

SYNCHRON[®] System(s) Chemistry Information Sheet

**FE
Iron
REF 467910**

For *In Vitro* Diagnostic Use

ANNUAL REVIEW

Reviewed by:	Date	Reviewed by:	Date

PRINCIPLE

INTENDED USE

FE reagent, when used in conjunction with SYNCHRON LX[®] System(s), UniCel[®] DxH 600/800 System(s) and SYNCHRON[®] Systems FE/IBCT Calibrator Kit, is intended for the quantitative determination of iron in human serum or heparinized plasma.

CLINICAL SIGNIFICANCE

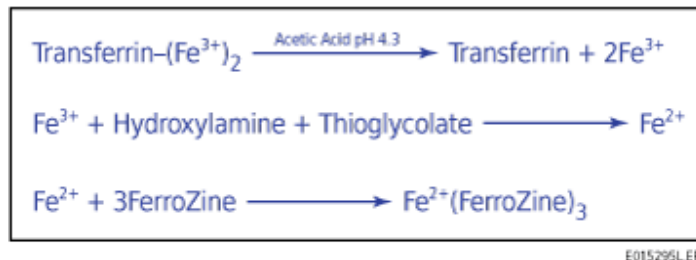
Alterations in iron and total iron binding capacity levels result from changes in iron intake, absorption, storage, and release mechanisms. Such changes are indicative of a wide range of dysfunctions including anemias, nephrosis, cirrhosis and hepatitis. Both iron and total iron binding capacity measurements are important for definitive diagnosis because they are interrelated. Tietz has presented a summary of these relationships and the patterns of iron/total iron-binding capacity associated with various disease states.¹

METHODOLOGY

FE reagent is used to measure the iron concentration by a timed-endpoint method. In the reaction, iron is released from transferrin by acetic acid and is reduced to the ferrous state by hydroxylamine and thioglycolate. The ferrous ion is immediately complexed with the FerroZine Iron Reagent.^a

The SYNCHRON[®] System(s) automatically proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 8 parts reagent. The system monitors the change in absorbance at 560 nanometers. This change in absorbance is directly proportional to the concentration of FE in the sample and is used by the System to calculate and express the FE concentration.

CHEMICAL REACTION SCHEME



SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.² Freshly drawn serum or heparinized-plasma is the preferred specimen. Whole blood, urine, and non-heparinized plasma are not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum or plasma be physically separated from contact with cells within two hours from the time of collection.³
2. Separated serum or plasma should not remain at room temperature longer than 8 hours. If assays are not completed within 8 hours, the separated sample should be stored at +2°C to +8°C. If assays are not completed within 24 hours, plasma samples should be recentrifuged and separated from precipitate before testing. If assays are not completed within 48 hours, or the separated sample is to be stored beyond 48 hours, samples should be frozen at -15°C to -20°C. Frozen samples should be thawed only once. Analyte deterioration may occur in samples that are repeatedly frozen and thawed.³

ADDITIONAL SPECIMEN STORAGE AND STABILITY CONDITIONS AS DESIGNATED BY THIS LABORATORY:

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SAMPLE VOLUME

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes and minimum volumes, refer to the Primary Tube Sample Template for your system.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet for information on unacceptable specimens.

CRITERIA FOR SAMPLE REJECTION AS DESIGNATED BY THIS LABORATORY:

PATIENT PREPARATION

SPECIAL INSTRUCTIONS FOR PATIENT PREPARATION AS DESIGNATED BY THIS LABORATORY:

SPECIMEN HANDLING

SPECIAL INSTRUCTIONS FOR SPECIMEN HANDLING AS DESIGNATED BY THIS LABORATORY:

REAGENTS

CONTENTS

Each kit contains the following items:

Two FE Reagent Cartridges (2 x 200 tests)

VOLUMES PER TEST

Sample Volume	25 µL
Total Reagent Volume	210 µL
Cartridge Volumes	
A	200 µL
B	--
C	10 µL

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

FerroZine ^b	0.4 mmol/L
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REAGENT CONSTITUENTS

Acetic acid	0.5 mol/L
Hydroxylamine hydrochloride	0.3 mol/L
Thioglycolic acid	22.3 mmol/L

Also non-reactive chemicals necessary for optimal system performance.

EUROPEAN HAZARD CLASSIFICATION

Iron Reagent (Compartment A)	Xn;R40-43	Limited evidence of a carcinogenic effect May cause sensitization by skin contact.
	S36/37	Wear suitable protective clothing and gloves.
	S61	Avoid release to the environment. Refer to special instructions/Safety data sheets.
Iron Reagent (Compartment C)	Xn;R40-43	Limited evidence of a carcinogenic effect May cause sensitization by skin contact.
	S36/37	Wear suitable protective clothing and gloves.
	S61	Avoid release to the environment. Refer to special instructions/Safety data sheets.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

SYNCHRON® Systems FE/IBCT Calibrator Kit
At least two levels of control material
Saline

REAGENT PREPARATION

No preparation is required.

ACCEPTABLE REAGENT PERFORMANCE

The acceptability of a reagent is determined by successful calibration and by ensuring that quality control results are within your facility's acceptance criteria.

REAGENT STORAGE AND STABILITY

FE reagent, when stored unopened at +2°C to +8°C, will remain stable until the expiration date printed on the cartridge label. Once opened, the reagent is stable for 60 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

REAGENT STORAGE LOCATION:

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CALIBRATION

CALIBRATOR REQUIRED

SYNCHRON® Systems FE/IBCT Calibrator Kit

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

SYNCHRON® Systems FE/IBCT Calibrator Kit is stable until the expiration date printed on the calibrator bottles if stored capped in the original container at room temperature. DO NOT FREEZE.

CALIBRATOR STORAGE LOCATION:

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CALIBRATION INFORMATION

1. The system must have valid calibration factors in memory before controls or patient samples can be run.
2. Under typical operating conditions the FE reagent cartridge must be calibrated every 14 days and also with certain parts replacements or maintenance procedures, as defined in the SYNCHRON LX *Maintenance Manual and Instrument Log*, or the UniCel DxH 600/800 System *Instructions For Use* (IFU) manual.
3. The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will be printed with error codes and the system will alert the operator of the failure. For information on error codes, refer to the SYNCHRON LX *Diagnostics and Troubleshooting Manual*, or the UniCel DxH 600/800 System *Instructions For Use* (IFU) manual.

TRACEABILITY

For Traceability information refer to the Calibrator instructions for use.

QUALITY CONTROL

At least two levels of control material should be analyzed daily. In addition, these controls should be run with each new calibration, with each new reagent cartridge, and after specific maintenance or troubleshooting procedures as detailed in the appropriate system manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.

The following controls should be prepared and used in accordance with the package inserts. Discrepant quality control results should be evaluated by your facility.

TABLE 1 QUALITY CONTROL MATERIAL

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

1. If necessary, load the reagent onto the system.
2. After reagent load is completed, calibration may be required.
3. Program samples and controls for analysis.
4. After loading samples and controls onto the system, follow the protocols for system operations.

For detailed testing procedures, refer to the SYNCHRON LX *Operations Manual*, or the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

CALCULATIONS

The SYNCHRON[®] System(s) performs all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

REPORTING RESULTS

Equivalency between the SYNCHRON CX, SYNCHRON LX, and UniCel DxC 600/800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The reference intervals listed below were taken from literature and a study performed on SYNCHRON Systems.⁴

TABLE 2 REFERENCE INTERVALS

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Literature	Serum/Plasma (Newborn)	100 – 250 µg/dL	17.9 – 44.8 µmol/L
	Serum/Plasma (Infant)	40 – 100 µg/dL	7.2 – 17.9 µmol/L
	Serum/Plasma (Child)	50 – 120 µg/dL	9.0 – 21.5 µmol/L
	Serum/Plasma (Adult Male)	65 – 175 µg/dL	11.6 – 31.3 µmol/L
	Serum/Plasma (Adult Female)	50 – 170 µg/dL	9.0 – 30.4 µmol/L

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
SYNCHRON	Serum (Adult Male)	45 – 182 µg/dL	8.1 – 32.6 µmol/L
	Serum (Adult Female)	28 – 170 µg/dL	5.0 – 30.4 µmol/L

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Laboratory			

Refer to References (5,6,7) for guidelines on establishing laboratory-specific reference intervals.

ADDITIONAL REPORTING INFORMATION AS DESIGNATED BY THIS LABORATORY:

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PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method, based on a study of 25 healthy volunteers:

Table 3 Acceptable Anticoagulants^c

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	AVERAGE PLASMA-SERUM BIAS (µg/dL)
Lithium Heparin	14 Units/mL	NSI ^d
Sodium Heparin	14 Units/mL	NSI
Ammonium Heparin	14 Units/mL	NSI

LIMITATIONS

1. EDTA, sodium citrate, and potassium oxalate are known to interfere with this method.
2. Samples showing evidence of hemolysis should not be used. Hemolysis may cause falsely elevated results.
3. Use disposable labware whenever possible. Rinse glassware with 0.1N HCl before use.
4. Ingestion of oral contraceptives will elevate iron and/or total iron binding capacity values.⁸
5. Iron-dextran administration can cause elevations in total serum iron with this methodology.
6. Use of this assay is not recommended for patients undergoing treatment with deferoxamine (e.g., Desferal[®]) or other iron-chelating compounds.
7. Ingestion of iron (including iron-fortified vitamins or supplements) may cause transient elevated iron levels.⁹
8. Some gadolinium magnetic resonance contrast agents such as Omniscan[®], Optimark[®], and Magnevist[®] may interfere with this method¹⁰.

INTERFERENCES

1. The following substances were tested for interference with this methodology:

Table 4 Interferences^e

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT ^f
Bilirubin (unconjugated)	Bovine	30 mg/dL	NSI ^g
Hemoglobin	RBC hemolysate	50 mg/dL	+7 µg/dL
Lipemia	Intralipid ^h	500 mg/dL	NSI
Copper	NA ⁱ	250 mg/dL	NSI
Magnesium	NA	5.0 mg/mL	NSI

2. Refer to References (11,12,13) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

Analytic Range

The SYNCHRON[®] System(s) method for the determination of this analyte provides the following analytical ranges:

TABLE 5 ANALYTICAL RANGE

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum or Plasma	5 – 500 µg/dL	0.9 – 89.5 µmol/L

Samples with concentrations exceeding the high end of the analytical range should be diluted with saline and reanalyzed.

REPORTABLE RANGE (as determined on site):

TABLE 6 REPORTABLE RANGE

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS

SENSITIVITY

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for FE determination is 5 µg/dL (0.9 µmol/L).

EQUIVALENCY

Equivalency was assessed by Deming regression analysis of patient samples to accepted clinical methods.

Serum or plasma (in the range of 12 to 494 µg/dL):

$$\begin{aligned} Y \text{ (SYNCHRON LX Systems)} &= 0.970X - 8.04 \\ N &= 59 \end{aligned}$$

Serum or plasma (in the range of 12 to 494 µg/dL):

MEAN (SYNCHRON LX Systems)	= 104.6
MEAN (SYNCHRON CX7 DELTA)	= 116.20
CORRELATION COEFFICIENT (r)	= 0.9971

Refer to References (14) for guidelines on performing equivalency testing.

PRECISION

A properly operating SYNCHRON[®] System(s) should exhibit imprecision values less than or equal to the maximum performance limits in the table below. Maximum performance limits were derived by an examination of the imprecision of various methods, proficiency test summaries, and literature sources.

TABLE 7 MAXIMUM PERFORMANCE LIMITS

TYPE OF PRECISION	SAMPLE TYPE	1 SD		CHANGEOVER VALUE ¹		% CV
		µg/dL	µmol/L	µg/dL	µmol/L	
Within-run	Serum/Plasma	3.5	0.6	140.0	25.1	2.5
Total	Serum/Plasma	5.3	1.0	140.0	25.1	3.8

Comparative performance data for a SYNCHRON LX[®] System evaluated using the NCCLS Proposed Guideline EP5-T2 appears in the table below.¹⁵ Each laboratory should characterize their own instrument performance for comparison purposes.

TABLE 8 NCCLS EP5-T2 PRECISION ESTIMATE METHOD

TYPE OF IMPRECISION	SAMPLE TYPE		No. Systems	No. Data Points ^k	Test Mean Value (µg/dL)	EP5-T2 Calculated Point Estimates	
						SD	%CV
Within-run	Serum	Control 1	1	80	51.2	1.2	2.4
	Serum	Control 2	1	80	262.6	2.2	0.9
Total	Serum	Control 1	1	80	51.2	1.8	3.5
	Serum	Control 2	1	80	262.6	3.1	1.2

NOTICE

These degrees of precision and equivalency were obtained in typical testing procedures on a SYNCHRON LX[®] System and are not intended to represent the performance specifications for this reagent.

ADDITIONAL INFORMATION

For more detailed information on SYNCHRON LX Systems or UniCel DxC Systems, refer to the appropriate system manual.

SHIPPING DAMAGE

If damaged product is received, notify your Beckman Coulter Clinical Support Center.

REFERENCES

1. Tietz, N. W., *Textbook of Clinical Chemistry*, W. B. Saunders Company, Philadelphia, PA (1986).
2. Tietz, N. W., "Specimen Collection and Processing; Sources of Biological Variation", *Textbook of Clinical Chemistry*, 2nd Edition, W. B. Saunders, Philadelphia, PA (1994).
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4. Tietz, N. W., *Clinical Guide to Laboratory Tests*, 3rd Edition, W. B. Saunders, Philadelphia, PA (1995).
5. National Committee for Clinical Laboratory Standards, *How to Define, Determine, and Utilize Reference Intervals in the Clinical Laboratory*, Approved Guideline, NCCLS publication C28-A, Villanova, PA (1995).
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7. Henry, J. B., *Clinical Diagnosis and Management by Laboratory Methods*, 18th Edition, W. B. Saunders Company, Philadelphia, PA (1991).
8. Weissman, M., Pileggi, V. J., *Clinical Chemistry: Principles and Techniques*, Harper and Row Publishers, Hagerstown, MD (1974).
9. Burtis, C. A., Ashwood, E. R., *Tietz Textbook of Clinical Chemistry* 3rd Edition, pp 1701, W. B. Saunders, Philadelphia, PA (1999).
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11. Young, D. S., *Effects of Drugs on Clinical Laboratory Tests*, 4th Edition, AACC Press, Washington, D. C. (1995).
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13. Young, D. S., *Effects of Preanalytical Variables on Clinical Laboratory Tests*, 2nd Edition, AACC Press, Washington, D. C. (1997).
14. National Committee for Clinical Laboratory Standards, *Method Comparison and Bias Estimation Using Patient Samples*, Approved Guideline, NCCLS publication EP9-A, Villanova, PA (1995).
15. National Committee for Clinical Laboratory Standards, *Precision Performance of Clinical Chemistry Devices*, Tentative Guideline, 2nd Edition, NCCLS publication EP5-T2, Villanova, PA (1992).



Beckman Coulter Ireland Inc., Mervue Business Park, Mervue, Galway, Ireland (353 91 774068)



Beckman Coulter, Inc., 250 South Kraemer Blvd., Brea, CA 92821

ENDNOTES

- a FerroZine is a registered trademark of Hach Chemical Co.
- b FerroZine is a registered trademark of Hach Chemical Co.
- c Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.
- d NSI = No Significant Interference (within ± 7 $\mu\text{g/dL}$ or 5%).
- e Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.
- f Plus (+) or minus (-) signs in this column signify positive or negative interference.
- g NSI = No Significant Interference (within ± 7 $\mu\text{g/dL}$ or 5%).
- h Intralipid is a registered trademark of KabiVitrum, Inc., Clayton, NC 27250.
- i NA = Not applicable.
- j When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test % CV to the guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.
- k The point estimate is based on the pooled data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer's instructions.