IN VITRO DIAGNOSTIC MEDICAL DEVICE

Hemoglobin A1c LR

Kit for HbA1c determination in human blood.
Class I Medical Device conformed by self certification D.Lgs. 332/2000 (directive 98/79/EC).

INDEX

1 Manufacturer
2 Device classification
3 Certification process
4 Applied standards list
5 Declaration of conformity
6 Compliance with the essential requirements
7 General product description
8 Documents of quality management system
9 Project information
10 Raw materials characteristics
11 Manufacturing process
12 Risk analysis
13 Project calculation results and inspections
14 Test report
15 Performance evaluation and bibliographic sources
16 Results of stability studies
17 Labeling plan and instruction for use
18 Quality insurance system

Att. 1 Instruction for use
Att. 2 Product variants
Att. 3 Risk analysis
Att. 4 Device performances
Att. 5 Labeling plan
Att. 6 Security sheet

Att. A Confirmation of compliance with the essential requirements
Att. B Packaging materials

1 MANUFACTURER

Company name	**Gesan Production Srl**
address	**71, Fiera dell'Eremita st.**
tel.	**+39 0924 912534**
fax	**+39 0924 912534**
e-mail	**overseas@gesanproduction.it**
website	**www.gesanproduction.it**
certification	**RINA SPA**
ISO 9001	**N° 5851/01/S Certificate**
ISO 13485	**N° DM/14/97/S Certificate**

2 DEVICE CLASSIFICATION

The device belongs in self certification class as it is not included in the II Annex, for performance evaluation, and as it is not a devices for self- diagnostic according to art. 9, paragraph 1 of D. Lgs. 332/2000, directive 98/79/EC related to in vitro diagnostic medical devices,

3 CERTIFICATION PROCESS

For the purpose of Medical Devices CE marking, we proceeded trough:

- Certification of company quality system according to the UNI-EN-ISO 9001:2008 norm with certificate released by Rina Spa,
- Certification of company quality system according to the UNI EN ISO 13485:2012 norm with certificate released by DNV,
- Declaration of conformity (as predicted by the annex III for devices not included in Annex II, nor intended for performance evaluations or self-testing),
- Notification to Ministry of Health based on art. 10, paragraph 1 of D. Lgs. 332/2000, directive 98/79/EC related to in vitro diagnostic medical devices.

4 APPLIED STANDARDS LIST

To draft this technical file, the rules in force have been complied according to the following decrees and UNI EN standard,

Basic regulation

DLGS 332:2000	Implementation of the Directive related to in vitro diagnostic medical devices
UNI EN ISO 9001:2008	Quality management system: requirements,

Labelling

EN ISO 18113-1:2009	In vitro diagnostic medical devices -- Information supplied by the manufacturer (labelling) -- Part 1: Terms, definitions and general requirements
EN ISO 18113-2:2009	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
EN 980:2009	Graphic symbols used for medical devices labelling

Stability testing

UNI EN 13640:2002	In vitro diagnostic stability tests

Performance evaluation

UNI EN 13612:2002	Evaluation of in vitro diagnostic medical devices performances
ISO 23640:2015	In vitro diagnostic medical devices - Evaluation of stability of in vitro diagnostic reagents

Traceability calibration and measurement values

ISO 17511:2002	Demostrating traceability
UNI EN 12287:2001	In vitro diagnostic medical devices - Measurement of quantities in samples of biological origin - Reference materials description

Risk analysis

DLGS 285/1998	Implementation of the Community Directive related to dangerous preparations and attachment with concentration limits
EN ISO 13485:2012	Quality system management – Requirements for regulatory purpose
UNI 14971:2012	Application of risk management to in vitro diagnostic devices
DLGS 52/1997	Implementation of Directive 92/32/EEC on classification, packaging and labelling of hazardous substances with regard to the safety data sheet
G.U. 20/5/93	List of prudence precautions and risk phrases
G.U. 116/1993	Symbols and indications of hazard, risk phrases, safety precautions
EN 13641:2002	Elimination or reduction of risk of infection related to in vitro diagnostic medical device.
REG. CE 1907/2006	Concerning registration, evaluation, authorisation and restriction of chemicals. (REACH),
(EC) Regulation n. 1272/2008	Concerning classification, labelling and packaging of substances and mixtures

5 DECLARATION OF CONFORMITY

I, the undersigned **Cudia Vito**, born in Campobello di Mazara on the 18th of July 1947, and living in Campobello di Mazara, 40 G. Mazzini st., as legal representative of Gesan Production s,r,l, based in Campobello di Mazara, 71 Fiera dell'Eremita st.

DECLARES

- That Gesan Production s,r,l, is manufacturer of this in vitro diagnostic medical device, belonging to "clinical chemistry, infectivity, immunochemistry kit" group with the following denomination:

Commercial name	**HbA1c LR**
Company code	**990**
EDMA Code	**11 02 01 14 00**

- That it satisfy all the Annex I requirements of directive 98/79/CE and as described in Annex III about in vitro diagnostic medical device and in Italian implementation (D. Lgs. 332/2000),
- That the device in not included in A and B list of Annex II of the abovementioned directive,
- That the subsequent will be conforming to the technical specifications of the first lot,
- Che i lotti successivi saranno conformi alle specifiche tecniche del primo lotto,
- That such conformity will be attested to on the quality control certificate,
- That the device is manufactured and placed on the market according to the application of a quality system declared compliant with UNI EN ISO 9001: 2008 standards as required by Annex III of the Directive,
- That the product technical file, the production and control document, as required by Annex I of directive 98/79/EC, can be consulted by authorized body for five years since the production of the last lot,
- That this device is manufactured and placed on the market not before the present date,
- That I established a procedure to ensure the after-sales control of the device in accordance with Directive 98/79/EC

This declaration has validity for a maximum period of five years.

In Faith

The legal representative of Gesan Production s.r.l.

Vito Cudia

Campobello di Mazara, 07/07/2017

6 COMPLIANCE WITH THE ESSENTIAL REQUIREMENTS

The technical file of the device was constructed by complying with the essential requirements in accordance with Annex I of D. Lgs. n. 332/2000, letter A and letter B.

For each point, the solutions adopted meet the requirements, and reference standards and internal documentation are indicated. The full analytical document is given in attachment A, "compliance with the essential requirements".

7 GENERAL PRODUCT DESCRIPTION

Kit for HbA1c determination in human blood.

Reference legislation

Device not included in the Annex II of directive 79/98/CE and not for self-diagnostic. In order to obtain the norm conformity, we refer to the Conformity Declaration required in the Annex III (I class device with self certification).

Product identification

Commercial name **HbA1c LR**

REF	SIZE	R1	R2	EXTERNAL LABEL CODE	R1 LABEL CODE	R12 LABEL CODE
9900140	1x40 ml	1x30 ml	1x10 ml	E9900140ES	E9900140R1	E9900140R2
A9900140	1x40 ml	1x30 ml	1x10 ml	EA9900140ES	EA9900140R1	EA9900140R2
C9900140P	1x40 ml	1x30 ml	1x10 ml	C9900140PES	C9900140PR1	C9900140PR2
C9900140A	1x40 ml	1x30 ml	1x10 ml	C9900140AES	C9900140AR1	C9900140AR2
CA9900140P	1x40 ml	1x30 ml	1x10 ml	CA9900140PES	CA9900140PR1	CA9900140PR2
CA9900140A	1x40 ml	1x30 ml	1x10 ml	CA9900140AES	CA9900140AR1	CA9900140AR2
C9900380D	1x76 ml	1x56 ml	1x20 ml + Lyse	C9900380DES	C9900380DR1	C9900380DR2
CA9900380D	1x76 ml	1x56 ml	1x20 ml + Lyse	CA9900380DES	CA9900380DR1	CA9900380DR2

Intended use

For the quantitative determination of Hemoglobin A1c (HbA1c) in human blood. The determination of HbA1c is most commonly performed for the evaluation of glycemic control in diabetes mellitus. HbA1c values provide an indication of glucose levels over the preceding 4-8 weeks. A higher HbA1c value indicates poorer glycemic control. For in vitro diagnostic use only.

Kit components

The kit is composed by:

- SEE TABLE Identification product paragraph
- N° 1 use instruction sheet

Reference legislation

Device not included in the Annex II of directive 79/98/Ec and not for self-diagnostic. In order to obtain the norm conformity, we refer to the Conformity Declaration required in the Annex III (I class device with self certification).

Reagents composition (initial concentration)

R1: Latex 0.13%, Buffer, stabilizer.
R2 (When combined): Mouse anti-human HbA1c monoclonal antibody 0.05mg/ml, goat anti-mouse IgG polyclonal antibody 0.08mg/dl, Buffer, stabilizers.

Compatibility with other devices

Procedure:	
Wavelength	**λ: 620 nm**
Working Temperature	**37 °C**
Optical path	**1 cm**
Reaction	**"end point".**

Therefore, in addition to normal laboratory glassware and small instrumentation (such as micropipettes, stirrers, etc.), it is necessary to have a colorimeter adjusted to the required parameters.

Reagent performance

The analytical performance of the device, detailed in the operating instructions (attachment 1) are:

Interference

Bilirubin to 50mg/dL, ascorbic acid to 50mg/dL, triglycerides to 2000mg/dL, carbamylated Hb to 7.5mmol/L and acetylated Hb to 5.0mmol/L do not interfere in this assay.

Linearity

The Hemoglobin A1c assay range is 0.83 – 17.93 %. If the limit value is exceeded, it is suggested to dilute sample with saline solution. Then, multiply, the result for diluting factor.

"Intra-Assay" precision (within-Run)

Within Run: The within run precision was established by assaying two blood samples following NCCLS protocol EP5 on a Hitachi 917.

Level	Mean	Std. Dev.	% C.V.
Low	5.48	0.078	1.43
High	10.28	0.176	1.72

Day to Day: The between day precision was established by assaying two blood samples following NCCLS protocol EP5 on a Hitachi 917.

Level	Mean	Std. Dev.	% C.V.
Low	5.48	0.152	2.77
High	10.28	0.275	2.68

Analytical sensitivity

The test sensitivity in terms of detection limit is: 0.56 g/dl. for 1% HbA1c.

Product variants

Basic device variants of this technical file are described in attachment 2 "Product variants"

8 DOCUMENTS OF QUALITY MANAGEMENT SYSTEM

Quality management system of GESAN PRODUCTION was verified on 09/11/2001 by RINA SPA, it was compliant with UNI EN ISO 9001:2000 standard requirements for planning and production of in vitro diagnostic medical devices. Its certificate is n. 5851/01/S and it is compliant with UNI EN ISO 9001:2008 as in the certificate released by RINA Services SPA on 08/01/2014.

Furthermore, GESAN PRODUCTION is compliant with EN ISO 13485:2012 norm with certificate released by RINA Services SPA for the activity of planning and production of in vitro diagnostic medical devices, sale of equipment and material for analysis laboratories, sale of medical products with certificate n° DM/14/97/S of 07/02/2014.

The Company constantly upgrades the Quality System in order to improve it and make it always in compliance with the changing needs. The certificate is available in the company.

9 PROJECT INFORMATION

The reagent was formulated according to bibliographic references found in the bibliography cited in the instructions for use, and optimized comparing the formulation to that one of the major manufacturers of the same product.

10 RAW MATERIALS CHARACTERISTICS

Specific chemistry products for that device are:

Contents of Reagents: R1 Latex	0.13%
Buffer: PIPES	
Stabilizers: Triton	
Sodium Azide	0.09%
R2	
Mouse anti-human HbA1c monoclonal antibody	0.05 mg/ml
Goat anti-mouse lgG polyclonal antibody	0.08 mg/dl
Buffer: PIPES	
Stabilizers: EDTA, PEG, Triton	
Gentamicin	0.01%
Sodium Azide	0.09%
Hemolysis reagent: (Included in 40ml kit, not 120ml kit)	
Water	
Stabilizers: EDTA, PEG	
Sodium Azide	0.05%

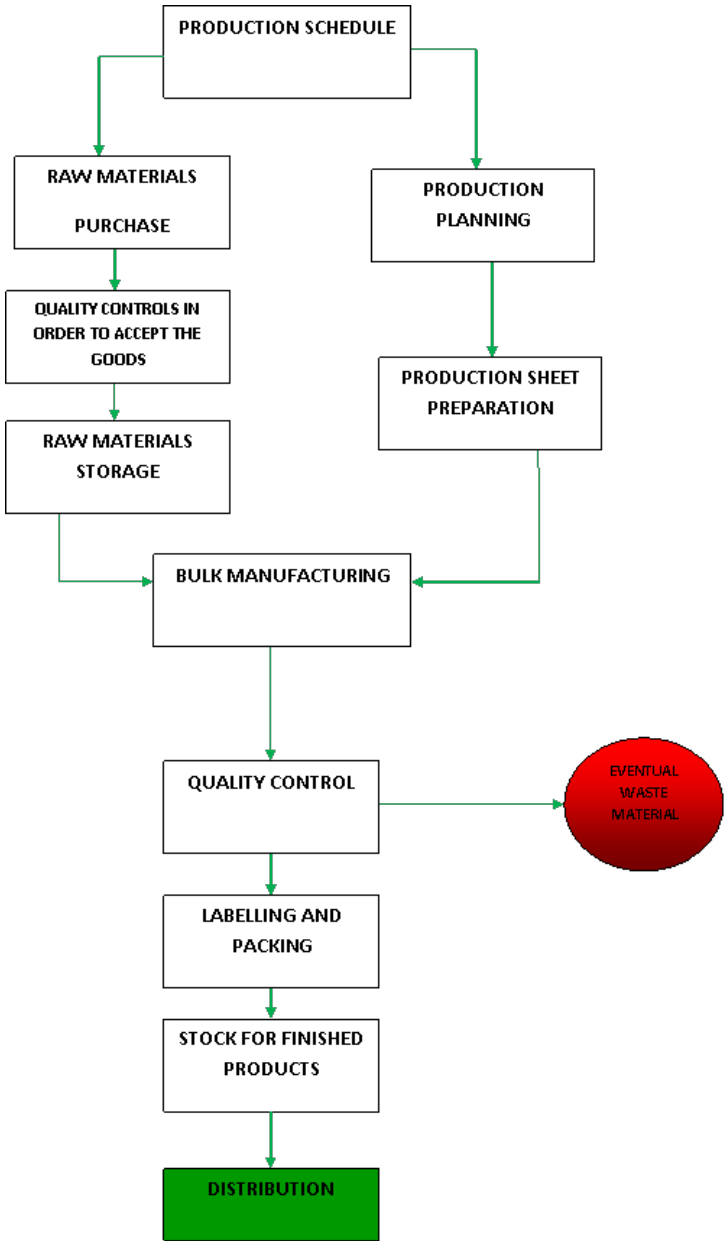
Packaging material characteristics are described in attachment B "Packaging materials" that specifies technical specifications of used materials as they are listed in "General product description".

The deionized water quality, produced by reverse osmosis and mixed bed resin columns, is constantly monitored by a conductometer measuring the resistance exiting. In addition, the water is subjected to a sterilization treatment by a suitable UV filter, in order to eliminate any microbial charges.

All stages are documented in accordance with the procedures of the company's quality system.

11 **MANUFACTURING PROCESS DESCRIPTION**

The flow diagram synthesizes the various stages of production, from the forecast to the storage of finished products



All the stages are described in detail in the following procedures and operating instructions integrated into the quality manual.

12 **RISK ANALYSIS**

Responsible for security and analysis: **Cudia Vito.**

The conclusions regarding the validation of the design and manufacture are in accordance with UNI CEI EN ISO 14971: 2012 "Medical Devices - Application of Risk Management to Medical Devices".

The results of the risk analysis are listed in attachment 3. The following rules were evaluated:

EN 13640:2002	Stability testing of in vitro diagnostic reagents
UNI CEI EN ISO 15223-1:2012	Medical devices – Symbols to use on medical device label, labeling and information provided
UNI EN ISO 9001:2008	Quality management system
UNI EN ISO 14971:2012	Application of risk management to medical devices
EN ISO 18113-1:2012	In vitro diagnostic medical devices -- Information supplied by the manufacturer (labelling) -- Part 1: Terms, definitions and general requirements
TS EN ISO 18113-2:2010	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use

Over the past few years, particular attention has been paid to the assessment of the potential risks associated with the production of diagnostic medical devices, in compliance with the 81/2008 law on Workers' Health Protection, in accordance with good manufacturing practice rules and with the procedures of our quality system (UNI EN ISO 9001: 2008).

13 **PROJECT CALCULATION RESULTS AND INSPECTIONS**

The descriptions, performances and limitations of the device have been verified and validated as required by the Gesan Production design control procedure. Anomalies due to its formulation and / or production process have not ever been reported.

Inspection visits, both internal and by the certifying body, did not show any significant deviation from the procedures of our quality system. During these visits, all points from the purchase of raw materials to the shipment of the finished product have been examined and checked.

The small remark that emerged have been improved by effective corrective actions.

14 **TEST REPORT**

This chapter describes the operating procedures of the various tests performed on the device.

SENSITIVITY

Method

The change of absorbance units per concentration unit was calculated for the up going part of the nonlinear curve.

Result

0.0458744 Absorbance/Concentration units

Normal values

Non-diabetics: < 6% Therapeutic Diabetics: < 7%

LINEARITY

Linearity was verified using:

- chemical standards prepared for those analytes for which international standards were not available:

-trough appropriate dilution of the sample and consequent stoichiometric calculation for the analytes mentioned in the previous point, but of enzymatic nature.

CORRELATION

The reagent has been correlated with another similar method highlighting the correlation factor as a comparison reference.

COMPARISON

Reagents were compared with other accredited European diagnostic manufacturers in terms of: method, analytical sensitivity, linearity and reference values. The data has been grouped in the diagram in the following chapter "Performance Evaluation and Bibliographic Sources".

STABIILITY

A stability study according to BS-EN 13640 standard has been carried out regarding:

REAL TIME STABILITY AND STABILITY AFTER THE 1ST OPEN

Finished products were used by storing reagents at the storage temperature. The vials were periodically opened and closed after taking reagent samples with clean glassware and according to good laboratory practice. At the end of the declared stability period, checks were carried out to verify that the values obtained were still within the range of controls acceptability.

After each day of exams, it is necessary to observe the evolution of the curves of the various parameters monitored. When one of them is outside the defined stability criteria, this is the end of the real-time stability study and gives the lifetime of the reagent.

ACCELERATED STABILITY

The Accelerated Stability Study allows for the market introduction of reagents before the real-time stability study is completed.

This study is based on the ISO 23640 standard. It makes it possible to calculate a lifetime of the reagent by means of a mathematical method based on the equation of the Arrhenius law and on a mathematical extrapolation.

Stability of the product was determined by subjecting reagents to a thermal stress. Therefore, according to the duration of the stress period and the temperature, the Arrhemius equation was used.

The principle of this method is as follows:

- The study requires at least 2 temperatures (T1 and T2 are taken here)
- for each temperature, one plots the evolution of a parameter as a function of time (one takes here X)
- The evolution of X as a function of time is plotted for the two temperatures
- For each curve, the times when X exceeds the defined stability criteria (t1 and t2)
- Then these two times (t1 and t2) are placed on a graph as a function of 1 / T (here 1 / T1 and 1 / T2)
- Draw the straight line connecting the 2 preceding points.
- By extrapolating the line, one can identify the time t, for a desired temperature, which will constitute the lifetime of the reagent.

STABILITY OF PRODUCTS DURING TRAFFIC AND STABILITY IN ROUTINE

The reagents used for stability tests were randomly picked up from the warehouse, to ensure "routine" stability on diagnostic devices. Prior to carrying out the storage and distribution of the reaction vials for stability tests, the same vials were subjected to stress temperatures to check their stability at non-optimal transport conditions (3 hours at 45 ° C, 21 hours at 37 ° C, 72 hours at 30 ° C). After this test, it has been found that the exposure to those temperatures does not affect the stability of the products.

PACKAGING

Tests have been carried out to verify the effectiveness of both the kit and the shipping box, simulating a shipment. During a whole month, a package containing products to ship, including the analyte, was randomly picked up every day. The package was dropped three times, each time on a different side, from a meter of height. It has also been overturned several times to simulate rolling and left, upside down, for three hours. At the end of the tests, the package was opened and the content was carefully inspected. There were no damage.

INTERFERENCES

Among the following analytes: Bilirubin – HB – Triglycerides, They have been selected those mentioned in the paragraph Interferences.

The maximum concentrations of mentioned substances have been found in bibliographic literature. These concentrations were simulated by enriching the sample with the required amount of potentially interfering element. The results were compared with those obtained without such enrichment. In the absence of significant divergences, this element was considered a non-interfering element, at least up to the tested concentration.

VIAL ENDURANCE CHECK

It has been carried out a endurance check on the vials used in the kit, listed in the "general product description" of this technical file. During the test, 10 bottles per type, filled with a highly colored solution, were turned in a vacuum ovens and put on a filter carton. Thanks to the vacuum ovens was reached a depression up to -300 millibars for 24 hours. At the end, there were no leakage and moisture at the bottom of the neck of the vials.

15 PERFORMANCE EVALUATION AND BIBLIOGRAPHIC SOURCES

Device performances have been compared to those reported by other reliable manufacturers for similar methods. They are compatible with the diagnostic expectations of those who use this device.

Bibliographic sources:

1. Trivelli, L.A., Ranney, H.M., and Lai, H.T., New Eng. J. Med. 284,353 (1971).
2. Gonen, B., and Rubenstein, A.H., Diabetologia 15, 1 (1978).
3. Gabbay, K.H., Hasty, K., Breslow, J.L., Ellison, R.C., Bunn, H.F., and Gallop, P.M., J. Clin. Endocrinol. Metab. 44, 859 (1977).
4. Bates, H.M., Lab. Mang., Vol 16 (Jan. 1978).

16 RESULTS OF STABILITY STUDIES

Stability tests on the device highlighted the following values:

Reagent stability: at least 18 months (until the expiration date)
Vial stability after opening: at least 30 days at 2-8 °C.

Stability tests were performed by simulating the conditions of transport and the treatment of the vial during its use in the laboratory routine. For a detailed description of the procedure, refer to the chapter "Report on Tests Made".

17 LABELLING PLAN AND INSTRUCTION FOR USE

The instructions for use and labeling comply with the requirements specified in UNI EN ISO 18113-2: 2009 and at paragraph 8 Information provided by the manufacturer of D. Lgs. 332/00 - Implementation of Directive 98/79/EC related to in vitro diagnostic medical devices.

The instructions for use are listed in attachment 1 "Instructions for Use".

The labeling plan, including primary and secondary labels of both the device and its variants, is given in attachment 5 "Labelling Plan".

Instructions for use and labels are available in Italian. If required (sale in the Common Market Countries), the information will be translated by qualified personnel (eg, interpreter or mother tongue retailer) in other languages.

18 QUALITY INSURANCE SYSTEM

Manufacturer's quality system is certified according to ISO 9001:2008 norm.
The chapter related to points:

- Organizational structure and responsibility;
- Manufacturing processes and production quality control;
- Means to control the performance of the quality system,

as well as the other chapters governing business activities both within and in relationships with third parties are described in the Company's Quality Manual and, more in details, in related procedures and operating instructions.
In particular, in the above-mentioned documentation, the following points are treated and regulated:

- Organizational Structure and Responsibility, and its organizational chart, which summarizes its functions and responsibilities and it is permanently posted in the corporate journal
- Manufacturing / packaging process: refer to the chapter "Description of the manufacturing process" in this technical file, where they are detailed process description, including the flow chart, production procedures and operating instructions.
- Inspection visits: inside the manual, internal inspection visits are regulated in order to verify the adherence of company behavior to quality system standards.
- Quality control: Tests, checks and trials are described in Q.M. and in the specific product design procedures and in the specific procedures for the production of the device components.

The following checks are carried out:

- Visual inspection of raw materials in acceptance.
- Check the quality certificate of the finished products in order to verify their correspondence to the features of the device.
- For enzymes and substrates: comparison of product specifications to the required requirements, through suppliers' quality check sheets.
- Sample control on the volume of products during the vials filling phase.
- In order to verify the stability of the product over time, even as a result of any claims, some samples of each batch of the device are preserved for ageing.
- Customer Satisfaction: This important function is ensured by the section 8.2.1 of the Company's Quality Manual.

Hemoglobin A1c

Reagent Set

CE IVD For in vitro medical device

Intended Use

For the quantitative determination of Hemoglobin A1c (HbA1c) in human blood. The determination of HbA1c is most commonly performed for the evaluation of glycemic control in diabetes mellitus. HbA1c values provide an indication of glucose levels over the preceding 4-8 weeks. A higher HbA1c value indicates poorer glycemic control. For *in vitro* diagnostic use only.

Summary and Explanation of Test

Throughout the circulatory life of the red cell, Hemoglobin A1c is formed continuously by the adduction of glucose to the N-terminal of the hemoglobin beta chain. This process, which is non-enzymatic, reflects the average exposure of hemoglobin to glucose over an extended period. In a classical study, Trivelli et al[1] showed Hemoglobin A1c in diabetic subjects to be elevated 2-3 fold over the levels found in normal individuals. Several investigators have recommended that Hemoglobin A1c serve as an indicator of metabolic control of the diabetic, since Hemoglobin A1c levels approach normal values for diabetics in metabolic control.[2,3,4]

Hemoglobin A1c has been defined operationally as the "fast fraction" hemoglobins (HbA_{1a}, A_{1b}, A_{1c}) that elute first during column chromatography with cation-exchange resins. The non-glycosylated hemoglobin, which consists of the bulk of the hemoglobin has been designated HbA_0. The present procedure utilizes a antigen and antibody reaction to directly determine the concentration of the HbA1c.

Principle

This method utilizes the interaction of antigen and antibody to directly determine the HbA1c in whole blood. Total hemoglobin and HbA1c have the same unspecific absorption rate to latex particles. When mouse antihuman HbA1c monoclonal antibody is added (R2), latex-HbA1c-mouse anti human HbA1c antibody complex is formed. Agglutination is formed when goat anti-mouse IgG polyclonal antibody interacts with the monoclonal antibody. The amount of agglutination is proportional to the amount of HbA1c absorbed on to the surface of latex particles. The amount of agglutination is measured as absorbance. The HbA1c value is obtained from a calibration curve.

Reagents

R1: Latex 0.13%, Buffer, stabilizer.
R2 (When combined): Mouse anti-human HbA1c monoclonal antibody 0.05mg/ml, goat anti-mouse IgG polyclonal antibody 0.08mg/dl, Buffer, stabilizers.

Reagent Storage and Preparation

Store all reagents refrigerated at 2-8°C.
All reagents are supplied as ready to use liquids.

Reagent Deterioration

Alterations in the physical appearance of the reagents or values of control materials outside of the manufacturer's acceptable range may be an indication of reagent instability.

Instruments

Refer to specific instrument application for suggested settings.

Precautions

1. This reagent is for *in vitro* diagnostic use only.
2. Not for internal or external use in humans or animals.
3.

Specimen Collection and Preparation

Special preparation of the patient is unnecessary. Fasting specimens are not required. No special additives or preservatives other than anticoagulants are required. Collect venous blood with EDTA using aseptic technique. All human specimens should be regarded as potentially biohazardous. Therefore, universal precautions should be used in specimen handling (gloves, lab garments, avoid aerosol production, etc.).

To determine HbA1c, a hemolysate must be prepared for each sample:

1. Dispense 1ml Hemolysis Reagent into tubes labeled: Control, Patients, etc.
   Note: Plastic or glass tubes of appropriate size are acceptable.
2. Place 20ul of well mixed whole blood into the appropriately labeled lyse reagent tube. Mix.
3. Allow to stand for 5 minutes or until complete lysis is evident. Hemolysates may be stored up to 10 days at 2-8°C.

Storage and Stability

1. All reagents are stable to the expiration date stated on the labels. Do not use the reagents past their expiration date.
2. R1 and R2 are stable for at least one month after opening stored at 2-8°C.
3. Hemoglobin A1c in whole blood collected with EDTA is stable for one week at 2-8°C.[5]

Interferences

1. Bilirubin to 50mg/dL, ascorbic acid to 50mg/dL, triglycerides to 2000mg/dL, carbamylated Hb to 7.5mmol/L and acetylated Hb to 5.0mmol/L do not interfere in this assay.
2. It has been reported that results may be inconsistent in patients who have the following conditions: opiate addiction, lead-poisoning, alcoholism, ingest large doses of aspirin.[6,7,8,9]
3. It has been reported that elevated levels of HbF may lead to underestimation of HA1c.[10] Also, it has been reported that labile intermediates (Schiff base) are not detected and do not interfere with HbA1c determination by immunoassay.[5]
4. It has been determined that Hemoglobin variants HbA2, HbC and HbS do not interfere with this method.
5. Other very rare variants of hemoglobin (e.g. HbE) have not been assessed.

Procedure

Wavelength	λ: 620 nm
Working Temperature	37°C
Optical Path	1 cm
Reaction	"end point"
Direction	Increase

Bring the reagents at 15-25°C before use them.

Reagent R1	240 µl
Sample	6 µl
	Mix, incubate at 37°C for 5' and then add:
Reagent R2	80µl
	Mix, make a reading after 5' at 37°C.

Procedure (automated-Hitachi 717)

TEST NAME	HbA1c
ASSAY CODE	[1-POINT]:[50]-[0]
SAMPLE VOLUME	[5] [3]
R1 VOLUME	[180] [50] [NO]
R2 VOLUME	[60] [20] [NO]
WAVELENGTH	[ ] [660]
CALIBRATION	[NONLINEAR] [4] [5]
STD (1) CONC-POS	[0.0*] [1]
TD (2) CONC-POS	[**] [2]
STD (3) CONC-POS	[**] [3]
STD (4) CONC-POS	[**] [4]
STD (5) CONC-POS	[**] [5]
STD (6) CONC-POS	-
SD LIMIT	[999]
DUPLICATE LIMIT	[1000]

Gesan Production s.r.l.
Via Fiera dell'Eremita, 71 – Campobello di Mazara (TP) – Part. IVA 01928730819
Tel +39 0924 912534 – Fax +39 0924 912534 // INTERNET : www.gesanproduction.it - e-mail: overseas@gesanproduction.it

Hemoglobin A1c

Reagent Set

CE IVD For in vitro medical device

SENSITIVITY LIMIT	[0]
ABS LIMIT (INC/DEC)	[32000] [INCREASE]
PROZONE LIMIT	[-] [-]
EXPECTED VALUE	[-] [-]
PANIC VALUE	[-] [-]
INSTRUMENT FACTOR	[1.0]

* Use Saline for the 0.0 Calibrator

** Input the values of the calibrator set being used

Hitachi 717™ is a Registered Trademark of Nissei Sangyo Co. Ltd., Japan

Limitations

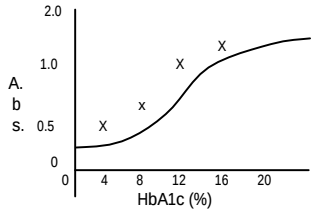
1. This assay should not be used for the diagnosis of diabetes mellitus.
2. Patient specimens should always be assayed using a calibration curve.
3. It has been reported that results may be inconsistent in patients who have the following conditions: opiate addiction, lead-poisoning, alcoholism, ingest large doses of aspirin.[6, 7, 8, 9]
4. It has been reported that elevated levels of HbF may lead to underestimation of HA1c and, that uremia does not interfere with HbA1c determination by immunoassay.[10] It has been reported that labile intermediates (Schiff base) are not detected and therefore, do not interfere with HbA1c determination by immunoassay.[5]
5. It has been determined that Hemoglobin variants HbA2, HbC and HbS do not interfere with this method.
6. Other very rare variants of hemoglobin (e.g. HbE) have not been assessed.

Quality Control

The reliability of test results should be monitored whenever patient samples are assayed using a standard and quality control materials analyzed in the same manner employed for the unknowns. We suggest the use of commercially available Hemoglobin A1c controls with an assayed range. If controls do not fall into the assayed range patient values from that run should not be reported. The run should be repeated, making sure that all mixing and handling instructions are strictly followed. Linearity of the assay should be verified with a commercial linearity check set, or dilutions of a high specimen, at least every six months.

Calculations / Results

HbA1c results for the unknowns and controls are determined using the prepared calibration curve. An example curve is illustrated below:



Expected Values[11]

Recommended Values: less than 6% for a non-diabetic, less than 7% for glycemic control of a person with diabetes.

Each laboratory should establish its own expected values. In using Hemoglobin A1c to monitor diabetic patients, results should be interpreted individually. That is, the patient should be monitored against him or herself. There is a 3-4 week time lag before Hemoglobin A1c reflects changes in blood glucose level.

Performance

1. Linearity: The Hemoglobin A1c assay range is 2.0%-16.0%.
2. Comparison: A study using 40 human specimens between this Hemoglobin A1c procedure and an automated HPLC procedure (Tosoh) yielded a correlation coefficient of 0.988 and a linear regression equation of y=1.050x – 0.481. (Syx = 0.332)
3. Precision:

   Within Run: The within run precision was established by assaying two blood samples following NCCLS protocol EP5 on a Hitachi 917.

Level	Mean	Std. Dev.	% C.V.
Low	5.48	0.078	1.43
High	10.28	0.176	1.72

   Day to Day: The between day precision was established by assaying two blood samples following NCCLS protocol EP5 on a Hitachi 917.

Level	Mean	Std. Dev.	% C.V.
Low	5.48	0.152	2.77
High	10.28	0.275	2.68

4. Sensitivity: Sensitivity was investigated by reading the change in absorbance at 660nm for a saline sample and a whole blood sample with a known concentration. Ten replicates of each sample were performed. The results of this investigation indicated that, on the analyzer used (Hitachi 717), the HbA1c reagent showed little or no drift on the zero sample. Under the reaction conditions described, a 0.073 absorbance change is approximately equivalent to 1.0% HbA1c.

References

1. Trivelli, L.A., Ranney, H.M., and Lai, H.T., New Eng. J. Med. 284,353 (1971).
2. Gonen, B., and Rubenstein, A.H., Diabetologia 15, 1 (1978).
3. Gabbay, K.H., Hasty, K., Breslow, J.L., Ellison, R.C., Bunn, H.F., and Gallop, P.M., J. Clin. Endocrinol. Metab. 44, 859 (1977).
4. Bates, H.M., Lab. Mang., Vol 16 (Jan. 1978).
5. Tietz, N.W., Textbook of Clinical Chemistry, Philadelphia, W.B. Saunders Company, p.794-795 (1999).
6. Ceriello, A., et al, Diabetologia 22, p. 379 (1982).
7. Little, R.R., et al, Clin. Chem. 32, pp. 358-360 (1986).
8. Fluckiger, R., et al, New Eng.J. Med. 304 pp. 823-827 (1981).
9. Nathan, D.M., et al, Clin. Chem. 29, pp. 466-469 (1983).
10. Engbaek, F., et al, Clin. Chem. 35, pp. 93-97 (1989).
11. American Diabetes Association: Clinical Practice Recommendations (Position Statement). Diabetes Care 24 (Suppl. 1): S33-S55, (2001).

CE	CE Mark (98/79 CE regulation)
IVD	in vitro medical device
LOT	Batch Code
	Use by
	Storage temperature limits
	Read instruction for use
	Gesan Production srl

Gesan Production s.r.l.

Via Fiera dell'Eremita, 71 – Campobello di Mazara (TP) – Part. IVA 01928730819

Tel +39 0924 912534 – Fax +39 0924 912534 // INTERNET : www.gesanproduction.it - e-mail: overseas@gesanproduction.it

1 – PRODUCT OFFERED IN VIALS

Commercial Name **HbA1c LR**

REF	SIZE	R1	R2	EXTERNAL LABEL CODE	R1 LABEL CODE	R12 LABEL CODE
9900140	1x40 ml	1x30 ml	1x10 ml	E9900140ES	E9900140R1	E9900140R2
A9900140	1x40 ml	1x30 ml	1x10 ml	EA9900140ES	EA9900140R1	EA9900140R2
C9900140P	1x40 ml	1x30 ml	1x10 ml	C9900140PES	C9900140PR1	C9900140PR2
C9900140A	1x40 ml	1x30 ml	1x10 ml	C9900140AES	C9900140AR1	C9900140AR2
CA9900140P	1x40 ml	1x30 ml	1x10 ml	CA9900140PES	CA9900140PR1	CA9900140PR2
CA9900140A	1x40 ml	1x30 ml	1x10 ml	CA9900140AES	CA9900140AR1	CA9900140AR2
C9900380D	1x76 ml	1x56 ml	1x20 ml + Lyse	C9900380DES	C9900380DR1	C9900380DR2
CA9900380D	1x76 ml	1x56 ml	1x20 ml + Lyse	CA9900380DES	CA9900380DR1	CA9900380DR2

2- PRODUCT OFFERED IN BULK

R1:

Commercial Name HbA1c LR R1

Packaging in adequate volume tank "PE"

Product Ref 990 R1

R2:

Commercial Name HbA1c LR R2

Packaging in adequate volume tank "PE"

Product Ref 990 R2

IVD

HbA1c UV LR

Kit for HbA1c determination in human blood.

INDEX

Introduction

Identification of qualitative and quantitative characteristics of the device

1 General description
2 Identification of potential hazards of the device
- 2.1 hazards related to the use of in vitro diagnostics
- 2.2 toxicological risks
- 2.3 danger factors associated with medical devices
  - 2.3.1 generalities
  - 2.3.2 risks related to energy
  - 2.3.3 biological risks
  - 2.3.4 environmental risks
  - 2.3.5 risks related to the use of the device
  - 2.3.6 risks due to functional failures, maintenance and aging

Acceptability of risks

- 3.1 methodology
- 3.2 toxicological risks
  - 3.2.1 risks associated with medical devices
    - 3.2.1.1 risks related to energy
    - 3.2.1.2 biological risks
    - 3.2.1.3 environmental risks
    - 3.2.1.4 risks related to the use of the device
    - 3.2.1.5 risks related to functional failures, maintenance and aging

Final evaluation

INTRODUCTION

The present document describes the risk analysis performed in order to identify in advance the dangers associated with the design, manufacture and use of the device. The study was conducted according to the guidelines of the UNI CEI EN ISO 14971 related to the definition of the operating goals and rules for the risk analysis of medical devices.

IDENTIFICATION OF QUALITATIVE AND QUANTITATIVE CHARACTERISTIC RELATED TO THE DEVICE

The following is the available information for a complete description of the device and / or accessories, obtained by applying the checklist suggested by UNI CEI EN ISO 14971. Based on the information collected will be structured the subsequent phases of analysis risk.

1 - GENERAL DESCRIPTION

The product consists of diagnostic reagents for clinical analysis as well as described in chapter "Product Overview".

2 - IDENTIFICATION OF POSSIBLE DANGERS OF DEVICE

Applying the checklist shown in the UNI CEI EN ISO 14971 relating to different types of risks have been identified the dangers related with the device. At this stage, are highlighted the characteristics of the device that must satisfy specific standards, when these can be applied, and the most critical points for the safety of the device.

POINT	QUERY	DESCRIPTION	RISK AND POSSIBLE CONSIDERATION
A.2.1	**What is the intended use / intended purpose and how should the medical device should be used?**	Factors that should be considered include the user expected, the physical and mental abilities, skills and training of the user, the ergonomic aspects, the environment in which it has to be used, by whom have to be installed and if the patient can control or influence the use of the medical device. It should be payed particular attention to the intended users with special needs, such as the disabled, the elderly and children. These particular requirements may include the assistance of another person to allow the use of the medical device. The medical device will be used by individuals with different levels of competence and culture? Which role is expected the medical device should play in the diagnosis, prevention, monitoring, treatment or disease alleviation, injury or disability compensation, anatomy replacement or modification, or conception control? The medical device is intended to support vital functions? Is it necessary a special action in case of failure of the medical device? There are particular concerns about the design features of the interface that could contribute to an inadvertent error of use.	The device is intended to be used by qualified personnel (technical or graduated) in the clinical chemical laboratory. Basic training necessary in a clinical chemical laboratory. Not expected any outdoor installation by qualified and competent personnel. The product does not require any contact with the user, nor with the final patient.
A.2.2	**Does the medical device is intended to come in contact with the patient or other persons?**	Factors that should be considered include the nature of the expected contact, or superficial contact, invasive and / or installation contact and, for each one, the period and the frequency of contact.	The device in its original form is handled only by laboratory personnel authorized to perform diagnostic in vitro tests; the processed device is non-invasive, being a product of in vitro diagnostic test biological liquids.
A.2.3	**Which materials and / or components are incorporated in the medical device or are used with it, or are in contact with the medical device?**	Factors that should be considered include if there are known characteristics relevant to the safety.	The device in its original form consists of chemical reagents whose composition and use is described in detail in the instruction sheet.
A.2.4	**Is supplied or extracted any energy to the patient and / or from him?**	Factors that should be taken into consideration include the type of transferred energy and its control, quality, quantity and length.	NOT APPLICABLE
A.2.5	**Are supplied or extracted any substances to the patient and / or from him?**	Factors that should be considered include whether the substance is supplied or extracted, whether it is a single substance or a series of substances, the maximum and minimum transfer rapidity, and its relative control.	NOT APPLICABLE

A.2.6	**Are there any biological materials processed from the medical device for subsequent re-use?**	Factors that should be taken into consideration include the type of process and the processed substance(s) (for example, auto-transfusion, dialysis).	NOT APPLICABLE
A.2.7	**The medical device is supplied sterile or is possible to schedule the sterilization by the user or are applicable other microbiological tests**	Factors that should be taken into consideration include whether the medical device is disposable or reusable and also any packaging, lifetime and any limit to the number of reuse cycles or the type of sterilization process to be used.	NOT APPLICABLE
A.2.8	**Is It expected that the medical device is cleaned and disinfected regularly by the user?**	Factors that should be taken into consideration include the types of cleaning or disinfection agents to be employed and the limits to the number of cleaning cycles. In addition, the design of the medical device can affect the efficiency of the cleaning and disinfection routine.	NOT APPLICABLE
A.2.9	**The medical device is set to change the patient's environment?**	Factors that should be taken into consideration include temperature, humidity, atmospheric gas composition, pressure and light.	NOT APPLICABLE
A.2.10	**Measurements are performed?**	Factors that should be taken into consideration include the measured variables and the accuracy and precision of the measurement results.	The diagnostic system provides a qualitative interpretation analysis using diagnostic tools with spectrophotometric calibration
A.2.11	**Does the medical device provides interpretative data?**	Factors that should be taken into consideration include the conclusions if they are submitted by the medical device through input or acquired data, used algorithms and confidence limits.	The diagnostic system provides a qualitative and interpretative analysis. Is specified in the operating instructions the need to complete the acquired data with other diagnostic tests in order to reach a conclusive picture.
A.2.12	**The medical device is intended to be used combined with other drugs or medical technologies?**	Factors that should be taken into consideration include the identification of medicines or other medical technologies that may be involved and the potential problems associated with such interactions, as well as patients joining to therapy.	NOT APPLICABLE
A.2.13	**There are unwanted outputs of energy or substances?**	The energy-related factors that should be taken into consideration include noise and vibration, heat, radiation (including ionizing radiation, non-ionizing and ultra-violet/visible/infrared), contact temperatures, leakage currents and electric and / or magnetic fields. The factors related to substances that should be considered include the discharge of chemicals substances, waste products and body fluids.	The waste products as described in the instructions for use must be treated as waste to be assigned to a specialized company.
A.2.14	**Is the medical device subjected to environmental conditions?**	Factors that should be taken into account include operating environments, transport and storage. These include light, temperature, vibration, leaking, susceptibility to variations of power and cooling sources and electromagnetic interference.	The device is stable under expected transport and storage conditions. Reagents should be stored at controlled temperature. Must be avoided contamination with dirt or dust; must be avoided the use of tools needed for the dispensation that may contaminate and modify the chemical-physical characteristics of the reagents.
A.2.15	**Does the medical device affect the environment?**	Factors that should be taken into consideration include the effects of power and cooling sources, emission of toxic materials and generation of electromagnetic interference.	NOT APPLICABLE
A.2.16	**To the medical device are associated consumables or essential accessories?**	Factors that should be considered include specifications for such consumables or accessories and restrictions on users' choice.	NOT APPLICABLE
A.2.17	**It is necessary maintenance and / or calibration?**	Factors that should be taken into consideration include yhe possibilities that the maintenance and / or adjustment is made by the operator or user or by a specialist. Are substances or equipment necessary for the proper maintenance and / or calibration?	NOT APPLICABLE

A.2.18	**Have the medical device got a software?**	Factors that should be considered include whether it is expected that the software is installed, tested, modified or exchanged by the user and / or operator.	NOT APPLICABLE
A.2.19	**Has medical device a limited life span?**	Factors that should be taken into account include the labeling or the indicators and the disposal of such medical devices.	The kit should be stored according to the instructions given in the instructions and on the labels (controlled temperature) and used within the expiry date printed on the label
A.2.20	**Are there delayed and / or long-term employment effects?**	Factors that should be taken into consideration include ergonomic and cumulative effects.	NOT APPLICABLE
A.2.21	**To which mechanical forces is subjected the medical device?**	Factors that should be taken into account includ the possibility that these forces are controlled by the user or by the interaction with other people.	NOT APPLICABLE
A.2.22	**What determines medical device duration of life?**	Factors that should be considered include aging and depletion of batteries.	Chemical and physical properties of raw materials and their combination, the conditions of storage and handling.
A.2.23	**Is the device intended for single use only?**		The device can be used until complete consumption of the reagents within the expiry date printed on the package and if stored and handled in a suitable way and in accordance with the instructions contained in the method.
A.2.24	**Is it needed a deactivation or a safe elimination of medical device?**	Factors that should be taken into account include the waste products generated during the elimination of medical device. For example, does it contain toxic or hazardous material, or the material is recyclable?	NOT APPLICABLE
A.2.25	**Does installation or normal use of medical device require special training?**	Factors that should be taken into consideration include the startup and the transition to the end user and if it is probable / possible that the installation can be carried out by persons without necessary skills.	The device requires no installation, and it is used by laboratory personnel authorized to perform in vitro diagnostic tests.
A.2.26	**Have to be established or introduced new manufacturing processes?**	The introduction of new manufacturing processes in the manufacturer's establishment, must be considered as a potential source of new(s) the danger(s) (for example new technology, new production scale).	Production is carried out taking into consideration the level of security required under current regulations; handling and storage of chemical products, used for the preparation of reagents, is carried out taking into consideration the dangers associated with each product, getting them from the relative safety data sheets. It was detected no biological risk or exposure to ionizing radiation.
A.2.27	**Does the success of medical device's application depends critically on human factors such as the user interface?**	Factors that should be taken into consideration are the characteristics of user interface design which can contribute to the error of use. The characteristics should be designed in such a way that it can not be used improperly by users engaged in an environment where distractions are common, for example device control, symbols used, ergonomic features, design and physical layout, operating hierarchy, menu for devices controlled by software, visibility of warnings, audibility of alarms, standard color coding. Such considerations include, without limitation, the following:	
A.2.27.1	**Has the medical device connection parts or accessories?**	Factors that should be taken into consideration include the possibility of incorrect connections, differentiation, similarity with links of other products, the connecting force, integrity feedback information about the connections and excessive or insufficient tightening.	NOT APPLICABLE

A.2.27. 2	**Has the medical device a control interface?**	Factors that should be taken into consideration include distance, coding, grouping, mapping, return mode, serious errors, minor errors, controls differentiation, visibility, direction activation or modification and whether the controls are continuous or intermittent and reversibility adjustments or actions.	NOT APPLICABLE
A.2.27.3?	**Does the medical device display information?**	Factors that should be taken into consideration include visibility in various environments, orientation, user groups and perspectives, clarity of the information presented,, color coding and accessibility of critical information.	NOT APPLICABLE
A.2.27. 4	**Is the medical device controlled by a menu?**	Factors that should be taken into consideration include the complexity and the number of levels, the hierarchical levels, the knowledge of the state, the location of settings, the navigation method, the number of steps per action and the clarity of sequences and the problems of storage, the importance of control function relating to its accessibility.	NOT APPLICABLE
A 2.28	**Is the medical device intended to be mobile or portable?**	Factors that should be taken into consideration are the necessary handgrips, handles, wheels, brakes, stability and mechanical durability.	NOT APPLICABLE

2.1 DANGERS RELATED TO THE USE OF IN VITRO DIAGNOSTIC (ANNEX A UNI CEI EN ISO 14971)

The in vitro diagnostic device does not generate any direct risk to the patient or the person under examination, as it is not in contact with the human body, but there may be indirect risks consist of dangers that lead or contribute to incorrect decisions and samples classifications with altered diagnosis and consequent incorrect therapy.

DANGER	COMMENTS
Non-homogeneity of the batch, incompatibilities from one batch to another	Each batch consists of reagents from a single process. Therefore, there is no possibility of kits that ate not uniform within the same batch. Also within the production of each component checks are performed in order to ensure homogeneity. Moreover within the production of each component there are performed controls in order to ensure homogeneity.
Common interference factors	Into the method are marked the most common interferences reported in the bibliography. They have been tested on the device up to the limits indicated for each interfering substance.
Carry-over effects	The risk is not applicable to manual methods. However, they are detectable only in automatic equipment use which also include washing accurate.
Errors in the identification of the samples	The samples that have to be used are clearly indicated in the instructions. The quality system of the laboratory that uses the device, must include the operating definition procedures for the collection, identification, handling, storage and traceability of patient's samples.
Stability problems (during storage, shipping, use, and after starting opening of the container)	The instructions for use of the device report the necessary information for conservation and handling to retain full functionality over time, during the whole period of stability declared.
Problems associated with the collection, preparation and stability of the samples	In the instructions for use are specified substances to be used for an adequate sample stability, and the stability of the same sample. In order to reduce the possibility of improper use of the device have been included in the instructions for use the following information: Sample type anticoagulants to avoid alanine stability in the sample and the its related conservation conditions. the observation of the information given, practically eliminates the risk of problems associated with the collection
Inadequate definition of the prerequisites	The instructions show in accordance with the requirements of Directive 98/79/EC and the UNI-EN 375, the information needed to ensure proper and totally safe operation of the device, treating the following topics: - Directions for use including clinical applications - Method principles and limitations -Warnings and precautions - Needed material - Method performances. The device is used by professionally trained personnel.

2.2 TOXICOLOGICAL RISKS (APPENDIX B UNI-EN 1441)

The in vitro diagnostic device presents in its compositionbiological origin substancesfor food use of animal and plant origin. Therefore, it is excluded any potential risks.

2.3 RISK FACTORS ASSOCIATED WITH MEDICAL DEVICES (APPENDIX C UNI-EN 1441)

2.3.1 ABSTRACT

In this phase are identified characteristics of the in vitro diagnostic device which must meet specific standards, when it is expected the application and the critical points for the safety of the same.

2.3.2 HAZARDS RELATED TO ENERGY

The device does not receive and does not supply energy, thus it is excluded any possibility of risk related to energy.

2.3.3 BIOLOGICAL RISKS

Danger	Comments
Biological load	The device isn't sold sterile and if it doesn't enter in contact with the human body it won't need further treatment
Biological contaminations	The device isn't sold sterile and if it doesn't enter in contact with the human body it won't need further treatment
Biological incompatibility	The product does not require any contact with either the user or the patient, therefore it is excluded any biohazard.
Incorrect emition (substance/energy)	Not applicable
Wrong formulation for an incorrect use of raw materials with a consequent device ineffectiveness.	Production procedures expected in the quality manual as well as final checks on the finished product, exclude this risk.
Improper mix of reagents with a consequent reduced effectiveness of the device	
toxicity	Not applicable
infection (crossed)	Not applicable
pyrogenicity	Not applicable
inability to maintain hygienic safety	Not applicable
degradation	Stability tests of the product ensure the proper maintenance of the materials contained in the device, if well observed the conditions of preservation.

2.3.4 ENVIRONMENTAL HAZARDS

Danger	Comments
electromagnetical interferences	Not applicable
inadequate supply of energy or refrigeration	Not applicable
operating probability outside the prescribed environmental conditions	If the conditions o fuse are not respected there could be the possibility of a wrong classification of patient's sample. However this risk is highly attenuated after checking required by the instructions for use.
incompatibility with other devices	The instructions show technical specifications necessary for proper use.
Accidental mechanical damage	It is the responsibility of the laboratory technician the correct use of the diagnostic system, the device is conform to the normal regulations concerning safety and hygiene. It is necessary to observe the rules of good laboratory practice.
Contamination due to waste products and / or disposal of the device	Wastewater processing and packaging parts found after provided manufacturing, shall be treated for the purposes of environmental protection, according to national and local regulations as stated in the instructions for use, taking care to follow all the rules of good manufacturing practice.

2.3.5 HAZARDS RELATED TO THE USE OF THE DEVICE

Danger	Comments
inadequate labeling	Both the label and the sheet of instructions have been compiled according to strict European regulations (Directive 98/79/EC and EN 375-92). Even the symbols and colors used meet these laws. The label was applied with permanent adhesive which does not allow accidental detachment, while printing is done with a thermal transfer process unalterable and that does not fade over time.
inadequate operating instructions	The instructions for use are in accordance with Directive 98/79/EC, Annex I Section 8 Information supplied by the manufacturer and the UNI EN 375, and includes the recommendations that came out risk analysis EEC
accessories inadequate specifications	The instructions for use are in accordance with Directive 98/79/EC, Annex I Section 8 Information supplied by the manufacturer and the UNI EN 375, and includes the recommendations that came out risk analysis EEC
inadequate specifications for the checks before use	The instructions for use are in accordance with Directive 98/79/EC, Annex I Section 8 Information supplied by the manufacturer and the UNI EN 375, and includes the recommendations that came out risk analysis EEC
too complicated operating instructions	The device is used by operators specialized in the sector, which in any case have the possibility to use a customer assistance service for explanations and every problem that can arise during normal use of the device itself.
istruzioni operative separate o indisponibili	The device is used by operators specialized in the sector, which in any case have the possibility to use a customer assistance service for explanations and every problem that can arise during normal use of the device itself.
use by staff not adequate / inexperienced	Not applicable
Incorrect use reasonably be expected. The following errors are presumable by the laboratorian	One or more errors hypothesized would have as a consequence an unreliability of the results obtained. However, the implementation of controls reduces this risk to very low levels. Was also highlighted in the instructions the need to understand the test results together with information derived from the patient's clinical examination that practice makes clear the possible misinterpretation.: if that practice is observed it is easier to find the possible misinterpretation.
Improper storage: with consequent low quality level of the product due to the deterioration of chemical nature active ingredients with performances result with different different from that expected.	
Wrong code: with consequent unreliability of the data that don't correspond to a control and to the lack of specificity of the system.	
Out of validity: low quality level given by the aging of the product and with performances different from that expected.	
Wrong reconstitution: error in the reconstitution of reagents with wron quantitative and / or not appropriate solvents.	
Misuse: in case of there is no respect of the conditions of use expressed in the instructions for use, such as: incorrect use of quantity (Qty), time not respected (t), not observed temperatures (T), agitation conditions not fulfilled (rpm) and dispensing sequences not observed (Sequences).	
inaccurate measurements and other aspects of metrology	Not applicable
inaccurate diagnosis	Resulting inadequate therapy with the possibility of damage to the patients' health
erroneous transfer of data	Inadequate transfer of data from analytical reporting with the consequent risk of providing incorrect diagnosis and then inadequate treatment. The quality system should provide appropriate operating procedures for the samples and patient identification and the data transfer in various areas of the laboratory.

incorrect data presentation	Resulting incorrect reporting due to information not associated with the correct normal values and the possible risk of incorrect interpretation of clinical data and possible errors in diagnosis and its treatment.
incompatibility with consumer products, accessories, other devices	Any problems using the device is properly reported in the method, highlighting all the restrictions according to current knowledge.

2.3.6 HAZARDS DUE TO OPERATING, MAINTENANCE AND AGING FAILURE

Danger	Comments
Performance characteristics unsuitable for use	Not applicable
Lack of or inadequate maintenance specifications including specific functional inadequate controls after maintenance	Not applicable
inadequate maintenance	Not applicable
Lack of a proper determination of the device expiry	The product will clearly report information about the stability of individual reagent and product and in accordance with Directive 98/79/EC to the UNI-EN-375.
Loss of mechanical integrity	Not applicable
Inadequate packaging (contamination and / or deterioration of the device)	The packaging system ensures the integrity of the product during handling, shipping and delivery.
Improper reuse	Not applicable

RISKS ACCEPTABILITY

3.1 METHODOLOGY

The criteria of acceptability can be graphically represented with a risk matrix, where in the abscissa there are the categories related to the magnitude (criticality) of the consequences arising from the situation of the considered danger, while in the ordinates there are positioned the different levels of probability or frequency.

This representation in matrix form constitute a simple and effective way to illustrate the combination of frequency and consequences that is synthesized in a level of risk.

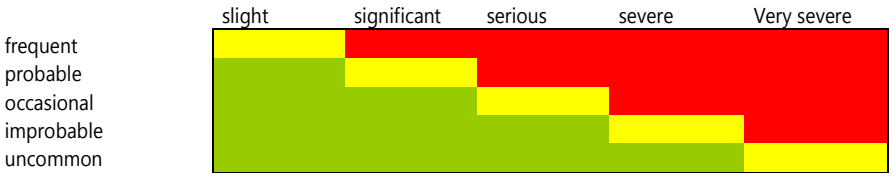
Generally the categories of magnitude may be defined as follows:

Slight damage that brings negligible consequences to the patient / user
Significant damage that quickly disappears without causing irreversible effects or prolonged
Serious damage that leads appreciable consequences that require some time before disappearing
Severe development of a damage which requires a treatment intense and / or prolonged over time, or requires the performance of a surgical procedure to be eliminated
Very severe damage enough severe to cause irreversible damage to the patient or user's body; damage, also mechanical, of vital organs or anyway of major organs, with effects no longer recoverable, with the possibility of compromising the patient or user's life

Frequency / probability categories can be defined as follows:

Common the dangerous situation occurs more than 1 time out of 10
Probable the dangerous situation occurs with a frequency from 1/10 to 1/100
Casual the dangerous situation occurs with a frequency from 1/100 to 1/1000
Improbabile the occurrence of the dangerous situation has a frequency from 1/1000 to 1/10000
Uncommon the occurrence of the dangerous situation has a frequency of less than 1/10000

The general matrix of risk is as follows:



Within the matrix can be identified three different areas:

- **Area of the unacceptability** of the risk, where the risk is intolerable and preventive or Protective measures must be readily identified and adopted. May be required a specific assessment of the risk / benefit ratio.
- **area intermedia o di rischio indesiderabile**, dove sono comunque suggerite misure di mitigazione, anche a seguito di una I verifica costi/benefici. **Intermediate area or undesirable risk**, where, however, suggested mitigation measures, also as a result of cost / benefit. verification.
- **negligible area of risk**, where the danger is fully acceptable

Each dangerous situation was analyzed and localized within the matrix.

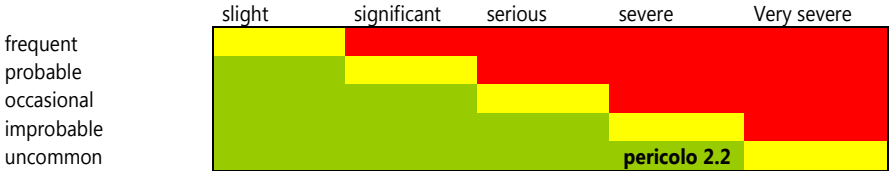
The magnitude associated with the dangerous situation was considered significant because:
device and samples errors of use, storage and identification can not achieve the diagnostic goal without causing substantial damage with prolonged and reversible effects to the patient.

The frequency associated with the dangerous situation was considered occasional, because the device is used exclusively by trained and informed personnel about the specific risks and moreover the operating instructions contain all the information necessary for a correct use of the device.

The risk falls within acceptable: it is suggested in any case, to maintain the acceptability of risk, an adequate level of information to users in order to obtain from them a constant level of attention.

3.2 TOXICOLOGICAL HAZARDS

The general matrix of risk processed is as follows:



The magnitude associated with the dangerous situation was considered serious because possible infection to the user from the use of materials of animal origin may cause diseases with intensive and prolonged care. The device never comes in contact with the patient.

The frequency associated with the hazardous situation has been considered rare, because:

- the device uses only raw food already adequately selected and controlled;
- The device never comes into contact with either the patient or the user;
- the device is used only by trained perdonnel that is informed on all the specific risks.

The risk falls within acceptable: it is suggested in any case to maintain the acceptability of risk an adequate level of information to users in order to obtain from them a constant level of attention.

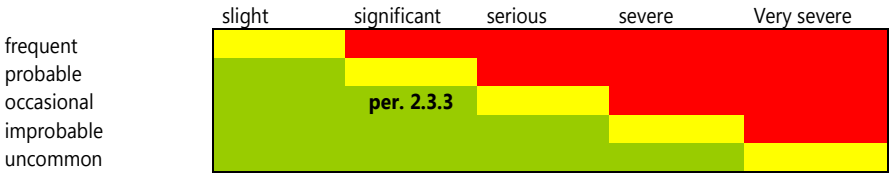
3.2.1 HAZARDS ASSOCIATED WITH MEDICAL DEVICES

3.2.1.1 HAZARDS RELATED TO ENERGY

The general matrix of risk is not applicable

3.2.1.2 BIOLOGICAL HAZARDS

The general matrix of risk is as follows:



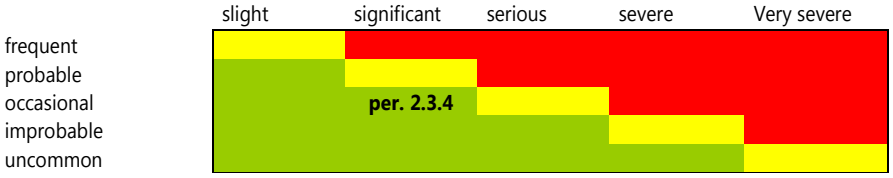
l'obiettivo diagnostico senza però, provocare danni rilevanti con effetti reversibili e prolungati al paziente. The magnitude associated with the dangerous situation was considered significant as any incorrect application of the device with the use of unsuitable samples can not achieve the goal diagnosis without, causing substantial damage with prolonged and reversible effects to the patient.

The frequency associated with the hazardous situation has been considered occasional, because the device is made according to specific processing and control procedures and the device is used exclusively by trained and informed personnel about the specific risks.

The risk falls within acceptable: it is suggested in any case to maintain the acceptability of risk an adequate level of information to users in order to obtain from them a constant level of attention.

3.2.1.3 ENVIRONMENTAL HAZARDS

The general matrix of risk is as follows:



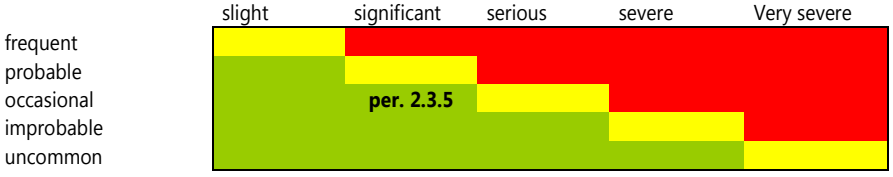
The magnitude associated with the dangerous situation was considered significant as any not suitable incorrect or storage application for the device can not reach the diagnostic goal without, causing substantial damage with prolonged and reversible effects to the patient.

The frequency associated with the dangerous situation was considered occasional, because the device is used exclusively by trained personnel informed about the specific risks and about the disposal procedures of laboratory waste.

The risk falls within acceptable: it is suggested in any case to maintain the acceptability of risk an adequate level of information to users in order to obtain from them a constant level of attention.

3.2.1.4 HAZARDS RELATED TO THE DEVICE USE

The general matrix of risk is as follows:



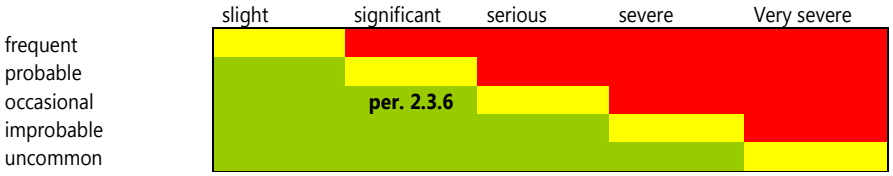
The magnitude associated with the dangerous situation was considered significant as any incorrect application of the device can not reach the diagnostic goal without, causing substantial damage with prolonged and reversible effects to the patient.

The frequency associated with the dangerous situation was considered occasional, because the device is used exclusively by trained personnel informed about the specific risks.

The risk falls within acceptable: it is suggested in any case to maintain the acceptability of risk an adequate level of information to users in order to obtain from them a constant level of attention.

3.2.1.5 HAZARDS RELATED TO FUNCTIONAL MAINTENANCE AND AGING FAILURES,

The general matrix of risk is as follows:



The magnitude associated with the dangerous situation was considered significant as any incorrect application of the device can not reach the diagnostic goal without, causing substantial damage with prolonged and reversible effects to the patient.

The frequency associated with the dangerous situation was considered occasional, because the device is used exclusively by trained personnel informed about the specific risks and about the disposal procedures of laboratory waste.

The risk falls within acceptable: it is suggested in any case to maintain the acceptability of risk an adequate level of information to users in order to obtain from them a constant level of attention.

FINAL EVALUATION

II device does not present significant risks or dangers for the use for which it is intended.

The residual risk is monitored and reassessed periodically to highlight further underestimated the dangers or to check whether the solutions adopted are always adequate. This review is from internal audits and not conformity reports expected by the procedures of quality system, and by the after-sales service questionnaire provided by these procedures too.

Internal audits are performed on an annual basis in order to monitor the proper implementation of procedures and proper risk assessment in the light of any changes that may arise. For this purpose the procedure of the quality system provides a specific guideline.

Hemoglobin A1c KIT

PRODUCT PERFORMANCES

9900140
990HCS
990L
990CAL
990CTL
A990CAL
A990CTL

INDEX

1. PRODUCT PERFORMANCES ON GESAN CHEM 400		3
1,1	REAGENTS	3
1,2	CALIBRATION	3
1,3	ACCURACY	4
1,4	INTRAREPRODUCIBILITY	6
1,5	INTERREPRODUCIBILITY	7
1,6	COMPARISON STUDY WITH ROCHE	8
1,7	SENSITIVITY	10
1,8	NORMAL VALUES	10
1,9	LIMITATION OF THE METHOD	11
1,10	CONCLUSION	11
1,11	DETERMINATION OF 3 DIFFERENT LOTNUMBERS	12
1,12	PROTOCOL FOR THE DETERMINATION OF HBA1C ON GESAN CHEM 400	13
2. APPLICATION VERIFICATION PROCEDURE		14
2,1	APPROVED STATUS	14
2,2	NOT APPROVED STATUS	14
3. APPROVED APPLICATIONS		15
3,1	DETERMINATION OF HBA1C ON SELECTRA PRO M	15
3,2	PROTOCOL FOR THE DETERMINATION OF HBA1C ON SELECTRA PRO M	16
3,3	DETERMINATION OF HBA1C ON COBAS MIRA	17
3,4	PROTOCOL FOR THE DETERMINATION OF HBA1C ON COBAS MIRA	18

1. PRODUCT PERFORMANCES ON GESAN CHEM 400

1.1 Reagents

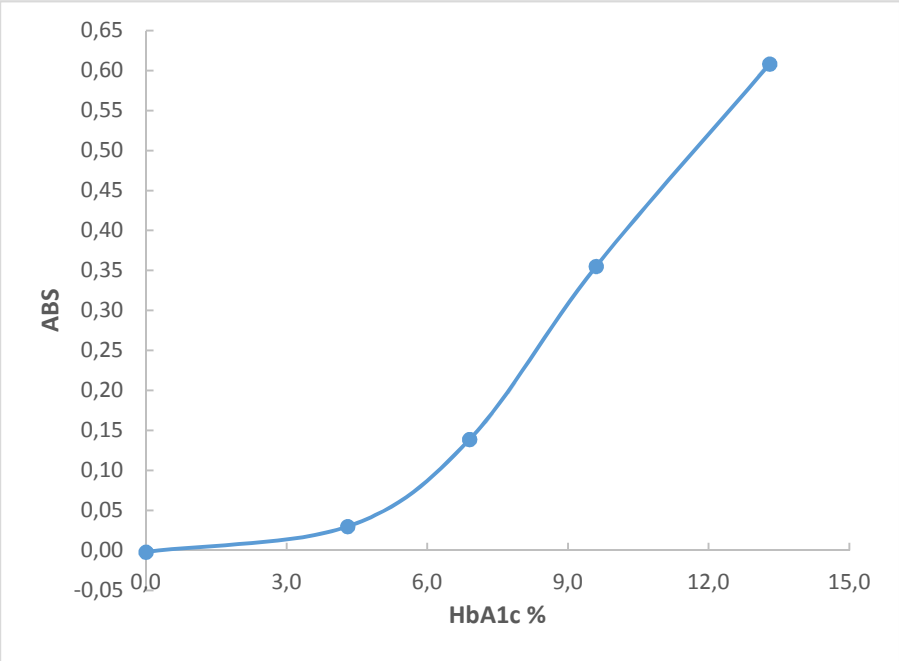
Hemoglobin A1c Standard Set	Lot. SH029	Exp. 2016/03	5 µL
Hemoglobin A1c Reagent R1	Lot. A1C020	Exp. 2017/03	180 µL
Hemoglobin A1c Reagent R2	Lot. A1C020	Exp. 2017/03	60 µL

1.2 Calibration

1.2.1 Raw data

HbA1c %	ABS
0,0	-0,00197
4,3	0,02998
6,9	0,13883
9,6	0,35518
13,3	0,60816

1.2.2 Curve



1.3 Accuracy

1.3.1 Controls

Controls from different companies were measured on Gesan Chem400. The results has to be measured within the range of the assigned value.

Controls	Lot	HbA1c %	
		Assigned value	Measured
GESAN HbA1c Control Low	CH023L	5.8 (4.9 - 6.7)	5,9
GESAN HbA1c Control High	CH022H	10.0 (8.5 - 11.5)	9,9
BIORAD Lyphochek Diabetes Control Level 1	33881	5.48 (4.39 - 6.58)	5,58
BIORAD Lyphochek Diabetes Control Level 2	33882	9.42 (7.54 - 11.3)	8,35

1.3.2 Standard Recovery

The standard set was measured on Gesan Chem 400. % recovery must be in the range 85 - 115%.

Standard Set Lot SH029	HbA1c %		
	Assigned value	Measured value	% Recovery
Level 1	4,3	4,5	105
Level 2	6,9	6,9	100
Level 3	9,6	9,7	101
Level 4	13,3	13,1	98

1.3.3 Precision of standard curve on Gesan Chem 400

1.3.3.1 Method

A calibration curve was performed 5 times on Gesan Chem 400 and the variation coefficient was calculated. The variation coefficient has to be < 5%.

1.3.3.2 Results

The individual values and their statistical interpretation are presented in the following tables. ΔAbs was calculated. The variation coefficient was 2.20%.

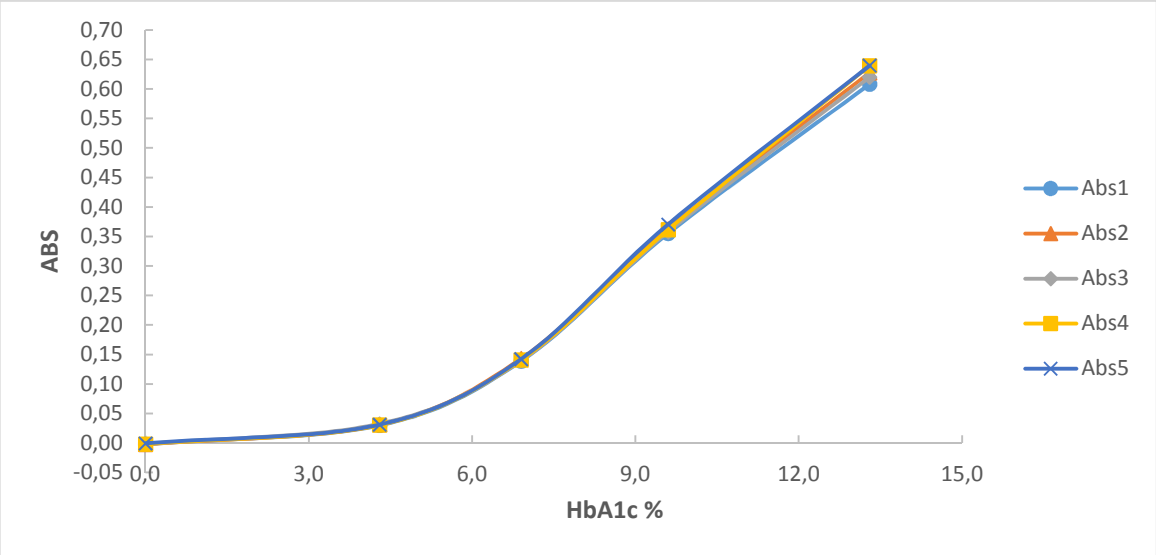
1.3.3.3 Raw data

HbA1c %	Abs1	Abs2	Abs3	Abs4	Abs5
0,0	-0,00197	-0,00240	-0,0023	-0,00207	-0,00061
4,3	0,02998	0,03105	0,03227	0,03047	0,03104
6,9	0,13883	0,14331	0,13931	0,14084	0,14217
9,6	0,35518	0,36292	0,35801	0,36139	0,37049
13,3	0,60816	0,62763	0,62008	0,63955	0,63963

calibration	ΔABS (12 - 4%)
1	0,4619
2	0,4764
3	0,4706
4	0,4863
5	0,4862

N°	Ave	SD	CV %
5	0,47628	0,0105	2,20

1.3.3.4 Curves



1.4 Intrareproducibility

1.4.1 Method

3 samples (Low – Medium – High) were consecutively measured 20 times on Gesan Chem 400 and the variation coefficient was calculated. The variation coefficient has to be < 5%.

1.4.2 Result

The individual values and their statistical interpretation are presented in the following tables. The variation coefficient were respectively 1.14%, 0.72% and 1.22% for the samples with HbA1c concentrations of 5.27 %, 8.45 % and 11.77 %.

N°	HbA1c %		
	Low	Medium	High
1	5,38	8,54	11,99
2	5,33	8,54	11,93
3	5,34	8,50	11,96
4	5,34	8,46	11,88
5	5,36	8,48	11,79
6	5,32	8,44	11,94
7	5,28	8,53	11,75
8	5,18	8,45	11,78
9	5,20	8,43	11,91
10	5,21	8,43	11,85
11	5,19	8,41	11,86
12	5,21	8,37	11,66
13	5,25	8,34	11,70
14	5,22	8,45	11,47
15	5,27	8,43	11,55
16	5,26	8,43	11,66
17	5,29	8,44	11,70
18	5,29	8,38	11,67
19	5,25	8,45	11,69
20	5,23	8,58	11,65

	N°	Ave %	SD	CV %
Low	20	5,27	0,06	1,14
Medium	20	8,45	0,06	0,72
High	20	11,77	0,14	1,22

1.5 Interreproducibility

1.5.1 Method

3 samples (Low – Medium – High) were measured daily on Gesan Chem.
The variation coefficient was calculated. The variation coefficient has to be < 5%.

1.5.2 Result

The individual values and their statistical interpretation are presented in the following tables.
The variation coefficient were respectively 1.85%, 2.05% and 2.97% for the sera with HbA1c concentrations of 5.13 %, 8.22 % and 11.28 %.

Date	HbA1c %		
	Low	Medium	High
10/10/2014	5,30	8,36	11,70
13/10/2014	5,22	8,19	11,16
14/10/2014	5,12	8,08	11,19
15/10/2014	5,03	8,06	10,74
17/10/2014	5,10	7,80	10,42
20/10/2014	5,15	7,94	11,08
21/10/2014	5,20	8,34	11,57
22/10/2014	5,07	8,28	11,38
23/10/2014	5,03	8,14	11,12
24/10/2014	5,07	8,24	11,10
27/10/2014	5,03	8,18	11,04
28/10/2014	5,03	8,16	11,11
29/10/2014	5,01	8,25	11,37
30/10/2014	5,07	8,19	11,30
03/11/2014	5,04	8,34	11,34
04/11/2014	5,15	8,53	11,79
05/11/2014	5,22	8,35	11,55
06/11/2014	5,27	8,45	11,77
07/11/2014	5,29	8,24	11,43
10/11/2014	5,16	8,30	11,41

	N°	Ave %	SD	CV %
Low	20	5,13	0,09	1,85
Medium	20	8,22	0,17	2,05
High	20	11,28	0,34	2,97

1.6 Comparison study with Roche

1.6.1 Method

Samples stored at 2-8°C were selected. These samples were measured at the same day for HbA1c on Gesan Chem 400 with Roche reagent Kit (HbA1c III Kit Lot. 682 980-01, C.f.a.s HbA1c Standard Lot. 171 434-01) and with the new GESAN reagent, Hemoglobin A1c Kit: (HbA1c Standard Set Lot. SH029, HbA1c Kit Lot. A1C020).
A regression analysis was performed using a spreadsheet program to determine the relationship between both HbA1c determination methods.

1.6.2 Results

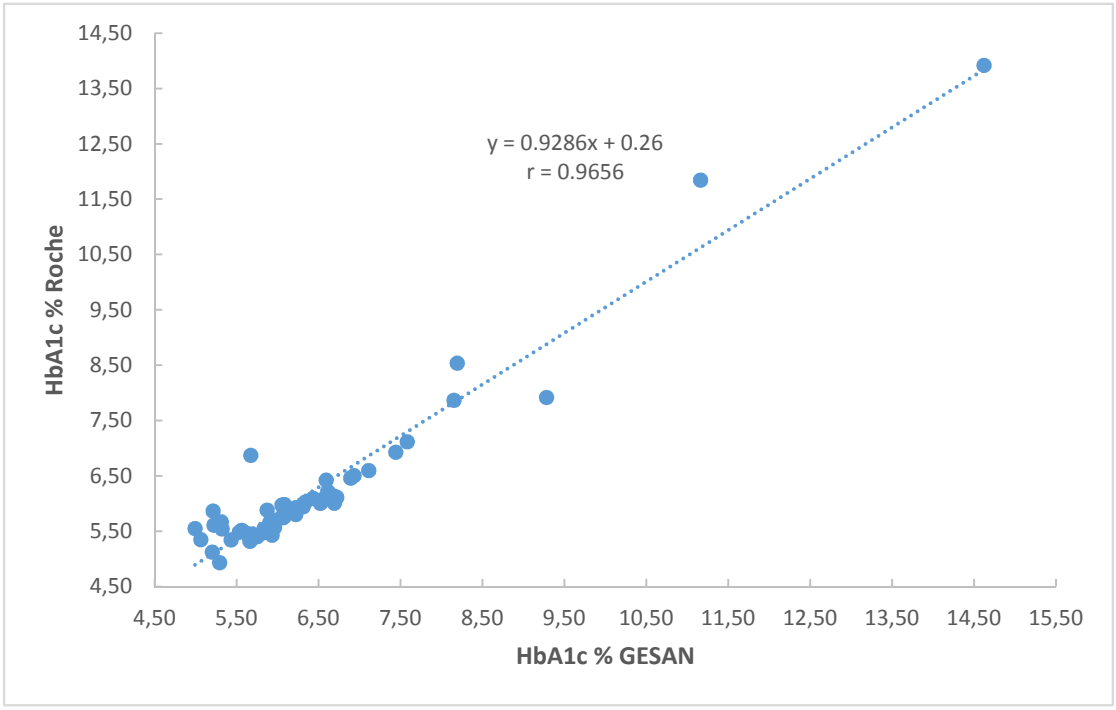
The individual values and their statistical interpretation are presented in the following tables. The correlation coefficient has to be > 0.95.

1.6.2.1 Individual data

Nr	GESAN Reagents %	ROCHE Reagents %
1	5,22	5,61
2	8,19	8,54
3	11,16	11,85
4	5,67	5,40
5	6,22	5,87
6	6,07	5,75
7	5,32	5,54
8	5,92	5,71
9	6,31	5,95
10	5,66	5,32
11	6,93	6,51
12	6,59	6,43
13	5,53	5,49
14	5,87	5,88
15	6,89	6,46
16	6,05	5,98
17	7,58	7,12
18	6,52	6,01
19	5,20	5,13
20	6,08	5,99
21	5,84	5,48
22	5,43	5,35
23	6,04	5,75
24	5,69	5,45
25	6,43	6,10
26	7,44	6,93
27	5,75	5,41
28	5,67	6,87
29	6,08	5,88

30	6,69	6,01
31	5,29	4,94
32	6,72	6,12
33	5,93	5,43
34	9,28	7,92
35	5,90	5,66
36	5,66	5,37
37	5,83	5,54
38	5,21	5,87
39	5,31	5,67
40	6,22	5,93
41	5,56	5,52
42	6,61	6,22
43	8,15	7,87
44	4,99	5,55
45	5,62	5,47
46	5,06	5,35
47	6,34	6,03
48	6,55	6,08
49	6,69	6,14
50	6,22	5,81
51	7,11	6,60
52	5,96	5,57
53	14,62	13,92

1.6.2.2 Correlation data



1.7 Sensitivity

1.7.1 Method
The change of absorbance units per concentration unit was calculated for the up going part of the nonlinear curve.

1.7.2 Result
0.0458744 Absorbance/Concentration units

1.8 Normal values

Non-diabetics: < 6%
Therapeutic Diabetics: < 7%

1.9 Limitation of the method

No known limitations

1.10 Conclusion

Normal values	Non-diabetics: < 6%
	Therapeutic Diabetics: < 7%
Measuring range	0 - 15%

1.11 Determination of 3 different lotnumbers

1.11.1 Method

A calibration curve was performed 3 times on Gesan Chem 400 and each time with a different Lot number of Reagent and Buffer.

1.11.2 Results

% difference in absorbance/concentration at Lot.1 , Lot.2 and Lot.3 is calculated according to GESAN Quality Control Procedure.
% difference has to be < 15%.

The individual values and their statistical interpretation are presented in the following tables.

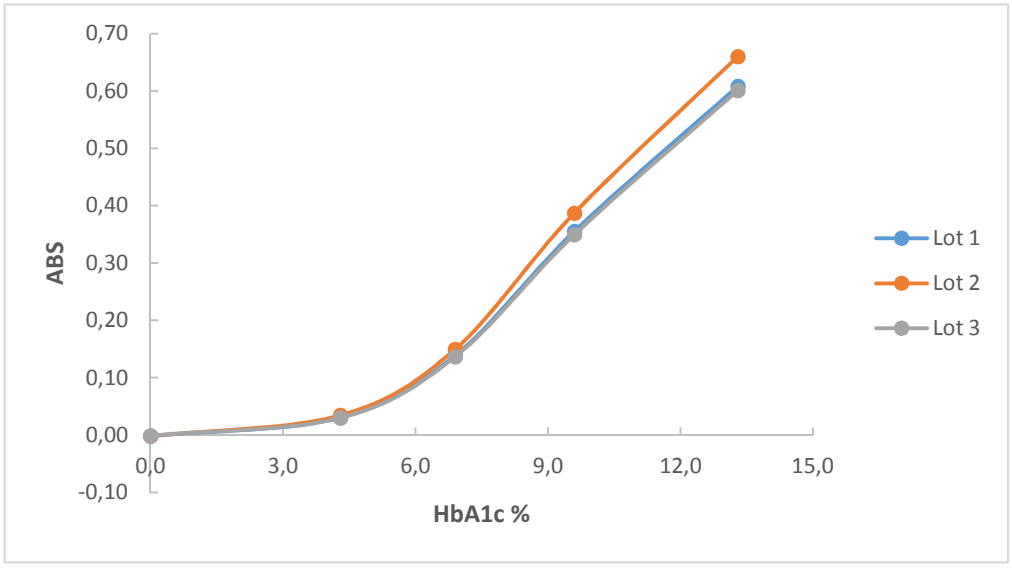
1.11.3 Raw data

HbA1c %	Abs		
	Lot 1	Lot 2	Lot 3
0,0	-0,00197	-0,00176	-0,0014
4,3	0,02998	0,03447	0,02985
6,9	0,13883	0,14956	0,13635
9,6	0,35518	0,38695	0,34933
13,3	0,60816	0,65998	0,60097

1) Delta ABS (12 - 4 %) Lot. : 0.4619
2) Delta ABS (12 - 4 %) Lot. : 0.5008
3) Delta ABS (12 - 4 %) Lot. : 0.4563

Difference 1 - 2 : 7.77%
Difference 2 - 3 : 9.75%
Difference 3 - 1 : 1.21%

1.11.4 Curves



1.12 Protocol for the determination of HbA1c on Gesan Chem 400

Test Item: Test Full Name: HbA1c Decimal Digit: 2 Unit: %

Assay: 2 point end Test time: 15 Sample Blank ×

Point: 6 22 0 0 Control Interval: 0 Always diluent ×

Main wave: 660 Second wave: 0

Sample Vol.

	Serum			Urine		
Normal:	6	0	0	6	0	0
Decrement:	0	0	0	0	0	0
Increment:	0	0	0	0	0	0

Reagent

	Vol.	Diluent	Pos.
R1	210	0	18
R2	70	0	12
R3	0	0	0
R4	0	0	0

Calibration Methods: Logit-log5P Point: 5 Span: 0

Calibration solution

(1)	0	1	6	0	0
(2)	4.4	2	6	0	0
(3)	7	3	6	0	0
(4)	9.9	4	6	0	0
(5)	13.3	5	6	0	0
(6)	0	0	0	0	0

2. APPLICATION VERIFICATION PROCEDURE

2.1 Approved status

An application made for the determination of serum proteins on a clinical chemistry analyzer is validated by:

a. The performance of a calibration curve and the validation of the curve by measuring controls.
b. Optional parameters
   - precision
   - detection limit

- comparison study

On the application is mentioned ‘approved application’.

Note: lot numbers of antiserum, standards and buffer have to be mentioned on the report

2.2 Not approved status

A lot of applications can be made on clinical chemistry analyzers by deduction.
These applications have to be validated by the client.

3. APPROVED APPLICATIONS

3.1 Determination of HbA1c on Selectra Pro M

3.1.1 Reagents

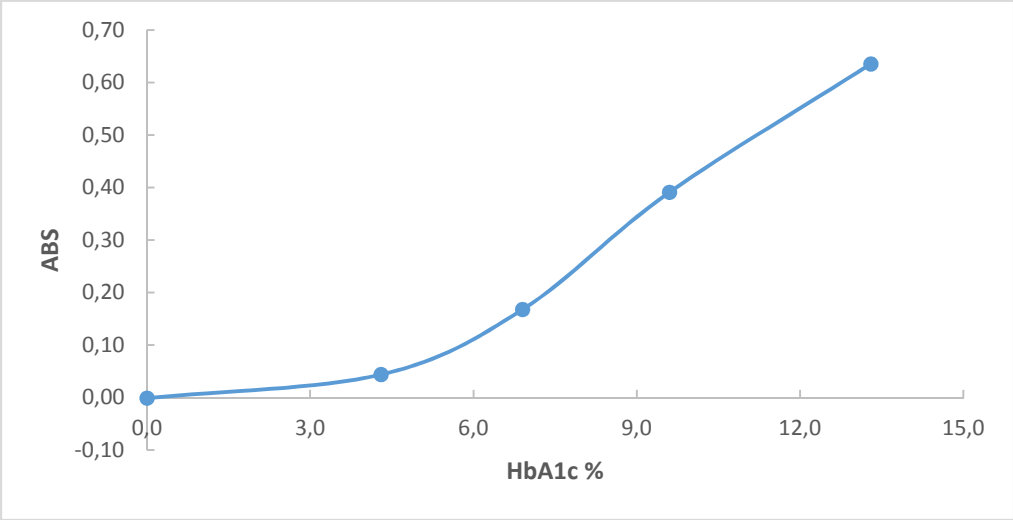
Hemoglobin A1c Standard Set	Lot. SH029	Exp. 2016/03	5 µL
Hemoglobin A1c Reagent R1	Lot. A1C0120	Exp. 2017/03	180 µL
Hemoglobin A1c Reagent R2	Lot. A1C020	Exp. 2017/03	60 µL

3.1.2 Calibration

3.1.2.1 Raw data

HbA1c %	Abs
0,0	-0,0012
4,3	0,0437
6,9	0,1676
9,6	0,3909
13,3	0,6353

3.1.2.2 Curve



3.1.3 Controls

Controls	Lot	HbA1c %	
		Assigned value	Measured
GESAN HbA1c Control Low	CH023L	5.8 (4.9 - 6.7)	5,9
GESAN HbA1c Control High	CH022H	10.0 (8.5 - 11.5)	9,9
BIORAD Lyphochek Diabetes Control Level 1	33881	5.48 (4.39 - 6.58)	5,38
BIORAD Lyphochek Diabetes Control Level 2	33882	9.42 (7.54 - 11.3)	9,16

3.2 Protocol for the determination of HbA1c on Selectra Pro M

Instrument setting

TEST PARAMETERS			
Name	: HbA1c	**Prozone check**	: N0
Abbr. Name	: HbA1c		:
Mode	: Two point	**Ref. male low**	: *
Wavelength	: 660nm	**Ref. male high**	: *
Units	: %	**Ref. female low**	: *
Decimals	: 1	**Ref. female high**	: *
Low Conc.	: 0.0 %	**Ref. ped. low**	: *
High Conc.	: 15.0 %	**Ref. ped. high**	: *
Calibrator Name	: HbA1c	**Control 1**	: *

Number of standards	: 5			*	
Calibration accepted	: Yes		**Control 2**	: *	
Number of points	: 5			*	
Repeats	: 1		**Control 3**	: *	
Interval	: 28 days			*	
Curve algorithm	: 5PLL		**Correlat. factor**	: 1.000	
Auto predilution	: No		**Correlat. offset**	: 0.000 IU/mL	

	Standard	**Predilution**	**Conc. %**	**Absorbance (dAbs)**	**Absorbance Low Limit**	**Absorbance High Limit**	**Dup-diff (dAbs)**
#1	Standard 1	None	0,0		0,0000	0,0000	0,0000
#2	Standard 2	None	**		0,0000	0,0000	0,0000
#3	Standard 3	None	**		0,0000	0,0000	0,0000
#4	Standard 4	None	**		0,0000	0,0000	0,0000
#5	Standard 5	None	**		0,0000	0,0000	0,0000

DUAL MODE PARAMETERS				
Sample blank	No			
Buffer reagent	No buffer			
(µL)	**R1**	**Sample**	**R2**	**R3**
Normal	180	5,0	0	60
Rerun	182	3,0	0	60
Predilution	: No	**Low Absorbance**	: - 0.100 Abs	
Slope Blank	: No	**High Absorbance**	: 3.000 Abs	
Point one:	: 6 sec	**R. Abs. L. Limit**	: - 0.100 Abs	
Point two:	: 236 sec	**R. Abs. H. Limit**	: 0.300 Abs	
Reagent Blank	: No	**Substr. depletion**	: 0.000 Abs	

* = can be selected freely

** = see insert for concentrations

3.3 Determination of HbA1c on Cobas Mira

3.3.1 Reagents

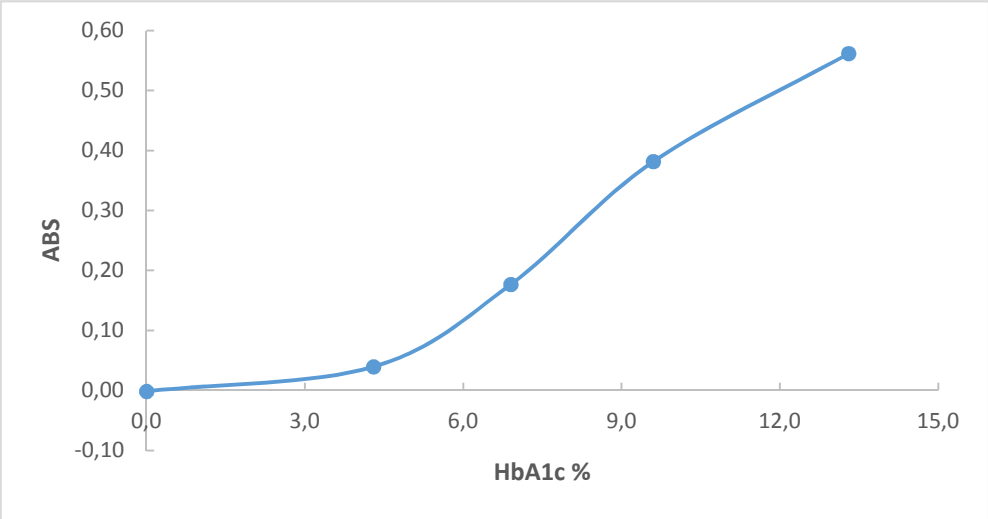
Hemoglobin A1c Standard Set	Lot. SH029	Exp. 2016/03	5 µL
Hemoglobin A1c Reagent R1	Lot. A1C0120	Exp. 2017/03	180 µL
Hemoglobin A1c Reagent R2	Lot. A1C020	Exp. 2017/03	60 µL

3.3.2 Calibration

3.3.2.1 Raw data

HbA1c %	Abs
0,0	-0,00160
4,3	0,03950
6,9	0,17670
9,6	0,38160
13,3	0,56160

3.3.2.2 Curve



3.3.3 Controls

Controls	Lot	HbA1c %	
		Assigned value	Measured
GESAN HbA1c Control Low	CH023L	5.8 (4.9 - 6.7)	5,9
GESAN HbA1c Control High	CH022H	10.0 (8.5 - 11.5)	10,1
BIORAD Lyphochek Diabetes Control Level 1	33881	5.48 (4.39 - 6.58)	5,51
BIORAD Lyphochek Diabetes Control Level 2	33882	9.42 (7.54 - 11.3)	8,61

3.4 Protocol for the determination of HbA1c on Cobas Mira

Instrument setting

GENERAL		CALCULATION		
MEASUREMENT MODE	ABSORB	SAMPLE	LIMIT	NO
REACTION MODE	R-S-SR1	REAC.	DIRECTION	INCREASE
CALIBRATION MODE	STD NONLIN		CHECK	OFF
REAGENT BLANK	NO BLANK	ANTIGEN	EXCESS	NO
CLEANER	NO	CONVERS.	FACTOR	1,00000
WAVELENGHT	600 nm		OFFSET	0,00000
DECIMAL POSITION	1			
UNIT	%	NORM. RANGE	LOW	NO

		HIGH	NO
		NUMBER OF STEPS	1
		CALC. STEP A	ENDPOINT
		READINGS FIRTS : 6	LAST: 25
ANALYSIS		CALIBRATION	
DILUTION NAME:	NACL	CALIBR. INTERVAL	ON REQUEST
FACTOR:	NO		
TIME:	NO	STD NON LINEAIR	CUP-POS: 1
		1: ** %	2: ** %
SAMPLE	CYCLE: 1	3: ** %	4: ** %
VOL: 5.0 µL	DIL: 0.0 µL	5: ** %	6: NO
REAGENT	CYCLE: 1	7: NO	8: NO
VOL: 180 µL			
START REAGENT 1	CYCLE: 5	REPLICATE	SINGLE
VOL: 60.0 µl	DIL: 0.0 µL	DEVIATION	NO
		CALCULATION MODEL:	LOGIT/LOG5
		CORRECTION STD:	NO

* = can be selected freely

** = see insert for concentrations

1: - IDENTIFICAZIONE DELLA SOSTANZA O DELLA MISCELA E DELLA SOCIETÀ/IMPRESA
IDENTIFICATION OF THE SUBSTANCE AND OF THE COMPANY

1.1. Identificatore del prodotto Product name	**HbA1c LR**
1.2. Usi identificati pertinenti della sostanza o miscela e usi sconsigliati Use of the substance	**IVD**
1.3. Dettagli del fornitore della scheda di dati di sicurezza Manufacturer	**Gesan Production s.r.l.** **via fiera dell'Eremita 71** **91021 Campobello di Mazara (TP)** **+39 0924 912534** **overseas@gesanproduction.it**
1.4. Numero telefonico di emergenza In case of emergency	**Centro Antiveleni Policlinico "A. Gemelli" Roma: +39 06 3054343**

2: - IDENTIFICAZIONE DEI PERICOLI
HAZARD INDENTIFICATION

2.1. Classificazione della sostanza o della miscela Classification of the substance or mixture	Il prodotto è un kit costituito da diversi ingredienti. La classificazione degli ingredienti è riportata nella sezione 3. The product is a kit made up by different ingredients. Their classification is quoted in Section 3. **Classificazione (REGOLAMENTO (CE) N. 1272/2008)/ Classification (REG. (CE) N. 1272/2008)** Sostanza o miscela non pericolosa secondo il Regolamento CE 1272/2008 No dangerous substance or mixture according to Reg. CE 1272/2008.
2.2. Elementi dell'etichetta Label	I preparati sono classificati come non pericolosi in accordo al Regolamento CE 1272/2008 The preparations are classified as no dangerous according to Reg. CE 1272/2008.
PITTOGRAMMA PICTOGRAM	Non applicabile/not applicable
AVVERTENZE WARNINGS	Non applicabile/not applicable
INDICAZIONI DI PERICOLO SIGNS OF DANGERS	Non applicabile/not applicable
CONSIGLI DI PRUDENZA CAUTION SUGGESTIONS	Non applicabile/not applicable
2.3 ALTRI PERICOLI OTHER DANGERS	Nessuno/none

3: - COMPOSIZIONE/INFORMAZIONI SUGLI INGREDIENTI
COMPOSITION/INFORMATION ON INGREDIENTS

nome componente Ingredient	N° CAS	N° CE	N° INDICE	Classificazione (REGOLAMENTO (CE) N. 1272/2008)	Concentrazione Concentration
Sodio Azide	**26628-22-8**	**247-852-1**	**01-004-00-7**	**Acute Tox. 2; Aquatic Acute 1; Aquatic Chronic 1; H300,H410,EUH032**	**< 0,1 %**
Succinic acid	**110-15-6**	**203-740-4**	**=====**	**Eye Dam. 1; H318**	**60 mmol/l**
Bromocresol green	**76-60-8**	**200-972-8**	**603-117-00-0**	**Flam. Liq. 2; Eye Irrit. 2; STOT SE 3; H225, H319, H336**	**0,15 mmol/l**

Nota: Le frasi di pericolo si riferiscono ai componenti intesi come materia prima.
Note: The hazardous phrases are referred to components intended as raw material.

4: - INTERVENTI DI PRIMO SOCCORSO
FIRST AID MEASURES

Dopo contatto con gli occhi Eyes	**Sciacquare con acqua corrente per alcuni minuti tenendo la palpebra aperta. Se l'irritazione persiste consultare l'oculista.** **Flush eyes with plenty of water for some minutes, occasionally lifting the upper and lower eyelids. If irritation develops, get medical aid.**
Dopo contatto con la pelle Skin	**Lavare accuratamente con acqua e sapone la parte esposta; togliere gli indumenti contaminati Consultare il medico se l'irritazione persiste.** **Flush skin with plenty of water and soap while removing contaminated clothing. Get medical aid if irritation persists.**
Dopo ingestione Ingestion	**Sciacquare la bocca con abbondante acqua senza ingerire. Consultare il medico o contattare il Centro Antiveleni locale.** **Wash mouth out with plenty of water without swallowing. Consult a doctor or the local poison center.**
Dopo inalazione Inhalation	**Portare il paziente all'aria aperta.** **Bring the patient to fresh air.**

5: - MISURE ANTINCENDIO
FIRE FIGHTING MEASURES

5.1. Mezzi di estinzione Extinguishing Media	**CO_2, polvere o getto d'acqua. Fronteggiare fiamme largamente sviluppate con getto d'acqua o schiuma resistente agli alcoli. Tenere comunque conto dei materiali nelle vicinanze.** **CO2, powder or water jet. Face flames largely developed with water spray or alcohol resistant foam. Take care of surrounding materials.**
5.2. Pericoli speciali derivanti dalla sostanza o dalla miscela Special hazards arising from substance or mixture	**Prodotto non combustibile. In caso d'incendio possibile formazione di gas e vapori pericolosi.** **This product is not combustible. In case of fire possible formation of hazardous gases and vapors.**
5.3. Raccomandazioni per gli addetti all'estinzione degli incendi Recommendations for fire-fighters	**Non sostare nella zona pericolosa senza adatti indumenti di protezione chimica e apparecchio autorespiratore.** **Do not stay in dangerous zone without suitable chemical protective clothing and breathing apparatus.**

6: - MISURE IN CASO DI RILASCIO ACCIDENTALE
ACCIDENTAL RELEASE MEASURES

6.1. Precauzioni personali, dispositivi di protezione e procedure in caso di emergenza Personal precautions, protective equipment and emergency procedures	**Evitare il contatto con la sostanza.** **Isolare la perdita e ripulire immediatamente la zona.** **Assicurare l'apporto di aria fresca nei locali chiusi.** **Avoid contact with the substance.** **Isolate the leak and clean up immediately the area.** **Ensure supply of fresh air in closed spaces.**
6.2. Precauzioni ambientali Environmental precautions	**Non permettere l'immissione nel sistema fognario** **Do not allow to enter into the sewerage system**
6.3. Metodi e materiali per il contenimento e per la bonifica Methods and materials for containment and cleaning up	**Asciugare, assorbire con materiali idonei (sabbia, diatonite, assorbenti universali).** **Smaltire secondo le informazioni del successivo punto 13.** **Dry, absorb with suitable material (sand, diatonite, universal absorbent).** **Dispose according to information from Section 13.**

7: - MANIPOLAZIONE E IMMAGAZZINAMENTO
HANDLING AND STORAGE

7.1 Precauzioni per la manipolazione sicura Precautions for safe handling	**Osservare le regole generali nella manipolazione di sostanze chimiche.** **Evitare inalazioni ed il contatto con gli occhi , la pelle e le mucose.** **Observe the general handling rules for chemicals substances.** **Avoid inhalation and contact with eyes, skin and mucous membranes.**
7.2. Condizioni per l'immagazzinamento sicuro, comprese eventuali incompatibilità Conditions for safe storage, including any incompatibilities	**Temperatura di conservazione: 15 - 25° C .** **Conservare ben chiuso, lontano da materiali combustibili e fonti di calore ed ignizione. Consultare le istruzioni per l'uso (metodica).** **Storage temperature: 15 - 25° C .** **Keep tightly closed, away from combustible materials and sources of heat and ignition.** **See the instructions for use (method).**
7.3. Usi finali specifici Specific end uses	**Nessuno** **N/A**

8: - CONTROLLO DELL'ESPOSIZIONE/PROTEZIONE INDIVIDUALE
EXPOSURE CONTROLS / PERSONAL PROTECTION

8.1. Parametri di controllo Control parameters	**Il prodotto non contiene quantità rilevanti di sostanze pericolose. I valori limite di soglia (TLV) non devono essere tenuti sotto controllo per l'esposizione del personale negli ambienti di lavoro.** **The product does not contain any relevant quantities of hazardous substances. The threshold limit values (TLV) shouldn't be monitored for personal exposure in the workplace.**	
8.2. Controlli dell'esposizione Personal Protective Equipment	Protezione occhi/viso Eyes	**Si consigliano occhiali di sicurezza o occhiali anti-schizzo** **Wear chemical splash goggles.**
	Protezione sulla pelle Skin	**Lavarsi le mani all'inizio ed alla fine del lavoro.** **Indossare guanti protettivi per le mani ed indumenti da laboratorio.** **Wash the hands at the beginning and at the end of the work.** **Wear appropriate protective gloves to prevent skin exposure.**
	Protezione respiratoria Respirators	**Nessuna normalmente richiesta in condizioni di ventilazione adeguata.** **None normally required with adequate ventilation.**

9: - PROPRIETÀ FISICHE E CHIMICHE
PHYSICAL AND CHEMICAL PROPERTIES

	R1
Aspetto / Physical State	**Liquido / Liquid**
Colore / Color	**Verde / Green**
Odore / Odor	**Caratteristico / Characteristic**
Temperatura di congelamento Freezing/Melting Point	**Simile all'acqua: circa 0°C** **Similar to water: about 0 ° C**
Temperatura di ebollizione / Boiling point	**Simile all'acqua: circa 100 °C** **Similar to water: about 100 ° C**
Punto di infiammabilità / Flash point	**Il prodotto non è infiammabile** **The product is not flammable**
Autocombustione / Spontaneous combustion	**Il prodotto non è autocombustibile** **The product is not auto-combustible**
Pericolo di esplosione / Danger of explosion	**Il prodotto non presenta rischi di esplosione** **The product doesn't present risk of explosion**
Pressione del vapore / Vapor pressure	**Simile all'acqua 23 hPa** **Similar to water 23 hPa**
Densità a 20° / Density at 20 ° C	**1.0 g/cm**
Solubilità in acqua / Solubility in water	**Totalmente miscibile** **Totally miscible**
Valore di pH a 20 °C / Value of pH at 20 °C	**N.A**

10: - STABILITÀ E REATTIVITÀ
STABILITY AND REACTIVITY

10.1. Reattività Reactivity	**Non si conosce nessuna reazione pericolosa se usato in condizioni normali.** **There is no known hazardous reactions when used under normal conditions.**
10.2. Stabilità chimica Chemical Stability	**Stabile.** **Stable.**
10.3. Possibilità di reazioni pericolose Possibility of hazardous reactions	**Nessuna nota, se usato correttamente.** **Any note, if used properly.**
10.4. Condizioni da evitare Conditions to Avoid	**Nessuna nota, se usato correttamente.** **Any note, if used properly.**
10.5. Materiali incompatibili Incompatibilities with Other Materials	**Forti agenti ossidanti.** **Strong oxidizing agents.**
10.6. Prodotti di decomposizione pericolosi Hazardous Decomposition Products	**Nessuno noto.** **N/A**

11: - INFORMAZIONI TOSSICOLOGICHE
TOXICOLOGICAL INFORMATION

Tossicità acuta Acute toxicity	**Non sono noti dati tossicologici per questo preparato.** **No known toxicological data for this preparation.**
Dopo contatto con la pelle After contact with skin	**Non noti** **N/A**

Dopo contatto con gli occhi After contact with eyes	**Non noti** **N/A**
Dopo ingestione After ingestion	**Non noti** **N/A**
Sensibilizzazione Sensitization	**Non noti** **N/A**

Nota: Gli effetti sulla salute indicati si basano sull'estrapolazione di dati sui componenti del prodotto puro. Per quanto a nostra conoscenza, non sono stati identificati effetti sulla salute per la miscela di prodotto in normali condizioni d'uso, benché gli effetti sulla salute del prodotto non siano stati completamente investigati.

Note: The health effects noted above are based on extrapolation of data on the pure product. According our knowledge, no health effects were identified for the product mixture under normal conditions of use, although the effects of the product have not been throughly investigated.

12: - INFORMAZIONI ECOLOGICHE
ECOLOGICAL INFORMATION

12.1. Tossicità Toxicity	**Non sono disponibili dati quantitativi sugli effetti ecotossicologici del prodotto. Utilizzare secondo le buone pratiche lavorative, evitando di disperdere nell'ambiente.** **There are no quantitative data on the ecotoxicological effects of the product. Use according to good working practices, avoiding waste in the environment.**

13: - CONSIDERAZIONI SULLO SMALTIMENTO
DISPOSAL CONSIDERATIONS

13.1. Metodi di trattamento dei rifiuti Methods of waste treatment	**Il prodotto tal quale è classificato come rifiuto speciale non tossico e nocivo.** **I residui chimici debbono sempre essere smaltiti come rifiuti speciali, secondo la normativa vigente. Riferimenti: DLGS 152/2006.** **Gli imballi, se contaminati, devono essere eliminati come il prodotto.** **The product is classified as not toxic and harmful special waste.** **The chemical waste should always be disposed as hazardous waste, according to current regulations. References: Legislative Decree 152/2006.** **The packaging, if contaminated, must be disposed as the product.**

14: - INFORMAZIONI SUL TRASPORTO
TRANSPORTATION INFORMATION

14.1 Numero ONU/ ONU number

ADR **Merci non pericolose/ No Dangerous Goods**
IMDG **Merci non pericolose/ No Dangerous Goods**
IATA **Merci non pericolose/ No Dangerous Goods**

14.2 Nome di spedizione appropriato ONU/ Appropriate ONU shipment name

ADR **Merci non pericolose/ No Dangerous Goods**
IMDG **Merci non pericolose/ No Dangerous Goods**
IATA **Merci non pericolose/ No Dangerous Goods**

14.3 Classi di pericolo connesso al trasporto/ Classes of danger related to transportation

ADR **Merci non pericolose/ No Dangerous Goods**
IMDG **Merci non pericolose/ No Dangerous Goods**
IATA **Merci non pericolose/ No Dangerous Goods**

14.4 Gruppo d'imballaggio/ Packaging group

ADR **Merci non pericolose/ No Dangerous Goods**
IMDG **Merci non pericolose/ No Dangerous Goods**
IATA **Merci non pericolose/ No Dangerous Goods**

14.5 Pericoli per l'ambiente/Environmental dangers

ADR **Merci non pericolose/ No Dangerous Goods**
IMDG **Merci non pericolose/ No Dangerous Goods**
IATA **Merci non pericolose/ No Dangerous Goods**

14.6 Precauzioni speciali per gli utilizzatori/Special warning for users

Merci non pericolose in termini di ADR/RID, ADNR, IMDG-Code, ICAO/IATA-DGR/ No Dangerous Goods in terms of ADR/RID, ADNR, IMDG-Code, ICAO/IATA-DGR

14.7 Trasporto di rinfuse secondo l'allegato II di MARPOL 73/78 e il codice IBC/ Bulk transportation according to annex II of MARPOL 73/78 and the code IBC

Osservazioni : non applicabile/ Observations: not applicable

This product is not subject to current regulations for the transport of dangerous goods

15: - INFORMAZIONI SULLA REGOLAMENTAZIONE
REGULATORY INFORMATION

15.1. Norme e legislazione su salute, sicurezza e ambiente specifiche per la sostanza o la miscela Standards and legislation on health, safety and environmental specifications for the substance or mixture	**Il prodotto non è soggetto ai regolamenti di identificazione secondo le normative CE sui materiali pericolosi.** **The product is not subject to identification regulations according to CE regulations on hazardous materials.**
15.2. Valutazione della sicurezza chimica Chemical Safety evaluation	**Il produttore non ha effettuato una valutazione della sicurezza chimica.** **The manufacturer hasn't conducted a chemical safety evaluation.**

16: - ALTRE INFORMAZIONI
OTHER INFORMATION

Questa scheda è stata redatta conformemente al REGOLAMENTO 1907/2006/CE (REACH) e successive modifiche ed integrazioni.
Le informazioni riportate in questa scheda di sicurezza sono basate sulle conoscenze del prodotto al momento della pubblicazione.
Tali informazioni hanno lo scopo di fornire all'utilizzatore un corretto e sicuro utilizzo, stoccaggio e trasporto del prodotto.
Avvertenze di formazione professionale
Le informazioni sono redatte al meglio delle nostre conoscenze. Il loro carattere è però informativo e non costituiscono garanzia. L'uso del prodotto avviene sotto il controllo degli utilizzatori ed è perciò loro responsabilità adeguarsi alle condizioni di corretto esercizio indicate nella scheda, nonchè adeguarsi a idonee pratiche di igiene industriale.

This sheet has been prepared in accordance with Regulation 1907/2006/EC (REACH) and subsequent amendments and additions.
The information in this MSDS are based on information and belief at the time of publication.
Such information are intended to provide the user with a correct and safe use, storage and transport of the product.
Training advice.
The information are edited to the best of our knowledge. Their aim is, however, informative and they cannot be a warranty. The use of the product is under the control of users and is therefore their responsibility to comply correct operating conditions in the schedule, as well as adapt to industrial hygiene practices.

Raccomandazioni per l'uso ed eventuali restrizioni
Non utilizzare il prodotto per usi differenti da quelli previsti. In tal caso l'utilizzatore potrebbe essere soggetto a rischi non preventivati

Recommendations for use and restrictions
Do not use the product for different uses from those projected. In this case the user may be subject to risks not estimated

Principali fonti bibliografiche:

Main literature sources:

ECHA – (Agenzia europea della sostanze chimiche) http: //www.echa.europa.eu/it/
ECDIN - Environmental Chemicals Data and Information Network - Joint Research Centre, Commission of the European Communities
IPCS INCHEM - Chemical Safety Informations from Intergovernmental Organizations. website -http://inchem.org
UNECE - United Nations Economic Commission for Europe - Dangerous Goods. Website http://www.unece.org/trans/danger/danger.htm

Fine delle informazioni
End of the information

DIRECTIVE DGLS 332/2000	ADOPTED SOLUTIONS	DIRECTIVE	INTERNAL DOCUMENTS
A. **General Requirements** A-1 The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise, directly or indirectly, the clinical condition or the safety of the paints, the safety or health of users or, where applicable, other persons, or the safety of the property. Any risks which may be associated with their use must be acceptable when weighed against the benefits to the patient and be compatible with a high level of protection of health and safety.	**Patient security or clinical records** : no risk has been underlined in the bibliography which instructions for use refer to. In the instructions for use it has been reminded to use control serums that highlight if the device does not work and guarantee the reliability of results obtained. Results must be evaluated considering clinical records and other analysis, as specified in the instructions attached to the device. **Operator security or health** Even if the vial is open, the device does not produce harmful vapors. It is not inflammable and corrosive and its pH is almost neutral. It is not risky for the operator if handled with caution according good practice regulation of laboratory. **Goods security** Even if put in automatic devices, reagents can not damage components because they are not subjected to precipitations that could obstruct circuits. As they are not corrosive and inflammable, they are not dangerous for devices or other goods in contact with them.	D.LGS. 285/98 Dir. 98/79 CE EN 1441/98 EN 12287/01 ISO 9001:2000	Risk management Quality Manual MSDS
A-2 The solutions adopted by the manufacturer for the design and construction of the devices must conform to safety principles, taking account of the generally acknowledged state of art. In selecting the most appropriate solutions, the manufacturer must apply the following principles in the following order: - eliminate or reduce risks as far as possible (inherently safe design and construction),	a) The production, distribution and packaging environments respect all the current security regulations. From the accurate device risk analysis , no danger has emerged. However, have been adopted the appropriate precautions in order to record risks at a minimum and acceptable level, as described in the following point (b).	D. LGS. 285/98 Dir. 98/79 CE EN 1441/98 EN 12287/01 ISO 9001:2000 DGLS 626/94	Risk management Quality Manual
- b) where appropriate take adequate protection measures in relation to risks that cannot be eliminated	b) All the operators that can be in touch with dangerous products (production, warehouse and others) can consult the security sheets . During the managing and manipulation of products, they can look the danger symbols found in the chemistry products warehouse and in the production laboratory. The chemistry products warehouse has an appropriate forced ventilation system to avoid possible vapors accumulation. Furthermore, in the preparation sheets consulted by the production operator, danger symbols, risk phrases and caution advices have been highlighted, as well as the appropriate individual protections and precautions for the production. The emergency lights, that are activated in case of black out, have a sufficient autonomy to consent the suspension of production activities and the storage of raw materials and semi finished products. If one or more components exceed the minimum concentration of not dangerous, the potential risk has been highlighted in the instructions for use, in labels and risk management, as well as in the MSDS sent to customers; label contain harmonized risk symbols on colored bottom with detailed explanations in the manual. Individual protection devices and security equipment are indicated.		b) Prepararion sheet "PREP" PR 7.5.1-1
- c) inform users of the residual risks due to any shortcomings of the protection measures adopted.	c) In the IFU, all the necessary detailed information for a correct and not risky use of the device can be found as well as risk phrases and caution advices		Instructions for use

DIRECTIVE DGLS 332/2000	ADOPTED SOLUTIONS	DIRECTIVE	INTERNAL DOCUMENTS
	for the dangerous components. In the MSDS can be found the phone number of Anti poison Centre of Rome University. Furthermore, with the first product supply, MSDS is sent to users.		MSDS
A- 3 The devices must be designed and manufactured in such a way that they are suitable for the purposes referred to in Article 1(2)(b), as specified by the manufacturer, taking account of the generally acknowledged state of the art. They must achieve the performances, in particular, where appropriate, in terms of analytical sensitivity, diagnostic sensitivity, analytical specificity, diagnostic specificity, accuracy, repeatability,reproducibility, including control of known relevant interference, and limits of detection, stated by the manufacturer. The traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.	Performance study with comparison with other producers products. Use of primary brand calibrators. All the test defining the performance have been done, as per the next attached documents.	UNI EN 13612/02 ISO 17511/02 UNI EN 12287/01 UNI EN 13640/02	Instructions for use Quality control certificate (Att. B1 – B2 – B3 – B4 – B5 – B6 – B7)
A-4 The characteristics and performances referred to in sections 1 and 3 must not be adversely affected to such a degree that the health or the safety of the patient or the user and, where applicable, of other persons, are compromised during the lifetime of the device as indicated by the manufacturer, when device is subjected to the stresses which can occur during normal conditions of use. When no lifetime is stated, the same applies for the lifetime reasonably to be expected of a device of that kind, having regard to the intended purpose and the anticipated use of the device.	Stability studies on closed vial and working solution. Routine stability studies.	UNI EN 13640/02	Stability study • Report on tests done
A- The device must be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected under storage and transport conditions (temperature, humidity, etc.) taking account of the instructions and information provided by the manufacturer.	Devices are normally shipped with forwarder that ensure controller temperature transportation or a delivery within 24/48 hours. An appropriate packaging has been studied (elevated carton thickness; use of insulated materials). Furthermore, devices have been subjects to heat stress, as described in the following paragraph 3J (report on tests done).	EN 13640/02 EN 1441/98 EN375/92	Stability study (see art. 3M) • shipping document
B. DESIGN AND MANUFACTURING REQUIREMENTS 1. B-1 Chemical and physical properties 1.1. The devices must be designed and manufactured in such a way as to achieve the characteristics and performances referrred to in section A on the 'General requirements'. Particular attention must be paid to the possibility of impairment of analytical performance due to incompatibility between the materials used and the specimens (such as biological tissues, cells, body fluids and micro-organisms) intended to be used with the device, taking account of its intended purpose. 1.2. The devices must be designed, manufactured	1.1 in the instructions for use, have been identified all the samples that the device can use. 1.2 Vilas used to contain reagents come from important brands. However they have been tested as well as reset cups. With reference to plastic vials, the supplier tests them in pressure conditions in order to find micro holes .	ISO 9001:2000	Report on endurance test Technical sheets: -vials PET - cups for vials in HD-PE -ferrules for vials in HD-PE

DIRECTIVE DGLS 332/2000	ADOPTED SOLUTIONS	DIRECTIVE	INTERNAL DOCUMENTS
and packed in such a way as to reduce as far as possible the risk posed by product leakage, contaminants and residues to the persons involved in the transport, storage and use of the devices, taking account of the intended purpose of the products.			
B-2 Chemical and physical properties	Not applicable		
B-3 Manufacturing and environmental properties	All the requirements have been considered during the production. Appropriate precautions have been highlighted in the IFU.	EN 1441/98 EN 575/92	Risk management Labeling plan
B-4 Devices which are instruments or apparatus with a measuring function.	Not applicable		
B-5 Protection against radiation.	Not applicable		
B-6 Requirements for medical devices connected to or equipped with an energy source.	Not applicable		
B-7 Requirements for devices for self-testing	Not applicable		
B-8 Information supplied by the manufacturer 8.1. Each device must be accompanied by the information needed to use it safely and properly, taking account of the training and knowledge of the potential users, and to identify the manufacturer. This information comprises the data on the label and in the instructions for use. As far as practicable and appropriate, the information needed to use the device safely and properly must be set out on the device itself and/or, where appropriate, on the sales packaging. If individual full labeling of each unit is not practicable, the information must be set out on the packaging and/or in the instructions for use supplied with one or more devices.	8.1 Each kit has its instruction for use. On primary and secondary labels are found the specific symbols. Labels are irremovable and humidity-resistant. Their print is done by thermal procedure.	EN 375/92 D.Lgs. 52/97 GU 20/5/93 D.Lgs. 285/98	Instructions for use
Instructions for use must accompany or be included in the packaging of one or more devices. In duly justified and exceptional case no such instructions for use are needed for a device if it can be used properly and safely without them. The decision whether to translate the instructions for use and the label into one or more languages of the European Union shall be left to the Member States, except that, for devices for self-testing, the instructions for use and the label must include a translation into the official language(s) of the Member State in which the device for self-testing reaches its final user. 8.2. Where appropriate, the information to be supplied should take the form of symbols. Any symbol and identification colour used must conform to the harmonized standards. In areas for which no standart exist, the symbols and colour used must be described in the documentation supplied with the device. 8.3. In the case of devices containing or a	8.2 harmonized symbols inherent to device are found on primary and secondary labels and on packaging. Color are compliant with regulation.		Labeling plan

DIRECTIVE DGLS 332/2000	ADOPTED SOLUTIONS	DIRECTIVE	INTERNAL DOCUMENTS
preparation which may be considered as basing dangerous, taking account of the nature and quantity of its constituents and the form under which they are present, relevant danger symbols and labeling requirements of 20 February 1988 n 141 and successive amendments to 16 July 1998 n° 285 and successive amendments. Where there is insufficient space to put all the information on the device itself or on its label, the relevant danger symbols shall be put on the label and the other information required by those Directives shall be given in the instructions for use. The provisions of the aforementioned Directives on the safety data sheet shall apply, unless all relevant information as appropriate is already made avaible by the instructions for use.	8.3 appropriate symbols and, where necessary, . risk phrases are have been applied.		MSDS Risk management
8.4. The label must bear the following particulars which may take the form of symbols as appropriate: (a) the name or trade name and address of the manufacturer. For devices imported into the Community with a view to their distribution in the Community, the label, the outer packaging, or the instructions for use shall contain in addition the name and address of the authorized representative of the manufacturer; (b) the details strictly necessary for the user to uniquely identify the device and the contents of the packaging; (c) where appropriate, the word 'STERILE' or a statement indicating any special microbiological state or state of cleanliness; (d) the batch code, preceded by the word 'LOT', or the serial number;	a) Supplier's data are reported (address, telephone, fax and web-site). Producer's and, if applicable, agent's name and address are in the instructions for use. b) Devices characteristics are reported in labels and instructions for use.		Labeling plan Instructions for use Quality manual
(e) if necessary, an indication of the date by which the device or part of it should be used, in safety, without degradation of performance, expressed as the year, the month and, where relevant, the day, in that order; (f) in case of devices for performance evaluation, the words 'for performance evalution only'; (g) where appropriate, a statement indicating the in vitro use of the device; (h) any particular storage and/or handling conditions; (i) where applicable, any particular operating instructions; j) Adequate warnings and precautions; k) if the device is intended for self-testing, that fact must be clearly stated. 8.5. If the intended purpose of the device is not obvious to the user, the manufacturer must clearly	e) Expiry date detected by stability study is reported on label . f) Not applicable. g) "In vitro medical diagnostic device is reported" and related harmonized symbol are reported in label and instructions for use. h) are reported in label and instructions for use. i) are reported in label and instructions for use. j) are reported in label and instructions for use. k) Not applicable.		

DIRECTIVE DGLS 332/2000	ADOPTED SOLUTIONS	DIRECTIVE	INTERNAL DOCUMENTS
state the intended purpose in the instructions for use and, if appropriate, on the label. 8.6. Wherever reasonable and practicable, the devices and separate components must be identified, where appropriate in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components.	8.5 The destination is indicated in the secondary label and in the instructions for use. 8.6 Label		

DIRECTIVE DGLS 332/2000	ADOPTED SOLUTIONS	DIRECTIVE	INTERNAL DOCUMENTS
8.7. Where appropriate, the instructions for use must contain the following particulars: points (d) and (e); (b) composition of the reagent product by nature and amount or concentration of the active ingredient(s) of the reagent(s) or kit as well as a statement, where appropriate, that the device contains other ingredients which might influence the measurement; (c) the storage conditions and shelf life following the first opening of the primary container, together with the storage conditions and stability of working reagents; (d) the performances referred to in section 3 of part A; (e) an indication of any special equipment required including information necessary for the identification of that special equipment for proper use; (f) the type of specimen to be used, any special conditions of collection, pre-treatment and, if necessary, storage conditions and instructions for the preparation of the patient; (g) a detailed description of the procedure to be followed in using the device; (h) the measurement procedure to be followed with the device including as appropriate; - the principle of the method, - the specific analytical performance characteristics (e.g.sensitivity, specificity, accuracy, repeatability, reproducibility, limits of detection and measurement range, including information needed for the control of known relevant interferences), limitations of the method and information about the use of available reference measurement procedures and materials by the user, - the details of any further procedure or handling needed before the device can be used (for example, reconstitution, incubation, dilution, instrument checks, etc.), - the indication whether any particular training is required; (i) the mathematical approach upon which tha calculation of the analytical result is made; (j) measures to be taken in the event of changes in the analytical performance of the device; (k) information appropriate to users on: - internal quality control including specific validation procedures,	8.7 All the detailed information required in the successive clauses: a), b), c), d), e), f), g), h), i), j), k) l), u) has been included in the instructions for use		Instructions for use

DIRECTIVE DGLS 332/2000	ADOPTED SOLUTIONS	DIRECTIVE	INTERNAL DOCUMENTS
- the traceability of the calibration of the device; (l) the reference intervals for the quantities being determined, including a description of the appropriate reference population; m), n), o), p), q), r), s), t) u) date of issue or latest revision of the instructions for use.	Not applicable u) The last revision number and the related updating date are indicated in the instructions for use.		