratio	CD	< 1.2 ratio
	LAC- Hexagonal Phase	CD	<10 seconds
	Interpretation		

[3006] Recurrent Pregnancy Loss Panel

Clinical Utility	Explores antibodies associated with recurrent pregnancy loss. References available upon request.
Specimen Req.	3 mL Serum & (2) 4.0 mL FROZEN Plasma Citrated
Methodology	IFA, EIA, Turb, CLIA, CD
Setup/TAT	3 – 5 days
CPT Code :	86146 X3, 86039, 86431, 86038, 86147 X3, 86800, 86376, 86148 X3, 85613, 85730, 85670, 85610, 85597, 85598
Reference Range:	

Test	Method	Reference Range
Anticardiolipin Ab, IgG (EIA)	EIA	< 15.0 GPL
Anticardiolipin Ab, IgA (EIA)	EIA	< 15.0 APL
Anticardiolipin Ab, IgM (EIA)	EIA	< 12.5 MPL
Anti-Beta-2 Glycoprotein Ab, IgG (EIA)	EIA	< 20 EU
Anti-Beta-2 Glycoprotein Ab, IgA (EIA)	EIA	< 20 EU
Anti-Beta-2 Glycoprotein Ab, IgM (EIA)	EIA	< 20 EU
Phosphatidylserine Ab, IgG (EIA)	EIA	< 11 GPS U/mL
Phosphatidylserine Ab, IgA (EIA)	EIA	< 20 APS U/mL
Phosphatidylserine Ab, IgM (EIA)	EIA	< 25 MPS U/mL
Anti-Nuclear Ab (IFA)	IFA	Negative
ANA Titer	IFA	<1.40
ANA Pattern	IFA	No Pattern
Anti-Thyroglobulin Ab	CLIA	< 4.1 IU/mL
Anti-TPO Ab	CLIA	< 5.6 IU/mL
LAC - dRVVT Screen	CD	< 1.2 ratio
LAC - Prothrombin Time (PT)	CD	12.5 – 14.6 seconds
LAC - PTT LA	CD	33 - 44 seconds
LAC - Thrombin Time (TT)	CD	< 21 seconds
LAC - dRVVT Confirm	CD	< 1.2 ratio
LAC - Normalized Ratio	CD	< 1.2 ratio
LAC- Hexagonal Phase	CD	<10 seconds
Interpretation		

FEATURED TESTS OF THE MONTH

Addition of Anti-phosphatidylserine/prothrombin antibodies (aPS/PT) IgG & IgM to RDL's Antiphospholipid Antibody Panel (APA) II

RDL will be adding anti-phosphatidylserine/prothrombin antibodies (aPS/PT) IgG & IgM to our Antiphospholipid Panel II. RDL has been offering PS/PT IgG & IgM antibodies as a standalone assay since 2013. After four years of testing, we are confident that our assay data supports the following findings as published in the literature.

- ✓ aPS/PT antibodies have a stronger correlation with LAC activity than Anti-Cardiolipin and Anti-Beta-2-glycoprotein antibodies and can therefore serve as a confirmatory test for the presence of true LAC, even while on anticoagulation therapy.
- ✓ These antibodies function as independent risk factors for thromboses-both arterial and venous[7]-and obstetric complications [8].
- ✓ These antibodies can identify APS patients that are considered seronegative (Anti-Cardiolipin, Anti-Beta-2-glycoprotein and LAC negative) [9].
- ✓ The presence of either IgG aPS/PT or IgM aPS/PT has a sensitivity of 52% and specificity of 86% for APS [10] .

A look forward: Antibodies to B2-glycoprotein 1 - Domain 1

It is widely known that anti-B2GPI antibodies mediate both thrombotic and obstetric complications in APS, and are an important pathogenic subset among the antiphospholipid antibodies. Further research has revealed that several different epitopes of B2GPI are targeted by autoantibodies; the main target epitopes are Domain 1 (D1) and Domain 4 and 5. D1 has been found to be the main immunogenic epitope targeted by anti-B2GPI in APS, while D4 and D5 are targeted in non-APS patients [11]. There is a very significant association between IgG B2GP1 (D1) and thromboembolic and obstetric events [12], RDL is currently investigating the IgG B2GP1 (D1) antibody and its ability to identify APS patients that are at the highest risk for these complications. We anticipate that B2-glycoprotein 1 - Domain 1 will soon be clinically available.

DID YOU KNOW ? ? ?

In an effort to provide evidence-based recommendations on the management of family planning and women's health issues in SLE and/or APS, a multidisciplinary panel of experts published the "EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome." This publication is available to the public, free of charge (open access).

Andreoli, L., et al. "EULAR recommendations for women's health and the management of family planning, assisted reproduction, pregnancy and menopause in patients with systemic lupus erythematosus and/or antiphospholipid syndrome." Annals of the rheumatic diseases (2016): annrheumdis-2016.

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SAMPLE PHYSICIAN QUESTIONNAIRE FOR LAC TESTING

APA panels include a physician consultative statement. Please refer to the RDL website for a list of panel components. If you do not want a consultative statement, please indicate when submitting your request.	
Patient History (check all that apply):	**Meds (check all that apply):**
☐ APS	☐ Argatroban
☐ Pregnancy loss	☐ Dabigatran
☐ Prolonged aPTT	☐ Rivaroxaban
☐ Arterial Thrombosis	☐ Apixaban
☐ Venous Thrombosis	☐ Warfarin
☐ SLE	☐ _____

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