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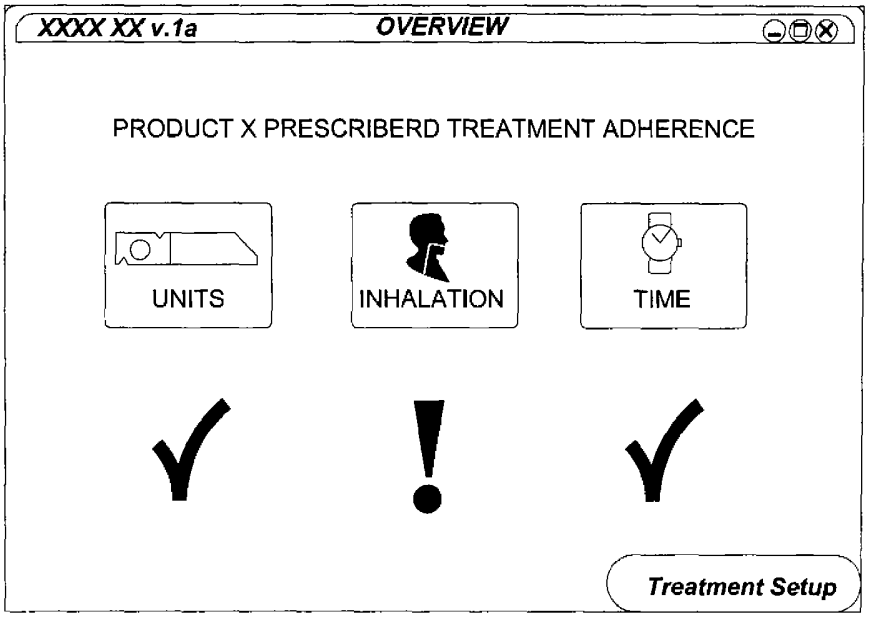
(54) **Title:** INHALATION THERAPY COMPLIANCE TRACKING SYSTEM AND APPARATUS



(57) **Abstract:** A system and method for allowing a patient and/or a health care provider determine when a patient is out of compliance with predetermined target values for parameters relating to inhalation therapy. In one embodiment the patient is informed about compliance with various parameters immediately following a dosing or inhalation episode. In a related embodiment, the patient can view in a single easy to read format whether he has been in compliance over a period of multiple days. Accordingly, in one glance a patient or health care provider can determine on which days a patient missed a target value for one or more parameters associated with his treatment.

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INHALATION THERAPY COMPLIANCE TRACKING SYSTEM AND APPARATUS

The present invention relates to the field of pulmonary drug delivery. It is particularly well-suited for, but is by no means limited to, delivery of blood glucose lowering agents and hormones in diabetic patients. For example, it can be applied to the area of pulmonary insulin delivery.

BACKGROUND OF THE INVENTION

Many conditions require periodic self administration of medications. While in most cases oral administration of a medication is probably most convenient for a patient, there are many medications that are not capable of being administered orally. One alternative route of administration is a pulmonary route in which a patient inhales a liquid or powdered medicine, usually in an aerosol form. While conventional inhalers and nebulizers are often used to treat lung and breathing aliments, the ability to systematically deliver to a patient's circulatory system through the patient's lungs a controlled, consistent, and precise dose of medication has proven more difficult. It is often not enough to merely deliver the same dose to the patient's airway. Getting a consistent and controlled dose absorbed often requires breath control, as well as controlling parameters of the aerosolized formulation. Thus, inhalation drug/ medication therapy for treating diseases, such as diabetes, is more difficult to control and may require sophisticated monitoring systems and methods in order to achieve a satisfactory treatment outcome for the patient.

A well-known problem in clinical trials, as well as regular disease treatment, is a patient's poor adherence to the prescribed treatment regimen. This is known as non-compliance. Usually the only source a health care provider ("HCP") has to monitor patient compliance is the patient's self-written diary, the accuracy of which is notoriously defective. In many cases it is impossible to get a patient to even track compliance, and if the patient can be convinced to track it, the data is often not collected contemporaneously by the patient, but is recorded later.

Situations where patients are non-compliant may require changes in regimens or substituting drugs in order to avoid a poor outcome. Typically, the poor outcomes that the HCP tries to avoid are not to due to the drugs characteristics but to incorrect dosing/use due to patient non-compliance with a prescribed treatment regimen. While this problem exists with all types

of drug delivery, including oral administration, injection, and inhalation, at least with oral administration the issue is more one of whether the medication was taken. Injection therapy adds a variable in the patient must inject the proper dose, but proper education can often minimize poor adherence with this variable. With inhalation therapy in general and inhalation of insulin and insulin like compounds in particular, there are numerous variables that the patient is not even aware of and therefore measuring compliance with these parameters is often impossible.

Thus, there is a medical need to monitor patient compliance with a treatment regimen. This need is particularly acute in the area of self-administered treatments, such as those employed in the treatment of diabetes and the need is even greater in the area of pulmonary administered treatments. The need is multifaceted in that the patient needs to know quickly whether he/she has done his/her part for a particular treatment or dosing episode and in that the HCP and/or patient also needs to know how well the patient is complying with a treatment regimen over a period of time, usually days, weeks, or months.

Many of the inhalation devices for delivery of medications to a patient's circulatory system via a pulmonary route can be quite sophisticated. For example the AERx® iDMS device described in US patent 6,167,880, which is hereby incorporated by reference, automatically records various data on inhalation performance, time and dose in the device memory and relieve the patient of recording these data. And thus these types of devices are readily useable with the present invention. Of course even simple devices can be used with the present invention. For example, metered dose inhalers can employ the apparatus of WO 97/13553, which is hereby incorporated by reference, and thus would be readily adaptable to work with the present invention described below.

SUMMARY OF THE INVENTION

The present invention provides methods and systems for assisting a patient and/or a health care provider in treating a disease where the treatment regimen is administered by the patient. In one aspect, the present invention is useful in helping a patient know that a particular administration of a medicament thru a pulmonary route has been successful. In another aspect, it is useful in allowing the patient and/or healthcare provider to determine how effectively the patient is complying with a prescribed treatment regimen over a period of time. Typically it is beneficial to monitor compliance from day-to-day over the period of time.

In a first aspect a system for assisting a patient in self treating a condition via pulmonary administration of a medicament is provided, the system comprising an inhalation device for aerosolizing a drug formulation, the device capable of administering multiple doses of the formulation over a period of time, and an input means for receiving target values for certain parameters relating to pulmonary administration of the formulation from a health care provider or a patient under the care of a health care provider. The system further comprises a monitoring system for monitoring values of a plurality of parameters relating to pulmonary administration of the formulation, the monitored parameters including those for which target values have been inputted and further including parameters relating to inhalation technique performed by the patient, and a processor configured to compare the monitored values to the target values for the certain parameters whose values have been inputted by the health care provider or the patient, the processor further configured to compare monitored parameters relating to inhalation technique with predetermined target values for inhalation technique parameters, wherein the process is further configured to generate indicators indicating whether monitored parameters had values within their respective targets. The system also comprises a display that displays in a single view whether a plurality of monitored parameters achieved their target values by displaying a first symbol where a target value or target values were achieved and a second symbol where a target value or target values were not achieved.

In the first aspect as well as in the other aspects described below, the condition may be diabetes and the formulation (or drug or agent) may be an anti-diabetic formulation. A value may be a value *per se*, and may represent an upper or a lower limit (e.g. >5 or <10), or the value may represent a range (e.g. 5-10). The display may comprises a single display unit (e.g. a single LCD screen) or may comprise two or more displays or indicators adapted to in combination provide a single view display of the defined information. In the above embodiment the system is adapted to monitor parameters including those for which target values have been inputted and further including parameters relating to inhalation technique performed by the patient, however, in alternatively embodiments, the system may be adapted to monitor either those parameters for which target values have been inputted or parameters relating to inhalation technique performed by the patient. The patient or health care provider inputted target values for parameters may include values for dose size and time the dose is to be administered, and the monitored inhalation technique parameters may include one or more of the following: inspiratory flow, chaser volume, and inspiratory volume.

In the context of the present application and as used in the specification and claims, the term processor covers any combination of electronic circuitry suitable for providing the specified functionality, e.g. processing data and controlling memory as well as all connected input and output devices. The processor will typically comprise one or more CPUs or microprocessors which may be supplemented by additional devices for support or control functions.

In a further aspect a method of assisting a patient in complying with a prescribed inhalation treatment regime is provided, the method comprising the steps of (a) receiving target values for a plurality of parameters relating to the inhalation treatment, (b) following a treatment episode displaying whether the patient achieved the target values for the plurality of the parameters, wherein the displaying occurs by presenting a single view showing a representation of each monitored parameter and a graphical indication indicating for each whether compliance was or was not met.

In a further aspect an inhalation system for assisting a health care provider in determining if a patient is complying with a self-treatment regimen that includes pulmonary administration of a formulation is provided, the system comprising an inhalation device for aerosolizing a formulation of the agent, an input means for receiving recommended target values for dosing parameters from a health care provider or patient under the care of a health care provider, and a monitoring system configured for monitoring actual values for the dosing parameters from each administration of the formulation, the monitoring system also configured for monitoring inhalation technique by monitoring one or more inhalation parameters that occurs during each administration of the formulation, thereby monitoring whether the inhalation technique performed by the patient was on target. The system further comprises a processor configured to compare the monitored values with the recommended values and to generate an indicator that indicates whether or not the monitored value comports with the target values, the processor further configured to compare inhalation technique with a predetermined proper inhalation technique and generate an indicator if the monitored inhalation technique comports with the predetermined proper target inhalation technique, wherein the processor is configured to display in a single view whether the patient was in compliance with recommended or predetermined proper values for one or more parameters over a period of multiple days.

In a yet further aspect, a method for assisting a health care provider in determining whether a patient is complying with a predetermined self-treatment regimen is provided, the method

comprising the steps of (a) inputting target values for various parameters associated with a self-treatment inhalation regimen for treating a condition, (b) comparing actual values that the patient achieves for the various parameters with the target parameters values of a period of multiple days, and (c) periodically displaying in a single view information for the period of multiple days along with an indicator that indicates when during that period the patient was out of compliance with a target values for one or more of the various parameters.

In a yet further aspect, a system for helping determine patient compliance with a predetermined self-treatment regimen that includes inhalation of a medicament, the system comprising a display configured to display in a single view whether the patient properly administered a dosage of a medicament via a pulmonary route, the display showing in a single view whether the patient was in compliance with target values for a plurality of parameters at least one parameter relating to inhalation technique and wherein the display utilizes one symbol to show compliance and one symbol to show no compliance.

In a further aspect a method for determining whether a patient is in incompliance with a prescribed treatment that requires inhalation of a medicament is provided, the method comprising the steps of (a) providing target values for a size of a dose of medicament to be inhaled, a time range for inhaling the predetermined dose size, and/or a predetermined inhalation technique to be used during the inhalation of a dose of medicament, (b) monitoring the actual dose, time of dosing, and/or inhalation technique that the patient employs to administer a dose, and (c) displaying in a single view an indication as to whether the dose, time of does, and /or the inhalation technique actual used by the patient was in compliance with the predetermined values of step a, the single view displaying multiple days worth of information thereby allowing a user to determine on which days within a period of treatment the patient was or was not incompliance.

In one embodiment, a patient in need of treatment with a blood glucose lowering agent, or some other drug that can be administered via inhalation, is provided with an inhalation device. The device is capable of converting the drug or agent into a form that can be delivered to the patient's lung(s). The device also contains or is interfaced with an electronic device that is capable of being programmed with various parameters and monitoring various parameters during patient use. I.e., target parameters can be inputted and the patient's performance or compliance with these predetermined parameters can be monitored.

In one embodiment, a health care provider or a patient may input desired dosages and time of dosing. For example, a doctor may prescribe a certain insulin dose at breakfast, which is to be administered within a range of times in the morning, a certain dose to be administered for lunch, which may also occur within a range of times, and a certain dose with dinner, which is prescribed to take place within a certain range of times. This may be done via the use of a set-up screen on the inhaler or on a peripheral device.

The device may have a preset of target values for an inhalation sequence or these values may be programmed into the device by the user or HCP. For example, the device may be preprogrammed with values for inspiratory flow, chaser volume, inspiratory volume and/or other parameters that affect absorption of the prescribed agent or drug thru the lung tissue. The device may be equipped to monitor a plurality of parameters associated with a patient's inhalation sequence (i.e., the manner in which the patient inhales the drug, for example the patient's inspiratory profile) for compliance with prescribed values. The device can also be programmed to compare the patient's actual inhalation sequence with the target values for the monitored parameters.

In one embodiment, a display apparatus that is interfaced with or integral to the inhalation device is provided and allows the patient or the health care provider to monitor whether a single dose administration was in compliance with predetermined key parameters. For example, a single screen view may be provided with a graphical representation of each important parameter and a graphical indication as to whether or not the patient was in compliance with predetermined range for each of the important parameters. In one example, number of units of insulin is displayed graphically on a PDA or computer. A graphical symbol can be used to indicate whether the patient was in compliance with the target a particular parameter (e.g., number of units of insulin). The display, in this example, also shows a graphical symbol for inhalation sequence or technique and a symbol denoting whether or not the patient inhalation sequence or technique comported with a predetermined target. For instance, it might monitor whether the patient inhales at the right speed with the right volume and whether he continues to inhale the right amount of chaser air. If the inhalation sequence comports with a predetermined set of rules or values, the display can display a symbol showing that the inhalation technique was satisfactory. The display might also display a symbol for time of dosing and an indicator showing whether the dose was taken on time. The symbol can be an icon, a character, a color, or any other suitable indicator.

In another embodiment, the present invention might include a data storage for storing multiple days worth of data relating to patient dosing. For example, in the typical day a diabetic might inhale 3 doses of insulin, one before each meal. The diabetic might not visit his doctor for months. Accordingly, there is a need for a HCP or even for the patient to quickly view whether or not he is in compliance with a prescribed treatment regimen over a period of time. Thus, the present invention may take the form of a system having a display that allows a HCP or patient to look at compliance with one or more prescribed parameters for a period of multiple days in a single easy to read screen view. By using a single screen view the user can see all the relevant, desired information in one view and need not change between views.

In one example, an inhalation device is interfaced with a display apparatus, such as a PDA or computer or, if the device is sufficiently sophisticated, a simply monitor that displays one or more months worth of data on a single screen. Typically, the display might include data for one monitored parameter and preferably also includes a graphical symbol indicating which portions of the data are out of compliance with a monitored event.

In another embodiment the device can graphically indicate on which days a patient was out of compliance with a monitored parameter. The user can then switch screen views and determine which parameters were out of compliance. Moreover the user can view a large number of days worth of data for a particular parameter on a single screen view. A graphical indicator can be used to highlight which days had a non-compliance associated with the particular parameter.

BRIEF DESCRIPTION OF THE DRAWINGS

In the following the invention will be further described with reference to the drawings, wherein

fig. 1 shows a set up screen that may be displayed on a PC, PDA or display incorporated within the hand-held inhalation device,

fig. 2 shows a compliance screen that displays feedback to the patient and health care provider, where “check marks” and “exclamation marks” are used to denote compliance and non-compliance with particular parameters,

fig. 3 shows an inhalation device suitable for delivering a drug via a pulmonary route,

fig. 4 shows a graphical display displaying 1 month of inhalation data in a single screen view with graphical indicators denoting 3 days where dose size was out of compliance, and

fig. 5 is an alternative single screen view that may be displayed in the place of that of fig. 4.

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

The shown figures are schematic representations for which reason the configuration of the different structures as well as there relative dimensions are intended to serve illustrative purposes only.

The present invention provides systems and methods for assisting a patient and health care provider in effectively treating a condition by ensuring compliance with a regimen that includes inhalation of a drug or medication. One key aspect of inhalation therapy for treating a disease, such as for example diabetes, is that a precise and controlled amount of the medication, such as insulin, must be absorbed into the patient's circulatory system in a controlled and repeatable manner so that effective treatment can occur. Various inhalation devices can administer drugs and can be equipped to monitor certain parameters related to inhalation therapy.

According to one embodiment of the present invention, data can be uploaded from an inhalation device to a personal computer, PDA or the like that processes calculations to determine compliance and, in simple manner, displays whether the patient complies with treatment regimen set individually for each patient.

In another embodiment, the inhalation device is equipped with a monitor which is either interfaced directly with the inhalation device processor (and may be integral with the inhalation device) which is programmed to perform the necessary calculation or is interfaced with a separate processor that uses data collected by the inhalation device. Of course, the monitor and/or processor needed to carry out one or more aspects of various embodiments of the present invention can be integrated with the inhalation device. The processor can be programmed to display on the display those parameters were monitored and whether the patient was in compliance with a prescribed treatment.

One of the many intended uses of the present invention is to provide a health care provider and/or patient with a compliance indicator tool by presenting feed-back on a number of parameter based on an underlying algorithm(s). Examples of parameters are inhalation technique, insulin units and dose time/frequency. The algorithm for each parameter, or set of rules applied to each parameter to determine compliance may be unique. In some cases a single algorithm may be applied to all parameters. Part of the algorithm may be a patient's individual treatment set up, e.g. the unit dosing interval.

In one embodiment of the present invention, the patient and/or health care provider is provided with simple feed-back that may take the form of simple symbols e.g. check- or exclamation mark and/or colors e.g. red, yellow and green, with respect to key parameters. In other words, one embodiment of the invention may comprise a mechanism for allowing individual targets to be set for a patient and a display showing whether the patient achieves some or all of those targets. The feed-back could be given directly on a medical device or on a device connected or interfaced with the inhalation device e.g. on a PC or PDA.

One particularly useful embodiment of the present invention is a method for assisting a patient and/or health care provider to determine whether a patient is in compliance with a self-administered inhalation therapy regimen. In accordance with this particular method, which is only an example of a particular embodiment, the compliance ranges for a patient are set. These ranges may include ranges for various parameters including chaser air parameters. In this example, chaser air, which in this case is air inhaled after drug flow to a patient's pulmonary system has begun, is a parameter used to determine compliance. After the ranges are set, data related to actual patient performance is collected. It is then determined whether the data is within the compliance ranges. Finally, an indication is displayed for each parameter or set of ranges that shows whether the patient was in compliance for that particular range for the particular parameter being monitored.

In an embodiment, the invention may also take the form of an apparatus. In one such embodiment, an apparatus for use with a medical treatment involving inhalation of a treating medication is provided. The apparatus may comprise a processor and/or memory, an input for allowing a patient or healthcare provider to input predetermined ranges for inhalation therapy parameters, including for example, a range for parameters related to chaser air inhaled after medication release into the patient's air way. The apparatus also may comprise a

display for patient or health care provider viewing. The processor can be programmed to compare data collected by the inhaler during actual administration of self-treatment with the predetermined ranges and can be further configured to create on the display a visual indication as to whether the patient is in compliance for each parameter. The processor can collect data and apply one or more algorithms to determine compliance. In one embodiment a "check mark" is displayed for parameters that are incompliance and an exclamation point or mark is displayed for parameters out of compliance. In some cases strict compliance is not necessary for the patient to be in compliance. For example being within a certain percentage of a target may be close enough for consistent and repeatable dosing.

Exemplary Inhalation Systems

In one embodiment of the present invention, the patient inhales a medication from an inhaler. The inhaler may be handheld size for convenience. If the patient achieves a target flow rate and volume, the device releases the medication in aerosol form. The patient may also be instructed to continue inhaling after medication release until a sufficient chaser air has been inhaled. The device preferably includes a means for recording a characterization of the inspiratory flow profile for the patient which is possible by including a microprocessor in combination with a read/write memory means and a flow measurement transducer.

For some medications, it may be desirable to instruct the patient to inhale a particular predetermined minimum volume at a particular flow rate following the release of an aerosolized medication, i.e., chaser air. For other medications, the flow rate may not be as critical. Moreover, the flow rate and volume required for the chaser may in some cases vary with properties of the aerosol, such as particle size, density, etc.

In some embodiments, the present invention can operate with an individual/personalized limit for chaser volume based on the patient's lung capacity. The limit may thus be described as a percentage of the patient's volume of lung capacity.

In some embodiments, drug release may occur within an inhaler from the instant (or thereabouts) that the patient begins inhaling from the device. In this case, the chaser air would be inhaled from the moment that the patient begins inhaling from the device. Thus, the chaser may start out having a high concentration of medicine to air and the concentration may decrease as the volume of chaser air that is inhaled increases. In fact, in some cases the concentration of medicine in the chaser may approach or become zero by the end of the inhala-

tion of the chaser volume. Thus, while the chaser may be pure air, in most cases it will be a combination of air and medicine where the concentration of medicine declines as the inhaled volume of the chaser increases.

In order to assist a patient carrying out the methods of the present invention, applicants disclose herewith exemplary novel and non-obvious devices, methods and systems that will assist the patient and/or the patient's health care provider.

The present invention may utilize a personal computer or a PDA that is configured to receive settings for various treatment parameters, monitor actual treatments and provide feedback to the patient.

Alternatively, the present invention may be practiced on an electronic inhalation device that is configured to carry out any or all of the method steps of the present invention. For example, if a processor controlled inhaler is equipped with a display, the feedback can be displayed directly on the device. The display can be a graphical display such as a LCD or it could be a simple display of different colored LEDs. Moreover, the inhaler can be equipped with an input means in some cases.

While many parameters can be monitored and feed back provided for each parameter, in one embodiment, the patient is merely provided with feedback as to whether the overall inhalation was successful. Various algorithms can be used to determine how stringently each individual parameter must be complied with in order to determine whether the overall inhalation is successful.

Additionally, individual parameters can be monitored and feedback provided on an aggregate basis for each parameter. Again, algorithms can be applied to determine what constitutes compliance. For example, in some cases, but not all cases, 100 % compliance, (i.e., strict compliance) with each parameter may be unrealistic and unnecessary for the patient to achieve satisfactory results. Thus, in one embodiment, a patient may be in compliance even though the patient has not always achieved the exact targets prescribed for each parameter.

As discussed above, numerous devices exist for administering a drug or medication to a patient via a pulmonary route. In many cases getting the medication or drug into a patient's lungs is only half the battle. The manner in which it gets deposited in the lungs, as well as the

properties of the particles and formulations often play a big part in determining how it will ultimately be absorbed, and for many medications (such as for example insulin) precision of dose size reaching the circulatory system are critical.

Breath control after administration also appears to greatly influence repeatability and absorption. It has now been shown that after a medication is released into the airway of a patient, the quantity of air the patient inhales after drug release (i.e., "chaser air") affects absorption and/or repeatability. In some situations, the rate at which the chaser air, as well as the volume of the chaser air, is also critical.

While repeatability and precision are required, repeatable may not always require precisely the exact quantity of drug delivered. In some cases it is sufficient that the quantity delivered in each dosing episode be sufficient to result in adequate blood glucose control within a medically acceptable range.

Various existing devices may be used to delivery a medication, such as insulin, to a patient's pulmonary system and ultimately to a patient's circulatory system. The AERx iDMS device described in US Patent 6167880 and shown schematically in fig. 3 is one such device. However, this device, like the numerous other currently available, do not provide feed back to a patient or guidance regarding chaser air inhaled after drug release from the device.

While a suitable device for use with the present invention is the AERx iDMS device described in more detail below and which is complete described in US Patent 6167880, the contents of which are hereby incorporated by reference, the present invention is not so limited. In fact, the present invention can be used with virtually any inhalation device suitable to deliver medication to a patient's circulatory system. The device and methods described herein are also particularly well-suited for, but by no means limited to, treating diabetes. The methodology for using the present invention for such treatment is also discussed in further detail below.

Treatment methodology for diabetics

Diabetes mellitus and many other conditions are generally treated by the injection of agents, such as for example insulin. One embodiment of the present invention provides alternatives to injection therapy. For example insulin can be aerosolized and administered to a patient's pulmonary system. Of course, successful treatment may require precise, controlled, and re-

peatable dose reach the circulatory system of the patient. Exact precision and control is not always required, but in general a treatment needs some level of predictability and repeatability to be effective. When insulin is deposited on the mucus membranes of the respiratory tract, it is absorbed by the body. The repeatability and predictability of absorption depend upon many things. Some parameters include how fine the particles are, how deep they penetrate into the pulmonary system and how difficult the pulmonary system finds it to reject these particles. It has been shown that some form of coached breathing can be beneficial in increase the predictability of insulin absorption.

One device that is well-suited for insulin delivery is the AERX device shown in fig. 3. All components are within a single, hand-held, portable breath actuated device. A microprocessor 26 and flow sensor 31 are used to provide electronic breath actuated release of a drug, such as insulin. The device includes a holding means and a mechanical means and may operate electronically, i.e., the actuation means is preferably not directly released by the user. The patient inhales through inspiratory flow path 29 which can form a mouth piece 30. Air enters the device via opening 38. The inhaling is carried out in order to obtain a metering event using differential pressure transducer 37. Further, when the inspiratory flow meets a threshold of a pre-selected criteria, the microprocessor 26 sends a signal to an actuator to release the electrical mechanism 28 which in turn actuates a mechanical means 23, thereby releasing a spring 22 and a plate 24 or equivalent thereof, forcing aerosolized formulation into the channel 11 and out of membrane 3 into the flow path 29 where the air surrounding the particles is optionally heated by the air heater 14.

Microprocessor 26 of fig. 3 includes an external non-volatile read/write memory subsystem, peripheral devices to support this memory system, reset circuit, a clock oscillator, a data acquisition subsystem and a visual annunciator subsystem. The discrete components are conventional parts which have input and output pins configured in a conventional manner with the connections being made in accordance with instructions provided by the device manufacturers. The microprocessor used in connection with the device of the invention is designed and programmed specifically so as to provide controlled and repeatable amounts of insulin to a patient upon actuation. The microprocessor must have sufficient capacity to make calculations in real time.

Adjustments can be made in the program so that when the patient's inspiratory flow profile is changed such is taken into consideration. This can be done by allowing the patient to inhale

through the device as a test (monitoring event) in order to measure air flow with preferred drug delivery points determined based on the results of several inhalations by each particular patient. This process can be readily repeated when the inspiratory flow profile is changed for whatever reason. When the patient's lung function has decreased the program will automatically back down in terms of the threshold levels required for release of drug. This "back down" function insures drug delivery to a patient in need but with impaired lung function. Determination of optimal drug delivery points in the inspiratory flow can be done at each dosing event, daily, weekly, or with the replacement of a new cellular array in the device.

The microprocessor 26, along with its associated peripheral devices, can be programmed so as to prevent triggering the actuation mechanism 28 more than a given number of times within a given period of time. This feature makes it possible to prevent overdosing the patient. The overdose prevention feature can be particularly designed with each individual patient in mind or designed with particular groups of patients in mind. For example, the microprocessor can be programmed so as to prevent the release of more than approximately 30 units of insulin per day when the patient is normally dosed with approximately 25 units of insulin drug per day. More specifically, the insulin can be inhaled from a separate device such as from a dry powder inhaler. Thereafter, the sensor portion of the device may be used to perform the inhale-exhale maneuver of the training.

The microprocessor 26 can be connected to external devices permitting external information to be transferred into the microprocessor of the invention and stored within the non-volatile read/write memory available to the microprocessor. The microprocessor of the invention can then change its drug delivery behavior based on this information transferred from external devices. All of the features of the invention may be provided in a portable, programmable, battery-powered, hand-held device for patient use which has a size which compares favorably with existing metered dose inhaler devices.

The microprocessor 26 can also be programmed so as to allow for monitoring and recording data from the inspiratory flow monitor without delivering drug. This is done in order to characterize the patient's inspiratory flow profile in a given number of monitoring events, which monitoring events preferably occur prior to dosing events. After carrying out a monitoring event, the preferred point within the inspiratory cycle for drug delivery can be calculated. This calculated point is a function of measured inspiratory flow rate as well as calculated cumulative inspiratory flow volume. This information is stored and used to allow activation of the

electronic actuation means when the inhalation cycle is repeated during the dosing event. In addition, data regarding chaser air can be collected, stored and analyzed.

One of the many inhalation parameters that may be critical to achieve uniform and repeatable dosing is volume of air inhaled after medication is released by the inhaler (i.e., chaser air). Other chaser air parameters such as inspiratory flow volume, rate, etc., can also effect dosing. Feedback about these and other inhalation parameters can greatly assist the patient in improving repeatable, consistent, and precise dosing. The AERx iDMS device, or other inhalation devices, can be incorporated with a display and/or processor to provide feedback to a patient and/or health care provider regarding chaser air inhaled after the device starts flowing medication to the patient. The device can also be interfaced with a processor and/or display, such as a PDA, computer, or the like, which can then be programmed to display feed back to the patient.

While chaser air may be the air inhaled after a drug is released by an inhaler, not all inhalers actively trigger drug release in response to the patient inspiratory flow profile hitting a predefined target. In some inhalers, drug release may occur within an inhaler from the instant (or thereabouts) that the patient begins inhaling from the device. In this case, the chaser volume is the air inhaled from the moment that the patient begins inhaling from the device. Thus, the chaser may start out having a high concentration of medicine to air and the concentration may decrease as the volume of chaser air that is inhaled increases. In fact, in some cases the concentration of medicine in the chaser may approach or become zero by the end of the inhalation of the chaser volume. Thus, while the chaser may be pure air, in most cases it will be a combination of air and medicine where the concentration of medicine declines as the inhaled volume of the chaser increases. Nonetheless, it may be advantageous to provide inhalation feedback about chaser air even in these types of inhalers.

Patient set-up and compliance monitoring

As discussed above, in order for therapy involving inhalation of a drug or medication to be effective in treating diseases like diabetes, it may be necessary to customize the treatment for individual patients and to monitor compliance with present parameters. For example, breath control after drug release is an important parameter to achieving consistent repeatable drug delivery into a patient's circulatory system via a pulmonary route of administration. One reason a patient may fail to achieve satisfactory blood glucose levels is that they are not properly inhaling their medications. Of course, the reasons could be that they are receiving

the incorrect dose or that they are using the wrong medication or insufficient doses are administered during the day. To aid both the patient and the patient's health care provider, applicants have discovered that presenting a quick view of the data relating to inhalation therapy as well as more detailed views can greatly improve the outcome for the patient. As is shown in fig. 1, a health care provider or a patient can set certain parameter related to the patient's inhalation therapy. These parameters may include dose size, time of dose administration or frequency of dosing, and inhalation related parameters, such a trigger points, chaser air values, etc. These parameters may be set directly on the device, or can be set by interfacing the inhalation device with a personal computer, PDA, or the like. It is also possible to make the inhalation device internet compatible and down load, either directly or indirectly the parameters from a web server. Thus, in some applications, the patient set-up screen shown in fig. 1 may be accessible over the internet.

Once the device is configured, it can store data related to how well the patient achieves compliance with targets. Various algorithms may be employed to monitor compliance. For example, adequate compliance may mean that the targets are achieved some percentage of the time, even though they are not hit 100% of time. The degree of compliance can, in some cases, be related to the ultimate goal in treating the patient, e.g. satisfactory blood glucose levels in a diabetic. Of course, in some cases, even one non-compliance may be worth noting.

To assist the patient and health care provider in tracking compliance or teaching a patient to inhale his medication, a simple output or display of compliance data is often preferred. Fig. 2 shows a simple display that uses a check mark and an exclamation mark to note compliance. Various color schemes can also not compliance or non-compliance. The screen in fig. 2 may be displayed either directly on a monitor on the inhalation device, on a PC, PDA or on a website that has received the data from the inhalation device. In one embodiment, a single screen view such as that shown in fig. 2 is displayed for a particular dosing episode. Preferably, it is shown immediately after the patient inhales a dose. The dose need not be an actual dose, it can be simulated and the screen view shown in fig. 2 can be part of a training apparatus or system.

One of the many uses of the present invention is to help determine which patients are or are not benefiting from inhalation therapy. For example, if a patient's blood glucose seems out of control and the patient is taking the wrong dose or dosing at the wrong frequency, this is eas-

ily corrected. However, if the patient is having trouble reaching inhalation targets, dose size or frequency may be adjusted to compensate. In some cases, the present invention is useful in determining that a patient is not a good candidate for inhalation therapy.

As is shown in fig. 4, a graphical image is shown in a single screen view. This single screen view can be employed to show multiple days or even months worth of data. In fig. 4 data relating to units of insulin administered to a patient over a one month period is shown in a single view. Alternatively the display could be configured to show multiple months in a single screen view. In this prophetic example, the patient might be instructed to inhale between 250-300 ml of insulin before dinner, which should be eaten between 5 and 7 pm. The patient would also be trained to continue inhaling at a certain predetermined rate until a certain predetermined volume of air had chased the insulin into his lungs. The days on which the patient administered a daily dose that is outside a preset range, e.g., 200-300 ml would be flagged with a symbol (e.g. an exclamation point) so that these days are readily apparent. This single screen view also shows the percentage of time (e.g. 22%) that the patient was out of compliance. The single screen view of fig. 4 can also be modified to show compliance with other predetermined parameters such as inhalation technique or time. In one embodiment, the user merely needs to click on an icon to change to these screen views.

Figure 5 shows an alternative single screen that may be used to show multiple days worth of data. In one embodiment, compliance with time and inhalation can be shown with the use of graphical symbols. For example an X can be used to denote non-compliance and a slash to denote compliance. Alternatively, actual values for the parameters could be shown with another indication when the parameter was measured to be out of range. For example, a certain color (e.g. red) could be used when displaying values that are out of range. Alternatively and as is shown in fig. 5 only days that are out of compliance could have values inserted. For example, as is shown in fig. 5, May 1 has a time and inhalation chaser volume value that is outside a predetermined range. Therefore, this date is the only date showing values as it is the only time in that month that the patient was out of compliance. Of course, if the patient is in compliance less frequently than he is out of compliance, it may be better to show values for when he is in compliance. While fig. 5 shows 1 month worth of data for dose timing and inhalation technique, it could show all parameters or just a single parameter.

In the above description of the preferred embodiments, the different structures and means providing the described functionality for the different components have been described to a

degree to which the concept of the present invention will be apparent to the skilled reader. The detailed construction and specification for the different components are considered the object of a normal design procedure performed by the skilled person along the lines set out in the present specification.

The explanation of the present invention in the foregoing is intended to exemplify and not limit the invention. Those skilled in the art will recognize numerous variations that are within the scope of the pending claims, which are the only limits intended by the inventors hereof. For example, as described herein the inhalation system might be embodied as a single device or it might be a multi-component device. In the multi-component embodiment, one component might be interfaced with another during operation or one component might merely download data to another. Further, in the disclosure of the present invention reference is mostly made to the treatment of diabetes by inhalation of insulin, however, this is only an exemplary use of the present invention. For treatment of diabetes, other drugs or formulations thereof may be used, e.g. GLP-1 and analogues thereof. Further, the invention may be used in the context of pulmonary delivery of any drug or formulation thereof suitable for inhalation treatment.

Unless stated otherwise, one should assume that examples or references to examples are illustrative and are merely prophetic. Applicant's specification is intended to illustrate various ways that their invention may be embodied and is not a representation that actual embodiments have been constructed.

CLAIMS

1. A system for assisting a patient in self treating diabetes via pulmonary administration of a medicament, the system comprising:

a. an inhalation device for aerosolizing an anti-diabetic formulation, the device capable of administering multiple doses of the formulation over a period of time,

b. an input means for receiving target values for certain parameters relating to pulmonary administration of the formulation from a health care provider or a patient under the care of a health care provider,

c. a monitoring system (31) for monitoring values of a plurality of parameters relating to pulmonary administration of the formulation by the patient, the monitored parameters including those for which target values have been inputted and further including parameters relating to inhalation technique performed by the patient,

d. a processor (26) configured to compare the monitored values to the target values for the certain parameters whose values have been inputted by the health care provider or the patient, the processor further configured to compare monitored parameters relating to inhalation technique with predetermined target values for inhalation technique parameters, wherein the process is further configured to generate indicators indicating whether monitored parameters had values within their respective targets, and

e. a display that displays in a single view whether a plurality of monitored parameters achieved their target values by displaying a first symbol where a target value or target values were achieved and a second symbol where a target value or target values were not achieved.

2. The system of claim 1, wherein the patient or health care provider inputted target values for parameters include values for dose size and time the dose is to be administered.

3. The system of claim 2, wherein the monitored inhalation technique parameters include one or more of the following: inspiratory flow, chaser volume, and inspiratory volume.

4. The system of claim 1, wherein the symbol for successfully achieving a target for a parameter is a check mark and wherein the symbol for not achieving a target is an exclamation point.

5. The system of claim 1, wherein the display displays an indication that a target was achieved or not achieved for at least three monitored parameters simultaneously.

6. A method of assisting a patient in complying with a prescribed inhalation treatment regime, the method comprising the steps of:

a. receiving target values for a plurality of parameters relating to the inhalation treatment,

b. following a treatment episode, displaying in a single view whether the patient achieved the target values for the plurality of the parameters, wherein the displaying occurs by presenting a single view showing a representation of each monitored parameter and a graphical indication indicating for each whether compliance was or was not met.

7. The method of claim 6 wherein there is a single symbol that represents when compliance with a target value was met and another distinct symbol that represents when compliance was not met.

8. The method of claim 7, wherein the display shows compliance or non-compliance for at least the following parameters: dose size, time of dose, and proper inhalation technique.

9. The method of claim 8, wherein proper inhalation technique is in compliance with a target only if a proper chaser volume is inhaled.

10. An inhalation system for assisting a health care provider in determining if a patient is complying with a self-treatment regimen that includes pulmonary administration of an anti-diabetic formulation, the system comprising:

a. an inhalation device for aerosolizing a formulation of the anti-diabetic agent,

b. an input means for receiving recommended target values for dosing parameters from a health care provider or patient under the care of a health care provider,

c. a monitoring system (31) configured for monitoring actual values for the dosing parameters from each administration of the formulation, the monitoring system also configured for monitoring inhalation technique by monitoring one or more inhalation parameters that occurs during each administration of the formulation, thereby monitoring whether the inhalation technique performed by the patient was on target, and

d. a processor (26) configured to compare the monitored values with the recommended values and to generate an indicator that indicates whether or not the monitored value comports with the target values, the processor further configured to compare inhalation technique with a predetermined proper inhalation technique and generate an indicator if the monitored inhalation technique comports with the predetermined proper target inhalation technique,

wherein the processor is configured to display on a display apparatus in a single view whether the patient was in compliance with recommended or predetermined proper values for one or more parameters over a period of multiple days.

11. The system of claim 10 wherein the dosing parameters include dose size and time of dose administration.

12. The system of claim10, wherein the display can display at least one month of information relating to at least one monitored parameter in the single view.

13. The system of claim 12, wherein the display displays an indication showing on which days the patient achieved target for one or more monitored parameters.

14. The system of claim 12, wherein the display further displays values for the one or more monitored parameters along with an indicator as to whether the monitored parameter or parameters were on target.

15. A method for assisting a health care provider in determining whether a patient is complying with a predetermined self-treatment regimen, the method comprising the steps of:

a. inputting target values for various parameters associated with a self-treatment inhalation regimen for treating diabetes,

b. comparing actual values that the patient achieves for the various parameters with the target parameters values of a period of multiple days,

c. periodically displaying in a single view information for the period of multiple days along with an indicator that indicates when during that period the patient was out of compliance with a target value for one or more of the various parameters.

16. The method of claim 15 wherein the display is graphical and does not include actual values for the various parameters but only a graphical indicator as to whether compliance was achieved.

17. The method of claim 15 wherein the display utilizes tables to display actual values for parameters that are out of compliance with targets.

18. A system for helping determine patient compliance with a predetermined self-treatment regimen that includes inhalation of a medicament, the system comprising a display configured to display in a single view whether the patient properly administered a dosage of a medicament via a pulmonary route, the display showing in a single view whether the patient was in compliance with target values for a plurality of parameters at least one parameter relating to inhalation technique and wherein the display utilizes one symbol to show compliance and one symbol to show no compliance.

19. The system of claim 18 wherein the user can switch the display to display in a single view an indicator for one or more predetermined parameters relating to the inhalation of the medicament whether the patient was in compliance with predetermined values or out of compliance and wherein the single view depicts multiple days worth of information thereby allowing a user to determine on which days in that period the patient was in or out of compliance for the one or more parameter.

20. A method for determining whether a patient is incompliance with a prescribed treatment that requires inhalation of a medicament, the method comprising the steps of:

a. providing target values for a size of a dose of medicament to be inhaled, a time range for inhaling the predetermined dose size, and/or a predetermined inhalation technique to be used during the inhalation of a dose of medicament,

b. monitoring the actual dose, time of dosing, and/or inhalation technique that the patient employs to administer a dose, and

c. displaying in a single view an indication as to whether the dose, time of does, and /or the inhalation technique actual used by the patient was in compliance with the predetermined values of step a, the single view displaying multiple days worth of information thereby allowing a user to determine on which days within a period of treatment the patient was or was not incompliance.

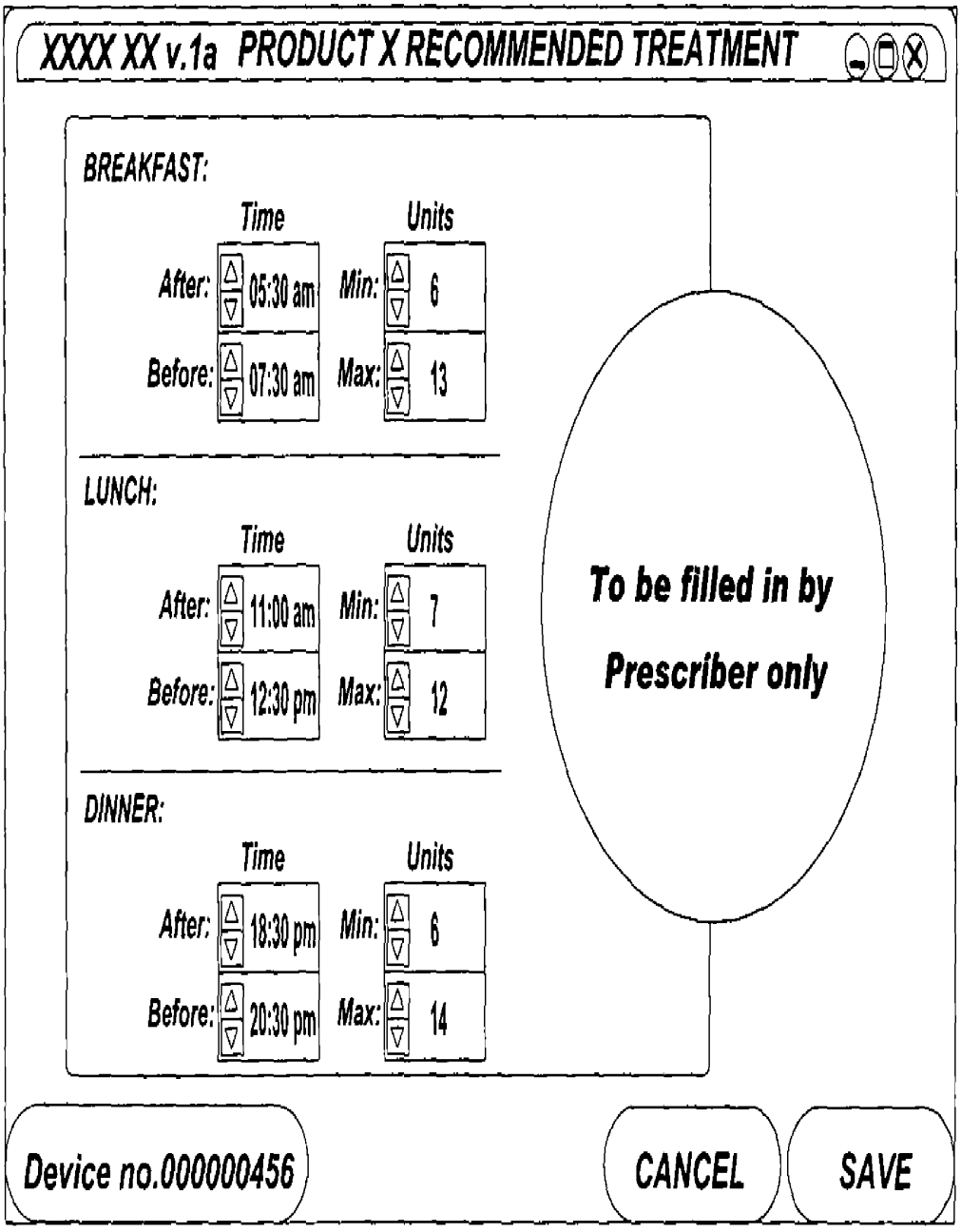

XXXX XX v.1a PRODUCT X RECOMMENDED TREATMENT
BREAKFAST:
Time
Units
After: 05:30 am
Min: 6
Before: 07:30 am
Max: 13
LUNCH:
Time
Units
After: 11:00 am
Min: 7
Before: 12:30 pm
Max: 12
DINNER:
Time
Units
After: 18:30 pm
Min: 6
Before: 20:30 pm
Max: 14
To be filled in by Prescriber only
Device no.000000456
CANCEL
SAVE

FIG. 1

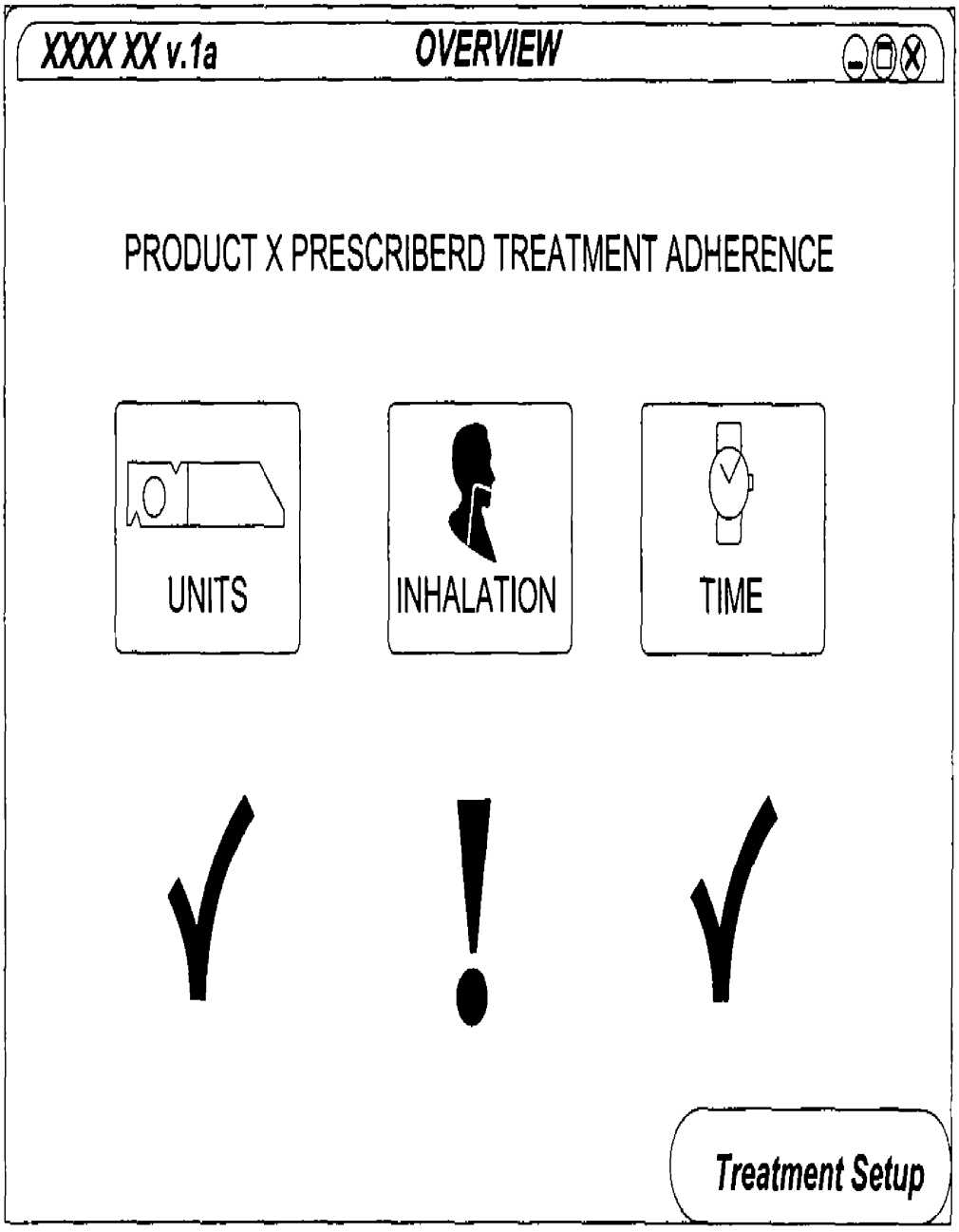
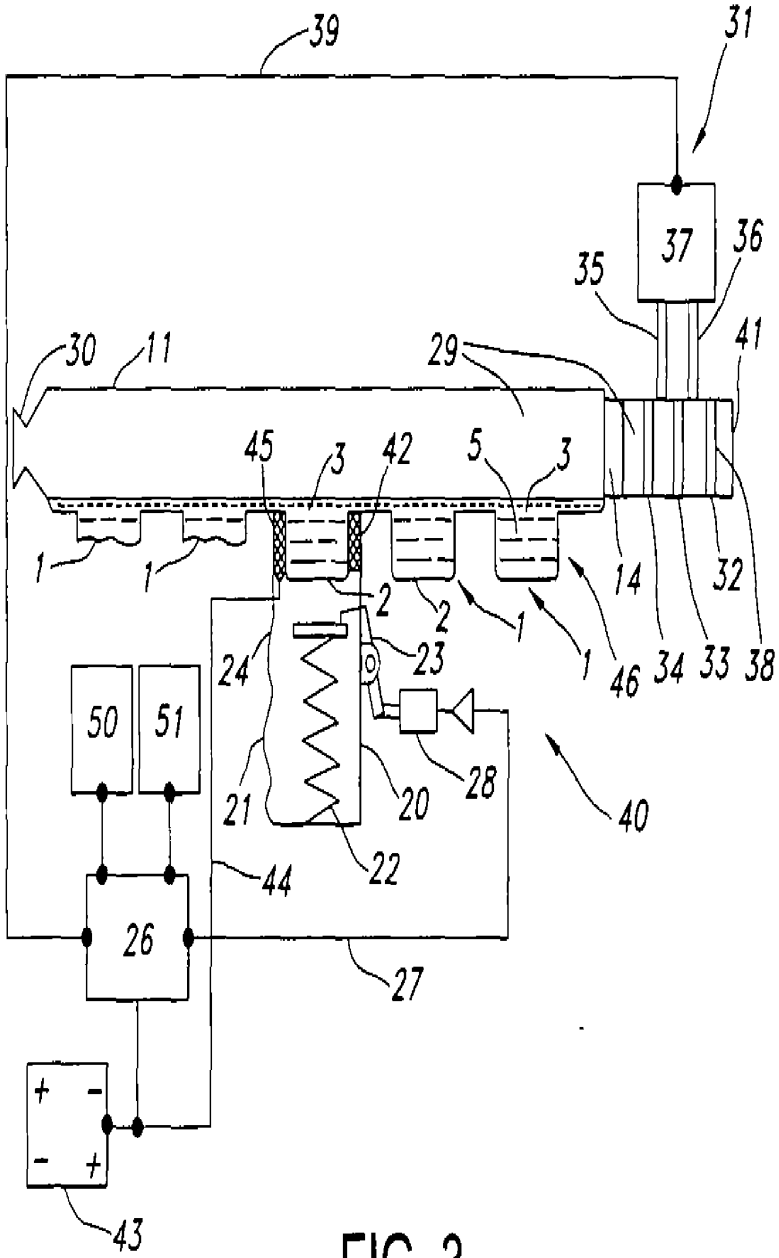

XXXX XX v.1a
OVERVIEW
PRODUCT X PRESCRIBERD TREATMENT ADHERENCE
UNITS
INHALATION
TIME
Treatment Setup

FIG. 2


39
31
37
36
35
41
30
11
29
45
3
42
5
3
14
32
1
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2
2
1
1
46
34
33
38
24
23
50
51
28
21
20
40
22
44
26
27
+
-
-
+
43

FIG. 3

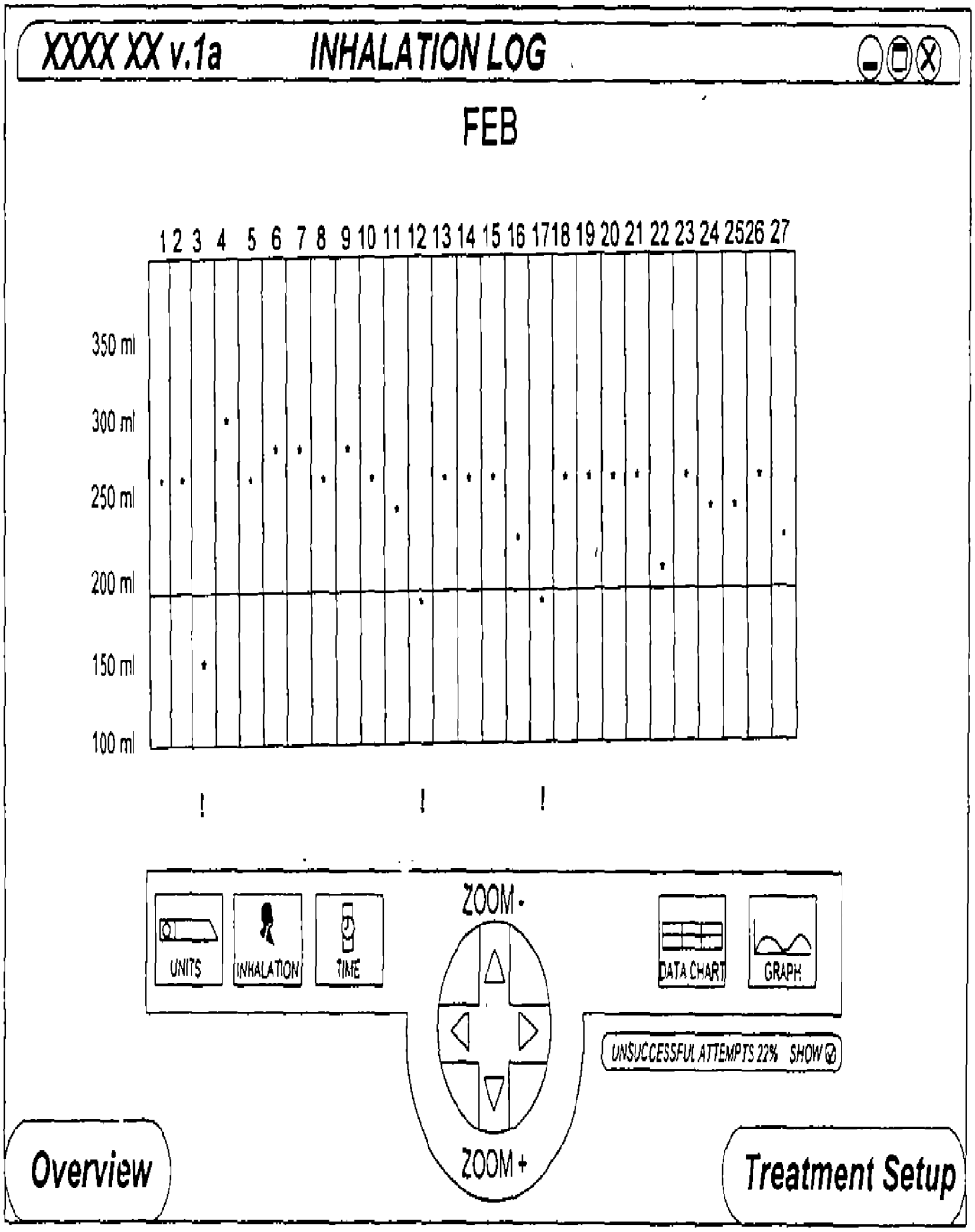
XXXX XX v.1a
INHALATION LOG
FEB
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27
350 ml
300 ml
250 ml
200 ml
150 ml
100 ml
UNITS
INHALATION
TIME
ZOOM -
ZOOM +
DATA CHART
GRAPH
UNSUCCESSFUL ATTEMPTS 22% SHOW
Overview
Treatment Setup

FIG. 4

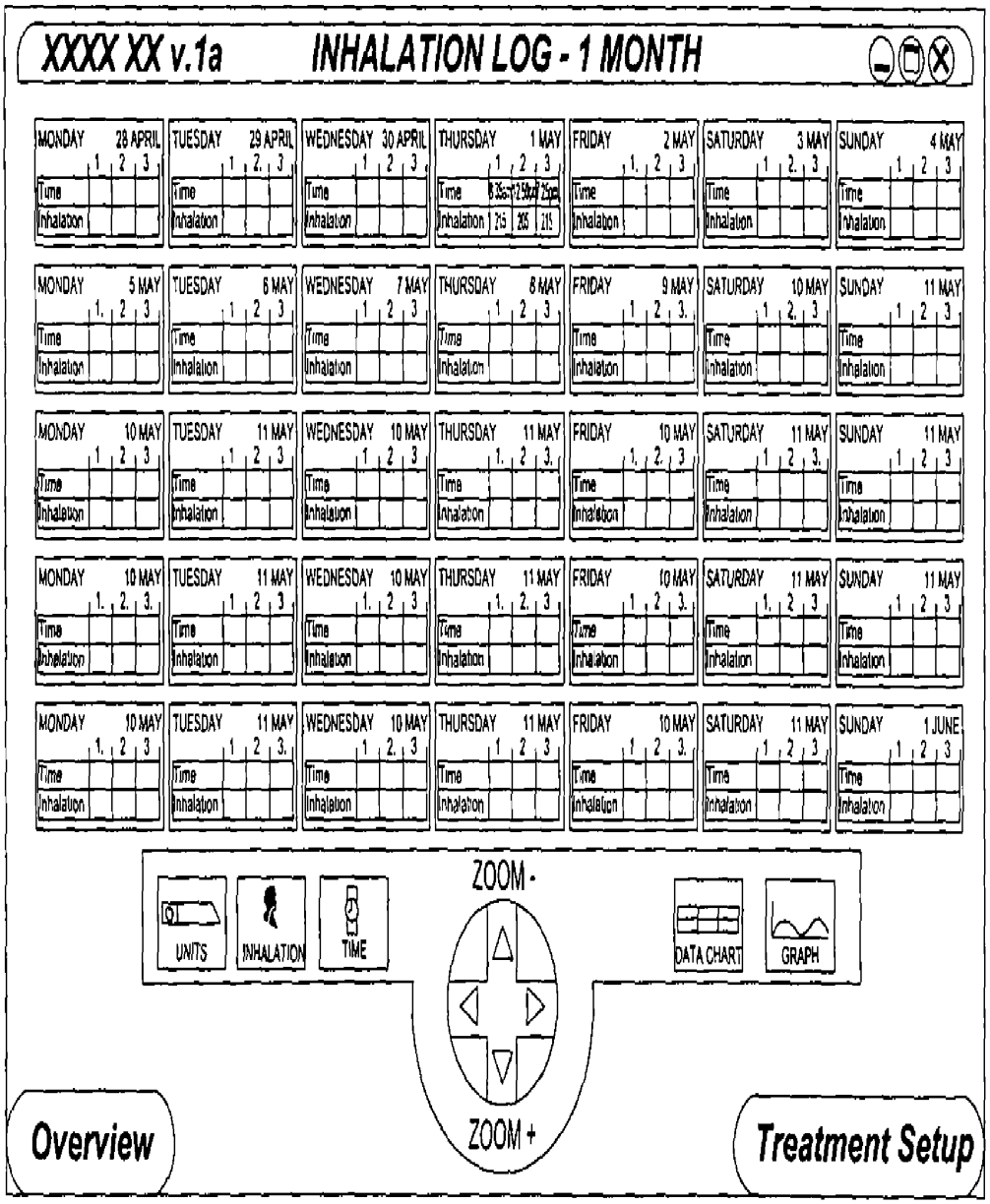
XXXX XX v.1a
INHALATION LOG - 1 MONTH
MONDAY 28 APRIL
TUESDAY 29 APRIL
WEDNESDAY 30 APRIL
THURSDAY 1 MAY
FRIDAY 2 MAY
SATURDAY 3 MAY
SUNDAY 4 MAY
MONDAY 5 MAY
TUESDAY 6 MAY
WEDNESDAY 7 MAY
THURSDAY 8 MAY
FRIDAY 9 MAY
SATURDAY 10 MAY
SUNDAY 11 MAY
MONDAY 10 MAY
TUESDAY 11 MAY
WEDNESDAY 10 MAY
THURSDAY 11 MAY
FRIDAY 10 MAY
SATURDAY 11 MAY
SUNDAY 11 MAY
MONDAY 10 MAY
TUESDAY 11 MAY
WEDNESDAY 10 MAY
THURSDAY 11 MAY
FRIDAY 10 MAY
SATURDAY 11 MAY
SUNDAY 11 MAY
MONDAY 10 MAY
TUESDAY 11 MAY
WEDNESDAY 10 MAY
THURSDAY 11 MAY
FRIDAY 10 MAY
SATURDAY 11 MAY
SUNDAY 1 JUNE
Time
Inhalation
UNITS
INHALATION
TIME
ZOOM -
ZOOM +
DATA CHART
GRAPH
Overview
Treatment Setup

FIG. 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/055678

A. CLASSIFICATION OF SUBJECT MATTER
A61M15/00 A61B5/00

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M A61B

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/092576 A (GLAXO GROUP LIMITED; LINTELL, DANIEL, THOMAS DE SAUSMAREZ) 13 November 2003 (2003-11-13) page 5, line 14 - page 24, line 21; figures	1,10,11, 18,19
X Y	US 5 363 842 A (MISHELEVICH ET AL) 15 November 1994 (1994-11-15) column 5, line 41 - column 12, line 24; figures	1-3,10, 11,18,19 4,5, 12-14
Y	WO 2004/017831 A (WELCH ALLYN, INC) 4 March 2004 (2004-03-04) paragraph '0182! - paragraph '0183!; figure 47 paragraph '0107!	4,5, 12-14

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 February 2006	22/02/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Zeinstra, H

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

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/055678

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 167 880 B1 (GONDA IGOR ET AL) 2 January 2001 (2001-01-02) cited in the application column 14, line 20 - column 22, line 26; figures 1-4	1,10,18

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2005/055678

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 6-9,15-17,20
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2005/055678

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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US 6167880 B1	02-01-2001	NONE	