



Direction de l'Evaluation des Dispositifs Médicaux
Département Surveillance du Marché
Unité Evaluation et Contrôle du Marché – DIV
Dossier suivi par Françoise CHEVENNE
Tél. : +33 01.55.87.42.61
Fax : +33 01.55.87.42.62
E-mail : Francoise.CHEVENNE@afssaps.sante.fr

HbA1c REAGENTS

INSTRUCTION FOR USE

GUIDELINES

Revised : January 10th 2006

Purpose:

These guidelines concerning the instruction for use of HbA_{1c} reagents have been developed for manufacturers.

National and international organizations recommendations for glycaemic control in diabetic patients have been brought together in this guideline. These recommendations are: the use of HbA_{1c} reagents for the glycaemic monitoring of diabetes (not haemoglobin glycated nor HbA₁ reagents) ; reagents standardization through reference materials of a higher order according to the 98/79/EC Directive and the use of the corresponding reference values according to the standardization system.

References :

- Gillery P, Bordas-Fonfrède M, Chapelle JP , Drouin P, Hue G, Lévy Marchal C, Périer C, Selam JL, Slama G, Thivolet C, Vialettes B. HbA_{1c} : concertation clinico-biologique pour la standardisation des méthodes de dosages. Rapport des experts de l'ALFEDIAM et de la SFBC. Diabète et Métabolisme (Paris) 1999 ; 25 ; 283-287.
- Jeppsson JO, Kobold U, Barr J, Finke A, Hoelzel W, Hoshino T, Miedema K, Mosca A , Mauri P, Paroni R , Thienpont L, Umemoto M, Weykamp C. Approved IFCC reference method for measurement of HbA_{1c} in Human Blood. Clin Chem Lab Med 2002 ;40 ;78-79.
- Hoelzel W, Weykamp C, Jeppsson JO, Miedema K, Barr JR, Goodall I, Hoshino T, John WG, Kobold U, Little R, Mosca A, Mauri P, Paron R, Susanto F, Takei I, Thienpont L, Umemoto M, Wiedmeyer HM ; (IFCC Working Group on HbA_{1c} Standardization). IFCC reference system for measurement of haemoglobin A_{1c} in human blood and the national standardization schemes in the United States, Japan, and Sweden : a method-comparison study. Clin Chem 2004 ; 50 ; 166-174.
- Standardisation du dosage de l'HbA_{1c} : suite et fin(?) M.Fonfrède, J.P.Chapelle, G.Hue, C.Périer, P.Gillery www.sfbc.asso.fr
- Report of the ADA/EASD/IDF Working group of the HbA_{1c} Assay London,UK,20 January 2004. www.easd.org
- Randie R. Little, Curt L. Rohlfing, Hsiao-Mei Wiedmeyer, Gary L. Myers, David B. Sacks, and David E. Goldstein, for the NGSP Steering Committee, The National Glycohemoglobin Standardization Program : A Five-Year Progress Report, Clinical Chemistry 47:11 1985-1992 (2001).
- Françoise Chevenne, Marianne Deschênes, Pascale Maisonneuve, Joelle Goudable, Jacques De Graeve, Bruno Guerci, Philippe Gillery, Philippe Passa, Eric Marsaudon, Réévaluation des performances techniques et des conditions d'utilisation des réactifs d'HbA_{1c} par l'étude des notices, Spectra Biologie, Vol. 22, N° 135, Décembre 2003.

According to the 98/79/EC Directive :

Essential Requirements of Annex I *A general requirements* and especially paragraph 3 :

"...taking account of the generally acknowledged state of the artThe traceability of values assigned to calibrators...must be assured through available reference measurement procedures and/or available reference materials of a higher order " and *B design and manufacturing requirements* and especially paragraph 8 concerning *the informations supplied by the manufacturers*.

Abbreviations :

IFCC : International Federation of Clinical Chemistry and laboratory medicine

NGSP : National glycohaemoglobin Standardization Program

DCCT : Diabete control and Complication Trial

ALFEDIAM : Association de Langue Française pour l'Etude du Diabète et des Maladies Métaboliques

ANAES : Agence Nationale d'Accréditation et d'Evaluation en Santé.

ADA : American diabetes Association

EADS : European association for study of Diabetes

IDF : International Diabetes Federation

SFBC : Société Française de Biologie Clinique

HAS : Haute Autorité de Santé

Type writing :

In bold type writing are HbA_{1c} specific characteristics.
In normal type writing are general requirements of the 98/79/EC Directive.

This guideline mentions the essential requirements of HbA_{1c} reagents instruction for use :

- 1) The Instructions for use written in French (for the devices put on the French Market),
- 2) The name or trade name and address of the manufacturer. The name and address of the authorised representative of the manufacturer,
- 3) **The intended purpose of the device must be stated :**
 - **HbA_{1c} tested**

or

 - **HbA_{1c} deducted by algorithm from glycated haemoglobin testing**
- 4) **The medical interest of testing : glycaemia follow-up in diabetes,**
- 5) The appropriate warnings and/or precautions to take; where appropriate, the word 'STERILE' or a statement indicating any special microbiological state or state of cleanliness,
- 6) The statement indicating the *in vitro* use of the device,
- 7) The composition of the reagent product by nature of the active ingredients and amount of dangerous ingredient(s) concentrations in the reagent(s) or kit,
- 8) The storage conditions and shelf life before opening and following the first opening of the primary container,
- 9) The storage conditions and stability of working reagents,
- 10) An indication of any special equipment required including information necessary for the identification of that special equipment for proper use,
- 11) 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,
- 12) the measurement procedure to be followed with the device including as appropriate:
 - a. the principle of the method,
 - b. the details of any further procedure or handling needed before the device can be used (for example, reconstitution, incubation, dilution, instrument checks, etc.),
 - c. a detailed description of the procedure to be followed in using the device;
 - d. the specific analytical performance characteristics :
 - sensitivity and specificity
 - **accuracy** : data from **comparison between tested method and standardized method through available reference material**
 - **recommended values NGSP/DCCT-SFBC : repeatability: <3%, reproducibility : ≤4%**
 - measurement range
 - information needed for the control of known relevant interferences and limitations of the method
 - **interferences (studies or references) due to main variants of haemoglobin : HbC, HbS, HbE, labile HbA_{1c}, HbF, carbamylated and acetyled Hb,**
 - **where appropriate, interferences with bilirubin and triglycerids,**
 - **limitations for the method in case of modified lifetime of red blood cells, physiological haemolysis, haemoglobin level (minimum haemoglobin level)**

- instruction for use must specify if interferences have been studied or not, are known or unknown, for the concerned technique.

- frequency and circumstances of calibration operations : in particular for HPLC techniques how using chromatographic column (number of test for one calibration),
 - e. the indication whether any particular training is required
- 13) **The indication of the mathematical approach used for the calculation of the analytical result is to be made if result obtained by using algorithm,**
 - 14) **Analytical result expressed in percentage of Hb A,**
 - 15) Measures to be taken in the event of changes in the analytical performance of the device;
 - 16) Information appropriate to users on :
 - **internal quality control including specific validation procedures,**
 - **the traceability of the calibration of the device through available reference materials of a higher order (indication of the standardization procedure and where to find information about this calibration),**
 - 17) **The reference intervals for the quantities being determined, and therapeutic threshold according to the international recommendations, and the standardization system,**

Compatibility of the data with HAS (Haute Autorité de Santé) recommendations (formerly ANAES) January 1999 “Follow-up of diabetes type 2 not including complications follow-up” (maybe included in leaflet annexed to package insert),

Suppress sentence “each laboratory should establish its own reference ranges” or replace “establish” with “verify the coherence”,
 - 18) If the device must be used in combination with or installed with or connected to other medical devices or equipment in order to operate as required for its intended purpose, sufficient details of its characteristics to identify the correct devices or equipment to use in order to obtain a safe and proper combination,

indication, where appropriate, of the requirement not to dissociate reagents and calibrators from the same batch,
 - 19) Precautions to be taken against any special, unusual risks related to the use or disposal of the device including special protective measures; where the device includes substances of human or animal origin, attention must be drawn to their potential infectious nature,
 - 20) Bibliography,
 - 21) Date of issue or latest revision of the instructions for use,
 - 22) CE marking of conformity.