Assessing limits of detection

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Concepts

- Critical value
  - instrument response used to trigger action
- Detection limit
  - amount of substance leading to action
- Quantitation limit
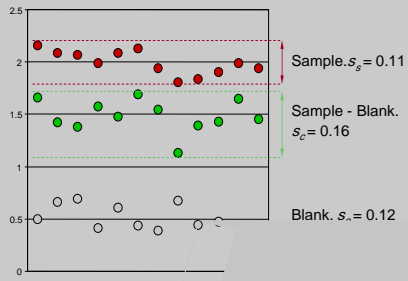 - lowest level at which uncertainty is acceptable

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- Standard deviation of blank response

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Sample. s_s = 0.11

Sample - Blank. s_c = 0.16

Blank. s_n = 0.12

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Quantitation limit (LoQ)

"Level at which the uncertainty becomes unacceptable"

- Common assumptions
  - acceptable uncertainty is 10%
    - leads to $10s_0$
- Other levels used:
    - $5s_0$, $6s_0$
- Recommendation
  - use $10s_0$ unless otherwise required

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Alternative procedures

- Instrument response

- ISO 11843-2
  - From calibration data

Usually based on repeatability

- SANCO
  - From multi-level, longer term precision data
  - Uses ISO 11843 procedure

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Setting limits from instrument response

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Current recommendations

- "Less than LOD" does NOT mean "invalid result"
  - Report the raw result and its uncertainty if you can

- Not all systems provide results below thresholds
  - A case for a different approach?
  - Maximum likelihood estimation...?

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Which standard deviation?

- Instrument noise?
  - If a signal is visible, there must be some analyte present!

- Repeatability?
  - Takes into account extraction/preparation

- In-house reproducibility?
  - Adds longer-term effects

- Suggestion: Smallest SD for critical value; largest for "LOD" addition.

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Conclusions

- Detection limits are based on statistical reasoning
- Detection limits determined during validation are indicative
  - for typical in-house validations, approximate values are usually adequate – e.g. $3s$ for "LOD"
  - decision limits on which action depends should be rigorously checked and monitored regularly
- Report raw values if you can
  - Investigate 'censored data' methods if you can't
- Some more work is needed on which standard deviation to use for critical decisions

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"A detection limit is something to stay well away from"

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