

ISO 9000 and Karl Fischer Titration

Instructions
**For Direct Volumetric
Determination of Water**

Instructions
**For Direct Coulometric
Determination of Water**

Instructions
**For a Volumetric
Titrator**

Instructions
**For a Coulometric
Titrator**



ISO 9000 and Karl Fischer Titration Over the years, the **HYDRANAL®**-laboratories have acquired a considerable know how in the design of guidelines to fulfil the requirements of their own ISO-9001 certification. This paper is intended to share this information with the reader.

Karl Fischer titration is an analytical method for the quantitative determination of water. It defines the quality of a given product and consequently becomes relevant to a quality assurance system like ISO 9001-9003. In practice three main issues have to be considered for this guideline:

1. Working instructions for the water determination analysis must be defined in writing.
2. Results must be documented to assure the retrieval of the analytical data at a later time.
3. The analytical instrumentation must be inspected periodically to assure delivery of exact and precise measurement.

The ISO 9001-9003 guidelines give only general recommendations but no specific instructions for practical implementation. Nevertheless, the guideline's focus is on instructions being appropriate, correct, unequivocal, and presented in writing. Over the years we have acquired a considerable know how in the design of proper and quality control conform guidelines with respect to our own ISO-9001 certification. This paper is intended to share this information with the reader.

The included analytical sample forms are intended as examples for quality control instructions. We have to point out that our Quality Management (QM) instructions can not be transferred directly to another laboratory without modifying the proposed method and integrating it into the local quality control system. The next few examples will illustrate the reasoning behind these requirements.

Testing instructions are only meaningful if the analyses are done in accordance with the QM guidelines of the company. It is

imperative that testing instructions and QM-guidelines are harmonized. Similar observations are also true for the Karl Fischer (KF) analyst. Instructions concerning which person will perform a particular analysis at a specific time and who will control, approve, and store the analytical data must be fixed in the QM-guidelines. The testing instructions have to be adapted to the actual analytical requirements. The requirements can include type of instrument, KF-reagent in use, working conditions in the laboratory, and finally expected criteria defined in the internal QM-guidelines. The adaption process centers around three main principles:

1. Instructions must be correct, clear, and practicable.
2. They must reflect actual conditions and analytical proceedings.
3. They must be integrated into the company's QM system.

Under these premises a variety of working instructions and numerous „correct“ instructions can be developed.

1. Writing a Measurement Procedure

Measurement procedures should be unabridged and specific to avoid errors in performing the instructions. Therefore, it must describe necessary working instructions in detail. It must focus on product characteristics, meaning that each analytical sample may have to be treated and described individually. Combining both requirements can lead to the collection of vast amounts of information. Eventually, it becomes so time consuming and impractical that nobody will spend time reading the guidelines.

It seems practical to divide the instructions into two parts. The first one should be a general guideline with detailed instructions concerning the method. The second part, a procedure of measurement for the product to be analysed, refers to the general guidelines. Only product specific aspects are listed here.

Two general procedural guidelines are presented in the next pages. The method KF-01 describes the volumetric KF titration while method KF-02 describes the coulometric determination. As an example, a product specific procedure of measurement will be illustrated for 1-propanol.

2. Documentation

Each analysis performed according to the procedure of measurement has to be documented. Records of the analytical data and notes must be kept and stored. The record keeping involves raw data such as sample weight or, reagent consumption, as well as

final results. Again, ISO 9001-9003 does not offer any precise definitions to which and how these records should be obtained. Consequently, a detailed set of in house quality control instructions has to be developed. Forms of record keeping can vary from a simple laboratory diary made by each technician up to a complex central data processing system. We generally use a variety of systems with different complexity to inventory our data. Raw data will be logged in laboratory diaries or saved in PC-controlled instruments. Final results will be filed depending on laboratory set up as hardcopy, PC-copy, or in the Laboratory Inventory Management System (LIMS). Initially, the choice of documentation system is up to the user. Once agreed on a particular system, the established analytical guidelines must be documented as a quality control procedure.

It is important to recognize that data for a particular product must be accessible at all times and independent of product location. The information available for every marketed product, must be traced from the final release specifications all the way back to the

initial laboratory notes of the technician who performed the analysis. The set of criteria (raw data) used to evaluate the product quality must allow a verification of results and specifications.

3. Control of Karl Fischer Titrators

Validating analytical instruments is necessary and ensures proper functioning of the titrator. The documentation of such tests suggests that the results obtained from the inspected unit are „correct“. A validation procedure is necessary and should be established following the same principles as outlined earlier. Examples of validation instructions for a volumetric and coulometric instrument will follow. The following example will illustrate an actual instruction report including an explanation of individual items.

Sample: General Instructions for a Direct Volumetric Karl Fischer [Method KF-01](#)

1. General Work Directions

The volumetric determination of water is based on the KF reaction, as described in detail in Appendix 1. KF volumetry is suitable for the determination of water ranging from 1 mg up to approximately 100 mg. Smaller or larger amounts of moisture can be determined under certain circumstances. A typical analysis contains sample water quantities between 5 and 20 mg. The weight of the sample has to be determined accordingly. Analysis samples should be soluble in methanol. Suitable solvent mixtures are discussed in Appendix 1.

The defined working directions become a binding routine for all water determinations. Alterations, such as titrating reagent, solvent system, sample weight, or working parameters necessary in the analytical procedure of a particular product will be specified in its respective testing procedure.

2. The Principle

The solvent system of choice will be added to the titration vessel of the KF instrument and titrated to dryness. After adding a weighed amount of sample, the water content is titrated with the same titrant.

3. The Instrument

KF-Titrator Model:
Instrument parameter:
Burette-Volume:
Titration Vessel Size:
End-Point Potential:

Here all instrument specific parameters like end-point potential, delay time etc. will be defined. Their choice should be made based on their universal applicability to most products tested.

4. The KF Reagents

Titrant:
HYDRANAL®-Composite 5
(Cat. No. 34805)
Solvent System:
HYDRANAL®-Methanol dry
(Cat. No. 34741)
Calibration Standard: **HYDRANAL®**-
Sodium-tartrate-2-hydrate
(Cat. No. 34803)
Titration Aids: **HYDRANAL®**-Benzoic
Acid (Cat. No. 37862)

5. Instrumentation Set Up

The titrator will be assembled according to the manufacturer's instructions (refer to Appendix 2 for details). The titration vessel and all parts of the titrator which come in contact with the KF reagent must be dry for assembly. The titrant will be added to the burette. Methanol will be dispensed into the titration vessel. Initiation of the pretitration step allows drying the inner titration vessel and its liquid content. This „conditioning“ phase remains constantly turned on (even overnight) to assure a dry titration cell. In case the instrument is not in use for several days the cell can be dismantled, cleaned and stored.

6. Performing a Titration

6.1 Check all instrument parameters and if necessary change to correct settings.

6.2 Add 30 mL methanol as working medium to the titration vessel.

6.3 Start the pretitration to dry the working medium and titration cell.

6.4 The sample to be analyzed will be weighed once the pretitration step is completed. The sample weight is documented in the testing instructions. Sample handling is explained in Appendix 1, page 46. (The numerical sample weight *S* will be added into the titrator once the instrument allows or prompts for it).

6.5 Upon addition, the sample will be titrated immediately.

6.6 Total consumption of KF reagent (in mL) will be recorded once the end-point of the titration is reached.

6.7 Calculation of sample water content *W*:

$$W = \frac{V \times Eq}{S \times 10} \%$$

W = Water content in sample, in weight %

V = Volume of consumed KF reagent, in mL

Eq = Water equivalent of titrant (titre or also known as factor), in mg/mL

S = Weight of analyzed sample, in g

(The titre calculation done at 7.7 becomes irrelevant if the titrator can compute the result automatically)

7. Determination of the „Water Equivalent“ (Titre)

The water equivalent of the KF reagent is determined daily in the morning. The plastic tubing which carries the KF reagent is flushed initially with one burette volume since it is not absolutely airtight.

7.1 All instrument parameters will be checked and if necessary changed to correct settings.

7.2 30 mL methanol will be added as working medium to the titration vessel.

7.3 Starting the pretitration dries the working medium and titration cell.

7.4 0.2 g **HYDRANAL**[®]-Standard Sodium tartrate-2-hydrate will be accurately weighed into the working medium (weighing by difference technique, *S*₂ in g) once the titrator permits or prompts for the standard.

7.5 Start the titration after addition of sodium tartrate-2-hydrate.

7.6 Total consumption of KF reagent (*V*₂ in mL) will be recorded once the end-point of the titration is reached.

7.7 Calculation of the „water equivalent“ (titre), *Eq*:

$$Eq = \frac{S_2 \times 156.6}{V_2} \text{ mg/mL}$$

Eq = Water equivalent of titrant (titre or also known as factor), in mg/mL

*V*₂ = Volume of consumed KF reagent, in mL

*S*₂ = Weight of analyzed sodium tartrate-2-hydrate standard, in g

(The titre calculation done at 7.7 becomes irrelevant if the titrator can compute the result automatically)

7.8 The determination is repeated if the water equivalent (titre) differs by more than 0.05 mg/mL to the value of the previous day.

8. Interferences

Compounds which react highly alkaline or acidic, strong oxidants or reductants, many aldehydes, ketones, aromatic or strong alkaline reacting aliphatic amines, certain phenol and sulphur compounds, boron salts, and other, or related compounds can interfere with the water analysis. Treatment of these samples is described in detail in Appendix 1.

9. Safety Precautions

Consult hazardous description and operating instructions on the label and Material Safety Data Sheet (MSDS) when working with KF reagents. The same recommendations apply to the sample to be analyzed.

10. Appendix

10.1 **HYDRANAL**[®]-Karl Fischer Titration Manual, published by Sigma-Aldrich Laborchemikalien GmbH

10.2 Instructions for
KF-titrator:.....
manufactured by:.....

Sample Test procedure**Sigma-Aldrich Laborchemikalien GmbH**

Cat. No. 24135 1-Propanol

Test procedure for

Department LC:

Code P-24135-1:

Valid from:

Page 1 of ...

This test procedure is related to the Specification Code S-24135-04

Assay (GC):**Boiling range:****Residue after evaporation:****Water content (Karl Fischer) 0,05%**

Method:

KF-01

Titrant:

HYDRANAL®-Composite 2

Sample amount:

Appr. 5 mL (exactly weighed)

This procedure has been produced by:**Signature:****Signature Supervisor:****Date:**

Sample: General Instructions for a Direct Coulometric Karl Fischer Titration Method KF-02

1. General Work Directions

The coulometric determination of water is also based on the KF reaction. KF coulometry is suitable for the determination of smaller amounts of water typically between 0.05 mg and 10 mg. Smaller or larger quantities of moisture can be determined under certain circumstances. A water quantity between 0.2 and 2 mg is generally satisfactory for a routine analysis. The weight of the sample has to be adjusted accordingly. Samples to be analyzed should be soluble in methanol. Alternative working conditions are discussed in Appendix 1.

The defined working directions become a binding routine for all future water determinations. Alterations in reagents, sample weight or working parameters necessary for the analytical procedure of a particular product are specified in the respective testing procedure of the sample.

2. The Principle

The sample is injected into the dried, conditioned titration cell of the KF coulometer. The instrument analyzes the sample automatically for water and reports its actual moisture content (or total quantity) at the end of the analysis.

3. The Instrument

KF-Coulometer:
Instrument Parameters:
End-Point Potential:
Delay Time:

(Here all instrument specific parameters like end-point setting, end-point delay time etc. will be defined. Their choice should be made based on their universal applicability to most products tested.)

4. Reagenzien

Anolyte:
HYDRANAL[®]-Coulomat AG (Cat. No. 34836)
Catholyte:
HYDRANAL[®]-Coulomat CG (Cat. No. 34840)
Control Standard:
HYDRANAL[®]-Water Standard 1.00 (Cat. No. 34828)
Titration Aids:
HYDRANAL[®]-Benzoic Acid (Cat. No. 37862)

5. Instrumentation Set Up

The titrator will be assembled according to the manufacturers instructions (refer to Appendix 2 for details). The titration vessel and all parts of the titrator which come in contact with the KF reagent must be dry for assembly.

100 mL of anolyte (unless otherwise specified) are added to the anode compartment and 5 mL of the catholyte (unless otherwise specified) to the cathode compartment. Both reagents must be added without delay to the respective compartment to protect them against absorbing atmospheric moisture. The cell is closed immediately after adding the reagents.

Once the titrator is turned on the cell and the reagents are dried automatically. The instrument does not permit the start of an analysis as long as residual moisture is present. This „conditioning“ stage remains constantly turned on (even overnight) to ensure a dry titration cell at all times. Further details can be found in Appendix 1, pages 29-34.

6. Performing a Titration

- 6.1 All instrument parameters must be checked and if necessary changed to correct settings.
- 6.2 The degree of dryness of the coulometric cell is monitored. The drift (background signal) should be below 20 pg/min. (0.3 hg/sec or less).
- 6.3 Initiate the analysis by pushing the „Start“ key of the titrator.
- 6.4 The sample to be analyzed is injected with a syringe within the next few seconds. The sample weight S (in g) is determined using the weighing-by-difference principle. The numerical value for the weight S will be added into the coulometer once the instrument allows or prompts for it.

7. Control and Validation

A weekly control determination ensures a proper coulometric performance (refer to Appendix 1, page 32). In order to do so 1 g of **HYDRANAL**[®]-Water Standard 1.00 is injected into the cell according to „Performing a Titration“ stated point 6. The standard is injected using a syringe. The sample weight is determined using the weighing-by-difference principle. The added amount of water must be recovered within a maximum deviation of 5 % from the theoretical value.

8. Interferences

Compounds which react highly alkaline or acidic, strong oxidants or reductants, many aldehydes, ketones, aromatic or strong alkaline reacting aliphatic amines, certain phenol, sulphur, and boron compounds, and other, or related compounds can interfere with the water analysis. Treatment of these samples is described in detail in Appendix 1.

9. Safety Precaution

Consult hazardous description and operating instructions on the label and Material Safety Data Sheet (MSDS) when working with Karl Fischer reagents. The same recommendations apply to the hazardous nature of the sample to be analyzed.

10. Appendix

- 10.1 **HYDRANAL**[®]-Karl Fischer Titration Manual published by Sigma-Aldrich Laborchemikalien GmbH.
- 10.2 Instructions for
KF-coulometer:.....
manufactured by:.....

Sample: Testing Instructions for a Karl Fischer Titrator according to the Requirements of ISO 9001-9003 Volumetric Determination

Instrument

Burette-Volume:	10 mL
Titrant:	HYDRANAL [®] -Composite 5 (Cat. No. 34805)
Solvent:	HYDRANAL [®] -Methanol dry (Cat. No. 34741)
Standard:	HYDRANAL [®] -Water Standard 10.0 (Cat. No. 34849)

Principle

The proportionality between water amount and reagent consumption is used as criteria to validate the instrument. The instrument is suitable for analysis if the proportionality relation is fulfilled.

Operating Instructions

1. Prepare instrument according to the general instructions listed in methanol KF-01.
2. Add 30 mL methanol to the titration vessel.
3. Titrate cell content to dryness with **HYDRANAL**[®]-Composite 5. A stable end-point must be achieved.
4. Load 1 mL or weigh 1 g of **HYDRANAL**[®]-Water Standard 10.0 in a syringe (expected weighing accuracy ± 0.1 mg). Record weight in report.
5. Inject the standard into the KF cell and titrate the water content with **HYDRANAL**[®]-Composite 5 to a stable end-point. Record consumed reagent volume (in mL) in testing report.
6. Follow steps 3 to 5 and titrate two further samples without delay in the same methanol solvent.
7. Replenish methanol reservoir and follow instructions 2-6 with now 2 g each of **HYDRANAL**[®]-Water Standard 10.0. Record readings in testing report.

8. Perform three titrations with approximately 4 g of **HYDRANAL**[®]-Water Standard 10.0. Replenish methanol in titration vessel each time
9. Determine mean and standard deviation (see **HYDRANAL**[®]-Manual, Chapter 4.1.6)
10. Complete and evaluate results in report, then sign. Present report for inspection and approval signature to department head. File the document in its designated location.

Interpretation

The working parameters of the instrument to be tested (burette size, end-point delay time etc.) must be defined in the working instructions. The respective reagents can be chosen freely. It is, of course, advisable to use the same reagents for testing a titrator as for measuring a product sample. This does not only add convenience but also ensures suitability of reagents and working technique. The number of validation or test runs can be chosen freely. A total of nine tests in three different moisture ranges seems to be a reliable approach for all statistical purposes. The choice of control standard is also free. Simplicity in handling and reliability should be the main criteria.

The injected water content of the standard should be adjusted to the burette in use. Typically, water quantities requiring 25 %, 50 % and 75 % of the burette volume are recommended. Statistical deviations will increase if the applied size of the standard was insufficient. Titrations which use more than one burette volume of reagent per test should be avoided. They should be performed only if the daily sample routine requires a similar reagent volume. The specific reagent volume (in mL water per mg reagent) consumed during the analysis will be used for the calculation of individual results. Mean and standard deviation are computed to evaluate the result. An acceptable standard deviation can be defined freely depending on the quality control requirements. We find a relative standard deviation of 2 % as acceptable. Using a reciprocal value, the „water equivalent“ in mg water per mL reagent is also acceptable for the evaluation of the test.

Sample: Test Report of a Karl Fischer Titrator according to the Requirements of ISO 9001-9003 Volumetric Determination

Instrument:		Location:	HYDRANAL®-Laboratory
Burette:	10 mL	Ident.-No.:	19/1
Working Parameters:			
Reagent (Titrant):	34805 HYDRANAL®-Composite 5	Lot. No.:	4075A
Working Medium (Solvent):	34741 HYDRANAL®-Methanol dry	Lot. No.:	4104C
Reference Standard:	34803 HYDRANAL®-Standard Sodium Tartrate <input type="radio"/>		
	34849 HYDRANAL®-Water Standard 10.0 <input checked="" type="radio"/>		9.99 mg/g
	Water <input type="radio"/>		

No.	Weight of Water Standard (g)	Water injected (mg)	Reagent consumption (mL)	Specific consumption (mL/mg)
1	1.0110	10.10	1.940	0.1921
2	0.9857	9.85	1.901	0.1930
3	1.0101	10.09	1.940	0.1923
4	1.9873	19.85	3.818	0.1923
5	2.0829	20.81	4.004	0.1920
6	2.0715	20.69	3.962	0.1915
7	4.0570	40.53	7.786	0.1921
8	4.0113	40.07	7.734	0.1930
9	4.0562	40.52	7.793	0.1923

Mean from 9 determinations:	0.1923	Standard Deviation Control Limit:	2 %
Relative Standard Deviation (found):	0.24 %	Control Requirements fulfilled (YES/NO):	yes
Performed by:		Approved by:	
		Date:	10.06.2004

Sample: Testing Instructions for a Karl Fischer Titrator according to the Requirements of ISO 9001-9003 Coulometric Determination

Instrument

Analyte (Vessel Solution):	HYDRANAL®-Coulomat AG (Cat. No. 34836)
Catholyte (Generator Sol.):	HYDRANAL®-Coulomat CG (Cat. No. 34840)
Control Standard:	HYDRANAL®-Water Standard 1.00 (Cat. No. 34828)

The Principle

Known amounts of water are injected into the cell and determined by coulometry. The water recovery rate will be evaluated statistically.

Operating Instructions

1. The instrument is prepared according to instructions listed in KF-02. Reagents are added to the titration vessel and the coulometer is turned on. The instrument will dry the cell automatically. Wait until drift (background) is stable and reaches pg water or less per min (or sec).
2. Prepare a 3 mL syringe.
3. Open a **HYDRANAL®-Water Standard 1.00** ampoule. Flush the syringe with approximately 1 mL of standard. Load sufficient amount of standard into syringe and weigh syringe plus content.
4. Start coulometer and inject 0.5 mL of standard into the cell (below surface of analyte).
5. Determine weight of syringe plus remaining content. Record injected sample weight in report. Enter the numerical value at the appropriate moment into the coulometer.
6. Once the titration is completed, register the found water content.
7. Repeat instructions 4-6 without delay and inject two further samples of similar weight.
8. Repeat control series (again 3 tests) with 1 mL each of **HYDRANAL®-Water Standard 1.00**.
9. Repeat control series (again 3 tests) with 2 mL each of **HYDRANAL®-Water Standard 1.00**.

10. Determine mean and standard deviation (see **HYDRANAL®-Manual**, Chapter 4.1.6).

11. Complete and evaluate results in report, then sign. Present report for inspection and approval signature to department head. File the document in its designated location.

Interpretation

Coulometry is an absolute method which determines the water content from the generated titration current. Therefore, the injected amounts of water must be known. The standard used must be precise and reliable. We prefer the **HYDRANAL®-Water Standard 1.00** since it is ampoule packaged and stored under argon.

Moisture ranges between 500 pg and 2000 pg are typical and sufficient for a routine coulometric analysis. Therefore, moisture measurements undertaken within this range are typically satisfactory. Other testing ranges can be defined. The reasoning behind the number of tests and choice of reagents is similar to the one for the volumetric validation process.

Coulometric instruments calculate the water content automatically once the numerical value for the sample weight is stored in the titration processor. Using this feature allows the calculation of the mean and standard deviation since same the titrators have a statistics program. The mean should be compared to the actual water content of the standard. Results will be compared with defined absolute and relative standard deviations specified in the analytical logbook.

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Sample: Test Report of a Karl Fischer Titrator according to the Requirements of ISO 9001-9003 Coulometric Determination

Instrument:		Location:	HYDRANAL®-Laboratory
Working Parameters:		Ident.-No.:	13/1
Analyt (Vessel Solution):	HYDRANAL®-Coulomat AG	Lot. No.:	4121D
Catholyte (Generator Solution):	HYDRANAL®-Coulomat CG	Lot. No.:	3258B
Control-Standard:	HYDRANAL®-Water Standard 1.00	Lot. No.:	30490
Water Content acc. Certificate:	1.001 mg/g		

No.	Weight of Water Standard (g)	Water injected (mg)	Water recovered (mg)	Water Content (mg/g)
1	0.5355	0.5301	0.5366	1.0021
2	0.5001	0.4951	0.5089	1.0176
3	1.4785	0.4737	0.4794	1.0019
4	1.0268	1.0165	1.0405	1.0133
5	0.9911	0.9812	0.9866	0.9955
6	0.9994	0.9894	1.0046	1.0052
7	1.9515	1.9320	1.9575	1.0031
8	1.9800	1.9602	1.9964	1.0083
9	2.0169	1.9967	2.0060	0.9946

Mean from 9 determination:	1.0046	Relative Standard Deviation (found):	0.75 %
Control Requirements fulfilled (YES/NO):	yes	Standard Deviation Control Limit:	2 %
Performed by:		Approved by:	
		Date:	10.06.2004

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