ENGLISH

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EXTEL HEMO • AUTO HS Latex
EXTEL HEMO • AUTO Buffer

IVD CE 0123

(Latex Agglutination Reaction Method)

"For Professional Use Only"

This product is an *in vitro* diagnostic reagent for professional use. Before using the product please read carefully this instruction for use.

[Intended Use]

EXTEL HEMO • AUTO HS is an immunological fecal occult blood test reagent for quantitative measurement of human hemoglobin in feces using an automatic analyzer by latex agglutination reaction. The reagent is intended to be used by professional users. Measurement of hemoglobin in feces is used for screening or aid to diagnosis of diseases with lower gastrointestinal bleeding, especially colorectal cancer, advanced adenoma and inflammatory bowel disease.

[Principle of the Test]

Human hemoglobin in feces react with anti-human hemoglobin antibody immobilized to latex particles and causes turbidity change with latex agglutination. Since the change in turbidity is proportional to the hemoglobin concentration in the sample, the hemoglobin concentration in the sample is measured optically by an automatic analyzer.

[Material Provided] (Both products are sold individually)

Code	Product Name	Constituent	Quantity
65553	EXTEL HEMO • AUTO HS Latex	Anti-human hemoglobin sheep antibody immobilized latex suspension (1.5-3.5 mg/mL)	18 mL x 4
65555	EXTEL HEMO • AUTO Buffer	Tris (0.1M)	250 mL x 1

EXTEL HEMO • AUTO HS Latex (The Latex) is provided with a Master Curve Card.

[Material Necessary but not provided]

- 65556 EXTEL HEMO • AUTO HS Calibrator
- 65557 EXTEL HEMO • AUTO HS Control
- 63927, 63631, 63632 EXTEL HEMO・AUTO MC Collection Picker

[Reference Material]

Internal reference material made from human hemoglobin is used and its concentration is determined using the cyanmethemoglobin method. In the case calibrators and controls are analyzed using the internal reference material, traceability is controlled to keep the deviation between the measured value and their assigned value within ±8% for high concentration and ±10% for low concentration.

[Procedure]

This reagent is specially designed for use in fully automated immunoassay analyzers, HM-JACKarc and HM-JACKarcⅡ. Do not use in any other analyzers. For details of the operation procedure, refer to the Instruction Manual for HM-JACKarc or HM-JACKarcⅡ.

Operation procedure in HM-JACKarc / HM-JACKarcⅡ

Be sure to carry out the measurements at the temperature range of 20-30°C with humidity range of 45-85%.

1. Reagent Preparation Method

(a) The Latex

Use the Latex directly after you have restored its temperature to 15-25°C. Just before use, invert to mix and obtain a homogenous reagent.

(b) EXTEL HEMO • AUTO Buffer (The Buffer)

Use the Buffer directly after you have restored its temperature to 15-25°C.

2. Sample Preparation

For fecal sampling, use EXTEL HEMO・AUTO MC Collection Picker in accordance with its Instruction for Use. Do not use any other collection device. Prior to measurement, have the buffer solution inside become 15-25°C and shake the bottle several times. Since the hemoglobin in some feces samples may degrade rapidly, it is recommended to analyze samples as soon as possible.

3. Establishing of Calibration Curve

(a) Enter the master curve in accordance with the Master Curve Card attached to the Latex whenever the lot number of the Latex changes.
(b) Calibrate the master curve with EXTEL HEMO • AUTO HS Calibrator when the lot number of the Latex changes or where appropriate.

4. Performing Quality Control

(a) Use EXTEL HEMO • AUTO HS Control to validate the calibration. Two levels of quality control material should be assayed on each day that samples are analyzed or when performing a two-point calibration. If the quality control results do not fall within the range given in Control Range Sheet of EXTEL HEMO • AUTO HS Control or within the laboratory's established values, check the instrument, reagents and technique for problems.

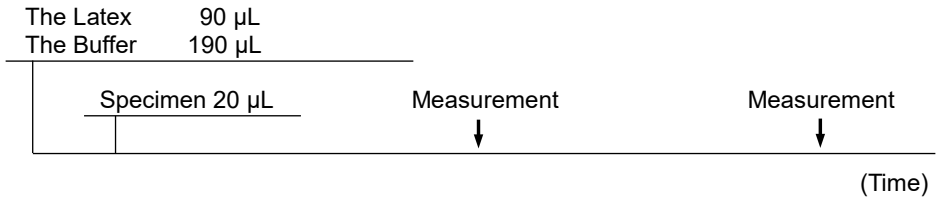
5. Assay Procedure

(a) Input the assay menu into the analyzer.
(b) Place the specimen on the sample rack and the reagent in the prescribed location.
Note: Place the sampler directly in such manner that the bottom of the sampler container faces upward.
(c) After you have depressed the START key, the entire process from sampling of the specimen up to the processing of the data after measurement will be fully automated.

(Reference Assay Procedure)

Be sure to use the appropriate assay parameter depending on each analyzer.

Assay parameter in HM-JACKarc / HM-JACKarc Ⅱ



[Assessment of Results]

1. Unit of measurement value is ng/mL.
2. Cut-off value should be determined by each Laboratory.
3. For clinical diagnosis based on the assay results, the physician in charge should assess the data in a comprehensive manner in conjunction with the clinical symptoms and the results obtained from other equivalent tests.

[Warnings and Precautions]

1. When handling human feces, note that specimens may, in some cases, be contaminated with HBV, HCV, HIV or bacteria. Be sure therefore to wear protective gloves when handling the specimens in order to prevent infection.
2. This product contains sodium azide (0.1% or less). When it has entered the eye or mouth or contacted the skin by accident, be sure to take the necessary emergency measures by rinsing with copious running water. If necessary, seek medical treatment and consult a physician.
3. Sodium azide (0.1% or less) is used as an antiseptic in this reagent. In contact with lead, it reacts vehemently with formation of highly explosive metal azides. When you discard the reagent, be sure therefore to dilute and wash with plenty of water.
4. Do not mix different lots of the Latex for use. Nor add reagent to supplement a shortage.
5. Do not use the Latex and Buffer that have expired their shelf life.
6. Do not use the Latex and Buffer which show obvious changes in appearance such as discoloration or aggregation. That indicates possibility of deterioration.
7. It is recommended to dispose of all waste material in accordance with local regulation.
8. Do not use the containers of this product for any other purpose.

[Storage and Shelf Life]

1. Storage: Store in a dark and cool place (at 2-8°C). Do not freeze under any circumstance.
2. Shelf life: The Latex: 12 months, The Buffer: 24 months

[Storage after Once Opening]

1. Once you have opened the reagent, be sure to close the lid and store at 2-8°C.
2. On-board stability after opening is 20 accumulated hours for the Latex and 14 accumulated days for the Buffer.

[Performance Characteristics]

The following performance data was obtained using HM-JACKarc. There is no difference in performance characteristics between HM-JACKarc and HM-JACKarcⅡ.

1. Analytical Sensitivity

EXTEL HEMO • AUTO HS has the following sensitivity specifications defined as slope of the calibration curve.
• A blank test is 100 or less in ΔIST.
• A test with a human hemoglobin standard solution of 10 ng/mL against a blank test is 80-450 in ΔIST.
When physiological saline solution as blank sample and 10 ng/mL hemoglobin solution were tested using 3 lots of reagent, blank ΔIST was 7 to 30, and 10 ng/mL ΔIST – blank ΔIST was 160 to 260 in our performance evaluation study.

2. Analytical Specificity (Interfering substances)

In our performance evaluation study, the deviation of a sample's measured value was within ±15% when the following substances were added into the sample.

- 100 ng/mL Bovine Hb (The deviation was 2.0% to 5.3%)
- 100 ng/mL Swine Hb (The deviation was 3.2% to 6.4%)
- 100 ng/mL Equine Hb (The deviation was 1.6% to 4.9%)
- 0.16% Barium sulfate (The deviation was -8.8% to -0.4%)

3. Accuracy (Trueness)

Accuracy specification is that the measured value of sample is within ±15% of the known concentration.
A representative data is shown below.

	Sample L			Sample M			Sample H		
	RUN1	RUN2	RUN3	RUN1	RUN2	RUN3	RUN1	RUN2	RUN3
Measured Value (ng/mL) (Mean of n=10)	22.0	22.5	22.5	52.7	52.4	52.2	90.9	90.0	89.7
Accuracy (%)	-5.4%	-3.2%	-3.0%	-2.9%	-3.5%	-3.8%	-5.0%	-6.0%	-6.3%

4. Repeatability

Repeatability specification is CV10% or less.
According to CLSI EP05-A3 SOP, three samples were assayed 2 times in 2 runs for 20 days (n=2 x 2 runs x 20 days) and the following data was obtained.

	Mean (ng/mL)	Repeatability SD	Repeatability CV
Sample L	17.43	0.53	3.0%
Sample M	34.64	0.41	1.2%
Sample H	171.99	1.25	0.7%

5. Reproducibility

Between-run, between-day, between-lot and between-site precision were evaluated in accordance with CLSI EP05-A3 SOP and the following data were obtained.

1) Between-run Precision Result
Three samples were assayed 2 times in 2 runs for 20 days (n=2 x 2 runs x 20 days)

	Mean (ng/mL)	Between-run SD	Between-run CV
Sample L	17.43	0.66	3.8%
Sample M	34.64	0.88	2.5%
Sample H	171.99	3.01	1.7%

2) Between-day Precision Result
Three samples were assayed 2 times in 2 runs for 20 days (n=2 x 2 runs x 20 days)

	Mean (ng/mL)	Between-day SD	Between-day CV
Sample L	17.43	0.77	4.4%
Sample M	34.64	1.09	3.2%
Sample H	171.99	3.27	1.9%

3) Between-lot Precision Result

Three samples were assayed in 10 replicates for 5 days with 3 lots reagent (n=10 x 5 days x 3 lots)

	Mean (ng/mL)	Between-lot SD	Between-lot CV
Sample L	22.04	0.20	0.9%
Sample M	51.31	1.41	2.8%
Sample H	87.57	3.15	3.6%

4) Between-site Precision Result

Three samples were assayed in 5 replicate for 5 days at 3 sites (n=5 x 5 days x 3 sites)

	Mean (ng/mL)	Between-site SD	Between-site CV
Sample L	25.62	0.22	0.9%
Sample M	47.39	0.66	1.4%
Sample H	93.29	0.71	0.8%

6. Detection Limit

Limit of blank (LoB), Limit of detection (LoD) and Limit of quantification (LoQ) were evaluated in accordance with CLSI EP17-A2.

- The LoB was 0.6 ng/mL
- The LoD was 1.5 ng/mL
- The LoQ was 4.7 ng/mL

7. Measuring Range

Measuring range is 7-400 ng/mL.

On “µg Hb/g feces” basis;

- 7-400 µg Hb/g feces for EXTEL HEMO • AUTO MC Collection Picker

Measuring range was determined based on the performance of LoQ and linearity.

In the linearity test, dilution recovery% was within ±15 up to 487.4 ng/mL as follows.

		Observed (ng/mL)	Expected (ng/mL)	Recovery %
Sample A (50 ng/mL)	1/10 dil.	4.3	4.8	-12.2%
	2/10 dil.	9.4	9.7	-2.9%
	3/10 dil.	14.4	14.5	-1.2%
	4/10 dil.	19.5	19.4	0.5%
	5/10 dil.	24.0	24.2	-1.0%
	6/10 dil.	29.2	29.0	0.4%
	7/10 dil.	33.2	33.9	-2.0%
	8/10 dil.	39.0	38.7	0.6%
	9/10 dil.	43.7	43.6	0.3%
	10/10 dil.	48.4	48.4	0.0%
Sample B (500 ng/mL)	1/10 dil.	54.1	54.2	-0.2%
	2/10 dil.	106.2	108.3	-2.0%
	3/10 dil.	166.1	162.5	2.2%
	4/10 dil.	228.0	216.6	5.2%
	5/10 dil.	280.4	270.8	3.5%
	6/10 dil.	339.7	325.0	4.5%
	7/10 dil.	376.2	379.1	-0.8%
	8/10 dil.	408.1	433.3	-5.8%
	9/10 dil.	449.0	487.4	-7.9%
	10/10 dil.	454.6	541.6	-16.1%

8. Clinical Performance

Through systematic review of scientific literatures, the following clinical performance data was obtained.
In the clinical studies covered by the literatures, cutoff value ranged between 0.6 and 50 μg Hb/g feces, and EXTEL HEMO・AUTO HS was used for screening or aid to diagnosis of various diseases including colorectal cancer (CRC), advanced adenoma (AA), higher risk adenoma (HRA) and inflammatory bowel disease (IBD).

		For Aid to Diagnosis				For Screening
		Diagnostic Sensitivity	Diagnostic Specificity	Positive Likelihood Ratio	Negative Likelihood Ratio	Positive Predictive Value
Target diseases	CRC	88.4%	87.2%	6.91	0.13	10.1%
	CRC + AA / HRA	61.4%	91.9%	7.60	0.42	24.3%
	CRC + AA / HRA + IBD	62.0%	92.0%	7.77	0.41	32.3%

For latest information on clinical performance of EXTEL HEMO・AUTO HS, please refer to Summary of Safety and Performance report in EUDAMED.

[References]

1). Allison JE, Fraser CG, Halloran SP, Young GP. Population screening for colorectal cancer means getting FIT: the past, present, and future of colorectal cancer screening using FIT. Gut and Liver 2014;8:117-30.

2). Godbler IM, Todd LM, Fraser CG, MacDonald LR, Younes HB; Use of a faecal immunochemical test for haemoglobin can aid in the investigation of patients with lower abdominal symptoms. Clin Chem Lab Med. 2015 Oct 10

3). Passamonti B, Malaspina M, Fraser CG, Tintori B, Carlani A, D'Angelo V, Galeazzi P.Di Dato E, Mariotti L, Bulletti S, et al; A comparative effectiveness trial of two faecal immunochemical tests for haemoglobin (FIT). Assessment of test performance and adherence in a single round of a population-based screening programme for colorectal cancer.Gut. 2016 Dec 14;.Epub 2016 Dec 14

Definition of Symbols:

Symbol	Definition
IVD	*In vitro* diagnostic medical device
	Manufacturer
CE 0123	CE Mark with identification number of notified body
	Consult instructions for use
CONT	Contents
REF	Catalog number
LOT	Batch/Lot code
	Temperature limitation
	Use by
EC REP	Authorized Representative in the European Community
FOBT	Fecal occult blood test reagent
	For professional use only

For all inquiries, contact:

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Please report any serious incident associated with the product to the above address and the competent authority of the Member State.

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EC REP

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