Titration Guide on Errors

Sources of Error
Avoiding Errors
Instrument Check

Titration Guide

How to Identify and Avoid Titration Errors

METTLER TOLEDO

Editorial

The primary goal of any chemical analysis is to get accurate and precise results as quickly as possible. No matter how routine the analysis, care must be taken when preparing fresh titrants and standardizing them; calibrating and maintaining appropriate sensors; and handling samples. Quality results are only obtainable from a system that is well-maintained. Neglecting small details can have an enormous impact on the reliability and quality of the final result.

This guide discusses critical factors that can affect titration results and provides insight into how to eliminate some of the more common sources of titration errors. Overviews provided here may be covered in greater detail in related METTLER TOLEDO application brochures. These supplemental resources are catalogued for your convenience in section 6.

We hope that this guide and related publications provide insight into ways you can ensure accuracy in your titration analyses and wish you great success achieving high-quality results in all your day-to-day lab routines.

Content

1. Titration System Schematics

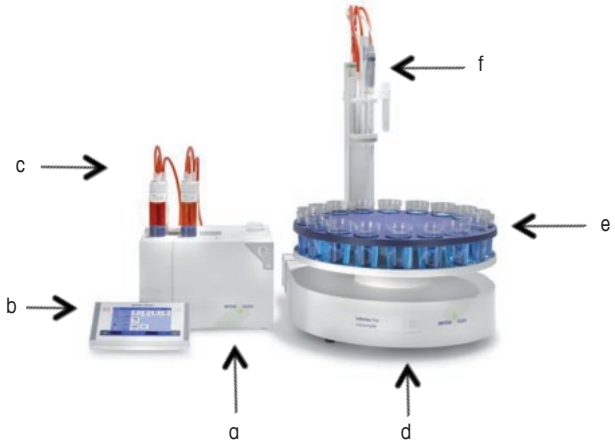
1.1 Potentiometric Titrator

Potentiometric titrators are used to determine concentrations of a wide variety of compounds in many industry segments. There are several assay reactions which are used in titration:

- Acid/base aqueous
- Acid/base non-aqueous
- Redox
- Precipitation (e.g. Argentometric titration)
- Complexometric

Potentiometric titration equipment generally includes the following features:

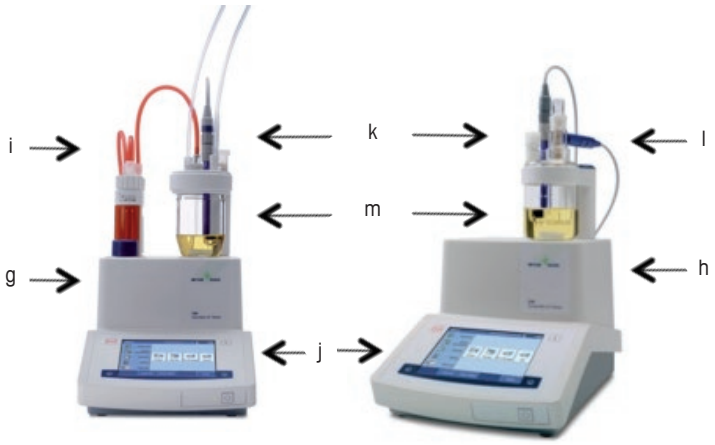
a. Titrator
b. Terminal (touchscreen)
c. Burettes
d. Autosampler (optional)
e. Titration beaker
f. Electrode(s)



1.2 Karl Fischer Titrator

Karl Fischer titration is the specific standard method for the determination of water content. There are two types of titrators generally used for this purpose. These two types are volumetric and coulometric titrators, and their general features include:

g. Volumetric titrator
h. Coulometric titrator
i. Burette
j. Touchscreen
k. Double pin electrode
l. Generator electrode
m. Titration vessel



2. Types of Error

An error is defined as any deviation from the true value and can be classified as systematic, random errors and gross errors. These types of errors are described in sections 2.1-2.3, while section 2.4 will help you identify and classify common errors. Section 3 will explore how errors that cause poor results can be avoided.

2.1. Systematic Errors

A systematic error is an error arising from a mistake made consistently throughout an analysis or analyses. This mistake causes consistently erroneous or slightly drifting results.

Typical systematic titration errors include:

- Analytical methods that do not compare directly to the method used to determine the "true" value
- Use of incorrect calculation formulas
- Consistent sampling errors
- Consistently incorrect sample sizes (such as those that arise from a constant weighing error)
- Incorrect titrant concentration
- False or missing blank value
- Incorrect or missing sensor adjustment
- A titration speed that is too quick to allow an actual chemical reaction endpoint
- A titration speed that is too quick to obtain an accurate sensor response

Once the source of a systematic error is identified, it is typically easy to correct.

2.2. Random Errors

A random error is a component of the overall error that varies in an unpredictable way. Because the sources of these errors vary, they are usually not easy to identify.

Typical sources of random errors include:

- Poor/inconsistent sample handling
- Inadequate equipment (including balance resolution too low for the process, wrong glassware grade, etc.)
- ncorrect method parameters (increments that are too large, insufficient waiting time between increments, etc.)
- Gas bubbles in burette tubes
- Ineffective/incomplete rinsing between samples
- Lack of operator training
- Inadequate environmental conditions (including fluctuating temperature and humidity)

If the source of a random error cannot be identified, the only solution is to increase the number of replicates performed to obtain a more trustworthy mean value.

2.3 Gross Errors

Gross errors are easily identifiable blunders or mistakes that usually arise from a blend of systematic and random errors. Another name for gross errors is avoidable mistakes.

Typical gross errors include:

- Notation mistakes
- Calculation errors
- Samples and/or reagent mix-up
- Wrong sample sizes
- Poor instrument operation
- Transcription errors

2.4 Possible Error Sources Defined by Type

Primary sources of titration error are described in the following table. Errors are grouped by where they arise within a given titration method and are defined by type (systematic, random or gross). Some cases may involve more than one error type.

Area	Error	Type		
		S	R	G
Primary standard	Impure, contaminated	•		
	Inhomogeneous		•	
	Unsuitable, no guaranteed primary standard quality			•
Sample size/balance	Balance not accurate, extant temperature gradient from titration vessel to balances		•	
	Careless weighing, concentration too low or high, improper sampling, contaminated balance			•
Titration vessel	Electrostatically charged, contaminated		•	
	Unsuitable			•
Dispensing unit	Leaky piston or burette tip, air in tubing system, 3-way stopcock leaking		•	
	Tube connection not tight			•
Sample	Matrix effect from similar species	•		
Solvent	Impure, poor solubilizing power, contaminated, wrong pH value or ionic strength	•		
	Not stable		•	
Titrant	Impure, contaminated, wrong pH value or ionic strength	•		
	Decomposed, light-sensitive		•	
	Very high or low concentration			•
Measurement	Contaminated sensor, blocked diaphragm, poor mixing of sample solution, excessive sensor response time, insufficient rinsing of sensor and stirrer		•	
	Unsuitable sensor type, loose contact at connector, unfavorable arrangement of burette tip and sensor			•
Titration parameters	Unsuitable titration mode, titration rate too fast or too slow, unsuitable evaluation procedure	•		
	Wrong measuring mode parameters			•
Temperature	Highly exothermic or endothermic reaction	•		
	Temperature fluctuations		•	
Environment	Changing, fluctuating, adverse conditions (humidity, temperature, UV light)		•	

Table 1: Possible error sources defined by type **S = Systematic R = Random G = Gross**

3. Avoiding Titration Errors

Many errors in analytical analysis arise from poor sample preparation or instrument set-up. This chapter will guide you through common preparation errors for both potentiometric and Karl Fischer titration methods and provide suggestions on how to avoid them. These points will help you achieve analytical excellence regardless of method used.

3.1. Potentiometric Titration

In a potentiometric titration, part of the sample containing the substance to be analyzed (the analyte) is dissolved in a suitable solvent. A second chemical compound, the titrant, is added as a solution of known concentration in a controlled manner until the analyte has reacted quantitatively. The reaction is monitored electrochemically by an electrode. From the consumption and concentration of the titrant as well as the weight of sample used in the analysis, the content of the analyte can be calculated. There are several assay reactions which are used in potentiometric titration:

- Acid/base aqueous
- Acid/base non-aqueous
- Redox
- Precipitation (e.g. Argentometric titration)
- Complexometric

To ensure high-quality results, the following aspects of the method and apparatus should be considered.

a) Titration beaker

Cleanliness

The first and most important rule for titration beakers is that they should be absolutely clean before using them for the analysis. Single use polypropylene beakers represent the perfect solution: they provide cleanliness without the hassle of cleaning. Glass beakers should be cleaned in a dishwasher and rinsed at least 2 times with deionized water before using them again.

Material

Plastic beakers can be used for almost any liquid sample, as polypropylene (PP) is resistant to virtually all chemicals. However, because plastic beakers have a tendency to accumulate electrical charges, solid samples that are susceptible to static charge should be weighed and measured in glass beakers (especially solids used in standard preparation). Glass beakers should never be used for samples that contain hydrofluoric acid as HF solutions can dissolve glass. Lye solutions can also corrode glass, but not as aggressively as HF.

Samples that contain analytes that are sensitive to ultraviolet light/UV radiation such as peroxide value and vitamin C content determination should be performed using protective dark red titration beakers.

b) Burette

Size (volume)

Burette size is an important factor in accurate titration analysis. Burette size is dependent on expected titrant consumption. In general, between 20 and 90 percent of the nominal burette volume should be used during titration. These limits help guarantee maximum accuracy for titrant addition and content determination.

Valve material

Standard valves in automatic titrator burettes are usually made of PTFE and have a very high chemical resistance. For applications where ruggedness or protection against wear and tear is required, ceramic valves should be used. Some applications where this makes a difference are methods in continuous operation (24/7 production or quality testing) and/or applications using titrants that crystallize easily (e.g. potassium permanganate, KMnO4).

c) Tubes

Gas bubbles

One of the most common error sources in titrimetric analysis with a semi-automatic or automatic titration system is the presence of gas bubbles in the tubes. Gas bubbles contribute to significantly elevated titrant consumption (it is a false titrant consumption: no titrant has been added and reacted with the analyte!) and reported analyte content will be too high, leading to a false result.

Bubbles are either introduced during aspiration or formed when titration tubes are already filled. They can often be dislodged by gently tapping the tubing and rinsing the burette several times, making sure that the suction tube is completely submerged in the titrant solution. Some bubbles can be avoided by placing the titrant solution at the same height (or a bit higher) as the titrator.

For titrants that contain either wanted or unwanted gas, bubbles can appear when the burette filling speed is too high, allowing the gas to be released by the titrant. In this case, the filling speed of the burette must be lowered.

Siphon

To stop diffusion of titrant out of titration tubes when no titration is running, all titration tubes should contain a siphon tip to limit titrant outflow. Diffusion becomes a serious threat to measurement accuracy, particularly when titrants have higher density (specific weight) than the sample solution.

d) Sensor

Since sensors are the effective measurement devices, their current state has a very large influence on titration results. Many factors contribute to sensor behavior, including maintenance, cleaning, conditioning procedure, and

Response

A sensor can be sluggish because of old age or poor maintenance. If this is the case, the measurement value detected by the sensor will be always different from the true value. In general this will lead to additional titrant consumption and measurements that are too high.

Calibration

Sensor calibration is particularly important for endpoint titrations. In endpoint titrations, titrant addition is stopped when a defined measured value is reached. The titrant consumption up to this point is used for the calculation of the required result. In this type of titration, used mostly for acid-base and ion selective titrations, the accuracy of the measurement value is thus directly related to the sample's determined analyte content. It also means that an accurate measurement value, possibly due to good calibration, gives an accurate content determination. For these reasons, the pH sensor must be calibrated with certified buffers (e.g. 4.00, 7.00 and 10.00) to check **slope**, which must be as near as possible to 59.16 mV/pH, and **zero point**, which must be as close to 0 mV (or pH 7) as possible, as in Fig.1. Depending on temperature fluctuations and measurement conditions, sensor calibration should be done at least once per day.

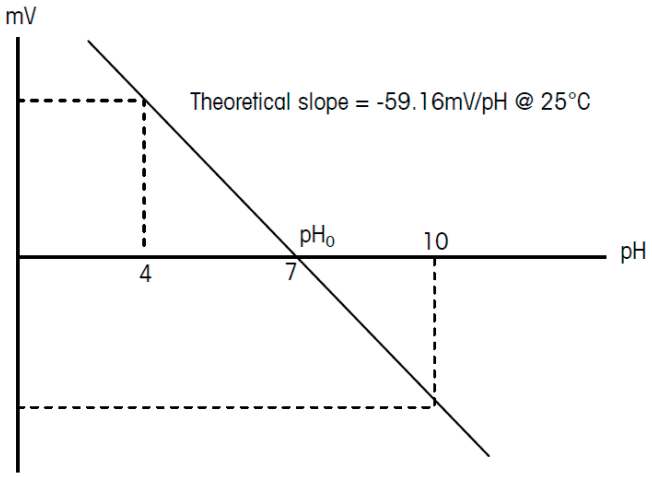


Figure 1: Calibration slope of an ideal pH electrode according to the Nernst equation

Conditioning

The ion-sensitive membrane of any pH or ion-selective electrode needs to be conditioned before the sensor can be used. If the sensor is not conditioned before use its response will be sluggish. Usually, conditioning is best done overnight with a dilute solution of the ion to be measured (e.g. 20 ppm). Also, when a pH sensor is used for longer times in non-aqueous media, the sensor needs to be conditioned in water or buffer solution before use to restore the hydration layer, without which a pH sensor cannot work properly (Fig.2).

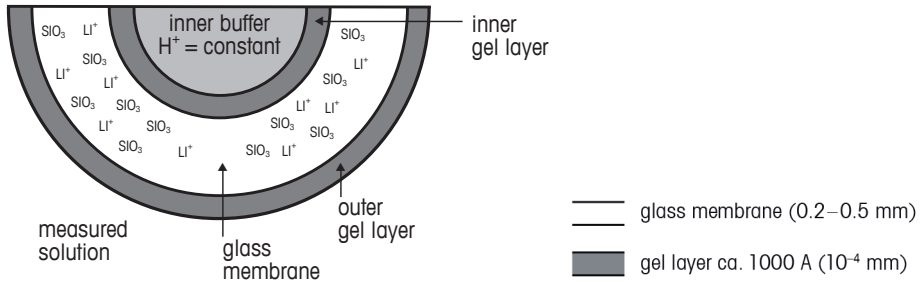


Figure 2: Cross section through the glass membrane of a pH electrode

Reference electrode

Another important factor for a sensor is the state of the corresponding reference electrode. The reference electrode provides the stable reference signal against which the measurement signal is determined. The reference electrode needs to be inert and provide a stable potential.

It is also important to use an electrolyte solution that is inert to the sample and titrant, and to maintain a fill level for the reference electrode that is always above the sample solution level. If not, the direction of flow will not be of electrolyte outwards, but of sample into the electrode!

To work properly, the reference electrode element must have good contact with the sample solution. Contact between reference system and sample is established via the junction (also known as diaphragm) of the reference electrode. The junction is an essentially open contact between the sample solution and the reference system that allows the flow of the reference electrolyte solution. The flow of ions in the reference electrolyte, which acts as a salt bridge, allows the closing of the circle in the electrochemical system.

Different junctions have been developed to provide the best contact for different kinds of samples (Fig. 3). The most common junctions in use today are ceramic junctions, which consist of porous ceramic material that allows slow electrolyte flow and are primarily used for "clean" samples; sleeve junctions, which are larger, ground-glass junctions that facilitate faster electrolyte flow and are mainly used for ion-poor or "dirty" media; and open junctions, which are completely open to the electrolyte and require a solid state electrolyte inside the reference electrode. For further information about electrode junctions, please refer to METTLER TOLEDO's "pH Theory Guide" (7).

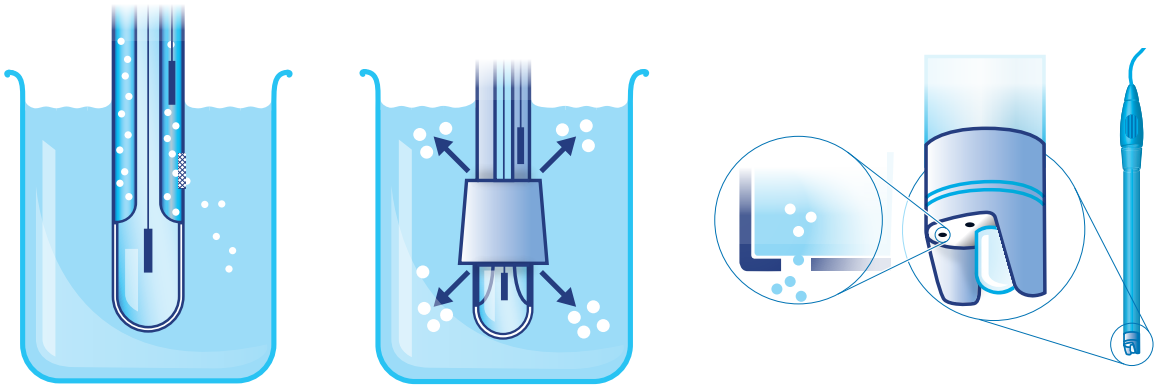


Figure 3: electrode with ceramic junction | electrode with sleeve junction | example of electrode with open junction

Maintenance

Depending on temperature fluctuations and measurement conditions, sensor calibration should be done at least once per day. Additionally, it is important that the electrolyte is replaced at least once every 3 months and that the sensor is cleaned regularly. Depending on potential contaminants, cleaning agents vary (please see Cleaning, below).

Cleaning

If a sensor is not clean (for example, when a film covers the sensing membrane and junction), the sensor is by definition not in direct contact with the sample solution. This can disrupt the measurement potential of the sample and deliver incorrect values. The cleaning solution to be used depends upon the type of material polluting the sensor, as listed in the following table. Please note that is important to recalibrate the sensor after taking any restorative action listed below.

If the pollutant is…	Then use…	Why cleaning is important
Protein	Pepsin	Proteins can block the junction with their bulky structure.
Ag_2S	Thiourea solution	If sulfides are present in a sample, silver in the reference electrode can precipitate, blocking the junction. This can be avoided altogether by using an ArgenthalTM reference system electrode, which prevents the exit of silver from the reference element.
AgCl	Concentrated ammonia solution	Chloride also precipitates with silver and appears in samples as common salt, which can block the junction or cause electrode malfunction. Soak the electrode in the solution.
Damaged surface membrane	Regeneration solution containing HF	After prolonged use, a glass membrane can become unresponsive. HF etches a thin pH glass layer from the membrane revealing a new layer of pH glass. This can only be performed a limited number of times. Do not over-soak or the entire membrane may dissolve.

Table 2: The four types of reference junction contamination and corresponding cleaning techniques

e) Stirrer

Speed

The speed and running time of the stirrer should be adapted to sample type. For normal, aqueous matrices with non-viscous samples that dissolve well, the standard titration speed of 30 percent is fine. For solid samples, the stirring time and speed should be increased to guarantee complete dissolution of the solid sample and avoid lower content findings caused by incomplete dissolution. This is especially important for solid titer standards, as incomplete dissolution would not only invalidate the titer determination itself, but also all consecutive sample measurements. Caution should also be taken not to use an excessive stirring speed as this can cause sample loss over titration beaker's rim.

Sensor cavities

In sensors types such as conductivity that have cavities, care must be taken to ensure no air is captured when the stirring speed is too high. If an air bubble is trapped, the signal will suddenly get noisy and change in intensity.

Surfactants

An excessive stirring speed is also an issue when measuring surfactants. Here, foam bubbles will be formed. With surfactants, all active molecules will accumulate on the surface of the soap bubble, causing the sample's surfactant concentration to be reduced and measured incorrectly. This problem can be avoided by lowering the stirring speed; or, when this is not possible, by adding methanol to the sample solution to reduce frothing.

f) Sample solution

Volume

The sample volume used for any titration should be sufficient to cover the sensor's active parts (junction and sensing membrane or metal ring). Normally this volume should be around 50 mL to also fit into the stirrer, titration tubes and dosing tubes when using an automatic titrator. For smaller sample sizes, special beakers like a microtitration beaker (15–20 mL) or 80 mL beaker (30–80 mL) should be used.

Analyte amount

Ideally, the amount of analyte in the sample to be determined should use up about half of the burette volume during titration. If the sample is in liquid form, it can be added to the sample solution with a pipette or dosing unit. When the sample is solid, the weight of the sample should be determined with a balance that has a resolution of at least 0.1 mg.

A special note about powdered samples: Be aware of electrostatic influences. If the titration beakers used are electrostatically charged, powdered samples will adhere to beaker walls and might not be accessible for titration, causing incorrect results. If the sample itself is susceptible to electrostatic build-up, it should be weighed either in glass beakers or through an antistatic kit that can be connected to an analytical balance.

Solvents and blank determination

For most titration analysis, sample amounts will be too small to be able to dip a sensor or stirrer into the sample and perform a titration. This means that the sample will have to be diluted. In titration, this diluent is called a solvent. The solvent should be inert, be able to dissolve the sample, and be easily obtainable in the quantities needed.

The most used solvents in titration are deionized water, organic solvents (mixture) and strong acids. Because the solvent does not participate in the reaction, the amount of solvent added is usually not relevant. However, solvents may interfere with the titration due to small inpurities or autodissociation (as is often the case with organic solvents) and cause inaccurate results. In this case a blank value determination for the solvent has to be performed by titrating the matrix without the actual sample and recording titrant consumption. This consumption is the blank value and should be subtracted from sample results. If a new batch of solvent is opened, a new blank determination must be performed.

pH value

Many redox and argentometric reactions require acidic environments, e.g. reactions with permanganate, dichromate or silver nitrate. For this reason, it is important to add an acid such as 20% H_2SO4 to the sample solution before titration. The exact amount and type of acid required can be found in the METTLER TOLEDO Application Brochures 34 (9).

Sample preparation

Sometimes, in specific methods, sample preparation plays a critical role. For example, samples may require heating or boiling, have specific waiting/reaction times, require different sensors for different measurements, necessitate serial dilution or consecutive sensor calibration, or require titer determination/sample series measurement without user interference.

In multi-step methods such as the ones listed above, automation can play an important role in obtaining accurate and precise results. It can also save lab time (see section 3h, Automation).

g) Titrants, titer, standards

Titer determination

Titrant concentration needs to be determined accurately to be able to calculate the content of the analyte in the sample solution. If the titrant concentration is unknown or inaccurate, the analyte content cannot be determined. Titer is calculated from the determined titrant concentration and the nominal titrant concentration. The titer is the ratio of determined concentration to nominal concentration and is generally ~1.

Standards

Primary standards are preferred for titer determinations. A primary standard is a highly pure, very stable, non-hygroscopic substance of a high molecular weight that reacts with the titrant in a known ratio. These combined properties ensure that an accurate determination of the titrant concentration can be performed.

Primary standards include TRIS/THAM for acids, potassium hydrogen phthalate for bases, NaCl/KCl for argentometric titrations and potassium dichromate for redox reactions. Further information about primary standards for specific titrations can be found in regulatory documentation such as NIST Standard Reference Materials (SRMs) as well as METTLER TOLEDO Application Brochures 8 and 9 (8).

Usable life

Titrants will deteriorate over time due to various external influences such as oxidation, precipitation, carbon dioxide absorption or degradation caused by UV radiation. Some of these influences can be counteracted. For example, drying tubes filled with NaOH on carrier material counteract CO_2 absorption while brown bottles counteract UV radiation, but this is not always possible and such fixes rarely offer complete protection.

Titrant deterioration changes the titrant concentration. Threat of deterioration determines how long titrant can be used without performing a new titer determination. This is called the usable life of a titrant. After the useable life has expired, a new titer determination has to be performed before any new titration analysis is attempted.

Lifespan

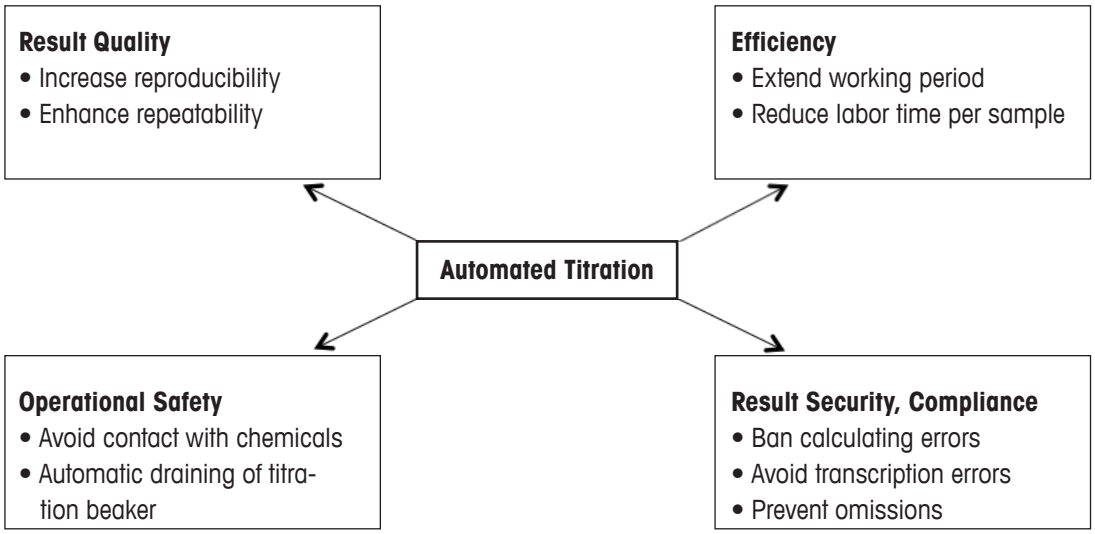
Titrant lifespan is the time after which a titrant should be replaced and is different for every titrant type. Acids, for example, are more stable than alkaline titrants. Therefore, an acid could have a life span of a year compared to just six months for a base. Throughout the lifespan of a titrant, titer determinations must be performed to obtain reliable results.

h) Automation

Automating a titration analysis means more than simply having the titration and results calculation performed by automatic titrators. It must also include sample preparation steps and operator-independent sample series analysis. The main focus of automation is keeping actions throughout the process consistent to eliminate systematic, random, and even gross errors during routine tasks.

When done well, automation:

- improves efficiency, offering high throughput with minimal operator effort;
- supports quality and data security by improving reproducibility and avoiding transcription errors; and
- enhances safety by limiting exposure to potentially dangerous reagents during dosing and disposal.



For more information about the benefits of automation, please refer to the Titration Automation Guide – Opportunities and Benefits (6).

Figure 4: A modern titration system with autosampler

3.2 Karl Fischer (KF) Titration

Water content determination is based on the following reaction described by R. W. Bunsen:

$$I_2 + SO_2 + 2\,H_2O \longrightarrow 2\,HI + H_2SO_4$$

Karl Fischer (KF) analysis, based on Bunsen's reaction, is one of the most-used analyses worldwide. The process has been refined over the years: toxic pyridine is no longer used, and new instruments and automation are now available. Also the reaction has been investigated and the reaction equation revised. But even with these improvements, special care must still be taken to avoid error and achieve true results, whether performing volumetric KF titration (for samples with water as a major component—100 ppm – 100 %) or coulometric KF analysis (for samples where water is trace—1 ppm – 5 %).

Ensuring accuracy

To ensure accuracy, the sample must release water completely. Only freely available water undergoes reaction with the KF reagent. A mixture of solvents can be used to achieve complete dissolution (or internal extraction).

Also, side reactions between the sample (or any sample component) must be avoided. There are essentially three side reactions that can affect results. These are:

1. **Reaction with methanol** (CH_3OH). In this side reaction, aldehydes and ketones react with methanol leading to additional water. Esterification with carboxylic acids also leads to additional water.
2. **Reaction with water** (H_2O). Ketones and aldehydes react with sulfur dioxide, a base and water so water is consumed, leading to inaccuracies.
3. **Reaction with iodine** (I_2). The reaction of iodine, for example, with oxides, hydroxides, carbonates, some amines, ascorbic acid, and mercaptans leads to higher iodine consumption leading to higher water content readings.

In each of these cases, precise action must be taken to avoid false results. These include using specific reagents, a KF oven, or external extraction procedure. Please refer to the Good Titration Practice™ in METTLER TOLEDO's Karl Fischer Titration guide (2) for more information and to create the perfect method for your particular sample.

Following are various additional aspects that must be taken into account to ensure accuracy when performing a KF titration.

a) Sample insertion

Syringe, septum and hole adapter

For coulometric titration, liquid sample insertion into the titration cell should always happen with a syringe that pierces the septum of the titration cell (Fig. 5). The water content detected with a coulometer is so low that any other insertion technique would allow introduction of a statistically significant amount of environmentally-present water, making accurate water content detection impossible. Since each sample insertion makes an additional hole in the septum, the septum needs to be exchanged on a regular basis to keep humidity influx and drift low (see section 3.2c for a discussion of drift).

For volumetric titration, sample insertion is not as critical. A sample can be injected into the titration vessel with a syringe by briefly opening the vessel to insert the solid or liquid. Since water content determined with volumetric analysis is much higher, any atmospheric water getting into the titration vessel with the sample will not disturb the measurements as much as it would for coulometric titration.

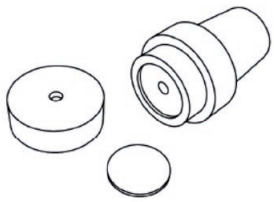


Figure 5: Septum and stopper for coulometer

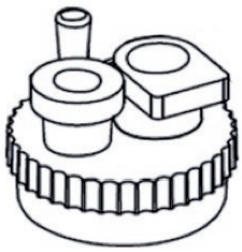


Figure 6: Three-hole stopper for Volumeter

Injecting the sample

First, a balance is used to tare the syringe filled with the sample. The sample can then be injected into the titration vessel. When pushing the sample out of the syringe, make sure that all sample is transferred into the solvent and not splashed against the walls of the titration vessel.

After the sample has been inserted, using the grading on the syringe to estimate the amount needed, slightly pull back the plunger to pull back any drops hanging on the needle of the syringe. If these drops remain at the end of the needle they get stuck inside the septum or inside the hole of the adapter when pulling the syringe out. This will cause a higher drift (see section 3.2c) as the water slowly evaporates and gets into the solvent.

When adding sample, it is also important that the drift in the titration vessel is low and stable (a drift of 1 ~ 4 µg/min should be achievable). Finally, the sample weight is determined via back weighing the syringe to obtain the absolute value and input it into the titrator. If a modern titrator and balance are used, it is possible to connect them with a cable and transfer the weight automatically from the balance to the titrator. This avoids transcription errors.

Weighing boat

For solid substances, a weighing boat (Fig. 7) is often the easiest way to weigh, insert and back-weigh a powder or a solid sample into a volumetric titration vessel. The most suitable boats are made from glass to avoid electrostatic influences and have a spout to pour the sample into the titration vessel. Depending on the size and length of the spout, either the whole three-hole adapter or only one of the stoppers has to be removed from the titration vessel.

Viscospoon™ (only for volumetric KF analysis)

Samples which are in the intermediate area between liquid and solid (viscous samples) can be inserted with METTLER TOLEDO Visco-Spoon™ (Fig. 8). With this spatula-like tool, a bit of very viscous sample can be picked up and placed in the titration beaker. Because of the Visco-Spoon™ length, the sample will be below liquid level so it can slowly dissolve and release its water.

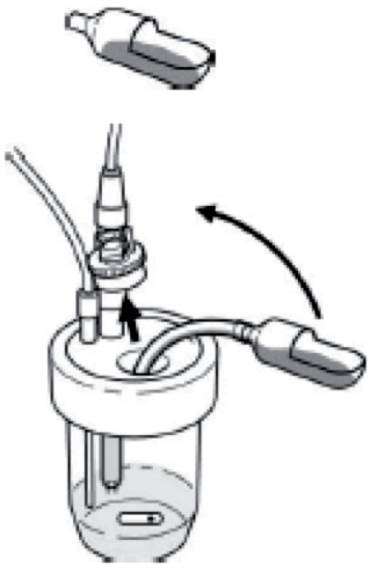


Figure 7: Weighingboat for adding a solid sample, e.g. powder

Figure 8: The Visco-Spoon is used for adding viscous samples

b) KF oven

Use of the KF oven is suitable for solids and liquids that cause side reactions with the KF reagent and/or release-water very slowly. In principle, the method involves heating a sample in an oven (Fig. 9) and causing the water in the sample to vaporize. The water is transferred to the titration cell on a current of dry inert gas (purge gas), and the amount of water is determined.

There are two main oven types: manual and automatic. With an automatic oven, a sample changer enables several samples to be titrated in unattended operation. The oven can be operated up to 300°C, and is usually completely controlled by the titrator. All determination parameters including oven temperature are managed by the titrator. Automation not only provides efficiency but also supports users in terms of quality and data security (2; 6).

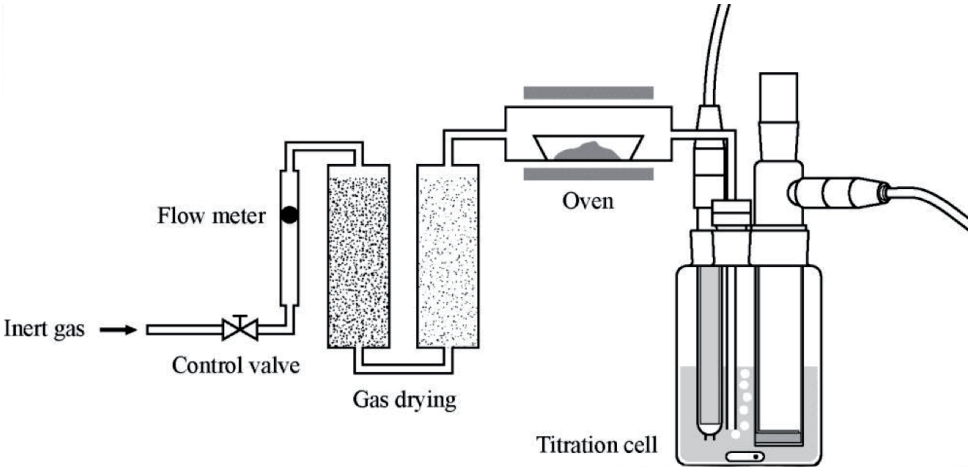


Figure 9: Setup to determine water with the oven method

c) Drift value

Humidity is the great enemy of accurate KF analysis. For this reason, modern titrator systems have very tight cells, and the entire system is protected by a drying tube filled with silica gel or a molecular sieve, both of which must be regenerated. Silica gel can be regenerated overnight at 150 °C, whereas molecular sieves require temperatures up to 300 °C.

The titration vessel should be sealed as much as possible against air coming in from the external environment. Any air entering the titration cell contains water and will influence the measurement. For this reason all the stoppers and inserts in the titration vessels are greased with silicone to make sure connections are airtight. As noted above, this is particularly critical for coulometric analysis.

Even with precautions, some water will get into the titration cell and show up as a water measurement baseline called drift. Usually, drift values of 4 µg/min or lower are achievable for volumetric titrators and 0.5-1 µg/min for coulometric titrators.

If it is not possible to keep a low drift value during the standby phase of the titration, check if all stoppers and electrodes going into the titration vessels are well lubricated, the septum is still intact, and whether or not the sample being analyzed can cause side reactions (see pag.14). If all these aspect are checked and confirmed, a high drift value means that it's time to clean the titration vessel and replace the solvent (section 3.2, introduction).

d) KF solvent and reagent

As noted, samples must release water completely for accurate analysis. Only freely available water undergoes reaction with the KF reagent. You can perform a so called internal extraction, i.e. use a mixture of solvents to achieve complete dissolution (such as chloroform or xylene in petrochemical products analysis). However, the largest part (at least 30-40 percent of the solvent mixture) must always be an alcohol, and generally methanol, to ensure that the KF reaction is strictly stoichiometric.

To obtain helpful results, important aspects that must be taken into account include:

- Use of solvents that contain as little water as possible (< 100 ppm), or the titration will take too long and titrant will be wasted.

- Use of buffering agents when acidic or basic samples are titrated to ensure that the titration is brisk and without side reactions. Imidazole is used for acidic samples, while salicylic or benzoic acid is used for basic samples.

Note: Sugar is the only type of sample that dissolves in formamide. On the other hand, formamide effectively extracts water from starch products. The extraction capacity can be improved by increasing the temperature—for example, 50°C. The amount of formamide at 50 °C should not exceed 30 percent, or the stoichiometry will change, falsifying results. Special thermostatable beakers for both coulometric and volumetric analysis can facilitate the dissolution of the sample inside KF solvents.

Various solvents for coulometric KF titration are available commercially. Solvents can be purchased specifically for samples like oils or ketones. A complete overview of titrants and solvents can be found in the Good Titration Practice™ brochure for Karl Fischer titration (2). For some specific samples there are also special catholytes available. One-component and two-component reagents are commercially available for volumetric analysis. Which one to use depends on the sample and user requirements. Titrants with different iodine concentrations are available for samples with lower or higher water content. Titrants with special solvents (not methanol) are available for samples that contain aldehydes or ketones that would react with methanol. For further information, please refer to the brochure Good Titration Practice™ brochure for Karl Fischer titration (2).

e) Concentration determination with "Water Standard" for volumetric analysis

Since KF titrants are not stable over long periods of time, a new concentration determination has to be performed regularly. If this is not done the accuracy of the analysis cannot be guaranteed.

When the titrants are freshly produced, the concentration will be higher than the nominal concentration on the bottle to make sure that they still have the nominal concentration on the "use by" date. For a titrant with a nominal concentration of 5 mg H_2O/mL, the concentration might be 5.5 mg H_2O/mL straight from the factory. Over time the concentration of the titrant will decrease; if titrant is not used up within a certain period (months if the bottle is opened, years if the bottle is closed), the concentration might get too low. If the titrant becomes so old that the concentration falls below 4 mg H_2O/mL, the titrant should be discarded, as titration speed will decrease too much.

It is also important to equilibrate the temperature of the titrant. The volume of KF titrants changes significantly with temperature, so if concentration is determined at a different temperature, subsequent samples will have erroneous results. Different water standards are available to determine the current concentration of the titrant.

Certified water standards

The standards which are easiest to use for KF titration are the certified liquid water standards that can be purchased from reagents suppliers. These standards have a certified water content per mass unit and can be dosed with a syringe. Available water contents are 10 mg/g, 1 mg/g and 0.1 mg/g (1%, 0.1% and 0.01%). Additionally, special standards are available for water in oils.

Solid water standards

Another option is to use a solid standard with a fixed amount of hydration water. The most used standard is disodium tartrate dihydrate ($Na_2C_4H_4O_6 \cdot 2\ H_2O$), which has a water content of 15.66% and can also be bought commercially for the purpose of KF titrant concentration determination. Since the solubility of sodium tartrate is limited in methanol (and even worse in ethanol), one has to be very careful that the tartrate is completely dissolved before the titration starts. After 3 concentration determinations in methanol (40 mL in titration vessel) with ~ 40 mg of sodium tartrate for each sample, the solvent will have to be exchanged.

A solid water standard is also available in tablet form. In this case, a fixed amount of water (10 mg) is present in every tablet. Handling here is simplified as the tablet can be added from the packaging straight into the titration vessel (use tweezers as hands contain moisture). However, comparisons showed that the reproducibility is somewhat lower when using tablet standards. Note that non-active tablet ingredients may not dissolve completely.

Pure water

Pure water can also be used to check the water content of a KF titrant. This is the most inexpensive option, but also the most difficult—and potentially the most inaccurate. When using pure water, practice the handling of micro-syringes beforehand and know the inserted volume or mass of the water precisely. Any deviation from the expected amount of water or any loss of water during handling will introduce a large error.

f) Replace the solvents

A common question about Karl Fischer titration is: When do I have to replace the electrolyte? Electrolyte stands for KF solvent, KF catholyte and KF anolyte. The common answer is to replace the electrolytes if their capacity is exhausted.

A more detailed answer is difficult. It has to consider several influences and depends on the very case. However, chemical facts about the Karl Fischer reaction and the reagents formulations lead to some practical rules and guidelines.

General rules of thumb

It is time to replace the electrolytes, if

- the drift is too high
- the solvent/anolyte has been used for two weeks
- the cathode compartment contains sulfides or mercaptans (obnoxious smell)

Dissolution capacity

Also replace the KF solvent/anolyte if the dissolving capacity of the solvent/anolyte is exhausted. This can occur rather likely with poorly soluble samples and typically clouds the solvent/anolyte.

Filling level

Replacement of the reagents is also recommended, when the level of solvent/anolyte, after adding samples, exceeds the 150 mL mark. The higher the solutions in the KF cell or anolyte compartment, the the worse the stirring efficiency will be. Insufficient stirring increases the risk of over-titration. Too vigorous stirring bears the risk for high drift and long titration times.

Conductivity

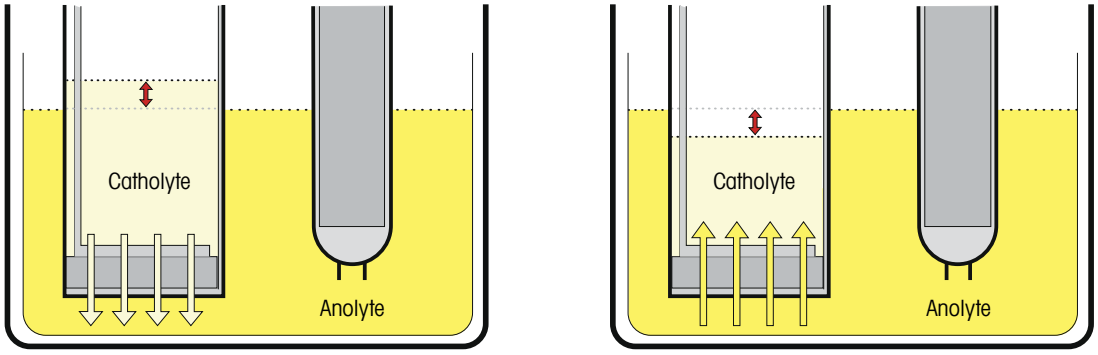
A minimum conductivity of the KF solutions - typically 10 µS/cm - is required for correctly indicating the endpoint. This applies especially to the coulometric anolyte. Conductivity can fall below the limit, when large sample amounts of low conductivity are titrated or when less polar solvents than methanol are used. However, modern KF titrators indicate a warning message in such cases to replace the KF solvent/anolyte.

Coulometric titration

- Anolyte reagent, typically 100 mL: Replace after 1000 mg water are titrated
- Catholyte reagent, typically 5 mL: Replace after 200 mg of water are titrated

It is common use to replace both the anolyte and catholyte at the same time for sake of ease.

Make sure that the level of the anolyte is approx. 3 - 5 mm higher than that of the catholyte. The catholyte always contains traces of water. If the level of the catholyte is the same or higher, catholyte flows slightly into the anolyte compartment, steadily entering moisture. This leads to a higher drift (Fig.10).



Incorrect: Lower anolyte level → drift is high

Correct: Higher anolyte level → low drift

Figure 10: Higher anolyte level ensures low drift and hence more accurate results

Note: It is best to avoid contact with KF chemicals due to their toxicity. The easiest and most secure way of draining and filling a titration cell is performed with an external liquid handling device. METTLER TOLEDO instruments include the Solvent Manger, a device mounted on top of the waste bottle that includes strong air (diaphragm) pump and an electromagnetic valve controlled by the titrator. A level sensor in the waste bottle prevents overflow. Any contact with reagent is avoided, and both draining and refilling of the titration cell are done automatically.

g) Cleaning the titration cell and platinum electrode

The titration cell and the electrodes should be cleaned, especially after dirty samples are analyzed. The generator electrode with diaphragm of a coulometric KF titrator must be cleaned periodically because contamination accumulates in the diaphragm over a period of time which leads to higher drift.

Contaminants can originate from samples or are side products that have been formed in the cathode compartment by reduction. For detailed instruction about the cleaning of the generator, please refer to Reference 2 in section 4, Good Titration Practice™ in KF Titration.

The titration vessel can be cleaned with a suitable solvent. Afterwards, dry the vessel at 100 °C in an oven. If immediate use is required, rinse with anhydrous methanol.

Generally, the indicating electrode does not need cleaning. A layer is formed on the platinum surface after the first few titrations. This leads to a higher potential jump. Therefore, the layer should not be removed.

However, samples may be deposited on the electrode's surface of the electrode, increasing the Ohmic resistance and preventing good indication. This becomes noticeable through a dark coloration of the anolyte at the end point.

In this case, the measuring electrode must be cleaned:

- Clean the platinum pin with a paper tissue. This is sufficient in most cases.
- With heavily contaminated electrodes, place the electrode in 0.5 mol/L sulfuric acid, and let an electrical current of about 400 mA flow across the platinum pins for 60 s by starting the KF titration.

1) Disconnect the indication electrode.
2) Connect the S7 screw cap connection of the generator cell with the indication electrode.
3) Stop the method when the cleaning is finished so that the polarization current at the indication electrode is stopped.

h) Gas bubbles (volumetric KF titration)

As already mentioned in section 3.1c, one of the most common error sources in titrimetric analysis with a semi-automatic or automatic system is the presence of gas bubbles in the tubes. Gas bubbles significantly contribute to false elevated titrant consumption, even though no titrant has been added to react with the analyte. Therefore, analyte content will be too high (leading to a false result).
As noted, bubbles can either be introduced during aspiration, or they can form when titration tubes are already filled. However they form, they can often be dislodged by gently tapping the tubing and rinsing the burette several times, making sure that the suction tube is completely submerged in the titrant solution. Some bubbles can be avoided by placing the titrant solution at the same height as the titrator (or just a bit higher).

Because KF titrants contain SO_2, bubbles can appear from titrant addition when the filling speed of the burette is too high so gas is released. Lowering the fill speed can help avoid this issue.

4. Service and Instrument Maintenance

Periodic maintenance is recommended to ensure accurate, precise titration results. This includes both day-to-day or more routine maintenance as well as regular service calls.

Routine maintenance can easily be carried out by a titrator's user or key user. Such performance verification includes checks of sensor and titrant performance and consideration of typical sample sizes and temperature influences (5).

Depending on process requirements, a certification of titration equipment is executed periodically, at least once per year. The tasks of certification are typically carried out by an expert, such as those who work in METTLER TOLEDO's Service Organization.

Certification & recertification

The certification is a check of the instrument in order to verify if technical specification are fulfilled, or verify if actual specifications meet the required level of a given use.

Certification is only a part of a list of measures to guarantee correct results. Other points that have to be considered are the general system suitability tests (GSST), the sensor calibration, the titrant standardization (8) and the method validation (4). Some of these topics are also already covered in this document.

A complete certification of the titrator can be performed by testing the following hardware:

Sensor input and amplifier

- Potential measurement with certified voltmeter
- Temperature sensor input (measurement with certified resistors)

Dosing accuracy

- Burette motor drive i.e. measurement of the piston stroke with a certified micrometer (this is very important, be cause the titrator calculates titrant consumption to the endpoint/equivalence point of any titration by looking up the spatial position of the piston at the exact point where the end of the titration was evaluated)
- The burette itself, by measurement of the deviations from the specified diameter value of the glass cylinder. Different volumes of water are dispensed and their mass is compared to the dispensing of a certified reference buette which is in its turn certified in regular intervals in the METTLER TOLEDO metrology department in Switzerland.

As already mentioned, in environments where very strict measurement accuracy and traceability to required standards need to be met, it is very important to follow the quality and performance of the system periodically. For this reason, depending on a customer's requirements, a recertification of the burettes, dosing unit and the sensor inputs is executed periodically by an expert.

Qualification

Quality management requires the documentation of the performance over the whole lifetime of the instrument, i.e. from the planning phase through manufacturing, installation, and operation through instrument disposal.

All steps are summarized in the comprehensive concept of qualification:

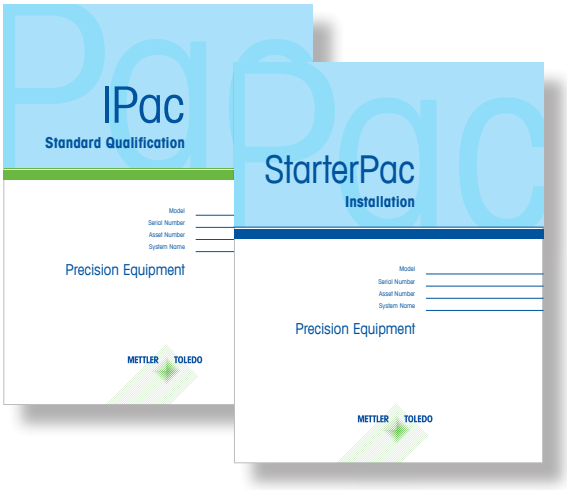
- Specification Qualification (SQ): Requirements, functions, design, HW/SW
- Construction Qualification (CQ): Production control for each product
- Design Qualification (DQ): Selection of correct instrument for intended use
- Installation Qualification (IQ): Evidence of correct installation at customer's facility
- Operational Qualification (OQ): Evidence and compliance to specifications, SOPs, initial calibration, user training
- Performance Qualification (PQ): Periodical calibration and certification
- Maintenance Qualification (MQ): Definition of preventive maintenance and calibration/certification intervals

METTLER TOLEDO titrators support the above requirement with the following quality package:

- Declaration of system validation, stating that the titrator was developed and manufactured in accordance to a strict quality management system
- Support with IPac, a service product that offers an initial equipment qualification including installation and operational qualification (IQ/OQ) of the titrator at the installation site and provision of the corresponding qualification documentation
- Support with EQPac, service product that offers complete qualification including full documentation of the instrument's history (IQ/OQ/PQ/MQ)
- Support with EduPac: with this education package, one of our METTLER TOLEDO specialists trains users on their instruments after installation, with refresher courses offered as needed

Validation of titration methods

As discussed, with titration, "correct" results are not necessary "true" results. To get the most accurate, precise and true result in this sensitive process, it is critically important to investigate factors affecting trueness and minimize influences that deviate from true results. Before this can be done, accuracy, precision and trueness must be defined for the process. The definition used here is made according to ISO 5725-1:1994. For more information on validation method procedure, please see the Application brochure 16 – Validation of titration method (4)



5. More Information

Application Database
The application chemists of the METTLER TOLEDO Analytical Chemistry market support group have prepared more than 500 of ready-made titration applications for use with the wide range of METTLER TOLEDO titrators. These proven and well-tested applications will help you to get accurate results quickly. Our online search engine allows you to search through the database.

www.mt.com/titration_applications

Webinars live and on-demand
Our web-based seminars (webinars) give you the opportunity to receive specific and relevant information concerning our products and applications. Please see the on-demand and the latest live webinars at

www.mt.com/webinars

For the titration automation webinar go to

www.mt.com/InMotion

Lab Library
The Lab Library is a one-stop portal to access knowledge resources such as webinars, literature, product info and much more.

www.mt.com/Lab-Library

6. References

1. GTP® - Hints & Tips – How to achieve the Best Result
2. Good Titration Practice™ in Karl Fischer Titration
3. How to Achieve the Best Results – Day-to-Day Titration Practice
4. Validation of Titration Methods – Application Brochure 16
5. Maintenance Guide – Sensor Performance, Titrant Performance & Standardization
6. Titration Automation Guide – Opportunities and Benefits
7. pH Theory Guide, METTLER TOLEDO, 51300047
8. Standardization of Titrants I & II – Application Brochure 8 & 9
9. Titration Excellence Application Brochure 34

Please contact your local METTLER TOLEDO representative for more information on our application brochures and titration solutions.

Good Titration Practice™

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GTP® – Good Titration Practice™

Dependable Titration in Practice – Reliable Results with GTP. A requirements-based selection of the titration system, as well as professional installation and training form the basis for dependable and risk-free titration.

GTP reduces the risks associated with titration and facilitates

- compliance with regulations
- preservation of the accuracy and precision of results
- increased productivity and reduced costs
- professional qualification and training

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Other Good Measuring Practices are available for weighing, pipetting, density and refractive index determination, thermal analysis, melting and dropping point determination as well as pH, conductivity, dissolved oxygen and redox measurements.

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