American College of Endocrinology/American Association of Clinical Endocrinologists: Reaffirmation of the 2003 ACE Insulin Resistance Syndrome (IRS) Position Statement

This statement was developed by an ACE/AACE Rapid Response Ad Hoc Committee comprised of:

Jeffrey I. Mechanick, MD, FACP, FACE, FACN, Chair
Rhoda H. Cobin, MD, MACE
Daniel Einhorn, MD, FACP, FACE
Yehuda Handelsman, MD, FACP, FACE
Richard Hellman, MD, FACP, FACE
Paul S. Jellinger, MD, MACE

In the past few months, several medical organizations have published statements reflecting changes in their definitions and assessment of "Metabolic Syndrome" (MS).[1,2,3] Bill Law, Jr., MD, FACP, FACE, American Association of Clinical Endocrinologists (AACE) President, appointed an ad hoc committee to examine these statements, especially in light of press reports which may have created uncertainty and controversy among clinical endocrinologists. The following comments summarize the discussions of this Committee.

ACE and AACE are pleased that several points in the statements referenced above reflect thinking that was promoted in the ACE 2003 Position Statement on the Insulin Resistance Syndrome (IRS),[4] a terminology which ACE and AACE feel more clearly describes the Syndrome.[4] This landmark document focused specifically on insulin resistance, which is a well-studied pathophysiological perturbation that is clearly associated with an increase in the risk of a number of disease consequences. The concept of IRS is based on this pathophysiology and is designed to *predict* and *prevent* such consequences, based on ACE's and AACE's growing understanding that resistance to the metabolic actions of insulin is a major driver of atherosclerosis and diabetes, and may play roles in diseases as disparate as infertility, malignancy, and abnormalities of liver function. As noted in the position statement, "IRS is used to describe the cluster of abnormalities that are more likely to occur in insulin resistant/hyperinsulinemic individuals."[4]

ACE and AACE specifically distinguished IRS from type 2 diabetes and cardiovascular disease (CVD), since one of their most important clinical goals was to identify individuals at risk *before* such consequences occurred. ACE and AACE also stressed the importance of expanding the concept of insulin resistance beyond CVD and recognizing other associated disease consequences, such as polycystic ovary syndrome and non-alcoholic fatty liver disease. ACE and AACE are pleased that the recent statement of the American Heart Association/National Heart, Lung, and Blood Institute endorsed the utility of the post-challenge glucose for early recognition of individuals at risk, which was an important contribution of the original ACE position statement.

From a clinician's perspective, ACE and AACE believe that it has been very useful to recognize the clustering of factors that increases the risk of an individual being insulin resistant as a "*syndrome.*" There clearly appears to be a relationship among factors in the cluster, even if the underlying pathophysiology may not be completely understood. The term "syndrome" implies this uncertainty. The concept of IRS has led physicians to search for related risk factors and associated illnesses. It is also useful from a patient perspective, as it provides a simple construct and supports the importance of the clustering. ACE and AACE recognize that there is an academic difference in discussing the various clinical manifestations of insulin resistance and calling the cluster a syndrome, but for didactic and

practical purposes, the term syndrome (whether *metabolic* or *insulin resistant*) is conceptually attractive and clinically useful.

The Metabolic Syndrome concept focused primarily on the cardiovascular disease predictive value of the clustering of a more limited number of risk factors. ACE and AACE agree that the term Metabolic Syndrome should not be misused as a disease unto itself. Although it may or may not be a more important predictor of CVD than its individual components, there is a great deal of evidence that insulin resistance underlies many of these conditions and may therefore be considered to have a key explanatory role, as well as offering the promise of allowing development of new therapeutic approaches to complement accepted treatment strategies directed at obesity, blood pressure, diabetes, and dyslipidemia. Furthermore, the linked concepts of Metabolic Syndrome/Insulin Resistance Syndrome have served a highly useful purpose by providing a simple construct to characterize the type of patients that clinicians see daily.

ACE and AACE have had a long-standing commitment to education and the promotion of understanding insulin resistance. ACE and AACE are co-sponsors of the annual World Congress on the Insulin Resistance Syndrome, to be held this year in San Francisco, November 17-19, 2005. Although ACE and AACE agree that the current wording of the descriptor is confusing, ACE and AACE were instrumental in obtaining the ICD-9 Code 277.7 ("Dysmetabolic Syndrome X") for the purpose of allowing clinicians to justify to payors of health care the medical necessity of testing for related risk factors when patients presented with some aspects of IRS. ACE and AACE developed its original position statement based on published scientific literature, and support additional research into better understanding insulin resistance and its disease consequences. ACE and AACE especially encourage the development of a standardized, validated insulin assay, which would greatly advance this field.

This area of medical knowledge is rapidly evolving and ACE and AACE both anticipate and welcome further changes in their definitions and understanding as new evidence is presented. With regard to this evolution, ACE and AACE hope that healthy debate will not be misconstrued as fractious controversy. ACE and AACE continue to believe that the concept of insulin resistance as a syndrome has been very helpful to practicing clinicians and the patients whose medical needs endocrinologists serve.

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[1] **International Diabetes Federation.** International Diabetes Federation consensus worldwide definition of the metabolic syndrome. Available at http://www.idf.org/webdata/docs/IDF_Metasyndrome_definition.pdf. Accessed September 29, 2005.

[2] **Kahn R, Buse J, Ferrannini E, Stern M.** The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care.* 2005;28(9):2289-2304.

[3] **Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F.** Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institutes scientific statement. *Circulation.* 2005; October 18:1-18.

[4] **Einhorn D, Reaven GM, Cobin RH, Ford E, Ganda OP, Handelsman Y, Hellman R, Jellinger PS, Kendall D, Krauss RM, Neufeld ND, Petak SM, Rodbard HW, Seibel JA, Smith DA, Wilson PW.** ACE Position Statement on the Insulin Resistance Syndrome. *Endocr Pract.* 2003;9(3):240-252.