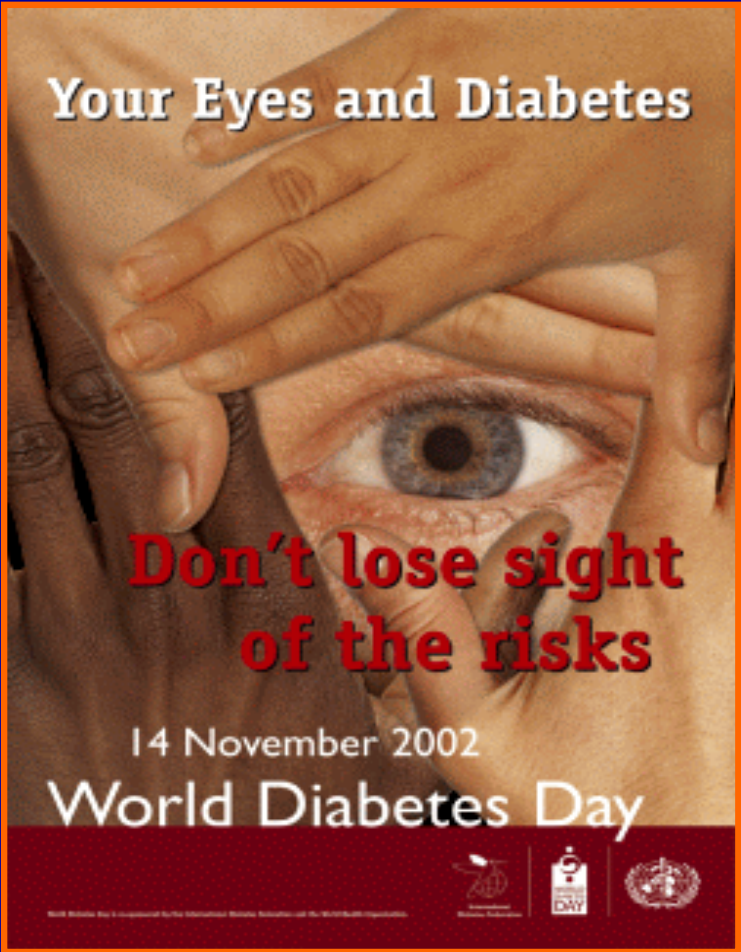


HbA_{1c} Standardisation

Have We a Choice?

Dr. Ned Barrett

Mid-Western Regional Hospital



Your Eyes and Diabetes

**Don't lose sight
of the risks**

14 November 2002

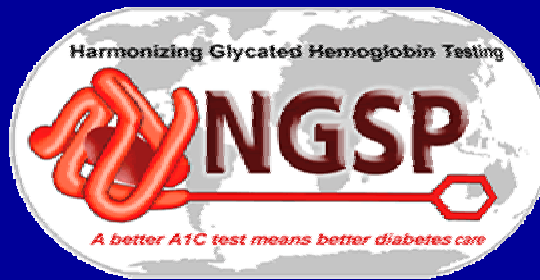
World Diabetes Day

World Diabetes Day is a day of action for the International Diabetes Federation and the World Health Organization.



Glucose Binding Sites on Haemoglobin

- N-terminal valine residue of the β -chain
 - 60% of bound glucose
 - Known as HbA1c
- ϵ -lysine amino groups
 - 44 per haemoglobin molecule
 - 34% of bound glucose
- N-terminal valine residue of the α -chain
 - 6% of bound glucose



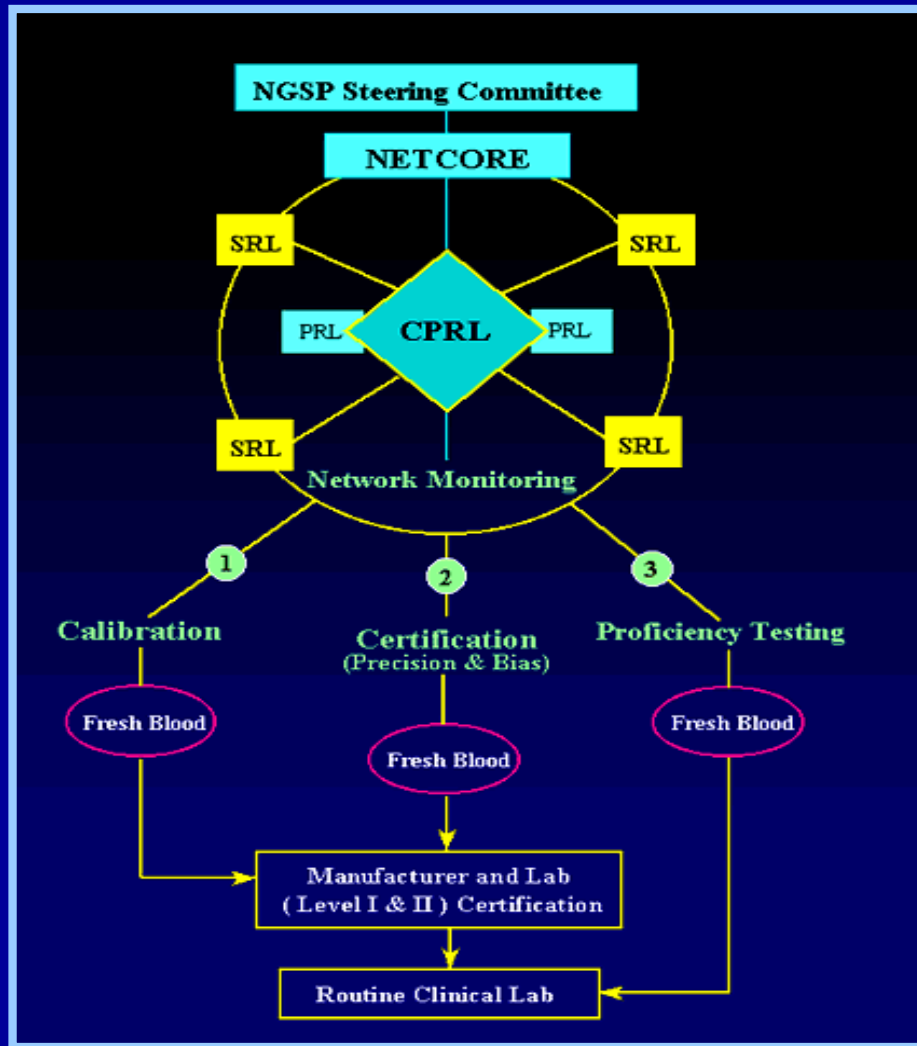
Purpose of the National Glycohemoglobin Standardization Program (NGSP)

To align reported results to clinical outcomes data (DCCT and UKPDS) and to assure optimal assay method and laboratory performance



NGSP Achievements

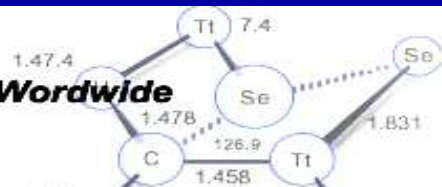
- 87% of US Laboratories use an NGSP certified method
- 70 – 75% of HbA1c test results in the US are traceable to the DCCT / UKPDS





Problems with NGSP

- Issue of chemical entity being measured is not addressed
- DCCT method is a designated comparison method and is not standardised or calibrated in the true sense
- DCCT method is not specific for HbA1c



- Publication of approved IFCC Reference Method for the Measurement of HbA1c in Human Blood (Jan 2002)
CCLM 2002; 40(1): 78-89
- The new reference method will be the basis for the uniform standardisation of HbA1c routine assays worldwide



IFCC HbA1c Standardisation is:

A programme to establish traceability of reported HbA1c results to the “highest order reference”



HbA1c

N-terminal hexapeptide of the β -chain

HbA0-peptide

Val-His-Leu-Thr-Pro-Glu

HbA1c-peptide

Glucose-Val-His-Leu-Thr-Pro-Glu

NGSP

- **Primary Reference Laboratories use a haemolysate as a calibrator**
- **Uses a Designated Comparison Method**
- **Established network with proven stability over many years**

IFCC

- **Network uses purified HbA1c calibrator**
- **Uses Reference Method**
- **Newly established network with limited stability data**

NGSP

- Reported test results can be directly related to clinical outcomes (DCCT, UKPDS) and published treatment goals
- Assists manufacturers in method calibration

IFCC

- Reported test results cannot be directly related to clinical outcomes except through conversion to NGSP /DCCT aligned results
- Supplies Secondary Reference Materials to manufacturers

NGSP

- **Certification programme for manufacturers and laboratories**
- **Sets limits for acceptable performance**

IFCC

- **Has plans to establish programme for manufacturers to verify their calibration**
- **Has not set limits for acceptable performance; an important role for EQA Schemes**



EU IVD Directive

With effect from the end of 2003

Manufacturers will be required to document the traceability of values assigned to calibrators and controls to available reference methods and/or reference materials of a “higher order”



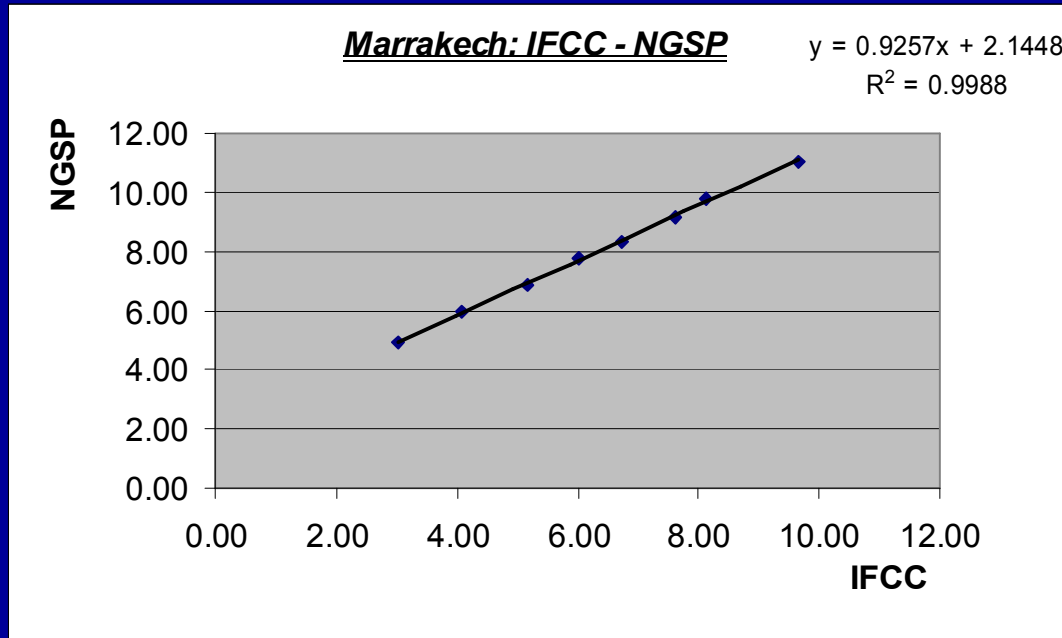
EU IVD Directive

Calibration of HbA1c assays within the EU will have to be traceable to the **IFCC Reference Method and Standards** by 31st December 2003

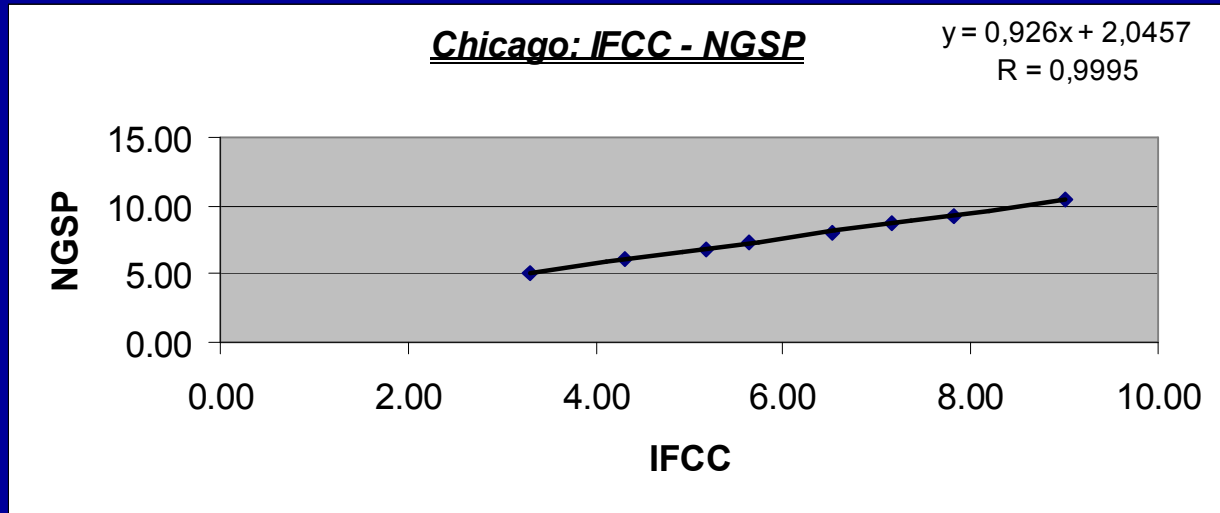
IFCC and NGSP Master Equation

- International progress continues on Master Equation (ME) relating NGSP to the IFCC Reference Values
- Stability of Master Equation will be monitored over time

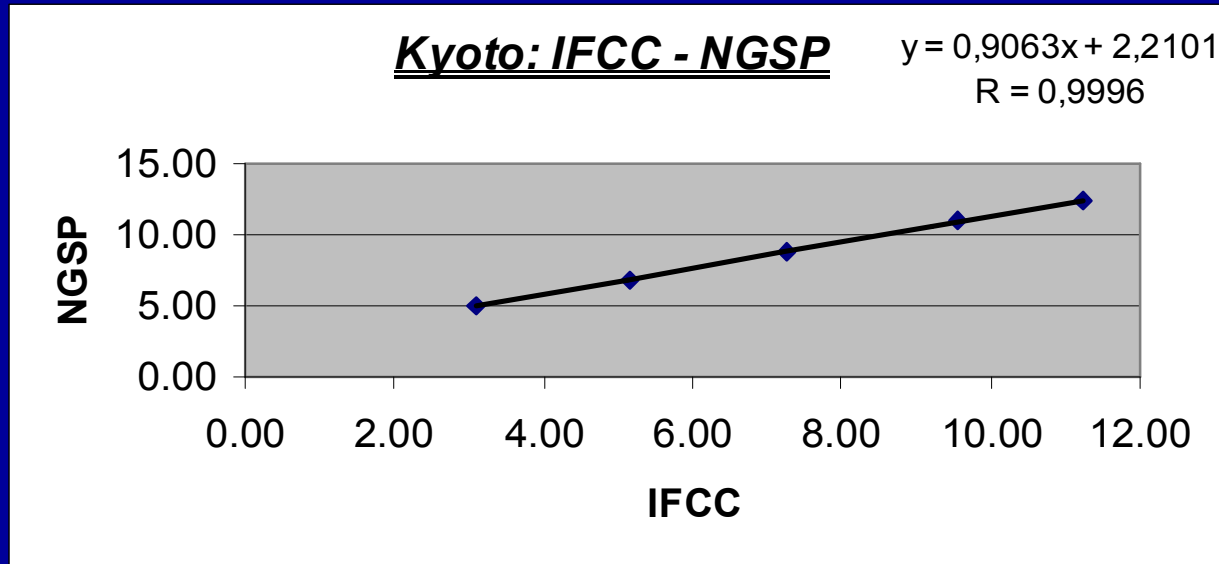
NGSP IFCC Relationship Marrakech (May 2001)



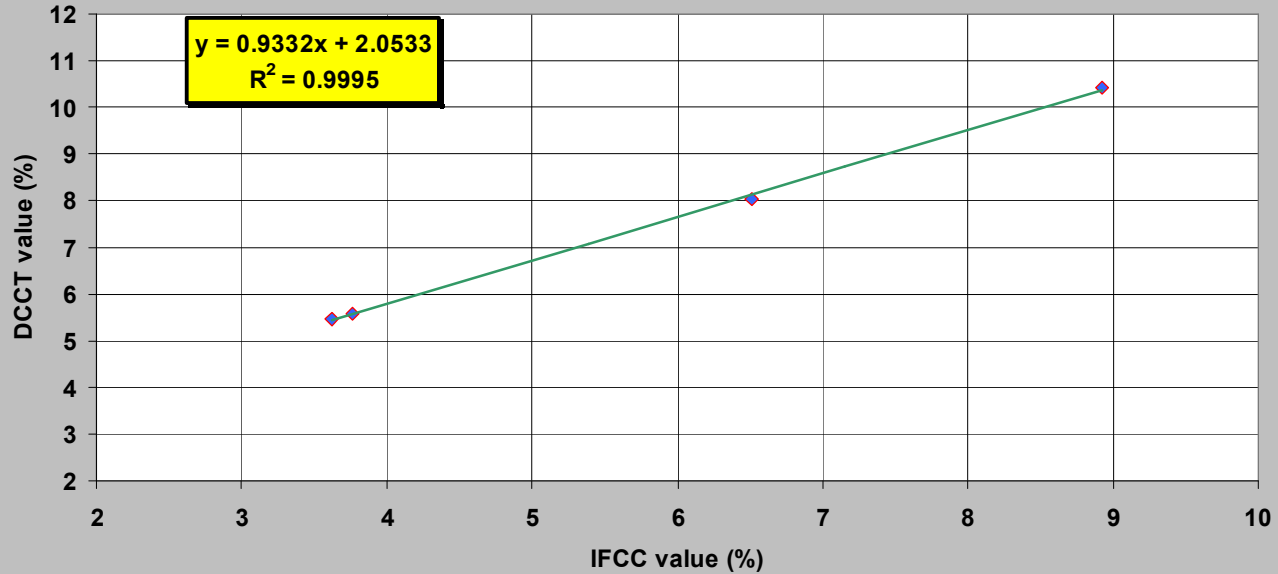
NGSP IFCC Relationship Chicago (September 2001)



NGSP IFCC Relationship Kyoto (April 2002)



IEQAS Specimens



Study	NGSP
Marrakech (May 2001)	$Y = 0.926x + 2.1448$
Chicago (Sept 2001)	$Y = 0.926x + 2.0457$
Kyoto (April 2002)	$Y = 0.906x + 2.2101$
IEQAS 2002	$Y = 0.933x + 2.0533$

IFCC and NGSP Master Equation

- Aim is for a resilient master equation linking NGSP to the IFCC Reference
- Master Equation will allow NGSP results to be reported while meeting the requirements of the EU IVD Directive

Issues relating to the Master Equation

- Where will the Master Equation reside in the traceability chain?
 - Network level / manufacturer's calibrator / clinical laboratory
- Is there a need for method-specific equations?



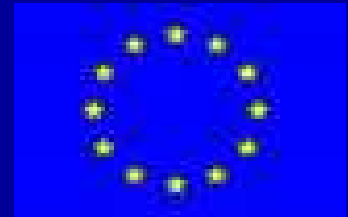
NGSP Plans ?

NGSP will probably “anchor” to the IFCC Reference Method within the next 3-5 years

NGSP and IFCC Results

(Based on Kyoto Study; April 2002)

NGSP (%)	IFCC (%)
4.0	2.0
5.0	3.1
6.0	4.2
7.0	5.3
8.0	6.4
9.0	7.5
10.0	8.6



E uropean Committee for External
Q uality
A ssessment Programmes in
L aboratory
M edicine



IEQAS

UKNEQAS

EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

“Communication is the bridge
between where you are now and
where you want to be”

Downey P , Youell D. *Exploring the Communication
Dynamic*. Dublin: Oak Tree Press, 1998.