PATENT ASSIGNMENT

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NATURE OF CONVEYANCE:	ASSIGNMENT
EFFECTIVE DATE:	02/20/2007

CONVEYING PARTY DATA

Name	Execution Date
HEARTLINK NA PATENT CORPORATION	02/20/2007

RECEIVING PARTY DATA

Name:	IFEM-CTAC LIMITED
Street Address:	P.O. Box 957 Offshore Corporations Centre
City:	Road Town
State/Country:	VIRGIN ISLANDS, BRITISH

PROPERTY NUMBERS Total: 1

Property Type	Number
Patent Number:	6245021

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NAME OF SUBMITTER:	Kenneth I. Kohn

Total Attachments: 67
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MEMORANDUM OF ASSIGNMENT OF PATENT RIGHTS

WHEREAS HEARTLINK NA PATENT CORPORATION of Bridgetown, Barbados ("ASSIGNOR") is the owner of certain inventions related to a METHOD FOR DIAGNOSING PSYCHIATRIC DISORDERS (the "INVENTIONS"), as disclosed in PCT Application No. PCT/AU98/00252 filed on 14 April, 1998, United States Patent No. 6,245,021 issued June 12, 2001, and a Canadian Patent Application filed on or about January 27, 2000 as a national continuation of said PCT Application (collectively the "APPLICATIONS");

AND, WHEREAS IFEM-CTAC LIMITED (the "ASSIGNEE"), with an address of PO Box 957, Offshore Corporations Centre, Road Town, British Virgin Islands, is desirous of acquiring and confirming that it has acquired all right, title and interest in the United States of America and Canada, in and to the said INVENTIONS, including without limitation all right, title and interest in the United States of America and Canada in, to and under said APPLICATIONS from said ASSIGNOR;

NOW, THEREFORE, in consideration of US$400,000 paid to the ASSIGNOR by the ASSIGNEE under the terms of an Intellectual Property Rights and Subsidiary Assignment Agreement dated February 20, 2007, and other good and valuable consideration paid to ASSIGNOR by ASSIGNEE, the receipt and sufficiency of which is hereby acknowledged by ASSIGNOR, ASSIGNOR hereby confirms that it has sold, assigned and transferred, and by these presents does hereby sell, assign and transfer to ASSIGNEE the entire right, title and interest in the United States of America and in Canada in and to said INVENTIONS, including without limitation:

(a) all right, title and interest in the United States of America and Canada, to and under said APPLICATIONS and any registration issuing thereunder and any other patents for such INVENTIONS;

(b) the right to file additional patent applications in any country for said INVENTIONS, and to do so in its own name (hereinafter "ADDITIONAL APPLICATIONS");

(c) all right, title and interest in the United States of America and in Canada in any and all existing or future substitute, divisional, continuation or continuation-in-part patent applications deriving directly or indirectly either in whole or in part from such APPLICATIONS or such INVENTIONS and any of such ADDITIONAL APPLICATIONS (hereinafter "DERIVATIVE APPLICATIONS");

(d) all right, title and interest in the United States of America and in Canada, in, to and under all patents granted directly or indirectly on or as a result of the APPLICATIONS, any of such ADDITIONAL APPLICATIONS and any of such

DERIVATIVE APPLICATIONS, and any reissues, renewals or extensions thereof;

(e) the right to claim benefits available in any country under the *International Convention For The Protection of Industrial Property*, and any like treaties or laws; and

(f) the right to claim and to the benefit of any priority dates established by the INVENTIONS or the APPLICATIONS.

the same to be owned, held and enjoyed by ASSIGNEE, its successors, assigns and legal representatives, as fully and exclusively as it would have been held and enjoyed by ASSIGNOR had this sale, assignment and transfer not been made.

ASSIGNOR hereby agrees that this assignment shall be binding upon their successors, assigns and legal representatives.

AND ASSIGNOR hereby covenants and agrees to do all such things and to execute or obtain execution without further consideration of such further lawful documents, assurances, applications and other instruments as may be reasonably required to make and prosecute any and all patent applications in the United States of America and in Canada on said INVENTIONS, to enforce any patents arising from or out of the INVENTIONS, the APPLICATIONS and any and all patents in the United States of America and Canada on said INVENTIONS, and to confirm in the ASSIGNEE or its successors and assigns, legal title in the United States of America and Canada to said INVENTIONS, the APPLICATIONS, all DERIVATIVE APPLICATIONS and ADDITIONAL APPLICATIONS and all United States patents and United States applications, Canadian patents and Canadian patent applications, on said INVENTIONS.

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IN WITNESS WHEREOF, ASSIGNOR has caused this Memorandum of Assignment to be executed at the locations and on the dates set out below and with effect as of February 20, 2007.

WITNESS

(Signature)

E. TAYLOR

(Print Name)

DAVIS + COMPANY, 2800-666 Burrard St

VANCOUVER

(Address)

HEARTLINK NA PATENT CORPORATION

Authorized Signatory

IFEM-CTAC LIMITED hereby accepts the foregoing assignment.

By: _____
(signature) (date)

Print Name: RICHARD TAN H.

Its: _____

AFFIDAVIT OF EXECUTION

I, Robert F. Baldock, 1513-989 Nelson St, Vancouver BC. V6Z 2S1, whose full post office address is , MAKE OATH AND SAY:

1. That I am CFO & DIRECTOR, an authorized signatory of HEARTLINK NA PATENT CORPORATION, one of the parties named in the Memorandum of Assignment dated with effect as of February 20, 2007 relating to the assignment of inventions set out in:

(a) PCT Application No. PCT/AU98/00252 filed on 14 April, 1998,

(b) United States Patent No. 6,245,021 issued June 12, 2001, and a Canadian Patent Application filed on or about January 27, 2000 as a national continuation of said PCT Application (collectively the "APPLICATIONS");PCT International Application No. PCT/US00/24920 filed 12 September 2000;

(b) United States Patent No. US 6,338,682 B1 issued January 15, 2002; and

(c) a Canadian national filing of said PCT Application

to IFEM-CTAC LIMITED.

2. I have read and understood the Memorandum of Assignment and the signature thereon is my own and was applied as my free act and deed and on behalf of and with the knowledge, approval and authority of HEARTLINK NA PATENT CORPORATION.

SWORN before me at Vancouver BC this 16th day of April, 2007.

E. TAYLOR

A Notary Public and Commissioner for taking oaths in and for the Province of British Columbia

[insert name and contact details below]

DAVIS & COMPANY
BARRISTERS & SOLICITORS
28th Floor - 666 Burrard St.
Vancouver, B.C. V6C 2Z7
687-9444

R.F. Baldock
Signature

Davis:1802195.2

CHAIN OF TITLE:

HEARTLINK PATENT RIGHTS

Chain of Title

1. Assignment of patent rights from Hans George Stampfer to HeartLink Pty Ltd., date July 19, 1999, effective April 10, 1997;

2. Australian Patent Application P0 6166, filed April 11, 1997 by HeartLink Pty Ltd.;

3. Assignment of rights from HeartLink Pty Ltd. to HeartLink World Patent Corporation, effective June 1, 1999;

4. Assignment of North American and Canadian rights from HeartLink World Patent Corporation to HeartLink N.A. Patent Corporation, effective June 1, 1999;

5. Licence of rights from HeartLink N.A. Patent Corporation to HeartLink Canada (1999) Inc. dated December 31, 1999.

1

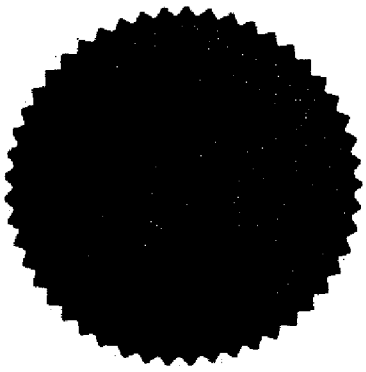
NOTARIAL CERTIFICATE

TO WHOM IT MAY CONCERN:

I, **GARRY EVAN SAME**, of Perth, Western Australia, Australia, Notary Public, duly admitted and sworn, HEREBY CERTIFY AND ATTEST:

THAT the photocopy of the Deed of Assignment between **HANS GEORGE STAMPFER** and **HEARTLINK PTY LTD (ACN 076 507 992)** which Deed is dated the 19th day of July 1999 annexed hereto and signed by me is a true photocopy of the aforementioned Deed of Assignment as sighted by me on this date.

GIVEN under my hand)
and official seal the 7th)
day of February 2000)



GARRY EVAN SAME
Notary Public
Perth, Australia

DEED BETWEEN

HANS GEORGE STAMPFER

- and -

HEARTLINK PTY LTD

Wray & Associates

PATENT AND TRADEMARK ATTORNEYS Est 1925

THIS DEED made this 19th day of July 1999 and effective from 10 April 1997.

BETWEEN

HANS GEORGE STAMPFER of 33A Owen Road, Darlington, Western Australia, Australia 6070 ("the Assignor")

AND

HEARTLINK PTY LTD an Australian Company of Level 1, 10 Kings Park Road, West Perth, Western Australia, Australia 6005 ("the Assignee")

RECITALS

A. The Assignor is the inventor of an invention entitled "Method for Diagnosing Psychiatric Disorders" ("the Invention") which is the subject of Australian patent applications PO 6166 and 68141/98 and International patent application PCT/AU98/00252.

B. By virtue of an earlier agreement between the Assignor and the Assignee, the Assignor assigned his entire right, title and interest in and to the Invention and of in and to any Letters Patent which may be granted therefor either to the Assignor as the Inventor or to the Assignee as Assignee together with the right to seek patent protection in respect of the Invention to the Assignee ("the earlier Agreement").

C. In the premises the parties hereto have agreed to execute this deed to supplement and confirm the earlier Agreement.

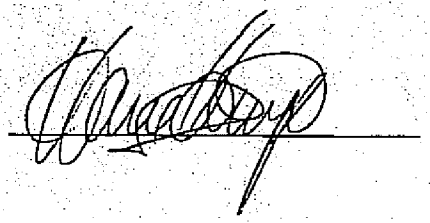
NOW BY THIS DEED

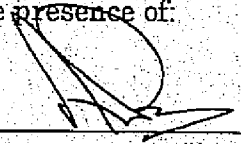
In confirmation of the earlier Agreement, the Assignor does hereby sell, assign, transfer and make over unto the Assignee all his entire right, title and interest of in and to the Invention with full power to the Assignee or his

assigns to apply for and/or obtain Letters Patent in Australia and/or elsewhere and the Assignor shall, at the expense of the Assignee or his assigns, execute and do all such documents and things as may be necessary or proper for legally vesting in the Assignee or his assigns the full benefit of the Invention and of any Letters Patent which may be granted therefor either in Australia and/or elsewhere.

EXECUTED BY THE PARTIES AS A DEED

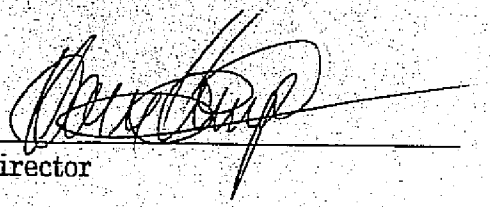
by the above named)
HANS GEORGE STAMPFER)
in the presence of:)





(WITNESS)

THE COMMON SEAL of)
HEARTLINK PTY LTD was)
affixed in accordance with its)
Articles of Association in the)
presence of:)



Director

Director/~~Secretary~~

Patent Office
Canberra

I, KAY WARD, TEAM LEADER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. PO 6166 for a patent by HEARTLINK PTY LTD filed on 11 April 1997.

WITNESS my hand this
Ninth day of February 2000

KAY WARD
TEAM LEADER EXAMINATION
SUPPORT AND SALES

ORIGINAL

AUSTRALIA

Patents Act 1990

PROVISIONAL SPECIFICATION

Invention Title: "Method for Diagnosing Psychiatric Disorders"

The invention is described in the following statement:

The present invention relates to a method for diagnosing psychiatric disorders using a subject's heart rate pattern and more particularly to a method for diagnosing psychiatric disorders by monitoring a subject's circadian heart rate pattern.

It has long been recognised that anxiety is associated with elevations in heart rate. However, whilst elevated heart rate may be a symptom of anxiety, the present invention is based on the surprising discovery that a subject's heart rate pattern provides useful information regarding the subjects psychiatric status.

The present invention seeks to provide a method for diagnosing psychiatric disorders or to at least provide a diagnostic method that may provide objective indications of clinical change and contribute to the diagnostic assessment of a subject.

Thus, the present invention provides a method for diagnosing a psychiatric disorder in a subject, the method comprising the steps of: measuring the subject's heart rate pattern and; comparing said pattern with at least one reference heart rate pattern indicative of a psychiatric disorder.

The present invention is based on the identification of a psychophysiological correlation between heart rate pattern and psychiatric status. In this respect, it has been found that certain clinical states are consistently associated with distinctly different heart rate patterns.

The heart rate pattern may be measured over a variety of time periods. Preferably, the heart rate pattern is a circadian heart rate pattern, in that it is measured over a 24 hour period. Whilst the entire circadian heart rate pattern may be used in the method of the present invention, certain portions of the circadian heart rate pattern may also be used to diagnose psychiatric disorders. In this respect, some psychiatric disorders may be identified via characteristic patterns within the circadian heart rate pattern.

Thus, the present invention also provides a method for diagnosing a psychiatric disorder in a subject, the method comprising the steps of: measuring the subject's circadian heart rate pattern or a portion thereof and; correlating said pattern or portion thereof with at least one reference circadian heart rate pattern or portion thereof indicative of a psychiatric disorder.

When the method comprises the measurement a portion of the circadian heart rate pattern the portion measured may be varied provided the portion is capable of exhibiting a pattern that correlates to a psychiatric disorder.

The heart rate pattern of a subject whilst asleep and during the transition from being awake to asleep and asleep to awake may be particularly useful in the method of the present invention. Thus, when the method comprises the measurement a portion of the circadian heart rate pattern, the portion of the circadian heart rate pattern is preferably the sleep portion and in particular the sleep portion including the transition of the subject into and out of sleep.

The heart rate pattern may be measured in a variety of formats. Preferably, the heart rate pattern is measured as beats per minute over time. Alternatively, the heart rate pattern may be measured as a difference plot which reflects variations or fluctuations in heart rate. When the heart rate pattern is a difference plot, the difference plot is preferably a plot of [heart rate (t+1) - heart rate (t)], where t is time in minutes, over time.

Of course, the heart rate pattern of a subject may be measured in a plurality of formats and the plurality of formats may be used together to diagnose psychiatric disorders according to the method of the present invention. Thus, the present invention also provides a method for diagnosing a psychiatric disorder in a subject, the method comprising the steps of: measuring the subject's heart rate pattern in a plurality of formats, such as beats per minute over time and [heart rate (t+1) - heart rate (t)], where t is time in minutes, over time and; comparing the patterns of said plurality of formats with a plurality of reference heart rate patterns indicative of a psychiatric disorder.

The method of the present invention may be computerised. In this respect, a subject's heart rate pattern may be measured and recorded in a form that allows it to be cross-checked with a database of heart rate patterns indicative of psychiatric disorders.

Thus, the present invention also provides a method for diagnosing a psychiatric disorder in a subject, the method comprising the steps of: measuring the heart rate pattern of the subject and; comparing said pattern with at least one reference heart rate pattern indicative of a psychiatric disorder wherein the reference heart pattern is provided in a computerised database.

The subjects heart rate pattern may be measured in a variety of ways. Preferably, the subjects heart rate is measured with a monitor that is unobtrusive and leaves the person freely ambulant. For example, the heart rate pattern may be measured using a POLAR® Sport Tester monitor (® registered trade mark of Polar Electro Oy).

The reference heart rate patterns of the present invention may be varied and may be developed by a person skilled in the art by collecting data from a sufficient number of patients with psychiatric disorders to determine a typical pattern.

When the heart rate pattern is a circadian heart rate pattern, the reference heart rate pattern may be selected from those illustrated in the examples and in particular those patterns illustrated in Figures 1 to 4.

The present invention may be used to diagnose a variety of psychiatric disorders. For example, the method of the present invention may be used to diagnose a psychiatric disorder selected from the group comprising; General Anxiety Disorder (GAD), Panic Disorder (PD), Obsessive-Compulsive Disorder (OCD), non-psychotic Major Depression, Somatoform Disorder (hypochondriacal type), Delusional Disorder (paranoid and somatic type) and acute Schizophreniform Disorder.

Heart rate patterns may be affected by a range of factors. Some factors may produce noise that may hamper the interpretation of the heart rate pattern, which is clearly undesirable. To assist in accounting for and thus negating the effects of noise, the method of the present invention may further comprise the recordal of a subject's activities throughout the time the subject is being subjected to the method.

Thus, the present invention provides a method for the diagnosis of a psychiatric disorder in a subject, the method comprising the steps of: measuring the subject's heart rate pattern; comparing the subject's heart rate pattern with a record of the subject's activities and; comparing said pattern with at least one reference heart rate pattern indicative of a psychiatric disorder wherein the comparison of the subject's heart rate pattern with the record of the subjects activities allows for the effects of noise in the subject's heart rate pattern to be negated.

Preferably, the record of the subject's activities comprises a daily diary that is completed by the subject when being subjected to the method of the present invention.

The present invention may also be useful for monitoring the effectiveness of a particular treatment administered to a subject suffering from a psychiatric disorder.

Thus, the present invention also provides a method for assessing the effectiveness of a treatment for psychiatric disorder, the method comprising the steps of: measuring the subject's heart rate pattern before and during said treatment and; comparing said patterns for changes to determine the effectiveness of the treatment.

Preferably, the treatment is a drug treatment in which the drug is administered to the subject. For example, the drug treatment may involve the administration of a drug selected from the group comprising; benzodiazepines; anti-depressants

such as Selective Serotonin Reuptake Inhibiters (SSRI's), Tri-cyclic Antidepressants (TCA's) and Reversible Inhibitor of Monoamines (RIMA's); and sertraline.

The present invention will now be described with reference to the following examples. The description of the examples in no way limits the generality of the preceding description.

The data presented in the examples illustrate the relationship between circadian pattern of heart rate and psychiatric disorders. The independent variable in the examples was an ACTIVE axis I DSM-IIIR disorder ("IIIR" - revised third edition of the diagnostic manual published by the American Psychiatric Association); the dependent variable, 24MAHR. Efforts were made to control for a number of possible confounding influences on heart rate. All subjects were given careful instructions in diary keeping. The diary consisted of a single card with provision for hourly ratings of potentially confounding influences that included: physical exertion, intake of tea/coffee/alcohol/nicotine and social interaction.

Only certain diagnoses were studied. The aim was to select readily diagnosed states between normality and psychosis and the following were included; Generalized Anxiety Disorder (GAD), Panic Disorder, Obsessive-Compulsive Disorder (OCD), non-psychotic Major Depression, Somatoform Disorder (hypochondriacal type), Delusional Disorder (paranoid and somatic type) and acute Schizophreniform Disorder.

Clinical subjects were selected from consecutive admissions to an adult psychiatric unit of a large teaching hospital. Normal control subjects (without any history of psychiatric illness) were obtained from students, nursing, clerical and medical staff. Patients were included in the study initially if they satisfied DSM-IIIR criteria for one of the above listed axis I disorders. Age was restricted to 18-65. Subjects were required to be physically healthy and were excluded, if after full physical examination and relevant laboratory investigations, there was

evidence of any physical disorder that might affect heart rate. Subjects were also excluded if there was any evidence of recent alcohol and illicit drug abuse.

Whilst efforts were made to select subjects who had not taken any medications within two weeks of admission, those who had been taking medications were not excluded if at the time of recording, they showed clear evidence of an active axis I disorder included in the study. Medication histories were recorded in all cases and the inclusion of both medication free subjects with those who had been or were taking medication at the time of recording, gave the opportunity to examine medication effects in each diagnostic category.

Measures of 24 hour, minute average heart rate (24MAHR) were obtained with the use of a POLAR Sport Tester monitor. Data acquisition is unobtrusive and leaves the person freely ambulant. A pre-study comparison was made between data obtained with a Polar and conventional Holter monitor. Simultaneous recordings were obtained from normal subjects and it was found that correlations of 0.97 and greater, obtained between the two sets of data. Similar findings were reported by Treiber et al (l989) who found that the correlation between a Sports Tester and conventional ECG monitor varied from 0.97 to 0.99.

The number of serial recordings per subject ranged from 2-10, with a rounded mean of 3 per subject. The purpose of taking serial recordings, was to examine the extent of intra-subject variation in circadian activity, depending upon changes in mental state. Typically, serial recordings were obtained every third day. Diagnostic reassessment was undertaken prior to each serial recording. As data were obtained over more than two years, it was possible to obtain serial recordings over relatively long periods in a percentage of subjects who were readmitted during this period.

Whilst plots of heart rate v's time of day can reveal the qualitative aspect of circadian activity at a glance, it is difficult to quantify this temporal aspect in a numerical form and there are certain difficulties in creating composite group data. There are a number of pitfalls in simply averaging the data. There are

obvious changes in heart rate depending on whether a person is awake or asleep (see Figure 1) and there is considerable variation in the sleep habits of different individuals - both in terms of when they go to sleep and the length of time they usually sleep. Hence, if one were to simply average group data, the resulting average would inevitably be confounded by overlapping segments of sleep/awake activity between subjects. Also, potentially relevant transient changes, such as a sudden elevation or reduction in heart rate during sleep and awake periods, would tend to become degraded or 'lost' with averaging. Hence averaging is not an appropriate method of group data reduction for comparing patterns of circadian activity between different diagnoses.

A comparison of the qualitative aspect requires a pattern classification of individual recordings in terms of particular 'morphological' features. This was the approach taken in the examples. Individual records of 24MAHR were superimposed on a VDU and classified into different pattern types, based on their circadian morphology. A frequency count was then made, of the pattern types found in each diagnosis and a Chi-square test applied to see if any particular pattern predominated.

Findings are presented below; Example 1 describes qualitatively different circadian patterns and illustrates how these data can provide clinically useful information. Example 2 shows the results of group data analysis and includes an analysis of medication effects.

EXAMPLE 1

Measures of 24MAHR provide a time history of two broadly different, but complementary, aspects of circadian activity. The first aspect, which is clearly evident in time plots of the raw data, consists of the broad contours of activity that are created by changes in the baseline mean around which minute pulse rates vary. The second aspect is revealed in a variability or difference plot,

[pulse rate (t+1) - pulse rate (t), with t in minutes], and consists of the changing trends in minute pulse variation that are to some extent independent of the broad mean contours. These two complementary aspects are illustrated in Figure 1, which shows typical examples of three broadly different circadian patterns. The patterns illustrated in Figure 1 were found commonly in subjects with General Anxiety Disorder (GAD), non-psychotic Depression (DEP) and normal subjects (NOR).

Plots of the corresponding first differential, are shown on the right. The respective 24 hour scalar means [$\bar{X}$] and [$\bar{X}$d], in beats per minute (BPM), are shown at the end of each plot. The plots on the left show visibly obvious differences in the broad circadian pattern or architecture, particularly in the pattern of activity extending over the sleep period. The sleep period is most clearly defined in normal data. There is a rapid decline in heart rate at the onset of sleep, an equally rapid rise on waking and a relatively flat pattern of low rate activity in between. By comparison, GAD data, show a well defined, large elevation of heart rate on waking, but no rapid decline to mark the onset of sleep. Instead, there is a progressive decline from awake rates to the lowest rates, just before waking. The opposite occurs in subjects suffering from Depression (DEP). Typically in these subjects the onset of sleep is marked by a relatively rapid decline in heart rate, that is followed by a fluctuating, but progressive elevation towards awake levels, without a clearly defined transition from sleep to waking. In GAD, heart rates are relatively high at the onset of sleep and at their lowest just before waking. In DEP it is the reverse.

Turning to the first differential plots on the right of Figure 1, it can be seen that normal data show the lowest differential mean of 3.4 BPM and the highest value of 7.0 BPM occurs in GAD. However, it should be noted that the 24 hour mean ($\bar{X}$) is not a reliable indicator of the amount or pattern of minute pulse variation. That is, the changes in minute pulse variation are to some extent independent of the broad contours of activity.

More generally, it can be seen that these differential plots also reveal something of a circadian pattern, which is created by variation in the amount of activity at different times of the day. Again, this architecture of circadian variation is most clearly defined in normal data, which show a clear reduction in pulse variation at the onset of sleep, followed by a visibly reduced level of activity during the sleep interval and a return to pre-sleep levels on waking. By comparison, Depression shows only a brief period of reduced activity at the onset of sleep, followed by a rapid return to pre-sleep activity, even while the mean trend is still below the pre-sleep awake values. GAD data show a discernible reduction in sleep activity similar to what is evident in normal data, but the reduction is less obvious and there is a much greater amount of activity during the sleep interval.

More generally, and compared to normal, the data for GAD and Depression show more spiking throughout the 24 hour period. The differences in activity extending over the sleep period, in both the broad mean contours and amount of minute pulse variation, are regarded as particularly significant, in that one would expect the least number of confounding influences during sleep. The evident differences over this period are likely to be particularly valid indicators of genuine physiological differences between these states. Apart from qualitative differences, the data in Figure 1 also show quantitative differences in the 24 hour means indicated at the end of each plot.

Figures 2a and 2b, show further typical patterns associated with Depression (Figure 2a) and GAD (Figure 2b) and their corresponding 24 hour means. It can be seen that typical GAD and DEP patterns can extend over a range of baseline offsets and whilst the 24 hour mean is usually found to be lower in Depression than GAD, Figures 2a and 2b show that this is not always the case. It can be seen that the 24 hour mean of 94 BPM for the top plot in Figure 2a is significantly higher than the 24 hour mean of 76 BPM for the bottom plot in Figure 2b. This shows that the qualitative differences between these two patterns, cannot be explained simply by quantitative differences in the 24 hour mean. This does not mean that quantitative differences within and between

particular patterns are irrelevant and the significance of such quantitative variation is discussed in more detail below in Example 2.

Although states of GAD and Depression will most commonly reveal the respective signature patterns of circadian activity as shown in Figures 1 & 2, individual recordings may show a number of minor variations that provide potentially useful information about particular individuals. For example, a typical GAD pattern might show the following variations while still retaining its signature contour.

There may be variation in baseline offset as shown in Figure 2. There may be variation in the gradient of declining activity during the sleep interval, as well as the gradient and relative elevation of heart rate on waking. There may be variation in the pattern of insomnia, as indicated by the amount of spiking activity to waking levels during the sleep interval. There may be a greater or lesser amount of minute pulse variation throughout the 24 hours or selected intervals of time. Hence, just as two individuals with an undoubted clinical diagnosis of GAD for example, may show some variation in the severity and number of clinical phenomena, so may the pattern of 24 hour show some variation, but still retain it's signature GAD contour.

However, subjects may also exhibit mixed heart rate patterns, with features of both GAD and DEP, that seem analogous to mixed mental state phenomena one finds in the clinical domain. These mixed patterns suggest a dynamic continuum of manifestations and the circadian pattern in individual cases may depend on the relative amount of activation in two broadly different physiological pathways. In this sense, it may be that the typical patterns for GAD and Depression shown in Figures 1 & 2, reflect 'pure' GAD and 'pure' Depression respectively, whereas mixed forms reflect activation of both GAD and Depression physiology. An example of such a mixed pattern ('MIX') is shown in Figure 3 together with a GAD and a Depression pattern.

Such patterns were found less commonly in subjects diagnosed as Panic Disorder, GAD and Depression, and it is emphasised in this regard, that these subjects were not given a mixed diagnosis on clinical assessment. However, their heart rate showed a circadian pattern that appears to fall between the more common typical patterns for GAD and Depression.

The mixed pattern in Figure 3 has been placed between further examples of typical GAD and DEP patterns, to facilitate an appreciation of what is meant by mixed. It can be seen that the mixed pattern shows a progressive decline of activity into the sleep period that closely resembles the GAD pattern above it. However, the similarity ends at around 4.00am. Thereafter there is a progressive increase in heart rate to awake levels, that resembles the Depression pattern immediately below. This suggests a combined activation of GAD and Depression physiology and even if this interpretation requires modification, the physiological perspective revealed by these data may contribute practically useful adjunct information in a variety of clinical and research applications.

In all, seven broadly different circadian patterns were identified and practically all the data obtained, could be broadly classified into one or other of these patterns. Four of these seven patterns, namely, Normal, GAD, Depression and Mixed, have already been presented above. The remaining three, shown in Figure 4, have been found to be most common in patients with Panic Disorder (PAN), Obsessive-Compulsive Disorder or Delusional Disorder (HSR) and acute Schizophreniform Psychosis (SCH).

The PAN pattern is characterized by a flat pattern of activity for much of the 24 hour period, a relatively low 24 hour mean and a relatively large amount of spiking pulse variation. There is a discernible flat sleep period (from around midnight to 8am), defined by a small baseline shift down and a slight reduction in the amount of minute pulse variation.

The HSR pattern resembles the normal pattern but differs in the consistently high rates of flat activity both in the awake and sleep periods. In the example shown, the sleep interval is clearly defined by a precipitous drop in heart rate at the onset of sleep, an equally precipitous elevation on waking and a relatively flat pattern of activity throughout the sleep period, with rates around 80 BPM. Elevations of sleep rate around and beyond such values, show a progressive disruption of the sleep architecture towards the grossly disorganized pattern which is found in acute schizophreniform states (SCH).

All but two out of all the recordings obtained could be classified broadly into one or other of the seven patterns discussed above. Those which did not conform to one or other of these types, were classified as other (OTH). Quite possibly further classificatory patterns might have been found by including more diagnostic states and by making finer pattern distinctions that included differences in minute pulse variation. Attention has been drawn to minute pulse variation to show how this perspective may also contribute clinically useful information. It was very apparent that the same broad circadian pattern in different individuals, can show considerable variation in the amount and distribution of minute pulse variation and the clinical significance of such variation will be explored in further studies. In this example, only the broad circadian contours were classified for group data comparisons.

Serial recordings were obtained from all subjects. However only the first recording from each subject was used for group data comparisons between the different diagnoses included in the study. Subsequent recordings were used to study intra-individual changes and did not contribute to group data. The aim of serial recordings, was to see whether a subject's change in mental state, eg from GAD to normal, was associated with a change in circadian pattern and if so, whether the change recapitulated the most common group data pattern for those states. Such intra-individual state-dependent recapitulation of group data patterns for those states, would give support to the proposed hypothesis of there

being a systematic link between psychiatric status and circadian pattern of heart rate.

EXAMPLE 2

Data presented in Example 2 show that, notwithstanding other influences, patterns of heart rate are demonstrably dependent on mental or psychiatric status. Where mental state alters, for example, from anxious to normal, the pattern of 24 hour activity shows corresponding changes in serial recordings. An example of such state dependent changes is shown in Figure 5.

The data were obtained from an individual whose symptoms of GAD abated with treatment. Raw data are shown on the left and the corresponding variability data on the right. The respective 24 hour means have been added at the end of each plot. It can be seen that the broad contours of activity change from a typical GAD pattern towards a normal NOR pattern and there are concomitant changes in minute pulse variation. In particular, there is a relative reduction in activity at the onset of sleep and during sleep. From a purely quantitative perspective, there is a reduction in the 24 hour mean ($\bar{X}$) from 98 to 77, and in the differential mean $\bar{X}d$ from 7.3 to 5.4. Taken together, these changes are intuitively consistent with someone becoming less anxious. The advantage of these physiological adjunct data is that they can provide objective indices of clinical change.

It is appropriate at this stage to make some comments about confounding noise. It is well recognised that heart rate is susceptible to a wide range of influences and the data presented here may be contaminated to some extent with noise caused by variation in fitness, age, sex, tea/coffee intake, motor activity, environmental stimulation. etc. Diary keeping can help to control for more obvious influences such as exercise, but a certain amount of noisy contamination will inevitably remain. It is found in this regard that whilst physical exercise and other unusual stimulation/exertion can undoubtedly produce confounding effects, these are readily identified with the help of diary information. Minor and brief influences do not appear to exert a significant

confounding effect on the broad contours of activity. Probably this is because such effects are brief and randomly distributed during the waking period. The diagnostically useful information is revealed more in the broad mean trends, which remain distinctly evident despite superimposed high frequency noise. Also, a large number of possible confounding effects do not operate during the sleep period and the pattern of activity during sleep is an important discriminatory feature.

More generally, and excepting unusual effects such as exercise, it appears to be the case that just as similar psychological phenomena (eg symptoms of anxiety and Depression) come to dominate the mental state of normally different individuals, so do mental state dependent patterns of circadian heart rate come to dominate in the physiological domain, despite differences in age, fitness etc. Thus, in the case of GAD for example, it is found that a sport fit 20 year old male and a decidedly unfit 60 year old female will both show a similar GAD pattern, even if there are baseline differences normally.

	CIRCADIAN PATTERN										
MENTAL STATE	NOR	DEP	PAN	GAD	MIX	HIS	SCH	OTH	N	$\bar{X}$	$\bar{X}d$
Normal	23	-	-	5	2	-	-	-	30	75	4.8
Depression	-	23	2	-	5	-	-	-	30	76	3.5
Somatoform	1	-	4	10	6	2	-	2	25	82	4.1
Panic	-	1	18	8	3	-	-	-	30	71	5.1
GAD	-	-	-	24	4	2	-	-	30	86	4.9
OCD	-	-	-	5	1	9	-	-	15	95	4.9
Delusional	-	1	-	8	2	14	-	-	25	99	4.1
Acute Schizophrenia	-	-	-	2	-	4	9	-	15	107	4.9

Table 1 shows a summary of group data, in terms of how frequently particular patterns occurred in the different diagnoses. The number of subjects (N), group 24 hour mean ($\bar{X}$) and group 24 hour differential mean ($\bar{X}d$), have been added for each diagnosis. It can be seen that whilst all diagnoses, including normal, are associated with more than one type of circadian pattern, certain diagnoses show a strong association with one particular pattern. If one assumes that the seven identified patterns should be equally distributed in each diagnostic group, then Chi square testing shows a significant predominance (with probabilities > 0.05 and 0.001) of a particular pattern in each of the diagnostic groups.

More generally, there are indications of an hierarchical grouping in these correlations. Thus normal subjects showed predominantly a NOR pattern, and of those who did not, all but two showed an anxiety (GAD) pattern. However no normal subject showed an HSR or SCH pattern, which predominate at the psychotic end of the clinical spectrum. Conversely, Delusional and acute Schizophreniform Disorder do not show a NOR pattern. A similar hierarchical grouping is evident for anxiety subtypes of Panic disorder, Generalized Anxiety and Obsessive-Compulsive Disorder. No subject diagnosed as OCD showed a PAN pattern which predominates in Panic Disorder and no subject diagnosed as Panic Disorder showed an HSR pattern which predominates in OCD. However a significant percentage of both Panic Disorder (27%) and OCD (36%) subjects showed a GAD pattern which predominates in Generalized Anxiety Disorder. Whilst larger samples may show a wider overlap, the findings obtained here suggest that statistically, these anxiety subtypes are associated with broadly different circadian patterns, with OCD showing a pattern that predominates at the psychotic end of the clinical spectrum.

Table 1 also shows variation in the 24 hour mean ($\overline{X}$) and 24 hour differential mean ($\overline{X}d$), between the different diagnoses. Taking the mean of 75BPM for normal subjects as the reference, there are statistically significant elevations with $p > 0.001$ in: GAD, OCD, Delusional Disorder and acute Schizophreniform Disorder. This shows that statistically, some diagnoses reveal circadian activity that differs from normal both qualitatively and quantitatively, whereas in others such as Depression, it differs qualitatively but not quantitatively. However individual recordings of any particular pattern can show quantitative variation in terms of 'baseline offset', as illustrated for DEP and GAD patterns in Figure 2. The clinical significance of such quantitative variation was not investigated systematically, but in the case of the GAD pattern for example, there is support for the likely explanation that the degree of baseline offset is related to severity.

Table 1 shows that the GAD pattern was found in normal subjects and all diagnoses other than Depression. However the combined 24 hour mean of the

GAD pattern in states of Normal, Somatoform and Panic Disorder is significantly lower than it is for states of OCD, Delusional and Acute Schizophreniform Disorder. This indicates that the quantitative aspect is also relevant and it does not seem surprising that in the example of the GAD pattern, the highest means are found at the psychotic end of the clinical spectrum. It is not known over what range of baseline offset different patterns can exist without undergoing a qualitative change and it may be that any particular pattern depends on the relative contribution and hierarchical progression, of only a few axes of physiological activation (possibly only anxiety and Depression). Thus, both the qualitative and quantitative aspects of circadian heart rate can contribute potentially useful information.

Compared to the raw scalar mean ($\overline{X}$), less difference was found in the differential mean ($\overline{X}d$). However compared to the value of 4.8 BPM for normal subjects, there is a significant reduction ($p > 0.05$) in Depression, Delusional Disorder and hypochondriacal Somatoform Disorder. Although not significantly different compared to normal subjects, Panic Disorder shows the highest absolute mean of 5.1 BPM whereas Depression shows the lowest absolute mean of 3.6 BPM. The difference in this regard between Panic Disorder and Depression is highly significant with $p > 0.001$.

The ratio of drug free to drug taking subjects varied between diagnoses as did the type of medication. Because of such variation, comparisons were confined to the largest N groups of Depression, GAD and Panic Disorder, and no claim is made for any systematic study of medication effects. The majority of subjects on medication in these three groups, had been or were taking a benzodiazepine at the time of recording and some had also been taking anti-depressants. Surprisingly, no statistically significant differences were found in pattern type or 24 hour means. One might have expected at least a lower 24 hour mean in subjects taking benzodiazepines. Possibly these subjects had a higher heart rates in the first place and whilst medication did have an effect, it did not lower the mean to a significant extent. The provisional conclusion drawn from these

findings is that unless medication is effective in changing mental state, it does not significantly alter the circadian pattern and may not significantly lower the 24 hour mean, even if one does see transient effects, especially with benzodiazepines and sedative major tranquillizers. This is illustrated in Figure 6, which shows transient benzodiazepine effects.

Figure 6a shows a typical GAD pattern obtained from a subject diagnosed as GAD. Figure 6b shows a typical DEP pattern from a subject diagnosed as Depression. By chance, both subjects were taking diazepam when the first recording was made. The subject with Depression had been prescribed diazepam initially because of agitation. It can be seen that diazepam resulted in a similar transient lowering of heart rate in both subjects. In neither case do these transient effects apparently alter the broad circadian pattern to any significant extent and the 24 hour mean would have been lowered only minimally by the briefly lower rates. It should be noted that after briefly dropping, the heart rate returns to the pre-medication baseline and even higher rates after some 40 or so minutes. It appears that only when benzodiazepines have been effective in the treatment of generalized anxiety, do the broad contours of activity alter significantly (as illustrated in Figure 4). In contrast to benzodiazepines, anti-depressants (including SSRI's TCA's and RIMA's) do not show any visibly obvious transient effects, but can lead to more profound changes when clinically effective. This is illustrated in Figure 7 which shows significant changes in a DEP pattern, after three weeks treatment with Sertraline and undoubted clinical improvement. A comparison of Figures 7(a) and 7(b) shows that the presumed effect of treatment with sertraline, has been to normalize the circadian pattern to where the sleep period resembles the pattern seen in normal subjects and there has been a general reduction in the amount of minute pulse variation over much of the 24 hour period.

The examples demonstrate that there are qualitatively different patterns of circadian heart rate which cannot be reduced to mere quantitative variation in the 24 hour mean. Evidence has been presented to show that the qualitative

aspect depends importantly on mental or psychiatric status and the predominance of particular patterns in broadly different diagnoses, suggests that the circadian pattern is an indication of broad physiological differences between these psychiatric states. Whilst some states show a strong association with a particular pattern, in others the pattern is more variable. Conversely, given a recording which shows a particular pattern, (eg GAD), the clinical phenomena may vary from generalized anxiety, Panic Disorder, hypochondriacal Somatoform Disorder and even normal subjects may show such pattern. It is likely, that broadly different circadian patterns, which reflect broadly different states of physiological activation, can be associated with different mental state phenomena and it is in this sense that these data can contribute a physiological dimension to clinical assessment.

Thus, the adjunct information provided by these data, may contribute significantly to the selection of more effective medication, the evaluation of treatment and the selection of more homogeneous populations in research. If broadly different patterns do reflect broadly different physiological states, it seems reasonable to expect that the qualitative and quantitative variation in circadian heart rate, would have an important bearing on a subject's response to a variety of study measures.

Controlling for the potentially wide variation in 24 hour activity, may be highly relevant in diverse physiological studies and the presented evidence suggests that the monitoring of heart rate in everyday practice can contribute practically useful indices in a variety of clinical applications. For example, the response to different medications may vary significantly depending on the circadian pattern such that information about this aspect can help to select more effective medication.

The examples show that changes in mental state are associated with variation in both the qualitative and quantitative aspects of circadian activity, such that serial recordings can provide practically useful indices of clinical change. Patients can serve as their own control and the changes in serial recordings may provide

more reliable indices of clinical change than those obtained with subjective rating scales.

The present invention includes within its scope adaptations and modifications apparent to one skilled in the art.

5

Dated this ELEVENTH day of APRIL 1997.

HEARTLINK PTY LTD
Applicant

Wray & Associates
Perth, Western Australia
Patent Attorneys for the Applicant

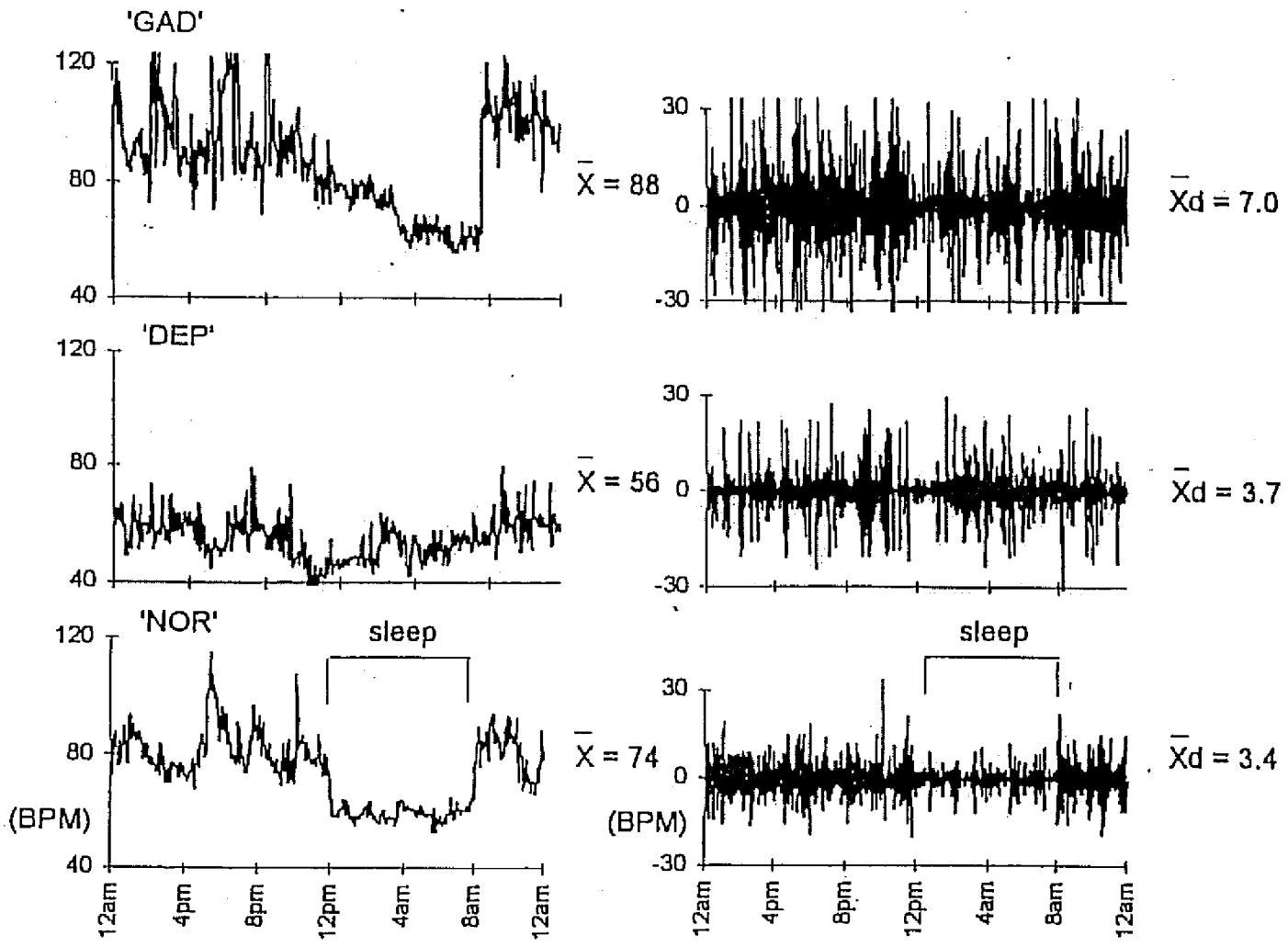
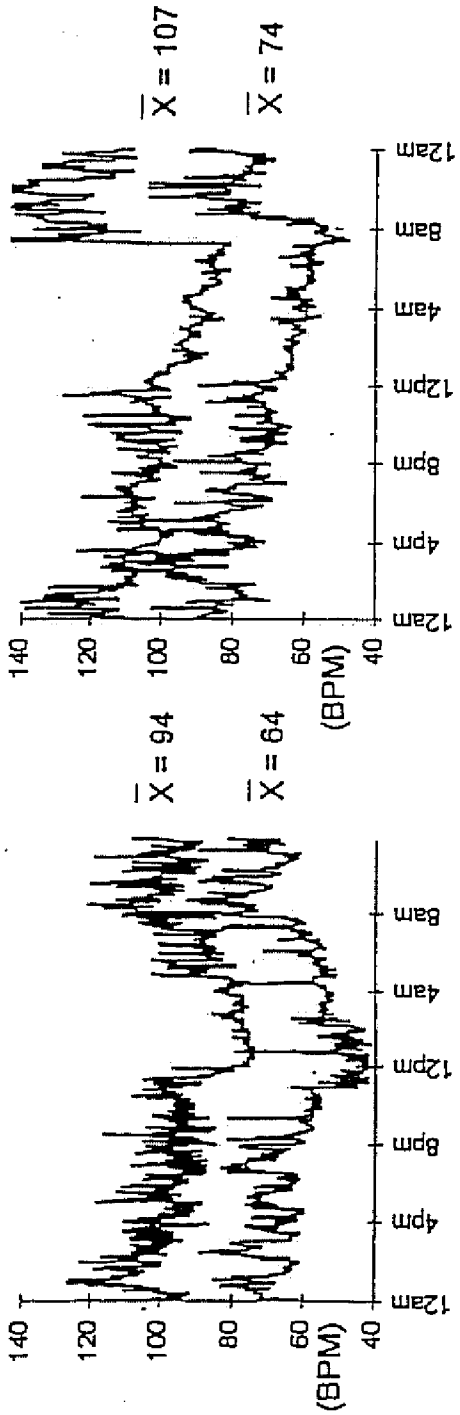


Fig. 1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$\bar{X}$ = 74
$\bar{X}$ = 94
$\bar{X}$ = 64
140
120
100
80
60
40
(BPM)
12am
4am
8am
12pm
4pm
8pm
12am

Fig. 2b

Fig. 2a

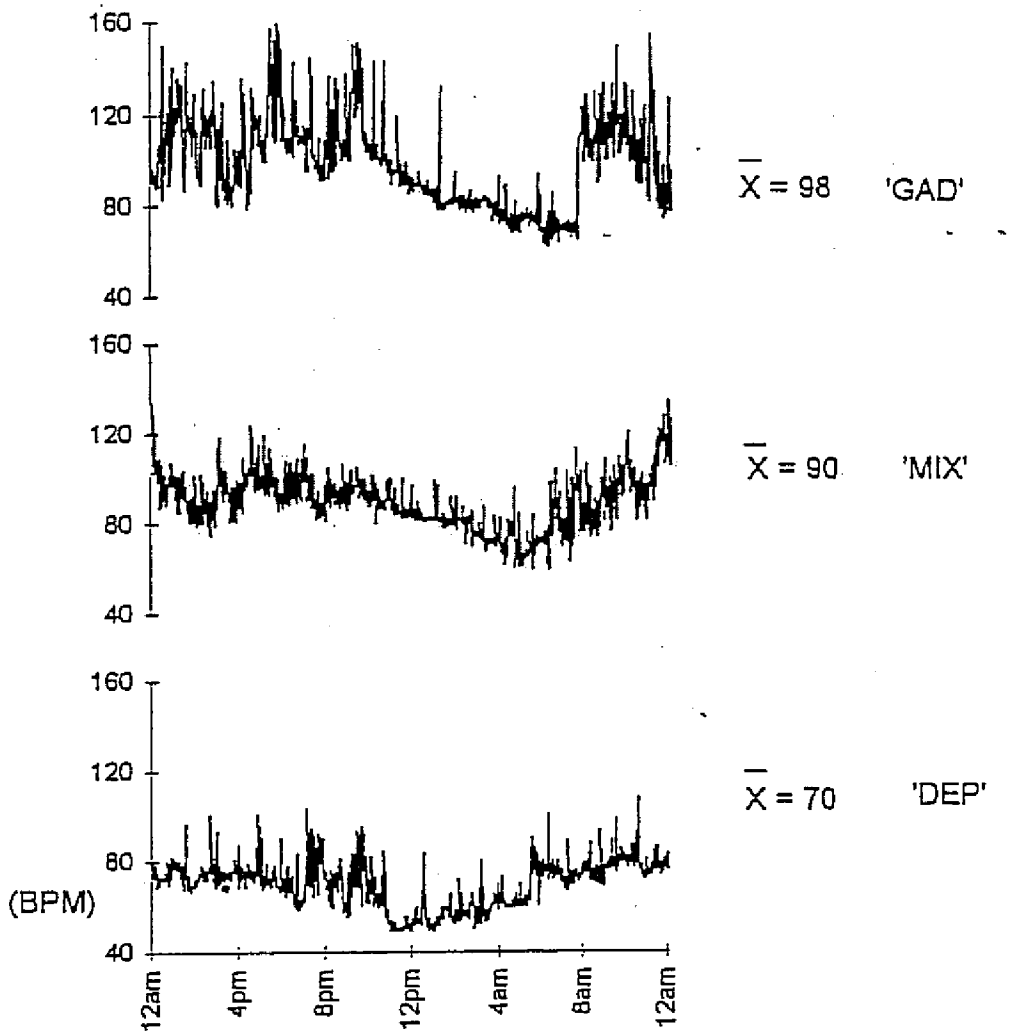
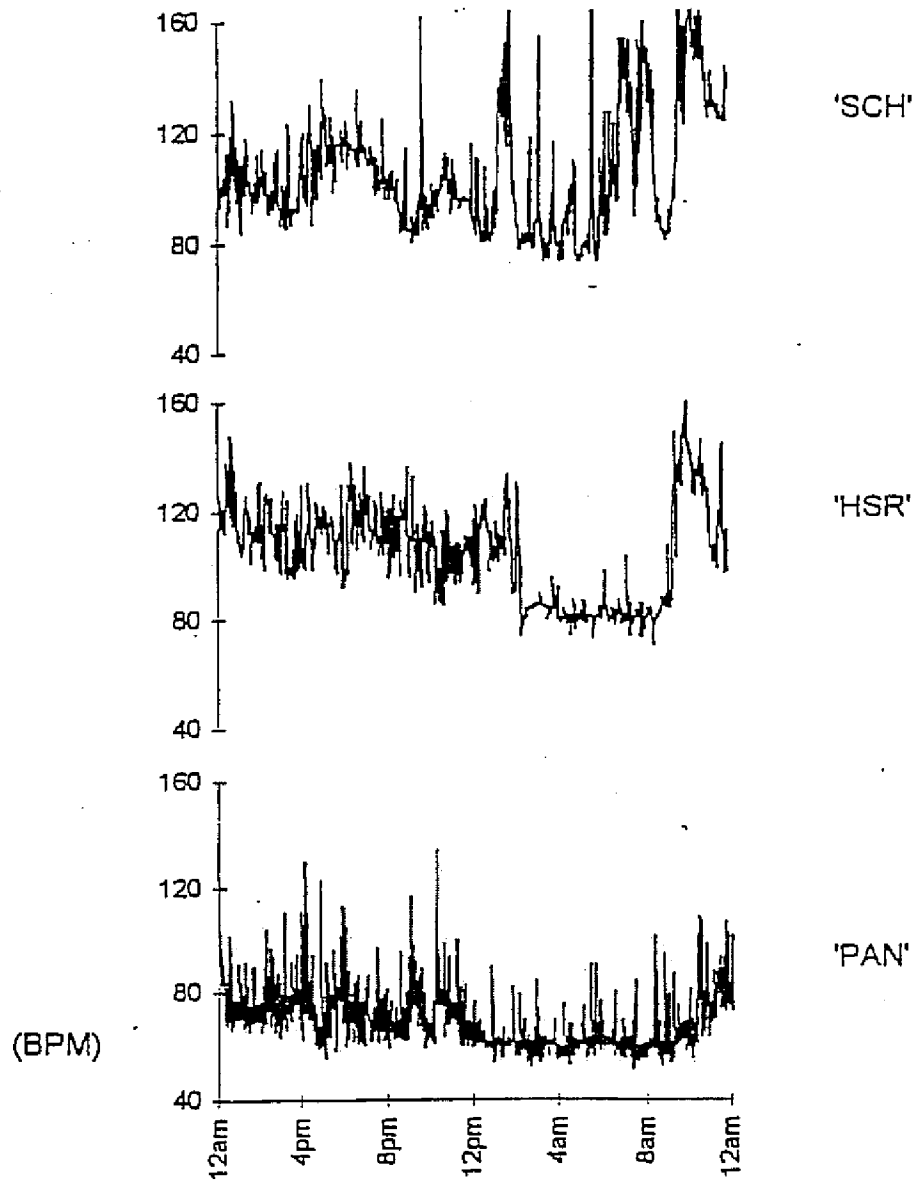

160
120
80
40
$\bar{X}$ = 98 'GAD'
160
120
80
40
$\bar{X}$ = 90 'MIX'
160
120
80
40
$\bar{X}$ = 70 'DEP'
(BPM)
12am
4pm
8pm
12pm
4am
8am
12am

Fig. 3


160
120
80
40
'SCH'
160
120
80
40
'HSR'
160
120
80
40
'PAN'
(BPM)
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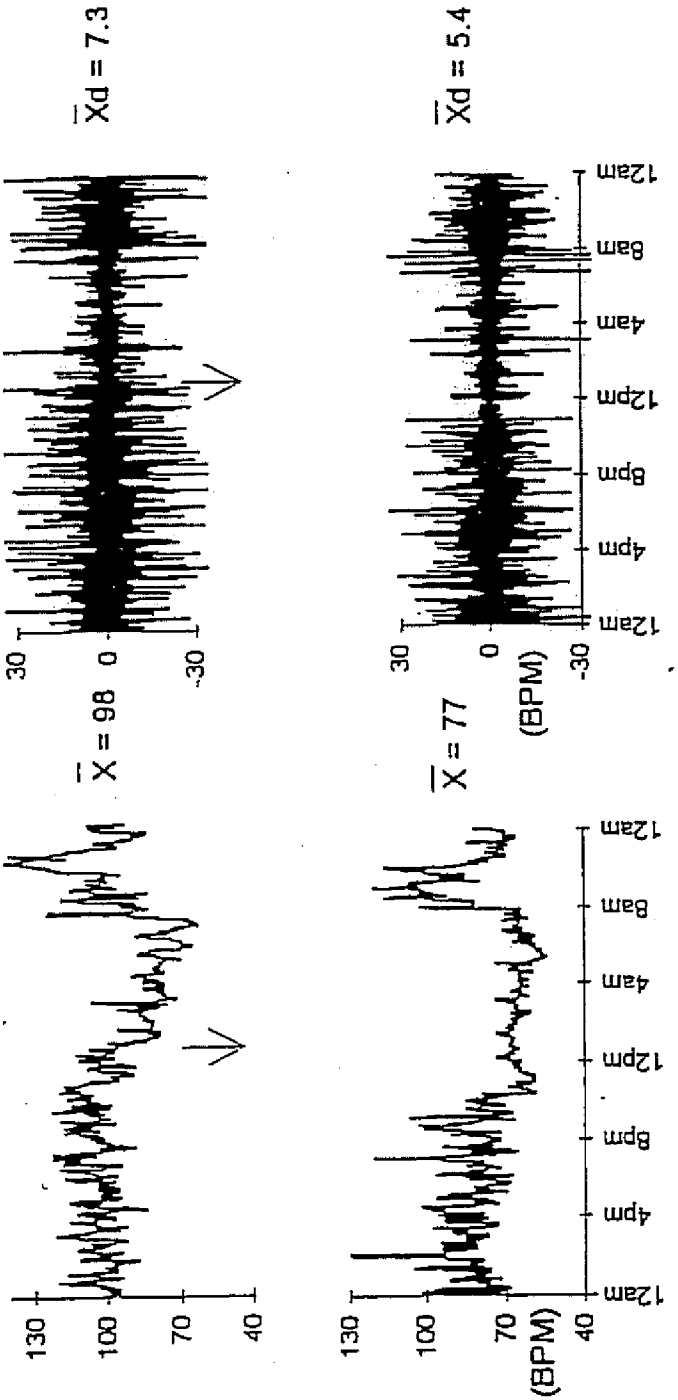
4pm
8pm
12pm
4am
8am
12am

Fig. 4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$\bar{X}$d = 5.4
130
100
70
40
30
0
-30
(BPM)
12am
4am
8am
12pm
4pm
8pm

Fig. 5

diazepam 5mg
160
120
80
40
(BPM)
12am
4am
8am
12pm
4pm
8pm
12am

Fig. 6a.

diazepam 5mg
160
120
80
40
12am
4am
8am
12pm
4pm
8pm
12am

Fig. 6b.

sertraline
160
120
80
40
(BPM)
12am
4am
8am
12pm
4pm
8pm
12am
4am
8am
12pm
4pm
8pm
12am

Fig. 7

MEMORANDUM OF ASSIGNMENT OF INTERNATIONAL PATENT RIGHTS

WHEREAS George Hans Stampfer (the "INVENTOR") has made certain new and useful inventions (the "INVENTIONS") as disclosed in International Application No. PCT/AU98/00252 filed April 14th, 1998, under the Patent Cooperation Treaty (hereinafter the "INTERNATIONAL APPLICATION");

AND, WHEREAS by assignment made effective April 10, 1997, the INVENTOR assigned to **HeartLink Pty. Ltd.**, a corporation organized and subsisting pursuant to the laws of Western Australia and whose principal office or place of business is at Sir Charles Gardner Hospital, Nedlands, Western Australia (hereinafter "ASSIGNOR"), all right, title and interest in and to the said INVENTIONS, including without limitation all right, title and interest in, to and under said INTERNATIONAL APPLICATION;

AND, WHEREAS by a License Agreement dated as of July 1, 1998, the ASSIGNOR granted to **HeartLink NA Patent Corporation**, a corporation organized and subsisting pursuant to the laws of Barbados and whose principal office or place of business is at "Whitepark House", White Park Road, Bridgetown, Barbados, as licensee by way of assignment, a license of certain rights to the INVENTIONS (the "LICENSE");

AND, WHEREAS **HeartLink World Patent Corporation**, a corporation organized and subsisting pursuant to the laws of Barbados and whose principal office or place of business is at "Whitepark House", White Park Road, Bridgetown, Barbados (hereinafter "ASSIGNEE"), is desirous of acquiring and confirming that it has acquired all right, title and interest in and to the said INVENTIONS, including without limitation all right, title and interest in, to and under said INTERNATIONAL APPLICATION, and to the LICENSE;

NOW, THEREFORE, in consideration of Ten Dollars ($10.00) and other good and valuable consideration paid to ASSIGNOR by ASSIGNEE, the receipt and sufficiency of which is hereby acknowledged by ASSIGNOR, ASSIGNOR hereby confirms that it has sold, assigned and transferred, and by these presents does hereby sell, assign and transfer to ASSIGNEE the entire right, title and interest in said INVENTIONS and LICENSE in all countries and other jurisdictions of the world, including without limitation:

(a) all right, title and interest in, to and under said INTERNATIONAL APPLICATION, including without limitation the right to enter the national phase of prosecution in any and all States designated in said INTERNATIONAL APPLICATION, and to do so in its own name wherever such right may be legally exercised, and to prosecute any and all such applications in the national phase (hereinafter "NATIONAL APPLICATIONS");

CERTIFIED TO BE A TRUE COPY THIS 16th
OF January, 2000.

DAVIS & COMPANY

Per: _____

LINDA I. PARSONS
BARRISTER & SOLICITOR
DAVIS & COMPANY
2800 - 666 Burrard Street
Vancouver, B.C. V6C 2Z7
687-9444

(b) the right to file additional patent applications on said INVENTIONS in all countries and other jurisdictions of the world, and to do so in its own name wherever such right may be legally exercised (hereinafter "ADDITIONAL APPLICATIONS");

(c) all right, title and interest in any and all existing or future substitute, divisional, continuation or continuation-in-part patent applications deriving directly or indirectly either in whole or in part from such INTERNATIONAL APPLICATION, any of such NATIONAL APPLICATIONS and any of such ADDITIONAL APPLICATIONS (hereinafter "DERIVATIVE APPLICATIONS");

(d) all right, title and interest in, to and under all patents granted directly or indirectly on or as a result of such INTERNATIONAL APPLICATION, any of such NATIONAL APPLICATIONS, any of such ADDITIONAL APPLICATIONS and any of such DERIVATIVE APPLICATIONS, and any reissues, renewals or extensions thereof;

(e) the right to claim available benefits under the *International Convention For The Protection of Industrial Property*, and any like treaties or laws; and

(f) the benefit of any license relating to the INVENTIONS granted by the ASSIGNOR or its predecessors in title to any person, including the LICENSE;

the same to be owned, held and enjoyed by ASSIGNEE, its successors, assigns and legal representatives, as fully and exclusively as it would have been held and enjoyed by ASSIGNOR had this sale, assignment and transfer not been made.

ASSIGNOR hereby agrees that this assignment shall be binding upon its successors, assigns and legal representatives.

AND ASSIGNOR hereby covenants and agrees to do all such things and to execute or obtain execution without further consideration of such further lawful documents, assurances, applications and other instruments as may be reasonably required to make and prosecute any and all applications on said INVENTIONS, to enforce any and all patents on said INVENTIONS, and to confirm in the ASSIGNEE or its successors and assigns legal title to said INVENTIONS and all patents and applications for patents on said INVENTIONS.

IN WITNESS WHEREOF, ASSIGNOR has caused this Memorandum of Assignment to be executed with effect June 1, 1999.

HeartLink Pty. Ltd.

By: _____ Witness: _____

Name: KEN BEARD

Position: DIRECTOR

TIMOTHY EDWARD COCKS
NOTARY PUBLIC

Date 31st August 1999

Place PERTH

HeartLink World Patent Corporation hereby accepts the foregoing assignment.

By: R. J. Babbick

Name:

Position:

AFFIDAVIT OF EXECUTION

I, KENNETH KESWICK BEARD, whose full post office address is 666 HEDLANDS WESTERN AUSTRALIA, MAKE OATH AND SAY:

1. That I am the DIRECTOR of **HeartLink Pty. Ltd.** one of the parties named in the attached assignment.

2. That I am an authorized signatory of **HeartLink Pty Ltd.** and, in accordance with the constitution and by-laws of the said company, I am authorized to execute, with or without affixing a seal, all instruments binding the company including the attached assignment.

SWORN before me at
PERTH this)
31 day of AUGUST, 1999.)
)
)
)
)

Notary Public in and for the State of Western Australia

My Commission expires PERMANENT

TIMOTHY EDWARD COCKS
NOTARY PUBLIC

VANSOL Library:135642.1

4

MEMORANDUM OF ASSIGNMENT OF NORTH AMERICAN PATENT RIGHTS

WHEREAS George Hans Stampfer (the "INVENTOR") has made certain new and useful inventions (the "INVENTIONS") as disclosed in International Application No. PCT/AU98/00252 filed April 14th, 1998, under the Patent Cooperation Treaty (hereinafter the "INTERNATIONAL APPLICATION");

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AND, WHEREAS **HeartLink NA Patent Corporation**, a corporation organized and subsisting pursuant to the laws of Barbados and whose principal office or place of business is at "Whitepark House", White Park Road, Bridgetown, Barbados (hereinafter "ASSIGNEE"), is desirous of acquiring and confirming that it has acquired all right, title and interest in and to the said INVENTIONS with respect to Canada and the United States (hereinafter "NORTH AMERICA"), including without limitation all right, title and interest in, to and under said INTERNATIONAL APPLICATION with respect to NORTH AMERICA, and to the LICENSE;

NOW, THEREFORE, in consideration of Ten Dollars ($10.00) and other good and valuable consideration paid to ASSIGNOR by ASSIGNEE, the receipt and sufficiency of which is hereby acknowledged by ASSIGNOR, ASSIGNOR hereby confirms that it has sold, assigned and transferred, and by these presents does hereby sell, assign and transfer to ASSIGNEE the entire right, title and interest in said INVENTIONS and LICENSE in NORTH AMERICA, including without limitation:

CERTIFIED TO BE A TRUE COPY THIS 16th
OF February, 2000
DAVIS & COMPANY
Per:

VANSOL Library:135642.1

LINDA I. PARSONS
BARRISTER & SOLICITOR
DAVIS & COMPANY
2800 - 666 Burrard Street
Vancouver, B.C. V6C 2Z7
687-9444

(a) all right, title and interest in, to and under said INTERNATIONAL APPLICATION with respect to NORTH AMERICA, including without limitation the right to enter the national phase of prosecution in NORTH AMERICA, and to do so in its own name wherever such right may be legally exercised, and to prosecute any and all such applications in the national phase in NORTH AMERICA (hereinafter "NATIONAL APPLICATIONS");

(b) the right to file additional patent applications on said INVENTIONS in NORTH AMERICA, and to do so in its own name wherever such right may be legally exercised, and to prosecute any and all such applications in NORTH AMERICA (hereinafter "ADDITIONAL APPLICATIONS");

(c) all right, title and interest in any and all existing or future substitute, divisional, continuation or continuation-in-part patent applications deriving directly or indirectly either in whole or in part from such INTERNATIONAL APPLICATION with respect to NORTH AMERICA, any of such NATIONAL APPLICATIONS and any of such ADDITIONAL APPLICATIONS (hereinafter "DERIVATIVE APPLICATIONS");

(d) all right, title and interest in, to and under all patents granted in Canada or the United States directly or indirectly on or as a result of such INTERNATIONAL APPLICATION, any of such NATIONAL APPLICATIONS, any of such ADDITIONAL APPLICATIONS and any of such DERIVATIVE APPLICATIONS, and any reissues, renewals or extensions thereof;

(e) the right to claim available benefits under the *International Convention For The Protection of Industrial Property*, and any like treaties or laws, in NORTH AMERICA; and

(f) insofar as the same pertains to any right, title or interest in North America, the benefit of any license relating to the INVENTIONS granted by the ASSIGNOR to any person, including without limitation the LICENSE;

the same to be owned, held and enjoyed by ASSIGNEE, its successors, assigns and legal representatives, as fully and exclusively as it would have been held and enjoyed by ASSIGNOR had this sale, assignment and transfer not been made.

ASSIGNOR hereby agrees that this assignment shall be binding upon its successors, assigns and legal representatives.

AND INSOFAR as the same pertains to any right, title or interest in North America, ASSIGNOR hereby covenants and agrees to do all such things and to execute or obtain execution without further consideration of such further lawful documents, assurances, applications and other instruments as

may be reasonably required to make and prosecute any and all applications on said INVENTIONS, to enforce any and all patents on said INVENTIONS, and to confirm in the ASSIGNEE or its successors and assigns legal title to said INVENTIONS and all patents and applications for patents on said INVENTIONS.

IN WITNESS WHEREOF, ASSIGNOR has caused this Memorandum of Assignment to be executed with effect June 1, 1999.

HeartLink World Patent Corporation

By: _____ Witness: _____

Name: R.F. BALDOCK

Position: PRESIDENT

Date 17TH AUGUST 1999

Place VANCOUVER B.C.

LINDA I. PARSONS
BARRISTER & SOLICITOR
DAVIS & COMPANY
2800 - 666 Burrard Street
Vancouver, B.C. V6C 2Z7
687-9444

HeartLink NA Patent Corporation hereby accepts the foregoing assignment.

By: _____

Name:

Position:

AFFIDAVIT OF EXECUTION

I, Robert Baldock, whose full post office address is 715 - 837 West Hastings St. Vanc. B.C. V6C 3N7, MAKE OATH AND SAY:

1. That I am the President of **HeartLink World Patent Corporation**, one of the parties named in the attached assignment.

2. That I am an authorized signatory of **HeartLink World Patent Corporation** and, in accordance with the constitution and by-laws of the said company, I am authorized to execute, with or without affixing a seal, all instruments binding the company including the attached assignment.

SWORN before me at
Vancouver, B.C. this)
17th day of August, 1999.)
)
)
)
)

R. J. Baldock

Notary Public in and for the Province of
British Columbia, Canada

LINDA I. PARSONS
BARRISTER & SOLICITOR
DAVIS & COMPANY
2800 - 666 Burrard Street
Vancouver, B.C. V6C 2Z7
687-9444

HEARTLINK LICENSE AGREEMENT - CANADA

THIS AGREEMENT is made as at the 31st day of December, 1999.

BETWEEN:

HEARTLINK N.A. PATENT CORPORATION, a corporation organized and subsisting pursuant to the laws of Barbados

(hereinafter called "**HLNAP**")

AND:

HEARTLINK CANADA (1999) INC., a corporation organized and subsisting pursuant to the laws of Canada

(hereinafter called "**HCI**")

WHEREAS:

A. A certain invention (the "**Invention**") as to the correlation between circadian heart rate patterns and psychiatric status of a patient as recorded by a monitor of heart rate patterns and analyzed by the HeartLink database was made in the course of research conducted by Dr. Hans Stampfer of HeartLink Pty. Ltd., and is now covered by HLNAP's Patent Rights as defined below;

B. HCI wishes to have the benefit of the HLNAP's Patent Rights in its commercialization of the Invention;

C. HLNAP wishes that HLNAP's Patent Rights be developed and utilized to the fullest extent so that benefits can be enjoyed by the general public.

NOW THEREFORE IN CONSIDERATION of the mutual covenants and agreements herein contained, the parties hereto agree as follows:

ARTICLE 1
INTERPRETATION

DEFINITIONS

1.1 Definitions - In this Agreement, the following terms will have the following meanings unless there is something in the context inconsistent therewith:

(a) "**Audited Net Profits**" means the gross revenues realized (or deemed to be realized) from the sale by HCI or any of its Affiliates of Licensed Product after deducting therefrom such reasonable costs and expenses as would be deductible under Canadian generally accepted accounting principles and practices consistently applied, including, without limitation (all of which have been subjected to audit by qualified licenced auditing firm of Canadian chartered accountants or certified general accountants acceptable to HLNAP):

(i) all overhead expenses, customer credits, refunds, and discounts;

(ii) all sales taxes, license fees and governmental levies of a similar nature; and

(iii) all costs associated with materials, equipment, facilities or clinical testing or other out-of-pocket costs or sub-contract costs;

(b) "**Affiliate**" means an affiliate as defined in the CBCA and includes agents appointed by HCI, joint venture or strategic alliance partners of HCI or any other business arrangement parties approved by HLNAP in respect of HCI's licence rights hereunder;

(c) "**CBCA**" means *Canada Business Corporations Act*, as amended from time to time;

(d) "**Commercialization**" shall have the meaning attributed to it in Section 6.1 hereof;

(e) "**Diagnostic Centre and Database**" means the Diagnostic Centre and Database being developed by HLNAP to be available to licensees under terms and conditions to be determined.

(f) "**Effective Date**" means the date first above written;

(g) "**First Commercial Sale**" means the first sale of any Licensed Product or Licensed Method by HCI following approval of its marketing by the appropriate governmental agency in the Territory;

(h) "**HCI**" means HeartLink Canada (1999) Inc.;

(i) "**HCI Sublicense**" shall have the meaning attributed to it in Section 3.1 hereof;

(j) "**HLNAP**" means HeartLink N.A. Patent Corporation, an International Business Corporation under the laws of Barbados;

(k) "**HLNAP's Patent Rights**" means patent rights to any subject matter claimed in or covered by any of the patent applications listed on Appendix A attached to this Agreement and held by HLNAP; any continuing applications thereof; patents issuing on these applications, including reissues and re-examinations; and any corresponding foreign patents or patent

applications; and any improvements thereof; all of which will be automatically incorporated in and added to Appendix A and made a part of this Agreement;

(l) **"License"** shall have the meaning attributed to it in Section 2.1 hereof;

(m) **"Licensed Method"** means any process or method which is covered by HLNAP's Patent Rights or whose use or practice would constitute an infringement of any claim within HLNAP's Patent Rights;

(n) **"Licensed Product"** means any article, composition, apparatus, substance, chemical, or any other material covered by HLNAP's Patent Rights or whose manufacture, use or sale would constitute an infringement of any claim within HLNAP's Patent Rights, or any service, article, composition, apparatus, chemical, substance, or any other material made, used or sold by utilizing or practicing a Licensed Method;

(o) **"Royalties"** shall have the meaning attributed to it in Section 5.1 hereof;

(p) **"Sublicensee"** means an Affiliate of HCI, who has entered into a sublicense agreement pursuant to Section 3.1;

(q) **"Sublicensing Income"** means income in the Territory received by HCI as a result of an HCI Sublicense; and

(r) **"Territory"** means Canada.

ARTICLE 2
GRANT

2.1 Exclusive License - HLNAP grants to HCI an exclusive license (the "**License**") under HLNAP's Patent Rights in the Territory to make, have made, use, sell, offer to sell, distribute, or otherwise dispose of or deal with the Licensed Products and to practice Licensed Methods. This includes access to and use of the Diagnostic Centre and Database under terms yet to be determined.

ARTICLE 3
SUBLICENSES

3.1 Exclusive Sublicense - HLNAP grants HCI the right to issue an exclusive sublicense or assignment (the "HCI Sublicense") to an HCI Affiliate ("**Sublicensee**") in the Territory.

3.2 Sublicensing Income - HCI shall charge its Sublicensee a Royalty on the same basis as HLNAP charges HCI Royalty under Article 5 and the net amount so charged and received by HCI shall be remitted by HCI to HLNAP concurrently with any other Royalties.

3.3 Copy of HCI Sublicense - HCI must provide to HLNAP a copy of all HCI Sublicenses.

3.4 Assignment of HCI Sublicense - If this Agreement is terminated for any reason (excluding the expiration of the term of this Agreement), the HCI Sublicense will be assigned by HCI to HLNAP.

ARTICLE 4
CONSIDERATION

4.1 Consideration - In consideration for the license, HCI will pay to HLNAP $10.00 forthwith upon the Effective Date.

ARTICLE 5
ROYALTIES

5.1 Royalty - HLNAP shall be paid for the sale of Licensed Products in the Territory an earned royalty (the "**Royalties**") of 10% of Audited Net Profits, calculated from the date of the First Commercial Sale.

5.2 Payment of Royalties - Royalties owed to HLNAP shall be paid on a quarterly basis in Cdn. funds, payable within 90 days of each calendar quarter.

5.3 Reduction of Royalty - The Royalties payable hereunder may be reduced by an amount equal to damages resulting from patent infringement, if any, payable to third parties as a result of sale of Licensed Products.

ARTICLE 6
DILIGENCE

6.1 Commercialization - Subject to HLNAP fulfilling its obligations under paragraph 6.4 hereof, upon the execution of this Agreement, HCI shall diligently proceed with the development and sale ("**Commercialization**") of Licensed Products, and must earnestly and diligently endeavour to market them within a reasonable time after execution of this Agreement, and in quantities sufficient to meet the market demands for them.

6.2 Commercialization Approvals - HCI must endeavour to obtain all necessary governmental approvals for the Commercialization of Licensed Products in the Territory.

6.3 Commercialization Discretion - HCI and, upon the granting of the HCI Sublicense, the Sublicensee, subject to the terms of the sublicense, shall have the sole discretion for making all decisions as to how to commercialize any Licensed Product, provided any marketing arrangements,

options or rights granted prior to the date of this Agreement by HLNAP or any of its Affiliates for the purpose of marketing, will be adhered to and honoured, if lawful in the Territory and a copy of such arrangements, options or rights is provided to HCI prior to its execution of this Agreement.

6.4 Monitors and Diagnostic Services - HLNAP shall provide monitors and diagnostic services to HCI or the HCI Affiliate, and technical support for all Licensed Product and Licensed Method on an "as needed" basis and on terms no less favourable than are or would be granted by HLNAP to any other third party. HCI or the HCI Affiliate shall pay HLNAP a fee for such service as reasonably set down from time to time by HLNAP.

6.5 Delivery of Monitors, Data, Reports and Assistance - Upon the request of HCI and/or the HCI Affiliate, HLNAP shall promptly deliver the required number of monitors, and HCI and/or the HCI Affiliate shall reimburse HLNAP for its cost of the same (including delivery). In addition, HLNAP shall provide such data, reports and technical or professional assistance as HCI and/or the HCI Affiliate may reasonably require in order to Commercialize the Licensed Product in the Territory, and provide HCI with all reasonable assistance in this regard.

ARTICLE 7
PATENT FILING, PROSECUTION AND MAINTENANCE

7.1 Patent Obligations - HLNAP will, at its sole expense, file, prosecute and maintain the HLNAP's Patent Rights and any applications comprising or improvements upon HLNAP's Patent Rights. These patents will be held in the name of HLNAP and shall be included within the scope of this License at no additional cost to HCI. HLNAP will provide HCI with copies of each patent application and any correspondence in respect to the same.

7.2 Abandonment - HLNAP will use its best efforts to not allow any of HLNAP's Patent Rights for which HCI is licensed to lapse or become abandoned without notice to HCI 180 days prior to the proposed abandonment. Within 60 days after receipt of the notice, HCI must, in writing, either:

(a) concur in the abandonment; or

(b) elect to assume responsibility for the prosecution and maintenance of all HLNAP's Patent Rights in which event, HLNAP will assign to HCI, without cost, all the HLNAP's Patent Rights.

ARTICLE 8
PATENT INFRINGEMENT

8.1 Patent Infringement - In the event that either HLNAP or HCI learns of the substantial infringement of HLNAP's Patent Rights, that party will inform the other party in writing and provide the other party with reasonable evidence of the infringement. Neither party will notify the third party

of the infringement of HLNAP's Patent Rights without first obtaining consent of the other party, which consent must not be reasonably denied or delayed. Both parties will use their best efforts to cooperate to terminate the infringement by third parties without litigation and at the reasonable cost of HLNAP.

8.2 Legal Action - HCI may request that HLNAP take legal action against the infringement of HLNAP's Patent Rights. This request must be in writing and must be include reasonable evidence of the infringement. If the infringing activity has not been abated within 30 days following the effective date of the request, HLNAP has the right to:

(a) commence suit on its own account; or

(b) refuse to participate in the suit.

HLNAP must give notice of its election in writing to HCI by the end of the 60th day after receiving notice of the request from HCI. HCI may thereafter bring suit in their own name or in the name of HLNAP for patent infringement if and only if HLNAP elected not to commence suit or unreasonably delayed or failed to prosecute such suit and if the infringement occurred during the life of the Agreement and in the Territory.

8.3 Cooperation in Litigation Proceedings - A party must cooperate with the other in litigation proceedings instituted under this Article but at the expense of the party who brings the suit. The litigation will be controlled by the party bringing the suit, although HLNAP may, at its cost, be represented by counsel of its choice if HLNAP joins a suit brought by HCI, and HCI may, at its cost, be represented by counsel of its choice if HCI joins the suit brought by HLNAP. Counsel retained by the party bringing the suit will consult and confer with counsel retained by the party not bringing the suit, but the final decisions will be made by counsel for the party bringing and having ultimate conduct of the litigation.

ARTICLE 9
PROGRESS REPORTS

9.1 Progress Reports - Beginning six months after the Effective Date, HCI must submit to HLNAP semi-annual progress reports covering HCI's activities related to the Commercialization of the Licensed Product in a report format mutually agreed upon by both parties.

ARTICLE 10
BOOKS AND RECORDS

10.1 Books and Records - HCI must keep accurate books and records in respect to the sale of all Licensed Product. HCI must preserve these books and records for at least two years from the date of the most recent Royalty payment to which they pertain.

10.2 Inspection of Books and Records - HLNAP's representatives or agents are entitled to inspect these books and records upon 24 hours' prior written notice and at reasonable business hours, provided that this right to inspect only includes the prior 12 months of books and records of HCI (calculated from the time of request). HCI will pay the fees and expenses of these inspections. If an error of more than 5% of the total annual Royalties is discovered and the error results in higher Royalties being payable by HCI, then HCI will pay the reasonable fees and expenses of these inspections.

ARTICLE 11
LIFE OF THE AGREEMENT

11.1 Life of the Agreement - Unless otherwise terminated by operation of law or acts of the parties in accordance with the terms of this Agreement, this Agreement is in force from the Effective Date recited on page one and remains in effect for the lesser of the life of the HLNAP's Patent Rights and five (5) years from the Effective Date, provided that if HCI duly pays the Royalty and performs the covenants herein contained, HLNAP will, at the option of HCI, grant successive renewals of this license for two further five (5) year periods on terms to be negotiated. At the commencement time for each of the renewals HCI must have paid all outstanding Royalties and performed the covenants herein contained. These terms will be no less favourable to HLNAP than those contained in this Agreement. If the parties cannot agree on the terms of renewal, the matter shall be determined by arbitration by a sole arbitrator appointed in accordance with Article 25.

11.2 No Further Rights Upon Termination - Upon termination of this Agreement, HCI will have no further right to make, have made, use or sell any Licensed Product during the life of HLNAP's Patent Rights.

ARTICLE 12
TERMINATION BY HLNAP

12.1 Termination by HLNAP - If HCI violates or fails to perform any material term or covenant of this Agreement, then HLNAP may give written notice of the default ("Notice of Default") to HCI. If HCI does not repair the default or refer the alleged violation or failure to arbitration pursuant to paragraph 25 hereof within 90 days after the effective date of the Notice of Default as provided in Article 19, then HLNAP has the right to terminate this Agreement and the License by a second written notice ("Notice of Termination") to HCI. If HLNAP sends a Notice of Termination to HCI, then this Agreement automatically terminates on the effective date of the Notice of Termination. Termination does not relieve HCI of its obligation to pay any Royalties owing at the time of termination, and does not impair any accrued right of HLNAP.

ARTICLE 13
TERMINATION BY HCI

13.1 Termination by HCI - HCI has the right at any time to terminate this Agreement in whole or with respect to any portion of HLNAP's Patent Rights by giving written notice to HLNAP. The notice of termination will be subject to Article 19 (Notices) and will be effective 90 days after the effective date of the notice. Any termination in accordance with this paragraph does not relieve HCI of any obligation or liability accrued prior to termination.

ARTICLE 14
DISPOSITION OF LICENSED PRODUCT ON HAND UPON TERMINATION

14.1 Disposal Upon Termination - Upon termination of this Agreement (excluding the expiration of the term of this Agreement), HCI will have the right to dispose of all Licensed Product on hand within a period of six months and otherwise HLNAP will purchase such Licenced Products from HCI, at no less than HCI's cost.

ARTICLE 15
PATENT MARKING

15.1 Marking Licensed Product - HCI must mark all Licensed Product made, used or sold under the terms of this Agreement, or their containers, in accordance with the applicable patent marking laws in the Territory.

ARTICLE 16
USE OF NAMES AND TRADEMARKS

16.1 Consent to Use - Neither party is permitted to use any name, trade name, trademark or other designation of the other party or its employees (including contraction, abbreviation or simulation of any of the foregoing) in advertising, publicity or other promotional activity, without the prior written consent of the other party, not to be unreasonably withheld.

ARTICLE 17
LIMITED WARRANTY

17.1 Right to Grant License - HLNAP warrants that it has the lawful right to grant this license to HCI on the terms of this Agreement.

17.2 No Warranty of Merchantability or Fitness for Purpose - This license and the associated Invention are provided without warranty of merchantability or fitness for a particular purpose or any

other warranty, express or implied. HLNAP makes no representation or warranty that any Licensed Product will not infringe any patent or other proprietary right.

17.3 Title and Infringement - HLNAP is the exclusive holder of HLNAP's Patent Rights and has not granted to any third party, other than HCI and HCI Affiliates, the right to use, license or otherwise participate in HLNAP's Patent Rights in the Territory. To the knowledge of HLNAP, it has not been served with any notice of injunction, judgment, order, decree, ruling , charge or claim related to HLNAP's Patent Rights and to its knowledge the HLNAP's Patent Rights are not subject to any claims of infringement or otherwise by third parties nor are there any events which might constitute material breaches or defaults of HLNAP's Patent Rights.

17.4 No Liability for Incidental, Special or Consequential Damages - In no event will either party be liable to the other party for any incidental, special or consequential damages resulting from exercise of this License or the use of the invention or Licensed Product or the use of the practice of Licensed Method.

17.5 Limitations - Except as may be provided in Section 17.3, nothing in this Agreement will be construed as:

(a) a warranty or representation by HLNAP as to the validity or scope of any of HLNAP's Patent Rights;

(b) a warranty or representation that anything made, used, sold or otherwise disposed of under any license granted in this Agreement is or will be free from infringement of patents of third parties; and

(c) an obligation to bring or prosecute actions or suits against third parties for patent infringement except as provided in Article 8 (Patent Infringement).

17.6 Notice from HLNAP in Certain Events - Notwithstanding Section 17.5, HLNAP agrees to provide notice to HCI forthwith upon the happening of any of the following events of which it becomes aware:

(a) if the performance of its obligations under this Agreement at any time conflicts with and will result in a breach of or default under any of the terms, conditions and provisions of any applicable law or regulation or judgment, injunction, order, decree or other instrument binding on HLNAP or HCI, or any Sublicensee, employee, director, officer, agent, successor or assign of HCI; or

(b) there are any proceedings before any court, administrative tribunal or other authority commenced, pending or threatened which would challenge the validity of HLNAP's Patent Rights or assert a right or interest of a third party in HLNAP's Patent Rights.

17.7 HLNAP Indemnity - HLNAP hereby agreed to indemnity and hold harmless and defend HCI, its officers, employees and agents, the inventors of the patents and other patent applications in HLNAP's Patent Rights, and their respective employers, from and against any and all liability, claims, suits, losses, damages, costs, fees and expenses resulting from or arising out of exercise of any breach of its warranty under Section 17.3. The amount of the indemnity will be limited to the amount of Royalties paid by HCI to HLNAP under this Agreement.

ARTICLE 18
INDEMNIFICATION

18.1 Indemnity by HCI - Subject to Section 17.6, HCI must indemnify, hold harmless and defend HLNAP, its officers, employees and agents, the inventors of the patents and other patent applications in HLNAP's Patent Rights, and their respective employers, from and against any and all liability, claims, suits, losses, damages, costs, fees and expenses resulting from or arising out of exercise of this License.

18.2 Insurance - HCI, at its sole cost and expense, must insure its activities in connection with the work under this Agreement and obtain, keep in force and maintain General Liability Insurance with such limits as HLNAP may reasonably request, provided the amount of such insurance is reasonable and such insurance is generally offered by the insurance industry.

18.3 Liability Not Limited by Insurance - HCI expressly understands, however, that the coverage and limits in paragraph 18.2 do not in any way limit HCI's liability. HCI must furnish HLNAP with certificates of insurance evidencing compliance with all requirements. HCI is not required to insure its activities pertaining to the products' liability risk until it begins to use Licensed Products.

18.4 Right to Set-Off - Without in any way limiting or restricting any rights or remedies available to HCI pursuant to this Agreement, at law or in equity, in the event of breach of this Agreement by HLNAP, HCI shall be entitled to set off against Royalties and other monies payable to HLNAP pursuant to this Agreement any and all liability, claims, suits, losses, damages, costs, fees and expenses resulting from or arising out of such breach.

ARTICLE 19
NOTICES

19.1 Notices - Any notice or payment required to be given to either party must be sent to the respective address given below and is effective:

(a) on the date of delivery if delivered in person, or

(b) five days after mailing by first class certified mail, postage paid.

For HLNAP: 715 – 837 West Hastings Street
Vancouver, British Columbia V6C 3N6

For HCI: 715 – 837 West Hastings Street
Vancouver, British Columbia V6C 3N6

Either party may change its designated address by written notice.

ARTICLE 20
ASSIGNABILITY

20.1 Assignments - This Agreement is binding upon and inures to the benefit of HLNAP, HCI, their successors and assigns. HLNAP acknowledges that HCI may assign its rights under this Agreement and grant a Sublicense to an HCI Affiliate, and HLNAP hereby consents to the same.

ARTICLE 21
WAIVER

21.1 No Waiver - The waiver of any breach of any term of this Agreement does not waive any other breach of that or any other term.

ARTICLE 22
FAILURE TO PERFORM

22.1 Right to Costs - If either party takes legal action against the other because of a failure of performance due under this Agreement, then the prevailing party is entitled to reasonable solicitor's fees in addition to costs and necessary disbursements.

ARTICLE 23
GOVERNING LAWS

23.1 Governing Laws - This Agreement is to be interpreted and construed in accordance with the laws of British Columbia and the laws of Canada applicable then, but the scope and validity of any patent or patent application will be governed by the applicable laws of the country of the patent or patent application.

ARTICLE 24
FORCE MAJEURE

24.1 Force Majeure - The parties will be excused from any performance required under this Agreement if performance is impossible or unfeasible due to any catastrophe or other major event beyond their reasonable control, including war, riot or insurrection; laws, proclamations, edicts, ordinances or regulations; strikes, lockouts or other serious labor disputes; and floods, fires, explosions or other natural disasters. When such events abate, the parties' respective obligations will resume.

ARTICLE 25
ARBITRATION

25.1 Arbitration - At the request of either party, any controversy or claim arising out of or relating to the provisions of this Agreement will be settled by arbitration by a sole arbitrator conducted in Vancouver, British Columbia, at the British Columbia International Commercial Arbitration Centre in accordance with the provisions of the International Commercial Arbitration Act of the Province of British Columbia. Judgment upon the award rendered by the Arbitrator will be binding on the parties and may be entered by either party in the court or forum, state or federal, having jurisdiction.

ARTICLE 26
CONFIDENTIALITY

26.1 Confidentiality Obligations - If either party discloses confidential information to the other party, the disclosing party will designate this information as confidential by appropriate legend or instruction, and the receiving party will:

(a) use the same degree of care to maintain the secrecy of the confidential information as it uses to maintain the secrecy of its own information of like kind; and

(b) use the confidential information only to accomplish the purposes of this Agreement.

26.2 Disclosure - Neither party will disclose confidential information received from the other party except to its employees, customers (including Sublicensees), distributors and other agents who are bound to it by similar obligations of confidence and only as required to accomplish the purposes of this Agreement.

26.3 Exceptions to Confidentiality Obligations - Neither party will have any confidentiality obligations with respect to the confidential information belonging to or disclosed by the other party that:

(a) the receiving party can demonstrate by written records was previously known to it;

(b) the receiving party lawfully obtained from sources under no obligation of confidentiality;

(c) is or becomes publicly available other than through an act or omission of the receiving party or any of its employees (such as any patent applications); and

(d) is required to be disclosed under a requirement of law.

26.4 Term of Confidentiality Obligations - The provisions of this Article 26 will continue in effect for three years after expiration or termination of this Agreement.

ARTICLE 27
CONFIDENTIALITY OF THIS AGREEMENT

27.1 Restrictions on Disclosure of this Agreement - Each party will not, without the prior written consent of the other party, disclose the contents of this Agreement to any third party, other than regulatory authorities (if required to do so), attorneys, accountants and consultants required in respect of this Agreement, and, in the case of HCI, Sublicensees and prospective Sublicensees, providing that in each such case the party receiving information relating to this Agreement shall have first agreed to maintain the confidentiality of information disclosed.

27.2 Public Disclosure Obligations - Each party acknowledges that it may be in the interest of the other party to distribute periodic informational releases and announcements to the news media that relate to this Agreement. Each of the parties agree not to release such materials without first sharing a draft of the release with the other party and receiving the prior written approval of the other party, such approval not to be unreasonably withheld or delayed. Should the party receiving a draft press release reject its public disclosure, the parties shall discuss the reasons for the rejection and make every effort to redraft the release in a form acceptable to both parties, provided that the above shall not apply to a particular situation if a party is advised by its legal counsel that certain disclosure or announcements, which the other party will not consent to after reasonable notice and attempts to redraft, are required to be made by applicable laws, stock exchange rules or policies of regulatory agencies or authorities having jurisdiction.

ARTICLE 28
MISCELLANEOUS

28.1 Headings - The headings of this Agreement are inserted for convenience of reference only and are not intended to be party of, or to affect the meaning or interpretation of, this Agreement.

28.2 Effective Date - This Agreement is not binding upon the parties until it has been signed below on behalf of each party, in which event it becomes effective as of the date recited on page one.

28.3 Amendments and Modifications - No amendment or modification of this Agreement will be valid or binding upon the parties unless made in writing and signed by each party.

28.4 Entire Agreement - Subject to Section 6.3, this Agreement embodies the entire understanding of the parties and supersedes all previous communication, representations or understandings, either oral or written, between the parties relating to the subject matter hereof including, without limitation, the Agreement between the parties dated as of June 9, 1999.

28.5 Severability - If any part of this Agreement is for any reason found to be unenforceable, all other parts nevertheless remain enforceable as long as a party's rights under this Agreement are not materially affected. In lieu of the unenforceable provision, the parties will substitute or add as part of this Agreement a provision that will be as similar as possible in economic and business objectives as was intended by the unenforceable provision.

28.6 Counterparts and Facsimile Copies - This Agreement may be executed in several counterparts, each of which when so executed shall be deemed to be an original and such counterparts shall constitute one and the same instrument and notwithstanding the date of execution shall be deemed to bear date as of the date of this Agreement. A facsimile transcribed copy of this Agreement signed by a party in counterpart or otherwise, shall be deemed to be and to constitute a properly executed, delivered and binding document of the party so signing, notwithstanding any variation in the dates of execution.

Both HCI and HLNAP have executed this Agreement in duplicate originals by their authorized officers on the dates written below:

HEARTLINK CANADA (1999) INC.

By: R.F. Baldock
(Authorized Signatory)

Name: R.F. BALDOCK

Title: PRESIDENT

Date: 2/17/2000

HEARTLINK N.A. PATENT CORPORATION

By: R.F. Baldock
(Authorized Signatory)

Name: R.F. BALDOCK

Title: PRESIDENT

Date: 2/17/2000

APPENDIX "A"

1 Australian patent applications PO6166 and 68141/98;

2 International patent application PCT/AU98/00252 (the designated inventor for US applications is shown as Stamfer (without the "p");

3 Canadian patent application number 2,284,553; and

4 Any equivalent US patent application.