FDA PUBLIC WORKSHOP:
ANTIBODY MEDIATED REJECTION IN KIDNEY TRANSPLANTATION

April 12-13, 2017

Tommy Douglas Conference Center
10000 New Hampshire Ave, Silver Spring, MD 20903

	DAY 1: Wednesday, April 12, 2017
7:30-8:00 am	**REGISTRATION**
8:00-8:10 am	**Welcome, Topics and Goals** Speaker: *Renata Albrecht, MD (FDA)* Goals of the Workshop: 1) Examine and emphasize the importance of immunosuppressive medication nonadherence in the development of de novo donor specific antibodies (DSA) and subsequent antibody mediated rejection (AMR) 2) Discuss the new developments in transplantation and their impact on patient management such as pretransplant sensitization not manifested by DSA, donor/recipient HLA epitope matching, routine posttransplant DSA monitoring 3) Discuss the natural course of the acute-chronic AMR continuum and its temporal association with cellular rejection and changes in GFR 4) Discuss unmet medical needs and potential clinical trial design challenges for the prevention and treatment of AMR
	Session 1: Overview, New Developments, Patients' Perspective and Diagnostic Challenges in Antibody Mediated Rejection Moderators (Part I): *Robert S. Gaston, MD and Ergun Velidedeoglu, MD*
8:10-8:30 am	New Developments in Kidney Transplantation since the 2010 FDA AMR Workshop – Nonadherence, HLA Mismatch, Banff updates, Kidney Allocation Speaker: *Roslyn B. Mannon, MD (University of Alabama)*
8:30-8:45 am	A New Paradigm: HLA Epitope Based Donor/Recipient Mismatch Assessment Speaker: *Peter Nickerson, MD (University of Manitoba)*
8:45-9:05 am	The Voice of the Patient in Transplantation *Dawn Edwards, Michael Mittelman and Jack Lennon*
9:05-9:20 am	The Relationship Between Acute AMR and Chronic AMR? Do Acute and Chronic AMR Represent a Continuum? Speaker: *Robert B. Colvin, MD (Massachusetts General Hospital)*
9:20-9:40 am	Impact of Acute and Chronic AMR on Graft and Patient Survival Is Acute AMR and Chronic AMR Related to Memory vs. De Novo DSA the Same Process or Fundamentally Different? HLA vs non HLA Antibodies Causing AMR Speaker: *Peter Nickerson, MD (University of Manitoba)*

9:40-10:25 am	**PUBLIC COMMENT AND DISCUSSION Part I** 1. Are early acute AMR and late acute AMR the same regardless of whether they are related to preformed or de novo DSA? Do either or both represent a continuum to chronic AMR? Discuss how. 2. If acute AMR and chronic AMR is a continuum, then can we predict who will or will not progress to chronic AMR? Are acute AMR and acute mixed AMR distinct entities? What is the significance of the presence of cellular rejection component in a biopsy demonstrating AMR?
10:25-10:40 am	**BREAK**
	Moderators (Part II): *Mark Haas, MD, PhD and Ergun Velidedeoglu, MD*
10:40-10:55 am	The Utility of Protocol Biopsies in the Follow-up of Acute AMR and in the Detection of Chronic AMR Speaker: *Mark D. Stegall, MD (Mayo Clinic)*
10:55-11:10 am	Tailored Immunosuppression Based on Routine DSA Monitoring (both in sensitized and nonsensitized patients Speaker: *Mark D. Stegall, MD (Mayo Clinic)*
11:10-11:25 am	Scientific Aspects; a General Overview of the Currently Used Antibody Measurement Methods, Issues of Standardization, Validation Speaker: *Howard M. Gebel, PhD (Emory University)*
11:25-11:50 am	Consideration of Quantitative Use of HLA Antibody Assays and a Summary of the 2017 AST/ASHI Antibodies in Transplantation Consensus Conference Speaker: *Anat Roitberg-Tambur, DMD, PhD (Northwestern University)*
11:50-12:40 pm	**PUBLIC COMMENT AND DISCUSSION Part II** 1. Discuss the utility of surveillance biopsies and single antigen bead (SAB) measurements of DSA in the management of immunosuppression. 2. Is quantification of DSA possible by SAB assays? 3. Is it possible to standardize assays to quantify recipient DSA and achieve consistency between sites in a multicenter study? Can this be accomplished via a central laboratory?
12:40-1:30 pm	**LUNCH**
	Session 2: Factors Contributing to Antibodies in the Pretransplant Period and Treatment Options Moderators: *Milagros Samaniego-Picota, MD and Marc Cavaillé-Coll, MD, PhD*
1:30-1:45 pm	Highly Sensitized Transplant Candidate – An overview Speaker: *Arjang Djamali, MD (University of Wisconsin)*

1:45-2:05 pm	Recognized and Unrecognized Sensitization: Assessment of the Pretransplant Immunologic Memory and Its Importance (with reference to the 2017 AST/ASHI Antibodies in Transplantation Consensus Conference) Speaker: *Howard Gebel, PhD (Emory University)*
2:05-2:20 pm	Prevention of Sensitization: Blood Transfusions, Nonadherence during the Previous Transplant and the Management of the failed graft Speaker: *Robert Gaston, MD (University of Alabama)*
2:20-2:35 pm	New Developments in Desensitization Protocols. Is there a Standard of Care? Speaker: *Robert A. Montgomery, MD, DPhil (NYU Langone's Transplant Institute)*
2:35-3:35 pm	**PUBLIC COMMENT AND DISCUSSION** 1. How important is to identify transplant candidates who have donor HLA specific quiescent memory B cells but do not have DSA and should their induction/immunosuppression regimens be different? 2. New developments in desensitization treatments?
3:35-3:50 pm	**BREAK**
	Session 3: Factors Contributing to Antibodies in the Post-Transplant Period Moderators: *Anat Roitberg-Tambur, DMD, PhD , and Ozlem Belen MD, MPH*
3:50-4:05 pm	The Choice of Induction / Maintenance Immunosuppression and their Impact on Preexisting and De Novo Antibodies Speaker: *Milagros D. Samaniego-Picota, MD (University of Michigan)*
4:05-4:20 pm	Calcineurin Inhibitor (CNI) and Corticosteroid Minimization/Avoidance Protocols and HLA Antibodies Speaker*: Arthur Matas, MD (University of Minnesota)*
4:20-4:35 pm	Nonadherence – Definitions, Monitoring, Prevention/Management Speaker: *Rita Alloway, PharmD (University of Cincinnati)*
4:35-4:50 pm	The Role of Acute Cellular Rejection Episodes in the Development of HLA Antibodies Speaker: *Robert S. Gaston, MD (University of Alabama)*
4:50-5:50 pm	**PUBLIC COMMENT AND DISCUSSION** 1.From a post-transplant DSA development perspective: a.Should induction treatment strategies be based on immunologic risk? b.Should CNI minimization be applied to all or selectively or not at all? c.significance of corticosteroid avoidance 2.Is T-cell mediated rejection (TCMR) early a risk factor for *de novo* DSA formation?
5:50-6:00 pm	**WRAP UP – DAY 1**

	DAY 2: Thursday, April 13, 2017
	Session 4: Post Transplant Monitoring, Diagnosis and Treatment of AMR Moderators: *Peter Nickerson, MD and Renata Albrecht, MD*
8:30-8:45 am	The Utility of Routine DSA Monitoring and Other Harbingers of AMR: • Is AMR underdiagnosed (due to lack of DSA monitoring and if older Banff criteria utilized)? • Monitoring of kidney function and its temporal association with antibody mediated graft damage Speaker: *Chris Wiebe, MD (University of Manitoba)*
8:45-9:00 am	Best Way to Assess Renal Functional Status: The Importance of Renal Functional Reserve, Glomerular and Tubular Stress Tests and their Potential Utility in Kidney Transplant Recipients Speaker: *Lakhmir Chawla MD (La Jolla Pharmaceutical Company)*
9:00-9:15 am	Diagnosis of Acute and Chronic AMR: Banff Classification and Pathologic Correlates of Graft Survival Speaker: *Mark Haas, MD, PhD (Cedars-Sinai, Los Angeles)*
9:15-9:30 am	Diagnosis of Acute and Chronic AMR: Molecular diagnosis and Correlation with Histology and Banff Classification Speaker: *Mark Haas, MD, PhD (Cedars-Sinai, Los Angeles)*
9:30-9:40 am	Treatment of AMR, Updates since 2010, Standard of Care, emerging therapies? Speaker: *E. Steve Woodle, MD (University of Cincinnati)*
9:45-10:45 am	**PUBLIC COMMENT AND DISCUSSION** 1. Should post transplant DSA monitoring be for: a. all kidney transplant recipients or b. high immunologic risk kidney transplant recipients or c. not necessary or useful in any patient group? 2. Is AMR underdiagnosed? Why or why not? 3. Do kidney transplant recipients have renal functional reserve? 4. Based on the information on diagnosis, treatment, what do we know about ability to select control therapy?
10:45-11:00 am	**BREAK**
	Session 5. Clinical trial design challenges for developing new treatments and Animal Models of AMR Moderators: *Roslyn B. Mannon, MD and Shukal Bala, PhD*
11:00-11:30 am	Potential Primary Endpoints in Clinical Trials of Antibody-Mediated Rejection a. Desensitization b. Prevention of acute AMR c. Treatment of acute AMR d. Prevention of chronic AMR

	e. Treatment of chronic AMR Speaker: *Gregory Knoll, MD (University of Ottawa)*
11:30-11:50 am	How to Perform Clinical Studies in Low Incidence Disease/Condition - Collaborative Clinical Studies, Pros and Cons of Composite Endpoints Speaker: *William Irish PhD (CTI Clinical Trial & Consulting Services)*
11:50-12:05 pm	Animal Models in AMR, How Can They Inform Clinical Studies Speaker: *Anita S. Chong, PhD (University of Chicago)*
12:05-12:20 pm	Animal Models in AMR (Presensitized Recipient Models) Speaker: *Stuart J. Knechtle MD (Duke University)*
12:20-1:30 pm	**PUBLIC COMMENT AND DISCUSSION** 1. Based on the information on diagnosis, treatment, what do we know about ability to select primary endpoints/secondary endpoints, control therapy? 2. Pros and cons of composite endpoints? 3. What are the major limitations to the applicability of the animal models of AMR to clinical transplantation?
1:20-1:30 pm	**CLOSING REMARKS and ADJOURN**