**Record of Technical Anomaly**

**Technical Anomaly No: TA433**

**PART 1: Issue, impact assessment and signing open**

**Raised by: Hannah Ford** **Date: 21/02/22**

**OP / Method: OP224**

**Analytical sequence(s) affected** *(where appropriate)***: EC0791 rerun**

**Details** *(please tick relevant box(es) and provide supplementary information where required)***:**

□ QC point(s) above/below ±2SD □ Bracketing standard(s) outside limits

R QC point(s) above/below ±3SD □ QC Recovery outside limits

R QC point(s) outside expanded uncertainty □ Other *(add details below)*

5th of 5 QCA points > expanded uncertainty due to partially resolved interfering peak.

Chart, histogram

Description automatically generated

**Figure 1. Chromatography of QCA peak > EU.**

Unlike previous instances of this QCA issue (see TA421 most recently) interfering peak did not creep gradually closer to EC peak through run but instead a sudden onset of poor resolution that also coincided with an increase in peak tailing. The shape of the interfering peak is also clearly distinguishable beneath the target peak, although coeluting. This gives more hope that the root cause is injector contamination rather than column deterioration and thus, that a front end clean will solve the issue.

Note that although point is >EU, is still within 2SD – evidence has already been noted that expanded uncertainty for this method is actually wider than the values in the uncertainty document.

4th of 5 QCB (spiked) points had no recovery. This was due to a detector issue causing an unstable baseline:

A picture containing diagram

Description automatically generated

**Figure 2. Chromatography of QCB (spiked) peak with no recovery**

This peak was caused by a malfunction in the detector as opposed to an interfering component physically coeluting with EC, as is clear from the troughs dipping to exactly 0 signal, the vertical edges and jagged top of the peak, and the presence of the same peak at the exact same time for the 64 deuterated EC ion. By unfortunate coincidence this malfunction exactly coincided with the target peak meaning it could not be quantified.

The malfunction also occurred intermittently during other injections in the run, but for only one other sample did the malfunction coincide with the target peak (S21-2208). This result will not be reported and the analysis repeated. There is satisfactory evidence to show that all other results are not compromised by this issue. In addition the corresponding QCB unspiked was quantified close to usual values, and all other QCB spikes in the run passed very close to chart means, showing that aside from these intermittent malfunctions the instrument was performing to specification. On this basis all results except S21-2208 can be accepted.

□ No apparent reason for this anomaly

**Recommended Action:**

□ No action required out with the usual close monitoring of the Quality Control data in subsequent runs.

QCA resolution issue: a front end clean will be performed before next run.

QCB malfunctioning detector issue will be investigated. Source will be cleaned and filament inspected.

**Explanation why the issue does not impact data quality & why it isn’t a departure:**

All QCA results are within 2SD. All QCB results except the one detailed above are also well within acceptable limits, and samples affected by the detector issue are clearly distinguishable and not reported.

**Management Review:**

***I agree to open this Technical Anomaly and confirm that this would not prevent results from being reported.***

**Authorised by:**

**(Technical/Services/Quality Manager)**

**Date:**

**PART 2: Follow-up actions and close-out**

**Follow-up actions conducted:**

□ No follow up required

**Signed off & closed by Quality Manager:**

**Date: \_\_\_\_\_\_\_\_\_\_\_\_**

