Global Standardization of HbA1c

Impact of the Consensus Statement of International Professional Organizations

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EQA organiser HbA1c in The Netherlands,

Berlin, EQALM, 1 July 2009

Obesitas

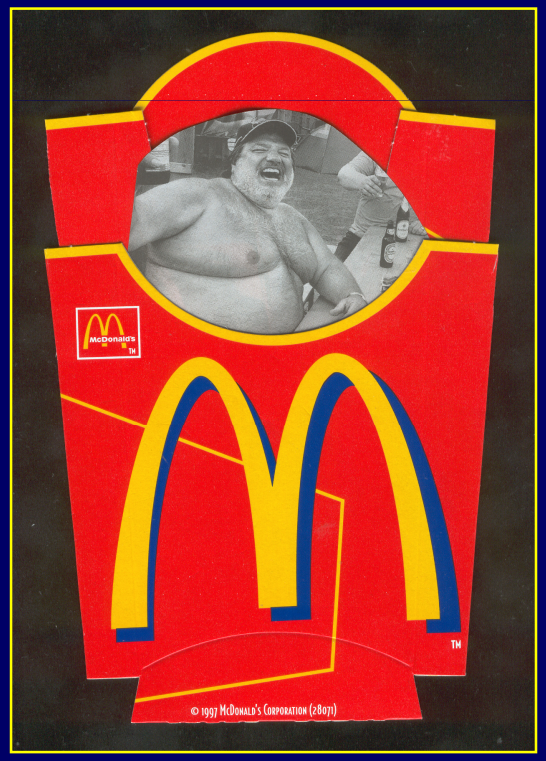
Diabetes

Long Term Complications

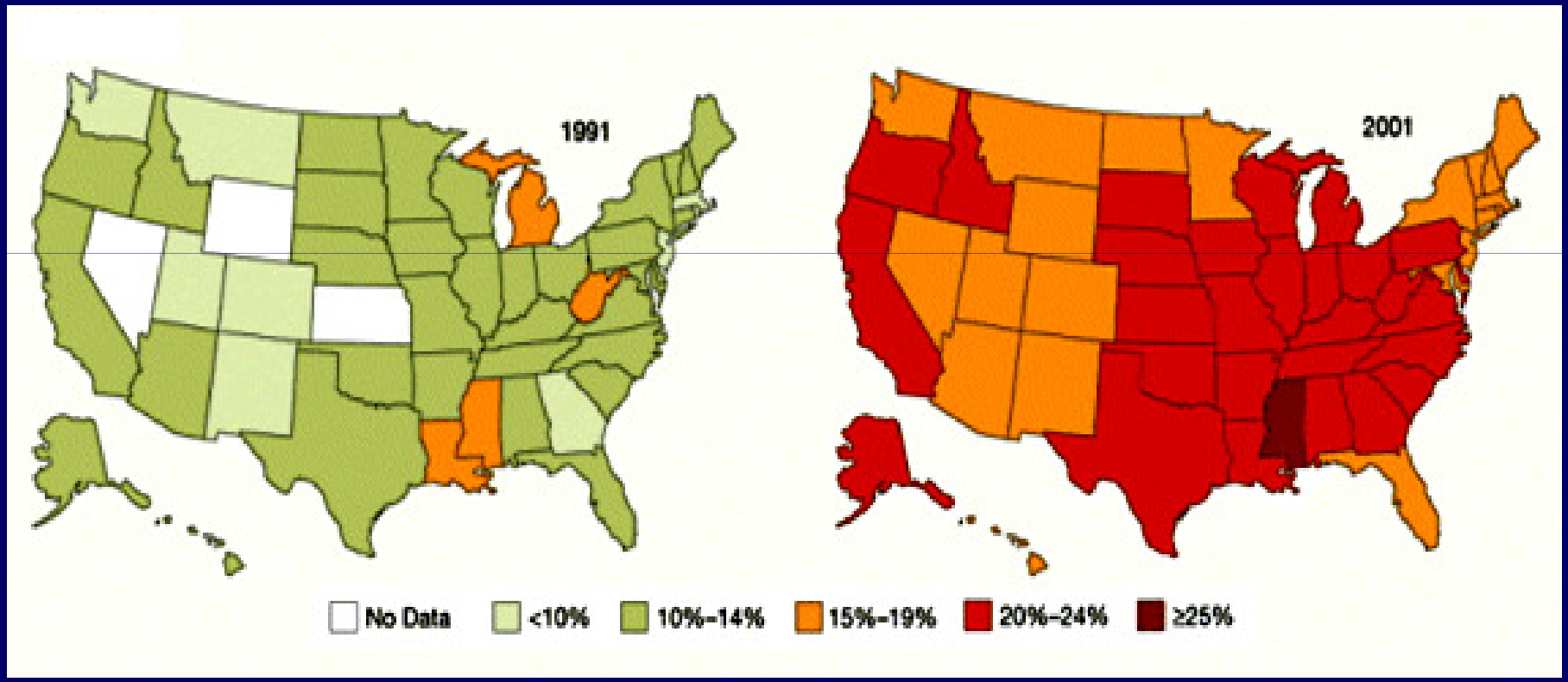
Glucose Memory

HbA1c: Risc factor

HbA1c: Standardization



Prevalence of Obesity Among U.S. Adults



JAMA 2003; 298:76

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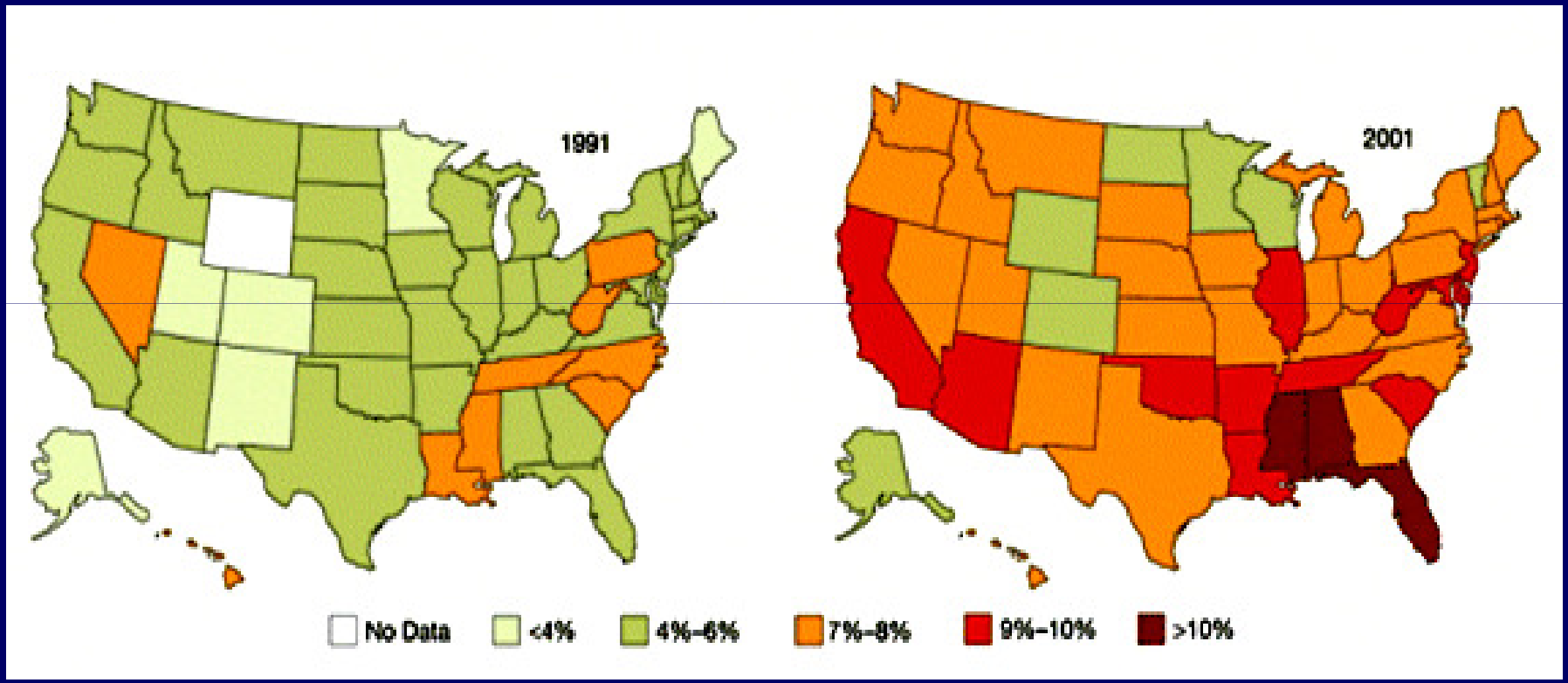
Prevalence of Diagnosed Diabetes Among Adults in the U.S.



JAMA 2003; 298:76

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Diabetes and HbA1c: the DCCT Study

The New England
Journal of Medicine

Volume 329 SEPTEMBER 30, 1993 Number 14

THE EFFECT OF INTENSIVE TREATMENT OF DIABETES ON THE DEVELOPMENT AND PROGRESSION OF LONG-TERM COMPLICATIONS IN INSULIN-DEPENDENT DIABETES MELLITUS

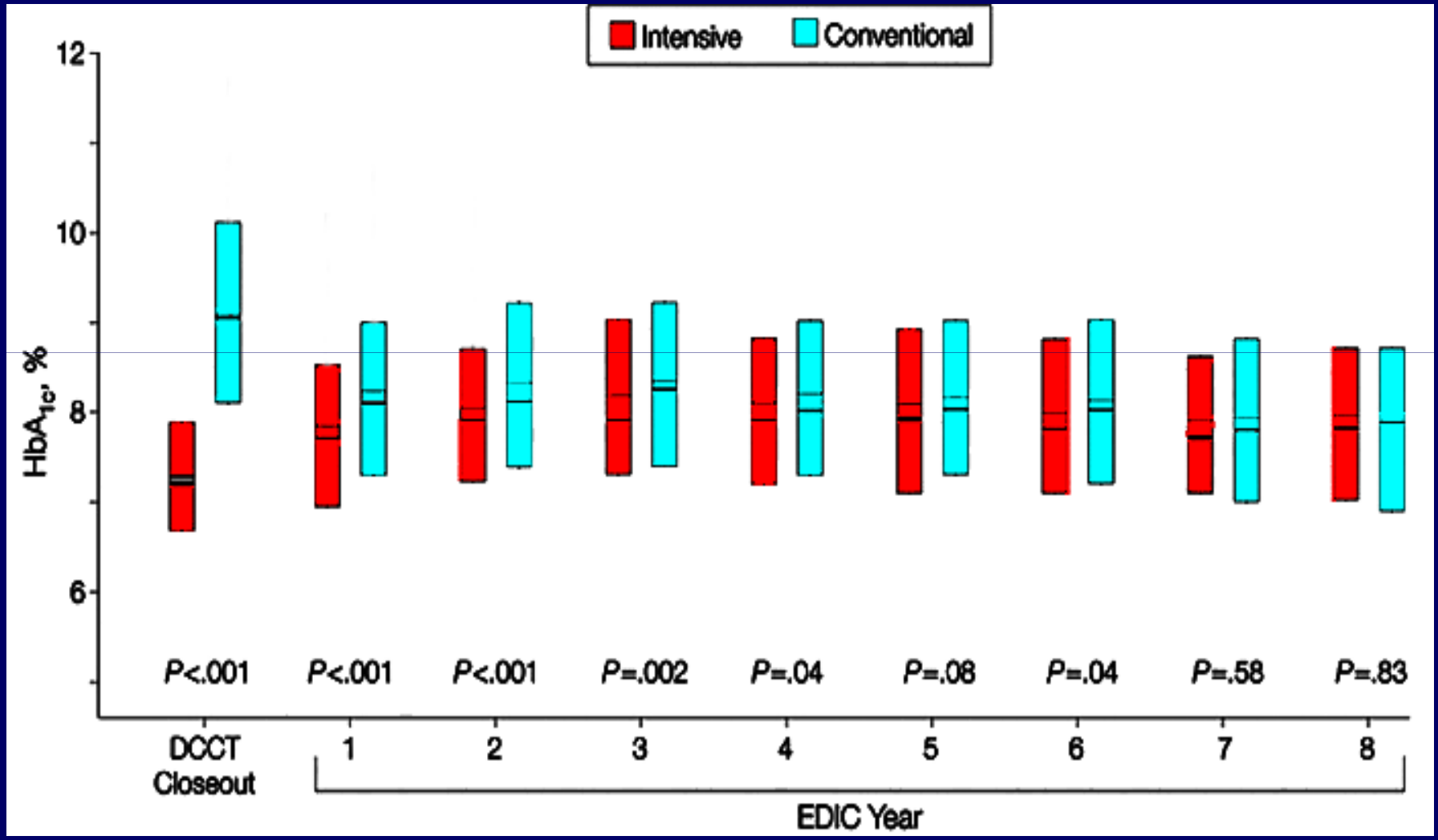
THE DIABETES CONTROL AND COMPLICATIONS TRIAL RESEARCH GROUP*

Abstract *Background.* Long-term microvascular and neurologic complications cause major morbidity and mortality in patients with insulin-dependent diabetes mellitus (IDDM). We examined whether intensive treatment with the goal of maintaining blood glucose concentrations close to the normal range could decrease the frequency and severity of these complications.

Methods. A total of 1441 patients with IDDM — 726 with no retinopathy at base line (the primary-prevention

interval, 62 to 85 percent), as compared with conventional therapy. In the secondary-intervention cohort, intensive therapy slowed the progression of retinopathy by 54 percent (95 percent confidence interval, 39 to 66 percent) and reduced the development of proliferative or severe nonproliferative retinopathy by 47 percent (95 percent confidence interval, 14 to 67 percent). In the two cohorts combined, intensive therapy reduced the occurrence of microalbuminuria (urinary albumin excretion of ≥40 mg

Distribution of HbA1c - EDIC



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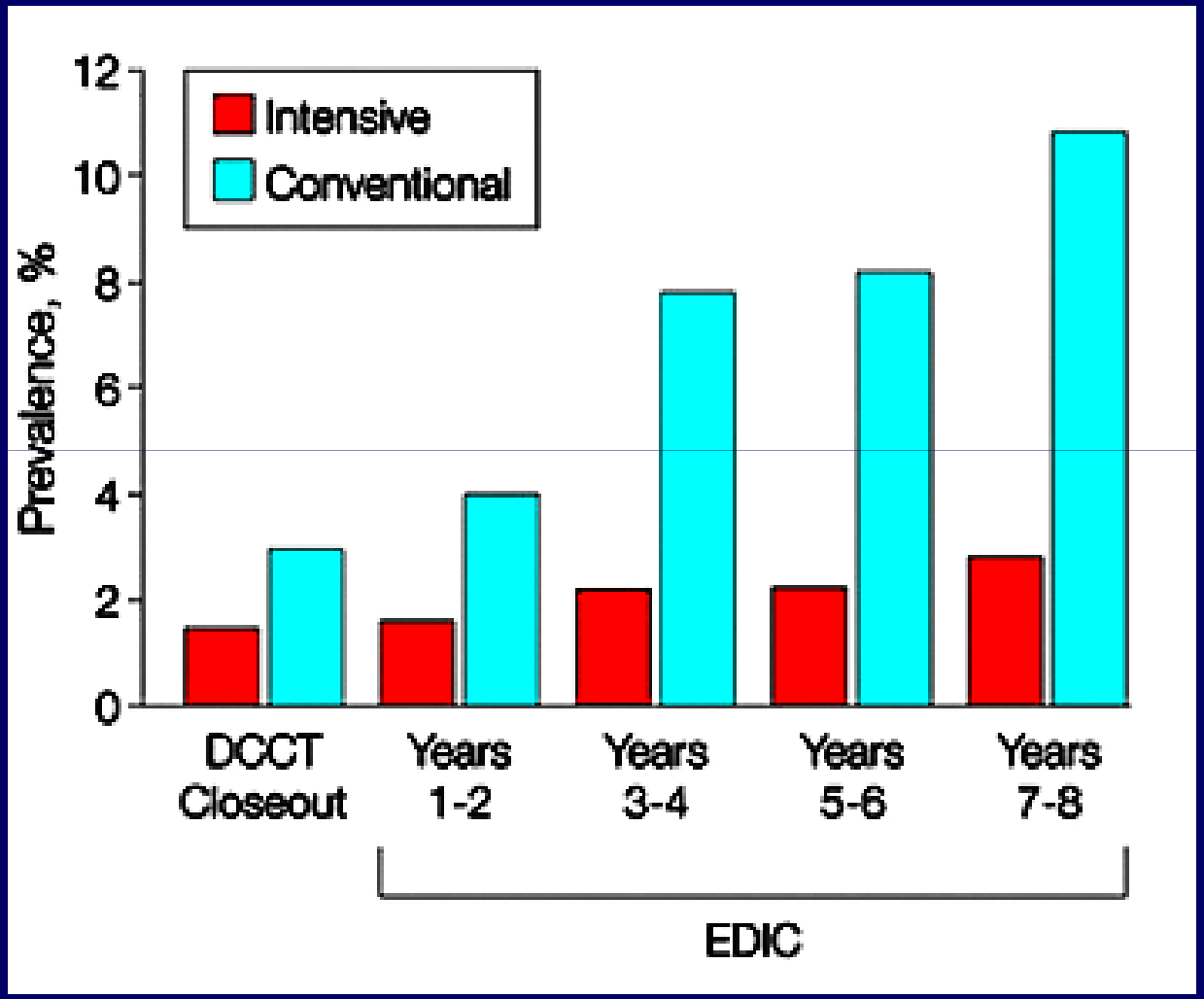
JAMA 2003; 290:2159

Prevalence of Albuminuria



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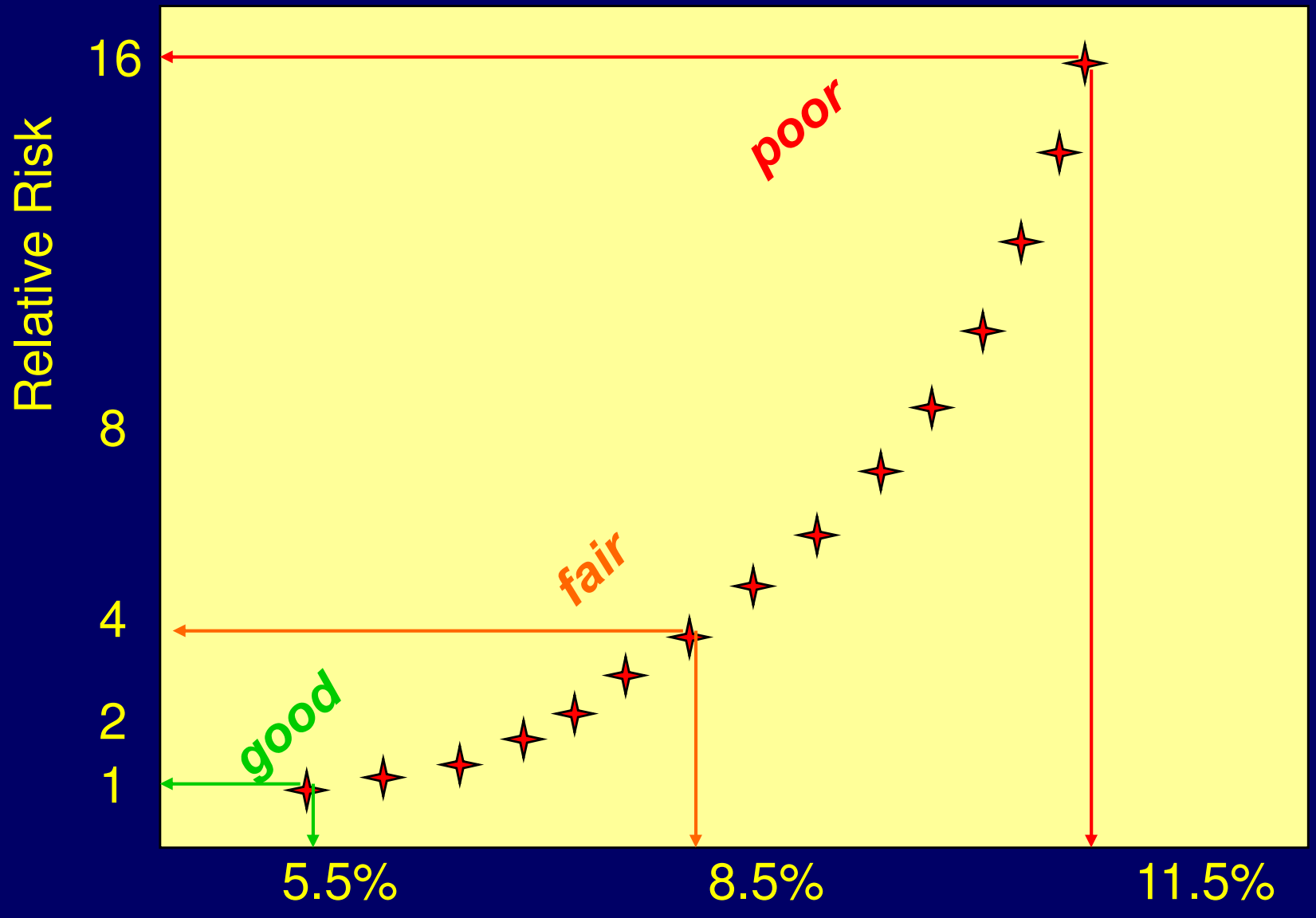
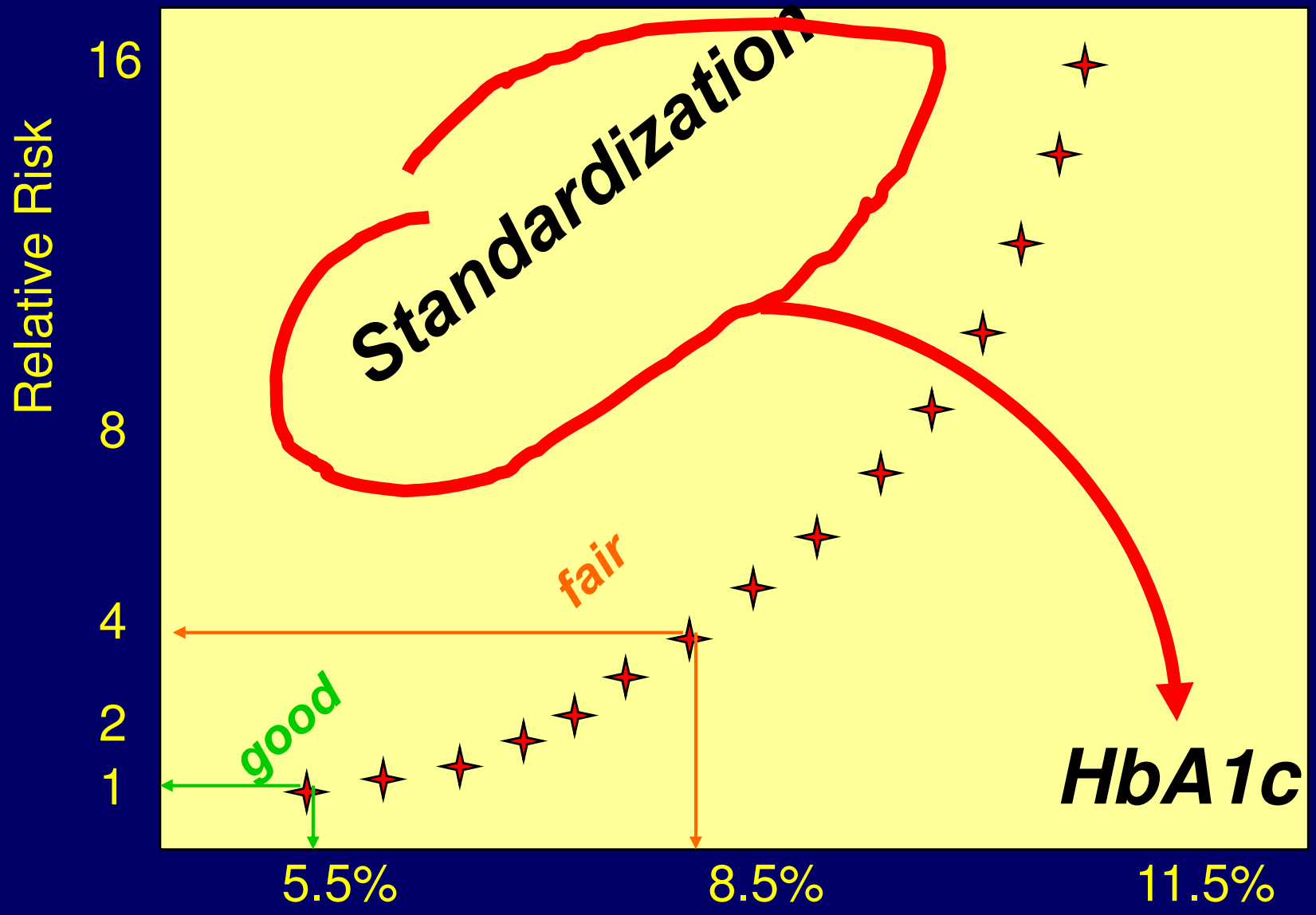
JAMA 2003; 290:2159

DCCT: HbA1c = Risk Factor



Reliable Risk Prediction = Reliable HbA1c



National Initiatives Standardisation

Approach

USA:	NGSP
Japan:	JDS/JSCC
Scandinavia:	Mono-S

Comparison
National Reference Methods

* *Arbitrarily Chosen*
* *Not Specific*
* *Different numbers*

Confusion!

Summary Situation

* *Confusion Different Numbers in USA, Japan, Scanidnavia, Europe*

* *Many Countries not standardized at all*

* *Traceability required by The European Law (IVD Directive)*

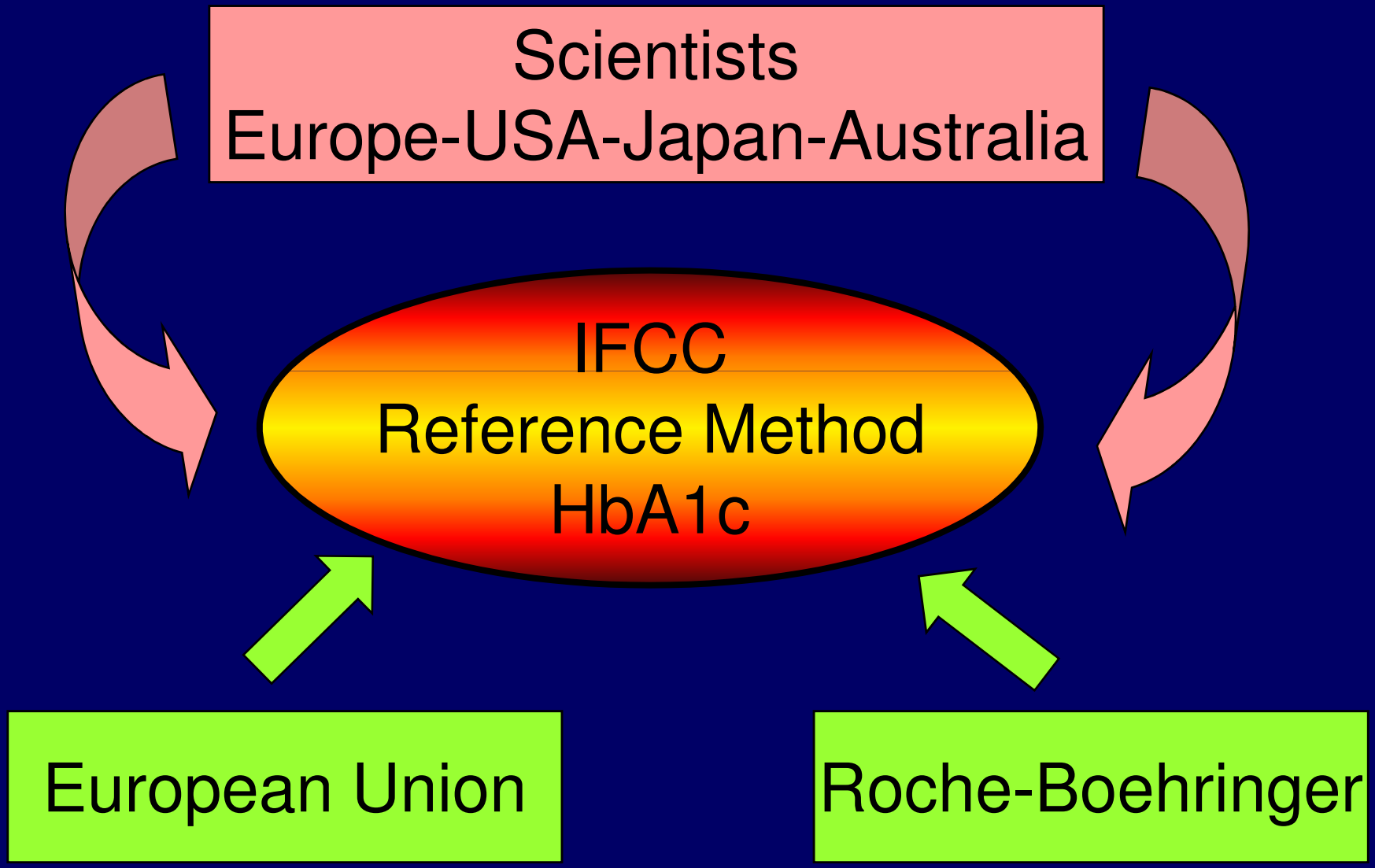
The IFCC: This is unacceptable

We want someone…….

……To develop an scientifically sound Reference Method

……As the anchor to achieve worldwide Harmonization of HbA1c

Where to find Fools to do this Job?



IFCC Working Group at Work

- Pure HbA1c HbA0
- Reference Method
- Worldwide Network
- Clinical Studies
- Implementation

Conclusions:

- *highly reproduceable over 8 years*
- *linear relationship*
- *tight relationship (low uncertainty)*

Similar results for Japanese and Scandinavian DCM's

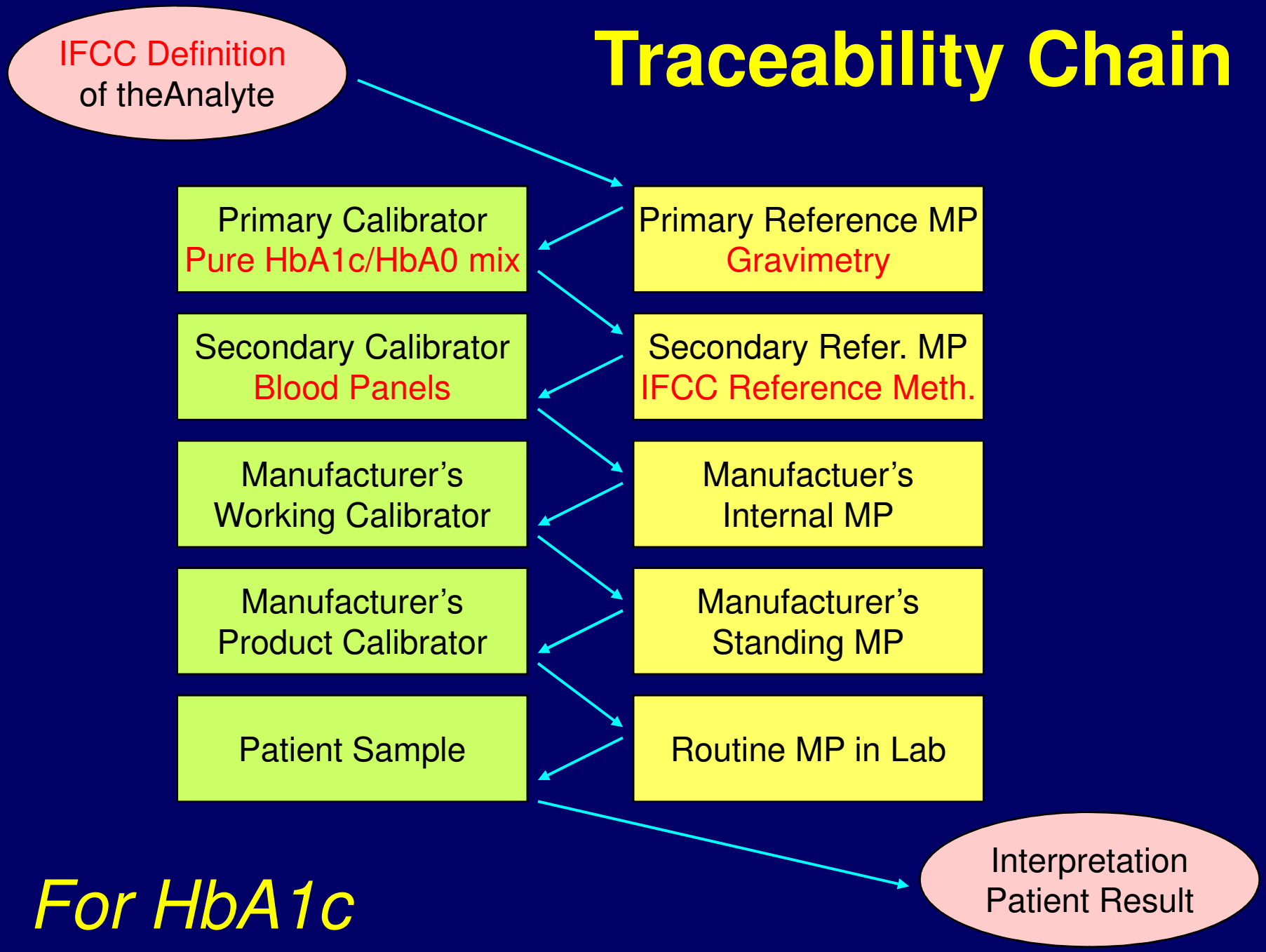
Clinical Chemistry

Clin Chem 2008

The IFCC Reference Measurement System for HbA1c: A 6-Year Progress Report

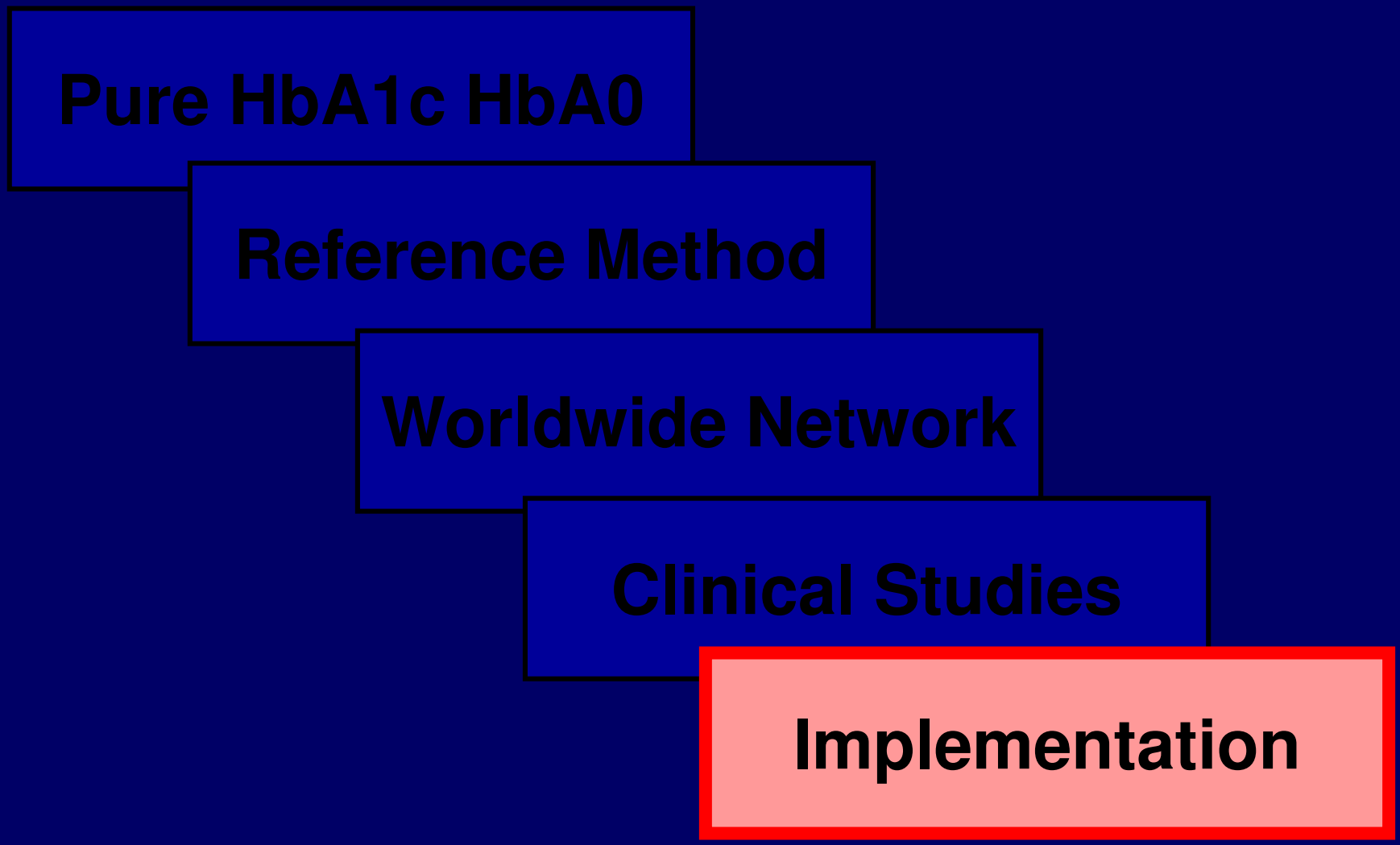
Cas Weykamp (1*), W. Garry John (2), Andrea Mosca (3)
Tadao Hoshino (4), Randie Little (5), Jan-Olof Jeppsson (6)
Kor Miedema (8), Gary Myers (9), Hans Reinauer (10)
David Sacks (11), Robbert Slingerland (8), Carla Siebelder (1)

Traceability Chain



For HbA1c

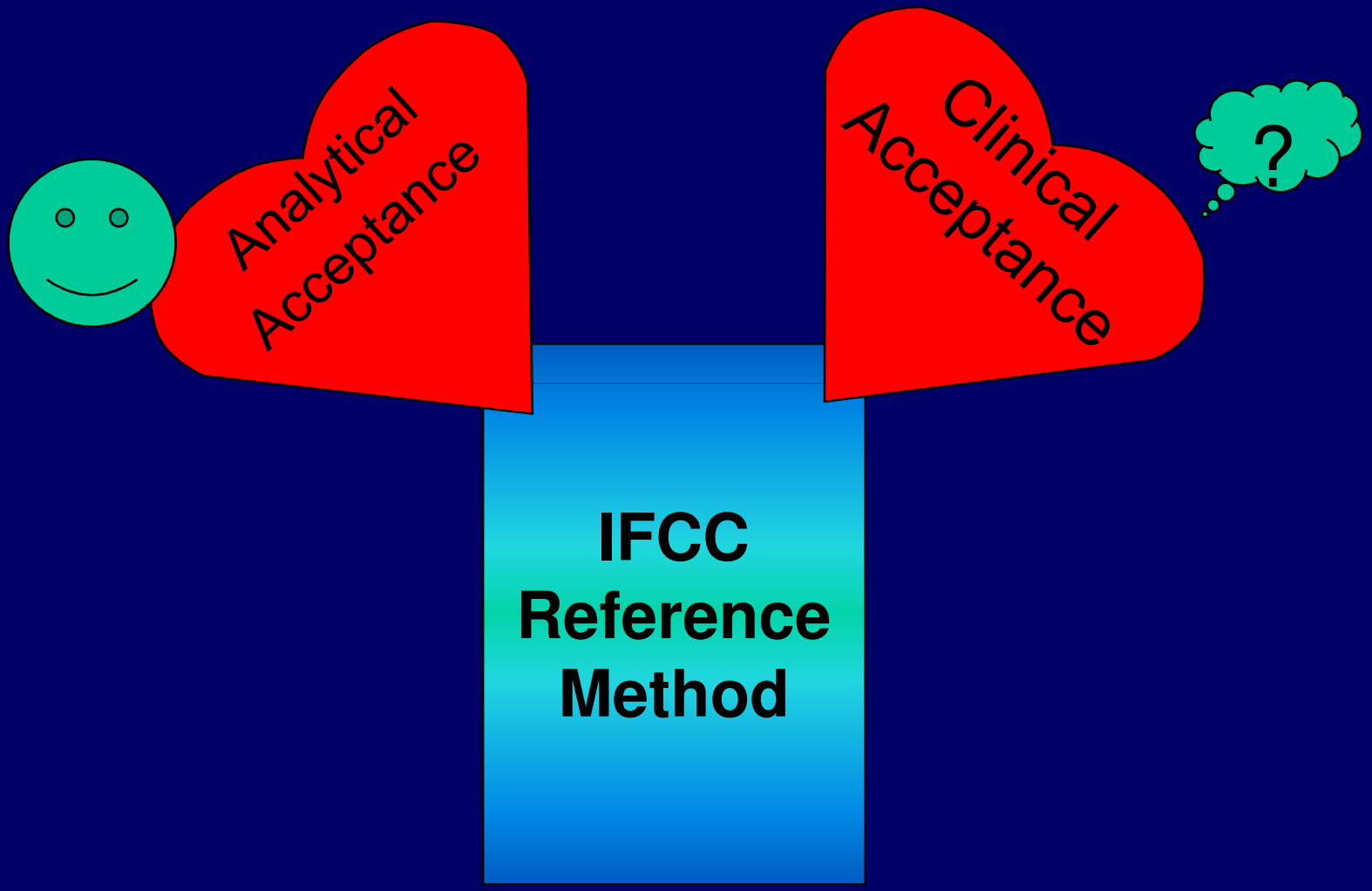
IFCC Working Group at Work



.....The IFCC Reference Method is ready for Implementation.....

But.....

Does the World love The IFCC?



But.....

The first Debate

But……in General

Fahrenheit	Celcius
Mark	Euro
Miles	Kilometers
Pints*	Liters
mg/dL	µmol/L
……	……

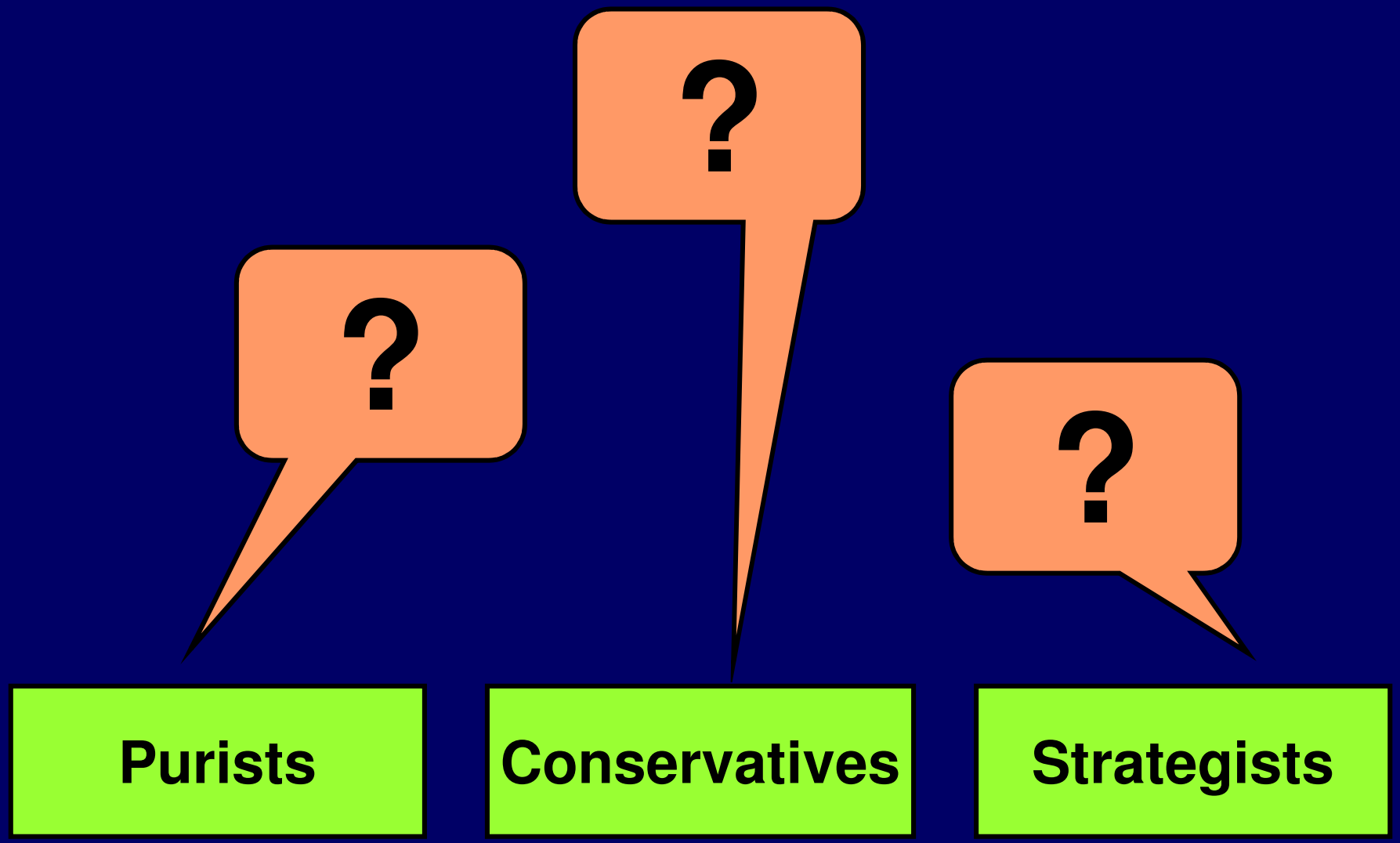
** Except Beer*

??????.....for HbA1c

Fahrenheit	Celcius
Mark	Euro
Miles	Kilometers
Pints	Liters
mg/dL	µmol/L
NGSP Numbers	***IFCC Numbers***

That is the Question!

Debate on HbA1c Numbers



Debate on HbA1c Numbers

Implement the new IFCC numbers

We have a new method: use it!

?

?

Purists

Conservatives

Strategists

Debate on HbA1c Numbers

Keep the old DCCT numbers

We are used to it: never change a winning team!

?

?

Purists

Conservatives

Strategists

Consensus Statement!

IFCC = International Federation Clinical Chemistry
IDF = International Diabetes Federation
EASD = European Association Study of Diabetes
ADA = American Diabetes Association

Milan, 4 May 2007

?

?

Purists

Conservatives

Strategists

1. We agree that the HbA1c results should be standardized worldwide, including the reference system and results reporting

2. We agree that the IFCC reference system for HbA1c represents the only valid anchor to implement standardisation of the measurement

3. We agree that the HbA1c assay results be reported worldwide in IFCC units (mmol/mol) and derived NGSP units (%), using the IFCC-NGSP master equation

4. We agree that if the ongoing “average plasma glucose study” fulfills its a priori specified criteria, an HbA1c-derived average plasma glucose (APG) value should also be reported as an interpretation of the HbA1c result

5. We recommend that all clinical guidelines be expressed in IFCC units, derived NGSP units, and APG

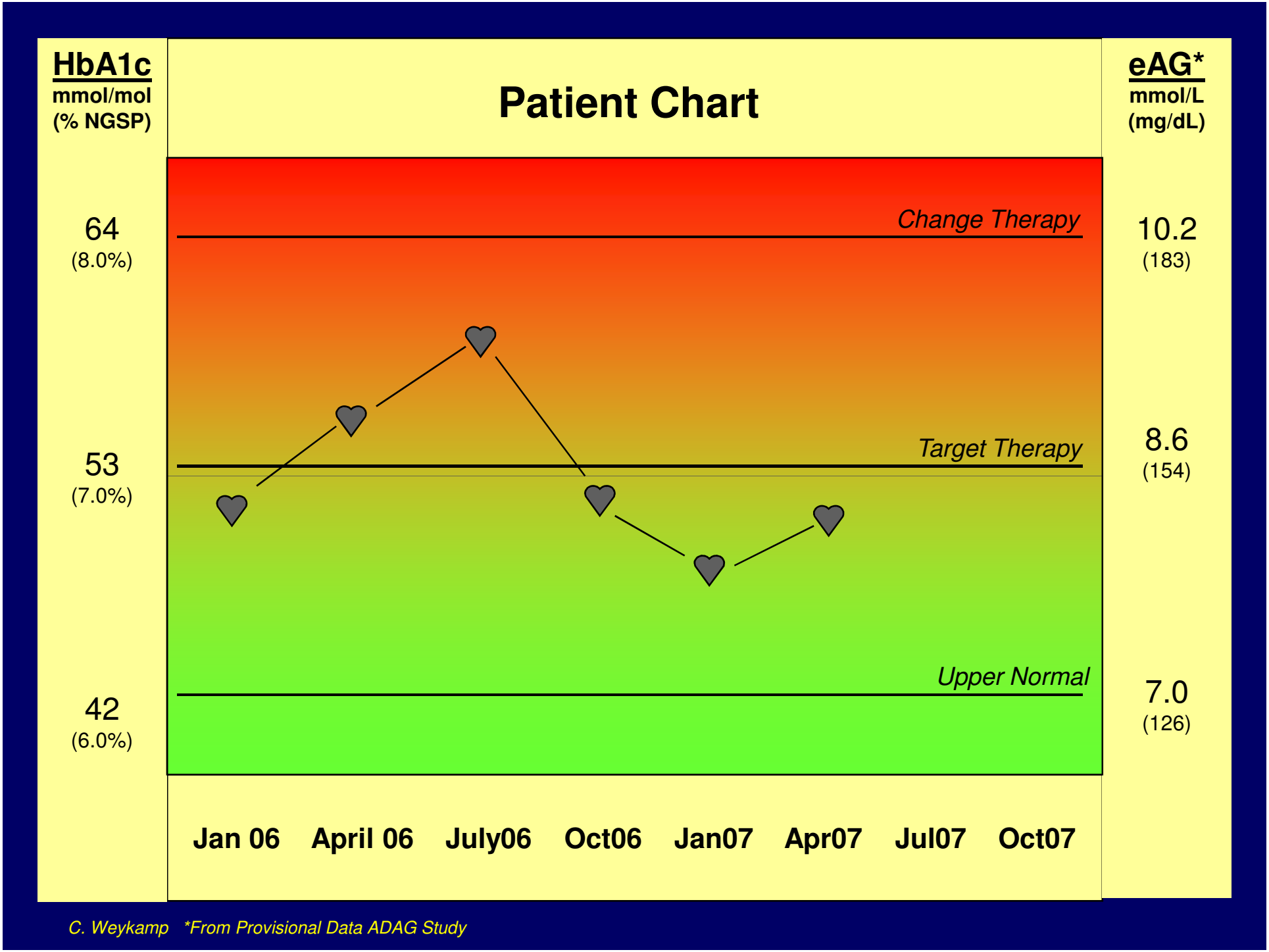
6. We agree that these recommendations should be implemented globally as soon as possible

HbA1c Dictionary

HbA1c				Average Plasma Glucose (APG)*		Interpretation
Mono-S Sweden %	JDS/JSCC Japan %	NGSP US %	IFCC mmol/mol	mmol/L	mg/dL	Normal Range and Action Limits
7.2	7.6	8.0	64	10.2	183	Change Therapy
6.1	6.6	7.0	53	8.6	154	Target Therapy
5.0	5.6	6.0	42	7.0	126	Upper Normal
2.9	3.6	4.0	20	3.8	69	Lower Normal

C. Weykamp

** From provisional results ADAG Study*



C. Weykamp **From Provisional Data ADAG Study*

Essention Consensus Statement

1. HbA1c Standardised Worldwide
2. IFCC is the Anchor
3. HbA1c reported IFCC and NGSP
4. HbA1c also reported eAG
5. IFCC, NGSP, eAG in Guidelines
6. Implementation Soon

But.....

The second Debate

Laboratory Report

Glucose	5.9 mmol/L (106 mg/dL)
Na	142 mmol/L (327 mg/dL)
K	4.6 mmol/L (18 mg/dL)
HbA1c	42 mmol/mol (IFCC Units)
	6.0 % (NGSP units)
	7.0 mmol/L (Average Plasma Glucose)
Urea	5.6 mmol/L (34 mg/dL)
Creatinine	83 µmol/L (0.94 mg/dL)
Ca	2.1 mmol/L (8.4 mg/dL)

Laboratory Report

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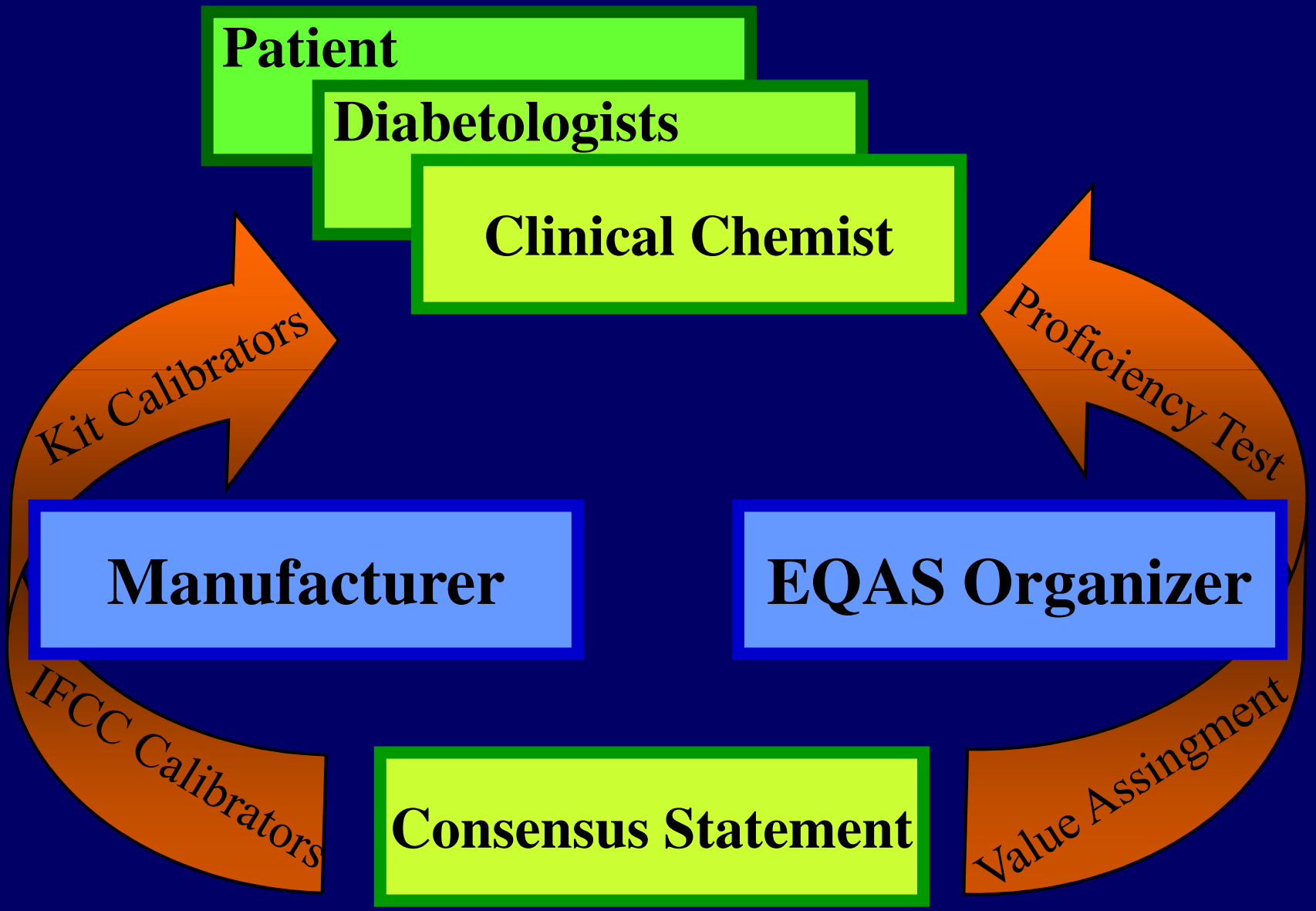
One Analyte: Three Numbers

Implementatation: Many parties Involved



One Analyte – Three Numbers !?

IFCC
ADA
EASD
IDF

** This is what We want*

One Analyte Three Numbers!?

Clinical Chemist

** Scientifically Sound?*

** Technically*
** Possible?*

** Do my*
** Physicians*
** want this?*

One Analyte – Three Numbers !?

Physicians

** Not too Fast*
Our Opinion
Is…….

One Analyte – One Number !?

Patients

** Know*
My Number….

…..What
Number?

One Analyte – Three Numbers !?

Manufacturer

<u>Give Us Time</u>

- Traceable 31 Dec 2009

- IFCC and NGSP
  "1-1-1-1"
  1 January 2011

- eAG not business
  Analytical Instruments
  (but lab information system
  like eGFR)

Lessons Learned

It is an **Illusion** to think that The Consensus Statement will be uniformly implemented Worldwide:
the views in the respective countries are too different

Implementation is not an issue for a single group but must be a **concerted action** of all parties involved (diabetologists, clinical chemists, patients, manufacturers, EQA organisers)

As global implementation is not achieveable, try at least uniform implementation at the **national level**

Implementation National Level

- National Committee of stakeholders
- Define: final situation
  transition period
  deadlines
- Consensus and Committment of Stakeholders
- Tasks of respective Stakeholders
- (Communication) Plan

Decisions National Level

Country	IFCC	NGSP	eAG	Other	Remark
UK	X	-	-	-	Transition
Italy	X	-	-	-	Transition
Germany	X	-	-	-	by Law
France	(X)	-	-	-	
Sweden	X	X	X	MonS	
Small EU	X	-	-	-	Transition
Japan	X	-	-	JDS	Transition
Australia	X	-	-	-	
USA	-	X	X	-	

One Analyte – Three Numbers !?

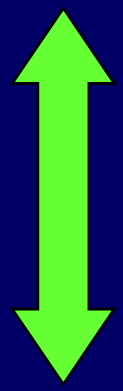
EQA Organiser

** Make a Policy*

EQA Organiser

(External Quality Assessment Programme)

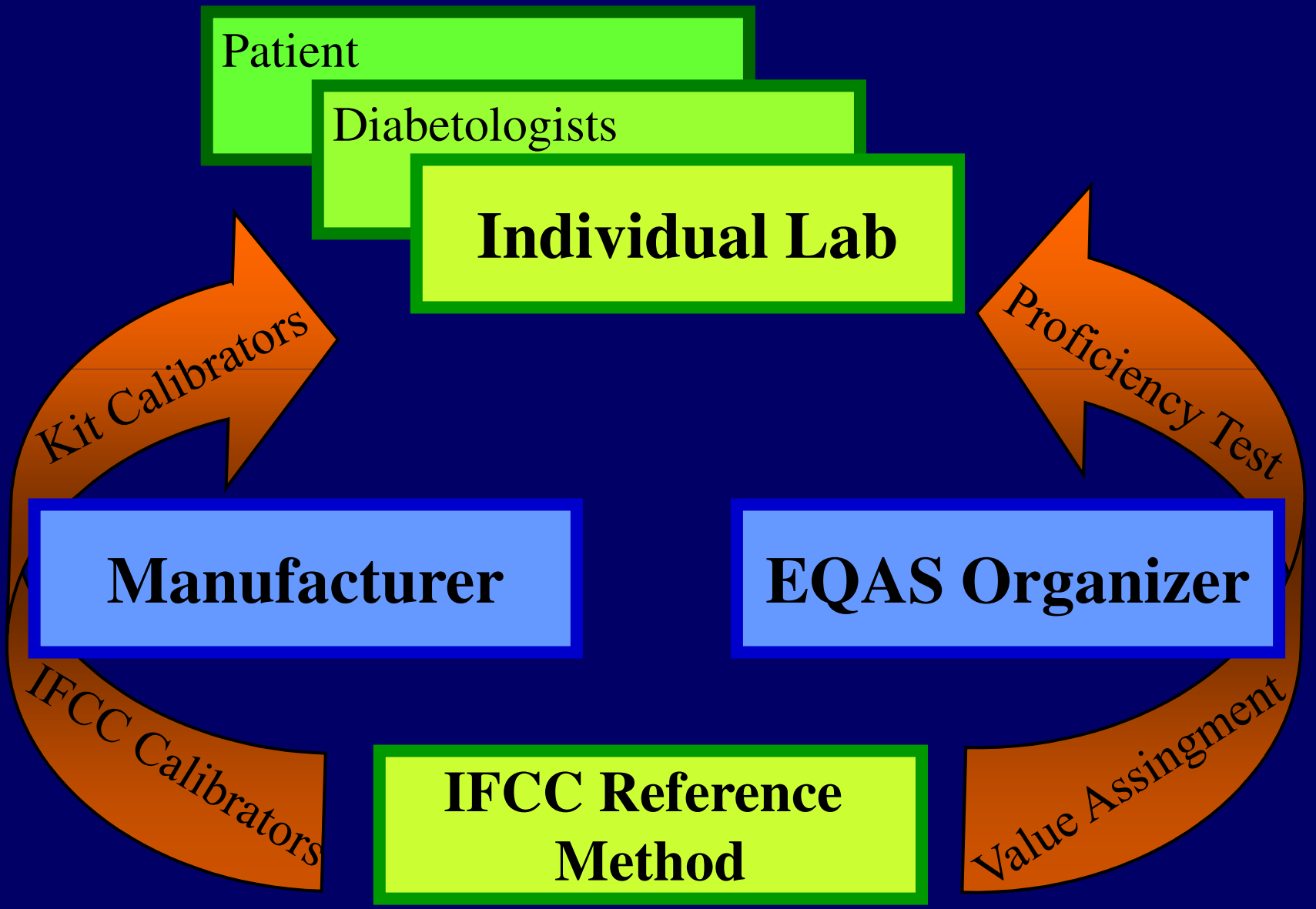
(Proficiency Testing)



Role?

Implementation Consensus Statement

EQAS Organizer:Monitor Implementation



Trend Quality in 15 years

JYear	*Deviation TargetCV*	*Intralab CV*	*Interlab*
1993	----	5.2%	22.0%
1999	+0.3%	4.9%	11.2%
2002	-0.1%	3.4%	8.5%
2005	-0.2%	2.9%	6.9%
2008	0.0%	2.1%	4.1%

Summary

1. Diabetes is emerging
2. HbA1c Anchor for Therapy
3. HbA1c requires Standardisation
4. Reference Method is in place
5. Global Debate on Units
6. EQA Organiser: Make your Decision
   implement in Concerted Action Stakeholders
7. EQA Organiser: Play a role
   in education and check Implementation

Thank you for your Attention