v 3

# Report

# European Co-ordinated Post Market Surveillance Operation under COEN authority

# Blood Glucose Meters

**Afssaps: France**
**Irish Medicines Board: Ireland**
**MHRA: United Kingdom**

# Summary

# I - Introduction

This operation was performed under the authority of COEN (Compliance and Enforcement group). COEN is a European Working Group of the Competent Authorities for medical devices set up to prevent non compliant medical devices being placed on the market by better co-operation, co-ordination and best practice at EU level in line with the requirements of article 2 of the respective Directives 90/385/EEC, 93/42/EEC and 98/79/EC.

Under COEN authority and within the scope of the directive 98/79/EC on *in vitro* diagnostic medical devices, the UK, Irish and French Competent Authorities undertook a coordinated action for a Post Market Surveillance Operation concerning blood glucose meters and associated test strips/electrodes.

The Ad Hoc group of COEN in charge of the project included: France (Afssaps), Ireland (IMB), and the United Kingdom (MHRA). The Member State in charge of coordination was: France (Afssaps).

The present Post Market Surveillance Operation concerns blood glucose meters for self-testing only and does not include hospital tests.

The coordinated action described in the protocol was a desk review: assessment of the "manual of use" of the meter and of the "instructions for use" (IFU) of the associated reagents (strips or electrodes).

The assessment was performed in conformity with the European Directive 98/79/EC.

# II - Background

Concern has been expressed by various stakeholders that Members States lacked a harmonized approach to Post Market Surveillance activities in the sense of there being:

- Little collaboration/cooperation between Competent Authorities.
- Results of investigations not being sent to other Competent Authorities.
- No collaborative evaluations or re-evaluation so as to share resources and experiences and outcomes of investigations.

It was agreed that a more formal approach should be adopted.

This situation lead COEN to approve a protocol for coordinated post market surveillance operation in September 2008 and to approve a new work item for blood glucose meters.
The protocol was approved by the IVD Technical Group and endorsed by the Competent Authority Meeting under the Czech Republic Presidency of the Council of Europe in February 2009.

The operation started in March 2009 and the final results were presented to the Competent Authority Meeting under the Spanish Presidency in March 2010.

## III - Evaluators

Afssaps – 143/147, boulevard Anatole France 93285 Saint-Denis Cedex

IMB – Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland

MHRA – Market Towers, 1 Nine Elms Lane UK London SW8 5NQ

## IV - Participation

***Annex 1 and 2***

28 manufacturers were contacted by mail (directly or via the Authorised Representative).

50% of them answered at the first request.
For the remainder, responses were received after the first reminder or after the intervention of the Competent Authority where the manufacturer or the Authorised representative had his place of business.

3 manufacturers never sent the required documents:
- I-Sens
- ISOTECH Co
- SAND COUNTY BIOTECHNOLOGY

Of the 28 companies originally identified, 7 were subsequently considered not relevant because they were only distributors or had declared products which were no longer on the market.

As such, only 21 companies were considered relevant for inclusion in the review, of which only 18 participated. As such the level of participation was 86%.

## V - List of manufacturers and products

***Annex 3and 4***

In total 54 meters and 44 reagents were assessed.

## VI - Generally-accepted agreements between evaluators

- When the meter and the combined strips are sold by the same manufacturer as a system, some information can be written in the IFU of the strips or in the manual of the meter (for examples, the performance or the traceability of calibration).

- This situation is acceptable if there is an explicit cross-reference between the IFU and the manual.
- During the assessment, the item was considered as 'conform' when an explicit cross-reference was written. The item was considered as 'not sufficient' when the cross-reference was not clear.

The generally-accepted abbreviations were as follows:

- Meter is the reader.
- Reagent is the strip.
- Insert for use (IFU) is the instruction for the test strips.
- Manual is the instruction for the meter.

## VII - Particular items

### VII – 1 - Change of Units.

Different scenarios on the market.

- Some meters are locked. In this case, the meter is placed on the market to display results in either mmol/L or in mg/dL. It is not possible to change the units of measure. This situation is very desirable as it is not possible for the user to change the unit of measure (neither involuntarily nor accidentally).

- Some meters can be used in either mmol/L or mg/dL formats. The user must choose the unit before the first use of the meter. In this case, there are 3 scenarios :

  - For 1 meter the change of unit is possible only after having unscrewed the back of the meter to turn a button. When the meter is screwed back, it is not possible to change the units by mistake.
  - For other meters, the manual outlines the procedure to change the units. In fact, the procedure to change the units is included in the procedure to configure other parameters such as date and hours or sound level and brightness of the screen. The risk of changing the units by mistake is very high. For example: "to change the hour push 3 times on the button in the menu and to change the units push 6 times".
  - In the final scenario, there is no information about the procedure to change the units in the user manual. In this case, it is unclear how to change the unit but if the procedure to change the units is also included in the menu of configuration of the meter, the risk of doing this by mistake is very high.

For information: in the framework of the revision of the standard EN ISO 15197, ISO was asked to include in the standard a requirement to only have meters with locked units of measure. The ISO committee decided that the manufacturer can choose the method in order to avoid change of units by mistake. This risk is now in the list of points to examine during the risk analysis.

**VII – 2 - Interferences with Maltose.**

Interference with maltose is described for enzymes such as GDH PQQ (pyrroloquinoline quinone glucose dehydrogenase). A high level of maltose is identified in blood of patients undergoing peritoneal dialysis with icodextrine. But, in this case, there is a risk of overestimation of blood glucose with risk of non identified hypoglycemia and coma or death of the patient. Identification of the enzyme and appropriate recommendations for patients under peritoneal dialysis with icodextrine is vital.

In France, Ireland and the UK, the Competent Authorities request that manufacturers include warnings and recommendations in the IFU and user manuals.

Only 2 manufacturers proposed systems with GDH PQQ at the time of the evaluation.

For these 2 products, warnings and recommendations are missing from the manual. Information is present in the IFU with no cross-reference between the manual and the IFU for the test strips. In these particular cases, the meters are no longer on the market. However the strips are still on the market.

For 4 manuals from the same manufacturer, information is present in the manuals but with differences from one meter to the next.

For systems with modified GDH PQQ, there is no risk of interference claimed by the manufacturer so, no special mention is required.

***Regarding the risk for patients undergoing peritoneal dialysis it seems more appropriate to have the same information about the risk with icodextrine in the IFU and in the manuals. It is desirable to have this information consistent for all products of the same range of systems for the same manufacturer.***

**VII – 3 - Calibration.**

Many deviations are observed regarding calibration items: traceability of the calibration, type of samples used for calibration and information regarding equivalence to blood or plasma results.

The assessment shows that, in many cases, information about traceability and type of sample is missing from both the IFU of the strips and the manual of the meter for a combined system. Moreover, in 14 manuals there is no information about the equivalence to blood or to plasma.

This lack of information is detrimental for the patient. A majority of vigilance reports concern a gap between the results found by a meter and the results found in a laboratory. In fact, often, this gap may not actually be an error but could be due to the fact that the results of the meter are not equivalent to plasma results.

***Therefore, we consider that information about calibration and equivalence to blood and plasma must absolutely be included in the IFU and in the manual.***

### VII – 4 - Use in New Born

***Annex 4***

Some Competent Authorities requested to have information about whether the meters and test strips may be used for New Borns.
This point was assessed.
Information is given in the strip Insert For use.
18% of the inserts claimed suitability for use in New Borns.
13% of the inserts did not contain any information on suitability for use in newborns.
The remainder state in the IFU that the strips are not validated for use in New Borns.

## VIII - 2 specific cases

### VIII – 1 - Case of the meter XX sold by XX.

The manufacturer places a meter on the market without a dedicated strip.
In the user manual, there is a table at the end of the manual which outlines the characteristics of the meter and recommends the use of the Ascencia ELITE strips (manufacturer BAYER).
There is no indication of performance and no information about the composition (in particular no information about the enzyme) in the manual.
Nevertheless, blood glucose monitoring is claimed in the user manual and diabetic associations of patients are mentioned as references for recommendations regarding diabetic care.

The IFU for the Ascencia ELITE strips mentions that the strips are “exclusively for use with the Ascencia ELITE XL/ELITE/Glucometer and ELITE XL/ELITE Blood Glucose Meter”. There is no mention of the GS meter.

If we consider that the meter is an accessory of the strips used to read the strips, all information regarding the claimed combination and the performance of the combination must be included as a minimum in the IFU of the strips (or explicit cross-reference).
The IFU must list the recommended meters and the user manual for the meter must list the strips to be used.
In any case, an agreement must exist between the manufacturer of the strips and the manufacturer of the meter to be sure of good practice in case of change of one of the components of the recommended combination.

All other situations were considered as ‘non conform’.

The Competent Authority who reviewed this meter is in communication with the Notified Body in charge of the certification of the meter and the relevant Competent Authority to resolve these issues.

**VIII – 2 - Case of the meters XX and XX sold by X.**

C. is described in the user manual as an “analyzer intended for *in vitro* diagnostic use to test whole blood”.

The manufacturer states in the user manual that this system “is capable of screening lipids (including Cholesterol, HDL Cholesterol and Triglycerides) and testing for diabetes and other disease states”.

The IFU of the glucose test strips for use with C. meters claims that the glucose test strips “are intended to be used by healthcare professionals to measure glucose in whole blood and by individuals with diabetes to measure glucose in finger-stick whole blood at home (for management of carbohydrate metabolism disorders)”.

The manual of the meter strips shows important deviations with the requirements of the directive and the standard for devices dedicated to diabetes management by lay persons at home. In particular, important information relating to precautions in the case of diabetes is missing.

The Competent Authority who reviewed this meter is in communication with the Notified Body in charge of the certification of the meter and the relevant Competent Authority to resolve these issues.

## IX - Practicality

***Annex 5***

Due to subjectivity to assess practicality items it was decided to present the results globally.
Assessment is based on requirements of the directive 98/79/CE and standard EN ISO 15197.

Particular items

- Warning not to deviate from these instructions on the basis of the results without first consulting a qualified healthcare provider (directive): in one case, there is no information in the IFU and in the manual. In the other cases there is no information in the IFU only.

- All the information needed to verify whether the device is properly installed and can operate correctly and safely (directive): this point concerns the verification, for example if there is sufficient information to verify the correct display of the screen before using the meter. Control to see if all the bars of the numbers are readable. This is considered as ‘non conform’ when there is no information about the control of the screen.

- Most of the deviations concern the size of the print. The standard recommends the use of large print, for example 12 point courier. This is not always the case and in several instances the size of the print is small.

- A reference to the instruction given by a physician and/or a qualified healthcare provider and a warning not to deviate from these instructions on the basis of the results without first consulting a qualified healthcare provider (directive and standard): this information is often incomplete.

- Advice on how to proceed if the result appears to be questionable: no information about a free phone number, the possibility to use a control solution…

## X - Conclusions

- The observed deviations are not of the nature to call into question the safety of the patients.
- There is no major deviation from directive 98/79/CE or from standard EN ISO 15197 which could lead to a withdrawal from the market. Nevertheless, two particular cases need to be discussed after receiving additional information.
- Information on the manufacturer: some deviations require information on the manufacturer. Update of the IFU and manual must be proposed to the manufacturer taking into account recommendations included in the report.
- Information of Notified Bodies: Notified bodies and NB-MED will be informed of the results and recommendations. They are responsible for the verification of the update of the IFU and manuals for their own customers.
- Standardization bodies regarding update of standard EN ISO 15197 will receive the report.

The complete results with conclusions will be published on the web site of each Competent Authority participating to the operation: France, Ireland, UK.

The report will be published anonymously. Therefore, the necessary information is available for the Competent Authorities.

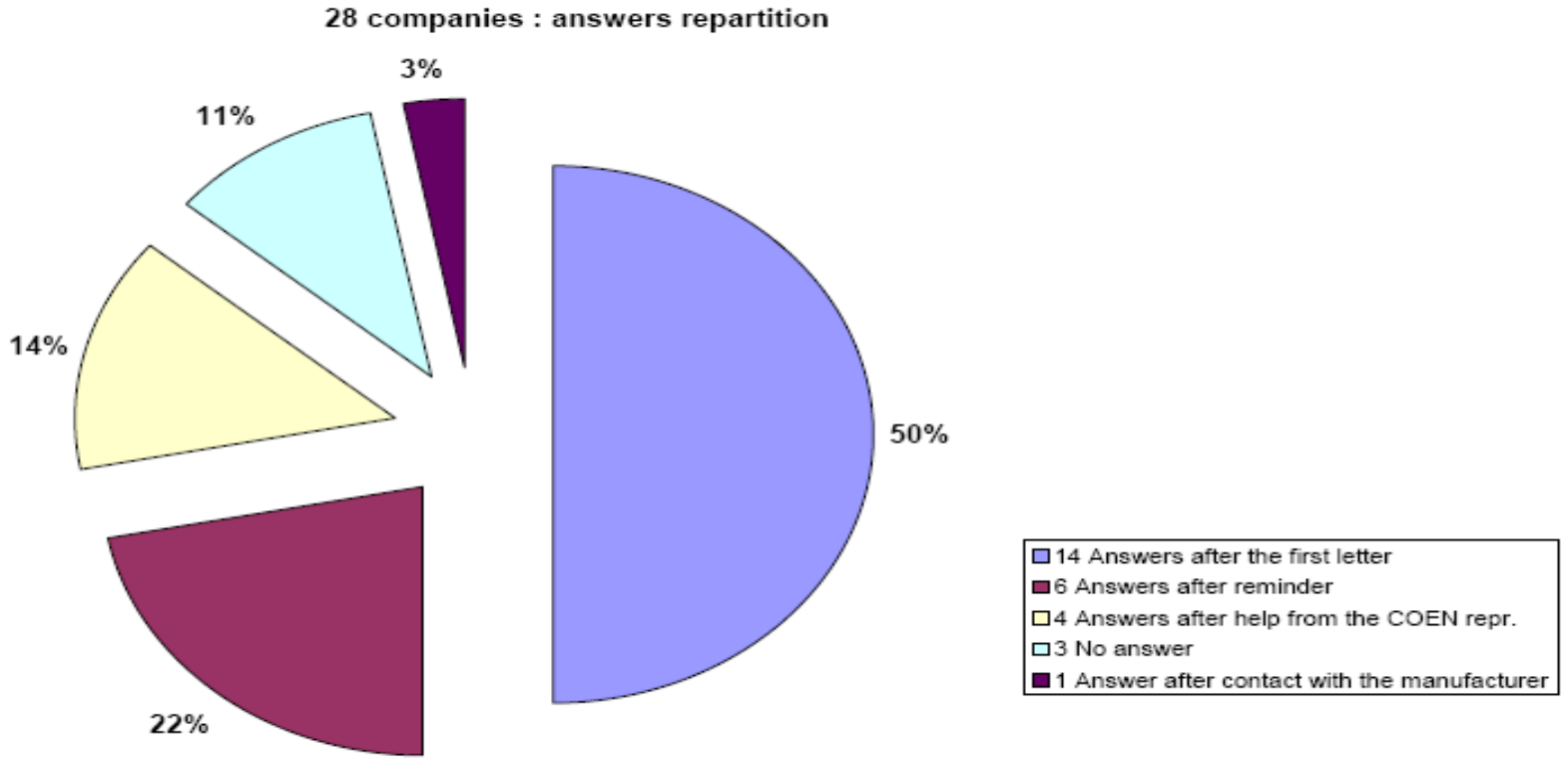
One of the objectives of this project was to provide all Competent Authorities with a book describing the method to conduct the same operation of market surveillance. This book will contain :

- The protocol,
- The list of items to be reviewed,
- A guideline for the evaluation,
- Models for letters, reports, graphs and tables, retro planning, type of decisions,
- Method for follow-up.

This book will be posted on CIRCA.

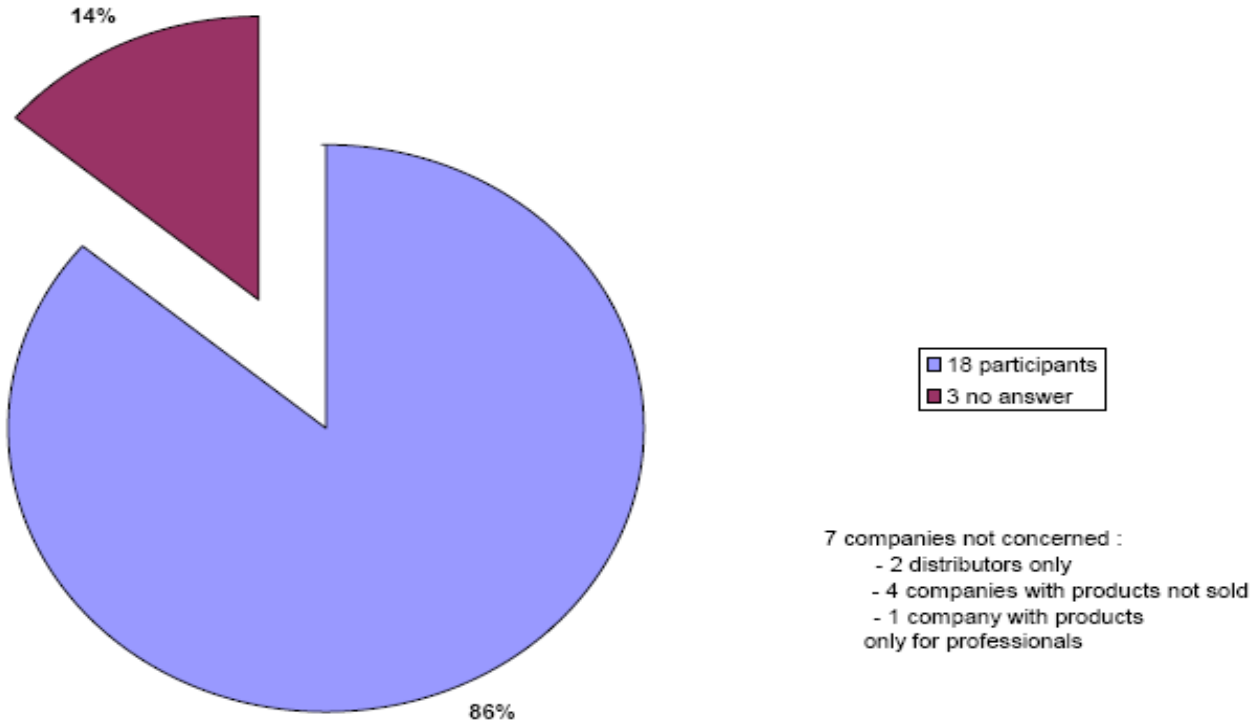
***Annex 6 results for each meter***
***Annex 7 results for each reagent***
***Annex 8 results by items/meter***
***Annex 9 results by items/reagent***
***Annex 10 rational of assessment for each item: meters***
***Annex 11 rational of assessment for each item: reagents***
***Annex 12 evaluation grid***

# Annex 1


28 companies : answers repartition
3%
11%
14%
50%
22%
14 Answers after the first letter
6 Answers after reminder
4 Answers after help from the COEN repr.
3 No answer
1 Answer after contact with the manufacturer

## Annex 2

**21 companies : participation assessment of the concerned companies**




7 companies not concerned :
- 2 distributors only
- 4 companies with products not sold
- 1 company with products only for professionals

# Annex 3

**BLOOD GLUCOSE DEVICES FOR GLYCEMIE SELF-MONITORING METER AND STRIPS**
**List of the manufacturers who sell products in FRANCE, UK and IRELAND**
**23th November, 2009**

| MANUFACTURER (METER AND STRIPS) : PARTICIPANTS | FRANCE | UK | IRELAND |
|---|---|---|---|
| ABBOTT DIABETES Care | YES | YES | YES |
| ACON Laboratoires | YES | YES | |
| AGAMATRIX | | YES | |
| BAYER DIABETES CARE | YES | YES | YES |
| BIONIME | YES | | |
| BIOPTIK | | | YES |
| CAMBRIDGE (Sensors) Ltd | | YES | |
| CARETEC | | YES | YES |
| HemoCue AB | | | YES |
| HOME DIAGNOSTICS | | YES | YES |
| INFOPIA | YES | | |
| LIFESCAN | YES | YES | YES |
| MENARINI DIAGNOSTICS | YES | YES | YES |
| NATIONAL DIAGNOSTIC PRODUCTS | | YES | |
| POLYMER Technology System | YES | YES | YES |
| ROCHE DIAGNOSTICS | YES | YES | YES |
| TAI DOC | YES | YES | |
| 77 ELEKTRONIKA | YES | YES | YES |

| **MANUFACTURER (METER AND STRIPS) : NO ANSWER** | **FRANCE** | **UK** | **IRELAND** |
|---|---|---|---|
| **I-SENS** | **YES** | | |
| **ISOTECH Co** | **YES** | | |
| **SAND COUNTY BIOTECHNOLOGY** | **YES** | | |

| OTHER CASES | |
|---|---|
| CARDIOCOM LLC | Not Sold |
| BBI HEALTHCARE | Distributor only |
| DINNO SANTE | Distributor only |
| ALLMEDICUS | Not Sold |
| B.BRAUN PETZOLD | Not Sold |
| HYPOGUARD | Not Sold |
| NOVA* | Only sold in hospital |

# Annex 4: Use in New Born

| FABRICANT | METER | STRIPS | use in new born |
|---|---|---|---|
| A. MENARINI Diagnostics | Glucomen Visio | Glucomen Visiosensor | no |
| | Glucomen LX | Glucomen LX Sensor | no information |
| | Glucofix MI0 | Glucofix Sensor | no |
| | Glucomen PC | Glucomen Sensor | no |
| 77 ELEKTRONIKA KFT | Sensocard | Test strips for Sensocard and Sensocard Plus BGM | no |
| | Sensocard Plus | Test strips for Sensocard and Sensocard Plus BGM | no |
| HEMOCUE AB | Hemocue Monitor | Hemocue Monitor Microcuvette | no information |
| AGAMATRIX Inc | WaveSense Jazz BGM syst. | WaveSense Jazz test strips | no |
| LIFESCAN | One Touch Ultra 2 | One Touch Ultra | no |
| | One Touch UltraEasy | *One Touch Ultra* | no |
| | One Touch UltraSmart | *One Touch Ultra* | no |
| | One Touch Vita | One Touch Vita | no |
| INFOPIA Co | Finetest | Finetest | no |
| Polymer Technology Systems | Cardiochek | PTS panel glucose t. s. | no |
| | Cardiochek PA | *PTS panel glucose t. s.* | no |
| Tai Doc | New Test 4237 | New Test 4237 | no |
| | Clever Check | Clever Check | no |
| ROCHE Diagnostics | Accutrend Plus | Accutrend Glucose | no information |
| | Accu-Chek Active | Accu-Chek Active test strip | yes |
| | Accu-Chek Go | Accu-Chek Go test strip | no |
| | Accu-Chek Performa | Accu-Chek Performa t.s. | yes |
| | Accu-Chek Performa nano | *Accu-Chek Performa t.s.* | yes |
| | Accu-Chek compact plus | Accu-Chek Compact test strip | no |
| | Accu-Chek Aviva | Accu-Chek Aviva | no information |
| | Accu-Chek Aviva Nano | *Accu-Chek Aviva* | no information |
| Home Diagnostic | TRUEtrack meter | TRUEtrack test strip | no |
| | TRUEone meter | TRUEone test strip | no |
| | | | |
| Bayer | Breeze 2 | Glucodisc 2 | no |
| | Breeze 2 | Breeze 2 | no |
| | Contour Link | Contour Link | no information |

| FABRICANT | METER | STRIPS | use in new born |
|---|---|---|---|
| | Contour Link | Contour | yes |
| | Contour | *Contour* | yes |
| | Ascensia Elite XL | Ascensia Elite | yes |
| | Ascencia Brio | Ascensia Easyfill | no |
| | Contour TS | Contour TS | no in France |
| | **Ascencia Confirm** | Ascencia Glucodisc | no |
| | **Ascensia Breeze** | Ascencia autodisc | no |
| Abbott Diabetes Care | **Sof-Tact meter** | Sof-Tact strip | no |
| | FreeStyle Papillon Vision | FreeStyle Papillon Easy | no |
| | FreeStyle Papillon Lite | *FreeStyle Papillon Easy* | no |
| | **FreeStyle Papillon Mini** | *FreeStyle Papillon Easy* | no |
| | FreeStyle Lite | *FreeStyle Lite* | no |
| | FreeStyle Freedom Lite | *FreeStyle Lite* | no |
| | **FreeStyle Freedom** | FreeStyle | no |
| | **FreeStyle mini** | *FreeStyle* | no |
| | **Precision QID** | Précis electrode | yes |
| | **Precision QID** | Precision plus test strip | yes |
| | *Precision QID* | G2 sensor electrode | yes |
| | Optium Xceed meter | Optium Plus test strip | no |
| | **Optium meter** | *Optium Plus test strip* | no |
| ACON (not sold) | On Call Now | On Call Now | no |
| | On Call Plus | On Call Plus | no |
| | On Call EZ | *On Call Plus* | no |
| Bionime | Bionime GM 100 | Bionime GS 100 | no |
| Cambridge Sensor Limited | Microdot | Microdot | no |
| Caretec Technische Hilfs. | Gluki Plus | Ascensia Elite (Bayer) | no information |
| National Diagnostic Prod. | Betachek G5 | Betachek G5 | no |
| Bioptik | Easy Touch GC | Easy Touch Strips | No |

bold : meter not sold anymore

# Annex 5: Practicality

**REAGENTS**

| ITEMS | % conform | % non conform | % not sufficient |
|---|---|---|---|
| Instructions provided by the manufacturer should be easily understood and applied by the user | 96 | | 4 |
| Measures to be taken in the event of changes in the analytical performance of the device | 96 | | 4 |
| Warning not to deviate from these instructions on the basis of the result without first consulting the qualified healthcare provider | 83 | **10** | 7 |

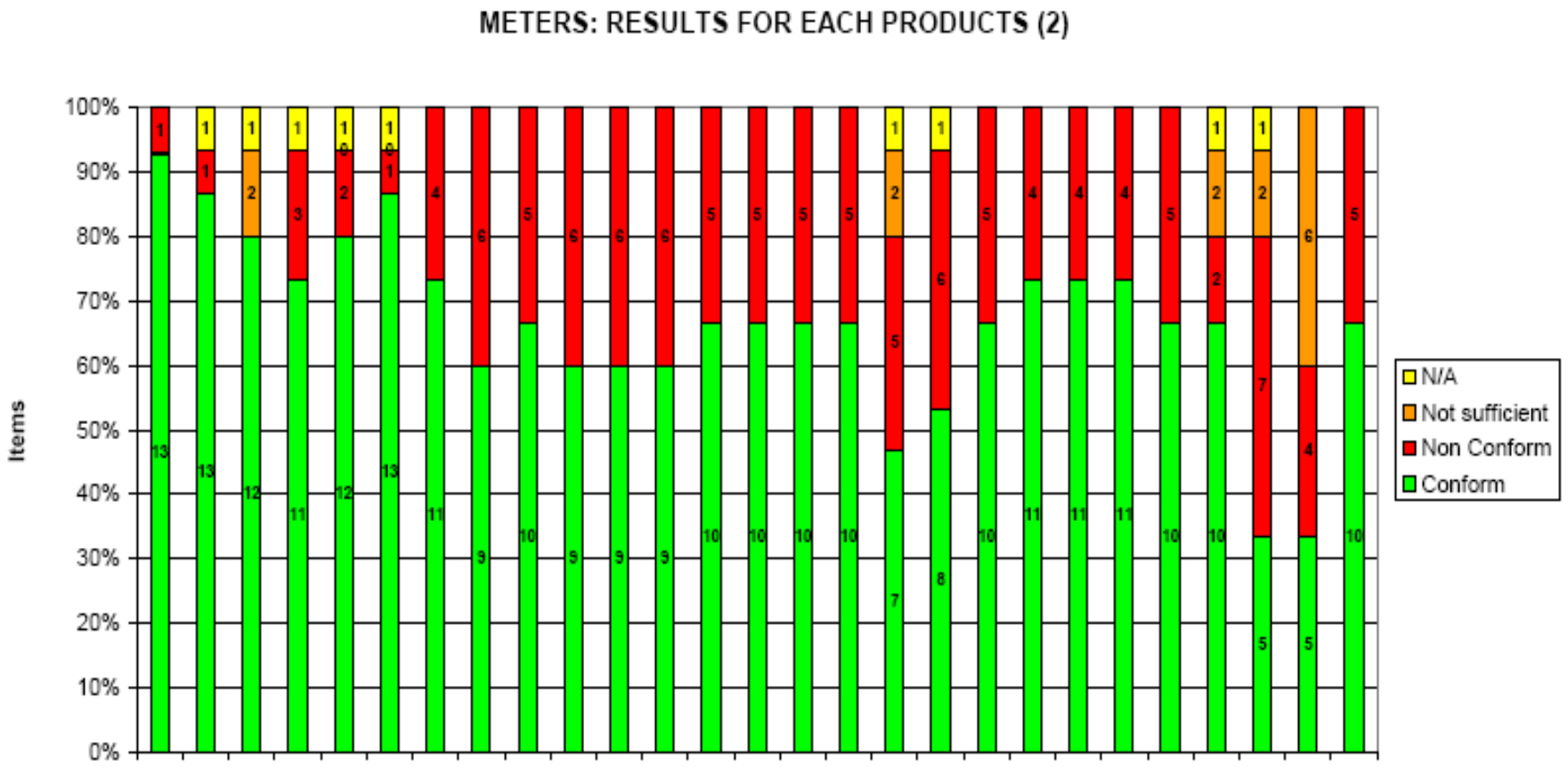
**METERS**

| ITEMS | % conform | % non conform | % not sufficient |
|---|---|---|---|
| All the information needed to verify whether the device is properly installed and can operate correctly and safety | 86 | **14** | |
| Manual of use presented in a clear and concise manner | 92 | 8 | |
| Plain terminology that is readily understood by a layperson | 94 | 6 | |
| Information well organized and easy to read | 100 | | |
| Large print | 39 | **51** | |
| Clearly state what actions to | 88 | 6 | 6 |

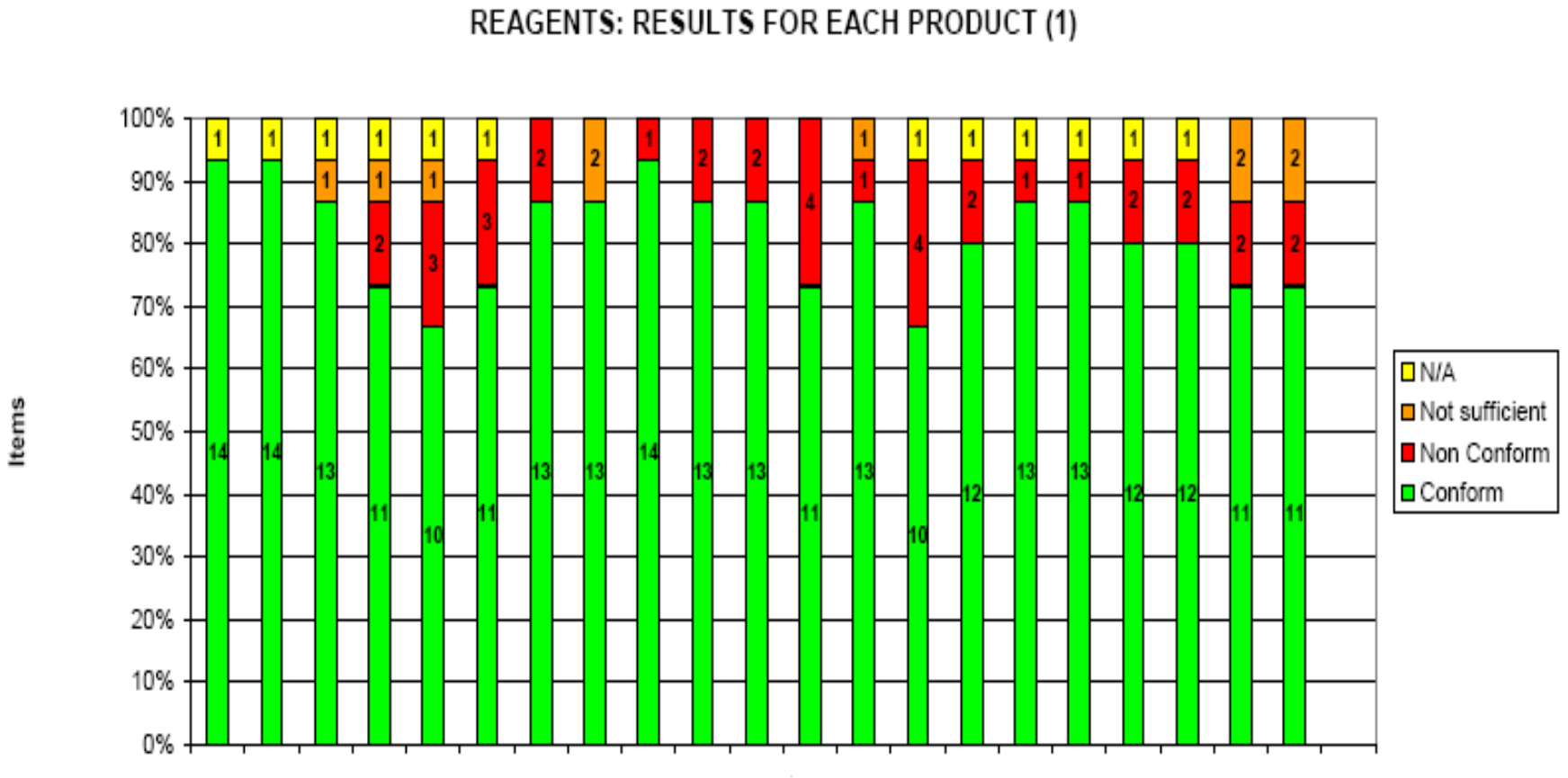
| | | | |
|---|---|---|---|
| take in the event of changes in the analytical performance of the device | | | |
| A reference to the instruction given by a physician and/or other qualified healthcare provider, and a warning not to deviate from these instructions on the basis of the result without first consulting the physician or other qualified healthcare provider | 55 | **14** | 31 |
| Advice on how to proceed if the result appears to be questionable to the user | 88 | **12** | |
| Indication how the monitoring system alerts the user when the result is outside the measurement interval | 94 | 6 | |

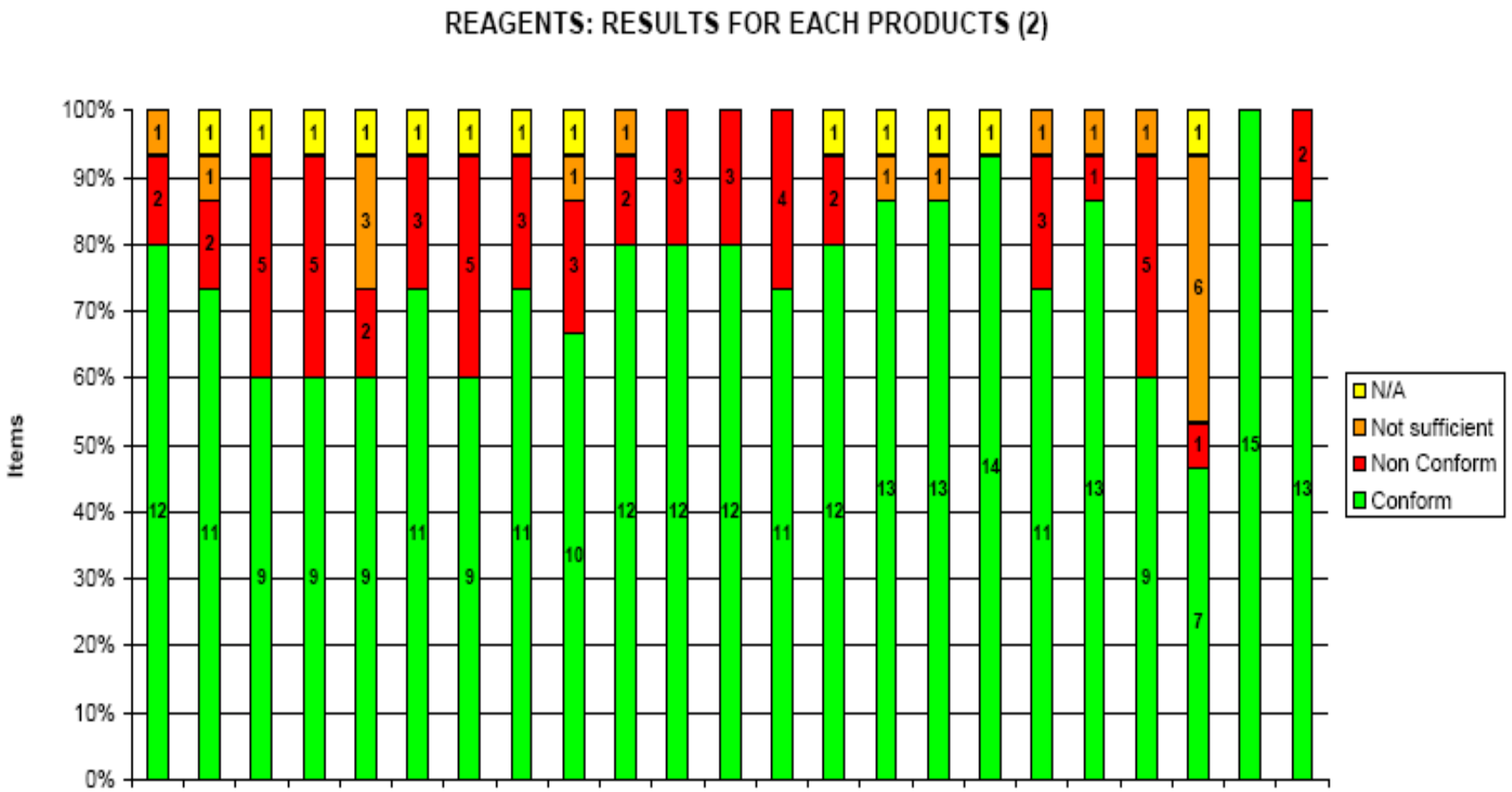
## Annex 6


METERS: RESULTS FOR EACH PRODUCTS (1)
Items
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
N/A
Not sufficient
Non Conform
Conform

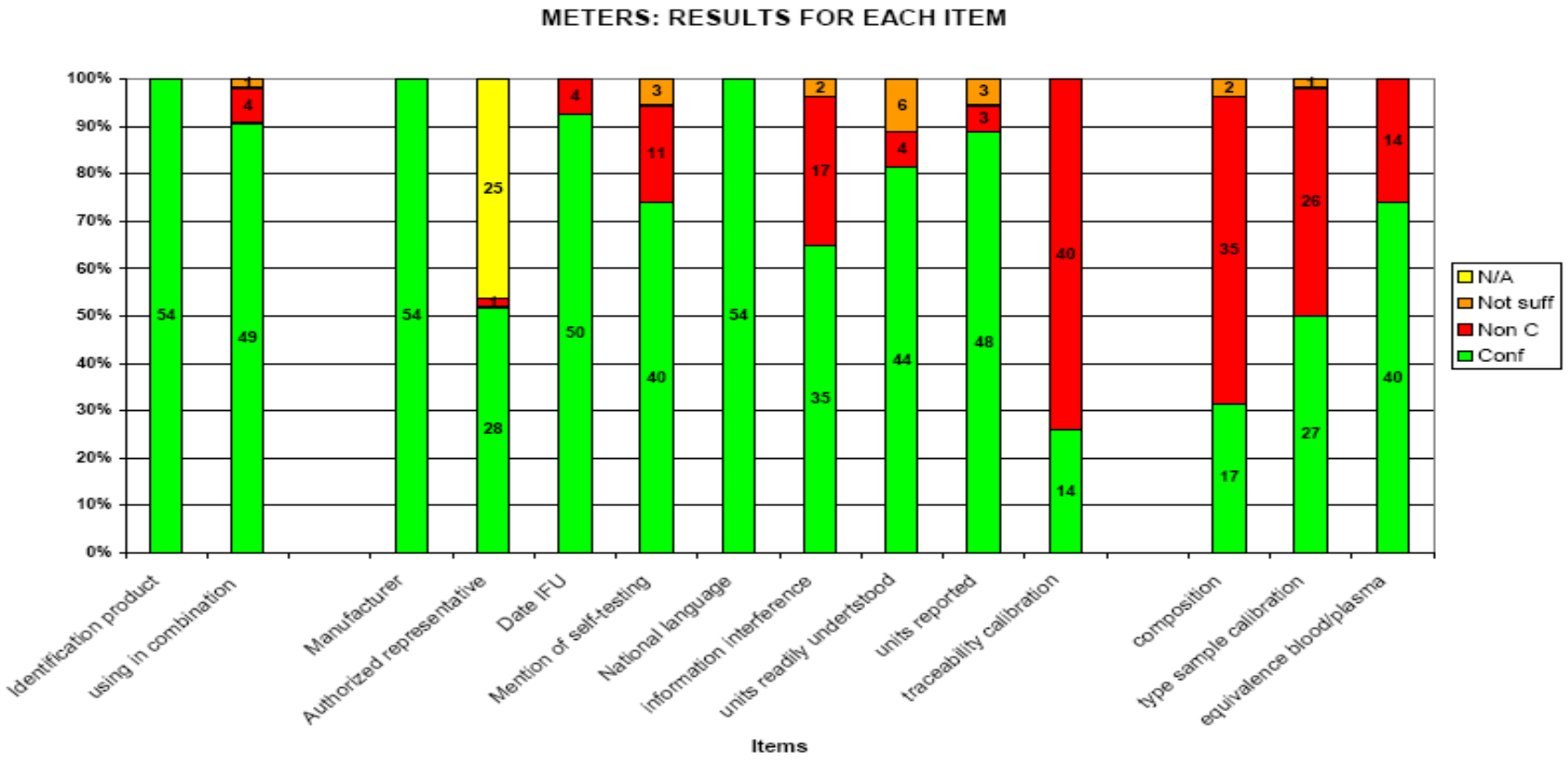

METERS: RESULTS FOR EACH PRODUCTS (2)
Items
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
N/A
Not sufficient
Non Conform
Conform

**Annex 7**

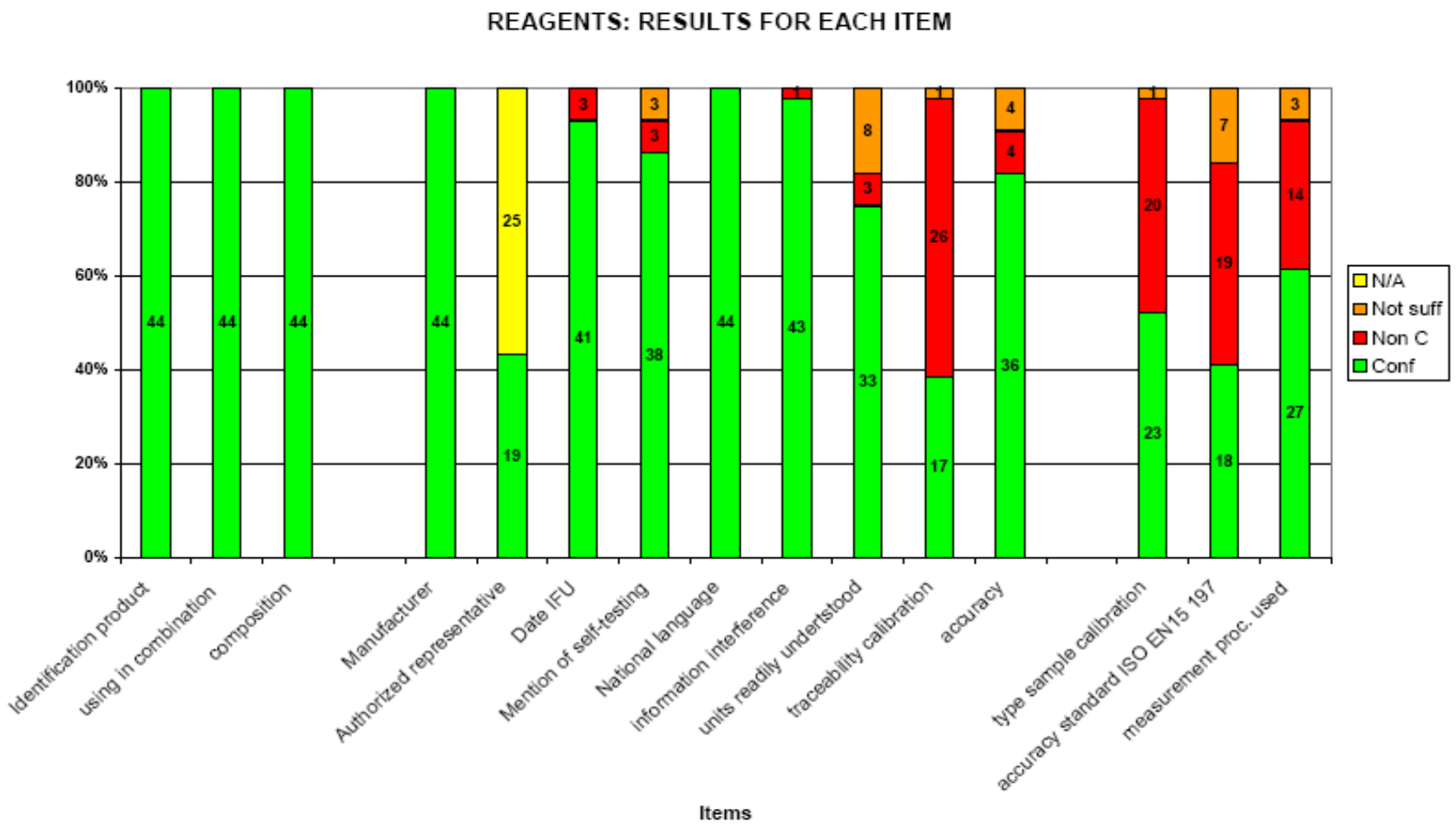

REAGENTS: RESULTS FOR EACH PRODUCT (1)
Items
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
N/A
Not sufficient
Non Conform
Conform


REAGENTS: RESULTS FOR EACH PRODUCTS (2)
Items
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
N/A
Not sufficient
Non Conform
Conform

## Annex 8


METERS: RESULTS FOR EACH ITEM
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
54
4
49
54
25
28
4
50
3
11
40
54
2
17
35
6
4
44
3
3
48
40
14
2
35
17
26
27
14
40
N/A
Not suff
Non C
Conf
identification product
using in combination
Manufacturer
Authorized representative
Date IFU
Mention of self-testing
National language
information interference
units readily undertstood
units reported
traceability calibration
composition
type sample calibration
equivalence blood/plasma
Items

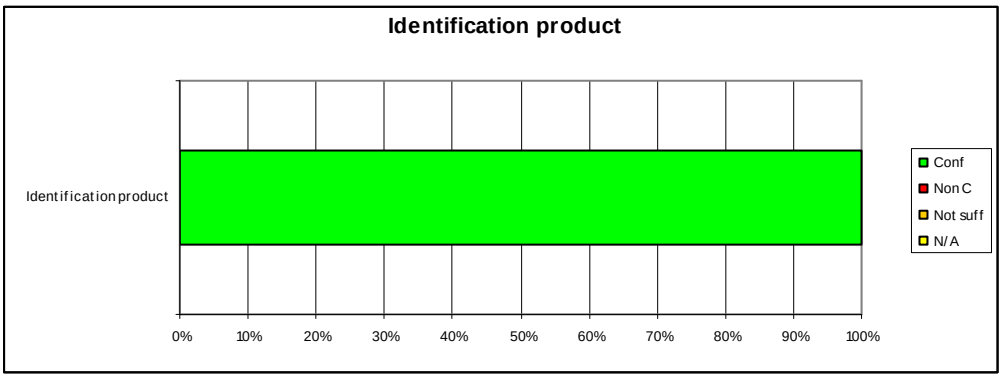
## Annex 9


REAGENTS: RESULTS FOR EACH ITEM
100%
80%
60%
40%
20%
0%
N/A
Not suff
Non C
Conf
Identification product
using in combination
composition
Manufacturer
Authorized representative
Date IFU
Mention of self-testing
National language
information interference
units readily undertstood
traceability calibration
accuracy
type sample calibration
accuracy standard ISO EN15 197
measurement proc. used
Items

# Annex 10

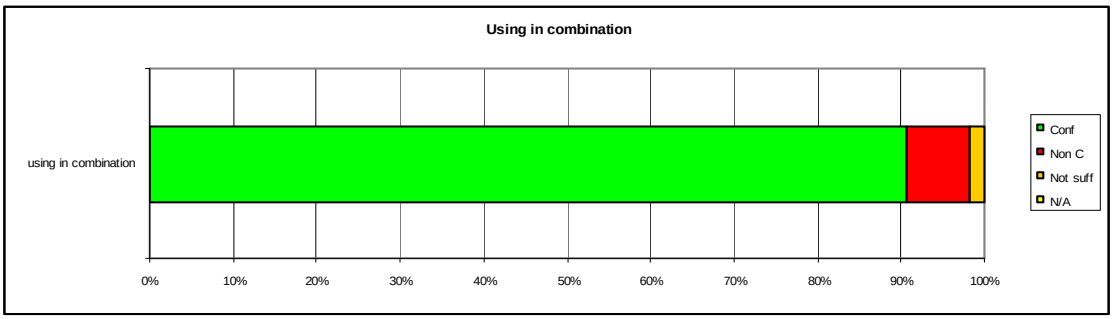
## Review of manuals of use of the meters.

## Items/meters




No deviation.

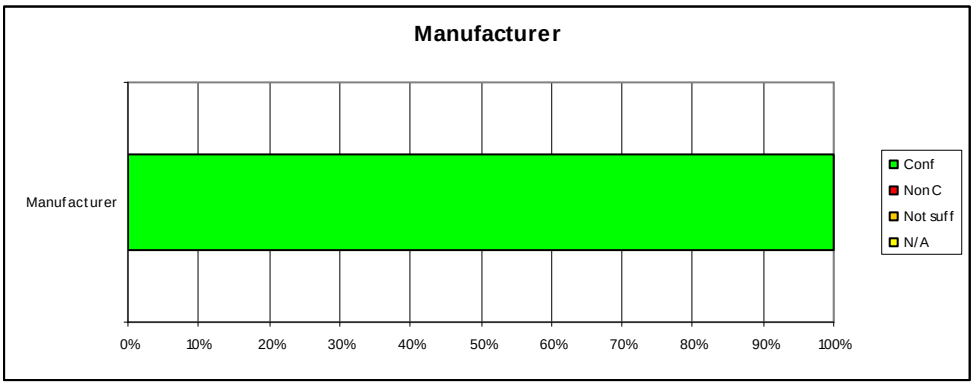
This item was considered as major insofar as, a correct identification of the strip and the relevant meter is essential to identify the combination claimed by the manufacturer.




A correct identification of the combination (strip + meter) is necessary to understand which system can be used in a safe manner. Performance evaluation must be performed for each combination claimed by the manufacturer.

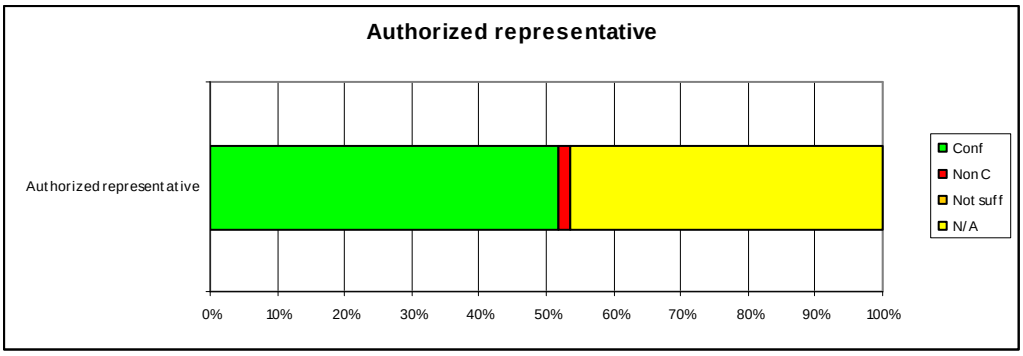
4 deviations : XX and XX.

1 information considered as not sufficient: there is only the reference of the strip but the name is missing.




No deviation.

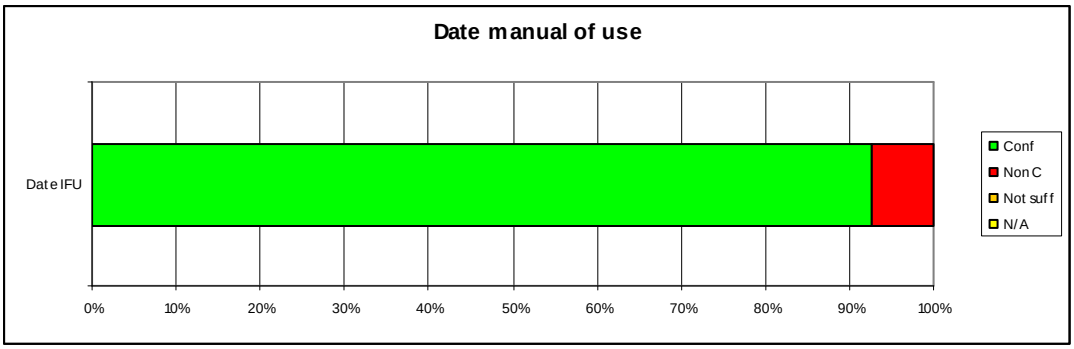
Name and address of the manufacturer as defined in the directive.



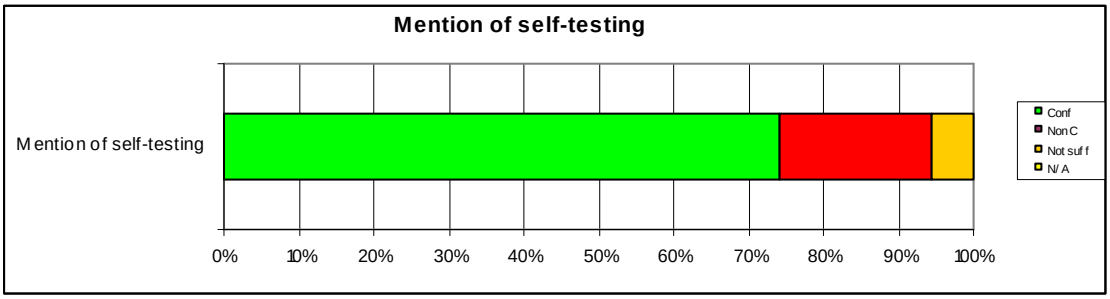

Name and address of the Authorised Representative (AR) as defined in the directive.

25 Not applicable when the manufacturer is located in European Union, EFTA and countries under specific convention.

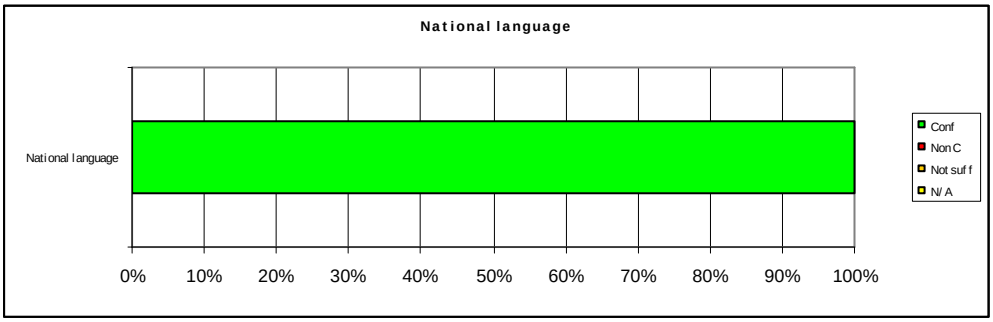
1 deviation : the name of the AR is missing in the manual but present in the IFU.




4 deviations : manual without any date.

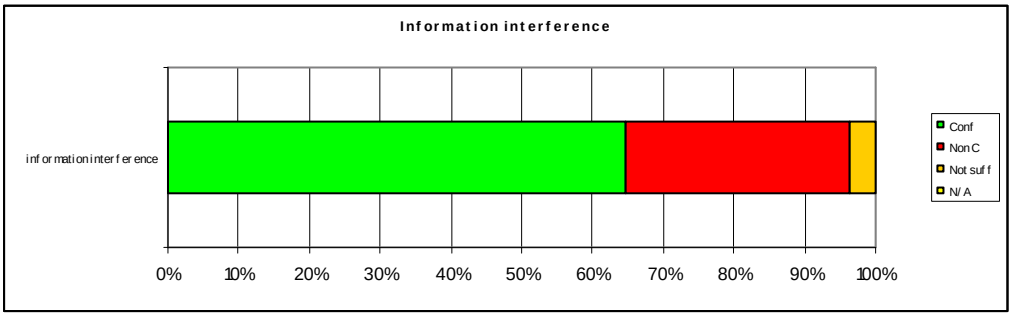



11 manuals without any mention of self testing.
3 manuals with no sufficient information : no clear mention of self-testing.




No deviation.

Products sold in France have a manual in French.
Products sold in UK and Ireland have a manual in English.



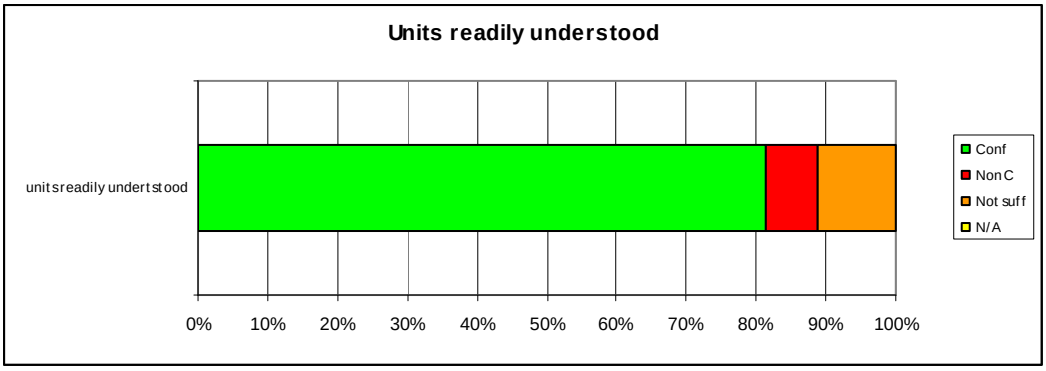

17 manual don't include information about the possibility of interferences. For one manufacturer there is no information in the manual nor in the IFU.

Interference with maltose is described for enzymes such as GDH PQQ (pyrroloquinoline quinone glucose dehydrogenase). High level of maltose is identified in blood for patients undergoing peritoneal dialysis with icodextrine. In this case, there is a risk of overestimation of blood glucose with risk of non identified hypoglycemia and coma or death of the patient.

In France, Ireland and the UK the Competent Authorities request warnings and recommendations in the IFU.

For 2 products, warnings and recommendations are missing in the manual. Information is present in the IFU with no cross-reference between manual and IFU of the strips.

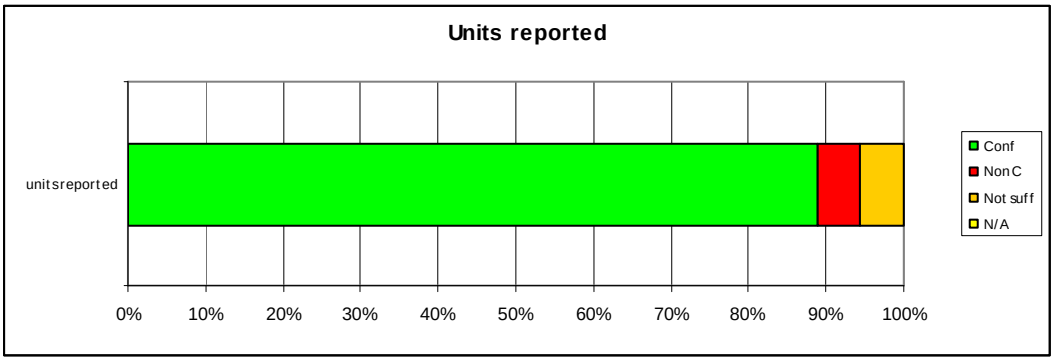
For systems with modified GDH PQQ, there is no risk of interference claimed so, no special mention.



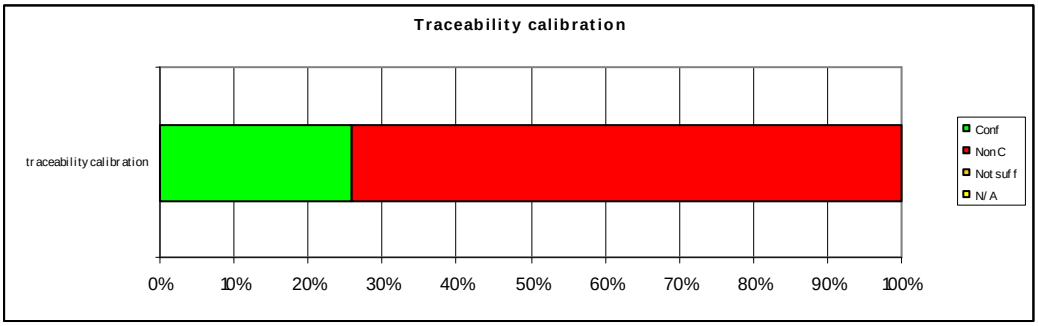
6 manuals are considered as not sufficient when the presentation of the units in a same document is not homogeneous (for example when 2 units of measure can be used: mg/L and mmol/L, the 2 units are not always presented in the same order).

In 6 cases : the meter allows the unit of measure to be changed. In the meter's manual results are given in mmol/L and in mg/dL but in the IFU of the strips, results are given in one sort of unit only.

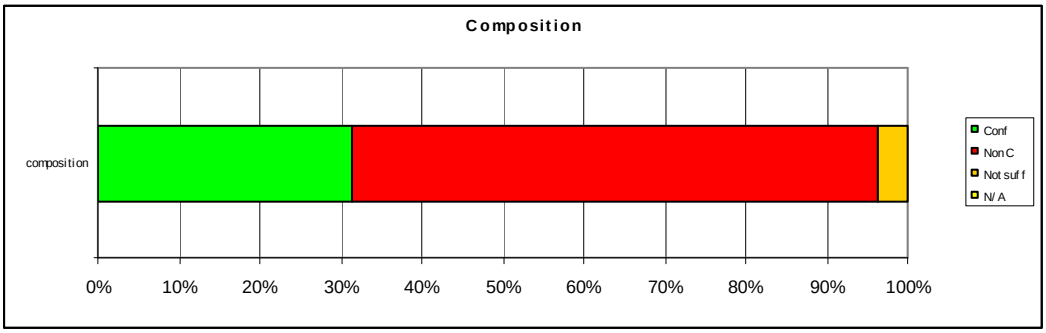
Important risk of confusion.




Presence of the unit on the screen of the meter.




40 deviations because the manual doesn't indicate the traceability to a glucose reference measurement procedure or to a reference material of higher order.

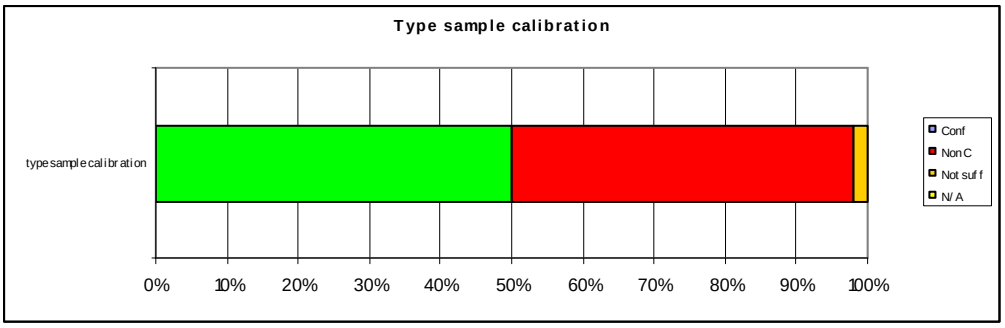



What is required in terms of composition is, at a minimum, the name of the enzyme which is the active ingredient which might influence the measurement as described in the directive.

35 deviations but information always present in the IFU of the strips.

Information not sufficient in 2 manuals.

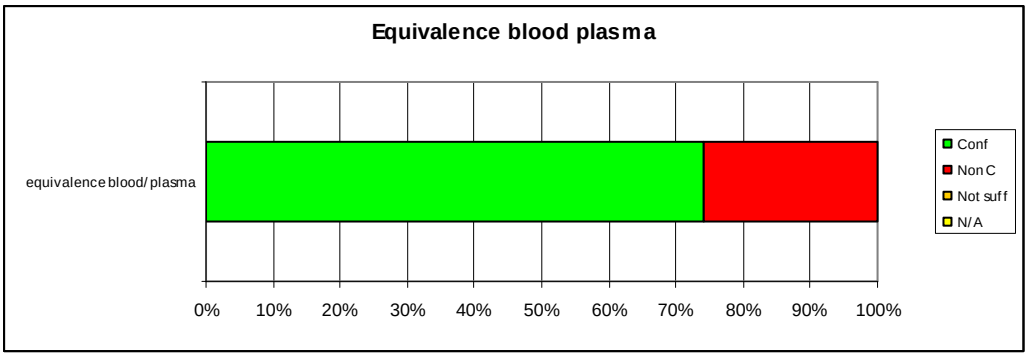
This information is major insofar as interference with maltose is described for enzymes such as GDH PQQ (pyrroloquinoline quinone glucose deshydrogenase). High level of maltose is identified in blood for patients under peritoneal dialysis with icodextrine. In this case, there is a risk of overestimation of blood glucose with risk of non identified hypoglycemia and coma or death of the patient. Identification of the enzyme and appropriate recommendations for patients undergoing peritoneal dialysis with icodextrine is vital.




The type of sample used for calibration is necessary to understand if the system is calibrated by using plasma or blood.

This is ‘non- conform’ in 26 cases as this information is missing.

In 1 case this information is not sufficient because there is no reference to the type of sample but the method used for calibration is described (YSI) and this method uses blood.



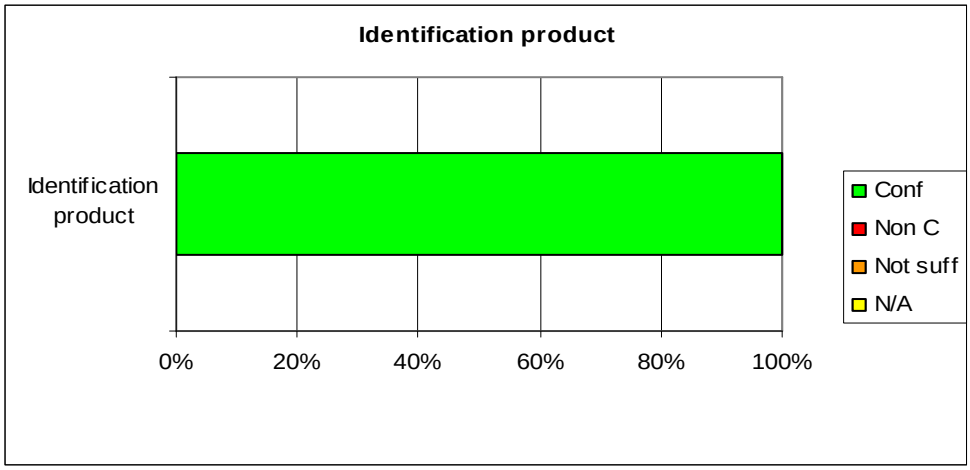

Information on whether reported results are equivalent to blood or to plasma results.
In 1 case, the strips are calibrated by using blood but the results are equivalent to plasma.

14 deviations for manuals with no information about equivalence.

## Annex 11

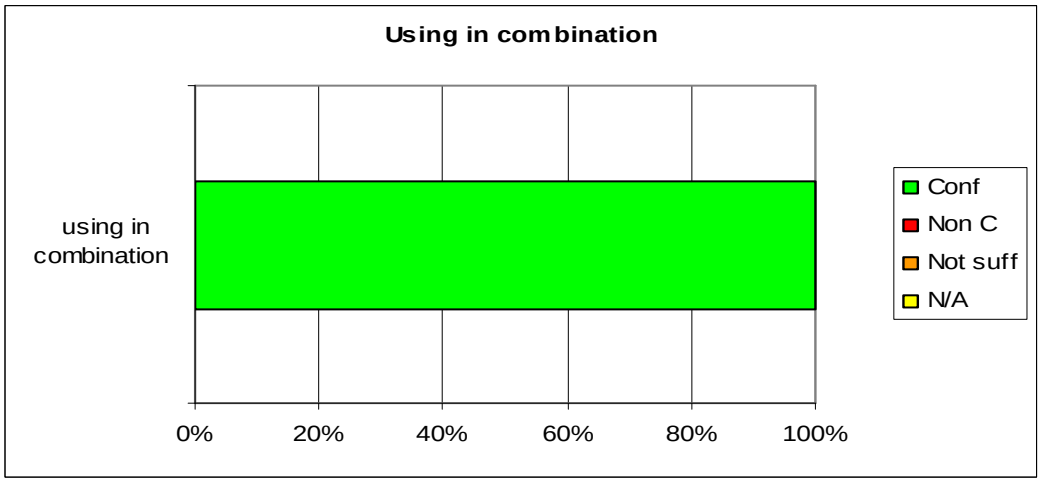
## Review of the instruction for use of the strips.

## Items/reagents



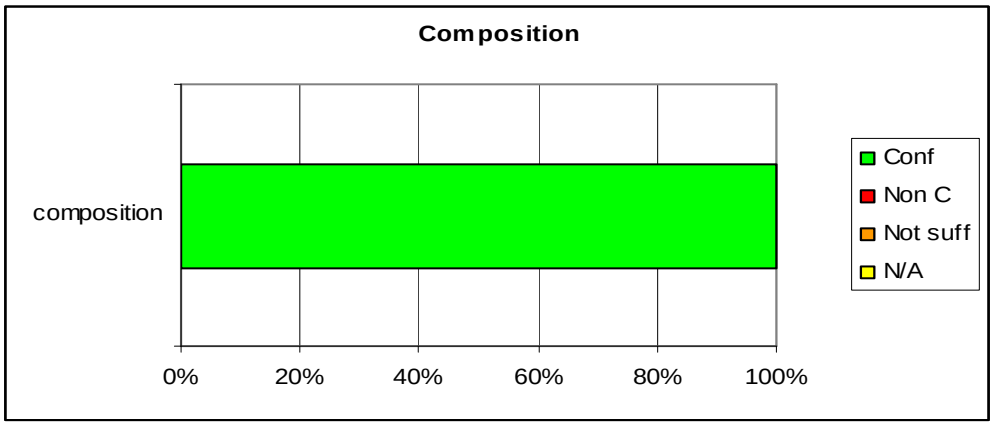

No deviation.

This item was considered as major insofar as, a correct identification of the strip and the relevant meter is essential to identify the combination claimed by the manufacturer.




No deviation.

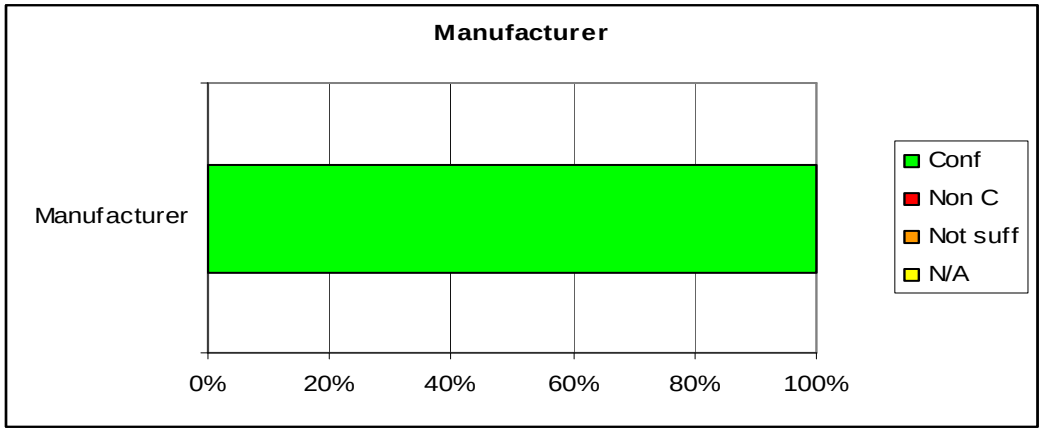
A correct identification of the combination (strip + meter) is necessary to understand which system can be used in a safe manner. Performance evaluation must be performed for each combination claimed by the manufacturer.




What is required in terms of composition is at a minimum, the name of the enzyme which is the active ingredient which might influence the measurement as described in the directive.

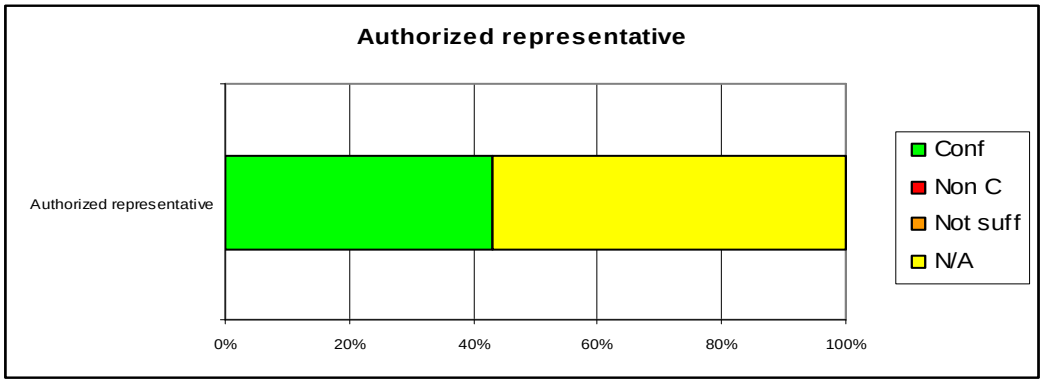
No deviation.

This information is major insofar as interference with maltose is described for enzymes such as GDH PQQ (pyrroloquinoline quinone glucose deshydrogenase). High level of maltose is identified in blood for patients under peritoneal dialysis with icodextrine. In this case, there is a risk of overestimation of blood glucose with risk of non identified hypoglycemia and coma or death of the patient. Identification of the enzyme and appropriate recommendations for patients under peritoneal dialysis with icodextrine is vital.



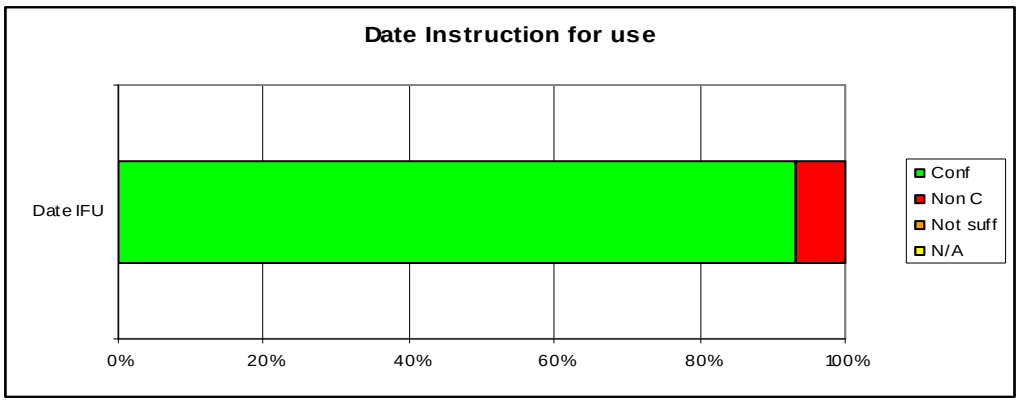

No deviation.

Name and address of the manufacturer as defined in the directive.

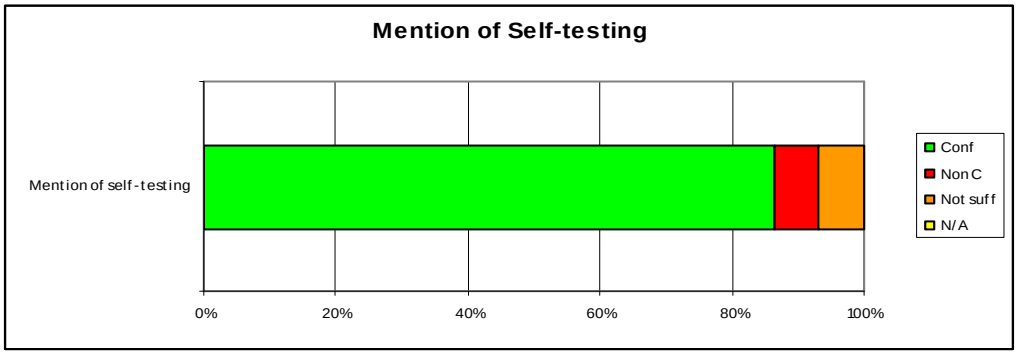



No deviation.

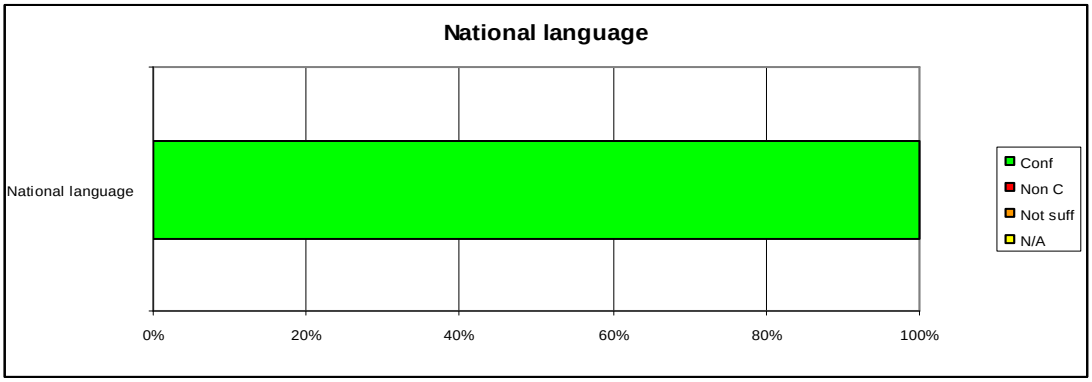
Name and address of the Authorised Representative as defined in the directive.
Not applicable when the manufacturer is located in European Union, EFTA and countries under specific convention.




3 deviations : IFU without any date.

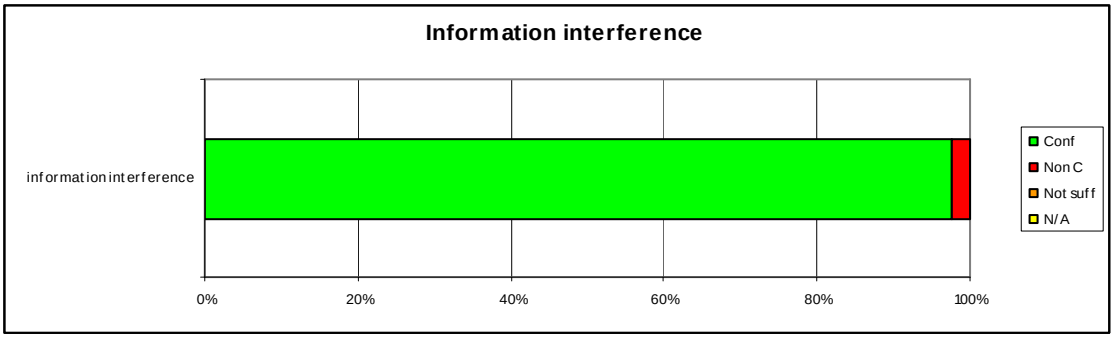


3 IFU without any mention.
3 IFU with no sufficient information : no clear mention of self-testing.




No deviation.

Products sold in France have an IFU in French.
Products sold in UK and Ireland have an IFU in English.

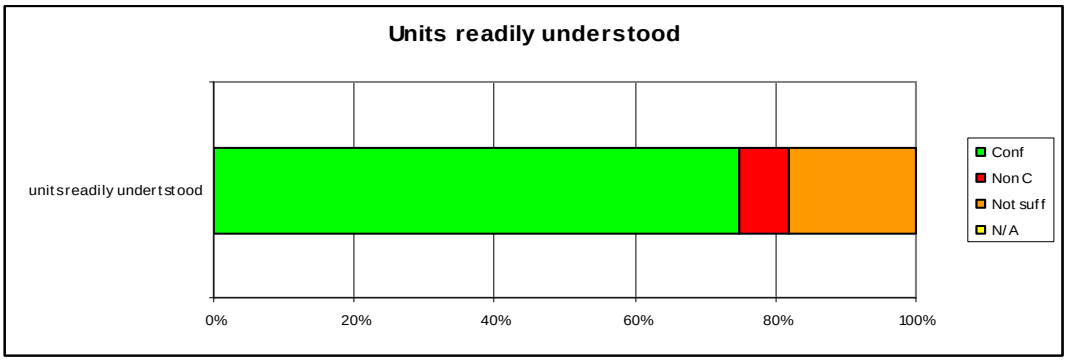



1 IFU doesn’t include information about possibility of interferences in general.

Interference with maltose is described for enzymes such as GDH PQQ (pyrroloquinoline quinone glucose deshydrogenase). High level of maltose is identified in blood for patients undergoing peritoneal dialysis with icodextrine. In this case, there is a risk of overestimation of blood glucose with risk of non identified hypoglycemia and coma or death of the patient.

In France, Ireland and the UK, the Competent Authorities request warnings and recommendations in the IFU.

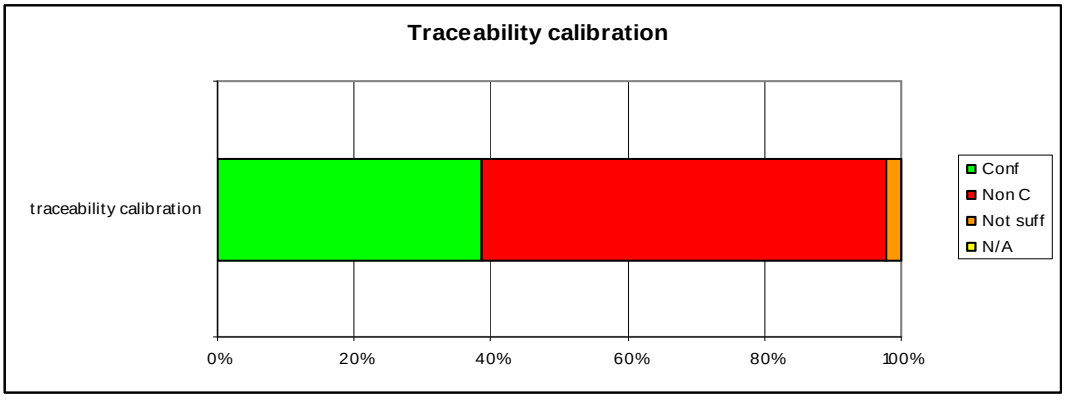
Warnings and recommendations are included in all the IFUs.



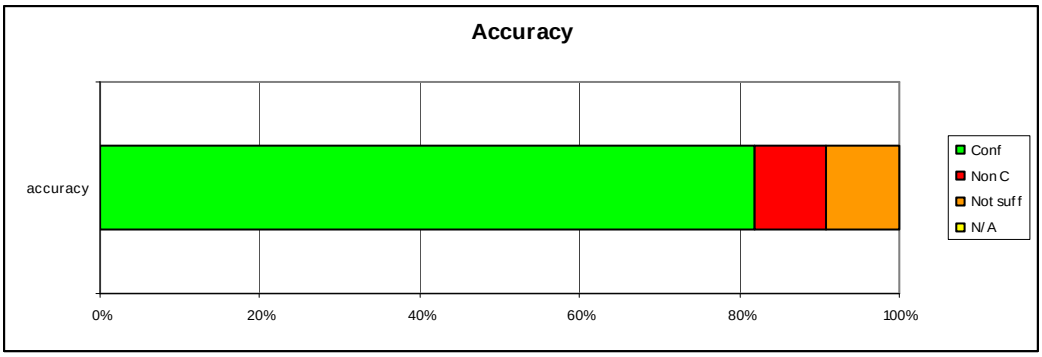

8 IFUs considered as not sufficient when the presentation of the units in a same document is not homogeneous (for example when 2 units of measure can be used: mg/L and mmol/L, the 2 units are not always presented in the same order).

In 3 cases: the meter allows the unit of measure to be changed. In the meter's manual results are given in mmol/L and in mg/dL but in the IFU of the strips, results are given in one sort of unit only.

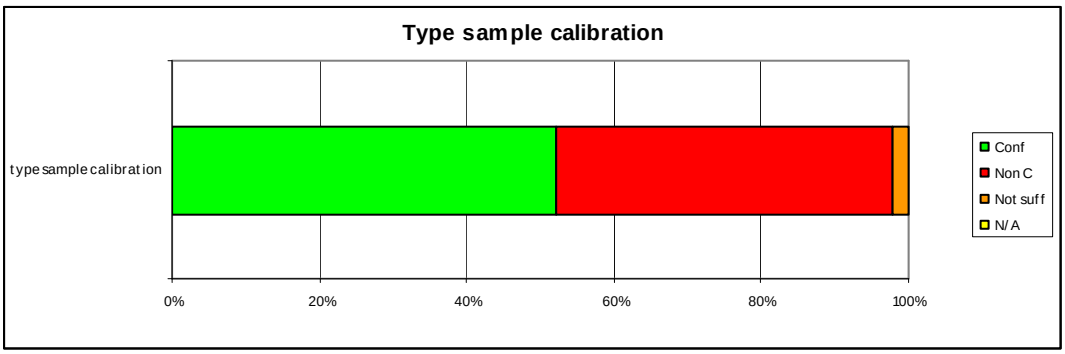
Important risk of confusion.




27 deviations because the IFU doesn't indicate the traceability to a glucose reference measurement procedure or to a reference material of higher order.



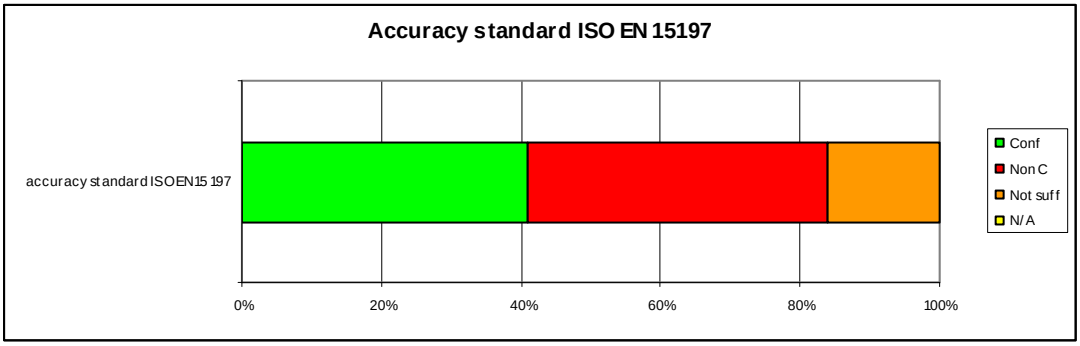

Accuracy as required in the directive can be a table, a correlation or a Clark diagram.
4 deviations because no performance data for accuracy is given.
4 results considered as not sufficient because no clear information is given.




The type of sample used for calibration is necessary to understand if the system is calibrated by using plasma or blood.

In 20 cases this information is missing.

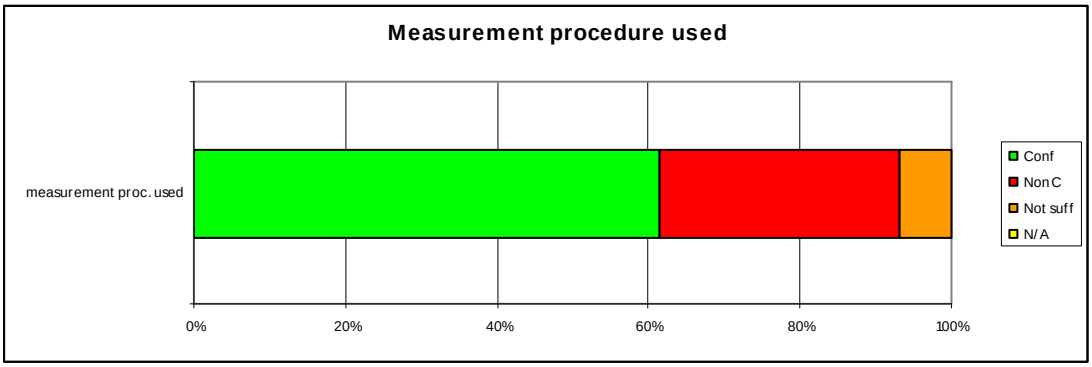
In 1 case this information is not sufficient because there is no reference to the type of sample but the method used for calibration is described (YSI) and this method uses blood.



The standard describes precisely how the accuracy data must be presented for the reagent in the form of a table with percentage of accuracy for different concentrations of glucose.

In 19 cases the results are not at all presented as described in the standard.

In 7 cases the information is not sufficient because for example, information required in the standard is given but this information is not supplied as required in the standard (general data or phrase replace the table with all the details).




Measurement procedure used to evaluate the performance characteristics of the system. Method of comparison.

In 14 cases deviations were noted because no information is given on the measurement procedure used to evaluate the performance characteristics of the system.

3 cases were identified as not sufficient because the comparison with one technique is mentioned but in general there is no precise information on the principle or on the name of the method used

# Annex 12

**BILATERAL POST MARKET SURVEILLANCE PROJECT : CONTROL OF BLOOD GLUCOSE MONITORING SYSTEMS**
**Checklist of instruction for use**
**of the reagents (strips and electrodes) and of the manual of use :**

**References :**

- European Directive 98/79/EC
- International Standard NF EN ISO 15197: In vitro diagnostic test systems. Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus
- European standard NF EN 592 : Instructions for use for in vitro diagnostic instruments for self-testing
- European standard NF EN 376 : Information supplied by the manufacturer with in vitro diagnostic reagents for self-testing

**Identification of the products and general points:**

| | |
|---|---|
| **Identification of the REAGENT** (name) (8.7a 98/79/EC) (5.3 EN 376) | |
| Name and address of the manufacturer (8.7.a 98/79/ EC) (5.2 EN 376) | |
| Name and address of the authorized representative if manufacturer is not located in EU (8.7.a 98/79/ EC) (5.2 EN 376) and if not indicated on the label, the outer packaging | |

| | |
|---|---|
| **Identification of the METER** (name) (8.7a 98/79/ EC) (5.4 EN 592) (5.2.b) NF EN ISO 15 197) | |
| Name and address of the manufacturer (8.7.a 98/79/ EC) (5.3 EN 592) (5.2.a NF EN ISO 15 197) | |
| Name and address of the authorized representative if manufacturer is not located in EU (8.7.a 98/79/ EC) (5.3 EN 592) (5.2.a NF EN ISO 15 197) and if not indicated on the label, the outer packaging | |

| **REAGENT** (strip or electrode) | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| If using in combination : sufficient details of its characteristics to identify the correct device to use in order to obtain a safe and proper combination (8.7.m 98/79/ EC) (5.4.b NF EN ISO 15197) | | | | | | |
| Date of issue or latest revision of the instruction for use (8.7.u 98/79/EC) (5.15 EN 376) | | | | | | |
| Mention of self-testing (8.7.a 98/79/EC, cf 8.4.k) (5.5 EN 376) | | | | | | |
| National language available (8.1 98/79/EC) (5.1 EN 376) (5.4 NF EN ISO 15 197) | | | | | | |

| **METER** | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| If using in combination : sufficient details of its characteristics to identify the correct device to use in order to obtain a safe and proper combination (8.7.m 98/79/EC) (5.2.g NF EN ISO 15 197) | | | | | | |
| Date of issue or latest revision of the instruction for use (8.7.u 98/79/EC) (5.19 EN 592) (5.2.r NF EN ISO 15 197) | | | | | | |
| Mention of self-testing (8.7.a 98/79/EC, cf 8.4.k) (5.7 EN 592) | | | | | | |
| National language available (8.1 98/79/EC) (5.1 EN 592) (5.2 NF EN ISO 15 197) | | | | | | |

**1) Interference in particular with maltose**

| **REAGENT** (strip or electrode) | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Composition of the reagent product by nature and amount or concentration of the active ingredient (s), other ingredients which might influence the measurement * (8.7.b 98/79/EC) (5.7 EN 376) | | | | | | |
| Information needed for the control of known relevant interferences (8.7.h 98/79/EC) (5.12.2 EN 376) (5.4.f NF EN ISO 15 197) | | | | | | |

| **METER** | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Composition of the reagent (strip or electrode) product by nature and amount or concentration of the active ingredient (s) (precision about the enzyme used in the associated reagent), other ingredients which might influence the measurement * (8.7.b 98/79/CE) | | | | | | |
| Information of limitation of use (5.10 EN 592) including relevant interferences (8.7.h 98/79/EC) | | | | | | |

*: if the enzyme is GDH-PQQ, the instruction for use and the manual of use must indicate: never use these meters with patients in peritoneal dialysis receiving dialysis solution containing icodextrine

**2) Units of the results**

| **REAGENT** (strip or electrode) | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Results presented in a way that is readily understood by a lay person (8.7.t 98/79/EC) (5.13 EN 376) | | | | | | |

| **METER** | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Results presented in a way that is readily understood by a lay person (8.7.t 98/79/EC) (5.13 EN 592)<br>The measurement units reported by the device (5.2.h NF EN ISO 15 197) | | | | | | |

Details of information assessed:

| **METER** | YES | NO | Comments |
|---|---|---|---|
| Are the units of measurement available with the result? | | | |
| Is it possible to change the unit of measure? | | | |
| If yes, is the procedure to be followed included? | | | |

3) **Information about the calibration of the system**

| **REAGENT** (strip or electrode) | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Information appropriate on the traceability of the calibration of the system (8.7.k 98/79/EC) (5.4.g NF EN ISO 15 197, see note 1) | | | | | | |
| Type of samples used for calibration (blood or plasma) (5.4.h NF EN ISO 15 197) | | | | | | |

Note 1: The traceability to a glucose reference measurement procedure or reference material of higher order

| **METER** | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Information appropriate on the traceability of the calibration of the system (8.7.k 98/79/EC) (5.2.e NF EN ISO 15 197) | | | | | | |
| Type of samples used for calibration (blood or plasma) (5.2.f. NF EN ISO 15 197) | | | | | | |
| Information whether reported results are equivalent to blood or plasma results (5.2.h NF EN ISO 15 197) | | | | | | |

### 4) Accuracy

| **REAGENT** (strip or electrode) | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Accuracy (8.7.h 98/79/EC) | | | | | | |
| 5.4.e NF EN ISO 15 197 : The performances characteristics : for system accuracy performance, the manufacturer shall report : (5.4.e)<br>- For glucose concentrations < 4.2 mmol/l (< 75 mg/dl) the percentage of results within +/- 2.28 mmol/l (5 md/dl), +/- 0.56 mmol/l (10 mg/dl), +/- 0.83 mmol/l (15 mg/dl) of the references values<br>- For glucose concentrations ≥ 4.2 mmol/l (≥ 75 mg/dl) the percentage of results within +/- 5 %, 10 %, 15 %, 20 % of the references values | | | | | | |
| The measurement procedure used to evaluate the performances characteristics of the system (5.4.g NF EN ISO 15 197) | | | | | | |

| **METER** | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Accuracy (8.7.h)<br>(5.10 EN 592, see note 2) | | | | | | |

Note 2: information on the performance

### 5) Practicality (Optional)

| **METER** | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| All the information needed to verify whether the device is properly installed and can operate correctly and safety (…) (8.7.n 98/79/EC). In this case: where applicable, the information that the user must verify the good display of the screen before using the meter | | | | | | |
| The information and instructions provided by the manufacturer should be easily understood and applied by the user : | | | | | | |
| Manual of use presented in a clear and concise manner (5.2. NF EN ISO 15 197) | | | | | | |
| Plain terminology that is readily understood by a layperson (7 98/79/CE) (5.2 NF EN ISO 15 197) | | | | | | |
| Information well organized and easy to read (5.2 NF EN ISO 15 197) | | | | | | |
| Large print (e.g. 12-point Courier) (5.2 NF EN ISO 15 197) | | | | | | |
| Clearly state what actions to take in the event of changes in the analytical performance of the device (8.7.j 98/79/EC)<br>Clearly state what actions to take if the verification indicates an invalid result (5.2 NF EN ISO 15 197) | | | | | | |
| A reference to the instruction given by a physician and/or other qualified healthcare provider, and | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| a warning not to deviate from these instructions on the basis of the result without first consulting the physician or other qualified healthcare provider (8.7.t 98/79/EC) (5.2.p NF EN ISO 15 197) | | | | | | |
| Advice on how to proceed if the result appears to be questionable to the user (5.2.p NF EN ISO 15 197) | | | | | | |
| Indication how the monitoring system alerts the user when the result is outside the measurement interval (5.2.p NF EN ISO 15 197) | | | | | | |

| **REAGENT** (strip or electrode) | Non-conform | Not sufficient | Conform | Not applicable | Information supplied | Comments |
|---|---|---|---|---|---|---|
| Instructions provided by the manufacturer should be easily understood and applied by the user (7 98/79/EC) | | | | | | |
| Measures to be taken in the event of changes in the analytical performance of the device (8.7.j 98/79/EC) | | | | | | |
| Warning not to deviate from these instructions on the basis of the result without first consulting the qualified healthcare provider (8.7.t 98/79/EC) | | | | | | |