Labsert Laboratuvar Hizmetleri ve Teknolojileri San.Tic.Ltd.Şti.
Adres: Mahmudiye M. Bahçeler C. Matiat İş Merkezi Kat:5 No:34
33070 Akdeniz - Mersin - Türkiye
Tel: +90850 3034076 / **E-posta:** info@labsert.com
Web: www.labsert.com / **Mersis No:** 0607037640900024

PURPOSE AND CORRECT USE OF REFERENCE STANDARD MATERIALS

As it is known, certified reference materials (CRM) are used frequently and often compulsory in laboratory analysis. A reference standard substance is a substance whose one or more measurable values can be defined by internationally valid methods or methods and determined as a standard value. If a detailed information document about this defined standard value is created and this document contains, for example, which analyzes were used to obtain this standard value, the methods by which the results were validated, which chemicals were used in the analyzes, then this document is called a certificate. When such a certificate is created for the reference substance, the name of the product becomes the certified reference standard substance.

As can be understood from the definition above, the main purpose of use of CRMs is to obtain the correct analysis result. Valid analysis results can be obtained by creating correct calibration curves in instrumental analyzes or by quality control studies to be performed before or after analyzes. Conversely, a systemic or methodical error can also be detected with similar studies.

What we need to understand from the correct use of CRMs is the correct interpretation of the data obtained by the use of CRM. When a systemic or methodical error is detected, two possibilities can be considered.

a) There is actually a systemic or methodical error

b) There is a manufacturing error of the CRM used for quality control

As with any production process, CRM productions cannot be expected to occur with absolute zero error. However, as a result of the levels achieved in international quality studies in CRM productions and increased internal and external quality audits in CRM productions, production errors have decreased to very low levels all over the world.

Therefore, if a systemic or methodical error is detected, starting the examination from the analysis processes firstly will provide both financial and time savings. Despite this, we can say that according to our domestic and international experiences, the following are considered first after the detection of such a mistake.

a) When a new lot numbered product of the usual CRM brand is used, it is considered that there may be an error in this product.

b) When a new CRM brand is used, it is also considered that there may be an error in the product.

As a result of these thoughts, new CRM purchases are made. Again, according to our experience, we can say that repeating the transactions by purchasing the same or a different CRM without examining the analysis processes, only causes a waste of time and money. Most of the time, errors can be detected with preliminary examinations, which we will detail below. In this way, the continuity of the work can be ensured without loss of money and time.

Labsert Laboratuvar Hizmetleri ve Teknolojileri San.Tic.Ltd.Şti.
Adres: Mahmudiye M. Bahçeler C. Matiat İş Merkezi Kat:5 No:34
33070 Akdeniz - Mersin - Türkiye
Tel: +90850 3034076 / **E-posta:** info@labsert.com
Web: www.labsert.com / **Mersis No:** 0607037640900024

WHERE SHOULD I START EXAMINATION WHEN THE ERROR IS DETECTED?

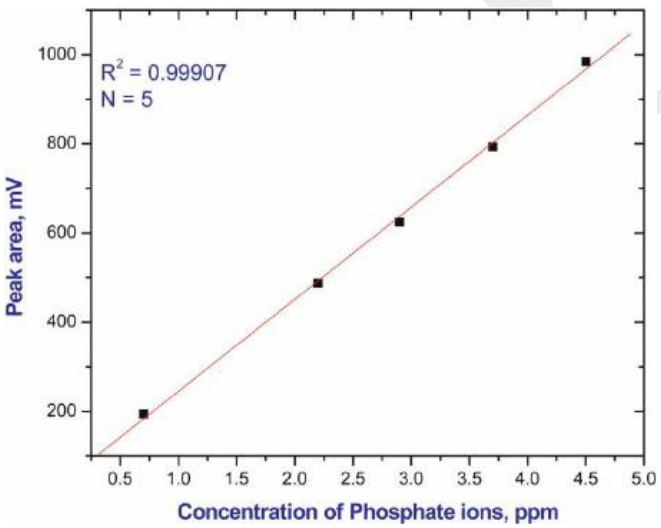
By applying one or more of the steps we will publish in this title, it can be easier to identify the source of error in the analysis results. In the technical support studies we offer as Labsert, we can identify the problem with 94% success by applying these steps.

1. CRM in Calibration Curve Studies

Chromatography and spectroscopy analysis devices make some mathematical calculations on the calibration curve prepared to provide quantitative analysis results. Therefore, the accuracy and validity of the calibration directly affect the analysis results. So what should we understand from the statement of calibration accuracy?

Whether single-point or multi-point calibration curves are created, the concentration of the prepared calibration solutions must be compatible with the concentration values entered in the program (software). Incorrect CRM dilutions or incorrect data entries are not an issue that can be understood by the R2 value of the calibration. When analysts only evaluate the R^2 value for the accuracy of the calibration curve, possible calibration errors can be overlooked.

What the R^2 value of the calibration curve represents is often a confused issue. We create calibration curves for quantitative analysis in chromatography devices. While creating these curves, we use solutions with known concentrations, that is, CRMs. For each reference standard concentration analyzed, the instrument obtains a peak and calculates the peak area. With the help of a software, the concentration value corresponding to the calculated area value is defined to the device. The device then obtains peak areas against the standard concentrations it reads at different levels. Finally, for each point, we define the concentration levels that the device uses for calculations. Thus, the calibration curve is prepared as multiple points.

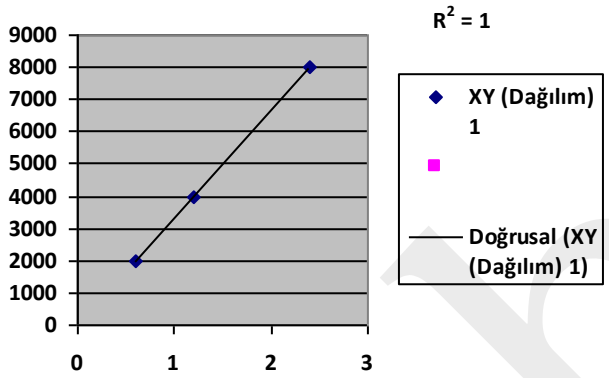


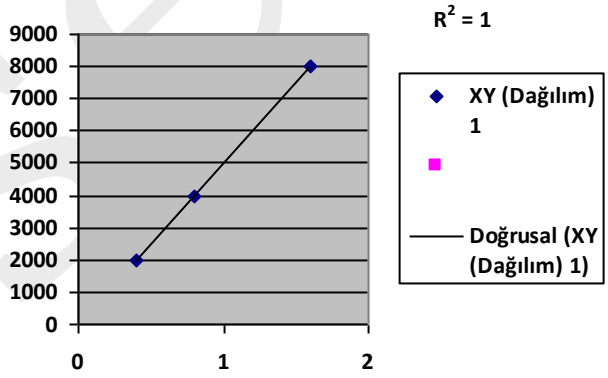
Labsert Laboratuvar Hizmetleri ve Teknolojileri San.Tic.Ltd.Şti.
Adres: Mahmudiye M. Bahçeler C. Matiat İş Merkezi Kat:5 No:34
33070 Akdeniz - Mersin - Türkiye
Tel: +90850 3034076 / **E-posta:** info@labsert.com
Web: www.labsert.com / **Mersis No:** 0607037640900024

Then, if the device obtains a peak in a sample read according to this calibration, it calculates the area of this peak and gives us the result of the concentration against this area according to the value we define in the calibration. The key definition here is this; While the device gives us the quantitative measurement result, it gives results according to the concentrations we have defined on the device. For example, let's assume that when we create a 3-point calibration, we define incorrect dilutions with incorrect values;

Correct Calibration Steps	
Calculated Area (mV)	Correct Concentration Enter (mg/l)
2000	0,6
4000	1,2 (1:2 Dilution)
8000	2,4 (1:2 Dilution)

Incorrect Calibration Steps	
Calculated Area (mV)	Incorrect Concentration Enter (mg/l)
2000	0,4
4000	0,8 (1:2 Dilution)
8000	1,6 (1:2 Dilution)





As can be seen, the value of R^2 was 1 in both calibration curves, as the dilution ratio between the calibration points corresponding to the areas was the same despite the incorrect dilution.

Now; let's suppose that we are analyzing a sample or quality control solution at a concentration of 1.2 mg/l. The peak area value that the device calculates for a given concentration is always constant (under good operating conditions). According to the example study above, the peak area to be calculated by the device for the substance with a concentration of 1.2 mg/l is 4000 units. However, since we mistakenly enter 0.8 mg/l instead of 1.2 mg/l for an area of 4000 units on software, we will read the analysis result, which should be 1.2 mg/l, as 0.8 mg/l. At this point, we find the answer to the question "Why do I get wrong results although the R^2 value is quite good".

Labsert Laboratuvar Hizmetleri ve Teknolojileri San.Tic.Ltd.Şti.
Adres: Mahmudiye M. Bahçeler C. Matiat İş Merkezi Kat:5 No:34
33070 Akdeniz - Mersin - Türkiye
Tel: +90850 3034076 / **E-posta:** info@labsert.com
Web: www.labsert.com / **Mersis No:** 0607037640900024

Therefore, when an error is detected in the analysis results obtained with the calibration curve prepared using CRM, a new calibration curve should be created first. The accuracy and validity of this calibration curve should be checked with a product with a different lot number than the CRMs used for the calibration curve or a different brand of CRM. The concentration of the CRM that you will prepare for quality control should preferably not be equal to one of the calibration curve points and should not be too close to the calibration upper-lower limit concentration values.

2. CRM in Quality Control Studies

The purpose of using CRM in quality control studies is to determine the accuracy and validity of the analysis results and to measure their change over time. The CRM to be used in quality control studies, as we mentioned above, unlike the CRMs used for calibration; either a different lot of the same brand or a different brand of CRM should be selected. When a deviation outside the acceptance range is detected in quality control studies, the main things to do are:

a) Preparing a new standard solution at different concentration levels and repeating the measurement in case of possible error while preparing the quality control standard solution.

b) The calibration validity should be checked by creating a new calibration curve as described in the heading number 1. It should not be forgotten that renewing the calibration curve means creating a calibration curve with new standard solutions, not creating a recalibration curve with previously prepared standard solutions.

If the source of error could not be detected as a result of these two operations performed in the first place, it means that there are 3 suspicious points to consider. These are:

a) There may not be an error in the processes performed to create the calibration curve (weighing of the standard material, dilution, dissolving, etc.), but the CRM used for the calibration curve may have a concentration deviation due to expiry date, stability problems or contamination.

b) There may be a general source of error in the system (column pollution, interference, mobile phase pollution, cone or detector pollution, etc.)

c) There may be a certification error in the production of the quality control standard.

At this point, there should be another reference point available for exact detection of the error. This independent reference point is either another standard reference material or another instrumental device compatible with the analysis. The most important requirement here is to make sure that both independent reference points are correct and valid.

Labsert Laboratuvar Hizmetleri ve Teknolojileri San.Tic.Ltd.Şti.
Adres: Mahmudiye M. Bahçeler C. Matiat İş Merkezi Kat:5 No:34
33070 Akdeniz - Mersin - Türkiye
Tel: +90850 3034076 / **E-posta:** info@labsert.com
Web: www.labsert.com / **Mersis No:** 0607037640900024

You can check the validity of your calibration curve by reading the second standard reference material as the quality control standard in your system as an independent reference point. If you find an error in the result of this second quality control standard, the error source is the calibration curve. If you get the correct result within the acceptance limits when this second quality control standard is used, it means that the error is in the first quality control standard.

Another independent reference source that can be used in investigations is using of an instrumental device whose accuracy and validity of results has been proven by quality control studies. It can be the same type of device (such as a 2nd ICP or GC) or another device compatible with analysis (such as the analysis of anions with UV-Vis instead of Ion chromatography “IC” or analysis of kations with ICP instead of IC). In this case, the following issues can be studied:

a) The first quality control standard is read as a sample in another device that is accepted as an independent reference point and the certification accuracy of the first quality control standard is checked.

b) The standard solution used in the preparation of the calibration curve is read as a sample in another device that is accepted as an independent reference point and the accuracy and validity of the standard solution are checked.

As a result of these studies, the source of error will be correctly identified. Avoiding these works will result in a loss of both money and time, and at the end of all these losses, these studies may still need to be done. For this reason, our recommendation to all users is not to make new purchases without any preliminary work (a new CRM, a new column, etc.). If you want, you can do these studies and ask for support by sharing your results with the reference material manufacturer or you can make this working plan with the reference material manufacturer.

Labsert Laboratuvar Hizmetleri ve Teknolojileri San.Tic.Ltd.Şti.
Adres: Mahmudiye M. Bahçeler C. Matiat İş Merkezi Kat:5 No:34
33070 Akdeniz - Mersin - Türkiye
Tel: +90850 3034076 / **E-posta:** info@labsert.com
Web: www.labsert.com / **Mersis No:** 0607037640900024

ERROR DETECTION SCHEMATIC OPERATION