

Has CE marking led to changes in pre-analytical requirements for patient samples?

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Annex 1 of the directive requires a manufacturer to provide information on:

- “The storage conditions and shelf life following the first opening of the primary container, together with the storage conditions and stability of working reagents”
- “The type of specimen to be used, any special conditions of collection, pre-treatment and, if necessary, storage conditions and instructions for the preparation of the patient”

- “The specific analytical performance characteristics (e.g. sensitivity, specificity, accuracy, repeatability, reproducibility, limits of detection and measurement range, including information needed for the control of known relevant interferences), limitations of the method and information about the use of available reference measurement procedures and materials by the user”

Since kits became CE marked we have found new information has “appeared”.

More has changed.

No obvious notification of changes.

Only came to light as we were routinely revising SOPs – need to check CE marked as against non CE marked package inserts.

Albumin

- Package insert from CE marked product states:

Separate from cells immediately. Separated plasma and serum is stable at 2 - 8°C for 30 days and at 18 - 25°C for 7 days.

No change in stability claim

As in all assays new information on calibration, sensitivity, interfering substances, linearity and precision.

The reference given for comment on specimen is:

Young DS, ed. Effects of preanalytical variables on clinical laboratory tests, 2nd ed. Washington: AACCC press, 1997; 3-15 to 3-16

Creatinine

- Same method but change of supplier.
- Dynamic range changed from 17-2000 to 23-1590 $\mu\text{mol/l}$.
- On board stability reduced from 30 days to 15 days.
- Calibration frequency changed from weekly to every two days.
- “Samples should be separated within 2 hours and must be stored in the dark at 2-8°C, only in these conditions stability is maintained for 3 days.”

Total Protein

Limitations:

“Absorption of atmospheric CO₂ by the reagent on board the analyser can impair calibration stability. This effect will vary depending upon the rate of use. Consequently each laboratory should set a calibration frequency in the instrument parameters appropriate to their usage pattern.”

Recalibrate following a change in the reagent bottle.

Triglyceride

- Samples should be separated from cells within 2 hours.
- Limitations:

“Triglycerides GPO enzymatic methodologies are subject to strong negative interference from patient samples with extremely elevated triglyceride levels....results can be erroneously reported as being within the linear range of the assay.”

“Grossly lipaemic samples under rare circumstances may evade the data check parameters and should routinely be diluted 1 part sample to 4 parts saline prior to analysis and results multiplied by 5 before reporting.”

Creatine Kinase

- Non CE marked – Serum, heparinised plasma or EDTA plasma. Loss of activity in serum after 7 days at 4°C = 2% and after 24 hours at 25°C = 2%
- CE marked – Serum is the recommended specimen. Haemolysed samples should be avoided. Allow specimen to clot and remove serum from cells promptly to minimise haemolysis and contamination by adenylate kinase from the red cells. Stable in serum, protected from light, for 8-12 hours when stored at 2-8°C and 4 hours at 18-25°C.
Heparinised plasma free from haemolysis can also be used. Plasma samples may occasionally produce unpredictable rate reactions resulting in false low results. Plasma with EDTA, oxalate or citrate is not recommended.

Iron

- Lipaemic samples should be avoided.
- Haemolysed samples may react with the reagent to produce spuriously low results and such specimens should not be used.
- In rare instances extremely high concentrations of monoclonal immunoglobulins, due to monoclonal gammopathies, may cause turbidity in the reaction cuvette and elevate direct colorimetric iron assays.

Amylase

- Discard reagents if any discolouration is observed.
- Haemolysed and strongly icteric samples should be avoided, separate from blood cells as soon as possible.
- Stable in serum and plasma for 7 days when stored at 2-25°C (was no activity lost after 5 days).
- Stable in urine for 10 days when stored at 2-8°C and 2 days when stored at 15-25°C (formerly no time given).

Other general issues

- Quoted calibration frequency has changed for a number of assays. A number now state that calibration should take place when a new bottle (as opposed to lot number) is placed on the instrument.
- Many assays recommend calibration after a major preventative maintenance visit or if “a critical part” of the analyser has been replaced.

- Do these changes matter?
- What are implications of deviating from the manufacturers instructions?
- What to do?

- We have ordered the following:

Samples:From the Patient to the Laboratory: The impact of preanalytical variables on the quality of laboratory results, 3rd Revised Edition 2003

Walter G. Guder, Sheshadri Narayanan, Hermann Wisser, Bernd Zawta
ISBN: 3-527-30981-0, Wiley, Weinheim
October 2003

Currently out of stock!