# New HbA1c system a valuable step forward

**The introduction of a new blood glucose reporting system has important implications for patient care, writes Ned Barrett**


**NEARLY EVERYBODY INVOLVED IN DIABETES CARE** is familiar with the HbA1c test. It features prominently in any review of blood glucose control. HbA1c is formed in the blood when glucose binds to a specific part of the haemoglobin molecule following a complex chemical reaction. The HbA1c level correlates with the average blood glucose over the preceding two months or so. The HbA1c test is used to assess the adequacy of blood glucose control over this period of time and as a guide in the management of diabetes.

The importance of the HbA1c test was not fully recognised until the completion of the US Diabetes Control and Complications Trial (DCCT) for people with type 1 diabetes in 1993 and the UK Prospective Diabetes Study (UKPDS) for people with type 2 diabetes in 1998. The DCCT showed that the risk for development and progression of the chronic complications of diabetes in people with Type 1 diabetes is closely related to the degree of blood glucose control as measured by HbA1c. The UKPDS showed similar results for people with type 2 diabetes.

The correlation between HbA1c levels and outcomes highlighted the need to measure HbA1c accurately and precisely so that results for a person with diabetes can be directly related to studies such as the DCCT and consequently to outcome risks. This requirement involves a consideration of one of the fundamental principles of measurement.

The science of measurement is called metrology and it sets out the requirements for measurement systems including those in laboratory medicine. Among these is the requirement for metrological traceability. Put simply, this is the linking of a measurement result from a patient sample through an unbroken chain of calibrations to a commonly accepted international reference. Doing this is a prerequisite to being able to link measurement results to a common reference when using different types of measurement equipment in different locations over time. The implications of all this are far-reaching. Measurement systems with full metrological traceability will enable the use of international reference ranges and the harmonisation of decision values.

All of this may appear esoteric but it will have very important benefits for patient care, the management of long-term conditions, the detection and control of disease, how we screen for disease, ongoing medical research and the control of healthcare costs.

An important driver for metrological traceability emerged in December 1998 with the publication of the European directive 98/79/EC on in-vitro diagnostic devices. The directive incorporated the requirement for metrological traceability into regulation. Earlier in 1998, in advance of the directive, the EU Commission provided funding to assist the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) in completing its programme to develop a reference method and pure standards for the HbA1c assay. That programme had commenced in 1995, two years after the publication of the DCCT results.

The IFCC reference method was published in 2002 and is now the means for the uniform standardisation of HbA1c assays worldwide. Measurements are traceable to an SI

unit, the mole (mol), and are expressed in mmol/mol rather than as % which is not an SI unit. The abbreviation SI, is universally used to signify the International System of Units (Le Système International d'Unités), colloquially known as the metric system of measurement. SI is the dominant measurement system used in science.

Both the DCCT and UKPDS predate the requirements for metrological traceability. The HbA1c assay systems used in both of these trials were not specific for HbA1c and were not standardised or calibrated in the true sense and would not now meet the standards required for the proper metrological traceability of the assay.

The principal officers of the American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), International Diabetes Federation (IDF) and the IFCC met at a summit conference in Milan on May 4, 2007. It was agreed that the HbA1c assay results be reported worldwide in IFCC units (mmol/mol) and derived DCCT units (%), using the IFCC-DCCT Master Equation.

The Master Equation expresses the mathematical relationship between the DCCT method results and the IFCC Reference Method results. This relationship has been stable and reproducible over several years. Countries have been asked to introduce the new way of reporting HbA1c results, known as dual reporting, beginning in 2010 after the agreed deadline of December 31, 2009 for HbA1c analytical equipment manufacturers to have traceability to the IFCC Reference System in place.

The HSE's Diabetes Expert Group (EAG) is leading the introduction of the new HbA1c reporting system in Ireland. A subcommittee of the EAG has been appointed for this purpose. The subcommittee members are: Dr Ned Barrett (chairman), James Conway (assistant national director, office of the CEO), Dr Graham Roberts, Dr Tony O'Sullivan, Louise McMahon and Dr Obada Yousif. The project team is chaired by Dr Ned Barrett and includes the EAG subcommittee members, health professionals and senior HSE management.

The agreed commencement date for dual reporting of HbA1c results in Ireland is July 1, 2010. The Project Manager is Loraine McGrattan, HSE, Oak House, Limetree Avenue, Millennium Park, Naas, Co Kildare.

For clinicians and people with diabetes in Ireland, the impact of all these developments will be evident in the laboratory reports giving HbA1c results with effect from Thursday, July 1, 2010. For example, a HbA1c (IFCC) result of 42mmol/mol will be accompanied by a derived HbA1c (DCCT-aligned) result of 6.0%; a HbA1c (IFCC) result of 53mmol/mol will be accompanied by a derived HbA1c (DCCT-aligned) result of 7.0%; a HbA1c (IFCC) result of 64mmol/mol will be accompanied by a derived HbA1c (DCCT-aligned) result of 8.0%.

These developments will enable the adoption of a national reference range for HbA1c *(See Table 1).*

It is important that all involved in diabetes care in Ireland note that under the new system of dual reporting of HbA1c results, each DCCT-aligned HbA1c result (expressed as %) will be reported alongside the new HbA1c (IFCC) result (expressed in mmol/mol). *Table 2* gives some examples of how the results compare.

Dual reporting will continue until December 31, 2011.

Table 1

**Reference range for HbA1c**

| | |
|---|---|
| **HbA1c (IFCC)** | **20-42 mmol/mol** |
| HbA1c (DCCT derived) | 4.0-6.0% |

Table 2

**Examples of how the new HbA1c results will relate**

| HbA1c (IFCC) mmol/mol | HbA1c (DCCT, derived) % |
|---|---|
| 45 | 6.3 |
| 55 | 7.2 |
| 65 | 8.1 |
| 75 | 9.0 |
| 85 | 9.9 |
| 95 | 10.8 |
| 105 | 11.8 |

Thereafter, HbA1c will be reported as a HbA1c (IFCC) result (expressed in mmol/mol) only. It is likely that each person with diabetes will have no more than three or four HbA1c measurements made during the period of dual reporting so it is important they become accustomed to the HbA1c (IFCC) numbers from early on.

The project team has put in place resources to advise and assist healthcare professionals and people with diabetes in dealing with these changes. A dedicated webpage on HbA1c is now accessible on the main HSE website. The web address is **www.hse.ie/go/diabetes** and it includes information and resources for:

- People with diabetes
- Healthcare professionals
- Laboratory professionals
- Suppliers of HbA1c equipment and reagents to Irish hospitals and clinics.

Information leaflets and conversion charts are available for download from this site. An online calculator is also available to convert units either way. Information for people with diabetes is available in English, Irish and Polish. Supplies of printed leaflets for healthcare professionals and people with diabetes can be ordered from the project office at 045-882588.

During March, seminars on the changes were held in Dublin, Cork, Galway and Sligo. The project team is willing to provide speakers to explain these changes at meetings relating to diabetes in the weeks leading up to the commencement of dual reporting in July.

The introduction of the new HbA1c reporting system is a valuable opportunity for all involved in diabetes care to emphasise once again the importance of sustained good blood glucose control in preventing the costly complications of diabetes.

**Ned Barrett is chairman of the HSE project team on the implementation of the international standardisation of HbA1c**