

## Recommendation for term and measurement unit for “HbA1c”<sup>1),2)</sup>

International Federation of Clinical Chemistry  
and Laboratory Medicine (IFCC)  
IFCC Scientific Division

Committee on Nomenclature, Properties and  
Units (C-NPU)

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### Introduction

The IFCC has recently approved a reference measurement procedure for measuring the property often designated ‘HbA1c’<sup>a)</sup> (1). This analytically specific procedure involving single molecular species allows

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<sup>a)</sup> Single quotation marks indicate a term and double quotation marks a concept.

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calculation of measurement results as “amount-of-substance fraction”<sup>b)</sup> rather than mass fraction. In addition, it provides well-defined metrological traceability to the International System of Units (SI).

As the numerical values of the measurement results will change with the new measurement procedure, it is timely to reconsider the current terms for the property in terms of system, component, and kind-of-property, as well as the expression of the measurement result.

### Current terms and measurement unit

The IFCC-IUPAC database on Nomenclature, Properties and Units (NPU) has up to now contained one entry for the dedicated kind-of-property term of ‘HbA1c’, as measured by various procedures, with the code NPU03835:

Haemoglobin(Fe; Blood)—

Haemoglobin A1c(Fe);

substance fraction

where the measurement unit is assumed to be “one” [1].

In routine reports, various abbreviated terms are used, such as ‘HbA1c’, or ‘A1c test’ referring to a chromatographic procedure, or just ‘GHb’ for glycated haemoglobin. The kind-of-property is mostly omitted – which renders the designation ambiguous – and the measurement unit generally is “0.01” (symbolised by %, percent) (2).

The abbreviated term or symbol ‘HbA1c’ in everyday speech has been criticised because it begins with ‘Hb’, which the layman might erroneously associate with a haemoglobin disorder instead of a metabolic disorder. It can also be argued that the correct understanding at least requires the inclusion of ‘fraction’.

Even with the kind-of-property ‘substance fraction’ stated, the use of “percent” as a unit is not encouraged (3). However, with the correct unit “one”, a typical measured value would be 0.034, which is an impractical format. Numerical values are recommended to lie in the interval 0.1 to 999 (4). Unfortunately, the use of SI terms or symbols for factors of 10<sup>n</sup> are not allowed with the unit “one”, so “34 m1” is forbidden. Instead an expression such as mmol/mol (but not μmol/mmol) can be used.

### NPU term and measurement unit

The IFCC reference measurement procedure, being analytically specific, measures a new property and requires a new entry in the IFCC-IUPAC database. The

<sup>b)</sup> The abbreviated term ‘substance fraction’ is used in the following.

substance fraction of the  $\beta$ -chains of haemoglobin that has a stable hexose adduct on the N-terminal amino acid valine may be expressed as follows:<sup>c)</sup>

Haemoglobin beta chain(Blood)—  
N-(1-deoxyfructos-1-yl)haemoglobin beta chain;  
substance fraction

The NPU database assumes that fractions are expressed with the unit "one", but "mole per mole" is also correct.

### Choice of measurement unit and numerical value

A consequence of changing from standardisation according to the U.S. National Glycohemoglobin Standardization Program (NGSP) to the new IFCC reference measurement procedure is that numerical values reported for patients would be approximately one-fourth lower, if reported in percent, than those currently observed. NGSP values of 6.0%, 7.0%, and 8.0% would become 4.2%, 5.3%, and 6.4%, respectively.

It has been emphasised that as the complete term of the property, including kind-of-property and specifications, is often abbreviated in informal contexts, there is a risk of confusion among healthcare personnel and patients when different, but overlapping, reporting intervals exist in parallel. Such situations may occur when data are compared in communication between the patient and physician or in interpretation of current guidelines with decision limits based on non-specific HbA1c measurement methods. It has also been pointed out that the new values being three-fourths of the previous values might give some patients a false impression of their condition (5).

These problems are eliminated if the measurement unit "millimole per mole" ( $\text{mmol/mol} = 10^{-3}$ ) is chosen instead of "percent" ( $\% = 10^{-2}$ ). For example, 3.4% would thus become 34  $\text{mmol/mol}$ , i.e., there would be no overlapping of values.

In parts of the world where the SI unit "millimole per litre" ( $\text{mmol/L}$ ) is used in reporting substance concentration of glucose in plasma, both the current and new values in percent reported for HbA1c can be misinterpreted because a numerical value, e.g. 3.4, would also be possible for a glucose concentration, and both properties are often reported together. Again, the much higher interval of numerical values in  $\text{mmol/mol}$  for the substance fraction of haemoglobin derivative would remove that risk.

### Abbreviated term

In everyday speech and even in reports, abbreviated terms are usually necessary. They are often contro-

versial and difficult to standardise. The following abbreviated terms are offered for discussion.

Abbreviated NPU term:

Hb(beta; B)—Deoxyfructosyl haemoglobin(beta);  
subst.fr.<sup>d)</sup>

Terms for everyday speech involving an acronym might be 'DOF haemoglobin fraction' or even 'DOF haemoglobin'.

### Recommendation

The joint IFCC Committee on Nomenclature, Properties and Units and IUPAC Subcommittee on Nomenclature, Properties and Units recognise that the substance fraction of the valyl-1-fructosylated haemoglobin  $\beta$ -chains among all haemoglobin  $\beta$ -chains can be measured specifically by the IFCC reference measurement procedure so as to be metrologically traceable to a substance fraction with the unit "millimole per mole".

The full NPU entry should be:

Haemoglobin beta chain(Blood)—  
N-(1-deoxyfructos-1-yl)haemoglobin beta chain;  
substance fraction  
millimole/mole

Abbreviated terms may vary with the context, as indicated above.

### Acknowledgements

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### References

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<sup>c)</sup> It is recognised that this expression does not specify that deoxyfructose is attached to the N-terminal valine. Currently there seems to be no authoritative way to express this.

<sup>d)</sup> "Hb( $\beta$ ; B)—Deoxyfructosyl haemoglobin( $\beta$ ); subst.fr." if type fonts including Greek letters are allowed.