EB (No. 152245)

ENGLISH

**Revised in February 2025 (Revision 01)
Issued in August 2023 (Revision 00)

EXTEL HEMO • AUTO NE

(Latex Agglutination Reaction Method)

IVD CE 0123 UKCA

SSP is available in EUDAMED.**

"For Professional Use Only"

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

[Intended Use]

EXTEL HEMO • AUTO NE 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 only by professional users. Measurement of hemoglobin in feces is used for screening or aid to diagnosis 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 can be measured optically by an automatic analyzer.

[Material Provided]

Code	Product Name	Component Name	Constituent	Quantity
66100	EXTEL HEMO • AUTO NE	EXTEL HEMO • AUTO NE Latex	Anti-human hemoglobin sheep antibody immobilized latex suspension (1.5-3.5 mg/mL)	14 mL x 4
		EXTEL HEMO • AUTO NE Buffer	Tris (0.1M)	50 mL x 4

EXTEL HEMO • AUTO NE Latex (The Latex) is provided with a Master Curve data by labeled barcode.

[Material Necessary but not provided]

- EXTEL HEMO • AUTO NE Calibrator
- EXTEL HEMO • AUTO NE Liquid Control
- EXTEL HEMO • AUTO MC Collection Picker

[Chemical hazard information]**

- Product identifiers:
  Product Name: EXTEL HEMO • AUTO NE Latex
  Substance Name: Imidazole
- Information of the supplier:
  See the last page written in each language.
- Quantity of mixture:
  See the section [Material Provided].
- Hazard pictgram:

- Signal word:
  Danger
- Hazard statements:
  H360D: May damage the unborn child.
- Precautionary statements:
  P201: Obtain special instructions before use.
  P202: Do not handle until all safety precautions have been read and understood.
  P280: Wear protective gloves/protective clothing/protective mask/eye protection.
  P308+P313: IF exposed or concerned: Get medical advice/attention.
  P501: Dispose of contents/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

[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-CODIAM. Do not use in any other analyzers. For details of the operation procedure, refer to the instruction for use for HM-CODIAM.

Operation procedure in HM-CODIAM

Be sure to carry out the measurements at the temperature range of 15-33°C with humidity range of 10-85% under non-condensing conditions

1. Reagent Preparation Method

(a) EXTEL HEMO • AUTO NE Latex (The Latex)

Use the Latex after you have restored its temperature to 15-25°C. Just before use, lay the latex bottle and rotate it to mix and obtain a homogenous reagent. (Homogenize by rotating is recommended, since shaking hard would generate too much foam.)

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

Use the Buffer after you have restored its temperature to 15-25°C. Just before use, lay the buffer bottle and rotate it to mix and obtain a homogenous reagent.

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, keep the picker in 15-25°C to restore the temperature of the buffer inside the picker to become 15-25°C and shake the picker until fecal sample is fully suspended. Since the hemoglobin in some feces samples may degrade rapidly, it is recommended to analyze samples as soon as possible.

3. Establishment of Calibration Curve

(a) Enter the master curve data by scanning barcode of each Latex bottle.

(b) Calibrate the master curve with EXTEL HEMO • AUTO NE Calibrator when the lot number of the Latex changes or whenever appropriate.

4. Performing Quality Control

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

5. Assay Procedure

(a) Place the reagent in the specified position of HM-CODIAM.

(b) Scan the barcode of the Latex and the Buffer bottles

(c) Place the specimen on the sample rack.

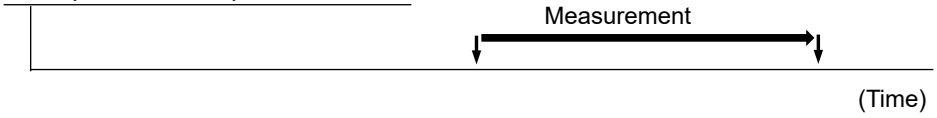
Note: Place the picker directly in a way that the cap of the picker faces downward.

(d) After you have touched 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)

Assay parameter in HM-CODIAM

The Latex	50 µL
The Buffer	130 µL
Sample	20 µL



[Assessment of Results]

1. Unit of measurement value is ng/mL.
2. It is recommended for each laboratory to set their own cutoff standard.
3. For clinical diagnosis based on the assay results, the physician in charge should assess the data in a comprehensive manner in a 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 HIV, bacteria and/or any other infectious factor. Be sure therefore to wear protective gloves when handling the specimens in order to prevent infection.
2. Be sure to wear protective gloves, protective clothing, protective mask and eye protection when handling or disposing of this product.** When liquid components of this product have 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. Do not allow this product to come in contact with lead/copper pipes because it may react with sodium azide (less than 0.1%, contained as a preservative) to form highly explosive metal azide.
4. Do not allow this product to come into contact with acids because it may react with sodium azide (less than 0.1%, contained as a preservative) to produce highly toxic hydrogen azide.
5. As described previous section (Chemical hazard information), HEMO • AUTO NE (Latex) contains imidazole, a hazardous substance of reproduction toxicity, (0.3% and more).** Be sure therefore to wear protective gloves, protective clothing, protective mask and eye protection when handling or disposing of this product.** When it has entered mouth or contacted the skin by accident, be sure to rinse with copious running water.** On the other hands, in case of eye contact, be sure to rinse with copious running water and remove contact lenses.** If necessary, call a physician or ophthalmologist.** Disposal of this product must be done according to official regulations.**
6. Do not mix different lots of the reagents. Nor add reagent to supplement a shortage.
7. Do not use the reagents that have expired their shelf life.
8. Do not use reagents which show obvious changes in appearance such as discoloration or aggregation. These changes indicate possibility of deterioration.
9. It is recommended to dispose of all waste material in accordance with local regulation.
10. Do not use the containers of this product for any other purpose.
11. When high concentration of barium sulfate are included in fecal sample, correct measurement result might not be obtained. In our study, the deviation of a sample's measured value was within ±15% when 0.16% Barium sulfate was added into the sample.
12. When high concentration of native animal (cow, pig, horse) derived hemoglobin are included in fecal sample, correct measurement result might not be obtained. In our study, the deviation of a sample's measured value was within ±15% when 100 ng/mL native animal derived hemoglobin were added into the sample.

[Storage]

1. Store in a dark and cool place (at 2-8°C).
2. Shelf life: 12 months after manufacturing

[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 the Buffer.

[Performance Characteristics]

The following performance data was obtained using HM-CODIAM.

1. Analytical Sensitivity

EXTEL HEMO • AUTO NE has the following sensitivity specifications defined as detection capability of lowest value of measurement range.

・ (ΔAbs (standard solution of lowest value of measurement range)-2×SD)- (ΔAbs(blank sample)＋2×SD) >0

When physiological saline solution as blank sample and about 7 ng/mL hemoglobin standard solution were tested using 3 lots of reagent, (ΔAbs (standard solution of lowest value of measurement range)-2×SD)- (ΔAbs(blank sample)＋2×SD) was 0.0221 to 0.0308 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 9.2% to 12.1%)
・ 100 ng/mL Swine Hb (The deviation was 7.6% to 11.3%)
・ 100 ng/mL Equine Hb (The deviation was 3.3% to 6.6%)
・ 0.16% Barium sulfate (The deviation was -8.7% to -13.5%)

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)	25.1	25.4	25.9	49.4	50.2	51.4	102.4	102.9	106.7
Accuracy (%)	-0.3%	0.8%	2.7%	0.5%	2.3%	4.8%	-2.1%	-1.6%	2.0%

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	24.7	0.68	2.8 %
Sample M	49.1	0.72	1.5 %
Sample H	98.8	1.77	1.8 %

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	25.4	0.00	0.0%
Sample M	49.6	0.32	0.6%
Sample H	101.8	1.06	1.0%

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	25.4	0.69	2.7 %
Sample M	49.6	1.06	2.1 %
Sample H	101.8	2.54	2.5 %

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	23.4	0.00	0.0 %
Sample M	46.3	0.72	1.6 %
Sample H	95.0	1.92	2.0 %

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	23.6	0.23	1.0 %
Sample M	46.8	0.00	0.0 %
Sample H	97.8	0.00	0.0 %

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 1.9 ng/mL
- The LoD was 2.8 ng/mL
- The LoQ was 5.2 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 408.0 ng/mL as follows.
※physiological saline solution was used as dilution buffer.

		Observed (ng/mL)	Expected (ng/mL)	Recovery %
Sample A (50 ng/mL)	1/10 dil.	4.0	4.3	-8.4%
	2/10 dil.	9.2	8.7	6.6%
	3/10 dil.	12.5	13.0	-4.1%
	4/10 dil.	16.9	17.3	-2.5%
	5/10 dil.	21.4	21.7	-1.2%
	6/10 dil.	25.6	26.0	-1.4%
	7/10 dil.	30.3	30.3	-0.1%
	8/10 dil.	34.4	34.7	-0.8%
	9/10 dil.	38.8	39.0	-0.5%
	10/10 dil.	43.1	43.3	-0.6%
Sample B (500 ng/mL)	1/10 dil.	39.5	40.8	-3.3%
	2/10 dil.	81.6	81.6	0.0%
	3/10 dil.	126.4	122.4	3.3%
	4/10 dil.	170.7	163.2	4.6%
	5/10 dil.	219.2	204.0	7.4%
	6/10 dil.	266.9	244.8	9.0%
	7/10 dil.	316.5	285.6	10.8%
	8/10 dil.	363.2	326.4	11.3%
	9/10 dil.	412.5	367.2	12.3%
	10/10 dil.	452.5	408.0	10.9%

8. Correlation (vs EXTEL HEMO・AUTO HS)

In our performance evaluation study, method comparison testing is conducted with about 150 samples and the following data were obtained.

- The slope was 0.9465.
- The correlation coefficient was 0.998.

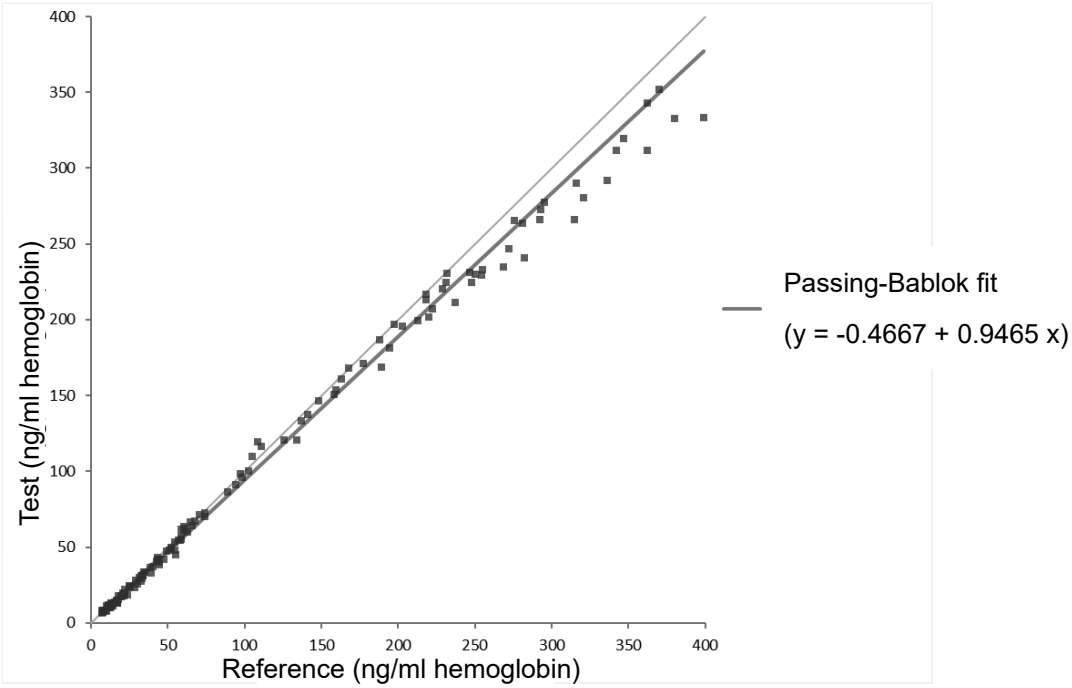


Fig. Comparison of HM-CODIAM (test) and HM-JACKarcII (reference)

9. Clinical Performance

Since the analytical performance of EXTEL HEMO・AUTO NE is equivalent to that of EXTEL HEMO・AUTO HS, the clinical performance is also comparable. The clinical performance of the EXTEL HEMO・AUTO HS is shown below.
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 400 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	91.7%	77.3%	4.04	0.11	10.1%
	CRC + AA / HRA	63.3%	88.1%	5.30	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 NE, 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

For all inquiries, contact:

Canon Medical Diagnostics Corporation**
Quality Assurance and Regulatory Affairs Department
1-8-10, Harumi, Chuo-ku, Tokyo, 104-6004 JAPAN

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

Canon Medical Diagnostics Corporation**
1-8-10, Harumi, Chuo-ku, Tokyo,
104-6004 JAPAN
Tel: +81-3-6219-7600
Fax: +81-3-6219-7614

EC REP
Obelis s.a.
Bd. Général Wahis 53
B-1030 Brussels, Belgium

UKRP
Alpha Laboratories Ltd.
40 Parham Drive Eastleigh
Hampshire SO50 4NU
United Kingdom

Definition of Symbols:

Symbol	Definition
	**EN:** *In vitro* diagnostic medical device **ES:** Dispositivo médico de diagnóstico *In vitro* **PT:** Dispositivo médico de diagnóstico *in vitro*
	**EN:** Manufacturer **ES:** Fabricante **PT:** Fabricante
	**EN:** CE Mark with identification number of notified body **ES:** Marca CE con número de identificación del organismo notificado **PT:** Marca CE com número de identificação do organismo notificado
	**EN:** Consult instructions for use **ES:** Consultar instrucciones para el uso **PT:** Consultar as instruções de utilização
	**EN:** Contents **ES:** Contenido **PT:** Conteúdo
	**EN:** Catalog number **ES:** Número de catálogo **PT:** Número de catálogo
	**EN:** Batch/Lot code **ES:** Código de lote **PT:** Código do lote
	**EN:** Temperature limitation **ES:** Limitación de temperatura **PT:** Limitação de temperatura
	**EN:** Use by **ES:** Usar antes de **PT:** Utilização por
	**EN:** Authorized Representative in the European Community **ES:** Representante Autorizado en la Comunidad Europea **PT:** Representante Autorizado na Comunidade Europeia
	**EN:** UK Responsible Person **ES:** Representante en el Reino Unido **PT:** Responsável no Reino Unido
	**EN:** Fecal occult blood test reagent **ES:** Reactivo para análisis de sangre oculta en heces **PT:** Reagente de teste de sangue oculto fecal
	**EN:** For professional use only **ES:** Solo para uso profesional **PT:** Exclusivamente para uso profissional