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## AutoAbSC.Org — Autoantibody Standardization Committee in 2006

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### Abstract

The Autoantibody Standardization Committee was established in the early 1980s based on the recognized needs for reference human autoimmune sera that were critical for academic, clinical, and industrial laboratories. To date, 14 reference reagents are available without charge from the Biological Reference Reagents distribution center at the Centers for Disease Control and Prevention. A web site has been developed under “AutoAbSC.Org” to communicate to the wider stakeholder community and to facilitate ongoing activities in continuing the mission in autoantibody standardization.

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## 1. Introduction

The Autoantibody Standardization Committee (ASC) in Rheumatic and Related Disorders operates as a subcommittee of the Quality Assessment and Standardization Committee of the International Union of Immunological Societies (IUIS) and reports to parent organizations including the World Health Organization (WHO), the Arthritis Foundation (AF) and Centers for Disease Control and Prevention (CDC). The primary objectives of ASC are consistent with the strategic directions of the parent organizations, particularly the IUIS, AF, and CDC, and to uphold the highest standards of patient care by promoting accuracy in autoantibody testing.

## 2. History

In the 1960s and 1970s, many investigators worldwide were engaged in the study of autoantibodies in the systemic rheumatic diseases and it had been established that autoantibodies were very important in clinical medicine as immunodiagnostic markers for certain disease conditions. At about the same time, in the late 1970s, some commercial organizations in the U.S., Europe and Japan were developing immunodiagnostic kits for the detection of antinuclear and other antibodies. In this milieu, much confusion was created because of lack of standardized reference sera for these autoantibodies with the result that detection of the autoantibodies with the use of commercially-available immunodiagnostic kits, as well as in the laboratory of academic investigators, was often inaccurate.

In 1980, a meeting between Dr. Eng M. Tan (then at the University of Colorado School of Medicine), Dr. Frederic McDuffie (then Sr. Vice President and Director of Medical Affairs at National Arthritis Foundation) and Dr. J. Steven McDougal (Centers for Disease Control) was convened to address the need for establishing authenticated standardized reference sera for antinuclear antibodies in the rheumatic diseases. The AF provided funding for the inaugural meetings of a group of scientific investigators who formed a committee to carry out this work. The CDC provided the expertise and laboratory resources to coordinate the activities of the committee and to lyophilize and package highly

characterized and validated serum samples for distribution to laboratories around the world. Within 2 years of the formation of the AF/CDC Reference Lab, five standardized reference sera for a number of antinuclear antibodies had been established, including standards for different patterns of nuclear immunofluorescence and antibodies reacting with native DNA, and the Sm, U1-RNP and SS-B/La autoantigens.

In 1982, at the urging of Dr. Ephraim Engleman who was then President of the International League Against Rheumatism (ILAR), the AF/CDC ANA Standardization Committee was expanded to include international participation. The standardization committee was recognized by ILAR, the World Health Organization (WHO) and the International Union of Immunological Societies (IUIS) and received support from these organizations. At this time, the committee included members from the U.S., U.K., Germany, Austria, Denmark, Netherlands, Japan, Australia and Canada. The work of this committee progressed rapidly and more reference sera were added to the serum bank at CDC. These reference sera have been distributed without charge to research laboratories, diagnostic laboratories and commercial organizations developing autoantibody diagnostic kits [1]. A survey performed in 1997 showed that more than 28,000 vials of reference sera had been distributed by the CDC and this activity has been sustained at a rate of approximately 350 vials annually.

## 3. Roles and responsibilities

The ASC sets priorities consistent with the strategic directions of the parent organizations to uphold the highest standards of patient care by promoting standardization and accuracy in autoantibody testing. The ASC ensures communication of strategies and activities to the parent organizations and cooperates with key science, research and technology organizations to enhance the accuracy and cost-effectiveness of autoantibody testing.

The ASC seeks the support and cooperation of relevant lay groups, institutions and researchers as well as industry. It undertakes or promotes studies and research projects that enhance the quality of autoantibody testing. The ASC

Table 1  
Reference standards available from the Centers for Disease Control and Prevention (CDC)

	Catalog no.	Reactivity/Specificity
ANA #1	IS2072	FANA (homogeneous/rim pattern); anti-native DNA
ANA #2	IS2073	FANA (speckled pattern); anti-SS-B/La
ANA #3	IS2074	FANA (speckled)
ANA #4	IS2075	Anti-U1 RNP (nuclear RNP)
ANA #5	IS2076	Anti- Sm
ANA #6	IS2100	FANA (nucleolar pattern); anti-fibrillar (U3 RNP)
ANA #7	IS2105	Anti-SS-A/Ro
ANA #8	IS2134	FANA (centromere pattern)
ANA #9	IS2135	Anti- Scl-70 (DNA topoisomerase I)
ANA #10	IS2187	Anti-Jo1 (histidyl-tRNA synthetase)
ANA #11	IS2310	Anti-PM/Scl
ANA #12	IS2706	Anti-Ribosomal P
	IS2717	human IgG anti-cardiolipin monoclonal HCAL
	IS2718	human IgM anti-cardiolipin monoclonal EY2C9

Abbreviations: ANA, anti-nuclear antibody; FANA, fluorescent antinuclear antibody; PM, polymyositis, RNP, ribonucleoprotein; Scl, scleroderma; SS, Sjögren's syndrome.

publishes key findings and recommendations of the Committee and critically reviews the cost-effectiveness of autoantibody testing and new technology that impacts on the detection of autoantibodies in human serum and plasma samples.

Some of the activities of this committee have included collaboration with immunodiagnostic companies in the validation of commercially available immunodiagnostic kits. These studies have been published in peer-reviewed journals and have improved the accuracy of diagnostic kits used by diagnostic laboratories in clinical diagnosis [2–4].

The ASC and its members evaluate and undertake to provide index reference sera to appropriate individuals, industry, manufacturers, hospitals, and academic institutions. During 2004–2005, the ASC established reference specimens for anti-ribosomal P protein antibodies and anti-cardiolipin and anti- $\beta$ 2-glycoprotein I antibodies. The latter reference samples are two human monoclonal antibodies directed to  $\beta$ 2-glycoprotein I that have been used to help reduce the well-known variability of  $\beta$ 2-glycoprotein I-dependent anti-cardiolipin assays [5] and are now included in the recently published “international consensus statement” in the advice on the use of antiphospholipid ELISA [6].

Currently a total of 14 reference reagents (Table 1) are available by request to Biological Reference Reagents,

NCID/SRP/BRR, Mailstop C-21, Centers for Disease Control and Prevention (CDC), 1600 Clifton Rd. N.E., Atlanta, GA 30333, USA (Email: [ncidsrpbr@cdc.gov](mailto:ncidsrpbr@cdc.gov)).

#### 4. Committee composition

The ASC has just reviewed the composition of the Committee at the last meeting held in November, 2005, during the annual meeting of the American College of Rheumatology (ACR) in San Diego. The new elected members are Pier Luigi Meroni (Chair), Edward K.L. Chan (Vice-Chair), Angela Tincani (Secretary/Treasurer), Luis Andrade, Marvin J. Fritzler (Chair, 1999–2005), Ignacio Garcia de la Torre, Falk Hiepe, Arthur Kavanaugh, Takao Koike, James Koziol, Robert Lahita, J. Steven McDougal, Westley H. Reeves (Secretary/Treasurer, 1999–2005), Joanna Sheldon, Yehuda Shoenfeld, Günter Steiner, Yoshinari Takasaki, Allan Wiik (Vice-Chair, 1999–2005), and Merlin Wilson. New members are being recruited with an aim to maintain wide international representation.

#### 5. Current initiatives

##### 5.1. Cyclic citrullinated peptide (CCP) antibodies

Anti-CCP have been established as an important marker for rheumatoid arthritis [7,8]. More importantly anti-CCP may be a strong predictor of erosive disease in early rheumatoid arthritis [9–14]. The ASC is establishing a reference specimen of human polyclonal anti-CCP.

##### 5.2. Anti-RNA polymerase I/III

Anti-RNA polymerase I/III antibodies are clinically useful markers of scleroderma and are associated with diffuse skin disease with cardiac and kidney involvement [15,16]. Anti-RNA polymerase III usually coexists with anti-RNA RNA polymerase I [17,18]. The ASC is establishing a reference specimen for anti-RNA polymerase I/III antibodies.

##### 5.3. Clinical practice guidelines

The ASC and its members will develop and promote Clinical Practice Guidelines for Autoantibody Testing [19,20] through educational Study Groups at major Rheumatology Meetings at the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) and the new web-site AutoAbSC.org ([AutoAb.org](http://AutoAb.org)).

**Take-home messages**

- Standardization of autoantibody testing is of major importance to ensure optimal usage in immunodiagnos- tics and clinical immunology.
- The ASC serves as an education, advisory and advocacy body for physicians, patients and industry.
- A major function of the ASC is to evaluate and make available consensus autoantibody standards distributed by the Centers for Disease Control and Prevention (CDC).

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