

Does the LSC include or ignore changes due to a different type of test device (say blood spot), a different device or the same type, a different person running the tester, different reagent sets, etc

The **Least Significant Change (LSC)** is a statistical measure used to determine the smallest difference between consecutive measurements that can be considered a "real" biological change (with 95% confidence), rather than random measurement error. Its calculation and applicability depend critically on the **consistency of testing conditions**. Below is a breakdown of how LSC accounts for variations in testing parameters:

1. Device Type and Methodology

- LSC **does not** account for differences between fundamentally distinct testing methods (e.g., serum-based assays vs. blood spot tests).
 - Each methodology has unique precision errors, requiring separate LSC calculations^[1]^[2].
 - For example, the LSC derived for serum 25(OH)D measurements (as in the attached paper) **cannot** be applied to blood spot tests without independent precision validation^[1]^[3].

2. Same Device Type, Different Instruments

- LSC **ignores** differences between instruments, even if they are the same model or from the same manufacturer.
 - Precision errors vary between devices due to calibration, maintenance, and technical variability^[2]^[3].
 - If a patient is monitored across different instruments, a **generalized LSC (GLSC)** must be calculated, incorporating cross-calibration data and precision errors from both devices^[4].

3. Operator Variability

- LSC **explicitly includes** operator-dependent factors.
 - Precision assessments (used to derive LSC) require each technologist to conduct their own reproducibility study^[5]^[2]^[3].
 - If a different operator performs the test, a new LSC must be established for that operator^[5]^[3].

4. Reagent Kits or Assay Kits

- LSC **does not accommodate** changes in reagent sets.
 - Reagent variability directly impacts precision error. Switching reagents invalidates the original LSC, necessitating a new precision assessment^{[1] [3]}.

Key Considerations from Research

- **LSC is context-specific:** It is valid only under identical testing conditions (device, operator, reagents, protocol)^{[1] [2] [3]}.
- **Monitoring across systems is discouraged:** ISCD guidelines advise against using different instruments for serial measurements due to accuracy drift and calibration differences^{[4] [3]}.
- **Practical Implication:**
If any testing parameter changes (device, operator, or reagent), the original LSC becomes obsolete. A new precision study must be performed to establish a valid LSC for the updated conditions^{[1] [2] [4] [3]}.

Example from the Attached Paper

The LSC of 4.0 ng/mL for 25(OH)D was derived using:

- **Same device:** IDS-iSYS chemiluminescence analyzer.
- **Same operator protocol:** Triplicate measurements per sample.
- **Consistent reagents:** IDS 25 VitDs kit^[1].
This LSC would not apply if any of these factors were altered.

Summary

LSC **ignores** changes in test devices, operators, or reagents. Its validity is strictly tied to the exact conditions under which precision was assessed. Altering any parameter requires recalculation of LSC to maintain statistical reliability in detecting true biological change^{[1] [2] [4] [3]}.

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1. least-significant-change.pdf
2. <https://iscd.org/knowledge-base/precision-assessment-calculator-faqs/>
3. <https://iscd.org/wp-content/uploads/2012/10/RadiationSafetyWhitePaperrevisedWebPosting2005-06-1.pdf>
4. <https://pubmed.ncbi.nlm.nih.gov/17616413/>
5. <https://pmc.ncbi.nlm.nih.gov/articles/PMC6216730/>