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(71) Applicant *(for DE only)*: **ROCHE DIAGNOSTICS GMBH** [DE/DE]; Sandhofer Strasse 116, 68305 Mannheim (DE).

(71) Applicant *(for all designated States except DE, US)*: **F. HOFFMANN-LA ROCHE AG** [CH/CH]; Grenzacherstrasse 124, CH-4070 Basel (CH).

(72) Inventors; and
(71) Applicants *(for US only)*: **SCHULAT, Jochen** [DE/DE]; Langer Schlag 123a, 68305 Mannheim (DE). **TRICK, Sebastian** [DE/DE]; Oberbergener Strasse 28, 68239 Mannheim (DE).

(74) Agents: **PFIZ, Thomas** et al.; Wolf & Lutz, Hauptmannsreute 93, 70193 Stuttgart (DE).

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(54) Title: METHOD FOR HEMATOCRIT CORRECTION AND GLUCOSE METER ADAPTED THEREFOR

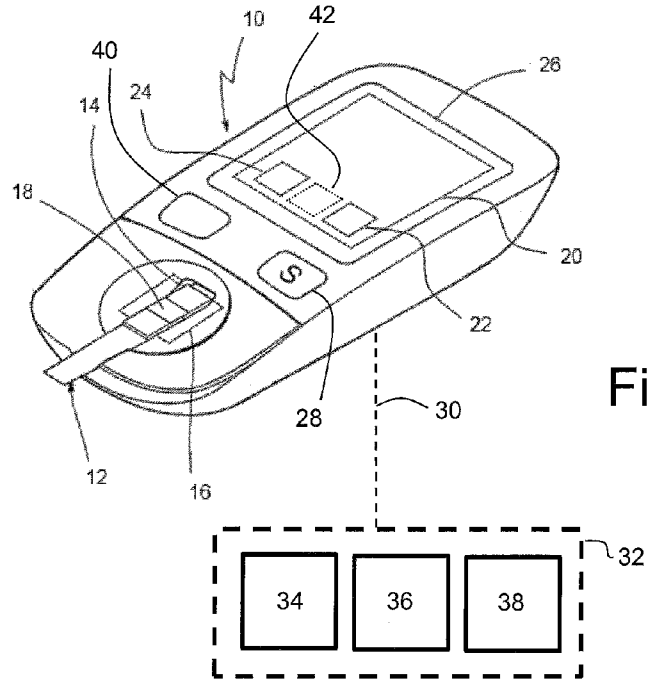

Fig. 1

(57) Abstract: The invention concerns a method and a device for hematocrit correction in connection with a glucose measurement, where the following measures are proposed: • - determining by means of a reference instrument (34), such as a laboratory analyser, a hematocrit reference value of a reference blood sample taken from a specific user, • - applying a fresh blood sample of said user on a disposable analytical test element (12), • - measuring the glucose value of the fresh blood sample by single use of said test element (12) in the glucose meter (10), • - determining a hematocrit correction value using at least the hematocrit reference value, • - adjusting the measured glucose value using the hematocrit correction value to receive an adjusted glucose value.

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Method for hematocrit correction and glucose meter adapted therefor

Description

The invention concerns a method for hematocrit correction and a glucose meter according to claims 1 and 15, respectively. The invention further concerns a system comprising a portable glucose meter and a reference instrument.

The hematocrit (HCT) may be defined as the volume percentage (%) of red blood cells in whole blood. The HCT is normally about 45% for men and 40% for women and may range from about 20% to about 70% in extreme cases. It is known that the hematocrit can impact the glucose level of a blood sample being tested. In order to account for such a hematocrit interference, it has been proposed to additionally measure the actual hematocrit value of a given sample, e.g. by multiple wavelength, conductivity or other tests in addition to the glucose test. However, such measurements imply unwanted complexity in self-testing devices and are prone to measurement uncertainty. As an alternative, efforts have been made to reduce the hematocrit influence by the design of the test chemistry or disposable, e.g. by retaining red blood cells through separating layers. However, such a measure can eliminate the hematocrit influence only to a residual dependency.

On this basis the object of the invention is to further improve the known methods and devices for hematocrit correction in glucose measurements and to provide improved measurement certainty specifically in a self-testing environment without undue effort.

The combination of features stated in the independent claims is proposed to achieve this object. Advantageous embodiments and further developments of the invention are derived from the dependent claims.

The invention is based on the finding that the mean/average hematocrit of a given person is (under normal life conditions) fluctuating only in a limited range. Accordingly it is proposed according to the invention that a method for hematocrit correction in a glucose meter comprises the steps of

- determining by means of a reference instrument preferably formed as a laboratory analyzer a hematocrit reference value of a reference blood sample taken from a specific user,
- applying a fresh blood sample of said user on a disposable analytical test element,
- measuring the glucose value of the fresh blood sample by single use of said test element in the glucose meter,
- determining a hematocrit correction value using at least the hematocrit reference value,
- adjusting the measured glucose value using the hematocrit correction value to receive an unbiased adjusted glucose value.

Such a procedure requires only once the determination of the hematocrit reference value, which can be exactly measured by use of a clinical or laboratory analyzer, whereas the routinely glucose measurements on the spot can be repeatedly conducted and corrected on the basis of one and the same hematocrit reference value without increased measurement effort. This is also due to the finding that the hematocrit dependency of typical self-monitoring blood glucose monitoring systems comprising a given test architecture and device is relatively constant. The adjustment of the measured glucose value can be easily implemented on processors which are already included in handheld devices or home meters for other data handling purposes. Thus, the system performance can be improved significantly, whereat the meter is then assigned to a specific user, i.e. as a personalized device. In this way, the hematocrit correction is easily feasible in a glucose monitoring system without the need for the patient to bring blood samples to a laboratory for determining the glucose bias in each and every case.

Advantageous for a convenient handling, the hematocrit reference value may be transferred via a wireless or wire-bound interface into a memory of the glucose meter.

For safety considerations, it is further advantageous when the hematocrit reference value is transmitted to the glucose meter using an external software on a device outside the glucose meter which is inaccessible to the user.

A further improvement for convenience may be achieved when the hematocrit reference value is stored in an external database outside the glucose meter in connection with a user identifier for the user.

To facilitate data exchange for a personalized device, the glucose meter may comprise machine readable means, specifically an RFID chip, for automatic user identification.

Another safety improvement provides that the user identity is checked by a query provided by the glucose meter, whereupon an input of a confirmation by the user is requested.

In order to account for eventual deviations of the hematocrit reference value, the user may be queried about a change in living conditions influencing hematocrit.

For a reliability check it is also favorable when the timeliness of the hematocrit reference value is verified within a given time interval.

For further awareness of the patient or user, it is advantageous when the user is informed that personalized data are used for correction of the measured glucose value.

In order to avoid unwanted loss of a test medium, an advantageous embodiment provides that the adjusted glucose value is displayed to the user upon fulfillment of given conditions including availability of the hematocrit reference value and optionally timeliness of this value, whereas otherwise in order to provide a fall back result the measured glucose value is displayed.

It is also advantageous for improved elimination of the hematocrit effect when the hematocrit correction value is determined in dependence of the hematocrit reference value and the measured glucose value.

Advantageously, determining of the hematocrit correction value involves using one or more correction functions or a lookup table determined empirically in connection with the architecture of the test element eventually in combination with the glucose meter.

The hematocrit correction is particularly effective when the glucose value of the fresh blood sample is measured by photometric or electrochemical detection on the analytical test element.

Advantageously, the glucose meter is construed as a portable handheld device usable by a proband or user for self-testing in a non-laboratory environment.

With regard to a glucose meter adapted for hematocrit correction, in order to solve the aforementioned object, the following combination of features is proposed according to the invention:

- means configured to receive at least one disposable test element on which a blood sample can be applied or is applied,
- a detector adapted for measuring a blood glucose value using the test element loaded with a fresh blood sample of a specific user,
- an interface configured to input a hematocrit reference value of a reference blood sample of said user,

- a processor adapted to determine a hematocrit correction value using the hematocrit reference value and the measured glucose value and to adjust the measured glucose value using the hematocrit correction value.

For a trusted execution of the hematocrit correction it is advantageous to provide means operable to allow hematocrit correction of the blood glucose measurement depending on the provision of a (valid) hematocrit reference value. It may also be conceivable that in case of a missing hematocrit reference value an uncorrected measurement result is provided together with a corresponding indication to the user.

A further aspect of the invention comprises a system adapted for hematocrit correction, comprising the glucose meter according to the invention and a reference instrument preferably formed as a laboratory analyzer to determine a hematocrit reference value of a reference blood sample taken from a specific user of the glucose meter.

The invention is further elucidated in the following on the basis of embodiment examples shown schematically in the drawings, where

Fig. 1 is a perspective and partially schematic view of a glucose meter in connection with an external reference system for hematocrit correction;

Fig. 2 is a plot of hematocrit-induced glucose bias Δ versus the glucose concentration C for a given hematocrit value.

FIG. 1 illustrates an exemplary handheld glucose meter 10 for insertion of a disposable test strip 12 usable by a proband or user for self-testing in an everyday environment. The meter 10 comprises a holder 14 to position the test strip 12 in the optical path of a reflection-photometric detector 16 to read

the reflectance of a test pad 18 of the strip 12. A small volume of a fresh sample of whole blood taken by the user on the spot can be applied to the test pad 18, wherein a reagent reacts with a glucose leading to a change in reflectance which is detectable from the bottom of the test pad 18 with the photometer 16. Such measurements are known to the skilled person per se and need not to be elucidated in more detail. It is further known that the hematocrit content of a blood sample can impact the glucose level to be tested e.g. by diffusion effects in the test pad 18.

In order to process and correct the measurement signals, a device electronics 20 comprises a processor 22, a memory 24, a display 26 and keys 28 for interaction with the user and an interface 30 for eventual connection to an external reference system 32. The processor 22 is adapted for hematocrit correction using the measured glucose value and a hematocrit reference value initially provided through the reference system 32 and stored in the memory 24.

The hematocrit reference value can be determined by means of an external reference instrument 34 formed as a laboratory analyzer. For this purpose, a specific user may provide a reference blood sample to be analyzed with the reference instrument 34 in a clinical or laboratory setting. Then, the determined hematocrit reference value can be transmitted into the memory 24 of the glucose meter 10 via the (wireless) interface 30 using an external software 36 running on a device outside the meter 10. In order to guarantee a safe handling, the software 36 should be inaccessible to the user and only operable by authorized personnel, e.g. by a health professional. For example, a physician may connect the glucose meter 10 of a patient to a computer in his medical practice running the software 36 such that configuration data of the meter 10 can be read out and the hematocrit reference value can be set only by the physician, to thereby ensure that the values are controlled and interpreted with the necessary medical knowledge and are not manipulated by a layperson.

It may also be conceivable that the hematocrit reference value is stored in a database 38 of the reference system 32 in connection with an identifier for the user who has provided the reference sample. An automatic data transfer to the glucose meter 10 assigned to said user could then be accomplished by an identification process enabled by machine readable means, specifically an RFID chip 40 mounted on the meter 10 and containing the user identifier.

It should be emphasized that such an initial procedure is only necessary once in a while, as the hematocrit value of a given patient is usually relatively constant over time. Given the living situation does not change, the hematocrit value of an individual typically fluctuates by less than 2%, which is small compared to the possible range of hematocrit values for different persons (typically 20 to 55%, eventually up to 70%).

By storing the hematocrit reference, the meter 10 is personalized for the specific user and can be employed for glucose measurements in a daily routine. In order to carry out such a measurement, the user takes a fresh blood sample and applies it on the test strip 12 before or after insertion into the meter 10, in which a glucose value can be measured automatically by means of the detector 16. At the beginning of the measurement routine, the user identity is checked e.g. by a query displayed to the user on the display 26 and requesting input of a confirmation by means of keys 28. The user can be informed by an indication on the display 26 that personalized data are used for correction of the glucose measurement. The user may further be asked about a change in living conditions which may influence the hematocrit, for example training in higher altitudes.

The processing routine may also include a verification of the timeliness of the hematocrit reference value, which should be updated regularly, e.g. once in a year.

The meter 10 may comprise an activation stage 42 e.g. in the form of a software routine or input field to allow a glucose measurement only if a valid hematocrit reference value is available. The validity and specifically the attribution to a specific user may be proved by a security query to be confirmed by the user. Alternatively, in case of a missing hematocrit reference value, the processing routine could provide the measured glucose value to the user together with information that no correction has been made.

If a valid hematocrit reference value is stored in the memory 24, the hematocrit correction value is determined in dependence of the hematocrit reference value and the measured glucose value. Then, the measured glucose value is adjusted using the hematocrit correction value to receive an adjusted glucose value unbiased by hematocrit.

The measured glucose concentration can be corrected in consideration of the hematocrit reference value by using one or more correction functions. For example, a correction function in the form of a correction equation may be used, in which one or more correction factors and/or one or more correction offsets are used. It has been found that the correction of the measured glucose concentration C(meas) can be effected for example according to the following equation:

$$C(corr) = C(meas) + m*HCT^{i} + n \qquad (1)$$

In this equation, HCT is the hematocrit reference value, C(meas) is the measured glucose concentration, C(corr) is the corrected glucose concentration, and the factor m and the exponent i are experimentally or empirically determined correction parameters, which may, for example, depend on the temperature and the concentration of glucose itself.

Fig. 2 illustrates the deviation Δ of the measured glucose concentrations from the actual glucose concentrations C(ref) determined by a means of a reliable

reference method. The uncorrected glucose concentration could be measured using the handheld glucose meter 10, and the actual glucose concentrations could be determined using a laboratory device, or in other ways. For a sample with a hematocrit of 30% the horizontal axis in Fig. 2 denotes the measured glucose concentrations C in milligram per deciliter, and the vertical axis shows the deviation Δ. For glucose concentrations below 100 mg/dL the deviations Δ are given as absolute values in mg/dL, whereas for glucose concentrations above 100 mg/dL, the deviations Δ are given as a percentage.

Such curves or polygons can be determined for a plurality of hematocrits and glucose levels, such that the curves can be put together to a hypersurface, wherein for example, the measured glucose concentration is plotted on a first axis, the hematocrit on a second axis and the deviation Δ on a third axis. Such hypersurfaces can be stored in the memory 24 for example as individual values in a lookup table or being defined analytically or in other ways, such that in each case for each hematocrit value and each measured glucose concentration, the corresponding deviation Δ can be easily deducted with the processor 22 in order to provide a corrected value of the glucose concentration. It has been found that the hematocrit dependency largely stable over different batches of test strips 12. The correction values determined are therefore generally valid for a combination of a meter 10 and a test strip 12 or other test element comprising a specific test chemistry.

Patent Claims

1. A method for hematocrit correction in a glucose meter (10) comprising the steps of
   a) determining by means of a reference instrument (34) preferably formed as a laboratory analyzer a hematocrit reference value of a reference blood sample taken from a specific user,
   b) applying a fresh blood sample of said user on a disposable analytical test element (12),
   c) measuring the glucose value of the fresh blood sample by single use of said test element (12) in the glucose meter (10),
   d) determining a hematocrit correction value using at least the hematocrit reference value,
   e) adjusting the measured glucose value using the hematocrit correction value to receive an adjusted glucose value.

2. The method of claim 1 further comprising transferring the hematocrit reference value via a wireless or wire-bound interface (30) into a memory (24) of the glucose meter (10).

3. The method of claim 1 or 2, wherein the hematocrit reference value is transmitted to the glucose meter (10) using a software (36) outside the glucose meter (10) which is inaccessible to the user.

4. The method according to any of claims 1 to 3, wherein the hematocrit reference value is stored in an external database (38) outside the glucose meter (10) in connection with a user identifier for the user.

5. The method according to any of claims 1 to 4, wherein the glucose meter (10) comprises machine readable means (40), specifically an RFID chip, for automatic user identification.

6. The method according to any of claims 1 to 5, further comprising checking the user identity by a query provided by the glucose meter (10) and requesting input of a confirmation by the user.

7. The method according to any of claims 1 to 6, further comprising asking the user about a change in living conditions influencing hematocrit.

8. The method according to any of claims 1 to 7, further comprising verifying the timeliness of the hematocrit reference value within a given time interval.

9. The method according to any of claims 1 to 8, further comprising informing the user that personalized data are used for correction of the measured glucose value.

10. The method according to any of claims 1 to 9, further comprising displaying the adjusted glucose value to the user upon fulfillment of given conditions including availability of the hematocrit reference value, and otherwise displaying the measured glucose value.

11. The method according to any of claims 1 to 10, wherein the hematocrit correction value is determined in dependence of the hematocrit reference value and the measured glucose value.

12. The method according to any of claims 1 to 11, wherein determining the hematocrit correction value involves using one or more correction functions or a lookup table determined empirically or experimentally for a given design of the test element (12) and/or the glucose meter (10).

13. The method according to any of claims 1 to 12, wherein the glucose value of the fresh blood sample is measured by photometric or electrochemical detection on the analytical test element (12).

14. The method according to any of claims 1 to 13, wherein the glucose meter is construed as a handheld device usable for self-testing on the spot.

15. A glucose meter (10) adapted for hematocrit correction, comprising

a) means (14) configured to receive at least one disposable test element (12) on which a blood sample can be applied or is applied,

b) a detector (16) adapted for measuring a blood glucose value using the test element (12) loaded with a fresh blood sample of a specific user,

c) an interface (30) configured to input a hematocrit reference value of a reference blood sample of said user,

d) a processor (20;22) adapted to determine a hematocrit correction value using the hematocrit reference value and the measured glucose value and to adjust the measured glucose value using the hematocrit correction value.

16. The glucose meter of claim 14, further comprising means (42) operable to allow hematocrit correction of the blood glucose measurement depending on the provision of a hematocrit reference value.

17. The glucose meter of claim 14 or 15, wherein the glucose meter is construed as a handheld device usable for self-testing on the spot.

18. A system adapted for hematocrit correction, comprising the glucose meter according to any of claims 15 to 17 and a reference instrument (34) preferably formed as a laboratory analyzer to determine a hematocrit reference value of a reference blood sample taken from a specific user of the glucose meter (10).

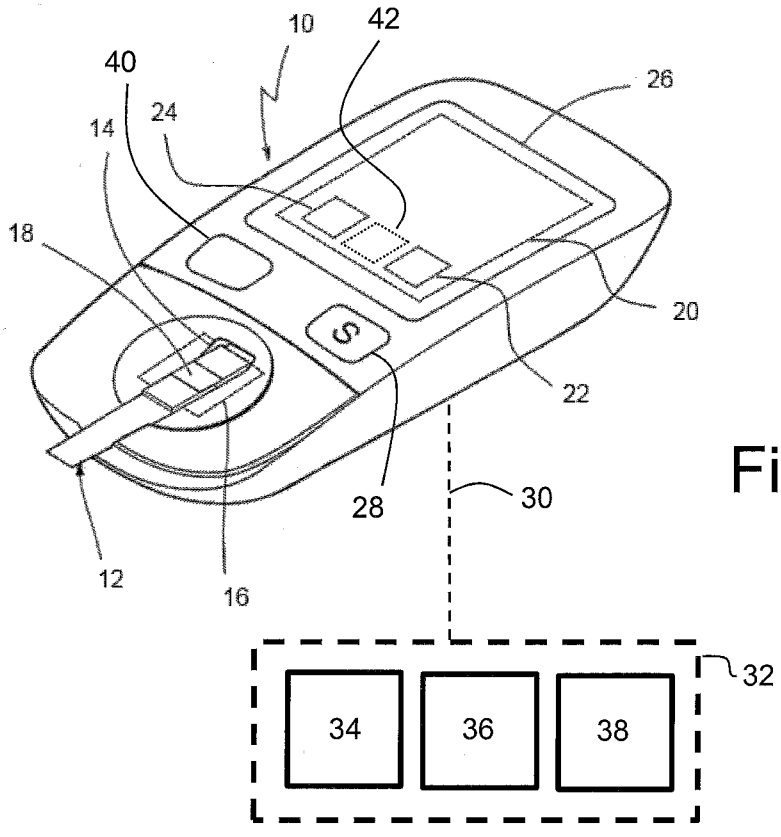
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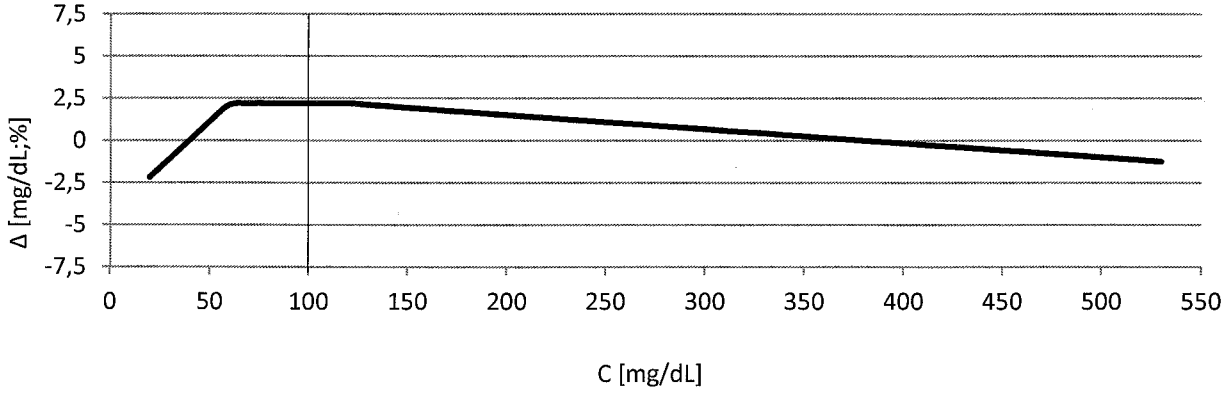
Fig. 1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0
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-5
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Δ [mg/dL;%]
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100
150
200
250
300
350
400
450
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550
C [mg/dL]

Fig. 2

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/075436

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N27/327
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2010/243476 A1 (FUJIWARA MASAKI [JP] ET AL) 30 September 2010 (2010-09-30) paragraphs [0077] - [0078], [0089], [0090], [0096], [0110], [0118] - [0125] figures 1,7,26,27 -----	15-17 1-14,18
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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 December 2013	02/01/2014

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Couteau, Olivier

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Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/075436

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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