A MEDICATION COMPLIANCE ACTION PLAN

Bruce A. Kehr, M.D.

MEDICATION MANAGEMENT TECHNOLOGIES, INC.

(a medication compliance company in formation)

March 31, 1994

A MEDICATION COMPLIANCE ACTION PLAN

Prepared for:

Hillary Rodham Clinton
and
Jennifer Kline

MEDICATION MANAGEMENT TECHNOLOGIES, INC.
5920 Hubbard Drive
Rockville, MD 20852

tel.301-984-1566 fax.301-816-0907

Table of Contents

MEDICATION MANAGEMENT TECHNOLOGIES, INC.
(A Corporation in Formation)
5920 Hubbard Drive
Rockville, MD 20852

EXECUTIVE SUMMARY

- Noncompliance with prescription medication costs the U.S. economy $150 billion per year.
  - Medication noncompliance is defined as the failure to take prescription medications as prescribed by the physician.
  - $100 billion per year is lost to the U.S. economy through direct and indirect medical expenses and lost productivity, attributable to noncompliance.
  - 10% of all hospital admissions, or over $25 billion per year in expense is caused by noncompliance-induced hospital admissions.
  - Of patients admitted to nursing homes, 23% had no high risk factor other than the inability to manage medications at home.
- Patient medication compliance is improved by the Procompliance Triad: patient education, medication counseling, and compliance technology.
  - Technology that prompts patients to take anti-hypertensive medication increases compliance from 78% to 95%, and decreases systolic blood pressure by 7.6 millimeters mercury and diastolic pressure by 6.8 millimeters mercury.
  - Technology that monitors patient compliance is supported by prominent physician organizations.
  - Physician-based electronic monitoring has improved diagnostic accuracy in cardio-vascular disease, epilepsy, asthma, depression, and hypertension.
  - Compliance technology is inexpensive to use.
- All constituents benefit from improved patient medication compliance.
  - Medicare and Medicaid budgetary savings result from reduced hospital admissions, laboratory testing, physician visits, and nursing home admissions.
  - Managed Care Companies reduce unnecessary utilization, thereby increasing profits.
  - Pharmaceutical manufacturers sell more drugs through increased "script yield," which offsets declining profit margins per drug.
  - Physicians diagnose and treat patients more efficiently through compliance technology, thereby stabilizing income in a managed care system.
  - Retail pharmacists sell more medication, and increase professional identity through compliance counseling and education.
  - Patients improve their health and well-being, and become more independent while reducing personal medical expenses.

Bruce A. Kehr, M.D
President

tele: (301) 984-1566/fax: (301) 816-0907

Compliance Assessment: A Diagnostic Test That Drives Down Healthcare Costs

I. Noncompliance is a human tragedy.

A. 125,000 people per year die cardiovascular deaths that are preventable by proper medication use.

B. 93% of diabetics risk loss of control of blood sugar and increased cardiovascular disease through noncompliance with treatment regimens.

C. 18% of organ transplant patients risk rejection through medication misuse.

D. 40% of hypertensive patients risk hospitalization and cardiovascular complications through failure to self-medicate properly.

E. 40% to 60% of adolescent cancer patients fail to take their medication as directed.

F. 50% of renal dialysis patients fail to adhere to their complex treatment regimen.

II. Proper medication compliance improves clinical outcomes.

A. In patients with congestive heart failure, there was a 40% reduction in mortality in patients who took their medications properly

B. Compliance with cholesterol lowering drugs directly correlates with reduced cholesterol in the blood--patients taking only 40% of the drug doses had a 25% increased risk of heart disease, patients who took less than 40% of the drug doses had a 50% increased risk of heart disease.

C. In organ transplant patients on immunosuppressants, 91% of noncompliant patients experience organ rejection or death, compared with 18% of the patients who had proper medication compliance.

III. Physician-led compliance interventions reduce disease severity.

A. In 191 studies of post-surgical care, psychoeducational intervention provided beneficial effects on length of hospital stay.

B. Single-session physician tutorials, focused on patient teaching techniques, resulted in increased patient compliance with drugs and decreased blood pressure for the patients of these physicians.

C. Two years after adding a counselling approach to physician care in a low income, minority community, hypertensive control in patients improved by 40%.

D. Hypertensives receiving compliance monitoring and counseling increased their medication adherence from 69% to 84% and reduced their blood pressure by 10 millimeters systolic and 7 millimeters diastolic.

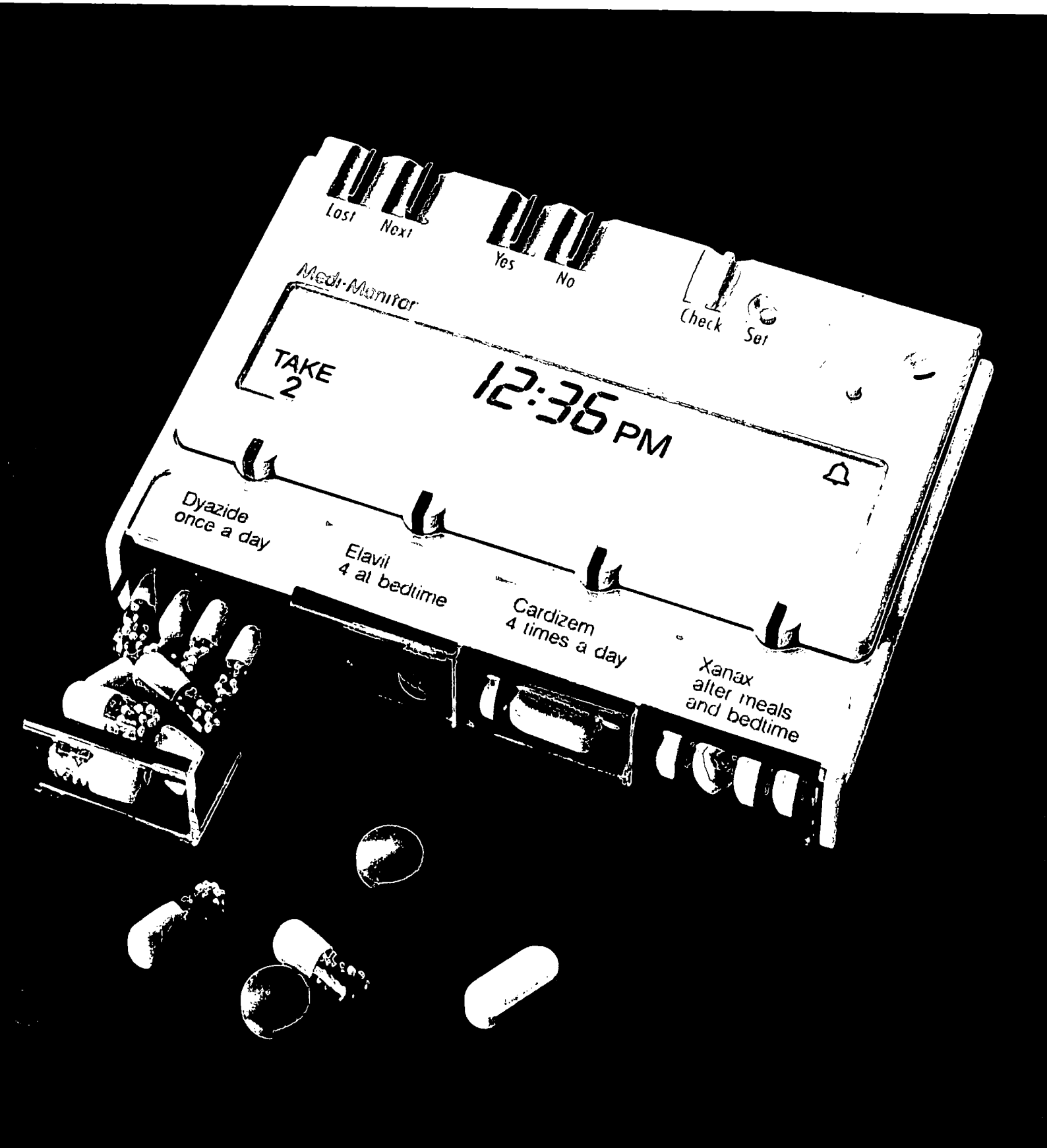
TABLE 5.
COST SAVINGS OF COMPLIANCE PROGRAMS

Program	Patients	Savings	Benefit/Cost	Reference
Pharmacy-based compliance clinic	25	$43,000 in 33 months	12/1	1
Medication-monitoring service for geriatric patients	14	$265-565/patient/month	7/1-4/1	2
Compliance education for hypertension	--	$100/patient/year	2.5/1	3
Asthma self-management	683	--	111/1	4
Education of schizophrenics at a day treatment center	18	$10,000	--	5
Asthma self-management in inner city*	58	--	5.9/1	6
Education for congestive heart failure	50	452 hospital patient-days	--	7
Telephone hotline service for diabetics*	6,000	$1.7-3.5 million in emergency and hospital admissions, and office visits for medications	--	8
Computer-assisted telephone refill reminders in a community pharmacy	450	--	1.26/1-1.67/1	9
Hospital-based clinical pharmacy program	355	$208,000	--	10

* Medication management was part of an overall education effort, involving life-style, diet, and general health measures.

1) Cable & Schneider, 1982; 2) Joyner et al., 1983; 3) Eastaugh & Hatcher, 1982; 4) Sperling, 1984; 5) Britt & Stowell, 1983; 6) Roccalla, 1976; 7) Rosenberg, 1971; 8) Miller & Goldstein, 1972; 9) Bryan et al., 1983; 10) Bond & Monson, 1984.

MEDICATION MANAGEMENT TECHNOLOGIES, INC.



PATENTED PRODUCT FEATURES

-- Single chamber and multi-chamber medication dispensers.

-- The technology covers pocket-sized and portable dispensers, as well as bedside and institutional versions for assisted living and nursing home settings.

-- Medications segregated by chamber.

-- Tells patient when to take a particular medication, which particular medication to take, and how much medication to take.

-- A wide variety of messages, prompts and cues can be used audibly (including synthesized speech) or visually on a display screen.

-- Alarm signals recur periodically to alert the patient, should they miss the first alarm signal.

-- Alarms and messages are automatically turned off after the patient has accessed the appropriate compartment. Accessing the wrong compartment will not turn off alarms.

-- Messages regarding particular medications (e.g., quantity to be taken) are displayed adjacent to the particular medication compartment to be referenced, thereby allowing for easy visual understanding of what the patient needs to do with a particular medication.

-- If medication is not taken within a given time after the alarm sounds, a "missed medication signal" alerts the patient, and the patient is instructed as to which medication was missed, and how many were missed.

-- Audible alarm may be suspended for a pre-set time period to allow for discretion in medication taking, while visual alarms silently indicate to the patient when to take medication, which medication needs to be taken, and how many need to be taken.

-- Displays a record of patient behavior, including which specific medications were taken and missed, and when they were taken or missed.

-- Prospective and retrospective review of medication schedules are presented "on-screen".

-- A "reload signal" can be given periodically to remind the patient or caregiver to place new medication in the dispenser.

-- Audible and visual alarms, signals, and messages can be set once, and recur indefinitely until reprogrammed.

-- When programming, the device displays standard doctor's orders on screen, which are then translated by the software into medication taking routines. (e.g.,"take two pills, three times a day", "one every other day", etc.).

-- Prescription taking routines may be set according to standard prescription dictates (e.g., "take two pills 4 times a day") or may be custom entered for specific times.

-- If time of day is changed (e.g., Daylight Savings Time or entering a new time zone), software automatically adjusts the medication taking routines.

-- If first dose time (i.e., the time of day at which the medication taking routines first begin) is changed to accommodate a later morning awakening, the software automatically adjusts the prescription taking routines for the remainder of the day.

-- If the patient opens a compartment at a time when they are not scheduled to receive medication, a separate alarm goes off and the patient is queried as to whether they want to take an unscheduled medication. If they answer "yes", the event is recorded in memory, if the answer is "no", it is not.

-- Volume of audible alarm may be preset.

ASSURANCE

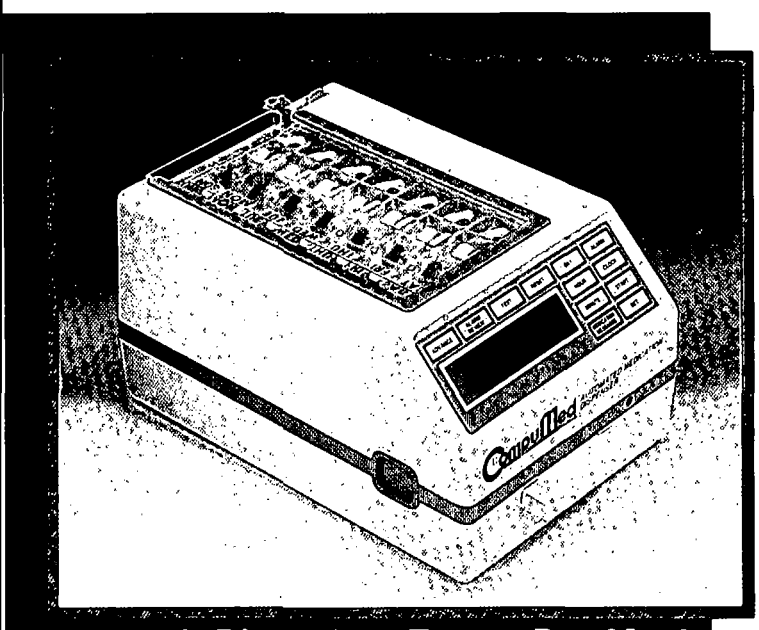
THROUGH MEDICATION COMPLIANCE

CompuMed®

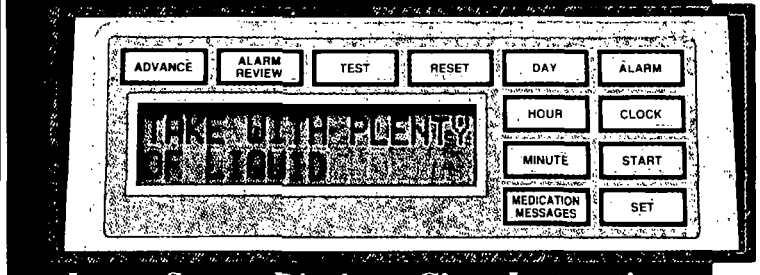
AUTOMATED MEDICATION DISPENSER

CompuMed

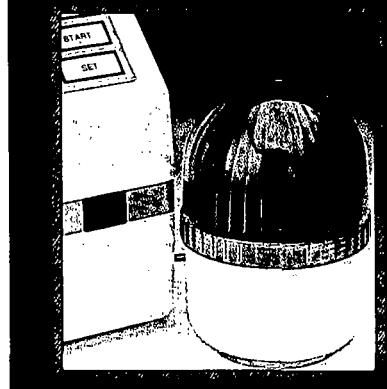
AUTOMATED MEDICATION DISPENSER



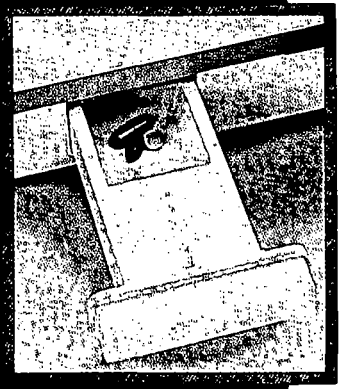
Automatic Dispensing • Tamper Proof Lock
Medication Advance Override
Reminders for All Medications
Battery Backup



Large Screen Display • Clear Instructions
Prescription Messages • Error Messages
Easy-to-read Clock



Volume & Pitch
Control/Audio &
Optional Visual Alarm



Easily Accessed
Drawer

CompuMed, Inc.
One Pitchfork Road
Meeteetse, WY 82433
1-307-868-2555

THE PROBLEM...
...Medication Non-Compliance

Have you or a loved one ever wondered if medication was taken correctly - or even at all?

Non-compliance with prescription medications has been called "America's other drug problem" and accounts for 25% of hospital admissions for those 65 and older.

Non-compliance increases the duration of chronic and temporary illnesses and conditions and costs patients and society dearly in terms of health, time and dollars.

THE SOLUTION...
...CompuMed

You and those you care about can rest assured that medication is taken properly with CompuMed.

Complex drug regimens are organized and simplified using CompuMed. In just minutes CompuMed can be programmed to ***automatically dispense*** pill-form medication and vitamins at the correct time and dosage.

Not only that, CompuMed will remind you of ***all your medications*** (creams, ointments, drops, etc.) at the proper time. CompuMed even displays directions on how the medication is to be administered!

THE BOTTOM LINE...

- Improves compliance
- Cost effective
- Reduces stress and worry
- Simplifies complex regimens
- Increases patient & caregiver independence

TO ORDER COMPUMED...

Phone 1-800-722-4417
Outside the USA, phone 1-307-868-2555
or FAX 1-307-868-2550
All Major Credit Cards Accepted

U.S. Patent No. 4,763,81
K10119

Action Plan for Pilot Programs in Medication Compliance

- Implement pilot programs in educating and counseling patients on medication compliance.
- Programs will be funded by pharmaceutical manufacturers, and conducted by The Task Force on Compliance.
- Perform outcome studies on patients in these pilot programs.
- Those patients who complete the program get a Certificate of Completion.
- The Certificate entitles the patient to an income tax credit or a credit toward their Medicare deductible, to encourage participation.
- Additional income tax credit or a credit toward Medicare deductible is given for proof of purchase of compliance technology.
- Provide SBA loan assistance for emerging compliance technology companies.

C.V. SUMMARY

BRUCE A. KEHR, M.D.

Bruce A. Kehr, M.D. graduated from The University of Pennsylvania and Georgetown University School of Medicine, and is Board Certified in Psychiatry. He is president of Contemporary Psychiatric Services, a group practice of 8 professionals located in Rockville, MD. Dr. Kehr has assembled a neurobehavioral team to evaluate and treat treatment resistant patients with neuropsychiatric conditions and patients with traumatic brain injury and behavioral problems. The team is also active in forensic neuropsychiatric evaluations. Dr. Kehr is President of American Neuroscience Centers, operating a laboratory for the assessment of brain function, soon to be acquired in a public offering by NeuroData. He is also an inventor. As the principal inventor for Medication Management Technologies, he holds three issued U.S. patents, 1 U.S. patent pending and issued patents in Europe, Canada, and Japan for computerized medication technology. His interest in medication compliance has led to the publication of articles in both professional and lay publications and to his collaboration on the production and national distribution of a video tape titled "The Other Drug Problem: Medication Misuse Among Older Americans." He has delivered over 100 public speaking engagements to professional and lay audiences, including both radio and television appearances.

KEHR PATENT SUMMARY

Date	Ref. No. and Title	Status	Territory	Owner
	United States			
8/30/84	4,768,176 Apparatus for Alerting a Patient to Take Medication	Issued 8/30/88	U.S.	B. Kehr, M.D.
8/30/84	4,768,177 Method and Apparatus for Alerting a Patient to Take Medication	Issued 8/30/88	U.S.	B. Kehr, M.D.
1/17/90	5,200,891 Electronic Medication Dispensing Method	Issued 4/6/93	U.S.	B. Kehr, M.D.
7/23/90	07,556,626 Electronic Medication Monitoring and Dispensing Method	Pending	U.S.	B. Kehr, M.D.
	Foreign Patents			
6/19/85	1,293,382	Issued 12/24/91	Canada	B. Kehr, M.D.
7/05/85	0172638B1	Issued	U.K.	B. Kehr, M.D.
	0172638B1	4/22/92	Germany	B. Kehr, M.D.
	0172638B1		Italy	B. Kehr, M.D.
	0172638B1		France	B. Kehr, M.D.
3/30/86	60-145921	Issued 1993	Japan	B. Kehr, M.D.

MMTI Trademark Summary

Trademark	MEDI-MONITOR Electronic Dispenser	Worldwide
Trademark	MEDI-MONITOR Medication Dispenser	Worldwide
Trademark	T. COMPliance Operating System	Worldwide

A MEDICATION COMPLIANCE ACTION PLAN

Bruce A. Kehr, M.D.

MEDICATION MANAGEMENT TECHNOLOGIES, INC.

(a medication compliance company in formation)

March 31, 1994

A MEDICATION COMPLIANCE ACTION PLAN

Prepared for:

Hillary Rodham Clinton
and
Jennifer Kline

MEDICATION MANAGEMENT TECHNOLOGIES, INC.
5920 Hubbard Drive
Rockville, MD 20852

tel.301-984-1566 fax.301-816-0907

Table of Contents

MEDICATION MANAGEMENT TECHNOLOGIES, INC.
(A Corporation in Formation)
5920 Hubbard Drive
Rockville, MD 20852

EXECUTIVE SUMMARY

- Noncompliance with prescription medication costs the U.S. economy $150 billion per year.
  - Medication noncompliance is defined as the failure to take prescription medications as prescribed by the physician.
  - $100 billion per year is lost to the U.S. economy through direct and indirect medical expenses and lost productivity, attributable to noncompliance.
  - 10% of all hospital admissions, or over $25 billion per year in expense is caused by noncompliance-induced hospital admissions.
  - Of patients admitted to nursing homes, 23% had no high risk factor other than the inability to manage medications at home.
- Patient medication compliance is improved by the Procompliance Triad: patient education, medication counseling, and compliance technology.
  - Technology that prompts patients to take anti-hypertensive medication increases compliance from 78% to 95%, and decreases systolic blood pressure by 7.6 millimeters mercury and diastolic pressure by 6.8 millimeters mercury.
  - Technology that monitors patient compliance is supported by prominent physician organizations.
  - Physician-based electronic monitoring has improved diagnostic accuracy in cardio-vascular disease, epilepsy, asthma, depression, and hypertension.
  - Compliance technology is inexpensive to use.
- All constituents benefit from improved patient medication compliance.
  - Medicare and Medicaid budgetary savings result from reduced hospital admissions, laboratory testing, physician visits, and nursing home admissions.
  - Managed Care Companies reduce unnecessary utilization, thereby increasing profits.
  - Pharmaceutical manufacturers sell more drugs through increased "script yield," which offsets declining profit margins per drug.
  - Physicians diagnose and treat patients more efficiently through compliance technology, thereby stabilizing income in a managed care system.
  - Retail pharmacists sell more medication, and increase professional identity through compliance counseling and education.
  - Patients improve their health and well-being, and become more independent while reducing personal medical expenses.

Bruce A. Kehr, M.D
President

tele: (301) 984-1566/fax: (301) 816-0907

Compliance Assessment: A Diagnostic Test That Drives Down Healthcare Costs

I. Noncompliance is a human tragedy.

A. 125,000 people per year die cardiovascular deaths that are preventable by proper medication use.

B. 93% of diabetics risk loss of control of blood sugar and increased cardiovascular disease through noncompliance with treatment regimens.

C. 18% of organ transplant patients risk rejection through medication misuse.

D. 40% of hypertensive patients risk hospitalization and cardiovascular complications through failure to self-medicate properly.

E. 40% to 60% of adolescent cancer patients fail to take their medication as directed.

F. 50% of renal dialysis patients fail to adhere to their complex treatment regimen.

II. Proper medication compliance improves clinical outcomes.

A. In patients with congestive heart failure, there was a 40% reduction in mortality in patients who took their medications properly

B. Compliance with cholesterol lowering drugs directly correlates with reduced cholesterol in the blood--patients taking only 40% of the drug doses had a 25% increased risk of heart disease, patients who took less than 40% of the drug doses had a 50% increased risk of heart disease.

C. In organ transplant patients on immunosuppressants, 91% of noncompliant patients experience organ rejection or death, compared with 18% of the patients who had proper medication compliance.

III. Physician-led compliance interventions reduce disease severity.

A. In 191 studies of post-surgical care, psychoeducational intervention provided beneficial effects on length of hospital stay.

B. Single-session physician tutorials, focused on patient teaching techniques, resulted in increased patient compliance with drugs and decreased blood pressure for the patients of these physicians.

C. Two years after adding a counselling approach to physician care in a low income, minority community, hypertensive control in patients improved by 40%.

D. Hypertensives receiving compliance monitoring and counseling increased their medication adherence from 69% to 84% and reduced their blood pressure by 10 millimeters systolic and 7 millimeters diastolic.

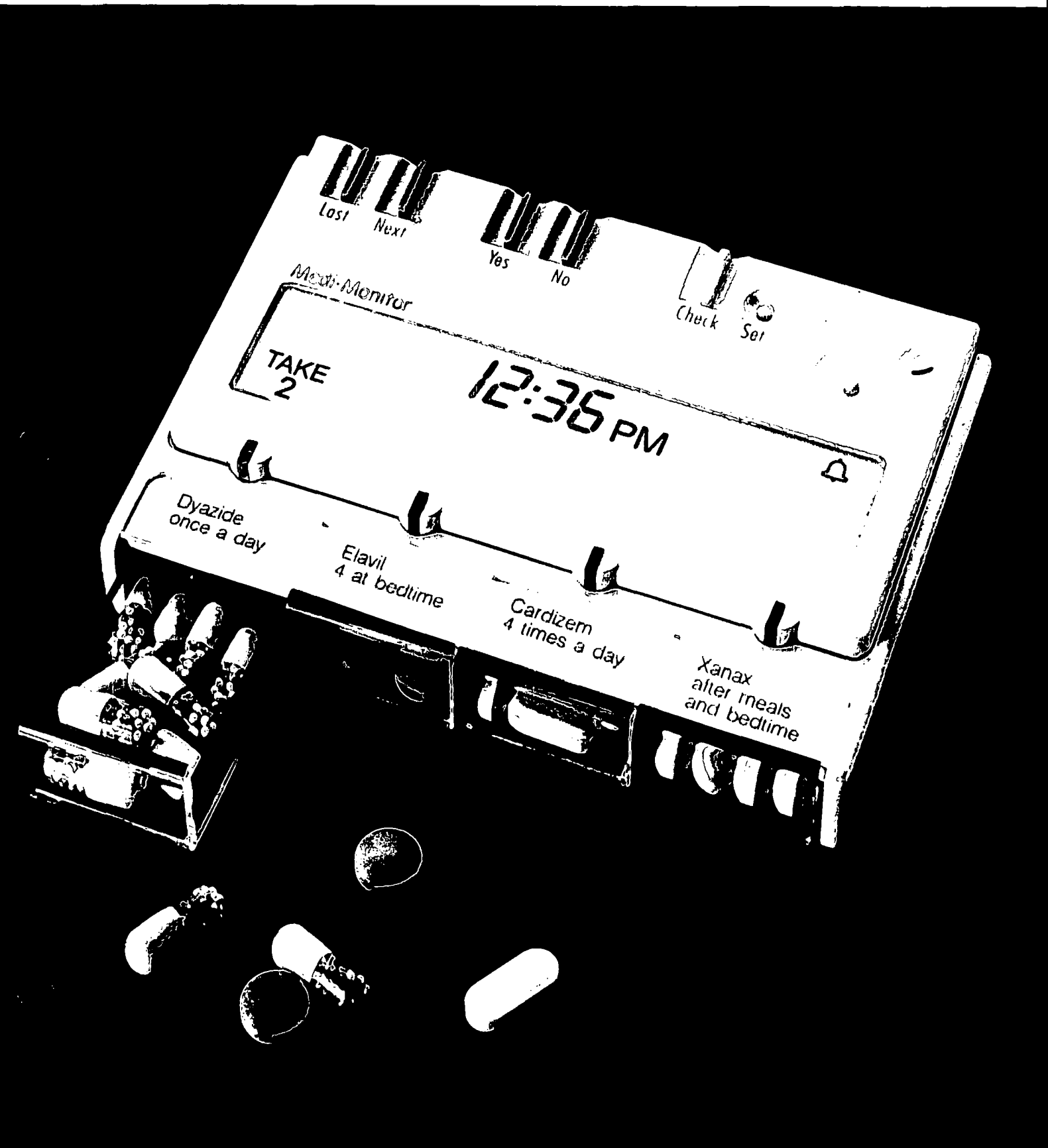
TABLE 5.
COST SAVINGS OF COMPLIANCE PROGRAMS

Program	Patients	Savings	Benefit/Cost	Reference
Pharmacy-based compliance clinic	25	$43,000 in 33 months	12/1	1
Medication-monitoring service for geriatric patients	14	$265-565/patient/month	7/1-4/1	2
Compliance education for hypertension	--	$100/patient/year	2.5/1	3
Asthma self-management	683	--	111/1	4
Education of schizophrenics at a day treatment center	18	$10,000	--	5
Asthma self-management in inner city*	58	--	5.9/1	6
Education for congestive heart failure	50	452 hospital patient-days	--	7
Telephone hotline service for diabetics*	6,000	$1.7-3.5 million in emergency and hospital admissions, and office visits for medications	--	8
Computer-assisted telephone refill reminders in a community pharmacy	450	--	1.26/1-1.67/1	9
Hospital-based clinical pharmacy program	355	$208,000	--	10

* Medication management was part of an overall education effort, involving life-style, diet, and general health measures.

1) Cable & Schneider, 1982; 2) Joyner et al., 1983; 3) Eastaugh & Hatcher, 1982; 4) Sperling, 1984; 5) Britt & Stowell, 1983; 6) Roccalla, 1976; 7) Rosenberg, 1971; 8) Miller & Goldstein, 1972; 9) Bryan et al., 1983; 10) Bond & Monson, 1984.

MEDICATION MANAGEMENT TECHNOLOGIES, INC.



PATENTED PRODUCT FEATURES

-- Single chamber and multi-chamber medication dispensers.

-- The technology covers pocket-sized and portable dispensers, as well as bedside and institutional versions for assisted living and nursing home settings.

-- Medications segregated by chamber.

-- Tells patient when to take a particular medication, which particular medication to take, and how much medication to take.

-- A wide variety of messages, prompts and cues can be used audibly (including synthesized speech) or visually on a display screen.

-- Alarm signals recur periodically to alert the patient, should they miss the first alarm signal.

-- Alarms and messages are automatically turned off after the patient has accessed the appropriate compartment. Accessing the wrong compartment will not turn off alarms.

-- Messages regarding particular medications (e.g., quantity to be taken) are displayed adjacent to the particular medication compartment to be referenced, thereby allowing for easy visual understanding of what the patient needs to do with a particular medication.

-- If medication is not taken within a given time after the alarm sounds, a "missed medication signal" alerts the patient, and the patient is instructed as to which medication was missed, and how many were missed.

-- Audible alarm may be suspended for a pre-set time period to allow for discretion in medication taking, while visual alarms silently indicate to the patient when to take medication, which medication needs to be taken, and how many need to be taken.

-- Displays a record of patient behavior, including which specific medications were taken and missed, and when they were taken or missed.

-- Prospective and retrospective review of medication schedules are presented "on-screen".

-- A "reload signal" can be given periodically to remind the patient or caregiver to place new medication in the dispenser.

-- Audible and visual alarms, signals, and messages can be set once, and recur indefinitely until reprogrammed.

-- When programming, the device displays standard doctor's orders on screen, which are then translated by the software into medication taking routines. (e.g.,"take two pills, three times a day", "one every other day", etc.).

-- Prescription taking routines may be set according to standard prescription dictates (e.g., "take two pills 4 times a day") or may be custom entered for specific times.

-- If time of day is changed (e.g., Daylight Savings Time or entering a new time zone), software automatically adjusts the medication taking routines.

-- If first dose time (i.e., the time of day at which the medication taking routines first begin) is changed to accommodate a later morning awakening, the software automatically adjusts the prescription taking routines for the remainder of the day.

-- If the patient opens a compartment at a time when they are not scheduled to receive medication, a separate alarm goes off and the patient is queried as to whether they want to take an unscheduled medication. If they answer "yes", the event is recorded in memory, if the answer is "no", it is not.

-- Volume of audible alarm may be preset.

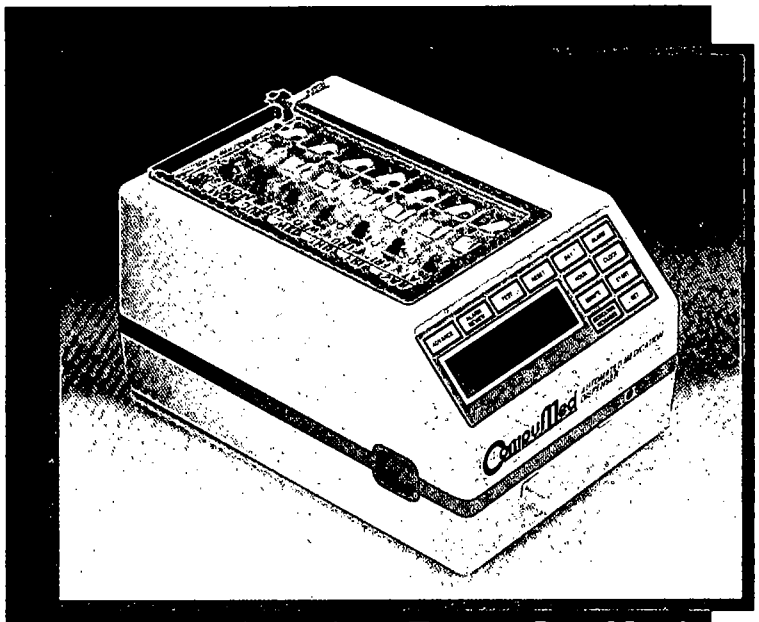
ASSURANCE

THROUGH MEDICATION COMPLIANCE

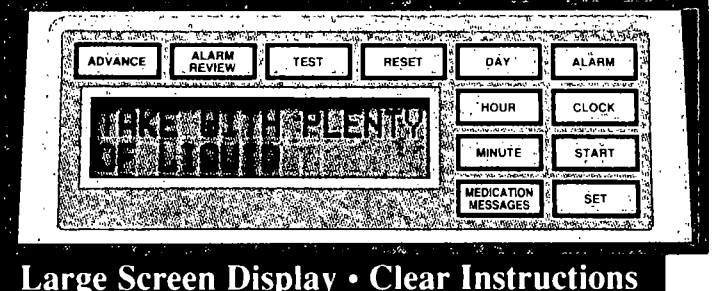
CompuMed®

AUTOMATED MEDICATION DISPENSER

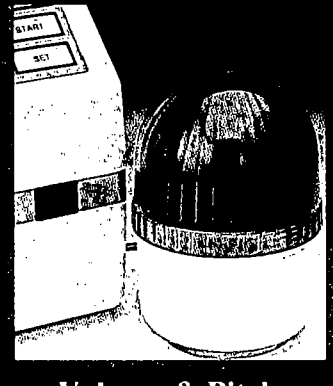
CompuMed AUTOMATED MEDICATION DISPENSER



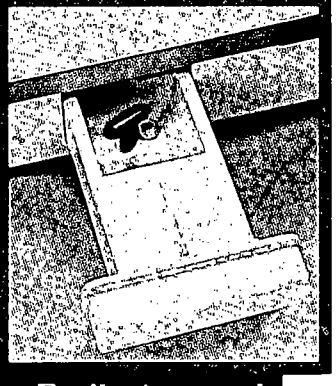
Automatic Dispensing • Tamper Proof Lock
Medication Advance Override
Reminders for All Medications
Battery Backup



Large Screen Display • Clear Instructions
Prescription Messages • Error Messages
Easy-to-read Clock



Volume & Pitch Control/Audio & Optional Visual Alarm



Easily Accessed Drawer

CompuMed, Inc.
One Pitchfork Road
Meeteetse, WY 82433
1-307-868-2555

THE PROBLEM...
...Medication Non-Compliand

Have you or a loved one ever wondered medication was taken correctly - or even at all

Non-compliance with prescription medicatio has been called "America's other drug proble and accounts for 25% of hospital admissions f those 65 and older.

Non-compliance increases the duration chronic and temporary illnesses and conditio and costs patients and society dearly in terms health, time and dollars.

THE SOLUTION...
...CompuMed™

You and those you care about can rest assure that medication is taken properly with CompuMe

Complex drug regimens are organized a simplified using CompuMed. In just minute CompuMed can be programmed to ***automatical dispense*** pill-form medication and vitamins the correct time and dosage.

Not only that, CompuMed will remind you ***all your medications*** (creams, ointments, drop etc.) at the proper time. CompuMed even displa directions on how the medication is to b administered!

THE BOTTOM LINE...

- Improves compliance
- Cost effective
- Reduces stress and worry
- Simplifies complex regimens
- Increases patient & caregiver independence

TO ORDER COMPUMED...

Phone 1-800-722-4417
Outside the USA, phone 1-307-868-2555
or FAX 1-307-868-2550
All Major Credit Cards Accepted

U.S. Patent No. 4,763,8
K101

Action Plan for Pilot Programs in Medication Compliance

- Implement pilot programs in educating and counseling patients on medication compliance.
- Programs will be funded by pharmaceutical manufacturers, and conducted by The Task Force on Compliance.
- Perform outcome studies on patients in these pilot programs.
- Those patients who complete the program get a Certificate of Completion.
- The Certificate entitles the patient to an income tax credit or a credit toward their Medicare deductible, to encourage participation.
- Additional income tax credit or a credit toward Medicare deductible is given for proof of purchase of compliance technology.
- Provide SBA loan assistance for emerging compliance technology companies.

C.V. SUMMARY

BRUCE A. KEHR, M.D.

Bruce A. Kehr, M.D. graduated from The University of Pennsylvania and Georgetown University School of Medicine, and is Board Certified in Psychiatry. He is president of Contemporary Psychiatric Services, a group practice of 8 professionals located in Rockville, MD. Dr. Kehr has assembled a neurobehavioral team to evaluate and treat treatment resistant patients with neuropsychiatric conditions and patients with traumatic brain injury and behavioral problems. The team is also active in forensic neuropsychiatric evaluations. Dr. Kehr is President of American Neuroscience Centers, operating a laboratory for the assessment of brain function, soon to be acquired in a public offering by NeuroData. He is also an inventor. As the principal inventor for Medication Management Technologies, he holds three issued U.S. patents, 1 U.S. patent pending and issued patents in Europe, Canada, and Japan for computerized medication technology. His interest in medication compliance has led to the publication of articles in both professional and lay publications and to his collaboration on the production and national distribution of a video tape titled "The Other Drug Problem: Medication Misuse Among Older Americans." He has delivered over 100 public speaking engagements to professional and lay audiences, including both radio and television appearances.

KEHR PATENT SUMMARY

Date	Ref. No. and Title	Status	Territory	Owner
	United States			
8/30/84	4,768,176 Apparatus for Alerting a Patient to Take Medication	Issued 8/30/88	U.S.	B. Kehr, M.D.
8/30/84	4,768,177 Method and Apparatus for Alerting a Patient to Take Medication	Issued 8/30/88	U.S.	B. Kehr, M.D.
1/17/90	5,200,891 Electronic Medication Dispensing Method	Issued 4/6/93	U.S.	B. Kehr, M.D.
7/23/90	07,556,626 Electronic Medication Monitoring and Dispensing Method	Pending	U.S.	B. Kehr, M.D.
	Foreign Patents			
6/19/85	1,293,382	Issued 12/24/91	Canada	B. Kehr, M.D.
7/05/85	0172638B1	Issued	U.K.	B. Kehr, M.D.
	0172638B1	4/22/92	Germany	B. Kehr, M.D.
	0172638B1		Italy	B. Kehr, M.D.
	0172638B1		France	B. Kehr, M.D.
3/30/86	60-145921	Issued 1993	Japan	B. Kehr, M.D.

MMTI Trademark Summary

Trademark	MEDI-MONITOR Electronic Dispenser	Worldwide
Trademark	MEDI-MONITOR Medication Dispenser	Worldwide
Trademark	T. COMPliance Operating System	Worldwide

THE WHITE HOUSE

February 25, 1994

The Honorable Constance A. Morella
U.S. House of Representatives
Washington, D.C. 20515

Dear Connie:

Thank you for your letter about Dr. Bruce Kehr and his work on medication noncompliance. I have asked Jennifer Klein on my staff to contact Dr. Kehr for more information about his research.

With best wishes, I am

Sincerely yours,

Hillary

Hillary Rodham Clinton

cc: Dr. Bruce Kehr

CONSTANCE A. MORELLA
8TH DISTRICT, MARYLAND

COMMITTEES:
POST OFFICE AND CIVIL SERVICE

SCIENCE, SPACE, AND TECHNOLOGY

WASHINGTON OFFICE:
223 CANNON HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-2008
(202) 225-5341

DISTRICT OFFICE:
51 MONROE STREET
SUITE #507
ROCKVILLE, MD 20850
(301) 424-3501

Congress of the United States
House of Representatives

November 8, 1993

Ms. Hillary Rodham Clinton
The White House
1600 Pennsylvania Ave.
Washington, D.C. 20501

Dear Hillary:

I am writing on behalf of one of my constituents, Dr. Bruce Kehr, who is a clinical psychiatrist practicing in Montgomery County, Maryland.

Dr. Kehr has been working for several years on the problem of medication noncompliance and has met with my staff to discuss the importance of this issue in the context of national health care reform. My staff was very impressed with Dr. Kehr's analysis of this issue, and I believe that he could be of assistance to the President's Health Care Reform Task Force in this important area (for your reference, I am enclosing a copy of an article written by Dr. Kehr on this subject).

In particular, I would appreciate your giving Dr. Kehr the opportunity to present to the Administration his findings with regard to medication noncompliance. He can be reached at (301) 984-9791, or at 5920 Hubbard Drive, Rockville, Maryland, 20852.

I hope that your staff will have a chance to meet with Dr. Kehr, and I thank you for your attention to this matter.

With best wishes, I am

Sincerely,

Constance A. Morella
Member of Congress

CAM:mc

Clinical Drug Trials: Fact or Fantasy?

Electronic monitoring of patient compliance—that both prompts medication-taking and records the event—could be incorporated into clinical drug trials in order to reach more accurate conclusions.

Bruce A. Kehr, M.D.*

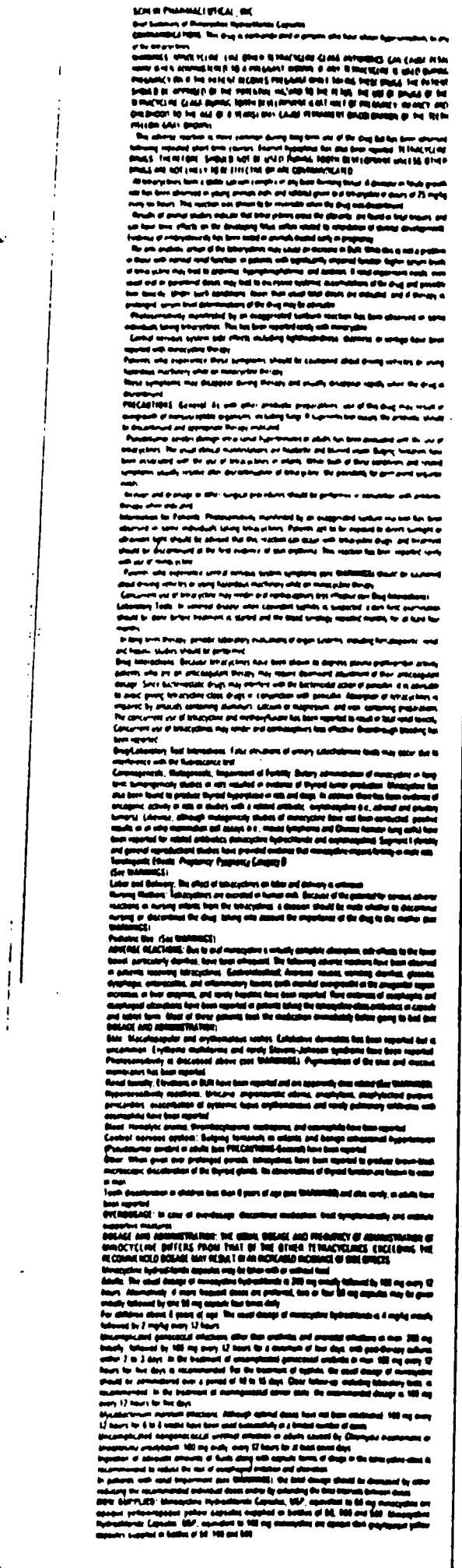
Fact: Modern medicine increasingly relies upon powerful, specific drug therapies. These drugs reach the marketplace following extensive clinical trials that examine their effects on the patient's illness, side effects, and toxicity. Then, postmarketing drug testing further examines their safety and efficacy. The average pharmaceutical manufacturer will spend between $150 million and $300 million to develop and test each new pharmaceutical agent. Hundreds, even thousands, of patients are tested with the new agent in a carefully designed, statistically elegant clinical study. And yet, a single glaring flaw exists in the design of most of these studies—under present methodology, investigators are unable to determine with any accuracy whether or not the patients are taking the medication as prescribed.

*Clinical psychiatrist and president of Contemporary Psychiatric Services, Rockville, Maryland, and chairman, Medi-Monitor Corporation

Impact of Noncompliance

Research documents consistently state that one-third to one-half of all patients on drug regimens fail to take prescribed medications correctly. In clinical trials, consistent underdosing and periodic drug holidays (taking a vacation from taking the medicine) create a large negative impact. So large, that a report in the *Annals of Allergy* states, "If the levels of noncompliance that we have demonstrated are indeed representative of the general level of compliance in clinical trials, they cast considerable doubt on the validity of many such trials."

What does this mean in practice? In the standard clinical trial, at each visit where the patient returns to the clinician/investigator, an interpretation is rendered as to how the clinical experiment is going. If the patient achieves the therapeutic goal, the clinician/investigator retains the regimen; if not, the regimen may change. This simple algorithm assumes near perfect medication com-



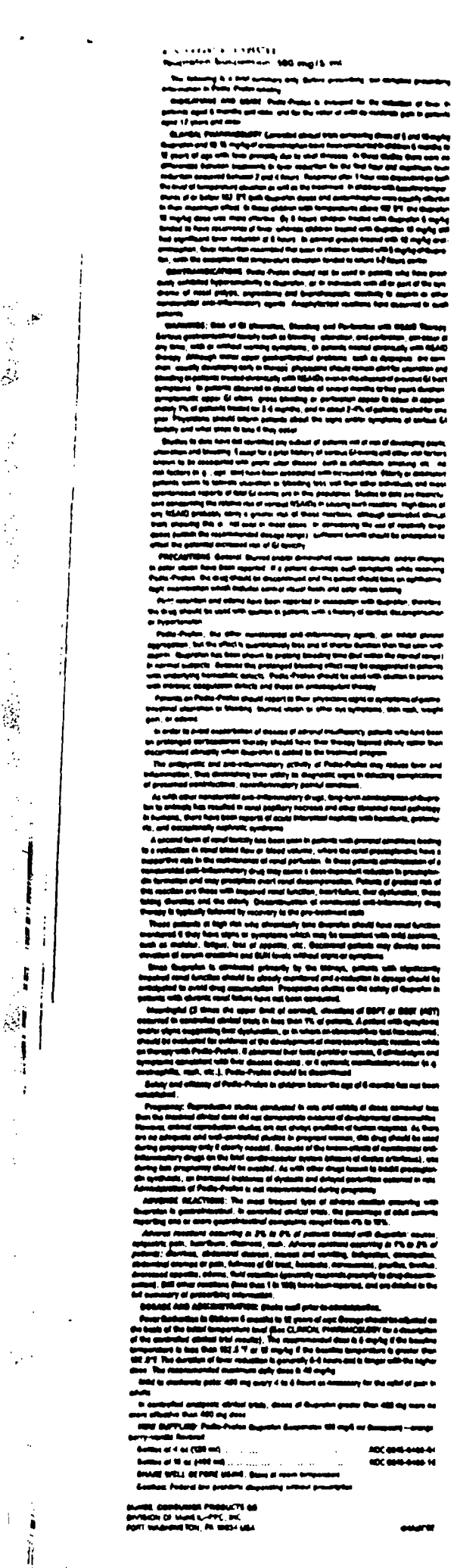
pliance. However, poor compliance in clinical trials could result in a number of erroneous conclusions regarding the medication. If patients take only a portion of the prescribed amount, it may be deduced incorrectly that the active treatment is of no therapeutic value. Preferential compliance with one of two regimens undergoing rigorous comparison can also mislead investigators into deducing that one regimen is less effective (or safer) when it is not. The end result? Potentially valuable medications may be discarded because unrecognized underuse leads to failure to demonstrate efficacy. Many medications released for clinical use may actually be more effective than the data from the clinical trials would suggest. Because of these errors in interpretation, in some cases of new drug introductions the minimal dose selected at first marketing was fourfold to sixfold higher than necessary.

Conversely, a medication may appear to have an unacceptable frequency of adverse reactions if inadvertent overuse leads to toxic effects. This too may lead to the drug being taken off the market. Then, also, toxic effects may be concealed by underuse during clinical trials, only to become apparent during postmarketing surveillance.

Measuring Compliance

Given the critical relevance of medication compliance monitoring to the interpretation of results in clinical drug trials, what are the traditional compliance measures? Industry standards to date have included patient self-report, pill counts, biologic assays, and investigators' opinions. Each of these measures is suspect. Regarding self-reports, Dr. F.W. Engstrom notes, "Some patients took medicine much less frequently than they said they did."

Commentary on pill count measures is even



more troubling. Dr. Peter Rudd has noted that pill counts misclassify compliance sufficiency in 22% of all patients. He notes that pill counts have been termed "punitive measures for research assistants. In our experience, pill counts offered little more than misleading reassurance." An editorial in *The Lancet* notes, "Residual tablet counts consistently overestimate compliance."

Biologic assays, measuring the amount of the drug in blood samples, offer little reliability as well. Even if the patient has a therapeutic blood level or urine level of a drug, this does not take into account the so-called "toothbrush effect." This refers to the fact that most patients dose correctly the day or so before visiting the physician-investigator, however erratic their compliance might have been weeks and months beforehand. If the physician then measures the level of the drug in a blood sample, it will appear normal. Dr. John Urquhart has termed this the "toothbrush effect" after the way people brush their teeth just before seeing a dentist. The "toothbrush effect" also applies to the pill counting method, as these same patients will discard the correct number of pills just prior to visiting the doctor, so that when the pills are "counted" at the visit, the patient will appear to have complied with the regimen.

In an overview of these disturbing findings, Dr. Peter Rudd noted, "It has been said that all science is measurement. The entire field of medication compliance suffers from the absence of good measures. The entire infrastructure of our understanding about suboptimal medication compliance is suspect: its prevalence, determinants, impact, detection, and amelioration." What then is the clinician/investigator to do?

Fortunately, advances in technology have recently been applied to compliance measurement in clinical trials and medical practice. Electronic

monitors that record the time and date that a patient accesses the medication container bring new insights into patient self-medication behavior and the potential for new reliability in clinical trials. These devices' special attraction lies in their dynamic assessment, close in time and space, to each medication-taking event. They reduce ambiguity about medication compliance, thereby enhancing the ability to interpret variability in the biology of the disease and the pharmacology of the drug. The use of these electronic monitors has begun to reveal some shocking patterns of patient behavior in clinical drug trials.

Drug Failure or Missed Doses?

Dr. W. Kruse notes in one study that "patient-initiated drug holidays occurred in 50% of patients." Dr. Rudd notes in a trial of hypertensive medications, "pill counts indicated near perfect compliance (92% to 99%), yet the electronic monitors showed fewer than half of all medications were taken at the prescribed interval. With one patient, the pill count method revealed a mean compliance of 93%, but the electronic monitor confirmed only 21% compliance. A clinical example from the trial supports the value of the electronic monitor: one patient who had achieved good blood pressure control when his prescribed dose of antihypertensive was raised from 2.5 to 7.5 mg/day, had an unexpected rise in blood pressure during a visit to the investigator. The electronic monitor confirmed that the time interval between the last dose and the visit rose from less than 5 hours in previous visits to more than 20 hours at the last visit, corresponding to the loss of blood pressure control. Without the electronic monitor, the rise in the patient's blood pressure would have been interpreted as a failure of the drug at the 7.5 mg/day dose. Either the dosage would have been raised, possibly causing toxic effects, or the drug would have been discontinued.

Using the electronic monitor, Dr. Joyce Cramer has demonstrated that 12 to 16 patients with breakthrough epileptic seizures had missed a dose prior to the onset of the seizure.

Finally, use of the electronic monitor in antidepressant treatment shows that 90% of patients taking 90% or more of their doses improve. Those who took less than 70% of their doses had a 0% chance of improving.

New Recommendations

Physician-investigators are beginning to adopt a tough new stance regarding methods used to measure compliance in clinical trials. A recent Task Force of the American Academy of Allergy and Immunology and others recommended that measures to monitor and enhance compliance be included in the design of all trials evaluating new antiasthma medications.

Monitor technology is far from perfect, as the circuitry can record each opening but cannot ensure actual drug consumption. As well, a survey of 368 medical outpatients on a variety of regimens revealed that remembering to take medications was a common obstacle to medication-taking. Fully 36% of all respondents indicated this problem, especially females under age 50. Clearly, if one is to both "monitor and enhance" compliance in clinical trials, additional features must be added to the electronic monitors.

Studies by Drs. Azrin and Powell confirmed via direct observation that when patients are given a pillbox that beeps when it is time to take medication, they indeed take the medication on time and do not throw it out. In a separate study, Dr. Marshall Becker concluded that an alarm pillbox substantially improved patient compliance, and

achieved a high degree of patient acceptance. Therefore, a medication monitor that both prompts patients when to take medications and then records the medication-taking event is as close to the "gold standard" as we can get.

Benefits of Electronic Monitoring

Pharmaceutical manufacturers could readily incorporate electronic monitoring of patient compliance into clinical drug trials and postmarketing drug testing. The expense of this electronic monitoring pales in comparison to the hundreds of millions of dollars spent to launch a drug, only to falsely conclude that the drug is either ineffective, or unacceptably toxic. Clearly, any rational approach to the interpretation of clinical drug trials must incorporate some type of electronic monitoring. Pharmaceutical companies must be strongly urged to incorporate these technologies as rapidly as possible.

As for the future, technologies are now in development that will first prompt the patients to take their medications and then record their behavior. In addition, these technologies will interact with the patients using a variety of language displays, further enhancing the likelihood that patients will take their medicines as prescribed.

Clinical medical practice will also benefit from these technologies, as patients and their physicians review together the history of the patient's self-medicating behavior during routine office visits. Instead of a poor patient outcome prompting the physician to increase the dose of the patient's medication, switch the patient to another medication, or add yet another medication, patient and physician will review the pattern of medication-taking behavior and make decisions based on science, not guesswork. The end result will be hundreds of thousand of lives saved and a reduction in unnecessary health care costs of billions of dollars. (PT)

FACTS ABOUT DIABETES

- **Approximately 14 million Americans suffer from diabetes.**
- **An estimated 200,000 of them will die from diabetes and its complications this year.**
- **The two major types of diabetes are juvenile (insulin-dependent or Type I) diabetes and maturity-onset (non-insulin-dependent or Type II).**
- **Juvenile diabetes is the more severe form of the disease, appearing at any age.**
- **People diagnosed with juvenile diabetes must take daily insulin injections to stay alive.**
- **People with diabetes are more likely to develop other complications, including kidney disease, heart disease, stroke, blindness, and gangrene.**
- **The death rate from kidney disease is 500 times higher in young adults with diabetes. Of all dialysis patients, 32% have diabetes-caused kidney failure, at an annual cost of over $1.7 billion in Medicare payments.**
- **People with diabetes are twice as likely to die of heart disease.**
- **The incidence of stroke is two to six times higher in people with diabetes.**
- **Blindness changes the lives of 6,000 people each year as a result of diabetes, the leading cause of new adult blindness in the U.S., costing over $75 million annually in federal and state aid.**
- **Amputations as a result of diabetes are performed on over 50,000 people each year. The likelihood of an amputation is 15 times greater for people with diabetes.**

THE WHITE HOUSE

February 25, 1994

The Honorable Constance A. Morella
U.S. House of Representatives
Washington, D.C. 20515

Dear Connie:

Thank you for your letter about Dr. Bruce Kehr and his work on medication noncompliance. I have asked Jennifer Klein on my staff to contact Dr. Kehr for more information about his research.

With best wishes, I am

Sincerely yours,

Hillary Rodham Clinton

cc: Dr. Bruce Kehr

CONSTANCE A. MORELLA
8TH DISTRICT, MARYLAND

COMMITTEES:
POST OFFICE AND CIVIL SERVICE

SCIENCE, SPACE, AND TECHNOLOGY

WASHINGTON OFFICE:
223 CANNON HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-2008
(202) 225-5341

DISTRICT OFFICE:
51 MONROE STREET
SUITE #507
ROCKVILLE, MD 20850
(301) 424-3501

Congress of the United States
House of Representatives

November 8, 1993

Ms. Hillary Rodham Clinton
The White House
1600 Pennsylvania Ave.
Washington, D.C. 20501

Dear Hillary:

I am writing on behalf of one of my constituents, Dr. Bruce Kehr, who is a clinical psychiatrist practicing in Montgomery County, Maryland.

Dr. Kehr has been working for several years on the problem of medication noncompliance and has met with my staff to discuss the importance of this issue in the context of national health care reform. My staff was very impressed with Dr. Kehr's analysis of this issue, and I believe that he could be of assistance to the President's Health Care Reform Task Force in this important area (for your reference, I am enclosing a copy of an article written by Dr. Kehr on this subject).

In particular, I would appreciate your giving Dr. Kehr the opportunity to present to the Administration his findings with regard to medication noncompliance. He can be reached at (301) 984-9791, or at 5920 Hubbard Drive, Rockville, Maryland, 20852.

I hope that your staff will have a chance to meet with Dr. Kehr, and I thank you for your attention to this matter.

With best wishes, I am

Sincerely,

Constance A. Morella
Member of Congress

CAM:mc