SIEMENS

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ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

Total IgE (tIgE)

Current revision and date [a]	Rev. U, 2020-03	
Product Name	ADVIA Centaur® Total IgE assay (250 tests)	**REF** 03359776 (110778)
	ADVIA Centaur Total IgE assay (50 tests)	**REF** 06843687 (110777)
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur Calibrator 80	**REF** 10492491
Specimen Types	Serum, EDTA plasma, lithium heparin plasma	
Assay Range	1.5–3000 IU/mL	
Reagent Storage	2–8°C	
Reagent On-System Stability	28 days	

a In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

For *in vitro* diagnostic use in the quantitative determination of total IgE in serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems.

Summary and Explanation

Immunoglobulin E (IgE) is a trace protein in serum, and normally accounts for less than 0.001% of total serum immunoglobulins. The concentration of IgE in serum is age dependent and normally remains at levels less than 10 IU/mL in most infants during the first year of life. The level of serum IgE rises during childhood and reaches adult levels during the teens. There is a wide distribution of expected serum IgE values in healthy individuals of the same age group.[1]

Because IgE is a mediator of the allergic response, quantitative measurement of serum IgE, when integrated with other clinical indicators, can provide useful information for the differential clinical diagnosis of atopic and non-atopic disease. Patients with atopic disease, including allergic asthma, allergic rhinitis, and atopic dermatitis commonly have moderately elevated serum IgE levels. However, a serum IgE level which is within the range of normally expected values does not rule out a limited set of IgE-dependent allergies.[2]

Total serum IgE measurements may be most valuable for children to assist in differentiating between atopic and non-atopic individuals and to predict the probability of developing allergic disorders. Elevated serum IgE in neonates and children under two years of age is often associated with the development of a clinically significant atopic allergic disorder. There is not, however, a close correlation between the severity of the allergic reaction and the concentration of IgE antibodies in serum.[3]

Total serum IgE levels may also be elevated in the presence of some clinical conditions that are not related to allergy. These clinical conditions include parasitic infections, immunodeficiency states, autoimmune diseases, Hodgkin's disease, bronchopulmonary aspergillosis, IgE myeloma, and Sezary syndrome.[4]

Principles of the Procedure

The ADVIA Centaur Total IgE assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of two antibodies to IgE. The first antibody, in the Lite Reagent, is a goat anti-human IgE antibody labeled with acridinium ester. The second antibody, in the Solid Phase, is a mouse anti-human IgE antibody, which is covalently coupled to paramagnetic particles.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur Total IgE ReadyPack® primary reagent pack; Lite Reagent	5.0 mL/reagent pack goat anti-human IgE antibody (~2.4 µg/mL) labeled with acridinium ester in buffer with sodium azide (0.12%), protein stabilizers, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 28 days
ADVIA Centaur Total IgE ReadyPack primary reagent pack; Solid Phase Reagent	22.5 mL/reagent pack mouse anti-human IgE antibody (~0.02 mg/mL) covalently coupled to paramagnetic particles in buffer with protein stabilizers, sodium azide (0.11%), and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 28 days
ADVIA Centaur Total IgE ReadyPack ancillary reagent pack; IgE Diluent[a] DIL	5.0 mL/reagent pack IgE-free human plasma with sodium azide (0.1%)	2–8°C.	**Unopened:** Until the expiration date on the pack **On-system:** 28 consecutive days after accessing the ancillary reagent pack
ADVIA Centaur IgE Diluent[a] DIL	10.0 mL/vial IgE-free human plasma with sodium azide (0.1%)	2–8°C.	**Unopened:** Until the expiration date on the vial

a See *Optional Materials*

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on www.siemens.com/diagnostics.

CAUTION POTENTIAL BIOHAZARD

Contains human source material. While each human serum or plasma donor unit used in the manufacture of this product was tested by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2, all products manufactured using human source material should be handled as potentially infectious. Because no test method can offer complete assurance that hepatitis B or C viruses, HIV, or other infectious agents are absent, these products should be handled according to established good laboratory practices.[5–7]

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

CAUTION

Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to the system operating instructions.

CAUTION

Discard the primary reagent packs at the end of the on-system stability interval.
Do not use reagents beyond the expiration date.

Storing and Stability

Store the reagents upright at 2–8°C.

Protect reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from heat and light sources.

All reagents are stable at 2–8°C until the expiration date on the packaging.

Specimen Collection and Handling

Serum and plasma (EDTA and lithium heparin) are the recommended sample types for this assay.

The following recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI):[8]

- Collect all blood samples observing universal precautions for venipuncture.
- Allow samples to clot adequately before centrifugation.
- Keep tubes stoppered and upright at all times.
- Do not use samples that have been stored at room temperature for longer than 8 hours.
- Tightly cap and refrigerate specimens at 2–8°C if the assay is not completed within 8 hours.
- Freeze samples at or below -20°C if the sample is not assayed within 48 hours.
- Freeze samples only once and mix thoroughly after thawing.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
03359776 (110778)	5 ReadyPack primary reagent packs containing ADVIA Centaur tIgE Lite Reagent and Solid Phase ADVIA Centaur and ADVIA Centaur CP tIgE Master Curve card	250
06843687 (110777)	1 ReadyPack primary reagent pack containing ADVIA Centaur tIgE Lite Reagent and Solid Phase ADVIA Centaur and ADVIA Centaur CP tIgE Master Curve card	50

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description	
REF 10492491	ADVIA Centaur Calibrator 80	2 vials of low calibrator CAL L 2 vials of high calibrator CAL H

Optional Materials

The following materials may be used to perform this assay, but are not provided:

Item	Description	
REF 02388586 (110324)	ADVIA Centaur IgE Diluent DIL	2 ReadyPack ancillary reagent packs containing 5 mL/pack
REF 07211110 (672265)	ADVIA Centaur IgE Diluent DIL	10 mL/vial
REF 672423	ADVIA Centaur IgE Master Curve Material	7 x 1 mL

Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following steps:

1. Dispenses 30 µL of sample into a cuvette.
2. Dispenses 100 µL of Lite Reagent and 450 µL of Solid Phase and incubates for 7.5 minutes at 37°C.
3. Separates, aspirates, and washes the cuvettes with reagent water.

   Note For information about reagent water, refer to the system operating instructions.
4. Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
5. Reports results according to the selected option, as described in the system operating instructions.

A direct relationship exists between the amount of total IgE present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Preparing the System

Ensure that the system has sufficient primary and ancillary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Load the ReadyPack reagent packs in the primary reagent area using the arrows as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about loading reagents, refer to the system operating instructions.

If automatic dilution of a sample is required, load ADVIA Centaur IgE Diluent in the ancillary reagent entry.

Preparing the Samples

This assay requires 30 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For detailed information about determining the minimum required volume, refer to the system operating instructions.

Note The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. For detailed information, refer to *Dilutions*.

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter.
- Samples are free of bubbles.

On-System Stability

The ADVIA Centaur Total IgE assay reagents are stable unopened until the expiration date on the carton or onboard the system for 28 days.

Performing Calibration

For calibration of the ADVIA Centaur Total IgE assay, use the ADVIA Centaur Calibrator 80. Perform that calibration as described in the calibrator instructions for use.

Calibration Frequency

Calibrate the assay at the end of the 28-day calibration interval.

Additionally, the ADVIA Centaur Total IgE assay requires a two-point calibration:

- When changing lot numbers of primary reagent packs.
- When replacing system components.
- When quality control results are repeatedly out of range.

Performing Master Curve Calibration

The ADVIA Centaur Total IgE assay requires a Master Curve calibration when using a new lot number of Lite Reagent and Solid Phase. For each new lot number of Lite Reagent and Solid Phase, use the barcode reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

For detailed information about entering quality control values, refer to the system operating instructions.

To monitor system performance and chart trends, as a minimum requirement, two levels of quality control material should be assayed on each day that samples are analyzed. Quality control samples should also be assayed when performing a two-point calibration. Treat all quality control samples the same as patient samples.

Siemens Healthcare Diagnostics recommends the use of commercially available quality control materials with at least 2 levels (low and high). A satisfactory level of performance is achieved when the analyte values obtained are within the Acceptable Control Range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme.

Taking Corrective Action

If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.

Results

Calculation of Results

For detailed information about how the system calculates results, refer to the system operating instructions.

The system reports total IgE results in IU/mL.

Dilutions

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to the following information for the sample volume required to perform onboard dilutions:

Dilution	Sample Volume (µL)
1:5	35

The following information pertains to dilutions:

- Samples with total IgE levels greater than 3000 IU/mL must be diluted and retested to obtain accurate results.
- Patient samples can be diluted automatically by the system or prepared manually. For automatic dilutions, ensure that ADVIA Centaur IgE Diluent is loaded and set the system parameters as follows:

  Dilution point: ≤ 3000 IU/mL

  Dilution factor: 5

  For detailed information about automatic dilutions, refer to the system operating instructions.
- Manually dilute the patient samples when patient results exceed the linearity of the assay using automatic dilution, or when laboratory protocol requires manual dilution.
- Use IgE Diluent to manually dilute patient samples, and then load the diluted sample in the sample rack, replacing the undiluted sample.
- Ensure that results are mathematically corrected for dilution. If a dilution factor is entered when scheduling the test, the system automatically calculates the result.

Interpretation of Results

Results of this assay should always be interpreted in conjunction with patient's medical history, clinical presentation and other findings.

Limitations

Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[9] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.

Expected Values

The expected results for the ACS:180® Total IgE assay were previously established. Data was obtained on serum samples from 103 clinically normal adults. The observed range of these samples was 0 to 378 IU/mL with a geometric mean of 17 IU/mL. Refer to the following table for the distribution:

% of Samples	Had IgE values less than . . . (IU/mL)
50	18
90	128
95	158

Samples from 109 healthy children were also assayed with the following results:

Age (years)	N	Geometric Mean (IU/mL)	Geometric Mean +/- 2SD (IU/mL)	Range (IU/mL)
< 1	7	8.5	0.61–117.4	1.4–52.3
1–4	45	9.3	0.28–313.5	0.4–351.6
5–10	30	18.5	0.61–555.1	0.5–393.0
11–15	27	25.7	1.40–481.1	1.9–170.0

These results were confirmed for the ADVIA Centaur Total IgE assay by analyzing 326 samples in the range of 2.0 to 2951.6 IU/mL. Refer to *Accuracy/Method Comparison*.

As with all diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.[10]

Performance Characteristics

Measuring Interval

1.5–3000 IU/mL

The lower limit of the measuring interval is defined by the analytical sensitivity. Report results below the measuring interval as < 1.5 IU/mL.

When sample results exceed the measuring interval, refer to *Dilutions*.

Specificity

The cross-reactivity of the ADVIA Centaur Total IgE assay with IgG, IgA, and IgM was determined by adding these immunoglobulins to samples containing IgE. The total IgE level in the sample then was determined.

Cross-reactant	Total IgE value without cross-reactant (IU/mL)	Total IgE value with cross-reactant (IU/mL)
IgG; 15 mg/mL	23.0	26.6
IgA; 4 mg/mL	23.4	24.6
IgM; 6 mg/mL	14.5	15.3

Interference testing was determined according to CLSI Document EP7-A2.[11]

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[12]

Limit of Blank (LoB)	1.5 IU/mL
Limit of Detection (LoD)	2.0 IU/mL
Limit of Quantitation (LoQ)	2.5 IU/mL

The LoB corresponds to the highest measurement likely to be observed for a blank sample with a probability of 95%.

The LoD corresponds to the lowest concentration of total IgE that can be detected with a probability of 95%.

The LoQ corresponds to the lowest amount of total IgE in a sample at which the within laboratory CV is ≤ 20%.

Sensitivity

The ADVIA Centaur Total IgE assay measures total IgE concentrations up to 3000 IU/mL with a minimum detectable concentration of 1.5 IU/mL as determined by the serial dilution of 10 serum samples.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[13] Samples were assayed in duplicate in 2 runs per day for 20 days. The following results were obtained:

			Repeatability		Within-Laboratory Precision	
Specimen Type	**N [a]**	**Mean IU/mL**	**SD [b] IU/mL**	**CV [c] (%)**	**SD IU/mL**	**CV (%)**
Serum A	80	10.89	0.68	N/A [d]	0.75	N/A
Serum B	80	43.13	1.26	2.9	1.44	3.3
Serum C	80	2155.94	154.02	7.1	189.39	8.8
Plasma, EDTA	80	1002.74	32.26	3.2	36.18	3.6
Plasma, Heparin	80	134.03	3.38	2.5	3.94	2.9
Control 1	80	361.48	11.12	3.1	14.58	4.0
Control 2	80	106.81	2.46	2.3	5.74	5.4
Control 3	80	142.55	3.11	2.2	4.50	3.2

a Number of results.
b Standard deviation.
c Coefficient of variation.
d Not applicable.

Assay results obtained at individual laboratories may vary from the data presented.

The assay was designed to have the following precision.

Concentration Interval	Design Requirements	
IU/mL	Repeatability (Within-Run)	Within-Laboratory (Total Precision)
≤ 15.0	≤ 0.75 IU/mL SD	≤ 1.05 IU/mL SD
15.0–100.0	≤ 5% CV	≤ 7% CV
100.0–500.0	≤ 7% CV	≤ 10% CV
500.0–3000.0	≤ 10% CV	≤ 15% CV

Accuracy / Method Comparison

For 326 samples in the range of 2.0 to 2951.6 IU/mL, the relationship between the ADVIA Centaur Total IgE assay and the ACS:180 Total IgE assay is described by the equation:

ADVIA Centaur Total IgE = 1.04 (ACS:180 Total IgE) + 2.91

Correlation coefficient (r) = 0.99

Specimen Equivalency

Specimen equivalency was determined with the weighted Deming linear regression model in accordance with CLSI Document EP09-A3.[14] The following results were obtained:

Tube (y) vs. Serum (x)	N [a]	Sample Interval	Slope	Intercept	r [b]
Dipotassium EDTA plasma	73	2.80–2748.84 IU/mL	0.99	0.28 IU/mL	1.00
Lithium heparin plasma	73	2.80–2748.84 IU/mL	1.00	0.18 IU/mL	1.00

a Number of samples tested.
b Correlation coefficient.

The assay is designed to have a slope of 0.90–1.10 for alternate tube types versus serum.

Agreement of the specimen types may vary depending on the study design and sample population used. Assay results obtained at individual laboratories may vary from the data presented.

Interferences

Interference testing was performed in accordance with CLSI Document EP07-ed3.[15] The following results were obtained:

Substance	Substance Test Concentration	Analyte Concentration IU/mL	Bias (%)
Dipotassium EDTA	9.0 mg/mL	121.51	-1.7
		1624.13	1.4
Heparin	75 U/mL	167.48	-1.7
		1450.12	-1.1

Assay results obtained at individual laboratories may vary from the data presented.

Hemolysis, Icterus, and Lipemia (HIL)

Serum specimens that are . . .	Have an insignificant effect on the assay up to . . .
hemolyzed	500 mg/dL of hemoglobin
lipemic	3000 mg/dL of triglycerides
icteric	20 mg/dL of bilirubin

Dilution Recovery

Ten human serum samples in the range of 563.4 to 2975.7 IU/mL of total IgE were diluted 1:2, 1:4, and 1:8 with IgE Diluent and assayed for recovery and parallelism. The recoveries ranged from 86.9% to 116.0% with a mean of 100.3%.

Sample	Dilution	Observed (IU/mL)	Expected (IU/mL)	Recovery %
1	—	1029.7		
	1:2	527.1	514.9	102.4
	1:4	260.7	257.4	101.3
	1:8	125.2	128.7	97.3
	Mean			100.3
2	—	1536.0		
	1:2	730.1	768.0	95.1
	1:4	394.0	384.0	102.6
	1:8	183.9	192.0	95.8
	Mean			97.8
3	—	582.7		
	1:2	279.7	291.4	96.0
	1:4	131.5	145.7	90.3
	1:8	63.3	72.8	86.9
	Mean			91.1
4	—	563.4		
	1:2	305.4	281.7	108.4
	1:4	147.0	140.9	104.4
	1:8	66.2	70.4	94.0
	Mean			102.3
5	—	712.3		
	1:2	363.2	356.2	102.0
	1:4	172.7	178.1	97.0
	1:8	86.6	89.0	97.3
	Mean			98.7
6	—	1461.9		
	1:2	730.4	731.0	99.9

Sample	Dilution	Observed (IU/mL)	Expected (IU/mL)	Recovery %
	1:4	363.8	365.5	99.5
	1:8	172.6	182.7	94.5
	Mean			98.0
7	—	1942.8		
	1:2	989.0	971.4	101.8
	1:4	519.8	485.7	107.0
	1:8	257.9	242.9	106.2
	Mean			105.0
8	—	2975.7		
	1:2	1525.9	1487.9	102.6
	1:4	707.0	743.9	95.0
	1:8	351.2	372.0	94.4
	Mean			97.3
9	—	2477.6		
	1:2	1287.1	1238.8	103.9
	1:4	645.6	619.4	104.2
	1:8	335.8	309.7	108.4
	Mean			105.5
10	—	2409.1		
	1:2	1253.5	1204.6	104.1
	1:4	698.9	602.3	116.0
	1:8	301.6	301.1	100.2
	Mean			106.8
Mean				**100.3**

Spiking Recovery

Varying amounts of total IgE were added to five samples with endogenous total IgE levels ranging from 9.9 to 43.1 IU/mL. The recoveries ranged from 88.5% to 128.6% with a mean of 102.1%.

Sample	Amount Added (IU/mL)	Observed (IU/mL)	Recovery %
1	—	36.0	
	20.3	62.1	128.6
	103.0	141.0	101.9
	566.0	585.0	97.0
	1292.0	1203.0	90.3
	Mean		104.5
2	—	18.9	
	20.3	44.0	123.6
	103.0	128.0	105.9
	566.0	595.0	101.8
	1292.0	1250.0	95.3
	Mean		106.7
3	—	9.9	
	20.3	30.0	99.0
	103.0	107.0	94.3
	566.0	542.0	94.0
	1292.0	1153.0	88.5
	Mean		94.0
4	—	43.1	
	20.3	64.7	106.4
	103.0	154.0	107.7
	566.0	563.0	91.9
	1292.0	1191.0	88.8
	Mean		98.7
5	—	15.8	
	20.3	41.5	126.6
	103.0	123.0	104.1
	566.0	596.0	102.5
	1292.0	1224.0	93.5
	Mean		106.7
Mean			**102.1**

High-Dose Hook Effect

Patient samples with high total IgE levels can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with total IgE levels as high as 10,000 IU/mL will assay greater than 3000 IU/mL.

Standardization

The ADVIA Centaur Total IgE assay is standardized to World Health Organization (WHO) 75/502. Assigned values for calibrators are traceable to this standardization.

Technical Assistance

For customer support, please contact your local technical support provider or distributor.

www.siemens.com/diagnostics

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11. Clinical and Laboratory Standards Institute (formerly NCCLS). *Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition.* Wayne, PA: Clinical and Laboratory Standards Institute; 2005. NCCLS Document EP7-A2.
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14. Clinical and Laboratory Standards Institute. *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2013. CLSI Document EP09-A3.
15. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2018. CLSI Document EP07-ed3.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat	UP	Up
	Use by	Σ (n)	Contains sufficient for (n) tests
LOT	Batch code		Shake the reagent pack vigorously. Refer to *Preparing Reagents* in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	Rev.	Revision
MC DEF	Master Curve Definition	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
LOT DTL	Lot Details	DER GRÜNE PUNKT	Green dot
	Recycle	PRINTED WITH SOY INK	Printed with soy ink

Trademarks

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