ReQuest® ANTI-Sm

REF 01-230 96-Test Set IVD

Intended Use: For the qualitative and semi-quantitative detection of human IgG antibodies to Sm in human serum by enzyme immunoassay, as an aid in the diagnosis of systemic lupus erythematosus (SLE). This assay has not been cleared / approved by the FDA for blood / plasma donor screening.

For in vitro diagnostic use only.

Summary of Test

1. Prepare 1:51 dilutions of Calibrator(s), Controls and samples in the Diluent. Mix well.
2. Place 100 µl of the dilutions in the Sm IgG Coated Wells; reserve one well for the reagent blank.
3. Incubate at room temperature for 30 ± 5 minutes.
4. Drain wells thoroughly. Wash wells 4 times with diluted Wash solution and drain.
5. Place 100 µl of Sm IgG Conjugate in wells.
6. Incubate at room temperature for 30 ± 5 minutes.
7. Drain wells thoroughly. Wash wells 4 times with diluted Wash solution and drain.
8. Place 100 µl of Substrate in wells.
9. Incubate at room temperature for 30 ± 5 minutes.
10. Stop the enzyme reaction with 100 µl of Stop.
11. Read absorbance at 405 nm against reagent blank.

Summary and Explanation of Test

The presence of one or more circulating autoantibodies to intracellular antigens is characteristic of the systemic rheumatic diseases. As the understanding of the nature of these antigens has grown, it has become increasingly clear that these diseases are distinguished by the presence of different sets of antibodies, giving each of the systemic rheumatic diseases a characteristic autoantibody profile. Therefore, the detection and identification of the circulating autoantibodies is helpful in the differential diagnosis of: systemic lupus erythematosus (SLE), polymyositis, Sjogren's syndrome, scleroderma, mixed connective tissue disease (MCTD), and drug-induced autoimmunity (1-3).
Autoantibodies to Sm are restricted to SLE, therefore they are highly specific marker antibodies for the differential diagnosis of this disease (1). Anti-Sm is present in approximately 35 % of SLE patients (2). Furthermore, anti-Sm in the absence of other autoantibodies has been related to isolated central nervous system disease in lupus (4).

The ReQuest® ANTI-Sm test is an ELISA which utilizes a microwell format. Test results are obtained after one and one-half hours incubation time. They are objective and normalized as Index values which are traceable to an in-house anti-Sm standard.

Principle of the Test

Diluted samples are incubated in antigen-coated wells. Sm IgG antibodies (if present) are immobilized in the wells. Residual sample is eliminated by washing and draining, and conjugate (enzyme labeled antibodies to human IgG) is added and incubated. If IgG antibodies to Sm are present, the conjugate will be immobilized in the wells. Residual conjugate is eliminated by washing and draining, and the substrate is added and incubated. In the presence of the enzyme, the substrate is converted to a yellow end product which is read photometrically.

Reagents

Coated Wells	Coated with calf thymus Sm antigen. 12 eight-well strips.
Well Support	One
Diluent*	25 ml (pink color). Diluent for specimens. Contains a protein stabilizer.
Calibrator 1*	0.3 ml. Human serum. Strongly reactive for Sm IgG antibodies. Index value shown on vial label.
Calibrator 2*	0.3 ml. Human serum. Moderately reactive for Sm IgG antibodies. Index value shown on vial label.
Positive Control*	0.3 ml. Human serum. Reactive for Sm IgG antibodies. Index value range shown on vial label.
Negative Control*	0.3 ml. Human serum. Non-reactive for Sm IgG antibodies.
Conjugate	12 ml (green color). Goat anti-human IgG labeled with Alkaline phosphatase (calf).
Substrate	12 ml. Substrate solution. *p*-nitrophenyl phosphate.

Note: The substrate may develop a slight yellow color during storage. One hundred microliters of substrate should yield an absorbance value less than 0.35, when read in a microwell against air or water.

Wash (30x)*	30 ml. Wash Solution (30x). Prepare Wash Solution by adding the contents of the Wash (30x) bottle to 1 liter of distilled or deionized water.
Stop Reagent	12 ml. Trisodium phosphate 0,5 M.

* Contains sodium azide.

Store these reagents according to the instructions on the bottle labels. Do not allow them to contact the skin or eyes. If contact occurs, wash with copious amounts of water.

Other Materials Required

1. Wash bottle
2. Pipettors for dispensing 4, 100 and 200 µl
3. Timer
4. 1 or 2 liter container for Wash Solution
5. Distilled or deionized water
6. Dilution tubes or microwells
7. Microwell reader capable of reading absorbance at 405 nm

CE

L-01-230-7
2017-06

ReQuest® ANTI-Sm

Precautions

1. For in vitro diagnostic use.
2. Test samples, Calibrator(s), Controls and the materials that contact them, should be handled as potential biohazards. The calibrators and controls have been found to be negative for HIV, hepatitis B surface antigen and HCV antibodies by licensed tests. However, because no method can offer complete assurance that HIV, hepatitis B virus, HCV or other infectious agents are absent, these materials should be handled at the Biosafety Level 2 as recommended for any potentially infectious serum or blood specimen in the Centers for Disease Control/National Institutes of Health Manual "Biosafety in Microbiological and Biomedical Laboratories", 1993, or latest edition.
3. The concentrations of anti-Sm in a given specimen determined from assays from different manufacturers can vary due to differences in assay methods and reagent specificity.
4. Avoid contact with open skin.
5. Never pipet by mouth.
6. Certain of the test reagents contain sodium azide. Azides are reported to react with lead and copper in plumbing to form compounds that may detonate on percussion. When disposing of solutions containing sodium azide, flush drains with large volumes of water to minimize the build-up of metal-azide compounds.
7. Do not interchange reagents from different reagent lots, except for Wash, Substrate and Stop Reagent.
8. Do not use reagents beyond their stated expiration date.
9. Incubation times recommended in the Test Procedure section should be adhered to.
10. Unused Sm IgG Coated Wells should be kept in their resealable bag with desiccant, and stored in the refrigerator.
11. This product should be used by qualified personnel.

Specimen Collection

Sera should be separated from clotted blood. If specimens are not tested within 8 hours, they should be stored at 2 to 8ºC for up to 48 hours. Beyond 48 hours specimens should be stored at -20ºC or below. Multiple freeze-thaw cycles should be avoided. Samples containing visible particulate matter should be clarified by centrifugation; and hemolyzed, icteric or grossly contaminated samples should not be used. Samples should not be heat-inactivated before testing.

Test Procedure

Allow all reagents and patient samples to reach room temperature before use. Return them promptly to refrigerator after use. The manual test procedure follows:

1. Prepare 1:51 dilutions of test samples, Calibrator(s), Positive and Negative Controls, in the test set Diluent. For example: add 4 µl of sample to 200 µl of Diluent in a dilution well or tube, and mix well.
   Note: For qualitative assays, a single Calibrator (Sm IgG Calibrator 2) may be used; for semi-quantitative and quantitative assays, use Sm IgG Calibrator 1 and Sm IgG Calibrator 2.
2. Place an appropriate number of coated wells from Sm IgG Wells in the Well Support.
3. Transfer 100 µl of each diluted Calibrator, Control and patient sample to the wells.
   Note: Include one well which contains 100 µl of Diluent only. This will serve as the reagent blank and will be ultimately used to zero the photometer before reading the test results.
4. Incubate the wells at room temperature (20 to 25ºC) for 30 ± 5 minutes.
5. Wash wells four times with diluted Wash solution, drain thoroughly.
6. Place 100 µl of Sm IgG Conjugate into each well.
7. Incubate the wells at room temperature for 30 ± 5 minutes.
8. Wash the wells four times with diluted Wash solution, drain thoroughly.
9. Place 100 µl of Substrate into each well.
10. Incubate at room temperature for 30 ± 5 minutes.
11. Place 100 µl of Stop into each well.
12. Read and record the absorbance of the contents of each well at 405 nm against the reagent blank.
    Note: Adjust the photometer to zero absorbance at 405 nm against the reagent blank. Readings should be made within 2 hours after the reactions have been stopped.

Calculation of Results

Qualitative results may be calculated using a single calibrator. For semi-quantitative results, use a calibration curve consisting of two or more calibrators.

Single Calibrator (Calibrator 2)
Determine the Index value for each test sample (or Control) using the following formula:

$$\frac{\text{Calibrator 2 Index}}{\text{Calibrator 2 Absorbance}} \times \text{Test Sample Absorbance} = \text{Test Sample Index}$$

If the Calibrator is run in duplicate, use the average absorbance value to calculate results.

Calibration Curve. Semi-quantitative determination.
Alternatively, test results may be calculated from a three-point curve comprised of: Sm IgG Calibrator 1 (high-point), Sm IgG Calibrator 2 (mid-point) and the reagent blank (zero / origin), using a point-to-point curve fit.
The upper range of the curve may be expanded by adding additional points. For example: the concentration of Calibrator 1 may be increased 1.5-fold, and 2-fold, by adding 6 µl and 8 µl of Sm IgG Calibrator 1 to 200 µl of the Diluent, and transferring 100 µl of each dilution to coated wells. The Index values, assigned to these points, should be 1.5 and 2 times respectively, the value shown on the Sm IgG Calibrator 1 label. The extent, to which the upper range of the standard curve may be expanded, will be limited by the calibrator(s) being used.

Quality Control

1. The Calibrator(s), Positive Control and Negative Control must be included in each test run.
2. The absorbance values of Calibrator 1 must be at least 0.4, when read against the reagent blank.
3. The absorbance value of the reagent blank should be less than 0.35.

L-01-230-7
2017-06

CE

4. The Negative Control must have an Index value less than 0.9. This control is used to validate the assay below the cutoff of the assay.
5. The Positive Control must have an Index value within the ranges printed on the label. When performing qualitative tests, users may supply alternative positive controls if they wish.
6. To validate the upper range of the assay when performing the semi-quantitative and quantitative procedures, the Positive Control should be run at higher concentrations. For example, the Positive Control should be assayed at 1.5-fold and 2-fold concentrations by adding 6 µl and 8 µl of the Positive Control, to 200 µl aliquots of the test set Diluent, and transferring 100 µl of each of these dilutions to coated wells. The expected value ranges for these concentrated controls would be 1.5 times and 2 times respectively, the expected value ranges printed on the Positive Control label. If the control values do not fall within the specified ranges, the assay is invalid and should be repeated. Optionally, users may supply alternative positive controls if they wish.
7. The Negative Control and Positive Control are intended to monitor for substantial reagent failure. The Positive Control will not ensure precision at the assay cutoff. Users may wish to establish an in-house control, having a quantitative value determined by replicate testing, at or near the cutoff of the assay, to monitor the precision of the assay cutoff. Additional controls may be tested according to guidelines or requirements of local, state and/or federal regulations or accrediting organizations. For guidance on appropriate quality control practices, please refer to NCCLS document C24-A, Internal Quality Control Testing: Principles and Definitions.
8. If any of these criteria are not met, the test is invalid and should be repeated.

Interpretation of Results

Index Value	Interpretation
<0.9	Negative for Sm IgG antibody.
≥ 0.9 to < 1.1	Equivocal
≥ 1.1	Positive for Sm IgG antibody.

Specimens which yield absorbance values above the range of the test set calibrator(s) may be reported as greater than the Index value of the uppermost point of the calibration curve. Alternatively, such specimens may be pre-diluted in the Diluent and reassayed. The resulting Index value must be multiplied by the dilution factor for reporting. *Example: If the specimen has been pre-diluted 1:5 before testing, the resulting Index value should be multiplied by 5.*
Differences in the antibody anti-Sm levels which are greater than the imprecision of the assay, i.e. > 20% (Mean intra-assay CV + 3 SD, see Tables 5, 6, 7 and 8) are considered significant.
The suggested method for reporting results is: The following results were obtained with the ReQuest® ANTI-Sm test. Values obtained with different manufacturer's assay methods may not be used interchangeably. The magnitude of the reported IgG level cannot be correlated to an endpoint titer. When the assay is used qualitatively, the magnitude of results above the cut-off is not an indicator of total antibody present.

Limitations

The results obtained with the ReQuest® ANTI-Sm test serve only as an aid to diagnosis and should not be interpreted as diagnostic in themselves. A positive result is suggestive of SLE and should be confirmed by other clinical findings.
Some individuals may have high levels of Sm antibodies, with no evidence of clinical disease. In contrast, some individuals with clinical disease may not exhibit detectable levels of anti-Sm.
This assays performance characteristics of ReQuest® ANTI-Sm have not been established for testing matrices other than human serum.
Titration experiments (please see Figure 1) have shown that the upper limit of linearity for ReQuest® ANTI-Sm index values is approximately 9.

Expected Values

The normal range of the ReQuest® ANTI-Sm test was determined with serum specimens obtained from 88 normal donors. The mean Index value was 0.2 and the standard deviation was 0.1. The positive Index cutoff value was set at 1.1.

373 serum samples obtained from 276 patients with clinically diagnosed disease, including systemic rheumatic disease and 97 normal donors were assayed by the ReQuest® ANTI-Sm test. The incidence of these values is shown in Table 1.

Table 1. Results of tests of 276 serum from patients with clinically diagnosed disease, including systemic rheumatic disease, and from 97 normal blood donors, performed at SeraQuest® (Lab B, Miami, FL), using the ReQuest® ANTI-Sm test.

Donor Group	n	Ranges : Index Values				
		Index	< 1.1	≥ 1.1 < 10	≥ 10 < 20	≥ 20
Asymptomatic Normal	97		97 (100%)	0	0	0
Systemic Lupus Erythematosus	171		118 (69%)	32 (22%)	16 (9%)	0
SLE/Sec. Sjogren's Syndrome	13		5 (38%)	5 (38%)	3 (24%)	0
Subacute Lupus	5		2 (40%)	3 (60%)	0	0
Sjogren's Syndrome	31		30 (98%)	1 (2%)	0	0
MCTD	8		3 (38%)	4 (50%)	1 (12%)	0
MCTD/Sec. Sjogren's Syndrome	5		1 (20%)	3 (60%)	1 (20%)	0
UCTD	2		1 (50%)	1 (50%)	0	0
Crest	1		1 (100%)	0	0	0
Raynaud's Phenomenon	2		2 (100%)	0	0	0
Rheumatoid Arthritis (RA)	16		16 (100%)	0	0	0
RA/Sec. Sjogren's Syndrome	5		5 (100%)	0	0	0
Osteoarthritis	2		2 (100%)	0	0	0
Hepatitis	2		2 (100%)	0	0	0
Neoplasia	1		1 (100%)	0	0	0
Thrombopenia	1		1 (100%)	0	0	0
Vasculitis	3		3 (100%)	0	0	0
Leukemia	4		3 (75%)	1 (25%)	0	0
Multiple Sclerosis	1		1 (100%)	0	0	0
Hypertension	2		2 (100 %)	0	0	0

n= total specimens in donor group; (%) = percentage of the donor group, Sec = secondary; MCTD = mixed connective tissue disease and UCTD = undifferentiated connective tissue disease.

L-01-230-7
2017-06

CE

Performance Characteristics

Comparative Testing

The results of ReQuest® ANTI-Sm tests correlate well with other commercial serological tests. Sera from clinically diagnosed patients, as well as from serum normal donors, were assayed for the presence of anti-Sm IgG antibodies, using the ReQuest® ANTI-Sm test, and another commercial EIA test. The assays were performed at two independent laboratory (Lab A, Barcelona, Spain and Lab B, Madrid, Spain), and at Quest International (Lab C, Doral, FL). The results obtained in these studies are shown below in Tables 2, 3 and 4, respectively.

Table 2. Results of tests of 89 specimens from clinically diagnosed patients and normal donors (100 % frozen), performed at Laboratory A (Barcelona, Spain), using the ReQuest® ANTI-Sm test and another commercial EIA test.

	Comparative ReQuest® ANTI-Sm test					
Test 1	Positive	Equivocal	Negative		%	95% CI**
Positive	14 {14}	0	0	Relative sensitivity	100	86.7 to 100 %
Negative	4 {3}	3 {3}	68 {40}	Relative specificity*	94.4	89.2 to 99.7 %
				Overall Agreement*	95.3	90.9 to 99.8 %

* Excluding equivocal results.
** Calculated by the Normal Method (5).
{ } Clinically diagnosed SLE.

Table 3. Results of tests of 120 specimens from clinically diagnosed patients and normal donors (100% frozen), performed at Laboratory B (Madrid, Spain), using the ReQuest® ANTI-Sm test and another commercial EIA test.

	Comparative ReQuest® ANTI-Sm test					
Test 1	Positive	Equivocal	Negative		%	95% CI**
Positive	37 {27}	0	2 {1}	Relative sensitivity	94.8	87.9 to 100 %
Negative	9 {5}	2 {2}	70 {33}	Relative specificity*	88.6	81.6 to 95.6 %
				Overall Agreement*	90.6	85.4 to 95.9 %

* Excluding equivocal results
** Calculated by the Normal Method (5).
{ } Clinically diagnosed SLE.

Table 4. Results of tests of 215 specimens from clinically diagnosed patients, normal donors (100% frozen), performed at Quest International (Lab C, Doral, FL), using the ReQuest® ANTI-Sm test and another commercial EIA test.

	Comparative ReQuest® ANTI-Sm test					
Test 1	Positive	Equivocal	Negative		%	95% CI**
Positive	10 {5}	0	1 {0}	Relative sensitivity	90.9	79.3 to 100 %
Negative	15 {7}	3 {0}	207 {38}	Relative specificity*	93.2	89.9 to 96.5 %
				Overall Agreement*	93.1	89.9 to 96.4 %

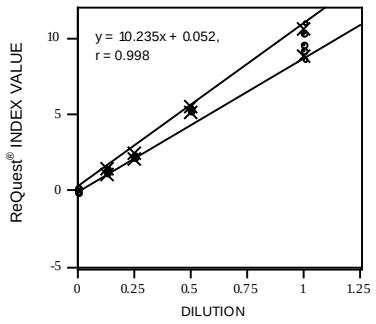
* Excluding equivocal results
** Calculated by the Normal Method (5).
{ } Clinically diagnosed SLE.

Please be advised that “relative” refers to the comparison of this assay’s results to that of a similar assay. There was not an attempt to correlate the assay’s results to disease presence or absence. No judgment can be made on the comparison assay’s accuracy to predict disease.

Titration curve

Several strongly positive serum specimens were serially diluted (two-fold) in triplicate, and assayed by the ReQuest® ANTI-Sm test. Typical results are shown in Figure 1.

Figure 1. Titration curve for a strongly positive specimen.



The triplicate data for each dilution are shown as points, the 95 % confidence limits for each set of triplicate data are indicated by (x's), and the 95 % confidence limits for the slopes and y-intercepts are represented by straight lines. The formula for the linear regression for the triplicate data is shown in Figure 1.

L-01-230-7
2017-06

CE

ReQuest® ANTI-Sm

Specificity

The ReQuest® ANTI-Sm test is specific for IgG antibodies directed against Sm, and does not cross-react with other nuclear antigens. Of 75 specimens which were unreactive in the ReQuest® Anti-Sm test, 42 were shown positive for IgG antibody directed against dsDNA antigen, 31 against Sm/RNP complex, 36 against SSA antigen and 17 against SSB.

Precision

Eight serum specimens (2 negative and 6 positive) and the Sm IgG Positive Control and Sm IgG Negative Control, were assayed in triplicate, on three separate occasions. The precision experiments were performed at a two independent laboratory (Lab A and Lab B), and at Quest International (Lab C). These results are shown below in Tables 5, 6, 7 and 8, respectively.

Table 5. Results Intra-assay and Inter-assay precision tests performed manually at Laboratory A. Values were calculated from ReQuest® Index value.

Sample	INTRA-ASSAY			INTER-ASSAY		
	Mean (Index)	S.D.	CV%	Mean (Index)	S.D.	CV%
Post. Contr.	2.4	0.000	0	2.7	0.255	9.6
Neg. Contr.	0.0	0.058	NA	0.1	0.053	NA
1	0.0	0.058	NA	0.2	0.173	NA
2	0.3	0.000	NA	0.4	0.117	NA
3	2.4	0.000	0.0	2.8	0.560	20.1
4	2.7	0.173	6.4	3.2	0.975	30.1
5	11.2	2.916	26.0	11.6	1.594	13.8
6	3.6	0.252	7.1	4.2	0.900	21.7
7	2.4	0.153	6.3	2.6	0.242	9.4
8	1.4	0.058	4.0	1.5	0.100	6.8

NA: Not applied

Table 6. Results Intra-assay and Inter-assay precision tests performed manually at Laboratory B. Values were calculated from ReQuest® Index value.

Sample	INTRA-ASSAY			INTER-ASSAY		
	Mean (Index)	S.D.	CV%	Mean (Index)	S.D.	CV%
Post. Contr.	2.6	0.058	2.2	3.0	0.492	16.3
Neg. Contr.	0.0	0.000	NA	0.0	0.000	NA
1	0.1	0.000	NA	0.1	0.033	NA
2	0.3	0.058	NA	0.3	0.060	NA
3	2.4	0.058	2.4	2.7	0.328	12.4
4	3.0	0.231	7.8	4.3	1.163	26.9
5	9.9	0.153	1.5	10.0	2.001	20.0
6	4.4	0.058	1.3	4.8	0.860	17.8
7	2.1	0.058	2.7	2.3	0.222	9.6
8	1.6	0.100	6.3	1.8	0.169	9.5

NA: Not applied

Table 7. Results Intra-assay and Inter-assay precision tests performed manually at Laboratory C. Values were calculated from ReQuest® Index value.

Sample	INTRA-ASSAY			INTER-ASSAY		
	Mean (Index)	S.D.	CV%	Mean (Index)	S.D.	CV%
Post. Contr.	2.6	0.100	3.8	2.6	0.101	3.8
Neg. Contr.	0.0	0.000	NA	0.0	0.000	NA
1	0.0	0.000	NA	0.0	0.033	NA
2	0.1	0.058	NA	0.2	0.044	NA
3	1.9	0.173	9.1	1.9	0.166	8.9
4	2.8	0.208	7.5	2.9	0.209	7.2
5	8.4	0.208	2.5	8.6	0.495	5.7
6	3.2	0.173	5.4	3.4	0.240	7.2
7	2.1	0.060	2.7	2.2	0.090	4.2
8	1.4	0.100	7.1	1.4	0.050	3.6

NA: Not applied

Table 8. Interlaboratory Precision. Tests were performed manually at Laboratory A, B and C. Values were calculated from the ReQuest® Index values.

Sample	Index		
	Mean	S.D.	CV%
Post. Contr.	2.8	0.283	10.2
Neg. Contr	0.0	0.018	NA
1	0.1	0.011	NA
2	0.3	0.015	NA
3	2.5	0.351	14.2
4	3.5	0.782	22.6
5	10.1	1.363	13.5
6	4.1	0.667	16.1
7	2.4	0.185	7.8
8	1.6	0.106	6.8

NA: Not applied

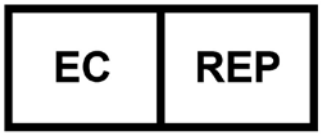
L-01-230-7
2017-06

CE

References

1. Tan, E.M. et al., Antinuclear Antibodies (ANAs): Diagnostically Specific Immune Markers and Clues Toward the Understanding of Systemic Autoimmunity. 47: 121-141, 1988.
2. Harley, J.B., Autoantibodies. Rheum. Dis. Clin. Nr. Am. 14: 43-56, 1988.
3. Tan, E.M. et al., Antibodies to Nuclear Antigens (ANA): Their Immunobiology and Medicine. Adv. Immunol. 33: 167-240, 1982.
4. Winfield, J.B. et al., Avidity of Anti-DNA Antibodies in Serum and IgG Glomerular Eluates from Patients with Systemic
5. Gardner, M. J. and Altman, D.G. Confidence Intervals Rather than Hypothesis Testing. Brit. Med. J., 292: 746-750 (1986)

Manufacturer:
Quest International, Inc.
8127 NW 29th Street
Doral, FL 33122
USA



EMERGO EUROPE
Prinsessegracht 20
2514 AP The Hague
The Netherlands

Symbols Glossary

Symbol	Standard Title and Number	Title of Symbol	Symbol reference #	Explanatory Text
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	Manufacturer	5.1.1	Indicates the medical device manufacturer, as defined in EU Directives 90/385/EEC, 93/42/EEC and 98/79/EC.
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	Authorized representative in the European Community	5.1.2	Indicates the Authorized representative in the European Community.
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	Use-by-date	5.1.4	Indicates the date after which the medical device is not to be used.
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	Batch code	5.1.5	Indicates the manufacturer's batch code so that the batch or lot can be identified.
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	Catalog number	5.1.6	Indicates the manufacturer's catalogue number so that the medical device can be identified.
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	Temperature limit	5.3.7	Indicates the temperature limits to which the medical device can be safely exposed.
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	Consult instruction for use	5.4.3	Indicates the need for the user to consult the instructions for use.
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	*In vitro* diagnostic medical device	5.5.1	Indicates a medical device that is intended to be used as an *in vitro* diagnostic medical device.
	ISO 15223-1: Medical Devices – Symbols to be used with medical device labels, labeling, and information to be supplied	Contains sufficient for 96 tests	5.5.5	Indicates the total number of IVD tests that can be performed with the IVD kit reagents.
Rx Only	Guidance for Industry and FDA on Alternative to Certain Prescription Device Labeling Requirements	Rx Only	N/A	Caution: Federal law prohibits dispensing without prescription.

L-01-230-7
2017-06

CE