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Add the following:

▲INTRODUCTION

This chapter describes three analytical procedures for the evaluation of the levels of iron (Fe). Use *Procedure 1*, *Procedure 2*, or *Procedure 3* as indicated in the individual monograph. *Procedure 2* or *Procedure 3* can be used in all circumstances, provided that suitability is demonstrated by meeting the *Requirements for Procedure Validation*. ▲ (Official 1-Jun-2023)

Change to read:

▲PROCEDURES

• PROCEDURE 1: CHEMICAL METHOD ▲ (OFFICIAL 1-JUN-2023)

This limit test is provided to demonstrate that the content of iron, in either the ferric or the ferrous form, does not exceed the limit for iron specified in the individual monograph. The determination is made by concomitant visual comparison with a control prepared from a standard iron solution.

Standard iron solution: Dissolve 863.4 mg of ferric ammonium sulfate $[\text{FeNH}_4(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}]$ in water, add 10 mL of 2 N sulfuric acid, and dilute with water to 100.0 mL. Pipet 10 mL of this solution into a 1000-mL volumetric flask, add 10 mL of 2 N sulfuric acid, dilute with water to volume, and mix. Each milliliter of *Standard iron solution* contains the equivalent of 0.01 mg (10 µg) of iron.

Ammonium thiocyanate solution: Dissolve 30 g of ammonium thiocyanate in water to make 100 mL.

Standard preparation: Into a 50-mL color-comparison tube pipet 1 mL of *Standard iron solution* (10 µg of iron), dilute with water to 45 mL, add 2 mL of hydrochloric acid, and mix.

Test preparation: Into a 50-mL color comparison tube place the solution prepared for the test as directed in the individual monograph, and, if necessary, dilute with water to 45 mL; or, dissolve in water and dilute with water to 45 mL the quantity, in grams, of the substance to be tested, calculated as follows:

$$\text{Result} = 1.0/(1000L)$$

L = limit of iron (%)

Add 2 mL of hydrochloric acid, and mix.

▲Analysis: ▲ (Official 1-Jun-2023) To each of the tubes containing the *Standard preparation* and the *Test preparation* add 50 mg of ammonium peroxydisulfate crystals and 3 mL of *Ammonium thiocyanate solution*, and mix. The color of the solution from the *Test preparation* is not darker than that of the solution from the *Standard preparation*.

• ▲PROCEDURE 2 AND PROCEDURE 3

Both *Procedure 2* and *Procedure 3* are ICP-based procedures and can be used for the determination of iron. *Procedure 2* can be used for the determination of iron by inductively coupled plasma atomic (or optical) emission spectroscopy (ICP–AES or ICP–OES). *Procedure 3* can be used for the determination of iron by ICP–MS.

Before initial use, the analyst should verify that the procedure is appropriate for the instrument and sample used (procedural verification) by meeting the *Requirements for Procedure Validation*.

Where a monograph specifies a limit for iron concentration, the value listed in the monograph should be used as the *J* value for the purposes of this test.

System standardization and suitability evaluation using applicable reference materials should be performed on the day of analysis.

Sample preparation: Forms of sample preparation include neat, direct aqueous solution, direct organic solution, and indirect solution. The selection of the appropriate sample preparation depends on the material under test and is the responsibility of the analyst. When a sample preparation is not indicated in the monograph, an analyst may use any appropriately validated preparation procedure. In cases where spiking of a material under test is necessary to provide an acceptable signal intensity, the blank should be spiked with iron using, where possible, the same spiking solution. [NOTE—All liquid samples should be weighed.]

Closed vessel digestion: This sample preparation procedure is designed for samples that must be digested in a concentrated acid using a closed vessel digestion apparatus. Closed vessel digestion minimizes the loss of volatile impurities. The choice of a concentrated acid depends on the sample matrix. The use of any of the concentrated acids may be appropriate, but each introduces inherent safety risks.

Therefore, appropriate safety precautions should be used at all times. [NOTE—Weights and volumes provided may be adjusted to meet the requirements of the digestion apparatus used.]

An example procedure that has been shown to have broad applicability is as follows. Dehydrate and predigest 0.5 g of the primary sample in 5 mL of freshly prepared concentrated acid. Allow to sit loosely covered for 30 min in a fume hood. Add an additional 10 mL of concentrated acid, and digest using a closed vessel technique until the digestion or extraction is complete. Repeat, if necessary, by adding an additional 5 mL of concentrated acid. [NOTE—Follow the manufacturer's recommended procedures to ensure safe use.]

Reagents: All reagents used for the preparation of sample and standard solutions should be free of elemental impurities, in accordance with [Plasma Spectrochemistry \(730\)](#).

Procedure 2: ICP–OES

Standardization solution 1: 1.5J of iron in a matched matrix

Standardization solution 2: 0.5J of iron in a matched matrix

Sample stock solution: Prepare as directed in *Sample preparation*. Allow the sample to cool, if necessary.

Sample solution: Dilute the *Sample stock solution* with an appropriate solvent to obtain a final concentration of iron of not more than 1.5J.

Blank: Matched matrix

Elemental spectrometric system

(See [\(730\)](#).)

Mode: ICP

Detector: Optical detection system

Rinse: Use diluent.

Standardization: *Standardization solution 1*, *Standardization solution 2*, and *Blank*

System suitability

Sample: *Standardization solution 1*

Suitability requirements

Drift: Compare results obtained from *Standardization solution 1* before and after the analysis of the *Sample solution*.

Suitability criteria: Not more than 20% for iron. [NOTE—If samples are high in mineral content, rinse the system well before introducing the *Sample* in order to minimize carryover.]

Analysis: Analyze according to the manufacturer's suggestions for program and wavelength. Calculate and report results on the basis of the original sample size. [NOTE—Appropriate measures must be taken to correct for matrix-induced interferences (e.g., wavelength overlaps).]

Procedure 3: ICP–MS

Follow *Procedure 2* except for *Detector* and *Analysis*.

[NOTE—An instrument with a cooled spray chamber is recommended. (A collision cell or reaction cell may also be beneficial.)]

Mode: ICP

Detector: Mass spectrometer

Analysis: Analyze according to the manufacturer's suggestions for program and mass-to-charge ratio. Calculate and report results based on the original sample size. [NOTE—Appropriate measures must be taken to correct for matrix-induced interferences.]▲ (Official 1-Jun-2023)

Add the following:

▲ REQUIREMENTS FOR PROCEDURE VALIDATION

The following section defines the validation parameters and the acceptance criteria for performance-based procedures. Meeting these requirements must be demonstrated experimentally using an appropriate system suitability procedure and reference materials. Any alternative procedure (e.g., an atomic-absorption-based procedure) that has been validated and meets the acceptance criteria that follow is considered to be suitable for use.

Meeting these validation acceptance criteria is sufficient to demonstrate that the procedure will produce comparable results to those obtained using the procedure prescribed in the monograph.

• ACCURACY

Standard solutions: Prepare solutions containing iron at concentrations ranging from 50% to 150% of J using appropriate reference materials.

Test samples: Spike the material under test with the appropriate reference materials before any sample preparation steps (digestion or solubilization). Prepare three replicate samples at concentrations ranging from 50% to 150% of J for iron.

Acceptance criteria

Spike recovery: 70%–150% for the mean of three replicate preparations at each concentration

• PRECISION

Repeatability

Test samples: Six independent samples of material under test (taken from the same lot) spiked with appropriate reference materials for iron at the indicated concentration

Acceptance criteria

Relative standard deviation: Not more than 20% ($N = 6$) for iron

Intermediate precision (ruggedness)

Analysis: Perform the *Repeatability* analysis again on a different day, with different instrumentation, with a different analyst, or a combination thereof. Combine the results of this analysis with the *Repeatability* analysis so the total number of analyses is 12.

Acceptance criteria

Relative standard deviation: Not more than 25% ($N = 12$) for iron

- **SPECIFICITY:** The procedure must be able to unequivocally assess (see [Validation of Compendial Procedures \(1225\)](#)) iron in the presence of components that may be expected to be present, including matrix components.
- **LIMIT OF QUANTITATION, RANGE, AND LINEARITY:** Demonstrated by meeting the *Accuracy* requirement. ▲ (Official 1-Jun-2023)

Add the following:

▲ **GLOSSARY**

Concentrated acid: Concentrated ultra-pure nitric, sulfuric, hydrochloric, or hydrofluoric acid or aqua regia.

Aqua regia: Aqua regia is a mixture of concentrated hydrochloric and nitric acids, typically at ratios of 3:1 or 4:1.

Matched matrix: Solutions having the same solvent composition as the *Sample solution*. In the case of an aqueous solution, a matched matrix would indicate that the same acids and acid concentrations are used in both preparations.

Target limit or target concentration: The acceptance value for the elemental impurity being evaluated, in this case iron. Where a monograph specifies a threshold limit, this shall become the target limit or target concentration of iron for the material. Exceeding the target limit indicates that a material under test exceeds the acceptable value. The determination of compliance is addressed in other chapters.

J: The concentration (w/w) of the element of interest, in this case iron, at the target limit, appropriately diluted to the working range of the instrument.

Appropriate reference materials: Where "appropriate reference materials" are specified in the chapter, certified reference materials (CRMs) from a national metrology institute (NMI), or reference materials that are traceable to the CRM of an NMI should be used. An example of an NMI in the United States is the National Institute of Standards and Technology (NIST). ▲ (Official 1-Jun-2023)

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