UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AGAMATRIX, INC.

Petitioner

v.

DEXCOM, INC.

Patent Owner

U.S. PATENT NO. 9,724,045

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

Case No. IPR2018-01716

PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 9,724,045

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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.

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 16-20, 23-25, 37-38, 41-43 ("challenged claims") of United States Patent No. 9,724,045 ("the '045 Patent," Ex. 1001) which is assigned to Dexcom, Inc. ("Dexcom" or "Patent Owner").

I. INTRODUCTION

The '045 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 a signal artifact in order to decide whether to accept or discard a glucose measurement.

This was not a new idea before the priority date of the '045 Patent. In fact, multiple prior art references disclose similar electrochemical glucose sensors and related error-detection and error-rejection techniques. Ex. 1003, ¶¶ 86-117.

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 which includes all the

elements of the claimed glucose sensor system. White's biosensor also employs sensor electronics to apply and switch 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 from the Cottrell relationship by a significant amount, then an error condition is reported and the glucose measurement will 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), in the same field of glucose monitoring as White and Beaty, discloses all the user interface limitations recited in the challenged claims.

Since at least these prior art references disclose, teach or suggest all the elements of the challenged claims of the '045 Patent, as shown in this Petition, the cited references render all the challenged claims obvious. Ex. 1003, ¶¶ 12-13.

II. TECHNOLOGY BACKGROUND

The technology at issue in the challenged claims relates to electrochemical sensors, specifically glucose sensors, and signal processing. Ex. 1003, ¶¶ 38-39.

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. Ex. 1003, ¶ 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. Ex. 1003, ¶ 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. Ex. 1003, ¶ 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 the glucose (*e.g.*, a blood

sample), 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, which is indicative of the glucose concentration in the chemical reaction. Ex. 1003, ¶ 43; *see also id*., ¶¶ 44-55.

It has long been discovered that, when a potential is applied to the electrodes, such electric current is diffusion-limited and its decay over time can be described with the following Cottrell equation (derived by Frederick Gardner Cottrell in 1903):

$$i = \frac{nFAc_j^0\sqrt{D_j}}{\sqrt{\pi t}}$$

where *i* denotes the measured current, *n* denotes the number of electrons (to reduce/oxidize one molecule of analyte *j*, such as a glucose molecule), *F* denotes Faraday constant, *A* denotes the area of the (planar) electrode, c_j^0 denotes the initial concentration of the oxidizable analyte *j*, D_j denotes the diffusion coefficient for species *j*, and *t* denotes time. Ex. 1011, pp. 162-163; Ex. 1003, ¶ 56.

According to the Cottrell equation, the current value (*i*) is inversely proportionate to the square root of time (*t*), and the slope of current plotted against $1/\sqrt{t}$ bears a linear relationship to the initial analyte concentration (c_j^0). As a result, the greater the concentration of analyte (c_j^0) in the chemical reaction, the greater the resulting electric current (*i*), thereby allowing glucose concentration to

be determined by measuring a current—a method known as amperometry, or alternatively as chronoamperometry. Ex. 1003, ¶ 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"); Ex. 1010, PCT International Publication No. WO 89/08713 ("Pottgen") (both disclosing amperometric techniques for determining glucose concentration). Ex. 1003, ¶ 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. Ex. 1003, ¶ 60. In particular, it was desirable and well known, based at least on common sense, 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. Ex. 1003, ¶ 59.

For example, U.S. Patent No. 6,558,351 ("Steil," Ex. 1012, filed June 1, 2000 and issued May 6, 2003), 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, filed April 9, 1987 and issued May 23, 1989) 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, filed Feb. 26, 1998 and issued Oct. 30, 2001), 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, filed Feb. 9, 1995 and issued Nov. 28, 2000), 4:42-65 (disclosing the use of a calibration curve to identify abnormal amperometric glucose measurements that deviate from the expected Cottrell relationship). Ex. 1003, ¶ 61.

III. OVERVIEW OF THE '045 PATENT

A. Prosecution History

The '045 Patent issued from U.S. Patent Application No. 15/481,347, filed April 6, 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, without providing any explanation or guidance to the examiner. Ex. 1002 at 230-298, 301-309.

In the next few weeks, the applicant communicated with the examiner primarily through a series of telephonic interviews and a few preliminary amendments. *See* Ex. 1002 at 228, 167, 53 (interview summaries); at 177-187, 193-203, 208-222 (preliminary amendments).

On June 1, 2017, a Notice of Allowance was issued without stating any reason for allowing the claims or discussing any of the 1,200 cited references. *Id*. at 43-45. On June 21, 2017, a Corrected Notice of Allowance was issued, again without stating any reason for allowing the claims or discussing any of the 1,200 cited references. *Id*. at 36-39.

The ’045 Patent issued on August 8, 2017. *Id*. at 2; Ex. 1001 at 1.

B. Summary of the Disclosure

The ’045 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:

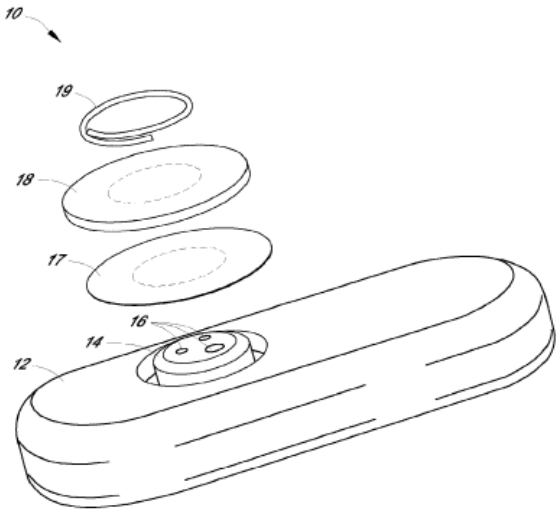


FIG. 1

Ex. 1001, FIG. 1; Ex. 1003, ¶¶ 62-63.

The glucose sensor 10 includes three electrodes 16. Ex. 1001, 20:25-27. An enzyme, glucose oxidase, contained in the sensing membrane 17 "catalyzes the conversion of oxygen and glucose to hydrogen peroxide and gluconate." *Id.*, 20:45-49; Ex. 1003, ¶ 64.

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. Ex. 1001, 20:41-59; Ex. 1003, ¶¶ 65-66.

The preferred embodiment disclosed in the '045 Patent is a continuous

glucose monitor (CGM)—*i.e.*, a "system [that] monitors a data stream[1] from a glucose sensor." Ex. 1001, Abstract. *See also id.*, 15:65-16:3; Ex. 1003, ¶¶ 67-69.

Because CGMs are implanted in the body or maintain constant contact with the body, they capture interferences from other conditions and sources in the body, causing significant signal errors. The CGM of the '045 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:

[1] "The terms 'raw data stream' and 'data stream,' as used herein … broadly encompass a plurality of time spaced data points from a substantially continuous glucose sensor, which comprises individual measurements taken at time intervals ranging from fractions of a second up to, e.g. 1, 2, or 5 minutes or longer." Ex 1001, 14:15-26.

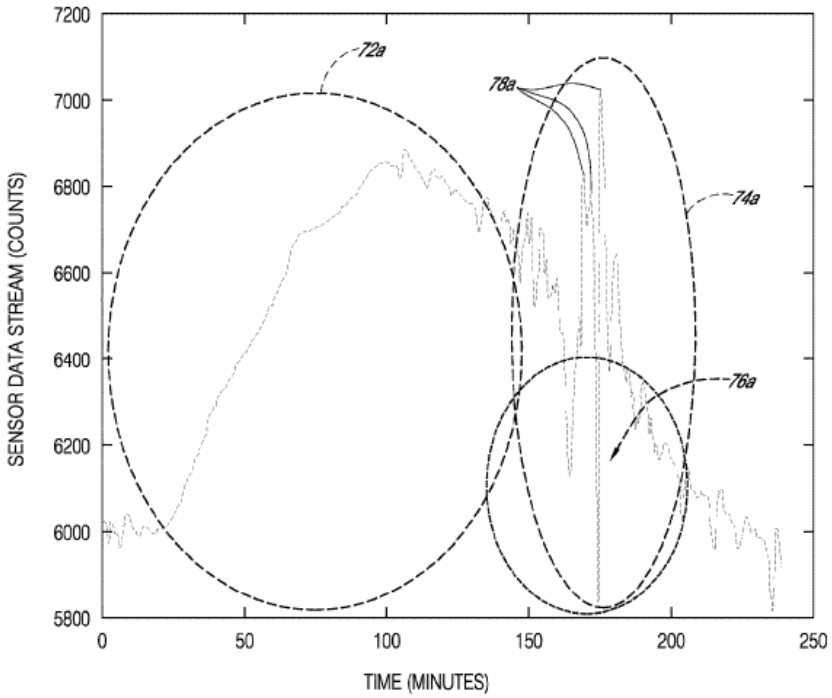


FIG. 7A

Ex. 1001, FIG. 7A; Ex. 1003, ¶¶ 67, 70-71.

Despite providing no meaningful discussion of any embodiment other than CGM in the specification, limiting the specification to a virtually exclusive description of CGM embodiments, the patent nevertheless claims:

> "***The glucose sensor can be <u>any</u> 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 <u>any</u> device capable of detecting a concentration of glucose and providing an output signal that represents the concentration of glucose***."

Ex. 1001, 20:11-18 (emphasis added). To the extent this characterization is true,

the inventive contribution of the challenged claims, if any, is not in sensor hardware or any specific glucose measurement methodology. Indeed, the challenged claims only recite generic, well-known sensor components and measurement operations. Nor is the claimed signal processing method novel or inventive since it merely applies a basic concept of error-detection and/or error-rejection to glucose data. Ex. 1003, ¶¶ 72-73.

C. Challenged Claims

The claims at issue in this Petition are claims 16-21, 23-25, 37-39, and 41-43, among which claims 16 and 37 are independent claims.

Claim 16 reads:

[16.preamble] A glucose sensor system, the system comprising:

[16.a] an electrochemical glucose sensor configured to be in contact with a biological sample for measuring a glucose concentration, wherein the electrochemical glucose sensor comprises a first electrode, a second electrode, and an enzyme-containing film;

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

[16.c] apply a voltage to the electrochemical glucose sensor at a first setting,

[16.d] switch the voltage applied to the electrochemical sensor to a different setting,

[16.e] measure a signal response of the electrochemical glucose sensor responsive to the switching,

[16.f] evaluate a severity associated with a signal artifact based on the measured signal response of the electrochemical glucose sensor to the switching, wherein the signal artifact is associated with a non-glucose rate limiting phenomenon, and

[16.g] generate an estimated glucose concentration value when the severity associated with the signal artifact is evaluated to be under a predetermined threshold, wherein the estimated glucose concentration value accounts for the severity associated with the signal artifact; and

[16.h] a user interface configured to display the estimated glucose concentration value.

Independent claim 37 includes almost identical limitations as independent claim 16 except that claim 37 recites "wherein the measured signal response is a time-varying voltage response of the electrochemical glucose sensor" and adds more "user interface" functions.

Thus, the overlapping limitations of the independent claims may be sorted into hardware elements and software elements. The hardware elements include "an electrochemical glucose sensor …" (*e.g.*, Element [16.a]), "sensor electronics comprising a processor …" (*e.g.*, Element [16.b]), and "a user interface …" (*e.g.*, Element [16.h]). The software elements include the steps of "apply" and "switch" a voltage (*e.g.*, Elements [16.c], [16.d]), "measure a signal response …" (*e.g.*, Element [16.e]), "evaluate a severity …" (*e.g.*, Element [16.f]), and "generate an estimated glucose concentration value …" (*e.g.*, Element [16.g]). Ex. 1003, ¶¶ 78-

79.

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. Ex. 1003, ¶¶ 80-81.

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 detected signal error is not too severe. Ex. 1003, ¶ 82.

Thus, the claimed invention is really directed to a broad, abstract concept of keeping good data and rejecting bad data—an idea that is basic and fundamental to any signal processing task—applied here to the basic operations of a generic electrochemical glucose sensor. It is then not surprising that, as shown in detail below, all of the claimed hardware elements, their operations, and the recited signal processing concepts, are indeed conventional, routine and well-known to the art. Ex. 1003, ¶ 83.

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 16-20, 23-25, 37-38, and 41-43 of the '045 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	16-20, 23-25
2	§ 103	White, Beaty, Schulman	37-38, 41-43

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 ("White")	Filed Dec. 15, 1989 Issued Sept. 7, 1993	102(a)/(b)
1007	PCT International Publication No. WO 99/32881 ("Beaty")	Filed Dec. 21, 1998 Published July 1, 1999	102(a)/(b)
1008	U.S. Patent No. 5,497,772 ("Schulman")	Filed Nov. 19, 1993 Issued March 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 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. Ex. 1003, ¶¶5-11.

The Schulman (Ex. 1008) patent was among the more than 1,200 references disclosed to the Patent Office 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, 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 how closely these two references out of the 1,200 cited references were analyzed by the examiner, if at all. Moreover, there is no evidence that the White-Beaty-Schulman combination was considered or discussed by the examiner. *See* Ex. 1002; Ex. 1003, ¶¶ 100, 108, 114.

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.[2] *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

[2] 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.

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[3]
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 sensor at a first setting	put to use a voltage to the electrochemical glucose sensor at a first specified condition	ITC judge
switch the voltage applied to the electrochemical sensor to a different setting	change the voltage that was put to use at the electrochemical glucose sensor to a different specified condition	ITC judge
signal artifact	a particular type of noise an artifact relating to signal noise	ITC judge Pat. Owner
non-glucose rate limiting phenomenon	a condition, other than glucose, that affects an electrochemical reaction rate of the electrochemical glucose sensor	Parties
generate an estimated glucose concentration value when the severity associated with the signal artifact is evaluated to be	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	Parties

[3] *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); *id*. at 36 (Patent Owner Dexcom's proposed definition of "signal artifact"); Ex. 1017 at 20 (fn. 7), 42-43, 50.

under a predetermined threshold	be less than a predetermined threshold value	
wherein the estimated glucose concentration value accounts for the severity associated with the signal artifact	wherein the degree of the signal artifact is taken into account in the estimated glucose concentration value	ITC judge
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 16-20 and 23-25 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) and PCT International Publication No. WO1999032881 by Beaty et al. ("Beaty," Ex. 1007) renders each of claims 16-20 and 23-25 obvious. Ex. 1003, ¶ 279.

1. Independent Claim 16

i. White discloses the preamble.

To the extent that the preamble of claim 16 is limiting, White discloses "[a] glucose sensor system." Ex. 1003, ¶ 280.

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."

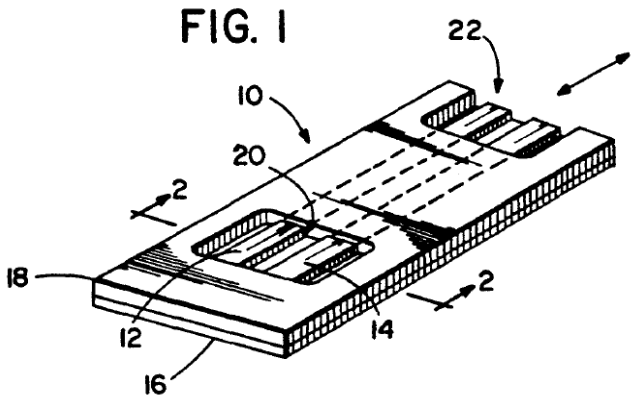
White, 1:5-11 (emphasis added). *See also id*., 2:56-59 ("It is another object of this invention to provide ***an amperometric biosensor and method for glucose concentration*** which provides an error indication, if an aberrant current curve results.") (emphasis added). A POSITA would have understood that "an amperometric biosensor … for glucose concentration" is simply another term for an electrochemical glucose sensor. Ex. 1003, ¶ 281.

Therefore, White discloses the preamble of claim 16. Ex. 1003, ¶ 282.

ii. White discloses "an electrochemical glucose sensor configured to be in contact with a biological sample for measuring a glucose concentration, wherein the electrochemical glucose sensor comprises a first electrode, a second electrode, and an enzyme-containing film" (Element [16.a]).

(1) "an electrochemical glucose sensor configured to be in contact with a biological sample for measuring a glucose concentration"

White discloses "an electrochemical glucose sensor … for measuring a glucose concentration" because White describes a biosensing instrument that, if it is used for "***glucose*** concentration determinations," will include an enzyme which "may be ***glucose*** oxidase (or ***glucose*** dehydrogenase)." White, 3:50-57 (emphasis added). In particular, White's biosensing system "includes ***a test cell*** with at least a pair of electrodes which extend into a reaction zone, which reaction zone includes analyte reactants." *Id*., 2:62-67 (emphasis added). Ex. 1003, ¶ 283. The test cell used with White's biosensing instrument is shown in FIG. 1:



White's biosensor is also "configured to be in contact with a biological sample" because White describes that "Opening 20 [in the test cell shown in FIG. 1] creates, in effect, a reaction zone or 'well' wherein ***a sample of body fluid can be emplaced to enable a reaction to occur***." White, 3:44-46 (emphasis added). White further teaches using "[a]n analog signal detector" of the biosensing system to take measurements "after a sample is ***placed in contact with the analyte reactants*** in the reaction zone." *Id*., 2:67-3:4 (emphasis added). Since the "sample of body fluid" which contains the "analyte reactant" (*i.e.*, glucose) constitutes a "biological sample," White's biosensor test cell (*i.e.*, "electrochemical glucose sensor") is "configured to be in contact with a biological sample" as claimed. Ex. 1003, ¶ 284.

It is also well known in the art that at least the enzyme portion of an electrochemical glucose sensor has to come in contact with the biological sample to react with any glucose content therein in order to measure the glucose concentration. Ex. 1003, ¶ 285.

(2) "wherein the electrochemical glucose sensor comprises a first electrode, a second electrode, and an enzyme-containing film"

White describes a biosensing test cell that includes multiple electrodes:

> "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***." White, 2:62-67 (emphasis added).

> "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. ***Electrodes 12 and 14*** 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 22 exposes ***electrodes 12 and 14*** so that the test cell 10 may be plugged into a female connector that makes electrical connections to ***the electrodes***." White, 3:35-49 (emphasis added).

Ex. 1003, ¶ 286.

In addition to the multiple electrodes, which comprise "a first electrode" and "a second electrode," White also discloses "an enzyme-containing film." Ex.

1003, ¶ 287.

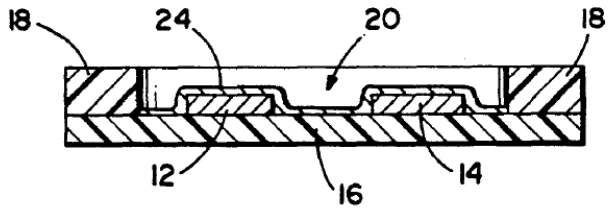
For example, White discloses:

> "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 (or glucose dehydrogenase)***; the buffer may be organic or inorganic; the electrolyte may be potassium chloride or sodium chloride; the mediator is preferably potassium ferricyanide and ***the film formers comprise gelatin and propiofin***."

White, 3:50-61 (emphasis added). Ex. 1003, ¶ 288.

In light of this description, a POSITA would have understood that the reaction layer 24 in White's test cell not only contains an enzyme (*e.g.*, glucose oxidase) but is also in the form of a film as a result of the "film formers" (although it may not be desirable to immobilize the enzyme in a BGM device with a much shorter test time than White's). Furthermore, White's FIG. 2 confirms that the reaction layer 24 is a thin layer formed over the surface electrodes 12 and 14:

FIG. 2



Ex. 1003, ¶ 289.

Thus, a POSITA would have found the reaction layer 24 to be a "thin layer that includes an enzyme" which is the plain and ordinary meaning of an "enzyme-containing film" as advocated by Patent Owner during the ITC proceeding. Ex. 1003, ¶ 290; Ex. 1017 at 41-42, 50.

Therefore, White discloses all the limitations of Element [16.a] as claimed. Ex. 1003, ¶ 291.

iii. White discloses "sensor electronics comprising a processor for executing a computer program code stored in a memory to cause the sensor electronics to [perform the recited functions]." (Element [16.b]).

White discloses "sensor electronics comprising a processor":

> "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.*** System communications occur over system bus 52 and each of the operating units within the instrument interface therethrough. ***A signal voltage module 54 converts digital commands from microprocessor 50 into analog outputs which are then applied***

> ***to cell 10 via line 56*** …"

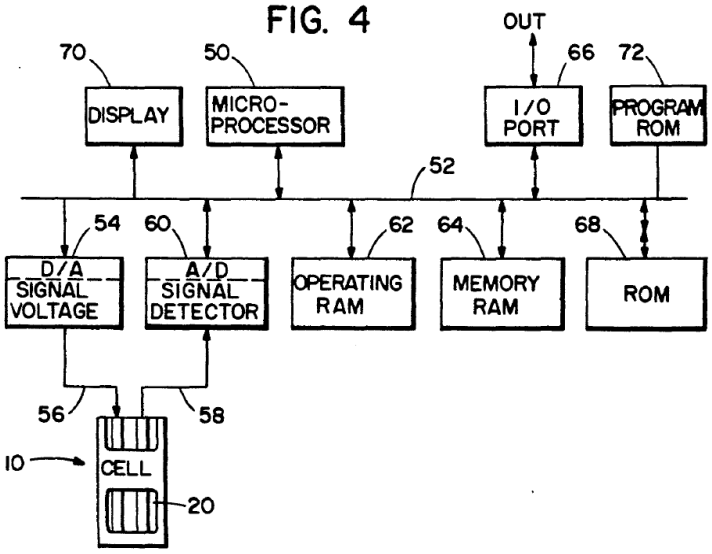
White, 5:26-37 (emphasis added). *See also id*., 6:51-54 ("The ***system's circuits*** are then initialized (box 102) and the autodrop voltage is applied to cell 10 (box 104). ***Signal detector*** 60 then awaits a current spike …"); 2:62-3:17 ("An ***analog signal detector***, in combination with ***a microprocessor***, take plurality of current measurements between the electrodes over a plurality of succeeding measurement times … The ***microprocessor*** also stores a plurality of succeeding comparison constants …) (emphasis added). Ex. 1003, ¶ 292.

White further teaches that the microprocessor is used "for executing a computer program code stored in a memory to cause the sensor electronics to [perform the recited functions]":

> "***Random access memories (RAM's) 62 and 64 provide the operating memory for the instrument.*** RAM 62 provides storage for operating parameters. RAM 64 provides additional storage which enables previous measurement cycles to be retained for comparison purposes or for later read-out to another processor via input/output port 66. A pluggable read-only-memory (ROM) 68 interfaces with bus 52, and in addition to other data, H contains precalculated comparison constants ($x_{1,2}$, $X_{2,3}$ etc.) for the batch of test cells from which test cell 10 is taken. ***Program ROM 72 contains the software to operate the microprocessor.***"

White, 5:49-60 (emphasis added). Ex. 1003, ¶ 293.

The "sensor electronics comprising a processor for executing a computer program code stored in a memory …" is also shown in White's FIG. 4:



Therefore, White discloses Element [16.b] as claimed. Ex. 1003, ¶ 295.

iv. White and Beaty disclose "apply a voltage to the electrochemical glucose sensor at a first setting" (Element [16.c]).

The claim limitation "apply a voltage to the electrochemical glucose sensor at a first setting" was construed as "put to use a voltage to the electrochemical glucose sensor at a first specified condition." Ex. 1016 at 24.

Beaty teaches a new technique to compensate for interferences in biosensors such as White's:

> "By way of example only, ***we have determined that in biosensors of the type described in U.S. Patents: 5,243,516***

> ***[White]; 5,288,636; 5,352,351; 5,385,846; 5,508,171; 5,437,999; and, U.S.S.N. 08/985,840, 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, 8:23-31 (emphasis added). Ex. 1003, ¶ 296.

More specifically, Beaty teaches adding the interference-correcting functionality to White's biosensor:

> "Referring to Fig. 2, a strip connector 30 of the general type illustrated in U.S. Patents: **5,243,516** [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. ***The indicated glucose concentration functionality of the instrument 32 is largely as described in those patents. However, additional functions, namely, the correction of the indicated glucose concentration for blood sample volume and the combined effect of sample temperature and hematocrit of the blood sample under test, are implemented in the instrument 32 according to the present invention.***"

Beaty, 11:20-28 (emphasis added). Ex. 1003, ¶ 297.

In particular, Beaty's additional functions involve applying "an AC signal having a frequency of, for example, 1300Hz … across terminals 34-2—34-3 of connector 34" and sampling the resulting current to determine if the blood sample is of a sufficient volume. Beaty, 15:3-12. "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" to determine "an indicated glucose-to-actual glucose correction factor." *Id*., 15:12-17. Ex. 1003, ¶ 298.

Beaty further teaches that, once its interference-correction procedure is completed, "the determination of the indicated glucose concentration ***proceeds generally as described in U.S. Patents: 5,243,516 [White]***; 5,288,636; 5,352,351; 5,385,846; and 5,508,171, for example." *Id*., 15:21-23 (emphasis added). In other words, Beaty contemplates its sample-detection and/or interference-correction procedure as an add-on module for White's glucose sensing method, replacing (or supplementing) White's sample-detection step and preceding to the amperometric measurement. Ex. 1003, ¶ 299.

A POSITA would have understood that the "AC signal" (1300Hz and/or 10KHz) applied to the electrode terminals for measurement of the resulting current is clearly a voltage signal and such voltage is applied at "a first specified condition" (or "a first setting") in at least two senses. Ex. 1003, ¶ 300.

First, a POSITA would have understood that with an AC voltage, as opposed to a DC voltage, applied to the electrodes, the voltage put to use at the test cell ("the electrochemical glucose sensor") would vary over time: at one moment the AC voltage would be at a first specified condition (or "a first setting"), and at a subsequent moment the AC voltage would be at a second specified condition (or "a different setting"). Ex. 1003, ¶ 301.

Second, the AC voltage applied to the test cell during Beaty's procedure is at a first specified condition (or "a first setting") distinguishable from the "measurement voltage" applied to the test cell which would be at a second specified condition (or "a different setting"). Ex. 1003, ¶ 302.

Thus, both White and Beaty disclose "apply a voltage to the electrochemical glucose sensor at a first setting" (Element [16.c]) as claimed. Ex. 1003, ¶ 303.

v. White and Beaty disclose "switch the voltage applied to the electrochemical sensor to a different setting" (Element [16.d]).

The claim limitation "switch the voltage applied to the electrochemical sensor to a different setting" was construed as "change the voltage that was put to use at the electrochemical glucose sensor to a different specified condition."

Case 1. Switch settings from sampling/correction to glucose measurement

Beaty teaches applying AC voltage(s) to the test cell to detect the volume of a blood sample and to correct inferences and further describes *then* "the

determination of the indicated glucose concentration ***proceeds generally as described in U.S. Patents: 5,243,516 [White]*** …" (Beaty, 15:21-23). Since White's subsequent glucose measurement includes applying the "measurement voltage," the transition from Beaty's sample-detection/interference-correction procedure to White's glucose measurement steps must involve switching the applied voltage from Beaty's AC voltage(s) to White's "measurement voltage" which in a typical amperometric measurement would be a DC voltage. Ex. 1003, ¶¶ 304-305.

Therefore, in Case 1, White discloses "switch the voltage applied to the electrochemical sensor [from a first setting] to a different setting." Ex. 1003, ¶ 306.

Case 2. Switch the AC voltage applied to the test cell

As explained above, Beaty teaches that, during sample detection and interference correction, AC signals having frequencies of 1300Hz and 10KHz are successively "applied across terminals 34-2—34-3 of connector 34." Beaty, 15:3-15. If the AC voltage(s) applied across the electrode terminals at a first moment have a first value (thus being "at a first setting"), then, when the AC voltage(s) swing to a different value at a subsequent moment, "the voltage applied to the electrochemical sensor" has switched to "a different setting." Ex. 1003, ¶¶ 307-308.

Thus, Beaty's application of the AC voltage(s) inherently requires "switch[ing] the voltage applied to the electrochemical sensor [from a first setting] to a different setting." Ex. 1003, ¶ 309.

Therefore, in both Case 1 and Case 2, White and Beaty disclose Element [16.d] as claimed. Ex. 1003, ¶ 310.

vi. White and Beaty disclose "measure a signal response of the electrochemical glucose sensor responsive to the switching" (Element [16.e]).

White's glucose current reading as "*signal response*" (in Cases 1 & 2)

Whether the "switching" refers to the switching of voltage settings from AC voltage(s) (during Beaty's sample-detection and interference-correction) to a "measurement voltage" or the inherent switching of such AC voltage(s), an ultimate goal (and the result) is the measurement of a glucose-indicating electrical signal based on the electrochemical reaction of the blood sample with a glucose enzyme:

> "At this point, the autodrop voltage is removed (box 108), and the system waits until the reaction time expires (box 110). ***Then, 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).***" White, 6:56-63 (emphasis added).
>
> "When the forward reaction has proceeded to completion, ***a***

> ***subsequent application of a voltage across terminals 12 and 14 will see <u>the creation of a small current</u> therebetween*** that results from the reverse reaction of potassium ferrocyanide back to potassium ferricyanide. ***<u>The flow of electrons during the reverse reaction is sensed and measured</u> and has been found to bear a known relationship to glucose concentration levels.***"

White, 4:8-15 (emphasis added). *See also id*., 6:25-28 ("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 . . .)"). Ex. 1003, ¶ 311.

Since the raw, glucose-indicating signal would not have been available but for the switching of the applied voltage from a previous AC setting to the "measurement voltage" setting and but for Beaty's application of the AC voltage(s), a POSITA would have understood that the measurement of the raw signal from White's test cell is indirectly or directly "responsive to the switching." Ex. 1003, ¶ 312.

Therefore, White discloses measuring the raw electrical signal as "a signal response of the electrochemical glucose sensor responsive to the switching." Ex. 1003, ¶ 313.

<u>Beaty's measured response to AC excitation as "*signal response*" (in Case 1)</u>

Beaty teaches measuring voltage and current responses to the excitation of AC voltages:

> "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, 15:3-15 (emphasis added). Based on this description, a POSITA would have understood that both the "resulting current" and the "response voltage" are "signal responses" responsive to the AC signal which inherently involves the switching of voltage levels. Ex. 1003, ¶ 314.

Thus, Beaty also discloses "measure a signal response of the electrochemical glucose sensor responsive to the switching." Ex. 1003, ¶ 315.

Therefore, both White and Beaty disclose Element [16.e] as claimed. Ex. 1003, ¶ 316.

vii. White discloses "evaluate a severity associated with a signal artifact based on the measured signal response of the electrochemical glucose sensor to the switching, wherein the

signal artifact is associated with a non-glucose rate limiting phenomenon" (Element [16.f]).

White discloses a method for determining "whether a measured current is varying in accordance with a predetermined Cottrell current relationship" (White, 2:62-64), which "evaluate[s] a severity associated with a signal artifact based on the measured signal response …" as claimed. Ex. 1003, ¶ 317.

When the raw glucose current is the "signal response," White teaches determining "whether a measured current is varying in accordance with a predetermined Cottrell current relationship" to evaluate the severity of signal artifacts:

> "Equation 5 shows that even though individual measurement currents taken at subsequent measurement times are not known in advance, that the ratio thereof, ***assuming a Cottrell curve is being followed***, will be a constant and will show a level of similarity with the ratio of the square roots of the measurement times. Of course, ***the ratios will rarely be exactly alike as the current measurements will show some variations due to test conditions***." White, 5:15-23 (emphasis added).
>
> "Additionally, microprocessor 50, in combination with the other modules in the system, carries out a series of tests ***to determine that the signals being detected by signal detector 60 are following the Cottrell current relationship***." White, 6:40-44 (emphasis added).

> "***At this point, the current value measured at t_n and t_{n+1} are accessed and the ratio thereof is derived. That ratio is then compared to the prestored comparison constant $x_{n, n+1}$.*** 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)." White, 6:64-7:5 (emphasis added).

Ex. 1003, ¶ 318.

Thus, the behavior of the glucose current as compared to "a predetermined Cottrell current relationship" reflects the severity of a "signal artifact," because any significant departure from this expected behavior is indicative of a poor or incorrect measurement. The evaluation of the "severity" is directly based on the glucose current which is "the measured signal response of the electrochemical glucose sensor to the switching." Ex. 1003, ¶ 319.

Moreover, White identifies various potential conditions, unrelated to the glucose concentration in the blood sample, that may cause the glucose measurement to deviate from the Cottrell curve:

> "Neither Nankai et al. or Pottgen et al. deal with certain real-life problems which occur during the use of a test cell. For instance, ***if 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***. These errors appear as baseline shifts in the Cottrell current or modulations of area during the measurement period."

White, 2:38-51 (emphasis added). Ex. 1003, ¶ 320.

Thus, monitoring the signal behavior in comparison to the predetermined Cottrell current relationship, as taught by White, can "evaluate a severity associated with a signal artifact based on the measured signal response of the electrochemical glucose sensor to the switching, wherein the signal artifact is associated with a non-glucose rate limiting phenomenon." Ex. 1003, ¶ 321.

Therefore, White discloses Element [16.f] as claimed. Ex. 1003, ¶ 322.

viii. White discloses "generate an estimated glucose concentration value when the severity associated with the signal artifact is evaluated to be under a predetermined threshold, wherein the estimated glucose concentration value accounts for the severity associated with the signal artifact" (Element [16.g]).

(1) "generate an estimated glucose concentration value when the severity associated with the signal artifact is evaluated to be under a predetermined threshold"

White teaches screening glucose current readings to eliminate poor or incorrect signals, such that only trustworthy glucose concentration values would be retained and displayed:

> "***At this point, the current value measured at t_n and t_{n+1} are accessed and the ratio thereof is derived. That ratio is then compared to the prestored comparison constant $x_{n, n+1}$.*** 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)." White, 6:64-7:5 (emphasis added).
>
> "In the event the comparison 'fails', an error condition is reported (box 122). ***If the comparison succeeds, the process continues*** … 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' glucose concentration value*** (box 134)." White, 7:6-17 (emphasis added).

Ex. 1003, ¶ 323.

The ratio between two successive current values, as "compared to the prestored comparison constant $x_{n, n+1}$", reflects "the severity associated with the signal artifact." Only when the calculated ratio is sufficiently similar to the

"prestored comparison constant," indicating a close enough fit to the Cottrell curve, will White's process continue to "generate an estimated glucose concentration value." Ex. 1003, ¶ 324.

In particular, White describes that the difference between the calculated current ratio and the precalculated comparison constant x—which constitutes or indicates the severity of signal artifacts—is compared with "a predetermined error value" (*i.e.*, "a predetermined threshold") to detect an error condition. White, 6:64-7:5. That is, a difference greater than that threshold would indicate a large deviation of the glucose current from the Cottrell curve (therefore an incorrect measurement), while a difference under the threshold would indicate conformality with the Cottrell curve (therefore an acceptable measurement). *Id*., 7:6-17. *See also* White, 5:20-25 (recognizing that "the ratios will rarely be exactly alike as the current measurements will show some variations due to test conditions" and therefore "any comparison of the ratios will require that standard deviations be taken into account when the comparison is made"). Ex. 1003, ¶¶ 325-326.

Therefore, White discloses "generate an estimated glucose concentration value when the severity associated with the signal artifact is evaluated to be under a predetermined threshold." Ex. 1003, ¶ 327.

(2) "wherein the estimated glucose concentration value accounts for the severity associated with the signal artifact"

The claim limitation "wherein the estimated glucose concentration value accounts for the severity associated with the signal artifact" was construed to mean "wherein the degree of the signal artifact is taken into account in the estimated glucose concentration value."

By performing the above-described data screening *before* calculating the estimated glucose concentration, White's biosensor takes into account the degree of severity of any signal artifact associated with deviations from the Cottrell curve. White's biosensing system would not proceed to compute the glucose value at all if that severity were above the predetermined threshold (*i.e.*, when the current values show significant departures from the Cottrell equation); in other words, the estimated glucose concentration value, if generated, indicates the severity is low enough and thereby "accounts for the severity associated with the signal artifact." Ex. 1003, ¶¶ 329-330.

Notably, Patent Owner has taken the same position in the related ITC proceeding, arguing that the severity of a signal artifact used to screen glucose measurements is effectively taken into account in a validated glucose concentration value:

> "By performing this partial fill check before calculating the estimated glucose concentration [Glucose], the AgaMatrix system takes into account or considers the degree of severity of any signal artifact associated with the available electrode

surface area. If that severity is below a certain threshold, that is to say the capacitance is above a set level, then the algorithm permits the system to compute the glucose estimate [Glucose]."

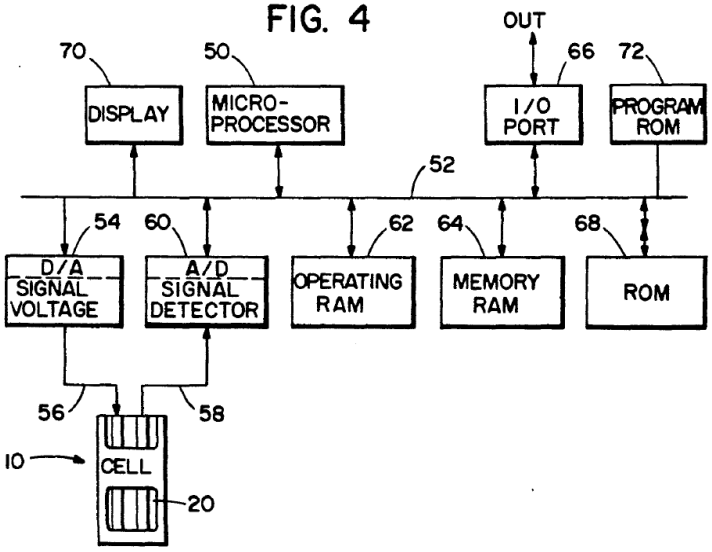
Ex. 1020 (Dexcom's Infringement Expert Report), ¶ 627.

Thus, White discloses "wherein the estimated glucose concentration value accounts for the severity associated with the signal artifact." Ex. 1003, ¶ 328.

Therefore, White discloses all the limitations of Element [16.g] as claimed. Ex. 1003, ¶ 331.

ix. White discloses "a user interface configured to display the estimated glucose concentration value" (Element [16.h]).

White discloses that "a display 70 enables the user to see the results of a concentration measurement taken through the use of cell 10." White, 6:2-4. *See also id*., FIG. 4 (Display 70). Ex. 1003, ¶ 332.



The display 70 is "a user interface configured to display the estimated glucose

concentration value" as claimed. Ex. 1003, ¶ 333.

Thus, White discloses Element [16.h] as claimed. Ex. 1003, ¶ 334.

Therefore, the combination of White and Beaty discloses, teaches, or suggests all the elements of claim 16. Ex. 1003, ¶ 335.

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

A POSITA would have been motivated to combine Beaty's disclosure with White's glucose sensor to improve its interference-correction capabilities. Ex. 1003, ¶ 336.

First, not only are White and Beaty in the same field of endeavor,[4] both being directed to biosensing systems for amperometric measurement of glucose, but Beaty also explicitly teaches incorporating its sample-detection and interference-correction functions into White's biosensor. For example, Beaty's disclosure cites White by its patent number (5,243,516) a total of twelve times, repeatedly confirming that Beaty's "methods and apparatus" are "for improving the accuracy of measurements made with instruments of the type described in" the White patent. Beaty, 1:4-8. Ex. 1003, ¶ 337.

[4] In fact, Beaty's applicant/assignee, Roche Diagnostics Corporation, is the successor-in-interest to the White's assignee, Boehringer Mannheim Corporation.

Second, Beaty's additional teaching is complementary to White because Beaty's interference-correction function helps achieve White's stated object of "prevent[ing] erroneous readings from being reported as true" (White, 2:52-55). Ex. 1003, ¶ 338.

Third, Beaty teaches how its methods fit into White's biosensing operations, specifying that, once Beaty's interference-correction procedure is completed, "the determination of the indicated glucose concentration ***proceeds generally as described in U. S. Patents: 5,243,516 [White]*** …" Beaty, 15:21-23 (emphasis added). Ex. 1003, ¶ 339.

Fourth, a POSITA would have been capable of modifying White's biosensing method to incorporate Beaty's sample-detection and interference-correction functions. Only a small amount of modification would be required, such as reprogramming the microprocessor and reconfiguring the voltage source to apply the AC voltage(s), measure the voltage/current responses, and determine a sample volume and a correction factor. At the time of the claimed invention (in 2003), no significant technological obstacle would have prevented a POSITA from making such modification. Ex. 1003, ¶ 340.

After all, the sample-detection and interference-correction functions are substantially independent from the subsequent glucose measurement functions. A POSITA would have considered Beaty's sample-detection and interference-

correction functions to be a modular component that could be easily copied and adapted to a similar glucose sensor system such as White's. Ex. 1003, ¶ 341.

Thus, modifying White with Beaty would require little more than: (a) combining one known element in the prior art (*i.e.*, Beaty's sample-detection and interference-correction functions) with other known elements (*i.e.*, White's biosensor system), or (b) simply substituting one known element (*i.e.*, the sample-detection step of White's biosensor system) with other known elements (*i.e.*, Beaty's sample-detection and interference-correction functions). Therefore, a POSITA would have a reasonable expectation of success in making the combination or modification. *See* Ex. 1003, ¶ 340.

In summary, because (1) White and Beaty are in the same field, (2) they disclose substantially overlapping amperometric methods for glucose measurement, (3) White itself offers the motivation to adopt Beaty's interference-correction function, (4) the insignificant amount of modification required would be well within the grasp of a POSITA, and (5) most importantly, Beaty explicitly teaches incorporating its teaching into White's system, it would have been obvious to combine the teachings of White and Beaty to make the claimed invention. *See* Ex. 1003, ¶¶ 337-342.

Since it would have been obvious for a POSITA to combine White and Beaty which collectively teach or suggest each and every element of claim 16,

White, in view of Beaty, renders claim 16 obvious. Ex. 1003, ¶ 342.

3. Dependent Claim 17

Dependent claim 17 incorporates the limitations of independent claim 16 (which are all disclosed, taught or suggested by White and Beaty) and additionally recites "*wherein the biological sample is blood*."

As shown above in connection with Element [16.preamble], White discloses "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, 1:6-11 (emphasis added). As shown above in connection with Element [16.a], White's test cell (*i.e.*, "electrochemical glucose sensor") is also configured to be in contact with "a sample of body fluid" containing the "analyte reactant" (*i.e.*, glucose) in order to measure its concentration. *Id*., 2:67-3:4, 3:44-46. Ex. 1003, ¶ 344.

Similarly, Beaty is directed to "[a]n apparatus (31, 32, 132) and method for determining the concentration of a medically significant component (for example, glucose) of ***a biological fluid*** (for example, ***blood***)." Beaty, Abstract (emphasis added). Ex. 1003, ¶ 345.

Therefore, both White and Beaty teach that the "biological sample is blood" as recited in claim 17, and the White-Beaty combination renders this claim obvious. Ex. 1003, ¶ 346.

4. Dependent Claim 18

Dependent claim 18 incorporates the limitations of independent claim 16 (which are all disclosed, taught or suggested by White and Beaty) and additionally recites "*wherein measuring the signal response comprises measuring a current output of the electrochemical glucose sensor*."

As shown above in connection with Element [16.e], White teaches measuring the current as a result of applying the "measurement voltage" to the test cell (*see* White, 4:8-15, 6:25-28, 6:56-63); therefore the measured glucose current is the "signal response." Ex. 1003, ¶ 348. Also as explained above, Beaty teaches measuring current responses to the excitation of AC voltages and that measured current response alternatively constitutes the "signal response." *See* Beaty, 15:3-15 ("***the resulting current is indirectly sampled*** by μP 54 by measuring the excitation and response voltages and using the scale factor ***to obtain current***") (emphasis added). Ex. 1003, ¶ 349. A POSITA would have understood that either of these current measurements, as taught by White and Beaty respectively, is "a current output of the electrochemical glucose sensor." Ex. 1003, ¶ 350.

Therefore, both White and Beaty disclose "wherein measuring the signal response comprises measuring a current output of the electrochemical glucose sensor" as recited in claim 18, and the White-Beaty combination renders this claim obvious. Ex. 1003, ¶ 351.

5. Dependent Claim 19

Dependent claim 19 incorporates the limitations of independent claim 16 (which are all disclosed, taught or suggested by White and Beaty) and additionally recites "*wherein measuring the signal response comprises measuring a voltage output of the electrochemical glucose sensor*."

As shown above in connection with Element [16.e], Beaty teaches measuring "response voltages" as a result of the excitation of AC voltages and that measured voltages constitute the "signal response." *See* Beaty, 15:3-15 ("the resulting current is indirectly sampled by μP 54 by ***measuring the excitation and response voltages*** …") (emphasis added). Ex. 1003, ¶ 353. A POSITA would have understood that Beaty's measured "response voltages" from the test cell constitute "a voltage output of the electrochemical glucose sensor." Ex. 1003, ¶¶ 354-355.

Therefore, Beaty discloses "wherein measuring the signal response comprises measuring a voltage output of the electrochemical glucose sensor" as recited in claim 19, and the White-Beaty combination renders this claim obvious. Ex. 1003, ¶ 356.

6. Dependent Claim 20

Dependent claim 20 incorporates the limitations of independent claim 16 (which are all disclosed, taught or suggested by White and Beaty) and additionally

recites "*wherein the measured signal response is a voltage response of the electrochemical glucose sensor*."

As shown above in connection with Element [16.e] and claim 19, Beaty teaches measuring "response voltages" as a "signal response" from the test cell ("electrochemical glucose sensor"). A POSITA would have understood that Beaty's "response voltages" from the test cell constitute "a voltage response of the electrochemical glucose sensor." Ex. 1003, ¶ 358.

Therefore, Beaty discloses "wherein the measured signal response is a voltage response of the electrochemical glucose sensor" as recited in claim 20, and the White-Beaty combination renders this claim obvious. Ex. 1003, ¶ 359.

7. Dependent Claim 23

Dependent claim 23 incorporates the limitations of independent claim 16 (which are all disclosed, taught or suggested by White and Beaty) and additionally recites "*wherein the non-glucose rate limiting phenomenon is associated with a temperature*."

As shown above in connection with Element [16.f], when the glucose current signal is the "signal response" and it is compared with a predetermined Cottrell current relationship to evaluate the severity of signal artifacts therein, a POSITA would have understood that such signal artifacts could originate from a number of conditions, other than glucose, that affect an electrochemical reaction

rate of the electrochemical glucose sensor. *See*, *e.g.*, White, 2:35-51; 4:28-50. Ex. 1003, ¶ 361.

It is well known that the sample temperature is an ever-present factor influencing the non-glucose conditions which cause the glucose current to deviate from the Cottrell curve. For example, Beaty's "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." Beaty, 7:28-31 (emphasis added). *See also id*., 8:23-31 (employing "AC signal in the range of less than about .1Hz to 10KHz or so with no DC offset to compensate for ***sample temperature***") (emphasis added). Ex. 1003, ¶ 362.

Furthermore, the Cottrell current includes the factor D, "the diffusion coefficient of the electroactive species." White 1:67-2:14. Ex. 1003, ¶ 363. A POSITA would have understood that the diffusion coefficient is also temperature dependent, and that the temperature of a blood sample can vary over the 30-second test period, creating a non-glucose rate limiting phenomenon. Ex. 1003, ¶ 364.

Therefore, the White-Beaty combination teaches, or at least suggests, "wherein the non-glucose rate limiting phenomenon is associated with a temperature" as recited in claim 23 and renders this claim obvious. Ex. 1003, ¶ 365.

8. Dependent Claim 24

Dependent claim 24 incorporates the limitations of independent claim 16 (which are all disclosed, taught or suggested by White and Beaty) and additionally recites "*wherein the non-glucose rate limiting phenomenon is associated with an available electrode surface area*."

The claim term "available electrode surface area" was construed as "surface area of an electrode where an electrochemical reaction occurs."

As shown above in connection with Element [16.f] and claim 23, when the glucose current signal is the "signal response," its associated signal artifacts could originate from a number of conditions, other than glucose, that affect an electrochemical reaction rate of the electrochemical glucose sensor. Ex. 1003, ¶ 367.

It is well known that the surface area of the measuring electrode is another factor influencing the non-glucose conditions which cause the glucose current to deviate from the Cottrell curve. For example, this is one of the factors in the Cottrell equation:

> "The current which results during the reverse reaction is known as the Cottrell current and is described by the following equation:
>
> $$\text{Cottrell Current} = i = \frac{nF\sqrt{D}\,CA}{\sqrt{\pi}\cdot\sqrt{t}}$$

where:

n=the number of transferred electrons;

F=Faraday's constant

A=<u>area of measuring electrode</u>;

C=concentration of the analyte;

D=diffusion coefficient of the electroactive species;

t=time"

White, 1:67-2:14 (emphasis added). Ex. 1003, ¶ 368. A POSITA would have understood that, in the context of glucose test strip, the "area of measuring electrode" (A) in the Cottrell equation refers to the electrode surface area actually covered by, or in contact with, the blood sample. Indeed, White recognizes that "[i]f the sample only covers a portion of the electrode areas, an erroneous reading will occur." White, 4:38-40. *See also id*., 2:41-43 ("if the blood sample does not totally cover the sensing electrode surfaces, an erroneous reading results."). Ex. 1003, ¶ 369.

Therefore, the White-Beaty combination teaches, or at least suggests, "wherein the non-glucose rate limiting phenomenon is associated with an available electrode surface area" as recited in claim 24 and renders this claim obvious. Ex. 1003, ¶ 370.

9. Dependent Claim 25

Dependent claim 25 incorporates the limitations of independent claim 16

(which are all disclosed, taught or suggested by White and Beaty) and additionally recites "*wherein the non-glucose rate limiting phenomenon is associated with a biochemical species*."

As shown above in connection with Element [16.f] and claim 23, when the glucose current signal is the "signal response," its associated signal artifacts could originate from a number of conditions, other than glucose, that affect an electrochemical reaction rate of the electrochemical glucose sensor. Ex. 1003, ¶ 372.

It is well known that the presence of biochemical species is a common factor influencing the non-glucose conditions which cause the glucose current to deviate from the Cottrell curve. For example, Beaty recognizes that "[i]n biosensors of the general types described in U.S. Patents: 5,243,516 [White]; …, such chemical interferrents include, for example, ***bilirubin***, ***uric acid*** and ***oxygen***." Beaty, 7:31-8:4 (emphasis added). A POSITA would have understood that each of bilirubin, uric acid, and oxygen (in the blood sample) is "a biochemical species." Ex. 1003, ¶ 373.

Therefore, the White-Beaty combination teaches, or at least suggests, "wherein the non-glucose rate limiting phenomenon is associated with a biochemical species" as recited in claim 25 and renders this claim obvious. Ex. 1003, ¶ 374.

B. Ground 2: Claims 37-38 and 41-43 are obvious under 35 U.S.C. § 103 in light of White, Beaty and Schulman.

The combination of White, Beaty, and Schulman renders each of claims 37-38 and 41-43 obvious. Ex. 1003, ¶ 375.

1. Independent Claim 37

Independent claim 37 recites identical limitations as independent claim 16 (which are all disclosed, taught or suggested by White and Beaty as shown above), except that claim 37 adds "wherein the measured signal response is a time-varying voltage response of the electrochemical glucose sensor" to the step of "measure a signal response …" and also adds more "user interface" functions. Ex. 1003, ¶ 376.

i. "wherein the measured signal response is a time-varying voltage response of the electrochemical glucose sensor"

As shown above in connection with Element [16.e] and claim 20, Beaty teaches applying AC voltages of chosen frequencies (e.g., 1300Hz or 10KHz) to the electrode terminals in White's test cell (*i.e.*, "electrochemical glucose sensor") and measuring "response voltages" as a "signal response" thereof. *See* Beaty, 15:3-15. Ex. 1003, ¶ 378.

A POSITA would have understood and expect that, since the AC voltage applied to the test cell changes over time (*e.g.*, oscillating at the chosen frequency), the "response voltages" responsive to such a "time-varying" excitation would also

be a "time-varying voltage response of the electrochemical glucose sensor." Ex. 1003, ¶ 378.

Furthermore, as shown above in connection with Element [16.e], White teaches measuring glucose current values, as "a signal response," at successive points in time. *See* White, 6:59-63 ("a measurement voltage is applied to cell 10 from signal voltage module 54, and ***a first current reading is taken at t0*** and recorded … Next, (in FIG. 6) ***a subsequent current reading is taken (e.g. t1)*** and recorded (box 118)."") (emphasis added). Ex. 1003, ¶ 379. Although such current readings constitute "a time-varying *current* response," a POSITA would have understood that a corresponding "time-varying voltage response" proportionate to the current response is available for measurement in the circuit. For example, the "current response" detected by the Signal Detector 60 is fed into an analog-to-digital converter (A/D) which conventionally processes a voltage input instead of current input. Ex. 1003, ¶¶ 380-381; White, FIG. 4.

Therefore, White and Beaty teach, or at least suggest, "wherein the measured signal response is a time-varying voltage response of the electrochemical glucose sensor." Ex. 1003, ¶¶ 377, 382.

ii. "user interface" limitation

Claim 37 recites "a user interface" configured to:

display a first screen presenting generated glucose

concentration data over a first time period,

display a second screen presenting generated glucose concentration data over a second time period, wherein the second time period is different in length from the first time period,

display a third screen presenting the estimated glucose concentration value,

allow a user to toggle between the first screen, the second screen, and the third screen, and

generate an alert responsive to detection of a hyperglycemic condition or a hypoglycemic condition.

As explained above, White generally discloses "a display 70" as a user interface which "enables the user to see the results of a concentration measurement taken through the use of cell 10." White, 6:2-4; FIG. 4 (Display 70). Ex. 1003, ¶ 385.

Although White does not elaborate on "the results of a concentration measurement" in connection with the user interface display functions, White describes elsewhere in its disclosure various forms of glucose measurement data, including: (1) "plots of Cottrell current variations at various glucose concentration levels" over a period of time (White, 2:32-34, 4:16-26, FIG. 3); (2) glucose concentration values (or "a single sample measurement") calculated from selected current measurements and based upon a precalibrated linear relationship (*id*., 6:29-34, 7:13-17, 7:39); and (3) glucose current values measured at a series of points in

time (or "current readings [provided] on continuing basis") and ratios derived from successive current values (*id*., 5:41-44, 6:59-7:5). These data may also include those from "previous measurement cycles" that have been "retained for comparison purposes or for later read-out to another processor via input/output port 66." *Id*., 5:51-55. Ex. 1003, ¶ 386.

In light of such variety of glucose measurement results, a POSITA would have understood White to teach, or at least suggest, displaying these results to a user. Furthermore, presenting current and previous glucose readings involves displaying multiple screens as the display of each of the current and previous glucose readings may provide a different screen "presenting generated glucose concentration data" over a corresponding time period or "presenting the estimated glucose concentration value" as claimed. Ex. 1003, ¶ 387.

Thus, White discloses, teaches, or suggests at least "a user interface configured to" display multiple screens presenting "generated glucose concentration data" or "the estimated glucose concentration value," and "allow a user to toggle between" the multiple screens as claimed. Ex. 1003, ¶ 388.

The only user interface limitations recited in claim 37 that are not explicitly described by White are the "glucose concentration data" being generated over "a first time period" and "a second time period" that are "different in length" and to

"generate an alert responsive to detection of a hyperglycemic condition or a hypoglycemic condition." Ex. 1003, ¶ 389.

U.S. Patent No. 5,497,772 to Schulman et al. ("Schulman," Ex. 1008), 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 37. 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 (emphasis added). *See also* Schulman, FIG. 10B ("Current Value" mode or "monitor mode"), FIG. 10C ("Graph" mode). Ex. 1003, ¶ 390.

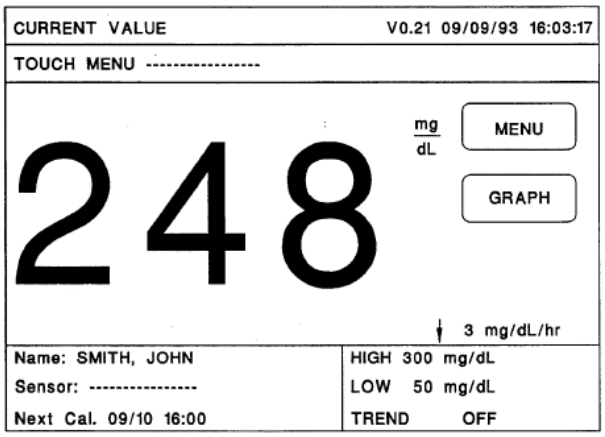


FIG. 10B

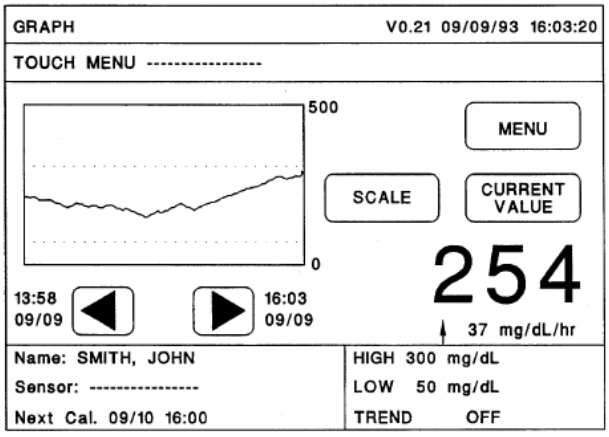


FIG. 10C

A POSITA would have understood that Schulman discloses all three types of user interface "screens" and related toggling as recited in claim 37. Ex. 1003, ¶ 391.

First, in the "graphic display mode," Schulman teaches that a user could select different time periods of 3 to 72 hours to plot glucose concentration data. Thus, if the user chose a 3-hour period for the graphic display, then the glucose monitor would "display a first screen presenting generated glucose concentration data 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 generated glucose concentration data over a second time period [of 72 hours], wherein the second time period is different in length from the first time period" as claimed. Ex. 1003, ¶ 392.

Second, in the "monitor mode," Schulman teaches that a different screen displays the glucose concentration is "in large numerals." In other words, the

monitor mode "display[s] a third screen presenting the estimated glucose concentration value" as claimed. Ex. 1003, ¶ 393.

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 (emphasis added). The ability to switch display modes, coupled with the above-described ability to select time periods of different length to plot data, "allow[s] a user to toggle between the first screen, the second screen, and the third screen" as claimed. Ex. 1003, ¶ 394.

In addition, Schulman teaches "generate 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"). Ex. 1003, ¶ 395.

Therefore, Schulman discloses all the "user interface" limitations of claim 37, and the combination of White, Beaty, and Schulman teaches or suggests all the elements of claim 37. Ex. 1003, ¶ 396.

iii. A POSITA Would Have Been Motivated To Combine Schulman with White and Beaty.

A POSITA would have been motivated to combine Schulman's disclosure with the White-Beaty glucose sensor to improve its user interface capabilities. Ex. 1003, ¶ 397.

First, White, Beaty, and Schulman are in the same field of endeavor, all being directed to glucose monitoring and disclosing complete glucose sensor systems including user interfaces. In all these systems, the glucose measurement generates a variety of data that need to be presented and utilized via a user interface. Ex. 1003, ¶ 398.

Second, the user interfaces disclosed by White and Schulman already have substantially overlapping display and alarm functions. For example, 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); Schulman describes "a large screen 126 wherein the sensor data, including glucose concentration, rates of change, and history (graphs of glucose concentration over time) may be

displayed" (Schulman, 11:14-18). The only significant difference is in Schulman's capability of displaying glucose graphs over different time periods and generating alarms. Ex. 1003, ¶ 399.

Third, Schulman's additional teaching is complementary to White because Schulman offers user interface functions suggested by, but not explicitly disclosed in, White. White, on the one hand, generally states the need for "enable[ing] the user to ***see the results*** of a [glucose] concentration measurement." White, 6:2-4 (emphasis added). Schulman, on the other hand, acknowledges the advantage of graphical visualization of glucose data 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 (emphasis added). That is, Schulman teaches displaying glucose graphs over user-selectable time periods to help visualize and detect the trends in glucose measurement. In light of these teachings, a POSITA could readily appreciate that Schulman's graphical display functions directly meet White's stated need for displaying glucose measurement results. Thus, White itself provides the reason and incentive for adopting Schulman's user interface functions. Ex. 1003, ¶¶ 400-403.

Fourth, a POSITA would have been capable of modifying White's biosensor display to incorporate Schulman's graphical display functions. Since White

already discloses many of the claimed user interface functions, only a small amount of modification would be required, such as reprogramming the microprocessor and reconfiguring the user interface with enhanced graphical display of glucose graphs over user-selectable time periods. At the time of the claimed invention (in 2003), no significant technological obstacle would have prevented a POSITA from making such modification. Ex. 1003, ¶ 404.

After all, the user interface and its functions are substantially independent from the glucose sampling and sensing components and related functions. A POSITA would have considered the user interface in White's system to be a modular component that could be easily copied and adapted from another glucose sensor system such as Schulman's. Ex. 1003, ¶ 405.

Thus, modifying White with Schulman 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 biosensor system), or (b) simply substituting one known element (*i.e.*, the user interface of White's biosensor system) with another known element (*i.e.*, Schulman's user interface module). Therefore, a POSITA would have a reasonable expectation of success in making the combination or modification. *See* Ex. 1003, ¶¶ 404-405.

To the extent Patent Owner points to the fact that Schulman is directed to continuous glucose monitoring while White and Beaty are directed to non-

continuous glucose sensors, it should be noted that the choice of user interface hardware (*e.g.*, display screen) here is a design choice well within a POSITA's technical capabilities. Ex. 1003, ¶ 406. In fact, a POSITA would have appreciated that a user interface module feasible for a continuous glucose monitor could generally be adapted for use with a non-continuous glucose monitor because the latter performs *in vitro* glucose measurement which actually places less constraint on the user interface component. Ex. 1003, ¶ 407.

In any case, Schulman teaches coupling its glucose monitor to multiple sensors through "a ***detachable connector*** that does not use a direct electrical contact (i.e., a ***'contactless' connector***)" (Schulman, 5:1-10, 11:28-12:13, FIGs. 7A-7B), which detachable design would have been found by a POSITA to be equally suitable for most types of glucose sensor systems, whether a continuous or non-continuous type. Ex. 1003, ¶ 408. In fact, it was known in the art to equip an *in vitro* (non-continuous) glucose sensor with user interface functions similar to those of Schulman's continuous glucose sensor. *See* Ex. 1003, ¶ 409, citing Buse (Ex. 1024), 38:35-42 (describing a sophisticated display, or a port for coupling such a display to an *in vitro* glucose sensor).

As a result, a POSITA would not have been discouraged or precluded from considering Schulman's user interface functions for incorporation into the White-

Beaty sensor system simply because they have different glucose sampling mechanisms in the front end. Ex. 1003, ¶ 410.

In summary, because (1) White, Beaty and Schulman are in the same field of electrochemical glucose measurement, (2) they already disclose substantially overlapping user interface functions, (3) White itself offers the motivation to adopt Schulman's enhanced graphical display function in order to help visualize glucose data, and (4) the insignificant amount of modification required would be well within the grasp of a POSITA, it would have been obvious to combine the teachings of White, Beaty, and Schulman to make the claimed invention. *See* Ex. 1003, ¶¶ 398-411.

Since it would have been obvious for a POSITA to combine White, Beaty, and Schulman which collectively teach or suggest each and every element of claim 37, White and Beaty, in view of Schulman, render claim 37 obvious. Ex. 1003, ¶ 411.

2. Dependent Claims 38 and 41-43

Dependent claims 38 and 41-43 each incorporate the limitations of independent claim 37 (which are all taught or suggested by White, Beaty and Schulman) and additionally recited limitations identical to those of dependent claims 17 and 23-25 respectively which are also disclosed, taught, or suggested by White and/or Beaty. Thus, White and/or Beaty disclose, teach, or suggest the

additionally recited limitations of claims 38 and 41-43. Ex. 1003, ¶ 412.

Therefore, based on the same reasons explained above for combining White, Beaty and Schulman, their combination renders each of claims 38 and 41-43 obvious. Ex. 1003, ¶ 413.

VII. CONCLUSION

In light of the above, it is respectfully submitted that claims 16-20, 23-25, 37-38, and 41-43 of the '045 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 '045 Patent is involved in litigation in the District of Delaware in *Dexcom, Inc. v. AgaMatrix, Inc.*, Case No. 1:17-cv-01310; and subsequently 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 (IPR2018-01715) to challenge the patentability of substantially the same claims of

the ’045 Patent on different, but equally compelling, grounds; and (b) IPR petitions (IPR2018-01717 and IPR2018-01718) to challenge the patentability of certain claims of U.S. Patent No. 9,750,460 which is commonly owned, and shares the same specification and parents, as the ’045 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*
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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 '045 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 '045 Patent, it is available for *inter partes* review, and that Petitioner is not barred from requesting *inter partes* review of the '045 Patent.[5]

Date: September 14, 2018

Respectfully submitted,

By */s/ Ira J. Levy*

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[5] The Complaint alleging infringement of the '045 Patent in *Dexcom, Inc. v. AgaMatrix, Inc.*, Case No. 1:17-cv-01310 (D. Del.) was served on Sept. 15, 2017.

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CERTIFICATE OF WORD COUNT

The undersigned hereby certifies that the foregoing **PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO. 9,724,045** complies with the type-volume limitation of 37 C.F.R. §§42.24(a)(1)(i) and 42.24(b)(1). The Petition contains 12,503 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. 9,724,045** 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:

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