Medication Adherence

University of Wisconsin – Madison College of Engineering – Biomedical Engineering BME 400 December 13, 2006

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Client: Timothy Juergens, M.D. UW/VA Hospitals Geriatric psychiatrist/sleep specialist

Advisor:

William Murphy Department of Biomedical Engineering University of Wisconsin – Madison Our client would like to monitor his patients' medication adherence. He would prefer to have a device that can be attached to a standard medication box that allows his patients to take pills up to four times a day. This device would record the time and date of when a specific compartment is accessed by the patient. This log file could be exported to a computer to be read by the client. He can then review the data with the patient in hopes of ensuring proper adherence. Future work includes adding an alarm to the unit to monitor how this reminder would affect the patient's routine of taking medications on time. We have purchased a new medication box that attaches to a circuit powered by a Texas Instruments microcontroller. This circuit is a prototype that will be replaced by a smaller and cheaper unit for research purposes.

Problem Statement:

Dr. Juergens would like us to construct a device that has the ability to record time and date information during daily operation of a patient's standard medication box. In addition, a stationary alarm should be attached in order to alert the user to take their medication at a certain time. This information should be easily accessed and read on a computer for the client to discuss with the patient, in efforts to ensure proper adherence.

Background – Motivation & History:

A number of resources were provided by our client for us to analyze. After further research it became quite clear that many adults do not take their medications correctly. In order for the pills, prescribed by our client, to serve their purpose, the proper amount must be taken at the correct time of day. Unfortunately, this improper adherence causes numerous deaths every year (Osterberg & Blaschke, 2005).

An article in *The New England Journal of Medicine* indicates that non-adherence adds almost \$100 billion to current hospital admissions. Patients often lie to their physicians in order to be perceived as an 'ideal patient.' This has a negative effect in many ways on both the patient and the physician. Seventy-five percent of patients simply

forget to take their pills while others do not feel that it is necessary to take the medication (Osterberg & Blaschke, 2005). Research is currently being conducted to develop a better understanding of the long-term results of non-compliance. In extreme cases, group intervention is necessary, but a reliable recording system could eliminate the need for large confrontation. Unfortunately, many physicians lack a reliable method of monitoring compliance. Our client would like to study his patients over time and see how many follow instructions carefully. By using a logging system to see when certain medications were accessed, Dr. Juergens can note whether or not his patients are following the recommended medication regimen. He can then discuss privately with the patient what can be done in order to improve their adherence.

The *Journal of Clinical Pharmacy and Therapeutics* featured a study focused on improving compliance in stages such as depression. Many studies were completed and it was quite clear that the rate of medication adherence is directly proportional to the patient's knowledge of their medication regimen (Bollina et al., 2006). Our client would like to monitor his patients with an electronic device that is safe to use in the home. The primary goals of this project are to improve patient adherence and to keep hospital admissions and costs to a minimum while learning more about why non-adherence exists.

Forgetfulness accounts for almost 30% of the reason that geriatric patients do not take their pills on time. To prevent such a large inaccuracy, a simple alarm can be implemented to assist the patient with taking medications appropriately and timely. Recently, alarms have been incorporated into common consumer electronics such as cell phones and wristwatches to fit a patient's medication regimen and individual lifestyle.

There are two current solutions to problems similar to the one proposed by Dr. Juergens. One solution is the Medication Event Monitoring System (MEMS). A MEMS system is a single vial which contains a single type of medication. When the patient opens the vial, the event is recorded to a micro-electronic circuit. The data is transferred to a computer and the time stamps can then be read by a professional. Unfortunately, because this design is only one vial for one medication type, it would not be satisfactory for Dr. Juergens. Our client requires a medication box capable of holding 28 separate dosages. To satisfy the client's requirements, each patient would need 28 vials; the number of vials would be confusing to geriatric patients.



Figure 1. Medication Event Monitoring System records when a single vial is accessed by a patient.

The other current solution is the E-Pill MD. 2, an automatic medication dispenser, monitors when a pill is dispensed. The MD.2 is about the size of an average coffee maker and stores three to four weeks of medication at a time. A built-in alarm reminds the patient to take their medicine through visual or auditory cues. The data is sent to a support center in a hospital for physician monitoring via an internet connection. This ensures that the data is sent immediately to the proper medical professionals, but it also means that the patient must pay for an internet connection, as well as a monthly fee for the monitoring services. Both of these fees add significant monthly expenditures to patients who are already living on limited finances. The device itself costs approximately \$900, which is also above the price range of many geriatric patients.



Figure 2. E-Pill MD.2 dispenses and records patient medications. Data can be sent to a doctor over the internet.

Design Specifications

Dr. Juergens set out a specific set of details that the design should follow. These major considerations need to be accounted for to ensure the design fulfills all of the necessary tasks without any unnecessary characteristics. The device should accurately obtain the data regarding the patient's adherence to their medication regimen. The final design should not alter the recorded data in any way. The final design should be lightweight and durable so that an elderly patient has no difficulty using the device and can use it as a normal pill box. Similarly, the device should not look fragile to ensure that the patient is willing to use the device and is not deterred by the thought of possibly breaking the apparatus. Cleaning the product will not damage the device. The patient should be alerted by an alarm on the pill box, either by vibration or auditory cues, to take their medication. In total, the device should cost no more than \$500 in its prototype stage, but the final production device should not exceed \$300. Finally, if the design uses batteries, the device should not consume large amounts of power to ensure that the user does not need to change batteries often. This should only need to be done occasionally by the pharmacist. To see the full list of design specifications, see the Product Design Specification in Appendix A.

Alternative Designs

While brainstorming for potential designs, many ideas were considered. The first idea was to use piezoelectric sensors under each compartment to determine when pills were removed from the box. The change in weight would be detected by the sensor and a signal will be sent to a microcontroller to record a time-stamp. This time stamp can then be downloaded to a computer. The piezoelectric sensors offer sufficient sensitivity, but the pills would move around each compartment too often, which would cause false readings. If the patients turned the pill box upside down to remove pills, the force on each of the sensors would change regardless of whether or not it is the compartment being emptied, causing multiple false readings in the box.

Another potential design involved a single door over the top of the entire 7x4 pill box. The user would have to open the large door to access the individual compartments containing the pills. This would mean that the doctor would be able to determine when the large door was opened, but not necessarily be able to tell if any individual doors were open, much less, which one in particular. We would like to be able to determine which specific compartment was opened by the patient.

The third possible design involves a photometer in each compartment. The photometer would shine light through each compartment; when pills are present, they would block the light from reaching the sensor. Once they are removed from the container, the light would reach the sensor and a signal would be sent to the microcontroller, which would record a time stamp. Unfortunately, each photometer costs about \$400, and there are 28 compartments in each pill box. As a result, the materials for the final product would cost \$11,200, which is significantly over the \$500 limit. Also, the

size of each photometer would cause the pill box to be drastically oversized for the average patient.

Our fourth potential design was a precise measurement device which uses a circuit to determine when each compartment is opened. The design would use a standard 7x4 pill box with a switch in each compartment compiled into a switch matrix. A microcontroller collects data from each compartment when it is opened and then sends the data to a computer via a parallel port. The circuitry would be hidden beneath the pill box so the user is not able to see it during normal use, to ensure that the patient is not intimidated by the device. The only visible sign of circuitry would be the connector for the parallel port. This design fulfills the vast majority of the client's requirements.

To determine which design to pursue, a design matrix was used. From general brainstorming, it was determined that the piezoelectric design, the single door box, and the photometer design would not be able to be used as they did not fulfill enough of the client specifications. We completed a design matrix with the precise measurement device, as well as the two current designs: the MEMS and the E-Pill MD. 2. The designs were graded on the ability to hold multiple medications, portability, ease of use, weight and cost for each option. The criteria were weighted based on their importance to the final design. Table 1 shows the matrix and the results.

	MEMS	Precise- Adherence	E-Pill MD.2
Capacity (3)	1	5	4
Portability (3)	5	3	1
Ease of Use (4)	4	5	3
Weight (2)	5	4	2
Cost (5)	5	5	1
Total	69	77	36

Table 1. A design matrix was used to determine which design would be best to pursue.

After analyzing the design matrix, it was determined that the precise adherence device would be the best design for the client's desired characteristics in a pill box.

Final Design

After considering the advantages and disadvantages of the various alternative designs the final design was developed. Most patients currently use a pill box which allows medication storage for four times a day (morning, lunch, evening, bedtime) per week. To accommodate such a common preference, we decided to build our final design using an Apex 7-day Medi Planner pill box, which measures 20.5cm x 12.5cm x 2.5cm (8in x 5in x 1in).

Michael Morrow, an Electrical and Computer Engineering professor at the University of Wisconsin- Madison, suggested that we obtain a microcontroller and program it based on the needs of our client. This microcontroller could then be attached to our client's current pill box through a circuit and be sent home with the patient. The patients would not have to do anything different, but could just follow their current routine. He also pointed out that this would allow the device to use less power. The system could wake up to scan the compartments, and then sleep for the majority of the time. This standby feature would use less power and then the patient would not have to deal with any battery changes. Using the information gathered up to this point, Craig Gehrke of VIASYS NeuroCare donated his microcontroller and a wealth of knowledge to our group. He said a switch matrix would also work and that a watch crystal may be needed to keep exact time.

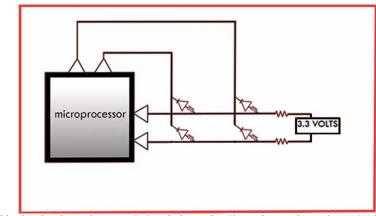


Figure 3. This circuit schematic uses a 2x2 switch matrix. The resistors pictured are $10K\Omega$ and diodes are model number IN4148.

We created a switch matrix in our final design that can be scaled up or down (See Figure 3 for schematic of circuit). The switch matrix consists of a Texas Instrument MSP430 microcontroller. By using a microcontroller in our design, we are able to develop a program that recognizes and stores the number of times a compartment is opened. Each one of these compartments will have a SPDT submini roller lever switch (item number 275-017A), which will be actuated when the compartment is opened. The microcontroller recognizes the change, and will record the number of times a compartment has been opened. Using the IAR Embedded Workbench IDE program, we can retrieve the amount of times each compartment switch has been activated. The microcontroller is programmed in the C language. A copy of the code used can be found in Appendix B.

To prevent pills from interfering with wires associated with the switch, and vice versa, a painted copper plate will be placed between the switch and the remaining pill compartment (see Figure 4). Each switch will be connected to a Texas Instruments MSP430 microcontroller in a switch matrix configuration. (Refer to the switch matrix section for further details). The microcontroller continuously scans the switch matrix in order to detect any compartments that may be open. If it detects a compartment to be

open, it will record which compartment was opened and at what time and date. At a later time, the microcontroller can output the data that has been stored on it, via a JTAG connector, to a computer.



Figure 4. Painted copper plates prevent pills from interfering with switch circuitry.

One of the problems of scanning switches in this manner is switch bounce. This is a phenomenon where a switch will open and close multiple times before coming to its final position. Switch bounce is usually not noticed by humans because it usually occurs during the first ten to twenty microseconds; however, when a microcontroller is used, it is able to detect these individual openings and closings. Thus the microcontroller could potentially record several switch closings, even though only one has officially occurred. To overcome this problem, a simple algorithm was implemented. The program uses a temporary counter that is incremented every time the switch is recorded as being closed. Only when this temporary counter reaches 1000 in consecutive runs, does the time and date get recorded. The microcontroller takes approximately 1 second to get to this limit. This algorithm also reduces false positives due to environmental electromagnetic noise. Another result of this algorithm is to prevent false positives when the compartment was not opened long enough to take a pill out. The number of 1000 may need to be fine tuned in the future.

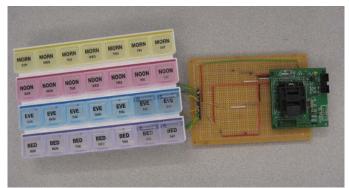


Figure 5. The pill box with circuit and microcontroller connected.

Switch Matrix

Switch matrix technology is most commonly used in computer keyboards. Even though there are over 100 keys on a keyboard, only six wires are connected to the corresponding computer. Using this same concept, the 7x4 pill box will require only 11 wires for 28 compartments. To use a switch matrix, switches must be connected using the layout specified in Figure 3. Outputs from the microcontroller must be connected to the rows and the inputs must be connected to the columns. While scanning the matrix, the microcontroller drives every output pin hi, or 1 (sends out a constant signal) except for the row of interest. This remaining row is driven low or 0 (no signal), and effectively acts as ground.

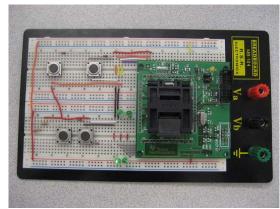


Figure 6. The switch matrix connected to a microcontroller.

When all switches are open, current from the power source goes to the inputs of the microcontroller, thus they each read 1. When switch is closed, current from the power source goes to the output pin that is driven low, and that the corresponding column input will read 0. When the microcontroller detects an input pin reading 0, it looks at which row was being driven low and which column read 0. Because the switches are on a grid, the microcontroller will be able to detect which compartment was opened.

Cost Analysis

To keep the final cost of the device under the \$500 limit set by the client, we were careful to use our budget in the most efficient way. The pill box we decided to base our design on cost \$4, but each switch cost \$3. Because we need 28 switches, the total cost for these switches will be \$84. The TI MSP430 microcontroller alone typically costs \$10, but for the initial construction of our design, a development kit will be used. The microcontroller with the development kit costs \$110. We have accounted for an extra \$30 for other parts and materials including a printed circuit board and circuit wires. In total, the cost of the final design is \$128 without the development kit and \$228 with the development kit, which are both significantly lower than the client's \$500 limit.

Advantages and Disadvantages

One of the advantages of this design is that is uses a 7x4 layout, one that most patients are familiar with. This will thwart patient confusion thus preventing incorrect medication compliance. Using the Texas Instruments MSP430 in this design, allows it to use energy efficiently, maximizing battery life.

As with any design, there are some disadvantages. Dr. Juergens mentioned that having an alarm system would be beneficial for his research; however, this design does

not currently incorporate an alarm. With the added circuitry, switches and a microcontroller, the weight of this design is increased. However, the total weight will still be within our design specifications.

Conclusion

The final design should not cause any injury to the patient. Specifically, there is a degree of safety that we must take into consideration upon developing an enclosure for the circuit. All wires and electrical components shall remain anonymous to the user except for a JTAG to parallel port converter. The circuitry enclosure will be made of the same material of the pill box, polyethylene. The final design should be accessible to all patients, regardless of disability. For example, brail text with respect to the time of dosage will be placed on each compartment lid to aid blind patients. By providing an alarm system, the patient will be reminded to take their medication on time, thus increasing the patient's medication adherence.

Currently the final design has a 2x2 configuration. This design establishes that our design functions properly and thus can be scaled up or down as desired. Therefore, to meet client requirements we will expand the pill box dimension to a 7x4. Secondly, we will enhance the microcontroller coding to log the date and time when a compartment is opened. The code will consist of a sleeping function to increase the efficiency of the microcontroller. Additionally, it is necessary that we develop a computer program that is user friendly to make data retrieval efficient. Lastly, we must test our final design to optimize its reliability and accuracy.

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Appendix A: Product Design Specification

Using Technology to Measure Adherence of Complicated Medication Regimens

Product Design Specifications

Team Members: Sujan Bhaheetharan, Cara Dunn, Farshad Fahimi, Nipun Yamdagni

Date Last Updated: December 12, 2006

Function: This device should record a patient's adherence to their medicine regimen and remind them with an alarm each time medications should be taken.

Client Requirements:

- Device must obtain data regarding patient's adherence of their medications.
- Device must be lightweight and durable.
- An alarm should alert patient to take medication.
- Total cost may not exceed \$500.
- Normal use may not interfere with recording.

• Must consume low amounts of power and be on standby for 2 weeks without power failure.

Design Requirements

1. Physical and Operational Characteristics

a. <u>Performance Requirements</u>: The user may access the device at any time and the prototype will record the exact time and date of operation. Everything will be logged so that the client may review the information when the device is returned. In addition, an alarm should be integrated into the final device in order to alert the user and remind them to take their medications; however, this feature may be done separately via a wristwatch. Alerting the user and recording the precise moment of operation are the key performance requirements for this design.

b. <u>Safety</u>: All safety issues associated with the client's standard medication box will pertain to this device. Chemicals that are harmful to the device must be clearly stated for the user during the cleaning process. If a wristwatch is implemented, the audible/vibration level must not be hazardous to the user's health.

c. <u>Accuracy and Reliability</u>: Accurate timing and logging is essential for this design. The final prototype must be able to record up-to-the-minute data on operation and store it correctly. Proper logging is necessary for the client's records. The alarm system should have a programmable alarm feature and should always have the correct time. The battery/power source for both the recording function and the alarm feature must be reliable in order to ensure accurate logging and to have correct medication alerts.

d. <u>Life in Service</u>: The final device should be able to last as long as the power source and there should be no functional dilemmas due to normal wear and tear. The device may be idle for numerous hours while sitting in the client's residence, but could also be accessed at any given moment. The device, which may surround the medication box, must not be negatively affected by normal medication refills or by being transferred between medication boxes or between patients. Given a good environmental setting, there should be no problem with the device traveling back and forth between the pharmacy and the patient every few weeks. The wristwatch system will last as long as the battery's life.

e. <u>Shelf Life</u>: The device should last for several years prior to being used, and should be operable for several years after purchase. To achieve this, proper materials must be selected and appropriate mechanisms must be employed.

f. <u>Operating Environment</u>: The device will be used mostly indoors, on a daily basis. Patients might like to store their medicine in a bathroom, thus it should not be damaged if exposed to high humidity, such as that caused by a shower. It should also not be damaged from any accidental water spills. If the device is left in a car accidentally, it should be able

to accommodate temperatures as low -20° C as high as 50° C. Furthermore, it should not be considered an extremely fragile device, which may deter patient usage.

g. <u>Ergonomics</u>: The typical user of this device will be elderly and or disabled, with reduced strength and motility. Thus, the device should be easy to hold and should not be physically challenging to operate. Additionally, the device should be intuitive for every patient and require little or no instruction.

h. <u>Size</u>: Despite the fact that the device will predominantly remain indoors, it will still need to be moved from time to time. Thus it cannot be a very large and bulky. The target size is approximately that of current pill boxes.

i. <u>Weight</u>. The device should not weigh more than between 5 and 10 pounds. It is vital that the patients, typically older, more fragile patients, be able to carry the adherence device. The alarm wristwatch should be of minimal weight to ensure no harm is done to the patient.

j. <u>Materials</u>: The materials for the device should be easily cleanable surfaces. Plastic would be optimal to prevent medicine contamination. Porous materials are not to be used to ensure a healthy storage situation. The preferred materials for the wristwatch would be plastic, but a fabric band would be possible. Any adherents used should be able to last in the normal operational atmosphere without failure or harm the user.

k. <u>Aesthetics, Appearance, and Finish</u>. The adherence device should be aesthetically pleasing, but has no specific requirements. A neutral color would be best with perhaps some color for easy recognition of the device. The form of the device should be easy for an elderly patient to hold and carry while still holding the maximum number of medications necessary. The wristwatch should be small and attractive. If the user does not find the wristwatch appealing, they will be less likely to wear it and, therefore, will not receive reminders to take their medications.

2. Production Characteristics

a. <u>Quantity</u>. One prototype of the medicine adherence device is necessary, but after a satisfactory design is created, a total of between 5 and 10 may be necessary. The client requests one wristwatch for every medicine adherence device created.

b. <u>*Target Product Cost*</u>. The Client would like the prototype (both the compliance device and the wristwatch) to cost no more than \$500, but when the design is in production, each device and wristwatch should cost approximately \$200.

3. Miscellaneous

a. <u>Standards and Specifications</u>: There are no national or international specifications for gathering information on when a patient takes their medication. This data is valuable information for clinicians, and will help in determining if additional medication is necessary. Also, the data can be used for improvement upon a patient's medication adherence. Our client also desired that we develop a device that would remind the patient to take their medication.

b. *Customer*: Device must be able to get customer's attention, reminding him/her to take their medications.

c. <u>*Patient-related concerns*</u>: The device does not have to be sterilized between uses. The data gathered from the instrument must be safeguarded for confidentiality purposes.

d. <u>*Competition*</u>: Currently there is an instrument which can monitor the date/time an individual medication pill bottle is opened; such instrument uses Micro-Electro-Mechanical Systems (MEMS.)

Appendix B: Microcontroller code written in C language

//Code to be used with TI MSP430f169

#include "msp430x16x.h"

void main(void)

{

WDTCTL = WDTPW + WDTHOLD;

#define COL1 0x02 #define COL2 0x04 #define ROW1 0x08 #define ROW2 0x10

volatile unsigned int Counter1; volatile unsigned int Counter2; volatile unsigned int Counter3; volatile unsigned int Counter4;

volatile unsigned int tcounter1; volatile unsigned int tcounter2; volatile unsigned int tcounter3; volatile unsigned int tcounter4;

volatile unsigned int ttcounter1; volatile unsigned int ttcounter2; volatile unsigned int ttcounter3; volatile unsigned int ttcounter4;

volatile unsigned int wasclosed1; volatile unsigned int wasclosed2; volatile unsigned int wasclosed3; volatile unsigned int wasclosed4;

Counter1 = Counter2 = Counter3 = Counter4 = 0; tcounter1 = tcounter2 = tcounter3 = tcounter4 = 0; ttcounter1 = ttcounter2 = ttcounter3 = ttcounter4 = 0; wasclosed1 = wasclosed2 = wasclosed3 = wasclosed4 = 1;

P1DIR |= COL1; P1DIR |= COL2; P1DIR |= 0x01; P1DIR &= ~ROW1;

P1DIR &= \sim ROW2;

```
P1OUT |= 0x01;
//to act as ground
P5DIR = 0x10;
P5OUT &=~0x10;
// for LEDS
P3DIR = 0x20;
P3DIR |= 0x40;
P3DIR = 0x80;
P4DIR = 0x01;
for(;;)
{
 COL2 D1;
 P1OUT &= ~COL1;
 P1OUT \models COL2;
 if (P1IN & ROW1) // button not pressed
 {
  ttcounter1++;
  if (ttcounter1 == 5000)
  {
   wasclosed1 = 1;
   ttcounter1 = 0;
   tcounter1 = 0;
   P4OUT &= ~0x01;
  }
 }
 else // button pressed
  if (wasclosed 1 == 1)
  {
   tcounter1++;
   ttcounter1 = 0;
  }
 }
 if (tcounter1 == 5000)
 {
  Counter1++;
  P4OUT = 0x01;
  tcounter1 = 0;
  wasclosed1 = 0;
 }
```

```
if (P1IN & ROW2) // button not pressed
ł
 ttcounter2++;
 if (ttcounter2 == 5000)
 {
  wasclosed2 = 1;
  ttcounter2 = 0;
  tcounter2 = 0;
  P3OUT &= ~0x40;
 }
}
else // button pressed
{
 if (wasclosed2 == 1)
 {
  tcounter2++;
  ttcounter 2 = 0;
 }
}
if (tcounter2 == 5000)
ł
 Counter2++;
 tcounter2 = 0;
 wasclosed2 = 0;
 P3OUT |= 0x40;
}
```

```
P1OUT |= COL1;

P1OUT &= ~COL2;

if (P1IN & ROW1) // button not pressed

{

ttcounter3++;

if (ttcounter3 == 5000)

{

wasclosed3 = 1;

ttcounter3 = 0;

P3OUT &= ~0x80;

}

else // button pressed
```

```
{
    if (wasclosed3 == 1)
    {
        tcounter3++;
        ttcounter3 = 0;
    }
}
if (tcounter3 == 5000)
{
    Counter3++;
    tcounter3 = 0;
    wasclosed3 = 0;
    P3OUT |= 0x80;
}
```

```
if (P1IN & ROW2) // button not pressed
 {
  ttcounter4++;
  if (ttcounter4 == 5000)
  {
   wasclosed4 = 1;
   ttcounter4 = 0;
   tcounter4 = 0;
   P3OUT &= ~0x20;
  }
 }
 else // button pressed
  if (wasclosed4 == 1)
  {
   tcounter4++;
   ttcounter4 = 0;
  }
 }
 if (tcounter 4 == 5000)
 {
  Counter4++;
  tcounter4 = 0;
  wasclosed4 = 0;
  P3OUT = 0x20;
 }
}
```

}