The Consensus Statement on the Standardization and Evaluation of Growth Hormone and Insulin-like Growth Factor Assays Lacks a Recommendation to Attempt Efficacious Harmonization

To the Editor:

Similar to the 2006 consensus statement on the standardization of growth hormone (GH) assays (1), the guidelines regarding improvement of assay comparability in a recent consensus statement in Clinical Chemistry (2) are limited to the recommendation of common use of the Second International Standard for Somatropin (IS 98/574), although it is recognized that discrepancies between different assays may remain. As a comment on this consensus statement, we pointed out that the recombinant IS 98/574 standard intrinsically lacks commutability, and therefore one can expect only a partial reduction in the variation between assay methods (3). The recent consensus report (2) states that a demonstration of commutability has not yet been published. The Endocrinology section of SKML (Dutch Foundation for Quality Assessment in Clinical Laboratories) performed such a study with the predecessor of IS 98/574 (numbered 88/624 and produced by an identical procedure) as part of a harmonization study that used a natural, commutable serum obtained from healthy individuals during exercise to stimulate GH secretion. In brief, the results (3) were as follows: the imprecision among the results of 6 different assay methods was reduced from 25% when all assays were performed with their own calibrators to 15% when IS 88/624 was used as a common standard. A further reduction to 6.7% was obtained by using the harmonization serum, to which was assigned a value equal to the mean of the results obtained by these 6 assay methods with IS 88/624 used as a standard. The harmonization procedure has since been adopted by the Dutch Growth Foundation as the best approach for using a common cutoff value for excluding GH deficiency after proper stimulation of GH secretion. Consequently, we assert that a harmonization procedure as implemented in the Netherlands may improve clinical decision making, especially with respect to the selection of patients who are eligible for treatment with GH. We wonder why this approach has not yet been adopted elsewhere.

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References


In Reply

We thank Ross and colleagues for their interest in the report of the consensus conference (1). The authors describe the improved harmonization of growth hormone results by use of calibrators made from sera obtained from healthy individuals during exercise (“harmonization serum”). They ask why such an approach was not recommended in the consensus document.

The consensus conference did not have agreement on the concept of using the “harmonization serum” as described in the 2008 Letter to the Editor of Ross et al. The related concept of using panels of sera to assess agreement among methods was discussed, however, and its importance was recognized. In fact, consensus was achieved on at least 3 related points: (a) The consensus group supported the statement, “Because no reference measurement procedure exists for GH (or IGF-1), the demonstration of equivalent results among a group of routine methods for a panel of patient samples will be necessary when method-specific calibrators are used.” (b) The consensus panel recommended “the establishment of a set of reference...