**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE PATENT TRIAL AND APPEAL BOARD**

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AGAMATRIX, INC.

*Petitioner*

v.

DEXCOM, INC.

*Patent Owner*

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U.S. PATENT NO. 9,750,460

TITLE: SYSTEMS AND METHODS FOR REPLACING SIGNAL ARTIFACTS IN A GLUCOSE SENSOR DATA STREAM

Case No. IPR2018-01718

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# PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 9,750,460

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| 1018 | J.D. Newman, et al., "Catalytic Materials, Membranes, and Fabrication Technologies Suitable for the Construction of Amperometric Biosensors," *Anal. Chem.* 1995, *67,* 4594-4599. |

| | |
|---|---|
| 1019 | S.J. Updike, et al., "The Enzyme Electrode," *Nature*, June 3, 1967, 214, 986-988. |
| 1020 | *Not used* |
| 1021 | PCT International Publication No. WO 96/00110 ("Tamada") |
| 1022 | *Not used* |
| 1023 | *Not used* |
| 1024 | *Not used* |
| 1025 | U.S. Patent No. 6,284,126 ("Kurnik") |
| 1026 | Joseph Wang, "Glucose Biosensors: 40 Years of Advances and Challenges," *Electroanalysis*, vol. 13, no. 12, pp. 983-88 (2001). |
| 1027 | U.S. Patent No. 5,322,063 ("Allen"). |
| 1028 | U.S. Patent No. 5,607,565 ("Azarnia"). |
| 1029 | R. Sternberg et al., "Covalent Enzyme Coupling on Cellulose Acetate Membranes for Glucose Sensor Development," *Analytical Chemistry*, vol. 60, no. 24 (1988) ("Sternberg"). |
| 1030 | U.S. Patent No. 4,757,022 ("Shults"). |
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| | |
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| 1040 | R. T. Kurnik, et al. "Design and Simulation of a Reverse lontophoretic Glucose Monitoring Device," *J. Electrochem. Soc.*, vol. 145, no. 12, pp. 4119-25 (1998) ("Kurnik-Article") |

Citations in this petition to patents use the column and line number found within the document, rather than the page indicated by the exhibit label. Citations to the remaining exhibits refer to the page number of the underlying document. Emphasis is added, unless noted otherwise.

# PETITION FOR *INTER PARTES* REVIEW

Pursuant to the provisions of 35 U.S.C. § 311 and 37 C.F.R. § 42.100 *et seq.*, Petitioner AgaMatrix, Inc. ("AgaMatrix," or "Petitioner") petitions the Patent Trial and Appeal Board to institute an *Inter Partes* Review ("IPR") of claims 14-18, 20-24, 26-30, 32-36, 38-42, 50-54, 62-66, and 68 ("challenged claims") of United States Patent No. 9,750,460 ("the '460 Patent," Ex. 1001) which is assigned to Dexcom, Inc. ("Dexcom" or "Patent Owner").

## I. INTRODUCTION

The '460 Patent relates generally to systems and methods for processing data received from a glucose sensor. In particular, the challenged claims are directed to glucose sensor systems which employ sensor electronics to apply voltage(s) to an electrochemical glucose sensor, to measure a signal response of the sensor, and to evaluate the severity of an erroneous signal in order to decide whether to accept or discard a glucose measurement.

This was not a new idea before the priority date of the '460 Patent. In fact, multiple prior art references disclose similar electrochemical glucose sensors and related error-detection and error-rejection techniques. Ex. 1003, ¶¶12-14 and 88.

For example, U.S. Patent No. 5,243,516 ("White," Ex. 1006), in combination with PCT International Publication No. WO 99/32881 ("Beaty," Ex. 1007), discloses a biosensor for glucose monitoring that employs sensor electronics

to apply and switch or cycle voltages to an electrochemical cell and to evaluate the resulting glucose current to determine whether it follows a predetermined Cottrell current relationship. If the measured current values deviate substantially from the Cottrell relationship, an error condition is reported and the glucose measurement is be discarded. Beaty teaches generating correction factors to account for various interferences in the glucose current measured with White's biosensor.

U.S. Patent No. 5,497,772 ("Schulman," Ex. 1008) is directed to a glucose monitoring system that continuously measures blood glucose concentration. Schulman also discloses a display unit that displays not only the glucose concentration but also graphs and trends of glucose concentrations over user-selectable periods. Thus, Schulman discloses all the user interface limitations of the claimed sensor.

Since at least these prior art references disclose, teach or suggest all the elements of the challenged claims of the '460 Patent, as shown in this Petition, the cited references render all the challenged claims obvious. Ex. 1003, ¶¶88-89; *see id.*, ¶¶90-119.

## II. TECHNOLOGY BACKGROUND

The technology at issue in the challenged claims relates to electrochemical sensors, specifically glucose sensors, and signal processing. Ex. 1003, ¶¶37-38.

### A. Electrochemical Glucose Measurement

Glucose sensors typically come in two forms: Blood Glucose Meter (BGM) or Continuous Glucose Monitor (CGM), both of which were well known long before the priority date of the challenged claims. In general, BGMs provide episodic measurements of glucose outside the body while CGMs provide continuous monitoring of glucose inside the body. *Id.*, ¶¶39-40.

For each glucose measurement with a BGM device, a patient must prick his/her finger to extract a new blood sample and apply that sample to a single-use test strip inserted into the BGM device. An electrochemical reaction between the blood glucose and the chemicals on the test strip allows the BGM device to analyze the blood sample to determine the amount of glucose in the blood at the time the blood is extracted. *Id.*, ¶¶40-41.

CGMs, on the other hand, monitor glucose levels on a continuous basis and, as such, involve implanting some type of device into the patient's body or attaching a device thereto. Since the CGM sensor device is constantly exposed to a complex environment in or on the patient's body, CGMs typically pick up interferences (*i.e.*, noises) from the body and from other conditions in the body that are not picked up by BGMs. As a result, compared to BGMs, CGMs typically require more signal processing to correct for the extensive interferences that they detect. *Id.*, ¶42.

Glucose levels are typically determined by measuring the concentration of an analyte in a chemical reaction based on electrochemistry. When a voltage is applied between two electrodes in a solution containing glucose (*e.g.*, a blood sample) and the required chemicals, electrochemical reactions at the electrodes may result in the consumption or release of electrons. These reactions cause the generation of electric current in an external circuit. It has long been discovered that, when a potential is applied to the electrodes in a solution containing an electroactive compound, such electric current is diffusion-limited and its decay over time generally follows the Cottrell relation in absence of significant errors. Such current can therefore indicate the analyte, e.g., glucose, concentration in the chemical reaction. *Id.*, ¶¶43-57.

This type of electrochemical glucose sensing method—applying a voltage across electrodes in an analyte solution to measure the resulting Cottrell current—and sensor devices implementing such a method—were well known in the art since at least the 1980s. *See*, *e.g.*, Ex. 1009, European Patent Application 0 230 472 ("Nankai") (disclosing amperometric techniques for determining glucose concentration); Ex. 1010, PCT International Publication No. WO 89/08713 ("Pottgen") (same). *Id.*, ¶58.

### B. Error-Detection & Error-Rejection

Similarly, signal processing techniques, especially the concept of error-detection and error-rejection (*i.e.*, "keeping good data and rejecting bad data"), were generally known to those having ordinary skill in the art. *Id.*, ¶¶59-60. In particular, it was desirable and well known to detect signal errors and/or noises so as to reject measurements when the errors or noises are too severe. Indeed, various methods for screening and rejecting noisy or erroneous signals were well known, well understood, and applied in the glucose sensing art. *Id.*, ¶60.

For example, U.S. Patent No. 6,558,351 ("Steil," Ex. 1012), which is also in the field of glucose sensors, teaches evaluating measurement data against noise thresholds and discarding the data "if more than three values are outside of the noise thresholds." Steil, 23:24-33. Likewise, U.S. Patent No. 4,832,034 ("Pizziconi," Ex. 1013) teaches using a microprocessor in a glucose sensor to "discard artifacts" and "to automatically measure and compensate for temperature changes." Pizziconi, 23:58-65. *See also* U.S. Patent No. 6,309,884 ("Cooper," Ex. 1014), 9:3-50 (disclosing a number of error analysis methods which reject the entire glucose measurement session when the data meet certain criteria); U.S. Patent No. 6,153,069 ("Pottgen-069," Ex. 1015), 4:42-65 (disclosing the use of a calibration curve to identify abnormal amperometric glucose measurements that deviate from the expected Cottrell relationship). *Id.*, ¶61.

## III. OVERVIEW OF THE ’460 PATENT

### A. Prosecution History

The ’460 Patent issued from U.S. Patent Application No. 15/488,190, filed April 14, 2017, which is a continuation of U.S. Patent No. 9,649,069 (“the ’069 Patent”). The ’069 Patent, in turn, is a continuation patent in a line of continuations, tracing back to U.S. Patent Application No. 10/648,849, filed on Aug. 22, 2003 (now U.S. Patent No. 8,010,174).

On April 20, 2017, the applicant submitted two Information Disclosure Statements citing over 1,200 references.

On June 15, 2017, the applicant filed a preliminary amendment, canceling original claim 1-20, adding new claims 21-89, and making remarks on patent eligibility under Section 101. Ex. 1002, pp. 220-52. The applicant also filed, and received approval of, an electronic terminal disclaimer with respect to U.S. Patent Application No. 15/481,347. Ex. 1002, pp. 212-19.

On July 6, 2017, a Notice of Allowance was issued and, on July 26, 2017, a Corrected Notice of Allowance was issued to correct some informalities in the claims. Ex. 1002, pp. 253-54 and pp. 385-88.

The ’460 Patent issued on Sept. 5, 2017. Ex. 1001.

### B. Summary of the Disclosure

The ’460 Patent is directed to systems and methods for processing data

received from glucose sensors, specifically continuous glucose monitors. FIG. 1 illustrates such a glucose sensor 10:

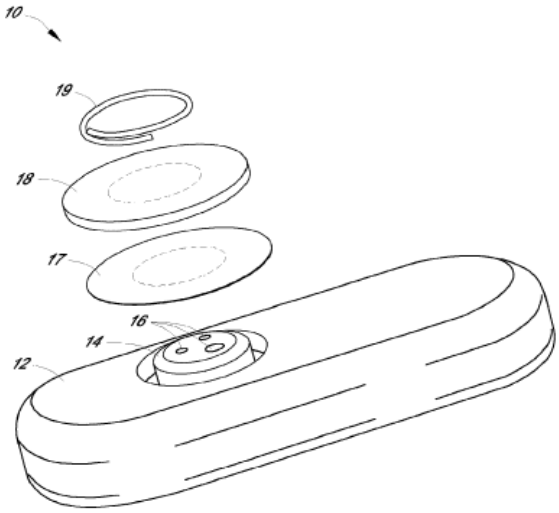



FIG. 1

Ex. 1001, FIG. 1.

The glucose sensor 10 includes three electrodes 16. *Id*. at 20:21-30. An enzyme, glucose oxidase, contained in the sensing membrane 17 "catalyzes the conversion of oxygen and glucose to hydrogen peroxide and gluconate[.]" *Id.* at 20:45-51.

Electronics connected to the electrodes measure the amount of hydrogen peroxide ($H_2O_2$) and this correlates to the amount of glucose in the sample, which is consistent with the prior art electrochemical glucose sensing method described above. *Id*. at 20:43-21:5.

The preferred embodiment disclosed in the '460 Patent is a continuous glucose monitor (CGM)—*i.e.*, a "system [that] monitors a data stream from a

glucose sensor." *Id*, Abstract. *See also id.*, 16:1-6 (defining CGMs). Because CGMs are implanted in or maintain constant contact with the body, they capture interferences from the body, causing significant signal errors. The CGM of the '460 Patent purports to detect signal errors and make appropriate corrections. Figure 7A is a graph of a raw data stream, that includes a signal artifact/erroneous signal (as shown at region 74a), from a glucose sensor spanning about four hours:

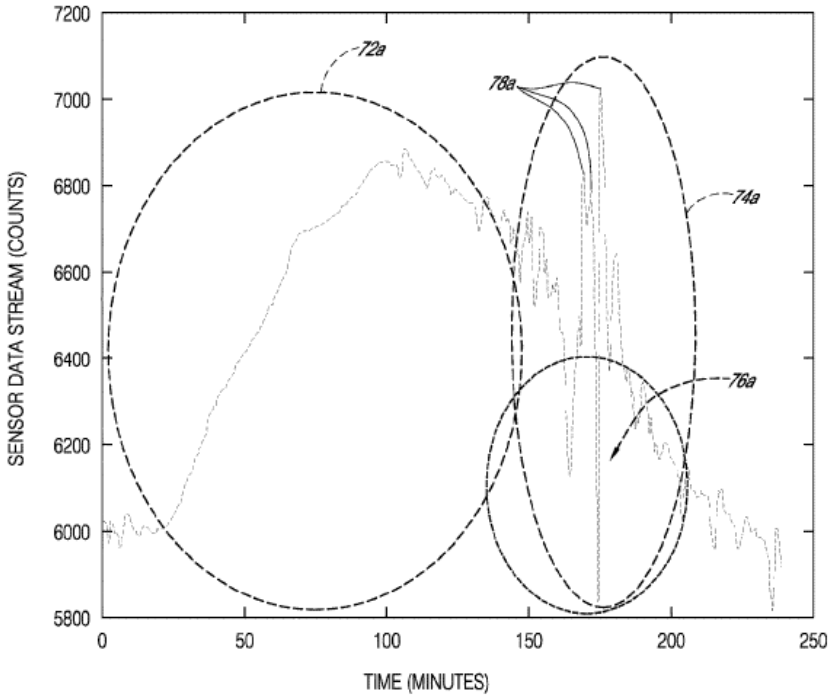



FIG. 7A

Ex. 1001, FIG. 7A.

The specification of the '460 Patent is limited to a virtually exclusive description of CGM embodiments, but the patent nevertheless states:

> ***The glucose sensor can be any device capable of measuring the concentration of glucose.*** One exemplary embodiment is

> described below, which utilizes an implantable glucose sensor. However, it should be understood that ***the devices and methods described herein can be applied to any device capable of detecting a concentration of glucose and providing an output signal that represents the concentration of glucose***.

Ex. 1001, 20:13-20.

Thus, the inventors of the '460 Patent do not even say or suggest that they invented any new type of electrochemical sensor or a new sensing technique. Instead, they allege describing a robust error detection and correction technique. That technique, however, was also not novel or unobvious, as discussed below. Just as electrochemical glucose sensors had been known for decades before 2003, the sources introducing errors in the sensor signal, and techniques for detecting and correcting those errors, had also been well known for decades prior to 2003, as the references discussed below demonstrate.

### C. Challenged Claims

The claims at issue in this Petition are claims 14-18, 20-24, 26-30, 32-36, 38-42, 50-54, 62-66, and 68, among which claims 14, 20, 26, 32, 38, 50, and 62-66, and 68 are independent claims.

Claim 14 reads:

| |
|---|
| [14.preamble] A glucose sensor system, the system comprising: |
| [14.a] an electrochemical glucose sensor configured to be in contact with a |

biological fluid to obtain a glucose measurement, wherein the electrochemical glucose sensor comprises a first electrode, a second electrode, and an enzyme-containing film, wherein the first electrode comprises an electrode surface; and

[14.b] sensor electronics comprising a processor for executing computer program code stored in a memory to cause the processor to:

[14.c] apply a voltage to the electrochemical glucose sensor, wherein applying the voltage comprises at least one process selected from the group consisting of switching, cycling, and pulsing a voltage applied to the electrochemical glucose sensor;

[14.d] measure a signal response of the electrochemical glucose sensor responsive to the applying,

[14.e] detect an erroneous signal based at least in part on the signal response of the electrochemical glucose sensor to the applying,

[14.f] wherein the erroneous signal is associated with at least one condition selected from the group consisting of an ischemia, a pH, a temperature associated with the electrochemical glucose sensor, a biochemical species, an available electrode surface area, a local environment associated with the electrode surface of the first electrode, a diffusion transport of glucose or a measured species, and a pressure or a stress associated with the electrochemical glucose sensor,

[14.g] determine a value associated with a severity of the erroneous signal, and

[14.h] discard a glucose measurement when the value associated with the severity of the erroneous signal is outside of a predetermined threshold value.

Each of independent claims 20, 26, 32, 38, and 50 includes substantially the same limitations as independent claim 14 except that: (1) the "wherein" clauses in

the "detect" step of those other independent claims each recites a single condition instead of a list of conditions as in claim element [14.f]; and (2) some of those other independent claims do not recite "wherein the first electrode comprises an electrode surface."

Independent claims 62-66 and 68 recite substantially the same limitations as independent claims 14, 20, 26, 32, 38, and 50 respectively, except that each of claims 62-66 and 68 adds a step of "generate a glucose value for display when the value associated with the severity of the erroneous signal satisfies a predetermined threshold value" and further includes more "user interface" functions.

The limitations of the independent claims may be sorted into hardware elements (i.e., electrochemical sensor and circuitry for its operation) and software elements (i.e., various signal analysis/processing and display operations).

As noted above, the universal applicability of the patent disclosure (as claimed in the specification) suggests that the combination of hardware elements is not novel or inventive. Indeed, those recited hardware elements are generic to any electrochemical glucose sensor device and were well known in the art.

Furthermore, the recited software elements (or functional steps) involve nothing more than basic operations of an electrochemical glucose sensor and the well-known signal processing concept of error-detection and error-rejection—that is, generating and displaying a glucose value only if a signal error is not too severe.

Thus, the claimed invention is really directed to a broad concept of "keeping good data and rejecting bad data" that is applied to conventional glucose sensors, i.e., an idea that is basic and fundamental to any signal processing system. As shown below, all these claimed hardware elements, their operations, and the recited signal processing operations were conventional, routine, and well-known prior to 2003.

## IV. STATEMENT OF THE RELIEF REQUESTED

### A. Claims for Which Review is Requested and the Statutory Grounds of Challenge

Petitioner respectfully requests that the Board institute an IPR of claims 14-18, 20-24, 26-30, 32-36, 38-42, 50-54, 62-66, and 68 of the '460 Patent and cancel those claims as unpatentable under pre-AIA 35 U.S.C. § 103, based on one or more of the following grounds:

| ***Ground*** | ***Statute*** | ***References*** | ***Claims*** |
|---|---|---|---|
| 1 | § 103 | White, Beaty | 14-18, 20-24, 26-30, 32-36, 38-42, and 50-54 |
| 2 | § 103 | White, Beaty, Schulman | 62-66, and 68 |

The grounds for unpatentability rely on the following references, which qualify as prior art under pre-AIA 35 U.S.C. § 102:

| ***Exhibit.*** | ***Prior art*** | ***Filing/Issued/Publication Date*** | ***Statute*** |
|---|---|---|---|
| 1006 | U.S. Patent No. 5,243,516 | Filed Dec. 15, 1989 | 102(a)/(b) |

| | | | |
|---|---|---|---|
| | ("White") | Issued Sept. 7, 1993 | |
| 1007 | PCT International Publication No. WO1999032881 ("Beaty") | Filed Dec. 21, 1998<br>Published July 1, 1999 | 102(a)/(b) |
| 1008 | U.S. Patent No. 5,497,772 ("Schulman") | Filed Nov. 19, 1993<br>Issued Mar. 12, 1996 | 102(a)/(b) |

Petitioner's arguments here were not considered by the Examiner, and Petitioner presents additional evidence not considered by the PTO, including the declaration of John L. Smith, Ph.D. (Ex. 1003). Dr. Smith has over 55 years of experience in electrochemical analytical instruments and systems, including 30 years in the glucose monitoring field. He worked at the LifeScan (diabetes care) division of Johnson & Johnson, as Vice President of Research, Development, and Engineering (and Chief Science Officer), for twelve years. Since his retirement from Johnson & Johnson, he has consulted for more than 40 blood glucose companies or their investors. From his extensive experience in the field, Dr. Smith has unparalleled knowledge of the glucose monitoring technology and its development history.

The Schulman (Ex. 1008) patent was among the more than 1,200 references disclosed to the Patent Office (which include seven Berner patents and applications) in an Information Disclosure Statement, which contained no explanation regarding the references and provided the examiner with no guidance regarding which of the more than 1,200 cited reference were most pertinent to the claimed inventions. Ex. 1002 at 230-298, 305-309. The prosecution history

confirms that neither patent was discussed by the examiner and there is no evidence in the prosecution history regarding how closely these two references out of the 1,200 cited references were analyzed by the examiner, if at all. *See* Ex. 1002, pp. 207, 262, 212-54, and 385-88.

The rest of the identified prior art references were not before the Patent Office and therefore never considered during prosecution.

### B. Level of Ordinary Skill

As explained by Dr. John L. Smith ("Dr. Smith"), who is an expert in this field, a person of ordinary skill in the art ("POSITA") at the time of the alleged invention would have had the equivalent of either (i) a bachelor's or master's degree in biology, chemistry, physics, electrical engineering, or related fields, and at least five years of experience developing glucose sensors or other biosensensors; or (ii) a Ph.D. with at least two years of experience in the same fields. Additional graduate education could substitute for professional experience, and significant work experience could substitute for formal education. Ex. 1003, ¶¶33-36 .

## V. CLAIM CONSTRUCTION

In an *inter partes* review, the claim terms should be given their plain meanings according to the broadest reasonable interpretation in light of the

specification.[1] *See Cuozzo Speed Technologies, LLC v. Lee*, 136 S.Ct. 2131 (2016).

In the related ITC proceeding (Investigation No. 337-TA-1075), the parties agreed on the interpretation of some claim terms, the judge construed some of the disputed terms, and Patent Owner offered "plain and ordinary meaning" interpretation of other disputed terms. Those terms, to the extent relevant to the challenged claims, are listed below with their definitions and indication of their sources. Petitioner believes that the broadest reasonable interpretation of the below-listed claim terms is *at least as broad as* the listed definitions.

| Claim Term | Definition | Source[2] |
|---|---|---|
| electrochemical glucose sensor | a device by which glucose can be quantified in which chemical energy is converted to electrical energy | Parties |
| enzyme-containing film | a thin layer that includes an enzyme | Pat. Owner |
| apply a voltage to the electrochemical glucose | put to use a voltage to the | ITC judge |

[1] Petitioner reserves the right to present different constructions in other forums (e.g., a district court, or the International Trade Commission) where a different claim construction standard applies.

[2] *See* Ex. 1016 at 14-15 ("Construction of the Agreed-Upon Claim Terms"); *id*. at 24, 28, 30, 37, 40 (judge-ordered definitions of disputed claim terms); Ex. 1017 (Dexcom's Petition for Review of ID) at 41-43, 50.

| Claim Term | Definition | Source[2] |
|---|---|---|
| sensor | electrochemical glucose sensor | |
| switching, cycling, and pulsing a voltage | changing a voltage, periodically repeating a voltage, and abruptly changing a voltage for a brief interval | ITC judge |
| erroneous signal | signal that is not indicative of the glucose level | ITC judge |
| generate an estimated glucose concentration value when the severity associated with the signal artifact is evaluated to be under a predetermined threshold | to generate an estimated glucose concentration value for display to a user when the severity related to the signal artifact (as defined herein) is evaluated by the sensor electronics to be less than a predetermined threshold value | Parties |
| a voltage response of the electrochemical glucose sensor | voltage responsive to a condition of the electrochemical glucose sensor | ITC judge |
| available electrode surface area | surface area of an electrode where an electrochemical reaction occurs | Parties |

## VI. DETAILED GROUNDS FOR UNPATENTABILITY

### A. Ground 1: Claims 14-18, 20-24, 26-30, 32-36, 38-42, and 50-54 are obvious under 35 U.S.C. § 103 in light of White and Beaty.

The combination of U.S. Patent No. 5,243,516 to White ("White," Ex. 1006) in view of PCT International Publication No. WO 99/32881 by Beaty et al. ("Beaty," Ex. 1007) renders each of claims 14-18, 20-24, 26-30, 32-36, 38-42, and 50-54 obvious. Ex. 1003, ¶305.

### 1. Independent Claim 14

#### *i. White discloses the preamble.*

To the extent that the preamble is limiting, White discloses a "glucose sensor system." Ex. 1003, ¶306. Specifically, White discloses "a ***biosensing instrument*** for quantitatively determining the concentration of an analyte in a fluid sample, and more particularly, to a method and ***apparatus for*** amperometrically ***determining the concentration of biological compounds, such as glucose,*** *cholesterol, etc.,* ***in a body fluid such as blood***." White, 1:5-11; Ex. 1003, ¶306.

#### *ii. White discloses "an electrochemical glucose sensor configured to be in contact with a biological fluid to obtain a glucose measurement, wherein the electrochemical glucose sensor comprises a first electrode, a second electrode, and an enzyme-containing film, wherein the first electrode comprises an electrode surface" (Element [14.a]).*

**<u>Part 1 of Element [14.a]:</u> "[A]n electrochemical glucose sensor configured to be in contact with a biological fluid to obtain a glucose measurement"**

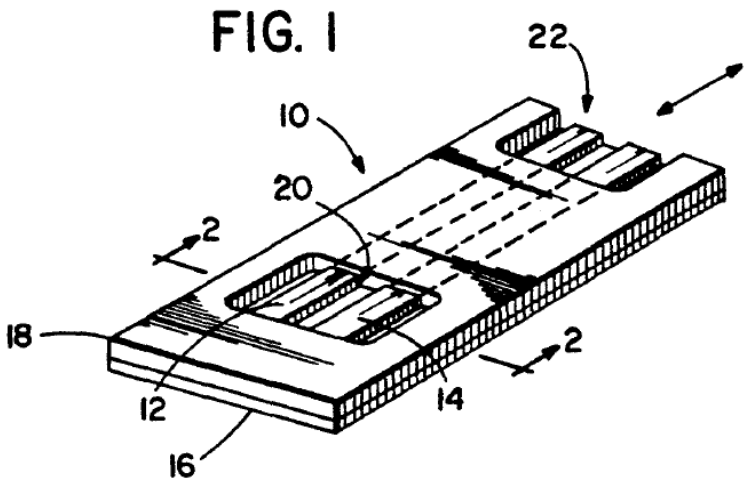
White discloses this feature because White's sensor "amperometrically determin[es] the concentration of biological compounds, such as glucose, cholesterol, etc., in a body fluid such as blood," White, 1:7-11, and "amperometric" is a term describing a form of electrochemistry. Ex. 1003, ¶¶307-309. White's "biosensing" system includes a "test cell 10" having a pair of electrodes and a reaction zone or a well for electrochemical reaction, so the test cell 10 is *an electrochemical glucose sensor*, and White's biosensor determines

whether the measured current varies according to a predetermined Cottrell current relationship. *See* White, 2:62-3:4; Ex. 1003, ¶309. Specifically, White discloses:

> A biosensing system is described which ***determines whether a measured current is varying in accordance with a predetermined Cottrell current relationship***. The ***system includes a test cell with at least a pair of electrodes which extend into a reaction zone***, which reaction zone includes analyte reactants. An analog signal detector, in combination with a microprocessor, take plurality of current measurements between the electrodes over a plurality of succeeding measurement times, after a sample is placed in contact with the analyte reactants in the reaction zone.

White, 2:62-3:4.

White also discloses that the test cell (i.e., *the electrochemical glucose sensor*) is placed in contact with a biological fluid to obtain a glucose measurement because White states that a sample of a body fluid is placed in the reaction zone of the test cell. White, 3:35-46 ("Referring now to FIG. 1, a pluggable test cell 10 includes a pair of electrodes 12 and 14" that "are sandwiched between a pair of polymeric sheet materials 16 and 18 with sheet material 18 having openings 20 and 22 that expose the electrodes. ***Opening 20 creates, in effect, a reaction zone or 'well' wherein a sample of body fluid can be emplaced to enable a reaction to occur.***"); FIG. 1; Ex. 1003, ¶310.




**<u>Part 2 of Element [14.a]:</u> "[W]herein the electrochemical glucose sensor comprises a first electrode, a second electrode, and an enzyme-containing film"**

White's "test cell 10," (i.e., the *electrochemical glucose sensor*) includes a working electrode and a reference electrode (i.e., *first and second electrodes*). Ex. 1003, ¶311. Specifically, White states:

> A biosensing system . . . includes a test cell with ***at least a pair of electrodes*** which extend into a reaction zone[.] * * *
>
> Referring now to FIG. 1, a pluggable test cell 10 includes a pair of ***electrodes 12 and 14***. Electrode 12 is termed the ***"working" electrode*** and is preferably comprised of platinum, palladium, or other noble metal. Electrode 14 is a ***reference electrode*** and is preferably comprised of silver/silver oxide or silver/silver chloride.

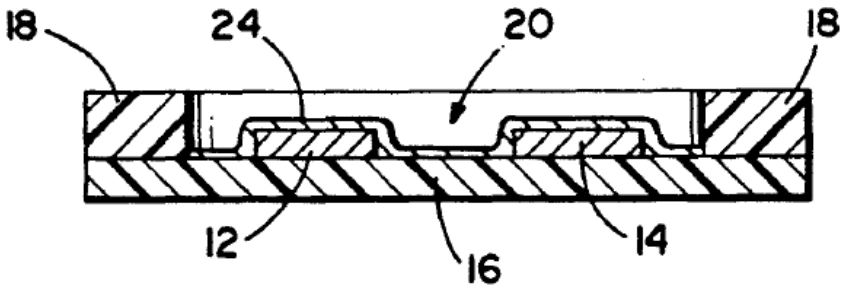
White, 2:62-3:4, 3:35-41; FIG. 1.

In addition, White's test cell 10 also includes a "reaction layer 24" that "includes an enzyme [and] certain film formers" such as gelatin. White states:

> In FIG. 2, a section of test cell 10 is shown. During manufacture, a reaction layer 24 is emplaced in well 20 and provides the reactants for the biosensing reaction. ***If the instrument is to be used for glucose concentration determinations, layer 24 will include an enzyme***, an electrolyte, a mediator, ***certain film formers***, and a buffer. For instance, the ***enzyme may be glucose oxidase*** . . . the mediator is preferably potassium ferricyanide and the ***film formers comprise gelatin*** and propiofin.

White, 3:50-61; FIG. 2; Ex. 1003, ¶312.

FIG. 2




Because an enzyme and a film former are included in the reaction layer 24, the reaction layer 24 is an "*enzyme-containing film.*" Ex. 1003, ¶313.

**<u>Part 3 of Element [14.a]:</u> "[W]herein the first electrode comprises an electrode surface"**

White discloses this limitation because electrodes 12 and 14 both are depicted as strips, where the strips have a top surface exposed to the reaction layer 24. *See* White, FIGS. 1 and 2; Ex. 1003, ¶314.

FIG. 1

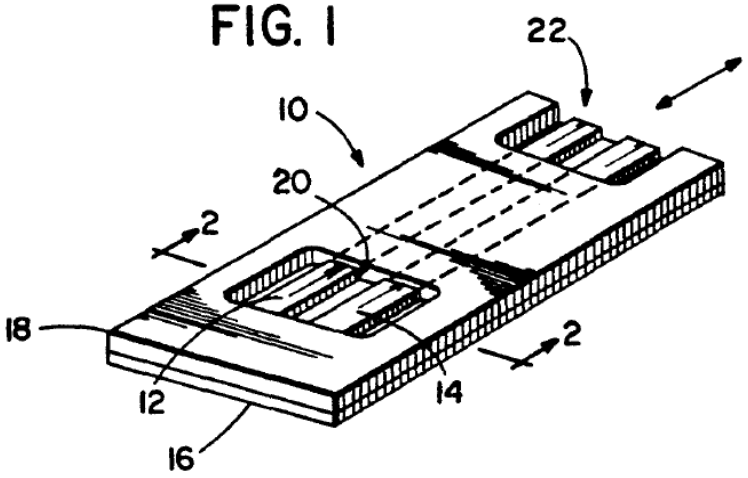
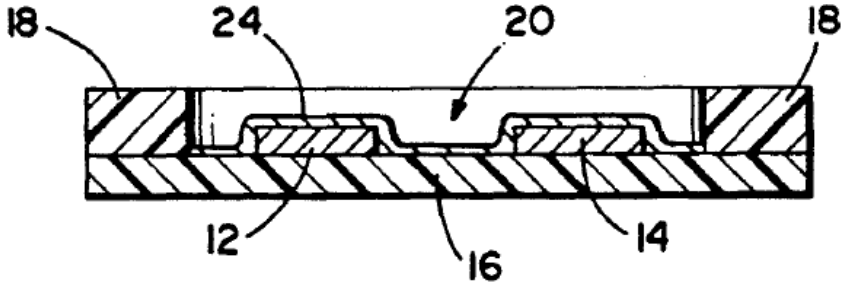



FIG. 2

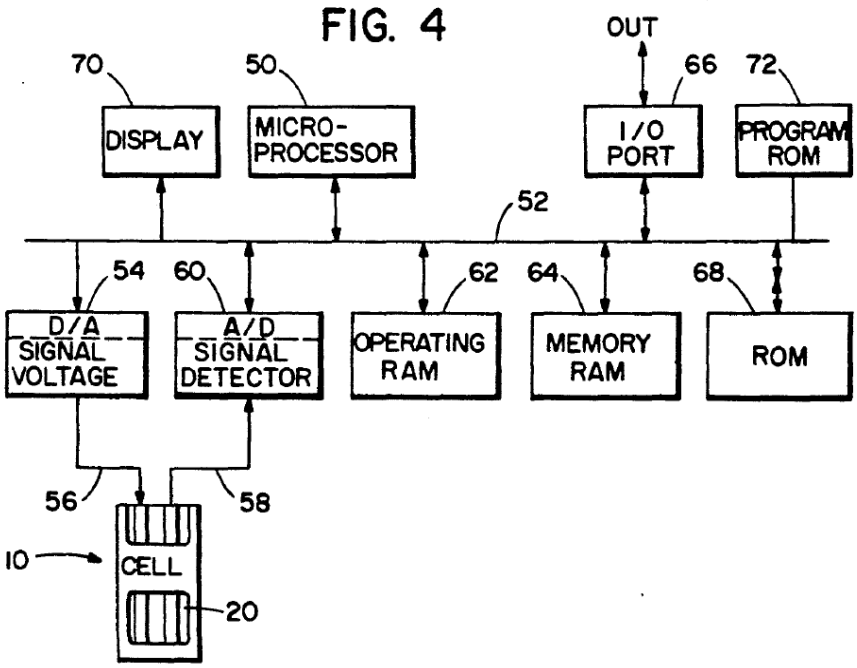



Therefore, White discloses Element [14.a]. Ex. 1003, ¶315.

***iii. White discloses "sensor electronics comprising a processor for executing computer program code stored in a memory to cause the processor to [perform certain recited functions]" (Element [14.b]).***

White discloses this claim element because White discloses a "microprocessor," and software (i.e., *computer program code*) stored in a ROM

(i.e., memory), where the software operates the microprocessor (i.e., *causes the processor to perform certain functions*). Ex. 1003, ¶¶316-317. Specifically, White states: "Turning now to FIG. 4, a high level block diagram of the biosensing instrument is illustrated. Overall system control emanates from ***microprocessor 50*** via system bus 52." White, 5:26-29. White also discloses "[p]rogram ROM 72 [that] contains the software to operate the microprocessor." White, 5:59-60; FIG. 4.




Therefore, White discloses Element [14.b]. Ex. 1003, ¶318.

***iv. White and Beaty individually and in combination disclose "apply a voltage to the electrochemical glucose sensor, wherein applying the voltage comprises at least one process selected from the group consisting of switching, cycling, and pulsing a voltage applied to the electrochemical glucose sensor" (Element [14.c]).***

As discussed below, White and Beaty describe at least three ways in which a voltage is applied to an electrochemical glucose sensor, where the applied voltage is changed by: changing the DC voltage value (Case 1); changing the frequency of an AC voltage (Case 2); and by switching from an AC voltage that is applied first, to a DC voltage that is applied subsequently (Case 3). Ex. 1003, ¶¶319-320.

**Case 1:**

White teaches this claim element because White discloses ***first applying*** an "autodrop" voltage to the test cell, for detecting the presence of a blood sample, and ***then switching*** the voltage to a "measurement voltage" for measuring the current. *Id.*, ¶321. In particular, White describes:

> Initially, cell 10 is plugged into the instrument, and the user depresses a key (not shown) to indicate that the test is about to begin. ***Microprocessor 50 then causes signal voltage module 54 to apply an 'autodrop' potential to the cell via line 56.*** Then, when a sample or 'drop' of blood is placed in well 20, an immediate spike of current occurs, indicating the presence of the blood sample, and is sensed by a signal detector module 60. * * *
>
> At this point, the forward reaction commences and continues until completion (e.g. some 20 seconds). At the end of the forward reaction time, ***microprocessor 50 causes signal voltage module 54 to apply a measurement potential to cell 10*** to commence the reverse reaction.

White, 6:5-24; FIG. 3. Changing the applied voltage from the "autodrop" potential to the "measurement potential" constitutes switching the applied voltage. Ex. 1003, ¶321.

**Case 2:**

Beaty teaches applying an AC voltage signal to electrochemical cells, and explicitly identifies White's biosensor. *See* Beaty, p. 11, ll. 20-23 ("Referring to Fig. 2, a strip connector 30 of the general type ***illustrated in U. S. Patents: 5,243,516 [i.e., White]***; 5,288,636; 5,352,351; 5,385,846; and, 5,508,171, ***makes contact between a disposable amperometric sensor cell or biosensor 31 of the general type illustrated in those patents and the instrument 32***."); Ex. 1003, ¶322.

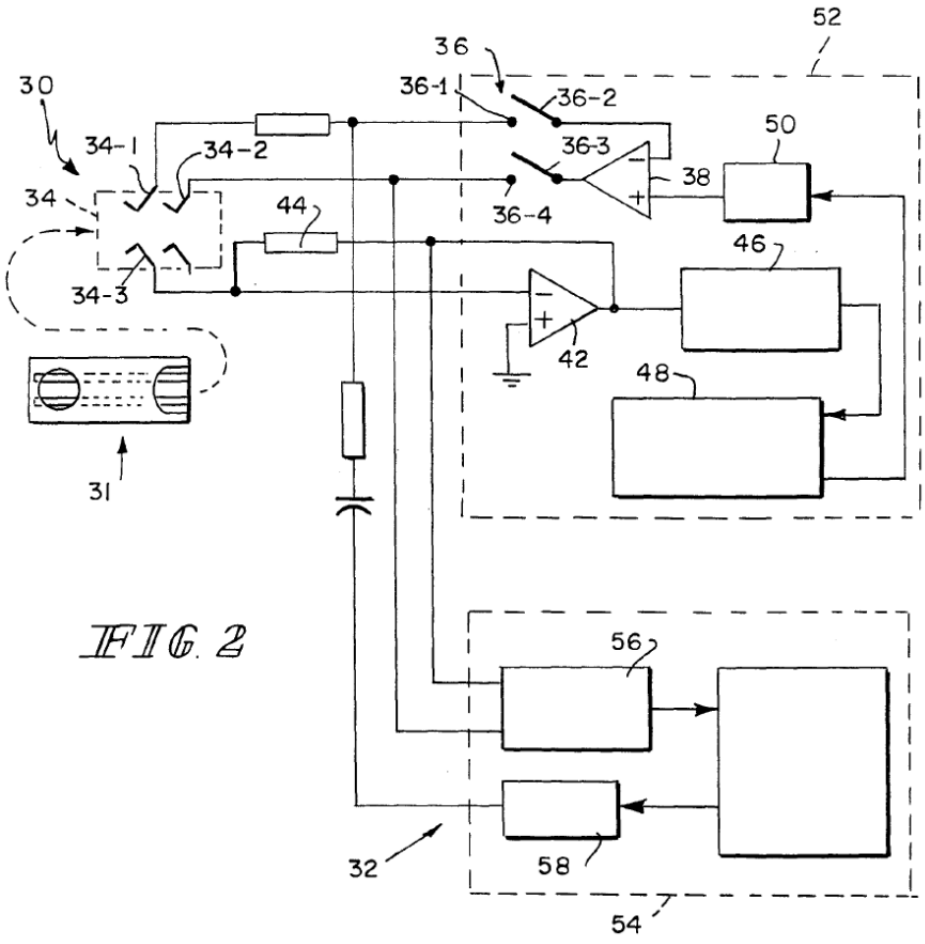



FIG. 2

Additionally, Beaty states:

> ***The calculations of the real and imaginary components of the AC impedance of the biosensor cell 31*** coupled to terminals 34-1, -2 and -3 ***are made by exciting terminal 34-2 of connector 34 at the desired frequency***, for example, 1300Hz or 10 KHz[.]

Beaty, p. 12, l. 31 – p. 13, l. 6.

An AC excitation continuously and periodically cycles (at the selected frequency) through a number of voltages. As such, the application of the AC

excitation signal at a selected frequency is "cycling" the applied voltage. Ex. 1003, ¶¶323-324.

Moreover, Beaty also discloses switching the applied excitation voltage during the determination of the glucose-measurement errors caused by the effect of temperature and interferents. *Id.*, ¶325. In particular, Beaty discloses ***first applying*** a voltage at one particular frequency to determine adequacy (or type) of sample volume and ***then applying*** a voltage at a different frequency (i.e., *switching the applied voltage*) to determine the effect of temperature and/or the hematocrit concentration of the sample on the glucose measurement. *See* Beaty, p. 8, l. 23 – p. 9, l. 13; Ex. 1003, ¶325. Specifically, Beaty describes:

> We have determined, for example, that ***at about 1300Hz***, . . . ***sample volume and sample identity have relatively substantially greater, fairly readily ascertainable, effects on AC impedance***. * * *
>
> We have determined that ***the combined effect of sample temperature and hematocrit can fairly effectively be isolated*** from other physical and chemical interferrents [sic] of interest ***using frequencies in the range of from about 2KHz to about 10KHz***. So, for example, ***once the adequacy of the sample volume for test has been established, a 2KHz signal can be applied to the biosensor*** and the real and imaginary components of impedance of the biosensor/sample system can be determined.

Beaty, p. 8, l. 23 – p. 9, l. 13.

**Case 3:**

Beaty states explicitly that its technique can be applied to White's biosensor prior to the amperometric measurement phase (that White describes). Ex. 1003, ¶326. Specifically, Beaty states that "we have determined that in biosensors of the type described in ***U. S. Patents: 5,243,516 [i.e., White]*** it is possible to employ a low-magnitude, for example, less than about 40mV rms or so, AC signal in the range of less than about .1Hz to 10KHz or so with no DC offset ***to compensate for sample temperature, hematocrit, bilirubin concentration***, uric acid concentration and oxygen concentration, ***and to determine identity of the sample*** with which the biosensor is dosed, ***and adequacy of dosed blood sample volume*** for a test for glucose concentration." Beaty, p. 8, l. 23-31; Ex. 1003, ¶326.

Beaty further states that using various AC signal "determinations" of adequacy and type of sample and/or effect of interferents such temperature and/or hematocrit "are made ***before*** the amperometric determination of the glucose concentration of the blood sample. DC offset may be avoided, if necessary, to reduce the likelihood of affecting the amperometric determination of the glucose concentration which, it must be remembered, is going to be conducted subsequently[.]" Beaty, p. 9, l. 19-23; Ex. 1003, ¶327.

Thus, Beaty expressly teaches and, hence, one of ordinary skill would have understood, that the step of applying a measurement voltage that White describes,

*see* White 6:21-24 (stating that "[a]t the end of the forward reaction time, ***microprocessor 50 causes signal voltage module 54 to apply a measurement potential to cell 10*** to commence the reverse reaction"), may be performed after one or more AC signals that Beaty describes are applied. Ex. 1003, ¶328. As such, the combination of White and Beaty teaches applying one or more AC voltage signals prior to applying the DC measurement potential and then switching the applied voltage to the measurement potential. *Id.*

Therefore, according to Cases 1-3, White and Beaty individually and in combination disclose Element [14.c]. *Id.*, ¶329.

***v. White and Beaty each discloses "measure a signal response of the electrochemical glucose sensor responsive to the applying" (Element [14.d]).***

**Case 1:**

White discloses this limitation because White teaches measuring a current response of the test cell ***after*** a measurement potential is applied. Ex. 1003, ¶¶330-331. For example, White states: "When the forward reaction has proceeded to completion, ***a subsequent application of a voltage across terminals 12 and 14 will see the creation of a small current therebetween*** that results from the reverse reaction of potassium ferrocyanide back to potassium ferricyanide. ***The flow of electrons during the reverse reaction is sensed and measured and has been***

***found to bear a known relationship to glucose concentration levels***." White, 4:7-15.

White also states: "At the end of the forward reaction time, ***microprocessor 50 causes signal voltage module 54 to apply a measurement potential to cell 10*** to commence the reverse reaction. Again, there is an initial surge of current which is ignored by the measurement circuitry. ***At the end of the surge time (e.g., t0), an initial current measurement is taken, followed by subsequent measurements at subsequent intervals (e.g. t1, t2, t3 . . . )***." White, 6:21-29. White describes a similar process of current measurement with reference to FIGS. 5 and 6. *See* White, 6:56-7:18; FIGS. 5 and 6; Ex. 1003, ¶¶332-333.

FIG. 5

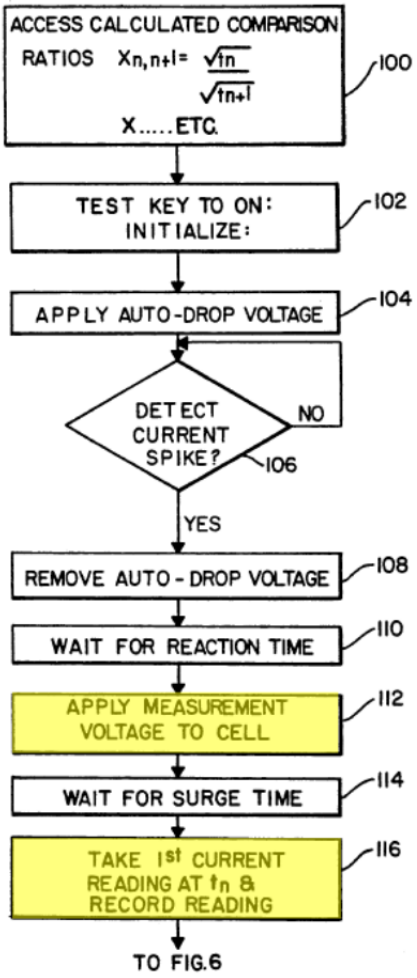
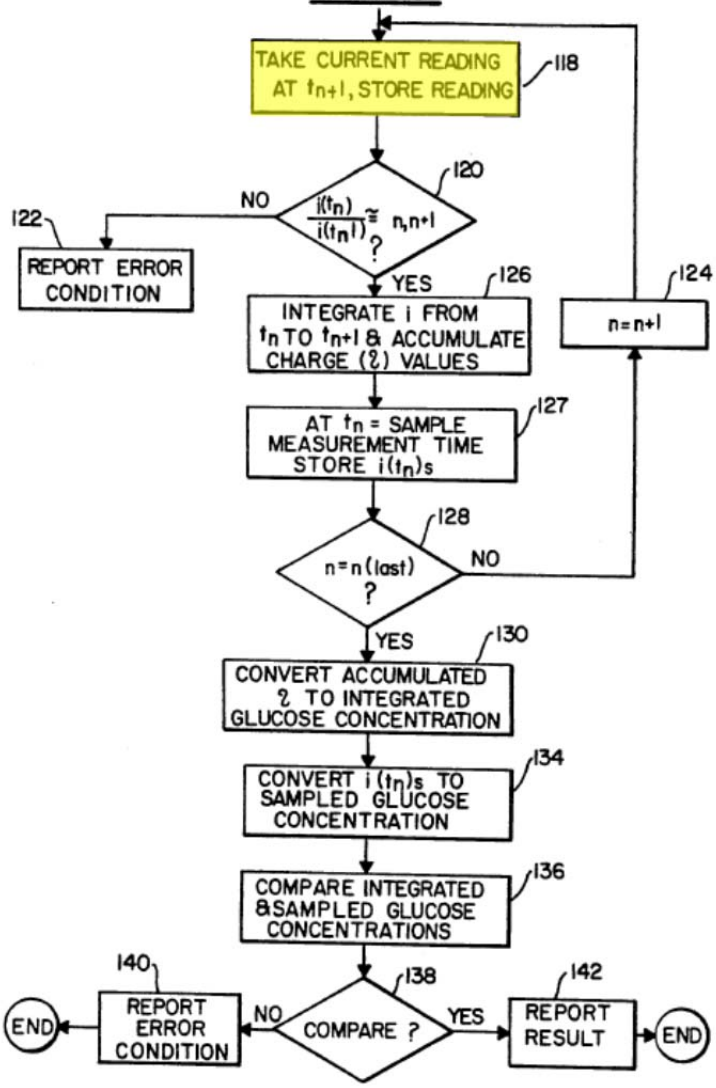



FIG. 6




**Case 2:**

Beaty also teaches this limitation because Beaty describes indirectly measuring a first current signal (using a voltage signal output by the biosensor) in response to applying an AC excitation at a first frequency, and also describes measuring a second current signal from the biosensor in response to switching the

applied AC excitation signal to a second, different frequency. Ex. 1003, ¶334.

Beaty states:

> A sample of blood is applied to the biosensor 31. Immediately after the instrument 32's electronics detect the deposit of the droplet on the biosensor 31, ***an AC signal having a frequency of, for example, 1300Hz is applied across terminals 34-2—34-3 of connector 34 and the resulting current is indirectly sampled by µP 54 by measuring the excitation and response voltages and using the scale factor to obtain current.*** * * * If there is sufficient volume to continue with the glucose determination, ***an AC signal at another frequency, for example, 10 KHz, is applied across terminals 34-2—34-3 of connector 34 and the resulting current is sampled by µP 54.***

Beaty, p. 15, ll. 2-15.

Therefore, White and Beaty each discloses Element [14.d]. Ex. 1003, ¶335.

***vi. White and Beaty each discloses "detect an erroneous signal based at least in part on the signal response of the electrochemical glucose sensor to the applying" (Element [14.e]).***

White describes:

> [I]f the blood sample does not totally cover the sensing electrode surfaces, an erroneous reading results. Furthermore, if the reaction area becomes hydrated, either prior to or during the test, an erroneous reading occurs. Likewise, if there is leakage along the length of the electrodes so that the blood sample covers not only the portion of the

> electrodes in the reaction zone, but also outside of the reaction zone, again, erroneous readings will occur.

White, 2:41-49; *see id.*, 4:28-51 (describing, in addition, that the presence of contaminants between the electrodes can also cause an error).

White also states: "These errors appear as baseline shifts in the Cottrell current or modulations of area during the measurement period." White, 2:49-51. Specifically, White describes determining whether certain ratios computed from the measured current are similar to the corresponding predetermined ratios and, if "the ratios are not 'similar,'" concluding "that the measured values of current are not following a predetermined Cottrell current relationship." White, 6:6-7:17; FIGS. 5 and 6; Ex. 1003, ¶¶336-338. Measuring the current response and determining whether or not the current follows the Cottrell relationship is therefore, "*detect[ing] an erroneous signal based at least in part on the signal response.*" *Id.*, ¶339.

Beaty also discloses this claim element because Beaty describes detecting from the measured current response: (a) the error condition of inadequate sample volume; and (b) the error introduced in the glucose measurement by the effect of temperature and/or various biochemical substances. *Id.*, ¶340.

In particular, Beaty states that "many presently available biosensors are ***sensitive to the volume of blood*** with which they are doped for determination of

glucose concentration." Beaty, p. 7, ll. 17-20. Furthermore, Beaty states that measurement systems, such as those used for blood glucose measurement are:

> known to be susceptible to ***variations in the temperature*** of the biological fluids and to ***interference by the presence in the biological fluids of other components, known and sometimes referred to hereinafter as interferrents***. In many cases, these sources of error have effects on the biosensor output of the same order of magnitude as the concentration of the component, measurement of which is sought.

Beaty, 7, ll. 2-12.

In addition, Beaty describes detecting the above-described errors by computing the cell impedance using the measured current. *See* Beaty, p. 15, ll. 1-17 ("***The impedance magnitude and phase angle are calculated. Using these values, a look-up table . . . is consulted to ascertain*** the nature of the sample and, if blood, ***whether there is sufficient volume in the blood sample***[.]"); *see id.*, 7:28-8:14 (stating that "measurement of the real component or the imaginary component, or both, of the AC impedance of an appropriately designed biosensor provides reasonable insight into sample temperature and the concentrations of certain physical and chemical interferrents"); Ex. 1003, ¶¶341-342.

Accordingly, in Beaty's biosensor, measuring the current response and determining whether or not the sample volume is adequate or determining the effect of temperature and/or biochemical substances on the glucose measurement

constitutes "*detect[ing] an erroneous signal based at least in part on the signal response.*" *Id.*, ¶343.

Therefore, White and Beaty each disclose Element [14.e]. Ex. 1003, ¶344.

> ***vii. White and Beaty each discloses "wherein the erroneous signal is associated with at least one condition selected from the group consisting of an ischemia, a pH, a temperature associated with the electrochemical glucose sensor, a biochemical species, an available electrode surface area, a local environment associated with the electrode surface of the first electrode, a diffusion transport of glucose or a measured species, and a pressure or a stress associated with the electrochemical glucose sensor" (Element [14.f]).***

**Part 1 of Element [14.f]: "[E]rroneous signal [] associated with at least one condition selected from . . . an available electrode surface area, [and] a local environment associated with the electrode surface of the first electrode"**

White discloses this feature because White explains that the measured current response can deviate from the expected Cottrell relationship due to at least three kinds of error conditions. *See* White, 2:41-51; Ex. 1003, ¶¶345-346. These error conditions are:

(a) "blood sample does not totally cover the sensing electrode surfaces,"

(b) "if there is leakage along the length of the electrodes so that the blood sample covers not only the portion of the electrodes in the reaction zone, but also outside of the reaction zone,"

where error condition types (a) and (b) are *associated with the available electrode surface area*,[3] which is either not fully utilized or is altered during the test, as discussed below in connection with claim 20;

(c) "if the reaction area becomes hydrated, either prior to or during the test," and

(d) "[i]f there is contamination in well 20 between electrodes 12 and 14," where error condition types (c) and (d) are *associated with a local environment associated with the electrode surface of the first electrode*, as discussed below in connection with claim 32.

White, 2:41-51 and 4:31-47; Ex. 1003, ¶346.

**Part 2 of Element [14.f]:** "**[E]rroneous signal [] associated with at least one condition selected from . . . a temperature associated with the electrochemical glucose sensor, a biochemical species, [and] a diffusion transport of glucose or a measured species**"

Beaty states that glucose "measurement systems are known to be ***susceptible to variations in the temperature*** of the biological fluids ***and to interference by the presence in the biological fluids of other components, known and sometimes referred to hereinafter as interferrents.***" Beaty, p. 6, l. 30 – p. 7, l. 5. In

[3] Parties agree that available electrode surface area is the surface area of an electrode where an electrochemical reaction occurs. *See* above, § V.

describing the effect of temperature and hematocrit on glucose measurement and the correction of the measurement error Beaty states:

> We have determined that the ***combined effect of sample temperature and hematocrit can fairly effectively be isolated from other physical and chemical interferrents of interest using frequencies in the range of from about 2 kHz to about 10 kHz***. So, for example, once the adequacy of the sample volume for test has been established, a 2 kHz signal can be applied to the biosensor and the real and imaginary components of impedance of the biosensor/sample system can be determined. ***This indicated impedance can be adjusted*** . . . and combined with an indicated glucose concentration ***to arrive at a glucose concentration compensated for the combined effects of sample temperature and hematocrit.***

Beaty, p. 9, ll. 8-18.

Dr. Smith notes that it is well understood that temperature and the hematocrit in the blood affect diffusion transport of glucose and the mediators involved in an electrochemical reaction occurring in the blood sample. Ex. 1003, ¶¶347-349. Therefore, errors corresponding to temperature and the level of hematocrit that Beaty describes are associated with the diffusion transport of glucose or a measured species such as a mediator. *Id.*, ¶350.

Beaty further states: "Similar procedures can be conducted, again . . . before the amperometric determination of the glucose concentration, to determine the concentrations of other interferrents . . . such as ***bilirubin, uric acid and oxygen***."

Beaty, p. 9, ll. 23-27. Hematocrit, bilirubin, uric acid, and oxygen are biochemical species and, hence, the error that Beaty describes corresponds to *a temperature associated with the electrochemical glucose sensor, a biochemical species,* and/or to the *diffusion transport of glucose or a measured species*." Ex. 1003, ¶351.

Therefore, White and Beaty each discloses Element [14.f]. Ex. 1003, ¶352.

***viii. White and Beaty each discloses "determine a value associated with a severity of the erroneous signal" (Element [14.g]).***

White describes computing pairwise ratios of current values measured at successive time intervals, e.g., ($t1$, $t2$); ($t2$,$t3$) . . . ($t$n, $t$n+1), etc., and comparing these ratios with respective predetermined constants to determine whether the measured current is following the Cottrell relation. *See* White, 6:6-7:17; FIGS. 5 and 6; Ex. 1003, ¶¶353-354. As explained in the discussion of claim element [14.e], White describes that the measured current may fail to follow the Cottrell relation if an error caused by one or more conditions is high. *See* White, 2:41-49, 4:28-51, and 2:49-51; Ex. 1003, ¶354.

Specifically, White states:

> [A] measurement voltage is applied to cell 10 from signal voltage module 54, and a first current reading is taken at t0 and recorded (box 116). Next, (in FIG. 6) a subsequent current reading is taken (e.g. t1) and recorded (box 118).

> ***At this point, the current value measured at tn and tn+1 are accessed and the ratio thereof is derived. That ratio is then compared to the prestored comparison constant xn, n+1.*** If the ratios are not "similar", then it is known that the measured values of current are not following a predetermined Cottrell current relationship. * * *
>
> In the event the comparison "fails", an error condition is reported (box 122). If the comparison succeeds, the process continues[.]

White, 6:6-7:17; FIGS. 5 and 6. Each ratio of the measured current values, thus indicates a severity of an error in the measured current signal, i.e., *a value associated with severity of the erroneous signal*. Ex., 1003, ¶354.

Beaty describes:

> Immediately after the instrument 32's electronics detect the deposit of the droplet on the biosensor 31, ***an AC signal having a frequency of, for example, 1300Hz is applied*** across terminals 34-2—34-3 of connector 34 ***and the resulting current is indirectly sampled by µP 54*** by measuring the excitation and response voltages and using the scale factor to obtain current. ***The impedance magnitude and phase angle are calculated. Using these values, a look-up table in the µP 54' s program memory is consulted to ascertain*** the nature of the sample and, if blood, ***whether there is sufficient volume in the blood sample*** to proceed with the glucose determination phase of the assay. ***If not, the assay is terminated*** and this outcome is displayed on the instrument 32's display. If there is sufficient volume to continue with the glucose determination, ***an AC signal at another frequency, for***

***example, 10 KHz, is applied across terminals 34-2—34-3 of connector 34 and the resulting current is sampled by µP 54. The impedance and phase angle are again calculated at this second frequency. A second look-up table in the µP 54's program memory is consulted for an indicated glucose-to-actual glucose correction factor.***

Beaty, p. 15, ll. 1-17.

Beaty also describes "measurement of the real component or the imaginary component, or both, of the AC impedance of an appropriately designed biosensor provides reasonable insight into sample temperature and the concentrations of certain physical and chemical interferrents" which, as discussed above, are sources of error. Beaty, 7:28-8:14; Ex. 1003, ¶¶355-356.

Thus, Beaty discloses computing the AC cell impedance (in terms of magnitude and phase) at one frequency (e.g., 1300 Hz) to determine the adequacy of the sample volume, (where inadequacy is a sever error condition), and computing the AC impedance at another frequency (e.g., 10 kHz) to quantify the effect of temperature, hematocrit, and/or other interferents, i.e., to determine the severity of corresponding errors in the glucose measurement. Ex. 1003, ¶357. Therefore, magnitude and phase of the cell impedance and the real and imaginary components of the cell impedance are *values associated with a severity of the erroneous signal*. *Id.*

Therefore, White and Beaty each discloses Element [14.g]. *Id.*, ¶358.

***ix. White and Beaty individually and in combination disclose "discard a glucose measurement when the value associated with the severity of the erroneous signal is outside of a predetermined threshold value" (Element [14.h]).***

As discussed below, White and Beaty individually teach this element (Cases 1 and 2, respectively), and they also teach this element in combination (Case 3). Ex. 1003, ¶¶359-360.

**Case 1:**

White states: "A pluggable read-only-memory (ROM) 68 interfaces with bus 52, and in addition to other data, [] contains ***precalculated comparison constants ($x_{1,2}$, $X_{2,3}$ etc.)*** for the batch of test cells from which test cell 10 is taken." White, 5:55-59. White also describes that after switching the applied voltage to the measurement voltage:

> ***[T]he current value measured at tn and tn+1 are accessed and the ratio thereof is derived. That ratio is then compared to the prestored comparison constant xn, n+1.*** If the ratios are not "similar", then it is known that the measured values of current are not following a predetermined Cottrell current relationship. * * *
>
> ***In the event the comparison "fails", an error condition is reported (box 122).*** If the comparison succeeds, the process continues[.]

White, 6:6-7:17; FIGS. 5 and 6.

Thus, White describes discarding a glucose measurement if a ratio of two measured current values (i.e., *a value associated with the severity of the erroneous signal*) is substantially different from, (i.e., *outside of*), a corresponding prestored comparison constant ($x_{1,2}$; $x_{2,3}$; etc., and $x_{n, n+1}$, in general), i.e., a *predetermined threshold value*. Ex. 1003, ¶¶361-362.

**Case 2:**

> Immediately after the instrument 32's electronics detect the deposit of the droplet on the biosensor 31, ***an AC signal having a frequency of, for example, 1300Hz is applied*** . . . ***and the resulting current is indirectly sampled by µP 54***[.] ***The impedance magnitude and phase angle are calculated. Using these values, a look-up table in the µP 54' s program memory is consulted to ascertain*** the nature of the sample and, if blood, ***whether there is sufficient volume in the blood sample*** to proceed with the glucose determination phase of the assay. ***If not, the assay is terminated*** and this outcome is displayed on the instrument 32's display.

Beaty, p. 15, ll. 1-12.

Thus, Beaty teaches this element because Beaty describes terminating an assay and discarding a glucose measurement when a computed cell impedance value (i.e., *a value associated with the severity of the erroneous signal* ) is different from (i.e., *outside of*) the corresponding value stored in a look-up table in memory (i.e., *a predetermined threshold value*). Ex. 1003, ¶¶363-364.

**Case 3:**

As discussed in Case 1, White teaches reporting an error condition and discarding the glucose measurement when the comparison between a ratio of measured current values and a stored constant fails. S*ee* White, 5:55-59 and 6:6-7:17; FIGS. 5 and 6. As discussed in Case 2, Beaty teaches discontinuing a test and discarding the current/glucose measurements if the sample volume is inadequate. *See* Beaty, p. 9, ll. 4-7, p. 11, ll. 13-19, and p. 15, ll. 1-12.

It is explained in the discussion of claim element [14.f] that Beaty describes that temperature, hematocrit, and/or other interferents can affect the glucose measurement (i.e., introduce an error in the glucose measurement), and further describes correcting that error by applying a correction factor based on the cell impedance that is measured in response to a suitable excitation signal and values stored in a second look-up table in memory. *See* Beaty, p. 15, ll. 1-17; Ex. 1003, ¶¶365-366.

Therefore, in light of White's and Beaty's express teachings, a POSITA would have understood that an error condition can be reported and a glucose measurement can be discarded if an impedance value and/or the corresponding correction factor indicative of the effect of temperature, hematocrit, and/or another interferent (i.e., *the value associated with the severity of the erroneous signal*) is too high (i.e., *outside of*) compared to a predetermined threshold value, such as that

stored in a second look-up table in memory. Ex. 1003, ¶¶367.

Thus, according to Cases 1-3, White and Beaty, individually and in combination, disclose Element [14.h]. *Id.*, ¶368.

In conclusion, in light of the White's and Beaty's disclosures, the combination of White and Beaty teaches or at least suggests each and every limitation of claim 14 and, as such, claim 14 is unpatentable as being obvious. *Id.*, ¶369.

### 2. A POSITA Would Have Been Motivated to Combine White and Beaty.

White and Beaty are in the same field of endeavor. They both are directed to glucose monitoring/display systems having electrochemical glucose sensors. Moreover, Beaty states: "This invention relates to ***methods and apparatus for improving the accuracy of measurements made with instruments of*** the type described in, for example, ***U. S. Patents: 5,243,516," i.e., White***, and of other U.S. patents. Beaty, 1:4-8. Beaty further states:

> [W]e have determined that ***in biosensors of the type described in U. S. Patent[]: 5,243,516 [i.e., White]*** it is possible to employ a low-magnitude, for example, less than about 40mV rms or so, AC signal in the range of less than about .1Hz to 10KHz or so with no DC offset ***to compensate for sample temperature, hematocrit,*** bilirubin concentration, uric acid concentration and ***oxygen concentration, and to determine identity of the sample*** with which the biosensor is dosed,

***and adequacy of dosed blood sample volume*** for a test for glucose concentration.

Beaty, p. 8, ll. 23-31; *see id.*, – p. 7, l. 15.

Thus, Beaty states that its techniques, that can detect and compensate for errors in glucose measurement caused by inadequate sample volume and the effects of temperature, hematocrit, and other interferents, can be applied to various electrochemical biosensors, and ***explicitly identifies White's biosensor that can be improved***, thus providing express motivation to combine White and Beaty. Ex. 1003, ¶¶370-372; *see* Beaty, 1:4-8; p. 6, l. 30 – p. 8, l. 17; and p. 8, ll. 23-31.

In light of White's and Beaty's express teachings, a POSITA would have understood that White's biosensor can be modified according to Beaty's techniques to detect various error conditions, and to correct for the errors if they are not too severe, or to discard the measurements otherwise. Ex. 1003, ¶373.

Moreover, to a POSITA combining Beaty's teachings with those of White would have been nothing more than using or applying a known technique (Beaty's sample volume detection and correction for effects of temperature and interferents) to improve a known device (White's electrochemical biosensor, that is similar to Beaty's electrochemical biosensor). Ex. 1003, ¶374. After such a combination, White's biosensor would function in the same way as before. *Id.*

To a POSITA, this combination would also be nothing more than combining prior art elements (measurement and analysis of signals of an electrochemical cell for determining glucose concentration, that both White and Beaty describe), according to known methods to yield the predictable result (of ensuring that adequate sample volume was available to the biosensor, and correcting for the effects of temperature and interferents). *Id.*, ¶375.

Because White and Beaty both describe electrochemical sensors for glucose measurement, and because the improved error condition detection and correction functionality that Beaty describes can be implemented readily using commonly used circuitry, such as AC voltage sources and amplifiers, and by modifying the software, and because these improvements do not require any modifications to the electrochemical cell of White, a POSITA would have had strong expectations of successfully combining the teachings of these two references. These straightforward modifications to White's glucose sensor according to Beaty's teachings, that Beaty expressly describes as applicable to White's biosensor, would have been well within the grasp of a POSITA and, as such, it would have been obvious to combine the teachings of White and Beaty to make an improved biosensor. *Id.*, ¶¶376-377.

For at least these reasons, a POSITA would have found it obvious to combine the teachings of White and Beaty to make an improved biosensor that can

detect and correct for different kinds of errors, i.e., the claimed invention. *Id.*, ¶377.

### 3. Independent Claim 20

This claim is substantially the same as independent claim 14 except for the claim element [14.f], which is replaced with the claim element "wherein the erroneous signal is associated with an available electrode surface area."

White describes that a measurement error can occur if the "blood sample does not totally cover the sensing electrode surfaces," White, 2:41-43, 2:49-51, and 4:31-41, or if the sample infiltrates cell components and comes into contact with the electrodes 12 or 14. White 4:43-47; Ex. 1003, ¶¶378-379. In the first case, the available electrode surface area is not fully utilized and thus can change during a test. In the second case also, the available electrode surface area changes during the test because a portion of the sample may contact electrode surface outside of the reaction zone. Ex. 1003, ¶379. The errors due to each of these conditions are therefore, errors *associated with the available electrode surface area*. *Id.*

As discussed above in connection with claim 14, the combination of White and Beaty teaches all of the other elements of claim 20. Therefore, White and Beaty, in combination, render claim 20 obvious. *Id.*, ¶380.

### 4. Independent Claim 26

This claim is substantially the same as independent claim 14 except for the claim element [14.f], which is replaced with the claim element "wherein the erroneous signal is caused by a temperature associated with the electrochemical glucose sensor."

Beaty teaches this element because Beaty describes that glucose "measurement systems are known to be ***susceptible to variations in the temperature*** of the biological fluids[.]" Beaty, p. 6, l. 30 – p. 7, l. 5. Beaty also states:

> We have determined that the combined ***effect of sample temperature*** and hematocrit can fairly effectively be isolated from other physical and chemical interferrents of interest using frequencies in the range of from about 2 kHz to about 10 kHz. So, for example, once the adequacy of the sample volume for test has been established, a 2 kHz signal can be applied to the biosensor and the real and imaginary components of impedance of the biosensor/sample system can be determined. This indicated impedance can be adjusted . . . and combined with an indicated glucose concentration to arrive at a ***glucose concentration compensated for the combined effects of sample temperature*** and hematocrit.

Beaty, p. 9, ll. 8-18.

As discussed above in connection with claim 14, the combination of White and Beaty teaches all of the other elements of claim 26. As such, White and Beaty,

in combination, render claim 26 obvious. Ex. 1003, ¶¶381-383.

### 5. Independent Claim 32

This claim is substantially the same as independent claim 14 except for the claim element [14.f], which is replaced with the claim element "wherein the erroneous signal is associated with a local environment associated with the electrode surface of the first electrode."

White teaches this element because White describes that a measurement error can occur: (A) "if the reaction area becomes hydrated, either prior to or during the test," and/or (B) "[i]f there is contamination in well 20 between electrodes 12 and 14[.]" White, 2:43-45 and 4:40-47; Ex. 1003, ¶¶384-385. The electrochemical reaction occurs within the reaction zone where the electrode surfaces are exposed to the reactants and, hence, each of the above-identified errors is *associated with a local environment associated with the electrode surface of the first electrode*. Ex. 1003, ¶385.

As discussed above in connection with claim 14, the combination of White and Beaty teaches all of the other elements of claim 32. As such, White and Beaty, in combination, render claim 32 obvious. *Id.*, ¶386.

### 6. Independent Claim 38

This claim is substantially the same as independent claim 14 except for the claim element [14.f], which is replaced with the claim element "wherein the

erroneous signal is associated with a diffusion transport of glucose or a measured species."

Beaty describes:

> [T]he ***combined effect of sample temperature and hematocrit*** can fairly effectively be isolated . . . using frequencies in the range of from about 2 kHz to about 10 kHz," "a 2 kHz signal can be applied to the biosensor and the . . . impedance of the biosensor/sample system can be determined," and that the "indicated impedance can be adjusted . . . and combined with an indicated glucose concentration to arrive at a ***glucose concentration compensated for the combined effects of sample temperature and hematocrit***.

Beaty, p. 9, ll. 8-18.

Prior to 2003, it was well understood that sample temperature and the hematocrit in the blood affects diffusion transport of glucose and the mediators involved in the electrochemical reaction. Ex. 1003, ¶¶387-389. Therefore, an error corresponding to sample temperature and hematocrit that Beaty describes is associated with the diffusion transport of glucose or a measured species such as a mediator. *Id.*, ¶390.

As discussed above in connection with claim 14, the combination of White and Beaty teaches all of the other elements of claim 38. As such, White and Beaty, in combination, render claim 38 obvious. *Id.*, ¶391.

### 7. Independent Claim 50

This claim is substantially the same as independent claim 14 except for the claim element [14.f], which is replaced with the claim element "wherein the erroneous signal is associated with a biochemical species."

Beaty teaches this element because Beaty describes that glucose "measurement systems are known to be ***susceptible*** to variations in the temperature of the biological fluids and ***to interference by the presence in the biological fluids of other components, known and sometimes referred to hereinafter as interferrents.***" Beaty, p. 6, l. 30 – p. 7, l. 5. In describing the effect of temperature and hematocrit on glucose measurement and the correction of the measurement error Beaty describes that cell impedance determined using a 2 kHz excitation signal can be used to compute a correction factor. *See* Beaty, p. 9, ll. 8-18.

Beaty further states: "***Similar procedures can be conducted***, again in the illustrated embodiments before the amperometric determination of the glucose concentration, to determine the concentrations of ***other interferrents*** with chemistry for the glucose concentration determination, ***such as bilirubin, uric acid and oxygen,***" each of which is a biochemical specie. Beaty, p. 9, ll. 23-27; Ex. 1003, ¶¶392-394.

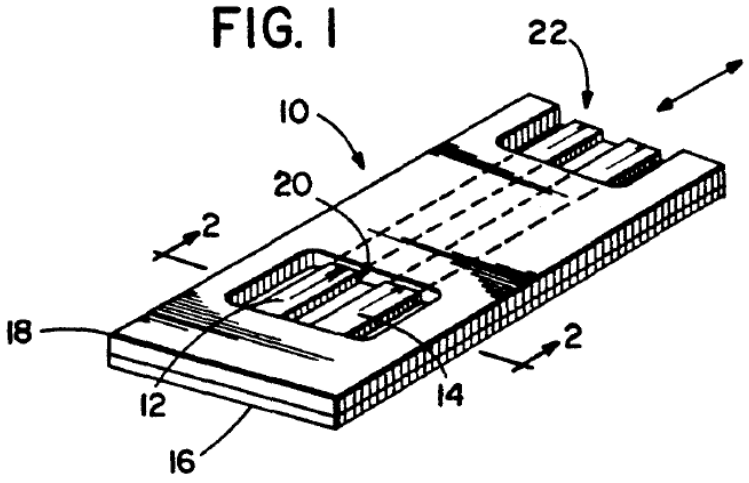
As discussed above in connection with claim 14, the combination of White and Beaty teaches all of the other elements of claim 50. As such, White and Beaty,

in combination, render claim 50 obvious. Ex. 1003, ¶395.

### 8. Dependent Claims 15, 21, 27, 33, 39, and 51

Dependent claims 15, 21, 27, 33, 39, and 51 each incorporates the limitations of independent claims 14, 20, 26, 32, 38, and 50, respectively (which are all disclosed by the combination of White and Beaty) and, additionally, each of these dependent claims recites: "*wherein the biological sample is blood*."

In the discussion of claim element [14.a] it is explained that the "test cell 10" of White's biosensor has an ***opening 20*** that creates "***a reaction zone or 'well' wherein a sample of body fluid can be emplaced to enable a reaction to occur***." White, 3:35-46; FIG. 1. White discloses blood as body fluid: "This invention relates to a biosensing instrument for . . . amperometrically ***determining the concentration of biological compounds, such as glucose***, cholesterol, etc., ***in a body fluid such as blood***." White, 1:5-11. Ex. 1003, ¶¶396-397. White also describes that "when ***a sample or 'drop' of blood is placed in well 20***, an immediate spike of current occurs, indicating the ***presence of the blood sample***, and is sensed by a signal detector module 60." White, 6:9-15; FIG. 1.




### 9. Dependent Claims 16, 22, 28, 34, 40, and 52

Dependent claims 16, 22, 28, 34, 40, and 52 each incorporates the limitations of independent claims 14, 20, 26, 32, 38, and 50, respectively (which are all disclosed by the combination of White and Beaty) and, additionally, each of these dependent claims recites: "*wherein measuring the signal response comprises measuring a current output of the electrochemical glucose sensor*." As explained above in discussing Element [14.d], White discloses this limitation. Ex. 1003, ¶398.

### 10. Dependent Claims 17, 23, 29, 35, 41, and 53

Dependent claims 17, 23, 29, 35, 41, and 53 each incorporates the limitations of independent claims 14, 20, 26, 32, 38, and 50 respectively (which are all disclosed by the combination of White and Beaty) and, additionally, each of these dependent claims recites: "*wherein measuring the signal response comprises measuring a voltage output of the electrochemical glucose sensor*."

Beaty discloses this limitation, because, as described below, Beaty describes measuring the "response voltage," i.e., voltage output of the biosensor, after applying an AC excitation signal. Ex. 1003, ¶¶399-401. In particular, Beaty states:

> A sample of blood is applied to the biosensor 31. Immediately after the instrument 32's electronics detect the deposit of the droplet on the biosensor 31, ***an AC signal having a frequency of, for example, 1300Hz is applied across terminals 34-2—34-3 of connector 34 and the resulting current is indirectly sampled by µP 54 by measuring the excitation and response voltages and using the scale factor to obtain current.***

Beaty, p. 15, ll. 2-7; Ex. 1003, ¶401.

Dr. Smith notes that it was well known prior to 2003 to use the voltage output/response of an electrochemical sensor for error correction and detection. Ex. 1003, ¶402; *see, e.g.*, Ex. 1005, Berner, 21:37-44 and 20:36-46 (disclosing measurements of "cathodal or anodal iontophoresis voltages" and/or "system voltage" for detecting various errors); Ex. 1032, Kermani (disclosing sensor electronics applying a voltage to a biosensor and receiving and processing voltage outputs from the biosensor); Ex. 1035, Ohara (same); Ex. 1036, Eppstein (same); Ex. 1033, Lall, (describing a Schmitt (or Schmidt) Trigger circuitry that Kermani's biosensor uses).

#### 11. Dependent Claims 18, 24, 30, 36, 42, and 54

Dependent claims 18, 24, 30, 36, 42, and 54 each incorporates the limitations of independent claims 14, 20, 26, 32, 38, and 50, respectively (which are all disclosed by the combination of White and Beaty) and, additionally, each of these dependent claims recites: "*wherein the measured signal response is a voltage response of the electrochemical glucose sensor*." As explained above in discussing claims 17, 23, 29, 35, 41, and 53, Beaty discloses this limitation. Ex. 1003, ¶¶403-405.

In summary, it is explained above that it would have been obvious for a POSITA to combine Beaty and White, which collectively teach all of the elements of 14-18, 20-24, 26-30, 32-36, 38-42, and 50-54. Therefore, White and view of Beaty renders these claims obvious. *Id.*, ¶406.

### B. Ground 2: Claims 62-66, and 68 are obvious under 35 U.S.C. § 103 in light of White, Beaty, and Schulman.

The combination of White, Beaty, and Schulman (Ex. 1008) renders independent claim 62 and also independent claims 63-66, and 68 obvious. Ex. 1003, ¶407.

#### 1. Independent Claim 62

Claim 62 is similar to independent claim 14, except for the following differences:

| Claim 14 | Claim 62 |
|---|---|
| Recites a glucose sensor "in contact with a *biological fluid*, | Recites a glucose sensor "in contact with a *blood sample*." |
| Recites:<br>"discard a glucose measurement, when the value associated with the severity of the erroneous signal is outside of a predetermined threshold value" | Recites:<br>"generate a glucose value for display when the value associated with the severity of the erroneous signal satisfies a predetermined threshold value, and<br>discard a glucose measurement when the value associated with the severity of the erroneous signal does not satisfy the predetermined threshold value" |
| Does not recite a "user interface" | Recites a "user interface" |

Ex. 1003, ¶408.

As discussed above, White teaches a glucose sensor "in contact with a *blood sample*." *See above*, §§ VI(A)(1)(ii) and VI(A)(8). White and Beaty, individually and in combination, teach the "generate" and "discard" operations recited in claim 62, and Schulman discloses the claimed "user interface," as discussed below. Ex. 1003, ¶409.

***i. White discloses "an electrochemical glucose sensor configured to be in contact with a blood sample to obtain a glucose measurement"***

As explained above in discussing dependent claim 15, White discloses this claim element. *See above*, §§ VI(A)(1)(ii) and VI(A)(8); Ex. 1003, ¶410.

***ii. White and Beaty, individually and in combination, disclose "generate a glucose value for display when the value associated with the severity of the erroneous signal satisfies a predetermined threshold value, and discard a glucose measurement when the value associated with the severity of the erroneous signal does not satisfy the predetermined threshold value"***

White and Beaty individually teach this element (Cases 1 and 2, respectively), and they also teach this element in combination (Case 3). Ex. 1003, ¶411.

**Case 1:**

As explained in the discussion of claim element [14.g], each of the pairwise ratios of current values that White describes is *a value associated with the severity of the erroneous signal*. *See* White, 6:6-7:17; FIGS. 5 and 6; Ex. 1003, ¶412. Moreover, as explained in the discussion of claim element [14.h], the respective prestored comparison constants $x_{1,2}$; $x_{2,3}$; . . .; $x_{n,\ n+1}$, etc., are the *predetermined threshold values* with which the respective current ratios are compared. *See* White, 5:55-59; Ex. 1003, ¶412. Only when the current ratios and the corresponding comparison constants are substantially the same, i.e., a *severity of the erroneous signal satisfies a predetermined threshold value*, the measured current is determined to follow the Cottrell relationship, and *a glucose measurement is*

*generated for display*. Otherwise, *the measured current values are discarded*, and an error condition is reported. *See* White, 6:6-7:17; FIGS. 5 and 6; Ex. 1003, ¶412.

Specifically, White describes that after switching the applied voltage to the measurement voltage:

> ***[T]he current value measured at tn and tn+1 are accessed and the ratio thereof is derived. That ratio is then compared to the prestored comparison constant xn, n+1.*** If the ratios are not "similar", then it is known that the measured values of current are not following a predetermined Cottrell current relationship. By the term "similar" is meant that the calculated current ratio does not differ from the precalculated comparison constant x by more than a predetermined error value (box 120).
>
> ***In the event the comparison "fails", an error condition is reported (box 122).*** If the comparison succeeds, the process continues with microprocessor 50 integrating the current values taken at $t_n$ and $t_{n+1}$ over the time period $(t_{n+1})$-$(t_n)$, and accumulating the value . . . . At some time during the measurement cycle, a sample measurement time is designated. At such time, the current reading taken at that time (box 127) is subsequently converted to a "sample[d]" glucose concentration value (box 134).
>
> *** * ***
>
> When it has been determined that the last current value has been measured (box 128), the system computes the integral glucose concentration (box 130) and the sampled glucose concentration (134).

> The system then compares the calculated integrated and sampled glucose concentrations (box 136) and determines whether they are similar or not (box 138) with ***the results being as shown in boxes 140 or 142***.

White, 6:6-7:35; FIGS. 5 and 6.

Box 142 reports, e.g., displays the result, i.e., the glucose concentration. *See* White, 6:2-4 ("[A] display 70 enables the user to see the results of a concentration measurement taken through the use of cell 10."); FIG. 4; Ex. 1003, ¶¶413-414. As such, White teaches this limitation. Ex. 1003, ¶414.

**Case 2:**

Beaty also teaches this element. As explained in the discussion of claim elements [14.g] and [14.h], Beaty describes computing cell impedance magnitude and phase values (i.e., *values associated with the severity of the erroneous signal*) and values stored in a look-up table in memory (i.e., *predetermined threshold values*). Ex. 1003, ¶415.

Additionally, Beaty describes using the impedance values and the stored values to determine the adequacy of the sample volume (i.e., determining that the *severity of the erroneous signal satisfies a predetermined threshold value*), and proceeding with the determination of error cause by temperature and/or interferents, subsequent glucose measurement, and correction, *if the sample volume is determined to be sufficient*. Otherwise, the assay is terminated and the glucose

measurements are discarded. *Id.*, ¶416. In particular, Beaty describes:

> [A] measurement of actual glucose concentration using an instrument 32 of the type illustrated in Fig. 2 proceeds as follows. A sample of blood is applied to the biosensor 31. Immediately after the instrument 32's electronics detect the deposit of the droplet on the biosensor 31, ***an AC signal having a frequency of, for example, 1300Hz is applied*** across terminals 34-2—34-3 of connector 34 ***and the resulting current is indirectly sampled by µP 54*** by measuring the excitation and response voltages and using the scale factor to obtain current. ***The impedance magnitude and phase angle are calculated. Using these values, a look-up table in the µP 54' s program memory is consulted to ascertain*** the nature of the sample and, if blood, ***whether there is sufficient volume in the blood sample*** to proceed with the glucose determination phase of the assay. ***If not, the assay is terminated*** and this outcome is displayed on the instrument 32's display.

Beaty, p. 15, ll. 1-12. Beaty further states:

> ***If there is sufficient volume to continue with the glucose determination***, an AC signal at another frequency, for example, 10 KHz, is applied across terminals 34-2—34-3 of connector 34 and the resulting current is sampled by µP 54. The impedance and phase angle are again calculated at this second frequency. A second look-up table in the µP 54's program memory is consulted for an indicated glucose-to-actual glucose correction factor. * * * [T]hat correction is stored, and ***the determination of the indicated glucose concentration proceeds*** generally as described in U. S. Patents: 5,243,516; 5,288,636; 5,352,351; 5,385,846; and 5,508,171, for example. Once

> the indicated glucose concentration has been obtained, the correction is then retrieved and applied to the indicated glucose concentration to arrive at the ***actual glucose concentration which is displayed*** on the instrument 32's display and/or stored in the instrument 32's memory.

Beaty, p. 15, ll. 12-27.

**Case 3:**

It is discussed above in Case 1 that White teaches generating a glucose concentration when the ratios of measured current values (i.e., values of error severity) are substantially the same as the respective stored constants (i.e., predetermined threshold values) and, otherwise, reporting an error condition and discarding the glucose measurement. S*ee* White, 6:6-7:17; FIGS. 5 and 6; Ex. 1003, ¶417. It is discussed in Case 2 that Beaty also teaches generating a glucose measurement if the sample volume is inadequate, which is determined using computed cell impedance and stored threshold values, and, otherwise, discontinuing the assay and discarding the current/glucose measurements. *See* Beaty, p. 9, ll. 4-7, p. 11, ll. 13-19, and p. 15, ll. 1-12; Ex. 1003, ¶418.

In addition, it is explained in the discussion of claim element [14.f] that Beaty also describes that temperature, hematocrit, and/or other interferents can affect the glucose measurement (i.e., introduce an error in the glucose measurement), and further describes correcting that error by applying a correction factor based on the cell impedance that is measured in response to a suitable

excitation signal and values stored in a second look-up table in memory. *See* Beaty, p. 15, ll. 1-17; Ex. 1003, ¶419.

Therefore, in light of White's and Beaty's express teachings, one of ordinary skill in the art would have readily understood and appreciated that if an impedance value and/or the corresponding correction factor indicative of the effect of temperature, hematocrit, and/or another interferent (i.e., *the value associated with the severity of the erroneous signal*) satisfies a stored threshold value, such as that stored in a look-up table in memory, the glucose concentration can be obtained and corrected and, otherwise, an error condition can be reported and the glucose measurements can be discarded. Ex. 1003, ¶420.

Thus, according to Cases 1-3, White and Beaty, individually and in combination, disclose this claim element. *Id.*, ¶421.

### *iii. Schulman discloses "a user interface"*

Regarding a user interface, claim 62 recites:

> a user interface configured to display the generated glucose value when the value associated with the severity of the erroneous signal satisfies a predetermined threshold value,
>
> wherein the user interface allows a user to toggle between a first screen, a second screen, and a third screen,
>
> wherein the first screen presents the generated glucose value in a glucose measurement trend graph extending over a first time

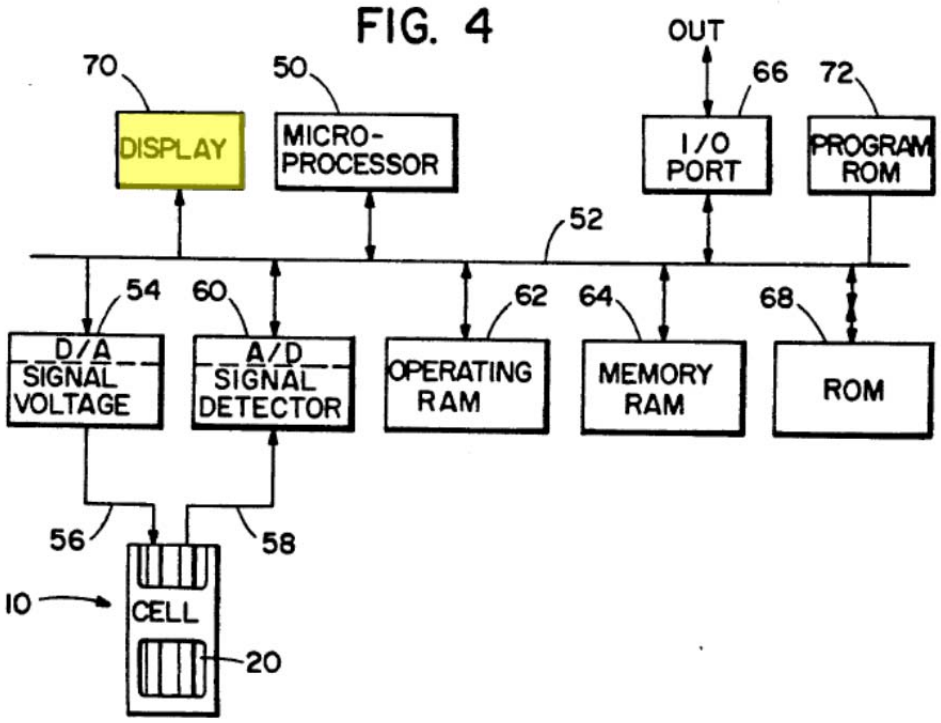
period,

wherein the second screen presents the generated glucose value in a glucose measurement trend graph extending over a second time period that is different in length from the first time period,

wherein the third screen presents the generated glucose value as a numerical value, and

wherein the user interface is configured to generate an alert responsive to detection of a hypoglycemic condition or a hypoglycemic condition based on the generated glucose value.

White discloses "a display 70 [that] enables the user to see the results of a concentration measurement taken through the use of cell 10." White, 6:2-4; FIG. 4. White does not explicitly disclose a multi-screen display and a user interface having alarms. Ex. 1003, ¶¶422-423.




Schulman, which is directed to "[a] glucose monitoring system that continuously measures the glucose concentration in a patient's blood," Schulman, 2:27-30, discloses all the user interface limitations of claim 62. Ex. 1003, ¶424. In particular, Schulman discloses:

> The glucose monitor 34 displays the ***current glucose concentration*** and the ***trend*** (the rate of change over a previous period of time, e.g., fifteen minutes). The glucose concentration is presented as either a digital display of the current value, or as a graph. The concentration value is updated once each minute (or other prescribed interval). ***In the graphic display mode, the concentration is plotted at user selected intervals, showing periods of 3 to 72 hours … In the monitor mode, the glucose concentration is displayed in large***

***numerals*** that can be easily seen from across the room, as illustrated, e.g., in FIG. 10B.

Schulman, 12:51-64. *See also* Schulman, FIG. 10B ("Current Value" mode or "monitor mode"), FIG. 10C ("Graph" mode).

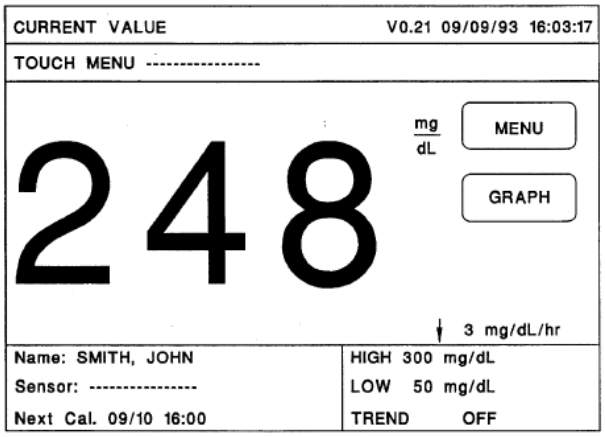



FIG. 10B

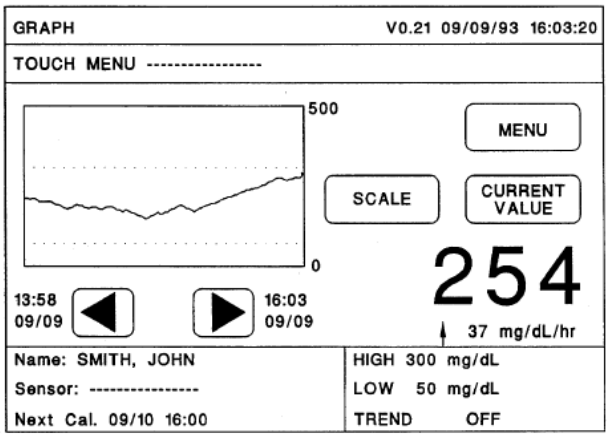



FIG. 10C

A POSITA would have understood that Schulman discloses all three types of user interface "screens" and the related toggling that claim 62 recites, as discussed below. Ex. 1003, ¶425.

First, in the "graphic display mode," Schulman teaches that a user could select different time periods ranging from 3 to 72 hours to plot "***trend*** (the rate of change over a previous [user-selected] period of time . . .)" of glucose concentration. Schulman, 12:51-62. Thus, if the user chose a 3-hour period for the graphic display, then the glucose monitor would display a first screen presenting "the generated glucose value in a glucose measurement trend graph extending over a first time period [of 3 hours]"; if the user chose a 72-hour period for the graphic

display, then the glucose monitor would display a second screen presenting "the generated glucose value in a glucose measurement trend graph extending over a second time period [of 72 hours], wherein the "second time period [] is different in length from the first time period." Ex. 1003, ¶426.

Second, in the "monitor mode," Schulman teaches that a different screen displays the glucose concentration is "in large numerals." Schulman, 12:62-64; FIG. 10B. Thus, the monitor mode displays a third screen presenting "the generated glucose value as a numerical value." Ex. 1003, ¶427.

Third, Schulman discloses that various menu buttons can be selected by the user to switch between the display modes and screens:

> FIG. 10A, for example, shows the main menu screen displayed by the glucose monitor when in use. ***FIG. 10B depicts the current value screen displayed by the monitor when the current value selection is made from the main menu.*** Note the large size of the glucose measurement displayed, providing easy-to-read numbers that are several inches high. ***FIG. 10C depicts a representative graph of the glucose concentration that is generated and displayed by the glucose monitor when the graphic selection is made from the main menu.***

Schulman, 14:42-51. The ability to switch display modes, coupled with the above-described ability to select time periods of different length to plot trend graphs, "*allow[s] a user to toggle between the first screen, the second screen, and the third screen*." Ex. 1003, ¶428.

In addition, Schulman also teaches "generat[ing] an alert responsive to detection of a hyperglycemic condition or a hypoglycemic condition." *See* Schulman, 2:29-32 ("The system further automatically determines whether the measured concentration and rate of change are within certain preset limits, and if not, generates an alarm signal."); 13:17-21 ("an alarm that signals when the value of the most recent reading is below or above user-set (or, if none, default) low or high limits"). *Id.*, ¶429.

Therefore, Schulman discloses all the "user interface" limitations of claim 62. *Id.*, ¶430.

The combination of White and Beaty teaches all of the other elements of claim 62, as discussed above in connection with claim 14. As such, the combination of White, Beaty, and Schulman teaches or suggests all the elements of claim 62. *Id.*, ¶431.

### 2. A POSITA Would Have Been Motivated to Combine White, Beaty, and Schulman.

A POSITA would have been motivated to combine Beaty's and Schulman's teachings with White's glucose sensor to improve its error handling and user interface capabilities. As a threshold matter, all three references are directed to glucose monitoring/display systems having electrochemical glucose sensors.

The motivation to combine White and Beaty is described above. *See above*, § VI(A)(2). In particular, Beaty states that its error detection and correction, that

includes determining adequacy of sample volume and the effects of temperature and interferents, can be applied to various electrochemical sensors, and explicitly identifies White's biosensor that can be improved using Beaty's techniques. Ex. 1003, ¶¶432-433; *see above*, § VI(A)(2). It is also explained above that improving White's biosensor using Beaty's teachings would have been within the grasp of a POSITA, who would have expected that the combination would predictably and successfully improve error detection/correction in White's biosensor. Ex. 1003, ¶433; *see above*, § VI(A)(2).

Furthermore, a POSITA would have readily understood that Schulman's display can further improve White's modified glucose sensor (modified according to Beaty's teachings) because Schulman describes the advantage of detecting "trends" and accordingly teaches that "[s]uch stored data may also advantageously be viewed, as selected, as a graphic display that indicates the last several hours of recorded values, ***thereby clearly showing any trends in the data over such time period***."). Schulman, 2:57-61; Ex. 1003, ¶434.

In addition, a POSITA would have been capable of modifying Whites's display to incorporate Schulman's graphical display functions because only a few well-understood modifications would be required, such as reprogramming White's microprocessor and reconfiguring or substituting White's display unit with

Schulman's enhanced graphical display showing glucose graphs over user-selectable time periods. Ex. 1003, ¶435.

At the time of the claimed invention (i.e., prior to 2003), no significant technological obstacle would have prevented a POSITA from making such modification. After all, the user interface and its functions are substantially independent of the electrochemical glucose cell and analysis of the sensed signals. A POSITA would have considered the display unit and the software program in White's biosensor to be modular components that could be easily adapted from or replaced with another display/user interface and software, respectively, from a similar glucose sensor system such as Schulman's. *Id.*, ¶436.

Thus, further modifying White's display unit/sensor (modified to incorporate Beaty's error-handling techniques) according to Schulman's teachings would require little more than: (a) combining one known element in the prior art (*i.e.*, Schulman's display functions) with other known elements (*i.e.*, White's display unit), or (b) simply substituting one known element (*i.e.*, the display of White's biosensor system) with another known element (*i.e.*, Schulman's user interface module). *Id.*, ¶437.

Because White and Beaty both describe electrochemical sensors for glucose measurement, and because the improved error condition detection and correction functionality that Beaty describes can be implemented readily using commonly

used circuitry, such AC voltage sources and amplifiers, and by modifying the software, and because this improvement does not require any modifications to the electrochemical cell of White, a POSITA would have had strong expectations of successfully combining the teachings of White and Beaty. *Id.*, ¶438.

Moreover, because Schulman also, like White and Beaty, describes electrochemical sensors for glucose measurement, and because the improvements to the display functionality that Schulman describes can be implemented readily by modifying the software and/or the display module, and because this improvement also does not require any modifications to White's biosensor (modified according to Beaty's teachings), a POSITA would have had strong expectations of successfully combining the teachings of White, Beaty, and Schulman. *Id.*, ¶439.

These straightforward modifications to White's glucose sensor according to Beaty's and Schulman's teachings would have been well within the grasp of a POSITA and, as such, it would have been obvious to combine the teachings of White, Beaty, and Schulman to make and improved glucose sensor, i.e., the claimed invention. *Id.*, ¶440.

### 3. Independent Claims 63-66, and 68

Each of these claims is substantially the same as independent claim 62, but the claim element "wherein the erroneous signal is associated with at least one condition selected from [a *Markush* group]" of claim 62 is replaced as shown in

the table below.

| Claim | Element "wherein the erroneous signal is associated with at least one condition selected from [a *Markush* group]" of claim 62 is replaced with: | Replaced element is also recited in claim |
|---|---|---|
| 63 | "wherein the erroneous signal is associated with an available electrode surface area" | 20 |
| 64 | "wherein the erroneous signal is associated with a temperature associated with the electrochemical glucose sensor" | 26 |
| 65 | "wherein the erroneous signal is associated with a local environment associated with the electrode surface of the first electrode" | 32 |
| 66 | "wherein the erroneous signal is associated with a diffusion transport of glucose or a measured species" | 38 |
| 68 | "wherein the erroneous signal is associated with a biochemical species" | 50 |

Ex. 1003, ¶441.

It is discussed above that the combination of White, Beaty, and Schulman teaches all of the elements of claim 62. Moreover, it is also explained above in the discussion of claims 20, 26, 32, 38, and 50 that the combination of White and Beaty teaches the respective elements of claims 63, 64, 65, 66, and 68 identified in the table above. *See above*, §§ VI(B)(1) and VI(A)(3)-(7). As such, White in view of Beaty, further in view of Schulman teaches all of the elements of claims 62-66

and 68, and renders these claims obvious. Ex. 1003, ¶442.

Since it would have been obvious for a person of ordinary skill in the art to combine White, Beaty, and Schulman, which collectively teach or at least suggest each and every element of independent claims 62-66 and 68, White in view of Beaty, further in view of Schulman renders claims 62-66 and 68 obvious. *Id.*, ¶443.

## VII. CONCLUSION

In light of the above, it is respectfully submitted that claims 14-18, 20-24, 26-30, 32-36, 38-42, 50-54, 62-66, and 68 of the '460 Patent are unpatentable under 35 U.S.C. § 103. Petitioner respectfully requests that an *inter partes* review be instituted and the subject claims be cancelled.

## VIII. MANDATORY NOTICES

### A. Real Parties-In-Interest Under 37 C.F.R. § 42.8(b)(1)

Petitioner identifies AgaMatrix, Inc. as the real party-in-interest.

### B. Related Matters Under 37 C.F.R. § 42.8(b)(2)

As of the filing date of this petition, the '460 Patent is involved in litigation in the District of Delaware in *Dexcom, Inc. v. AgaMatrix, Inc.*, Case No. 1:17-cv-01310; and before United States International Trade Commission, in *Certain Electrochemical Glucose Monitoring Systems And Components Thereof*, Investigation No. 337-TA-1075.

Concurrently with this petition, Petitioner is also filing: (a) an IPR petition (2018-01717) to challenge the patentability of claims 14-69 of the '460 patent on different, but equally compelling, grounds; and (b) IPR petitions (2018-01715 and 2018-01716) to challenge the patentability of certain claims of U.S. Patent No. 9,724,045 which is commonly owned, and shares the same specification and parents, as the '460 Patent.

Petitioner is not aware of any other judicial or administrative matter that would affect or be affected by a decision in this IPR.

### C. Lead and Back-Up Counsel Under 37 C.F.R. § 42.8(b)(3) and Service Information Under 37. C.F.R. § 42.8(b)(4)

| *Lead Counsel* | *Back-up Counsel* |
|---|---|
| Ira J. Levy<br>(Reg. No. 35,587)<br>ILevy@goodwinlaw.com<br>GOODWIN PROCTER LLP<br>620 8th Avenue<br>New York, NY 10018<br>(212) 813-8800 | Suhrid Wadekar<br>(Reg. No. 65,595)<br>SWadekar@goodwinlaw.com<br>GOODWIN PROCTER LLP<br>100 Northern Avenue<br>Boston, MA 02210<br>(617) 570-1000 |

Pursuant to 37 C.F.R. § 42.8(b)(4), counsel agrees to service by mail as detailed above, and to electronic service by email to the email addresses above. A Power of Attorney executed by Petitioner accompanies this Petition.

Fees: The required fees are submitted herewith. If any additional fees are due at any time during this proceeding, the Office is authorized to charge such fees

to Deposit Account No. 506989.

### D. Service on the Patent Owner

Pursuant to 37 C.F.R. § 42.105(a), this petition and its exhibits were served simultaneously with this filing on Patent Owner at the correspondence address of record on file at the USPTO for the '460 Patent, per the attached Certificate of Service, with a copy to Patent Owner's counsel in the above-referenced litigation matters.

## IX. GROUNDS FOR STANDING

Pursuant to 37 C.F.R. § 42.104, Petitioner certifies that this Petition is being filed within one year of AgaMatrix, Inc. being served with a complaint for infringement. Petitioner has not filed a civil action challenging the '460 Patent, the patent is available for *inter partes* review, and that Petitioner is not barred from requesting *inter partes* review of the '460 Patent.[4]

Date: September 14, 2018

Respectfully submitted,

By */s/ Ira J. Levy*

Ira J. Levy
(Reg. No. 35,587)
ILevy @goodwinlaw.com

[4] The Complaint alleging infringement of the '460 Patent in *Dexcom, Inc. v. AgaMatrix, Inc.*, Case No. 1:17-cv-01310 (D. Del.) was served on Sept. 15, 2017.

GOODWIN PROCTER LLP
620 8th Avenue
New York, NY 10018
(212) 813-8800

Ce Li
(Reg. No. 70,305)
CLi@goodwinlaw.com
GOODWIN PROCTER LLP
901 New York Avenue NW
Washington, DC 20001
(202) 346-4000

Suhrid Wadekar
(Reg. No. 65,595)
SWadekar@goodwinlaw.com
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
(617) 570-1000

Attorneys for Petitioner

## CERTIFICATE OF WORD COUNT

The undersigned hereby certifies that the foregoing **PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 9,750,460** complies with the type-volume limitation of 37 C.F.R. §§42.24(a)(1)(i) and 42.24(b)(1). The Petition contains 13,913 words, excluding the parts of the Petition exempted by 37 C.F.R. §42.24(a)(1), as measured by the word-processing system use to prepare the Petition.

## Certificate of Service

Pursuant to 37 C.F.R. §§ 42.6(e) and 42.105, I hereby certify that on September 14, 2018, I caused a true and correct copy of the foregoing **PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 9,750,460** and copies of all supporting materials to be served by Federal Express Next Business Day Delivery on the patent owner at the correspondence address of record for the subject patent as listed on PAIR:

Rose M. Thiessen
**KNOBBE, MARTENS, OLSON & BEAR, LLP**
DEXCOM, INC.
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE CA 92614

With an additional copy to:

Kirk R. Ruthenberg
Nicholas H. Jackson
**Dentons US LLP**
1900 K Street NW
Washington, DC 20006

/Ce Li/
Registration No. 70,305