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Determination of Chloramphenicol Residues in Crustaceans: Preparation and Evaluation of a Proficiency Test in Germany

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11 **Determination of Chloramphenicol Residues in Crustaceans:**
12 **Preparation and Evaluation of a Proficiency Test in Germany**
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Abstract

Chloramphenicol (CAP) is banned for use in food producing animals and is thus controlled on the basis of the National Residue Control Plans in the European Union. Due to the current problems with residues of CAP in shrimps, crayfish and prawns, a sensitive GC/NCI/MS method was optimised and in-house validated. The validation study resulted in a decision limit (CC_{α}) of 0.07 $\mu\text{g}/\text{kg}$, a recovery of 95 % and a within-laboratory reproducibility of 9 %. The method was used for preparing a proficiency test in order to assess the quality of residue control in Germany. The proficiency test involved analysis of five samples and the results were very satisfactory. The reproducibility standard deviation for five samples ranged from 17 to 24 %, and the median concentrations lay between 0.43 and 0.51 $\mu\text{g}/\text{kg}$ CAP. These values are clearly below the corresponding Horwitz standard deviation of about 50%. From the study it can be concluded that there are – irrespective of the method applied - well established and properly working analytical procedures for the control of CAP around the MRPL of 0.3 $\mu\text{g}/\text{kg}$.

Keywords: Chloramphenicol, proficiency testing, shrimps, validation, GC-NCI-MS, MRPL, residue control

Introduction:

Chloramphenicol (CAP) is banned for use in food producing animals in the European Union (Annex IV of Council Regulation 2377/90/EC) and is thus to be controlled on the basis of the National Residue Control Plans (Council Directive 96/23/EC). Even though it is an effective broad-spectrum antibiotic, its use was forbidden in the European Union in 1994 due to severe side effects, as e.g. aplastic anemia. Since these toxic effects are not dose dependent, a no effect level could not be established and consequently a zero tolerance level was set for CAP in food.

In 2003, with Commission Decision 2003/181/EC, a minimum required performance limit (MRPL) of 0.3 µg/kg for residues of CAP in different matrices, as e.g. muscle and aquacultures, was fixed. The MRPL was introduced with Commission Decision 2002/657 EC and was meant as the “minimum content of an analyte in the sample, which at least has to be detected and confirmed”. The aim of the MRPL was a harmonisation of the control of substances for which no MRL could be established. Since the level of the MRPL is not based on a risk assessment but on an assessment of a residue level which could be controlled by a majority of laboratories in residue control, it is clear that lower control limits are possible and welcome in order to meet scientific progress (as far as the method is validated according to the requirements of Commission Decision 2002/657 EC). This paper describes a sensitive GC/NCI/MS method, which is able to achieve decision limits for CAP below 0.1 µg/kg and which is validated according to this decision using the in-house validation approach (Jülicher et al. 1998) by applying a statistical software (“InterVal™”, quo data Ltd., Dresden, Germany).

1
2 This method was developed because of recent problems with residues of CAP in
3
4 import samples of shrimps and crayfish. According to these recent findings, also the
5
6 number of publications dealing with the analysis of CAP has increased significantly
7
8 since 2003. Meanwhile a number of different methods is available, which allows the
9
10 control of the actual MRPL (e.g. Rupp et al. 2005, Peng et al. 2005, Penney et al.
11
12 2005, Santos et al. 2005, Hammack et al. 2003, Ramos et al. 2003, Mottier et al.
13
14 2003).

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20
21 One of the tasks a National Reference Laboratory should fulfil according to Council
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23 Regulation 882/2004/EC and Commission Decision 96/23/EC is to organise
24
25 comparative tests between official national laboratories. In order to meet these
26
27 requirements, proficiency test material was prepared and tested for homogeneity and
28
29 stability by applying the above mentioned method. Using this material (five different
30
31 test samples from four different laboratory samples), a proficiency test according to
32
33 the International Harmonised Protocol for the Proficiency Testing of (Chemical)
34
35 Analytical Laboratories (Thompson and Wood 1993, IHPPT) was organised and the
36
37 official residue control laboratories in Germany were offered to participate. The NRL
38
39 took part in this study as one of the participants. The second part of the paper gives
40
41 the results of this proficiency test. Additionally the potential influence of parameters
42
43 on the analytical results is evaluated in detail. This is done on the basis of the
44
45 information about the various methods applied by the participating laboratories.
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50

51 52 53 **Materials and methods**

54
55 *GC-MS (negative chemical ionisation) method*

56
57
58 *Materials and instrumentation*
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Standards were obtained from Sigma Aldrich (CAP, >99 %) and from Euroisotope/Cambridge Isotope Laboratories (deuterated CAP, D5-CAP, >98 %). For the evaporation of solvents TurboVap LV™ and TurboVap II™ stations (Zymarck, United States) were used.

An Agilent 5973N mass spectrometer coupled with a GC (HP 6890 plus) and equipped with an automatic sampler (HP 7683) was used for the measurements. The mass spectrometer was operated in the negative ion chemical ionisation mode (NCI with methane) with the following ions for confirmatory purposes: m/z 466, 468, 470, 376 (CAP), 466, 468 (meta-CAP), 471 D5-CAP.

2 µl of the sample are injected splitless into the GC. The separation is performed on a 30 m * 0.25 mm id column, 0.25 µm ZB5 (Phenomenex) using a flow rate of 1 ml/min (Helium 5.0) and the following temperature programme: 85°C (0.1 min); 12°C/min to 240°C; 5°C/min to 260°C/min; 15°C/min to 290°C (5 min hold). The injection block is operated at 280 °C, the transfer line at 290 °C and the ion source at 160 °C.

Sample preparation

Freeze-dried laboratory sample (2 g) was reconstituted with water to the original fresh sample weight (10 g). The internal standard (CAP-D5) was added to the sample followed by 20 ml of an extraction mixture (acetonitrile / 4% NaCl in water solution 1+1 V+V). The mixture was homogenised in a stomacher (Seward, United Kingdom) and transferred into a centrifuge tube. The stomacher bag was rinsed twice with 4 ml of an extraction mixture, the solution was added to the centrifuge tube and centrifuged (4000 rpm for 15 min). The supernatant was separated and de-fatted twice with 10 ml of n-hexane. Water-saturated ethyl acetate (7 mL) was added to the remains, the mixture vortexed and the supernatant was transferred to a TurboVap

1
2 tube. This extraction procedure with ethyl acetate was repeated. The combined
3
4 supernatants were evaporated to dryness and re-dissolved in 3 ml of
5
6 water/acetonitrile (95+5 V+V). The re-dissolved sample was applied onto a C18
7
8 cartridge (500 mg, Separtis, Switzerland, preconditioned with 10 ml of methanol and
9
10 10 ml of water/acetonitrile (95+5 V+V). The sample was eluted with 3 ml of
11
12 water/acetonitrile (45+55 V+V). Water-saturated ethyl acetate (4 ml) was added to
13
14 the eluted sample, the mixture vortexed and the supernatant separated. This
15
16 extraction procedure was repeated. The combined extracts were evaporated to
17
18 dryness under a nitrogen stream. The dry residue was re-dissolved in 1 ml of
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20 acetone/toluene (20+80 V+V) and then applied onto a Silica cartridge (1 g, Separtis,
21
22 Switzerland, preconditioned with 6 ml of acetone/toluene (20+80 V+V).
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30 The cartridge was washed twice with 3 ml of acetone/toluene (20+80 V+V) and the
31
32 sample was eluted into a derivatisation tube with 6 ml of acetone/toluene (70+30
33
34 V+V). The extract was evaporated to dryness. 50 μ l of the derivatisation mixture N,O-
35
36 bis (trimethylsilyl)acetamide (BSA)/n-heptane (1+1 V+V) were added to the dry
37
38 extract. The derivatisation tubes were closed carefully and set aside to react for
39
40 approx. 45 min at 60°C. The amount of 2 μ l of the mixture was directly injected into
41
42 the GC-MS system.
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50 **Validation and validation data**

51 The validation of the method was carried out according to the alternative validation
52
53 model suggested in Commission Decision 2002/657 ("in-house validation approach").
54
55 This model is based on an experimental plan, which was created by means of the
56
57 validation software InterVal™. In the validation study, 16 different factor-level-
58
59 combinations (using 16 different matrices) were tested. The following factors were
60

1
2 varied during the validation on two levels each: species (as a leading factor),
3
4 operator, cartridge lots, storage times of the extracts, sample amount, extraction and
5
6 centrifugation conditions. The resulting experimental plan is given in table 1. In order
7
8 to get reliable validation data, it is required that firstly, for each of the runs a different
9
10 matrix is used, and secondly, the experiments are carried out at different times (not
11
12 more than one or two runs at a time). This study was carried out within 10 weeks.
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18 [Insert table 1 about here]
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23 For each of the 16 factor level combinations, five analysis were carried out (blank
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25 material was spiked at levels of 0.05, 0.08, 0.12 and 0.2 ng/g and a blank with only
26
27 internal standard); i.e. a total of 80 analyses was carried out. The resulting
28
29 concentrations were calculated by using a standard calibration curve. The results of
30
31 these analyses are shown in figure 1. The figure gives the 16 “calibration curves” for
32
33 the different factor level combinations as well as the prediction interval.
34
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39 [Insert figure 1 about here]
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44 From these data, the method validation characteristics are calculated. The data are
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46 summarised in table 2.
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51 [Insert table 2 about here]
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56 Furthermore, it is possible to estimate the contributions of the selected factors and
57
58 the uncertainty due to the matrix/run deviations to the total uncertainty of the result.
59
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Details can be found e.g. described by Uhlig et al. (2003).

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4 [Insert figure 2a,b about here]
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10 11 **Incurred material**

12 **Production of proficiency test samples**

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16 Incurred material was provided by a German import control point. This material
17
18 consisted of non-compliant samples, remainders of import control tests. There were
19
20 three different types of material, two from shrimps and one from crayfish (see table
21
22 3). The samples were frozen and homogenised when they arrived in the laboratory.
23
24
25 The samples were pre-tested for their CAP content, subsequently freeze-dried and
26
27 the water content was calculated. The lyophilised material was homogenised in a
28
29 Grindomix mixer (Retsch, Germany) and in an overhead rotary tumbler for two days.
30
31 Two of the samples were used directly in this form. The third sample was diluted with
32
33 blank material (obtained from the grocery, tested for compliance prior to use) in order
34
35 to achieve more relevant residue levels. The preparation of the proficiency test
36
37 samples targeted at concentration levels close to the MRPL-level of 0.3 µg/kg.
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46 [Insert table 3 about here]
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50 The material was portioned and filled into dark glass vials, each with a quantity of
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52 approximately 4 g. Although the water content was different for the different materials
53
54 (60 to 88 %), a joint value of 80 % was given in order to avoid the possibility of
55
56 identifying the samples by their water content. So each portion of lyophilised material
57
58 referred to a theoretical amount of approximately 20 g of fresh sample. After having
59
60

1
2 packed the samples, the dark glass vials are labelled with randomised sample codes
3
4 (prepared by using the software "Prolab™").
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8
9 Approximately 100 aliquots of each of the samples were available. Five samples
10 each were combined in a set of samples. The sets contained, as shown in table 3,
11 one blank sample (CAP004) and four non-compliant samples (CAP001,-002,-003,-
12 005). One of the non-compliant samples was sent in duplicate, but without indicating
13 this fact to the participants, in order to be able to check the repeatability of the
14 measurements (CAP002/CAP005).
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25 **Homogeneity and stability**

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27 For testing homogeneity, 10 randomly selected aliquots of each sample (prior to
28 combining it in test sets) were analysed in duplicate using the method described
29 above. The results were evaluated by analysing variance and by comparing the
30 standard deviation occurring between different aliquots S_S with the Horwitz standard
31 deviation S_H . It turned out that all samples belonged to the same population and had
32 a ratio $S_S/S_H < 0.3$ as requested in the IHPPT, see table 4.
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44 [Insert table 4 about here]
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49 For stability testing, the samples were stored under different conditions (-80°C, -
50 30°C,+4°C, +20°C) and analysed after storage periods of one day to one year. The
51 storage of aliquots at +20°C was stopped after one month since this storage
52 condition was primarily chosen to prove the stability of the samples during shipping
53 and sample handling (and due to the limited number of available samples for stability
54 testing). For each of the storage time/storage condition combinations, two aliquots
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1
2 were randomly selected. Each aliquot was analysed in double. The use of an
3
4 isochronous approach as suggested by Linsinger et al. (2004) was not suitable for
5
6 this study, because in this connection, two significant disadvantages would come into
7
8 effect: great number of samples to be analysed at one time and the results not being
9
10 available until the very end of the stability study. Hence, as a compromise, the tests
11
12 were performed using a „semi-isochronous“ approach. Analysis was done after three
13
14 different periods of time (2 days, 1 month, 1 year), so that, on the one hand, an
15
16 acceptable number of samples has be analysed at a time and, on the other hand,
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18 stability data which were sufficient to start the proficiency test were already available
19
20 after one month. In the stability study, no degradation of the analyte could be
21
22 observed as can be seen in figure 3.
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30 [Insert figure 3 about here]
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35 **Proficiency test**

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37 The proficiency test started in November 2004 with the shipment of the samples. The
38
39 frozen samples (-20°C) were shipped without dry-ice because even at room
40
41 temperature the material proved to be stable for some weeks (see figure 3). Each
42
43 laboratory received a set of five samples. The samples should be analysed with the
44
45 method routinely applied (a confirmatory method according to Commission Decision
46
47 2002/657EC) and results submitted within six weeks.
48
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56 **Evaluation**

57
58 The proficiency test was organised and evaluated according to the prescriptions of
59
60 the IHPPT, ISO/IEC-Guide 43-1: 1977 and DIN 38402-45: 2003-09 using the

1
2 statistical software “Prolab™” (quo data Ltd. Dresden, Germany). The z-scores for
3
4 the laboratories’ quantitative results were calculated from the laboratory results x , the
5
6 target value X (here: consensus value of all submitted results) and the target value of
7
8 the standard deviation σ .
9

$$10 \quad z\text{-score} = \frac{x - X}{\sigma}$$

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18 x : laboratory result

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20 X : target value

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23 σ : target value of the standard deviation
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27 The laboratories were asked to analyse the samples in double each and to submit
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29 the recovery corrected results. The mean value of these determinations was used
30
31 and taken as the laboratory result (x) without any further correction.
32
33

34 The target value X was determined by calculating the median of the results of all
35
36 laboratories (consensus value). The National Reference Laboratory; Berlin, took part
37
38 in the study as one of the laboratories. As target value of the standard deviation, the
39
40 reproducibility standard deviation was calculated using the Q-method as described in
41
42 DIN 38402-45. The reproducibility standard deviation was taken instead of the
43
44 Horwitz standard deviation (Horwitz et al. 1980, Boyer et al. 1985) because at these
45
46 low concentrations, the latter would allow significantly higher standard deviations and
47
48 considerably limit the significance of the quantitative assessment of the proficiency
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50 test.
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55 In addition to the individual quantitative assessment of each sample, the NRL uses a
56
57 point system with the purpose of evaluating the overall proficiency of the laboratories.
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60 In order to take into account not only the quantitative but also the qualitative

1
2 evaluation (especially meaningful for banned substances as CAP), the following rules
3
4 within a point system were applied:
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9	z-scores:	z-score > 2: (qualitative detection is carried out,	+1.0 point
10		quantification outside tolerance limits)	
11			
12		z-score > 2: (qualitative detection is carried out,	+1.5 points
13		quantification within tolerance limits)	
14			
15		false positive results:	- 1 point
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17		false negative results:	0 points
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26 This system is applied per analyte and per sample, i.e. in this case, there are a
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28 maximum of six attainable points ($4 * 1.5$). The minimum score for passing this
29
30 proficiency test was set at 4.0 points (corresponding to 66.7 % of the maximum
31
32 score). The score for banned compounds is generally set in such a manner that it is
33
34 possible to be successful in the overall proficiency by simply identifying the banned
35
36 compound (which is, in principle, sufficient), if there are no false positive findings in
37
38 the blank samples.
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44

45 **Results and discussion**

46
47 A total of 20 participants submitted results. For each sample, the median was
48
49 calculated as a target value, including all results into the calculation (no outlier
50
51 elimination). No false negative results and only one false positive result were
52
53 reported for a total of 100 analyses. For the quantitative evaluation on the basis of z-
54
55 scores, the reproducibility standard deviation was used, the results and the used
56
57 techniques are summarised in figure 4. Four of the results (from three different labs,
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60

1
2 but from one matrix, namely CAP002/CAP005) lay outside the range of +/- 2,
3
4 nevertheless three of these four results were close to a z-score of 2.
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9 [Insert figure 4 about here]
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11
12
13 In contrast to the other samples, this matrix was a processed food sample. With the
14 method applied by the NRL, an unusual behaviour during the extraction process
15 (problems in phase separation) was observable. The difficulties with this sample are
16 also reflected in the results of the proficiency test (results out of the z-scores and
17 high reproducibility standard deviations for GC methods)).
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28 [Insert table 5 about here]
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33 The Horrat ratio (see table 5), which gives a certain indication of the overall
34 performance level of the laboratories, should be between 0.5 to 2 for acceptable
35 method performance as suggested by Pocklington 1990. The ratio here is even
36 below 0.5, indicating a very good performance of the laboratories.
37
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42 The evaluation of the overall proficiency based on the point system (see above)
43 added up to a mean of 5.85 points (out of six attainable points, referring to 97.5 %),
44 all laboratories have been successful.
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48

49 The participants were asked to provide details of their analytical method. The results
50 were also evaluated with respect to this additional information. The very different
51 sample clean-ups (extraction with different solvents; clean-up with solid phase
52 extraction, liquid-liquid extraction, silica clean-up, or a combination thereof) as well as
53 a hydrolysis step, which was included by some of the laboratories, did not have any
54 significant effect on the results. Most of the laboratories used deuterated CAP as the
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1
2 internal standard. Meta-CAP was used only in three laboratories as the internal
3
4 standard all of them applied GC-methods. The use of meta-CAP as an internal
5
6 standard showed a tendency towards a higher scatter of the results but this
7
8 conclusion is uncertain because of the very small number of measurements.
9

10
11 The only parameter which showed a bias was the comparison of GC/MS(MS) and
12
13 LC/MSMS results (see table 6). GC/MS results showed a tendency towards higher
14
15 concentration levels with a worse reproducibility compared to the LCMSMS results.
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21 [Insert table 6 about here]
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25
26 This effect would be similar, if the results of the two labs, which applied GC/MSMS,
27
28 would be treated separately. An explanation of this effect is difficult due to the
29
30 principle difference between the methods, e.g. the different ionisation mechanism,
31
32 the necessary derivatisation for GC analysis and the different selectivity of the
33
34 detection systems. Further studies using certified reference material would be
35
36 necessary in order to verify whether there is a bias between the two techniques or
37
38 whether it is just a matrix dependent effect.
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41
42 All in all, the results of the study were very positive. The median concentrations were
43
44 between 0.43 and 0.51 $\mu\text{g}/\text{kg}$ CAP, the reproducibility ranged from 17 to 24 %
45
46 (clearly below the Horwitz standard deviation of about 50%). None of the laboratories
47
48 found false negative samples.
49

50
51 A conclusion of the results of the study is that the analysis of CAP residues is well
52
53 established in many labs and the decision limits between 0.05 and 0.36 ng/g ,
54
55 indicated by the labs, were realistic because all labs were successful in confirming
56
57 the analytes in the non-compliant samples. Accordingly the methods tested in the
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1
2 study, including the one used by the NRL, proved to be suitable for the control of
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4 residue levels around the MRPL of 0.3 µg/kg.
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Table captions:

Table 1: Experimental plan for the in-house validation

Table 2: Method performance characteristics

Table 3: Matrix information of test kit submitted to the participants and sample codes

Table 4: Results of homogeneity tests

Table 5: Median, Horrat ratio, repeatability and Horwitz standard deviation (S_R and S_H of the individual samples

Table 6: Median and repeatability standard deviation (separate calculation for the different systems applied)

Tables:

Table 1: Experimental plan for the in-house validation

run	species	operator	cartridge lot	test sample	storage of extracts	centrifugation	extraction	elution
S_16	pig	B	Y	15 g	2-3 days	with 4000 rpm	with 2 * 8 ml	60/40 ACN/water
S_06	crustaceans	B	X	15 g	2-3 days	with 3000 rpm	with 2 * 10 ml	50/50 ACN/water
S_01	crustaceans	A	X	10 g	0-1 day	with 3000 rpm	with 2 * 8 ml	50/50 ACN/water
S_10	pig	A	X	15 g	2-3 days	with 3000 rpm	with 2 * 10 ml	60/40 ACN/water
S_12	pig	A	Y	15 g	0-1 day	with 3000 rpm	with 2 * 8 ml	50/50 ACN/water
S_09	pig	A	X	10 g	2-3 days	with 4000 rpm	with 2 * 8 ml	50/50 ACN/water
S_14	pig	B	X	15 g	0-1 day	with 4000 rpm	with 2 * 10 ml	50/50 ACN/water
S_15	pig	B	Y	10 g	2-3 days	with 3000 rpm	with 2 * 10 ml	50/50 ACN/water
S_04	crustaceans	A	Y	15 g	2-3 days	with 4000 rpm	with 2 * 8 ml	50/50 ACN/water
S_02	crustaceans	A	X	15 g	0-1 day	with 4000 rpm	with 2 * 10 ml	60/40 ACN/water
S_11	pig	A	Y	10 g	0-1 day	with 4000 rpm	with 2 * 10 ml	60/40 ACN/water
S_03	crustaceans	A	Y	10 g	2-3 days	with 3000 rpm	with 2 * 10 ml	60/40 ACN/water
S_08	crustaceans	B	Y	15 g	0-1 day	with 3000 rpm	with 2 * 8 ml	60/40 ACN/water
S_13	pig	B	X	10 g	0-1 day	with 3000 rpm	with 2 * 8 ml	60/40 ACN/water
S_05	crustaceans	B	X	10 g	2-3 days	with 4000 rpm	with 2 * 8 ml	60/40 ACN/water
S_07	crustaceans	B	Y	10 g	0-1 day	with 4000 rpm	with 2 * 10 ml	50/50 ACN/water

Table 2. Method performance characteristics

Decision limit CC_{α}	0.074 $\mu\text{g}/\text{kg}$
Detection capability CC_{β}	0.087 $\mu\text{g}/\text{kg}$
Recovery*	95%
Repeatability*:	8%
Within-laboratory reproducibility*:	9 %.

*) at the concentration of CC_{β}

Table 3: Matrix information of test kit submitted to the participants and sample codes

Sample code	Kind of sample
CAP 001	CraYfish; non-compliant import sample, Asia
CAP 002	Shrimps, salted, non-compliant import sample, Asia
CAP 003	Prawns, non-compliant import sample; diluted with blank material, Asia
CAP 004	Polar sea shrimps, blank
CAP 005	As CAP 002

Table 4: Results of homogeneity tests

Sample	Test statistic F	Critical F-value	Mean [$\mu\text{g}/\text{kg}$]	s_s	s_H	s_s / s_H
CAP 001	1.876	3.020	0.452	0.011	0.230	0.05
CAP 002/5	1.227	3.020	0.460	0.015	0.234	0.06
CAP 003	1.578	3.020	0.356	0.048	0.188	0.26

s_s : Standard deviation between different samples ($n = 10$)

s_H : Horwitz standard deviation at the respective concentration

Table 5: Median, Horrat ratio, repeatability and Horwitz standard deviation (S_R and S_H of the individual samples

Sample	Median [$\mu\text{g}/\text{kg}$]	Horrat ratio		S_R		S_H	
		S_R / S_H	abs.	%	abs.	%	
CAP 001	0.512	0.49	0.124	24.3	0.256	50.0	
CAP 002	0.500	0.37	0.093	18.6	0.251	50.2	
CAP 003	0.427	0.34	0.073	17.0	0.219	51.4	
CAP 005	0.491	0.43	0.107	21.7	0.247	50.4	

Table 6: Median and repeatability standard deviation (separate calculation for the different systems applied)

Sample	GC-MS (including GC-MS/MS) n=10 (n=2)		LC-MS/MS n=10	
	Median [$\mu\text{g}/\text{kg}$]	S_R	Median [$\mu\text{g}/\text{kg}$]	S_R
CAP001	0.619	0.133 = 21.5 %	0.477	0.101 = 21.2 %
CAP002	0.525	0.128 = 24.4 %	0.469	0.075 = 16.9 %
CAP003	0.425	0.090 = 21.2 %	0.427	0.067 = 15.7 %
CAP005	0.503	0.155 = 30.8 %	0.486	0.067 = 13.8 %

Figure captions:

Figure 1: Confidence interval of the 16 calibration curves calculated from the 16 different runs (factor-level-combinations) according to table 1.

Figure 2a and 2b : Matrix blank (2a) and spiked matrix blank (2b) in crustaceans, spike level at 0.08 ng/g (m/z 471 referring to the internal standard, the other ion traces to CAP)

Figure 3: Results of the degradation study (CAP_002), concentration in ng/g

Figure 4: Summary of the z-scores of the participating laboratories (dark triangles indicating results out of the accepted tolerance of +/- 2)

Figures:

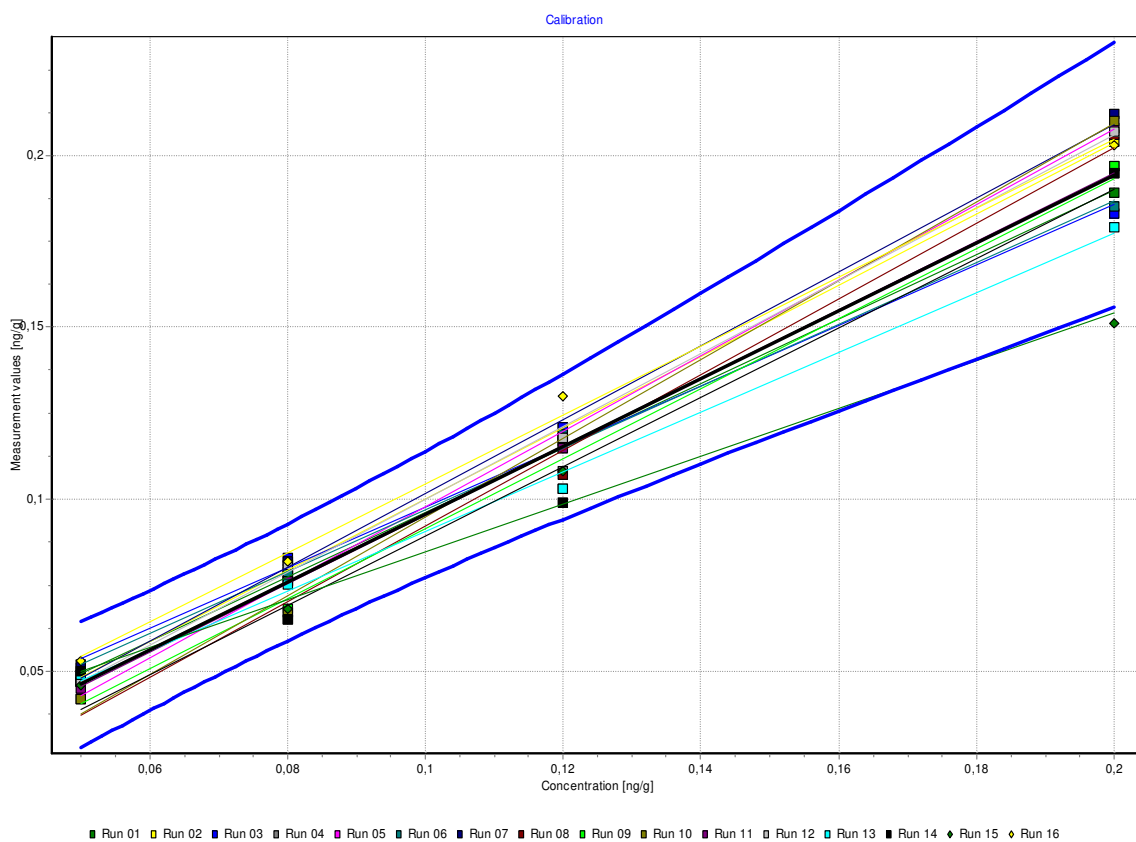


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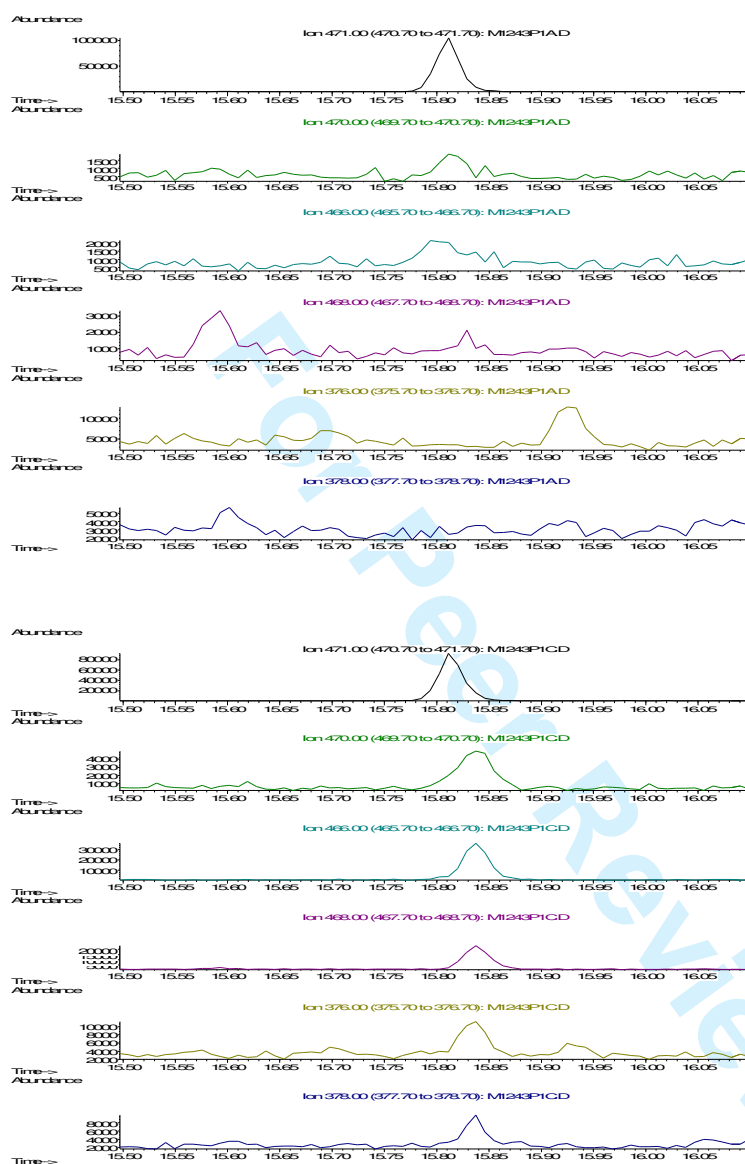


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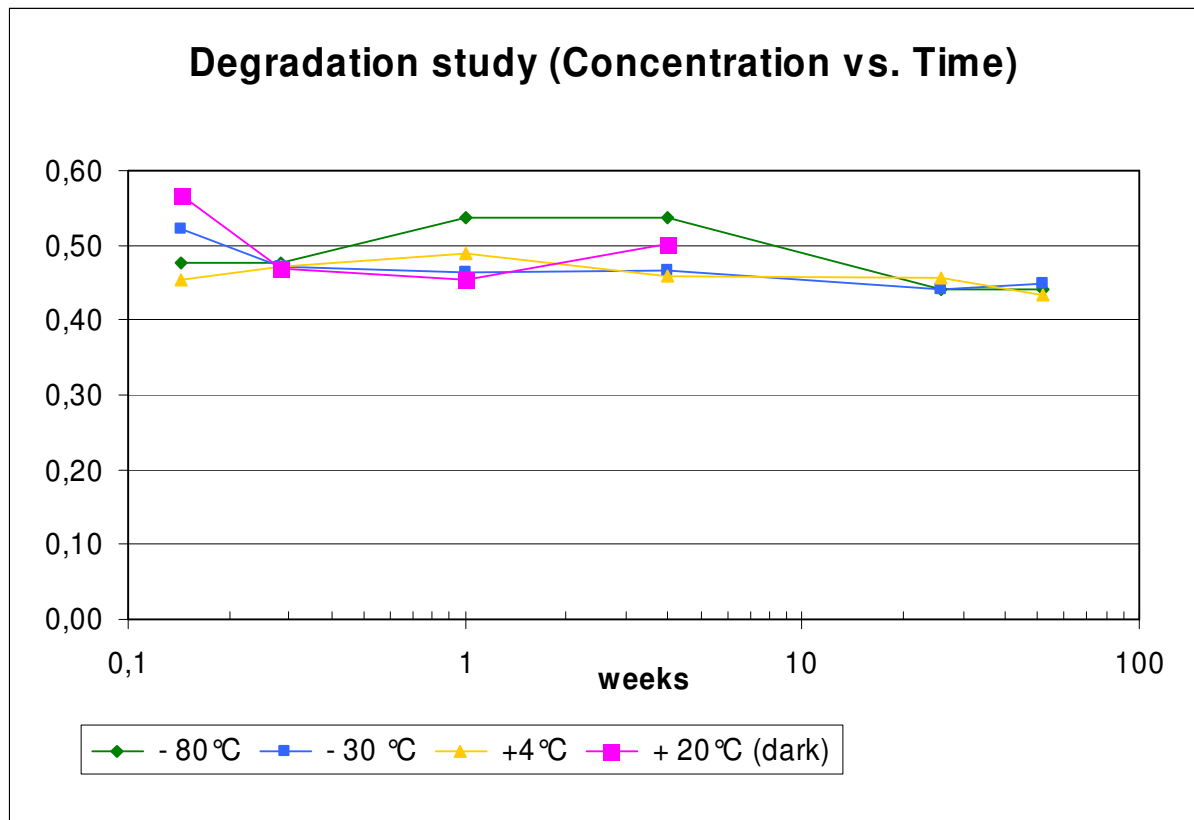


Figure 3: Results of the degradation study (CAP_002), concentration in ng/g

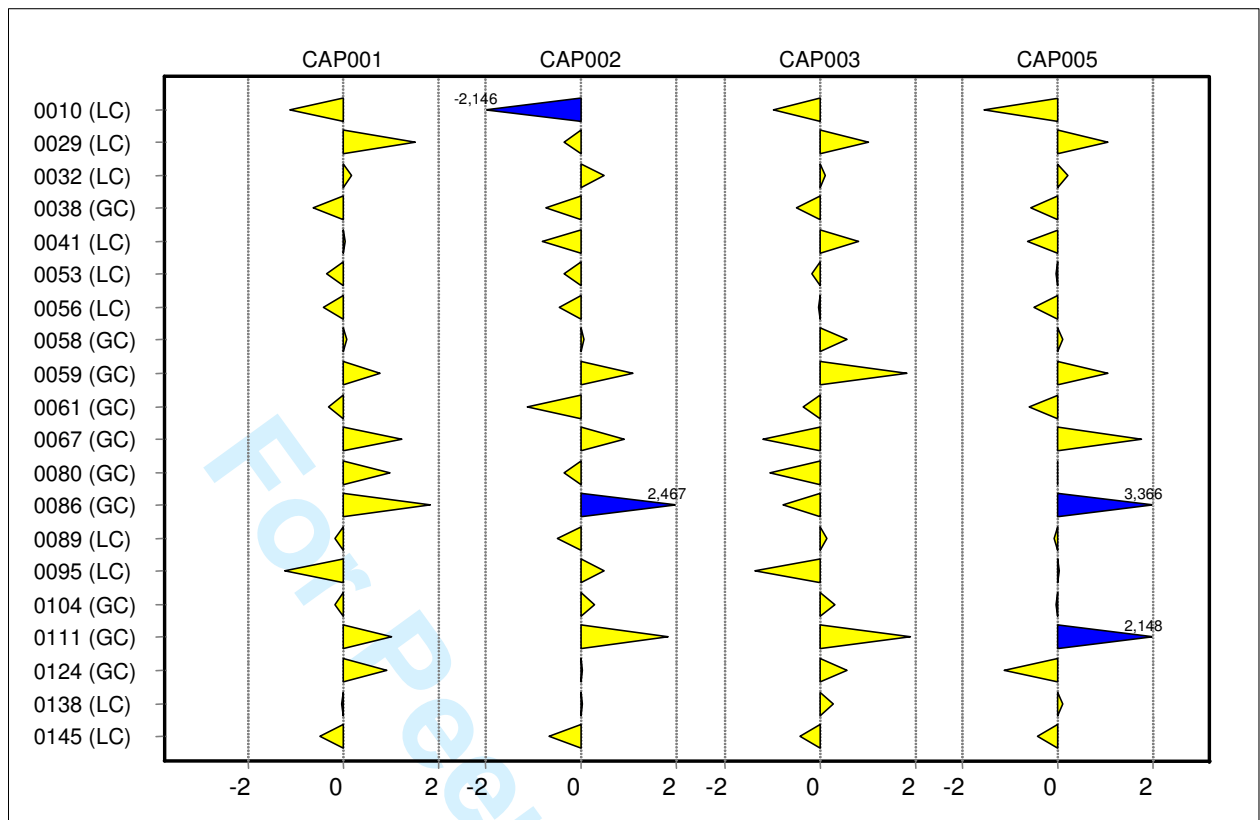


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