



## HbA<sub>1c</sub> Standardisation

### For Clinical Health Care Professionals

From 1 June 2009, the way in which HbA<sub>1c</sub> results are reported in the UK is changing. This leaflet explains why and how this will happen.

#### What is HbA<sub>1c</sub>?

Glucose in the blood binds irreversibly to a specific part of haemoglobin in red blood cells, forming HbA<sub>1c</sub>. The higher the glucose, the higher the HbA<sub>1c</sub>. HbA<sub>1c</sub> circulates for the lifespan of the red blood cell, so reflects the prevailing blood glucose levels over the preceding 2-3 months.

#### What does it tell us?

The Diabetes Control and Complications Trial (DCCT) in Type 1 diabetes and the UK Prospective Diabetes Study (UKPDS) in Type 2 diabetes both showed that the risk of microvascular and macrovascular complications of diabetes increases as HbA<sub>1c</sub> increases. HbA<sub>1c</sub> thus gives a measure of an individual's risk of the long-term complications of diabetes.

#### Why measure it?

Serial measurements of HbA<sub>1c</sub> show how an individual's glucose control, and thus risk of complications, changes in response to alterations in management. HbA<sub>1c</sub> should be measured 2-6 monthly. Target HbA<sub>1c</sub> levels can be set for individual patients and therapy adjusted accordingly.

#### How is HbA<sub>1c</sub> reported currently?

Current HbA<sub>1c</sub> assays in the UK and other parts of the world are aligned to the assay used in the DCCT, so that an individual's risk of complications can be inferred from the result.

#### What are the current targets?

General targets for HbA<sub>1c</sub> of 6.5 - 7.5 % should be set for an individual, taking into consideration their risk of severe hypoglycaemia, cardiovascular status and co-morbidities.

#### Why Change?

After the DCCT, a new standard specific for HbA<sub>1c</sub> was prepared by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). In future, manufacturers will supply IFCC standardised values for their calibrators as well as DCCT-aligned values. The units for reporting HbA<sub>1c</sub> will also be changed so that HbA<sub>1c</sub> reported by laboratories is traceable to the IFCC reference method. Global comparison of HbA<sub>1c</sub> results will therefore be possible.

#### What are the IFCC units?

HbA<sub>1c</sub> results traceable to the IFCC reference method will be expressed as mmol per mol.

### How do old and new relate?

A guide to the new values expressed as mmol/mol is:

| DCCT- HbA <sub>1c</sub><br>(%) | IFCC-HbA <sub>1c</sub><br>(mmol/mol) |
|--------------------------------|--------------------------------------|
| 6.0                            | 42                                   |
| 6.5                            | 48                                   |
| 7.0                            | 53                                   |
| 7.5                            | 59                                   |
| 8.0                            | 64                                   |
| 9.0                            | 75                                   |
| 10.0                           | 86                                   |
| 11.0                           | 97                                   |
| 12.0                           | 108                                  |

### What are the targets in IFCC units?

The equivalent of the DCCT HbA<sub>1c</sub> targets of 6.5 % and 7.5 % are 48 mmol/mol and 59 mmol/mol in the IFCC units, with the non-diabetic reference range of 4.0 % to 6.0 % being 20 mmol/mol to 42 mmol/mol.

### When is the changeover to IFCC units?

HbA<sub>1c</sub> results expressed in the IFCC units are obviously very different to those currently in use.

From **1 June, 2009**, results will be provided in the UK as both IFCC-standardised units (mmol/mol) and DCCT-aligned units (%). This will give everyone time to become familiar with the new units and how they relate to DCCT numbers, and thus to the risk of complications.

From **1 June 2011**, results will be reported only in the IFCC units.

### What are the limitations of HbA<sub>1c</sub> measurement?

HbA<sub>1c</sub> results (DCCT or IFCC) will be misleading in certain situations eg a variety of haematological conditions where there is abnormal red cell turnover, where there is an abnormal haemoglobin, and in some patients with renal or

liver disease. In pregnancy, HbA<sub>1c</sub> falls by around 0.5 % due to haemodilution and other factors. In the presence of abnormal haemoglobin, HbA<sub>1c</sub> results can vary depending on the method used to measure HbA<sub>1c</sub> and the particular haemoglobinopathy involved. For these reasons, such HbA<sub>1c</sub> results should be used to detect trends in a patient's glycaemic control rather than for target setting.

If any condition leads to a change in red cell survival, then HbA<sub>1c</sub> measurement by any means can, at best, be used to track changes in glycaemia. Other measures of glycaemia may then be required, such as more reliance on self monitored blood glucose values or the use of a serum fructosamine assay, if available.

### Why not report eAG?

Conceptually, converting the HbA<sub>1c</sub> result to an equivalent "average glucose" level might help our understanding and interpretation of HbA<sub>1c</sub>. A recent large study reported on how to calculate an estimated average glucose (eAG) from an HbA<sub>1c</sub> result.

However, the study was carried out in a restricted population; issues have been raised about the study design; and an eAG will have limited applicability to the majority of patients who do not measure their own blood glucose levels. In some patients, the estimate may also prove inaccurate enough to be misleading. It has been agreed that in the UK, eAG results will not be reported the moment. Further research into the applicability and utility of eAG to the wide range of people with diabetes is on-going and eagerly awaited.