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REPORT OF A WORKSHOP

Drug Development
for the
Geriatric Population

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Institute of Medicine

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This meeting summary was prepared by Laura Ost, Kimberly Kasberg, and the staff of the Institute of Medicine's Division of Health Sciences Policy, Forum on Drug Development. Major themes are reported to provide highlights of the conference discussions; however, they do not represent policy statements by the Institute of Medicine.

The Institute of Medicine was chartered in 1970 by the National Academy of Sciences to enlist distinguished members of the appropriate professions in the examination of policy matters pertaining to the health of the public. In this, the Institute acts under both the Academy's 1863 Congressional charter responsibility to be an advisor to the federal government, and its own initiative in identifying issues of medical care, research and education.

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DRUG DEVELOPMENT FOR THE GERIATRIC POPULATION

Proceedings of a Workshop

Despite widespread recognition of the "graying of America," and the greater need for health care among older people, there is a dearth of information about their appropriate use of drugs. Problems of over-medication, under-medication, and adverse drug interactions are disturbingly common among older patients. Difficulties in prescribing drugs for them are caused by factors that include polymorbidity, polypharmacy, and individual variations in the physiological changes of aging.

Only half of the drugs used by those over 65 years of age contain specific information in package insert literature about geriatric use. Furthermore, the most senior of the elderly -- age 85 and over -- seldom have been included in sample populations for drug studies. This may reflect the slow response of researchers to address the most basic questions in geriatric pharmacology, such as why the effectiveness of drugs varies so widely among older persons.

Geriatric pharmacology also needs to dispel some widely-held myths and misunderstandings about the aging process. According to a study by Lawrence Klein, 40 percent of older outpatients view their side effects to drugs as a result of normal aging. These misunderstandings can be propagated by physicians themselves. In a recent survey by Gerald Avorn, it was revealed that a large proportion of primary care physicians in Boston mistakenly believe senile dementia is caused by insufficient blood flow to the brain.

Persons aged 65 and over are only 12 percent of the population but account for approximately 30 percent of all drugs prescribed. There are indications that the average older patient has 14 to 18 prescriptions a year. However, it is unclear how many different prescriptions are used concurrently or are refills of the same prescription. According to a review by Mark Beers, approximately 40 percent of the drugs taken by this population are either overused or misused. Furthermore, Gerald Avorn suspects that many older persons do not receive sufficient medication for certain conditions, such as hypertension.

WHAT IS KNOWN ABOUT THE BIOLOGY OF AGING

Although older persons vary widely in their overall health status and physiological response to drugs, some generalizations are possible. Beers summarized many uniform physiological changes associated with aging:

The Brain As the body ages, the volume of blood circulating through the brain decreases. In some instances, the blood circulation through the brain may diminish to the point where any sudden drop in blood pressure, perhaps caused by an antihypertensive drug, may result in fainting.

The aging process may also effect changes in brain chemistry. Many older persons become increasingly sensitive to drugs which affect cholinergic neurotransmission. Many medications, including antidepressants, cold remedies, and over-the-counter sleeping pills, can inhibit the action of the cholinergic system leading to confusion, delirium, and dementia-like symptoms. Such drugs have also been shown to increase urinary retention and aggravate existing conditions such as blurred near vision.

The Heart Maximal cardiac output appears to decline with age, and the response to physical demands slows. The number of pacemaker cells decreases. The heart muscle thickens and becomes stiffer requiring more contractions to move the same volume of blood. Drugs that affect the heart's ability to pump, such as some calcium channel blockers and beta blockers, may precipitate congestive heart failure. Vasodilators, used to treat angina, may cause fainting. Despite increased levels of the neurotransmitter norepinephrine in many older persons, their bodies are less responsive to its effects. Thus, a classic warning sign of toxicity -- a rapid heart rate -- may not alarm the physician.

GI Tract The aging gastrointestinal tract is subject to constipation because of physiological changes and increased sensitivity to factors that affect motility. Anticholinergics and narcotics, which may further slow the digestive system, can lead to impaction. It is also common for gastric acid secretion to decrease in older persons. Thus, drugs that are adversely altered by an acidic environment, such as penicillin G, will be more efficiently absorbed. Conversely, drugs that require an acid environment for absorption, such as iron preparations, would be less efficiently absorbed.

The ability of the kidneys to concentrate urine and regulate internal blood flow decreases in many older persons. Therefore, nonsteroidal anti-inflammatory agents can precipitate renal failure. A reduction in renal blood flow also slows the ability of the kidneys to eliminate drugs. Bladder capacity decreases and consequently the risk of diuretics causing incontinence increases. Analgesics and anticholinergics can weaken bladder muscles in such a way as to cause urinary retention.

Sexual Function Testosterone levels and the concentration of other sex hormones decrease in many older men. This, in conjunction with atherosclerosis, contributes to the higher incidence of impotence in men over 75. Drugs such as anticholinergics can further complicate sexual dysfunction.

Other Changes Blood concentrations of albumin, the main binding protein for most acid drugs, generally decrease in older persons. Therefore, to obtain the same drug concentration in older patients as observed in a younger patient, more free (unbound)

drug must be available to act and to be eliminated by the liver and kidneys. As lean body mass declines in older persons there is a decrease in the distribution of water-soluble drugs and a concurrent increase in the distribution of fat-soluble drugs.

Although there are many physiological changes that occur more frequently in older people, not all individuals will necessarily experience each of these changes. According to T. Franklin Williams, the most recent studies show little or no degeneration in maximum cardiac output, renal or sexual function, or serum albumin in many older people. When changes are found they are largely secondary to disease. Nonetheless, because chronic disease is common in older persons -- particularly those taking multiple medications -- physicians should look for changes that may affect a patient's responses to drugs.

COMMON PROBLEMS IN STUDYING OLDER POPULATIONS

How Old is Old? Individual biological responses to aging may be influenced by a variety of factors, including overall physical or nutritional condition, smoking, and weight. Age alone cannot be considered the sole determinant for augmented biomedical or pharmaceutical research. Researchers arbitrarily select ages to designate older populations, and some research literature does not even define the label "elderly." Moreover, studies of hypothetical physiological responses to drugs as a function of age may not even specifically address the question they pose. Most studies are cross-sectional rather than longitudinal because it is easier to compare different people at different ages. The results may not be due to the effects of aging, but rather to individual variations that are better explained by factors other than age.

Mistaken Assumptions Although logic may seem to indicate that all biological functions are impaired with age, Michael Mayersohn's review of the body's absorption capability disproves such sweeping assumptions. What Mayersohn found was that the body's ability to absorb medications does not diminish with age. The fact that elderly test subjects do not excrete as much of a drug in urine as younger test subjects is a function of the aging kidney's reduced ability to clear the drug from the body. Further testing with different chemical compounds corroborated these findings that age does not affect the body's ability to absorb drugs.

Drug Metabolism Researchers still have many questions about how the body absorbs, distributes, metabolizes, and excretes drugs -- the study of pharmacokinetics. Many factors can affect drug metabolism, including liver weight, volume, and blood flow, all of which decline with age. However, scientists do not know how to predict the metabolic capabilities of the aging liver, largely because they have not found a reliable means of measuring such processes.

Although numerous pharmacokinetic studies of the elderly have been undertaken, many of these are flawed, according to Darrell Abernethy. The studies often are based on single or short-term doses of medications (i.e. acute), yet actual usage often continues for a long period of time (i.e. chronic). Abernethy's laboratory studied hypertensive patients, one group over age 65 and the other younger than 40, who were taking diltiazem, a calcium channel blocker used to treat angina and other conditions. Drug clearance (a measure of the ability of the body's organs to eliminate drugs) was the same in both groups, whether the dose use was acute or chronic. However, the time required to eliminate half of the drug from the body was increased with chronic use in both young and old. This increase in half-life was due to increased distribution in the body, and not a result of a change in clearance by the kidney and liver.

Abernethy hypothesizes that the duration of dosage may be a much more important variable than aging in determining pharmacokinetic features. Furthermore, he believes that the proper method for extrapolating acute-use data to chronic dosing situations is "simply unknown" for most drugs. He concluded that the development of a database for chronic dosing situations will be very important for the future if scientists are to be able to predict the effects of aging on determining appropriate drug dosing.

Adverse Drug Interactions The extent of adverse drug interactions in the elderly is uncertain. However, it is known that 3 to 8 percent of all admissions to general medical wards are attributed to adverse drug reactions (ADRs). Those using multiple medications, including many older persons, are considered especially vulnerable to adverse drug interactions. There is a paucity of data on drug interactions, which are not part of the evaluations for safety and efficacy that must be done before a drug is marketed.

A classic example of adverse drug interactions is digoxin (a drug that strengthens the pumping action of the heart) combined with quinidine (a drug for the control of cardiac arrhythmias). Digoxin clearance decreases in the presence of quinidine. This results in the body storing more digoxin than the pre-marketing testing indicated, thus increasing the risk of an individual accumulating toxic amounts of digoxin at recommended dosing levels.

SUGGESTIONS FOR IMPROVING GERIATRIC PHARMACOLOGY

Design drugs specifically for older people. In general, older patients have less tolerance for drug-induced biological changes than do their younger counterparts. Therefore, ideal drugs for the elderly would produce effects at a pace that maintains physiological balance -- slowly enough to avoid undue shock to their systems, yet quickly enough to relieve symptoms at minimal doses. Despite the special attention warranted by the geriatric

population, drugs often are not tested in many subjects over 75, although dosages can be adjusted for that age group. Now, however, through advanced technology, drugs could be designed to fit the particular needs of the aging body.

For example, the elderly lose elasticity in blood vessels and the heart. Therefore, the ideal cardiostimulant agent would counteract this condition by relaxing the stiff walls of the ventricle, to enhance filling. At the same time, the aging body's maximum cardiac output decreases and its peripheral vascular resistance increases (the blood vessels become less elastic requiring the heart to work harder). Hypothetically, an ideal hypertensive drug would not decrease cardiac output but rather decrease peripheral vascular resistance.

Consider quality-of-life endpoints. According to Gerald Avorn, cognitive deterioration may be the most important adverse effect of a drug, even though the drug may be prescribed for completely unrelated conditions. In evaluating drugs for the elderly, researchers should not restrict evaluation to efficacy and physical side effects, but also consider the patient's ability to function normally. The questions should be asked: Does this drug increase independence? Is this drug causing confusion, depression, or incontinence?

Consider cost-containment policies. Drugs are probably the most cost-efficient means of treating medical conditions. Prescription prices, however, have been increasing. The rise in the cost of prescription drugs has attracted the attention of policy makers who are concerned about holding down escalating health care costs. Research has shown that policies aimed at containing the costs of prescription drugs should be considered very carefully to prevent unexpected negative repercussions.

For example, Avorn's research of the New Hampshire Medicaid program's decision to pay for only three drugs for each beneficiary per month showed that the number of insulin prescriptions filed for reimbursement dropped dramatically. When the state discarded the cap in favor of a \$1 co-payment system, the number of insulin prescriptions rose. That led researchers to conclude that the drug was important to the patients but was dropped -- perhaps instead of less critical drugs -- for financial reasons. The research team now is determining how many patients became seriously ill as a result of the cap and whether it cost more to treat them than it would have cost to pay for the medication.

Study the very old, and get the results to physicians. During the next decade, the population over 85 will almost double. Yet, in past studies of some drugs, such as the antimicrobial sulfanilureas, and their use in the aged, none of the subjects was over 75. Those over 85 years old, the "oldest old," must be included in future studies if possible. Furthermore, the results of this type of research must be disseminated to physicians who

may have difficulty gaining access to the latest information about pharmacodynamics (the effect of a drug on the body), pharmacokinetics, and drug interactions. Possible methods for widely disseminating recent findings include connecting a central information bank to computers in physicians' offices, or encouraging more interaction between pharmacists and health care providers.

Whatever programs for disseminating research findings should be developed, they must be planned and managed carefully. According to Jeffrey Halter, "If tomorrow there were development of a tremendous data base on people over age 85, it would probably take me two years to get to it. The information overload possibilities are tremendous."

Discontinue use of unsafe and/or unneeded drugs. Some drugs are not significant advances over existing products. Sidney Wolfe argues that the Food and Drug Administration should not be allowed to waste its time considering, or be allowed to approve, drugs with no advantages in safety or effectiveness over those already on the market. Other scientists disagree, arguing that no one can forecast whether a drug will be clinically significant until it has been in widespread use for some years.

Some drugs are used more widely than just those for whom the medication has been proven safe and/or effective. Furthermore, according to Wolfe, more than two million older Americans take a sleeping pill or tranquilizer every day for at least a year. Yet, he said, there is no evidence that the sleeping pills are effective beyond 15 to 30 days, or the tranquilizers for more than four months.

"Many of these people are suffering one or more of the side effects or adverse reactions from the drugs, and yet there is no clear evidence that they are benefiting at all from them," Wolfe said. Furthermore, some drug side effects include conditions that can be wrongly attributed to old age. Wolfe estimates that thousands of people have symptoms of Parkinson's disease that are induced by drugs.

There is need for increased training in geriatrics, pharmacology, and pharmacoepidemiology. People over 65 use nearly a third of all medical resources. However, fewer than 300 faculty members in U.S. medical schools are specialists in geriatrics, T. Franklin Williams has noted. Moreover, according to a new survey, less than one teaching faculty member in geriatrics per school has had formal training in the field.

"How are you going to develop a research environment under these circumstances?" William Abrams asked. ". . . With deficits in geriatrics, gerontology, education and training programs, deficits in clinical pharmacology education and training programs, there is little wonder why there are insufficient experts in centers to study the drugs used by this preponderant medicine-using segment of the population."

Some improvement in the supply of clinicians with training in geriatrics is expected. Beginning this fall, residency programs in internal medicine must include geriatrics to be approved by the Accreditation Council for Graduate Medical Education. In addition, the National Institute on Aging has issued a request for proposals in geriatric pharmacology, and The Merck Company Foundation is sponsoring a training program in the field in which six fellows are enrolled. However, there are as yet no graduates of formal training programs in pharmacoepidemiology.

IMPROVEMENTS UNDER WAY IN DRUG MONITORING

Throughout the 1980s, the FDA has increased its monitoring of drugs in the geriatric population. The agency is trying to ensure that older subjects continue to be included in clinical trials and that research results are analyzed with respect to age and other relevant factors, such as multiple medical conditions or drug use. The agency encourages measurement of steady-state blood levels in essentially all subjects to learn whether the elderly have higher levels of a drug on average and to detect unexpected influences of concomitant conditions and medications.

Beginning in 1986, the agency asked manufacturers to analyze the influence of demographics and other relevant patient characteristics as part of applications for drug approval. A survey showed that, for 20 drugs approved in 1988, about 30 percent of the subjects were over 60 years old, and that pharmacokinetic studies for the elderly were conducted for 7 of the 9 drugs approved that involved chronic use. These analyses detected only minor side effects. For instance, with the calcium channel blocker, nifedipine, facial flushing was less common in older patients. In the near future, FDA regulations are expected to require a section on geriatric use in drug package inserts. This regulation would cover all new medications and eventually be retroactive to drugs already on the market.

In another fairly recent change, the FDA has centralized and restructured reporting of adverse drug reactions. Prior to 1983, the FDA logged 10,000 to 20,000 adverse drug reactions per year. Now the agency logs about 50,000 in a year. Reports for patients over age 65 have increased proportionately. Companies now must classify ADR forms in terms of severity and forward them to a central location within the FDA. In addition, the vague definition of reportable unexpected reactions was changed to mean any reaction not listed on the drug label. Serious reactions (hospitalization or death) must be reported within 15 days. Reports are screened by a pharmacist or physician, and incidents deemed worthy of discussion are reviewed weekly by an FDA committee. Problems requiring further study are forwarded to epidemiologists.

SUMMARY OF THE NEEDS

Achieving appropriate medication usage in the older population will require further research on drug metabolism and distribution in the aging body. More physicians and researchers must become knowledgeable in the fields of geriatrics and pharmacology to improve both the treatment of patients and the design and extent of research on prescription drugs in the elderly. Many more post-marketing epidemiological studies need to be conducted to find links between drug use and biological effects, particularly when multiple drugs and diseases are present. In addition, there should be greater public awareness of the special needs of the elderly, particularly as the government develops new methods for controlling health-care costs and scientists harness advanced technology for drug design.

ANSWERING SOME OF THE QUESTIONS

In order to conduct post-marketing epidemiological studies, researchers must have access to large, computerized databases. Such databases must represent adequate numbers of older people and track them over time. The data also should contain answers to several critical questions, including the medical condition being treated, and the date, dosage, and schedule of medication. In the United States, these data are available from Medicaid, Medicare, health maintenance organizations, and state-run pharmacy reimbursement programs.

A Model Database The province of Saskatchewan, Canada, has what may be a model system for epidemiological studies. Data are fully accessible, and researchers can track down extensive information if necessary, including patients' medical records or even the patients themselves. Furthermore, a special government unit has been established to assist researchers.

In Saskatchewan, each of the one million inhabitants has a health services number, making possible both longitudinal and cross-sectional tracking of virtually the entire population. Specific information on drug use by older persons is extensive. In 1986-87, the province's prescription drug services branch paid for prescriptions that were used by 85 percent of the population over age 65. Each data entry includes: the drug dispensed by brand name, active ingredient, the strength, the form, the quantity dispensed, the date dispensed, prescriber, pharmacy, and cost.

According to Linda Strand, concerns about possible misuse of the data are outweighed by recognition of the importance of this kind of research. Confidentiality of all involved is protected, and more than 30 research projects have been completed without causing problems for the government, she noted. "It is recognized that the data are available and that they are a valuable resource for drug epidemiology studies, and therefore systems are in place to enable their use." However, the database

is not perfect. It does not include, for example, laboratory data on patient responses to drugs. To add that feature, health officials would need \$1.5 million to computerize the provincial laboratory.

Medicaid Data These records represent only the low-income U.S. population, but otherwise are fairly complete. The data include diagnostic information, which can be used to identify cases, and prescriptions filled, which can indicate drug exposure. The data also contain some demographic characteristics of patients, which can be linked to other sources, such as death certificates, to obtain specific information such as date and cause of death. However, the data are not organized for ease of research. Medicaid is run by individual states, so there is wide variation in availability of diagnostic information and in numbering systems for patients.

The biggest problem is the potential for misclassifications of medical conditions. Researchers must confirm computerized entries of a disease through a structured review of medical records. Failure to do so can skew the results, Wayne Ray emphasized. Misclassification "will give us a false sense of security. It will tend to dilute the association" between a drug and an undesired result, he said. That is because the study population will include people who do not really have the condition and thus are less likely to have used the drug.

In a study of the 1976-84 Tennessee Medicaid population, for example, Ray confirmed only 122 of 159 possible cases of fatal peptic ulcer disease, or 77 percent. The researchers were looking for a link to non-steroidal anti-inflammatory drugs, requiring disease onset close to the time of hospital admission. Of the 122 cases, 96 had onset within 14 days of admission. So, without the confirmation process, the computer records would have been only 59 percent accurate.

Medicare Data These records, maintained by the Health Care Financing Administration, represent all economic groups but are not as complete as researchers would like. For instance, diagnosis is included in part A (hospitalizations) but not in part B (physicians' office visits). Additionally, there is no information about the frequency with which a drug is taken.

"The HCFA data system is both one of the very richest that I've ever encountered, and also in many ways one of the most frustrating," Stephen Jencks said.

More extensive data on drug use may become available in the next few years. The Medicare Catastrophic Coverage Act of 1988, which is designed to help Medicare beneficiaries with unusually high health care expenses, includes a provision for outpatient prescription drug benefits.¹ The benefits, scheduled to go into

¹. The Medicare Catastrophic Coverage Act of 1988 was repealed by Congress subsequent to this workshop.

effect in 1991, would pay partial costs of prescribed FDA-approved drugs that are administered at home.

Data from this program (sometimes referred to as Medicare part C) would be gathered by participating pharmacies in a point-of-sale electronic billing system connected to the HCFA central database. The data would then be organized into summary files for each drug, each doctor, and each pharmacy. For longitudinal studies, files for a 5 percent sample of the population would contain complete billing records. Through health insurance claims or Social Security numbers, the files could be linked to parts A and B, provided those records are incorporated into an accessible database.

Concerns About "Part C" Congress wanted to have a system for identifying doctors and pharmacists involved in patterns of "inappropriate prescribing" or "substandard care," and for correcting the problem through educational programs. This will prove to be a difficult task because diagnoses would not be listed on prescriptions. The only computerized method of tracking down a patient's diagnosis would be to link part C records to other HCFA data. The easiest solution would be to list the diagnosis on the prescription. However, this approach could invite the sort of inaccuracies that Ray found in Medicaid records, with doctors listing only superficial symptoms or only one of several conditions present. Another concern is the mechanism for educating doctors about problems with their aging patients' drug use. Pharmacists would be expected to counsel patients on drug use, but feedback to doctors might depend on the patients themselves. Many older persons have cognitive deficits that can make it difficult to understand technical health care problems without assistance, or to accurately communicate the pharmacists' advice to a doctor. Furthermore, they may have several different doctors, all of whom are prescribing, unknown to each other, a variety of drugs that could have undesired interactions.

The government assumes that problems will be managed through professional judgments and thoughtful discussions. "There is supposed to be a learned discourse between the actual parties based on a review of the claims to determine if there is a funny pattern," Ann Morgan Vickery said. However, it would be impossible for HCFA to administer an elaborate system for monitoring prescribing practices.

"We need to have some system that really responsibly addresses this issue when some flagging of a potential interaction appears," T. Franklin Williams said. Scientists are concerned about HCFA relying on claims processors rather than medical experts to warn of possible adverse interactions of mail-order drugs. One solution might be to require Medicare beneficiaries to select a primary pharmacist, who would have access to the patient's complete drug records and be responsible for counseling. However, this type of access raises the issues of confidentiality. A pharmacist who sees a patient's complete

medication profile would note drugs that imply sensitive conditions, such as AIDS. Furthermore, there is no guarantee that the advice of the pharmacist would be consistent for each potential drug-to-drug interaction. This concern is supported by a study cited by Daniel Everitt which found little consensus among medical experts about which drugs interact.

Maximizing Use of HCFA Data for Research About \$50 million in the HCFA 1990 budget was earmarked for effectiveness research, but none was allocated for research on medications. Similarly, the FDA has for 20 years been constrained by a small and stagnant budget for epidemiological studies on reports of adverse drug reactions. Their annual budget is only \$1.5 million.

In addition to hoping for improved funding for drug research, scientists emphasized that HCFA data must be as complete and accessible as possible. They need, for example, adequate samples of sub-groups such as the very old and ethnic populations. At the same time, they must provide for some control of the users to ensure that the data are not used improperly. "Some system needs to be built into the access process . . . that would in effect be a peer review of the quality of the scientists and of their proposal, up front," Williams said.

Scientists hope the expanding HCFA data base can be used creatively, not only to improve drugs and drug prescribing for the aging population, but also to detect patterns of drug use. Researchers might learn, for example, how use of a particular medication or medical technology varies by geographic area. Are some advances essentially unknown to rural practitioners? Other studies might show whether physicians are prescribing drugs for conditions outside of their specialty.

"Potentially this data base is a gold mine of that sort of information that is not (now) in the academic or public domain," Daniel Everitt said. "The incredibly large numbers of people . . . give unbelievable statistical power to look at certain associations, but I think the greater the power we have, the greater the responsibility . . . to develop (a more refined) science of this kind of work."

**Forum on Drug Development and Regulation
Drug Development and Aging Populations
Institute of Medicine**

Lecture Room
2101 Constitution Avenue, NW
May 24-25, 1989

DAY I: The Science of Aging and Drug Development

8:00am Continental Breakfast

**8:30 Introduction: William Kelley
Identification of the issues.**

8:45 Biology of aging

Moderator: Leslie Benet

**The physiologic changes in normal aging.
Mark Beers**

**Aging as a variable in pharmacokinetics.
Michael Mayersohn**

**Aging as a variable in pharmacodynamics.
Darrell Abernethy**

**Common diseases in the elderly and drug effects: Known
and potential interactions.
Janice Schwartz**

12:00 - 1:15pm Lunch

**1:15 The side effects of drugs: The special sensitivities
of the elderly.
Gerald Avorn**

**Rational drug dosing in the elderly: The known,
speculation, myths and needs for further study.
Jeffrey Halter**

2:45 - 3:00 Break

3:00 **Panel Discussion: Drug Development in the Elderly.**
 Moderator: Frank Williams

What additional questions need to be answered?
Sidney Wolfe

What is the current practice?
Robert Temple

What restrictions/barriers exist to studies in the elderly?
William Abrams
Dan Azarnoff

4:30pm **Adjourn**

4:30 - 5:30pm **Reception in the Members Room**

**Forum on Drug Development and Regulation
Drug Development and Aging Populations
Institute of Medicine**

DAY II: Data Bases: Impact on Utilization and Development

8:00am Continental Breakfast

**8:45 Identification of the issues.
Moderator: Gerald Avorn**

**Post-Marketing Surveillance in the Geriatric
Population.**

**Spontaneous reporting and how it is managed.
Charles Anello**

**Existing drug epidemiology data bases.
Linda Strand**

**Impact of Provisions of the Catastrophic Coverage Act
of 1988 on Geriatric Populations.**

**What is the relevant law?
Ann Vickery**

**The role of HCFA: The database and its uses.
Stephen Jencks**

12:00 - 1:15pm Lunch

**1:15 Quality of the HCFA data base.
Wayne Ray**

**Potential uses of the HCFA data base: Benefits and
risks.
Dan Everitt**

3:00 - 3:15 Break

**Discussion: "What Must Be Done for the Law to Work?"
Improvements in the HCFA data base.**

4:00 Summary: William Kelley

4:30pm Adjourn

**Speakers for Workshop on
Drug Development and Aging Populations
May 24-25, 1989**

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