We thank Drs Stepman and Thienpont for their comment on our recent article in which we reported what we called "*a relatively high measurement uncertainty for the measurement of serum 25(OH)D levels*" (1). Indeed, we found that if one wants to be sure that the 25(OH)D serum concentration of a given patient is >80 nmol/L, a value >100 nmol/L should be targeted. Drs Stepman and Thienpont underlined that this translates into an analytical coefficient of variation (CV) of approximately 8% which compares well with the analytical CV of the measurement of most steroid compounds (2). Thus, what we called "*a relatively high measurement uncertainty*" is in fact very common when measuring steroid hormones. We agree that one must aim to achieve the best analytical performances for the measurement 25(OH)D serum levels (as well as for the measurement of any biological parameter). However, 25(OH)D measurement has become an increasing routine practice and, from a very pragmatic point of view, we must deal with the assays that are currently available on the market. This means that measurement uncertainty must be taken into account for an optimal interpretation of the measured values which, according to our data, means that the "true" concentration of a patient whose measured value is 100 nmol/L for example, could be (grossly) anywhere between 80 and 120 nmol/L. On the one hand it will be above the desired value of 80 nmol/L, but on the other hand it may be as high as approximately 120 nmol/L. This seems to alarm Drs Stepman and Thienpont. However, in our opinion, it cannot be considered as a potential "burden" for the patients, as 25(OH)D serum levels up to 250 nmol/L (and probably largely more) are safe (3). Moreover, many experts argue for increasing the minimum 25(OH)D levels that defines optimal vitamin D status to at least 100 nmol/L (4-6). We acknowledge that the 25(OH)D threshold level below which one can consider that the vitamin D status is insufficient is not consensual as some other experts consider a value of 50 nmol/L as sufficient (7). It must be underlined that measurement uncertainty must be applied with any cut-off and that, according to our experience (unpublished for this level of

concentration), if one wants to ensure that a measured 25(OH)D concentration is really >50 nmol/L, a value of 70-75 nmol/L at least should be targeted. We also agree with Drs Stepman and Thienpont that averaging 25(OH)D results from repeated sampling when monitoring vitamin D supplementation would significantly (but not completely) reduce measurement uncertainty of 25(OH)D results. However, this is impossible in routine practice. So, if a clinician wants to know if a patient's 25(OH)D serum level is above or below the cut-off that defines vitamin D insufficiency, he or she must consider the measurement uncertainty and target a measured value that is above the cut-off. Thus, from a very pragmatic point of view, we suggest to measure 25(OH)D once and consider quite a large measurement uncertainty (for example 100 nmol/L if the cut-off is 80 nmol/L as proposed by us but also by others (8)) instead of measuring 25(OH)D several times (how many times?) and target the mean concentration of the repeated measurement to a level that will be closer to the cut-off that in our proposal, but remains to be determined. For practical reasons (cost and simplicity), and because we are convinced of the safety of 25(OH)D serum levels in the 100-250 nmol/L range, we clearly prefer the first solution as this will be the case, we believe, for most physicians and patients.

Reference List


1. Cavalier E, Rozet E, Gadisseur R, Carlisi A, Monge M, Chapelle JP et al. Measurement uncertainty of 25-OH vitamin D determination with different commercially available kits: impact on the clinical cut offs. Osteoporos Int 2009.
2. Taieb J, Mathian B, Millot F, Patricot MC, Mathieu E, Queyrel N et al. Testosterone measured by 10 immunoassays and by isotope-dilution gas chromatography-mass spectrometry in sera from 116 men, women, and children. Clin Chem 2003;49:1381-95.
3. Hathcock JN, Shao A, Vieth R, Heaney R. Risk assessment for vitamin D. Am J Clin Nutr 2007;85:6-18.
4. Heaney RP. Vitamin D: criteria for safety and efficacy. Nutr Rev 2008;66:S178-S181.

5. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006;84:18-28.

6. McKenna MJ, Freaney R. Secondary hyperparathyroidism in the elderly: means to defining hypovitaminosis D. Osteoporos Int 1998;8 Suppl 2:S3-S6.

7. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev 2001;22:477-501.

8. Binkley N, Krueger D. Evaluation and correction of low vitamin D status. Curr Osteoporos Rep 2008;6:95-9.