PART IV. REPORTS TO THE COMMISSION

Chapter 8. Philosophical Perspectives

Papers on the ethical issues involved in research with prisoners were prepared for the Commission by Roy Branson, Ph.D., Cornel Ronald West, M.A., and Marx W. Wartofsky, Ph.D.

Dr. Branson first analyzes the ethical principles underlying the standard arguments for and against research involving prisoners, and, secondly, examines several policy alternatives. He concludes by recommending a moratorium, appealing to the principles of free and informed consent and justice.

In reviewing arguments for experimentation, Dr. Branson cites three justifications generally advanced in support of research involving prisoners: (1) that it contributes to the good of society, of which prisoners are members and therefore recipients of benefits; (2) that it is an appropriate way for prisoners to make reparation; and (3) that prisoners can, in fact, give free and informed consent. A varient of the third argument is that criminal conviction presupposes competence and responsibility; therefore, prisoners must be presumed to have the capacity to volunteer. In fact, advocates of this position point out that prisoners are permitted to choose work in hazardous industries and so should be permitted to choose work as research subjects as well.

Opponents of prison research assume that experimentation is different from other occupations. A person's relationship to his body is not his relationship to his goods. A person's body, in a special and real sense, is

the person. In experimentation risk to bodily integrity is primary to the activity, whereas in other occupations, the risk is secondary.

The two fundamental principles to which opponents of experimentation appeal are free and informed consent and justice. Those citing consent can say that prisoners cannot in principle give free consent because of the inherent nature of prisons as coercive, total institutions. Other opponents appealing to free consent do not go so far. They claim that sufficiently free consent to experimentation cannot in fact be given in American prisons. They cite not only the coercive structure of prisons, but such administrative features as limited alternative to earn money in prisons (none for equivalent rates of pay), and indeterminate release dates with nonobjective or unknown conditions for leaving the prison. Dr. Branson identifies himself with the second position, saying that empirical analyses leave a serious and reasonable doubt that inmates of American prisons can in fact give a sufficiently free consent to experimentation.

Justice is the other principle to which opponents of prisoner experimentation appeal. Injustice can take the form of injury, when a person is wrongfully harmed through exploitation or negligence by others. Injustice can also result from failure to follow the basic requirement of distributive or comparative justice: that like cases are to be treated alike and different cases be treated differently. Since prisoners are in relevant respects equal to free persons, the burdens of risk and harm should be proportional to those of free-living citizens, which would entail a significant reduction in at least phase 1 drug trials. On the other hand, prisoners are unequal to free persons in important respects in that they have been placed in total institutions.

Dr. Branson, citing comparative justice, says the similarities of prisoners to free persons requires that the proportion of experimentation utilizing prisoners should be reduced. The differences between experimentation conducted on prisoners and those conducted on free persons require that prisoner experimentation be stopped, at least until conditions change.

In applying principles to policy alternatives, Dr. Branson sees remuneration as a major and finally insurmountable practical obstacle to prisoner experimentation. The principle of informed consent dictates that in order for prisoners to give consent that is not coerced, they should not be paid more for experimentation than for other prison jobs. But the principle of justice requires that rates of remuneration to prisoners should be equivalent to the rates paid to free volunteers. Schemes relying on committees of prisoners (or prisoners and prison officials) controlling funds created by the difference between the standard amount paid by drug companies and what an individual prisoner received run into practical problems, for the committee itself could manipulate and coerce prisoners.

Dr. Branson's recommendation, therefore, is that the Commission declare a moratorium on prison research and suggest that if and when conditions in American prisons have improved, then research might be resumed in those facilities which can meet the requirements of informed consent and justice. He would not preclude the possibility of offering innovative therapy to an individual inmate in need of treatment, but this, he says, should be distinguished from programs of "therapeutic research" which blur the distinction between individual therapy and experimentation. He suggests, in addition, that the moratorium extend to behavioral research, since new behavioral therapies may

be evaluated first on nonprisoners, but that observational research (noninterventional behavioral research), as well as educational programs, be permitted to continue.

Mr. West advocates a contractual approach to human experimentation which requires full disclosure, written consent and choices that are rational. These requirements reflect the human rights to know, to choose and to be treated fairly He distinguishes between coercion (which involves threats) and bribery (which involves manipulation of incentives). Mr. West considers requests for prisoners to participate in research to be bribery, not coercion; hence, choice is at play. The paucity of alternatives and the conditions of domination within prisons, however, undermine the rational basis for such choice. Mr. West concedes that a certain degree of control over prisoners might be warranted, but only to the extent that basic human rights are not violated. The necessity for such control, he believes, suggests that prisoners are less appropriate subjects for research than are nonprisoners. Therefore, he urges that normal volunteers be recruited, instead; but he cautions against shifting the burden of research to Third World populations.

Mr. West views behavioral research in prisons to be nontherapeutic, inasmuch as the rehabilitative efficacy of behavior modification programs has not been demonstrated. Thus, he would restrict such research according to the same principles he applied for nontherapeutic biomedical research.

Mr. West recommends termination of both nontherapeutic biomedical and "therapeutic" behavioral research involving prisoners until such time as prison reform creates the conditions necessary for their legitimate participation in such research.

Dr. Wartofsky begins his essay on selling the services of one's body for research by discussing the extent to which being a subject is similar to other forms of wage-labor. He examines the nature of that which is being sold (and bought), and the extent to which a person has the right to offer his or her body in exchange for money. His position is that whereas one may not sell one's body, as such, nevertheless one may sell the disposition over the use of one's body for specified purposes, for a specified time and under specified conditions. In other words, while one's life and liberty are inalienable rights (which cannot be separated from one's person and sold), one's services or capacities are commodities which, in our free-market social and economic system, are regularly exchanged for wages.

Dr. Wartofsky then considers the problem of risk-taking. In general, he says, no ethical question arises concerning the risks inherent in dangerous occupations, since the workers are seen as having free choice in undertaking or refusing such jobs, and the risks involved are secondary to the needs of society which the occupations (e.g., coal mining, construction work, chemical manufacturing) are designed to meet. By contrast, the nature of risk in research is such that one is placing one's health or well-being at risk not as a by-product of some other purpose, but as the primary commodity; and it is the intimacy of the relation between one's person and one's well-being which makes the exchange disturbing.

With respect to motivation, Dr. Wartofsky observes, it is generally assumed that placing oneself at risk for monetary gain is for one's own benefit, whereas doing it without tangible reward is more altruistic. However, he points out that one may place oneself at risk for monetary gain and, at the same time, be self-sacrificing (if, for example, the purpose is to support

one's family or otherwise satisfy the needs of others). Whether working for the abstract "good of society" is a higher motive than working for one's family is a question which cannot be settled. Thus, he concludes, motivation should be considered (if at all) only to the extent that the seriousness of the motivation should be commensurate with the degree of risk to be undertaken.

Next, he considers the extent to which prostitution is like wage-labor, involving, as it were, the sale of a disposition over one's body for a certain purpose, at a certain rate and for a certain time. The relevance of the inquiry lies in the fact that what is being bought and sold in prostitution is (just as in participation in research) something which is "so intimate to one's person that there is something disturbing in the notion that it is alienable, as a commodity." In his view, the ethical objections to prostitution, and to being a paid research subject, derive from the translation of relations which are supposed to express fundamental aspects of humanity into an economic exchange. In the paid research context, both the investigator and the subject are reducing an essential human capacity (putting oneself at risk for others) to a commodity; so doing, they may dehumanize each other.

Here, he observes, society is faced with a dilemma: on the one hand, research with human subjects is important for the preservation and well-being of the species; on the other hand, the only means of conducting such research is ethically questionable. He sees three obvious solutions: (1) to stop paying the subjects; (2) to conduct only that research which can be carried out with unpaid volunteers; and (3) to restructure society in order to eliminate the economic need which induces (or coerces) the disadvantaged into making up the largest portion of paid research subjects. All of these "solutions,"

however, are impractical. The pragmatic solution which he recommends, therefore, is to minimize the exploitive elements which "commodify" the situation. An alternative would be to follow the model proposed by Hans Jonas in which the most valuable members of society (rather than the most expendable) undertake the risks, but Dr. Wartofsky considers this also to be impractical. Finally, he proposes that both paid and unpaid research subjects be organized, educated as to their rights, and represented at all levels of review (Institutional Review Boards as well as state and federal commissions). This, he believes, would socialize the interaction, reduce the alienation, and ameliorate the dehumanizing effects of the commodity relationship for both the paid subjects and the researchers.

Chapter 9. Sociological and Behavioral Perspectives

In order to obtain an understanding of the nature of the social structure of a prison and its implications for the prisoner's freedom and competence to make a choice for or against involvement in research, the Commission requested papers by two sociologists: Jackwell Susman, Ph.D., and John Irwin, Ph.D. In addition, Martin Groder, M.D., prepared a paper on behavioral research aimed at rehabilitation of prisoners. These essays are summarized below.

Dr. Susman suggests that a determination regarding prisoners' participation in biomedical or behavioral research depends on understanding their value system and how it deviates from conventional norms. He describes two sets of norms in prison society: (1) the norms which the staff and officials endorse and which support their authority, and (2) the norms of the inmates, which encourage diversity of behavior and subversion of the official system.

It is generally agreed that custody involves profound attacks on the prisoner's self-image through deprivation and control. Inmates cope with the "pains of imprisonment" through various social structures, norms and values. From the sociological literature on prisons and prison life, Dr. Susman identifies two descriptive models of prison society: the "prisoner solidarity" image and the "prisoner diversity" image.

As described by Dr. Susman, the prisoner solidarity image classifies prisoners according to their conformity to or deviation from the inmate code which encourages cohesion and mutual support among prisoners vis-a-vis their captors. Adherence to the inmate code helps protect the average inmate and strengthens

his dignity. A negative aspect of this social structure is the dependence of most prisoners on the few leaders for privileges and protection. The convict leaders are granted special privileges by the administration in return for maintaining order, and thus seem to have little incentive to participate in biomedical and behavioral research. The rest of the inmates may adapt differently to prison life. Some may conform with varying degrees of intensity to the demands of the inmate code, and might reject biomedical and behavioral research since the code rejects conventional values and cooperation. Others may deviate from the norms of the prisoners' world and participate in research to obtain the goods and services their outcast status denies them. Still others may combine conformity and deviance to maximize their chances of leaving prison emotionally and physically unscathed; their participation in research would depend on a careful analysis of the costs and benefits, in terms of their life in prison and their chances of getting out. Finally, some may conform completely to the official norms and may volunteer for research for both altruistic and pragmatic reasons.

The second model of prison society, the prisoner diversity image, focuses on the inmates' identification with persons or groups outside the prison. In this view, the inmates bring subcultural norms and values with them into prison, and, thus, prison society is diverse. This model describes inmates according to three categories. First is the career criminal or professional thief, who assumes a commitment not to prison life but to criminal lifestyles. His objective is to do his time and get out, not to manipulate the prison environment. He may volunteer for research believing that it will be considered favorably by the parole board, or merely to maximize his comfort until he is released. Second

is the "convict," who is oriented primarily to prison life and seeks status by manipulating the environment, winning special privileges and asserting influence over others. His participation in research is improbable because it might imply cooperation with the staff. The third group of inmates identify with "legitimate" subculture outside the prison. They have no commitment to the values of thieves or convicts and seek status through the means provided by the prison administration. They are usually rejected by the convict and thief subcultures, and might be expected to volunteer for research projects.

Dr. Susman examines the implications of these models of prison society for the requirements of informed consent: competency, knowledge and voluntariness. Rejecting the Kaimowitz court's view of the effects of institutionalization, Dr. Susman believes that prisoners are able to maintain an identity. He suggests that prisoners' autonomy may expand or contract depending on their circumstances, and that at least some prisoners have sufficient autonomy to give informed consent to participate in research. Providing prisoners with knowledge of the risks associated with research may be difficult, but Dr. Susman believes in principle that it can be done satisfactorily. With respect to voluntariness, both images of prison society indicate that prisoners have a great deal of power and influence over how the prison is run. This implies that mechanisms could be developed to insulate research activities from staff and peer pressure. Dr. Susman concludes that prisoners can have the freedom and competence to give informed consent.

Dr. Irwin agrees with Dr. Susman that biomedical research involving prisoners should not be categorically denied, but rather permitted under conditions

that protect against the disparity of bargaining power between prisoners and authorities. Instead of a contract model (which assumes relatively equal bargaining power) Dr. Irwin suggests a "rights model," in which minimal rights are established and guaranteed against abuse of power. He observes that conditions of degradation and coercion vary with the degree of autonomy and isolation under which prisons operate, and he believes that most of the constraints (including arbitrary use of discretionary powers) are, in fact, unnecessary and could be abandoned without interfering with effective operation of the penal system. This, he says, would make the prison environment compatible with conditions necessary for the ethical conduct of research.

Dr. Irwin recommends, therefore, an accreditation process and an ongoing review mechanism, in which prisoners, their families and civil rights groups all participate, with a concomitant reduction of discretionary powers now held by prison authorities. He would also require that drug firms pay at the same rate that they pay nonprisoner participants, but that the difference between those wages and the prevailing prison wages be placed in a fund to increase the wages for the general prison population. He would also eliminate any leakage of information to parole boards about research participation. Finally, he recommends that there be established a review and grievance mechanism independent of the prison system in which prisoners, their families and civil rights organizations would participate. This mechanism would review all decision-making relative to prisoners' rights and perhaps consider, as well, such factors as the adequacy of the health care available to the prisoners.

Dr. Groder, formerly warden-designate of the Federal Correctional Institution at Butner, North Carolina, observes that of all research involving

prisoners, only therapeutic psychosocial research directly addresses "the promise of rehabilitation." Unless society is willing deliberately and intentionally to abandon its commitment to rehabilitation, he argues, research of high quality is essential if services are to be provided to offenders in a safe, effective and humane manner. He believes that offenders, as wards of the state, have a "right to treatment" that will be abridged if correctional research is abolished or stifled through overregulation.

Dr. Groder accepts the likelihood that the Commission will wish to recommend additional regulatory procedures, and suggests the following goals: (1) "wards of the state" should be provided an opportunity to rejoin the social mainstream; (2) the quality of consent should be audited to protect basic rights of volunteers; (3) provision should be made for care, compensation, and possible reversal if a bad effect occurs; and (4) the outcome of all research should be published. Dr. Groder recommends that Congress appoint regional boards with the responsibility of achieving the four goals and ensuring prisoner rights. The boards would approve or disapprove projects, and appeals could be made to the federal court of appeals. The boards should sponsor studies of the correctional process and the impact of research, and make recommendations to Congress regarding pertinent legislation.

Dr. Groder believes, on the basis of his experience, that therapies can be devised to enable prisoners to reenter and remain in the mainstream of society, and he cautions that a ban or limitation on such research will ensure that no correctional innovations will be developed. Therapeutic techniques that become available in nonprison society may also be denied to prisoners, and that would pervert the desire to rehabilitate prisoners as well as infringe upon their right to treatment.

Chapter 10. Legal Perspectives

The Center for Law and Health Sciences, Boston University School of Law, prepared for the Commission an analysis of the law relevant to determining the validity of consent by prisoners to their participation in research. This analysis proceeded on the assumption (consistent with the findings of the Commission) that quality of information and ability to comprehend do not generally constitute problem areas in prison research. The key issues reviewed by the Center are whether consent can be given voluntarily in the prison environment, and whether voluntary consent to treatment (and, by extension, to behavioral programs that might not constitute "treatment") is required. The first of these issues is discussed primarily in the context of nontherapeutic biomedical research, and the second is raised in connection with behavior modification programs.

Motivations of prisoners to participate in nontherapeutic research include financial reward, hope for reduction of sentence, seeking of medical or psychiatric help, relief from tedium, desire for better or more secure living conditions, attraction of risk-taking, altruism, etc. The conditions that give rise to these motivations may constitute duress such as would render a contract voidable and, by analogy, render it difficult if not impossible to uphold a prisoner's "informed consent" to participation in research. It has been argued, but not determined as a matter of law, that incarceration inherently constitutes such coercion (or duress) that nontherapeutic research should not be conducted in prisons. In the absence of such a determination, courts will examine particular prison situation for evidence of duress in obtaining consent to participation in research.

Thus, as to financial reward, the questions to be asked are whether there are alternative sources of equal income and, more importantly, whether participation in research is the only way prisoners can earn enough money to maintain a minimum standard of living. As to living conditions, the questions would concern the extent of deprivation in the prison, and the contrast between the prison environment and conditions in the research center. These are matters of fact that would be examined in a particular situation to determine whether a consent was voluntary.

Promise of reduction of sentence is now generally thought to be inherently coercive, but, at least with respect to rehabilitative treatment that may be of experimental nature, sentence reductions have been tied to prisoners' consent. Cases involving waiver of rights indicate that even in a coercive situation, rights may be waived if adequate safeguards, e.g., counsel, are provided.

Medical treatment generally constitutes a battery if the patient has not consented to it. Although one jurisdiction has not applied this rule in cases involving prisoners, other jurisdictions have held to the effect that imprisonment does not deprive a person of the capacity to decide whether or not to consent to health care. The latter rule has been applied in cases dealing with physically invasive behavior modification techniques, but there is no holding on the right to withhold consent to noninvasive behavior modification techniques. Whether or not the techniques were experimental does not appear to have been material in any of the holdings. Rather, the courts appear to have taken into account the degree of invasiveness.

State regulations and statutes dealing with experimentation on prisoners cover the entire spectrum, from permission to total bans of such research.

Where any sort of research involving prisoners is permitted, a requirement that informed consent be obtained is explicitly set forth. Where financial or other rewards are explicitly covered, they are generally limited or prohibited. The recently published DHEW proposals related to research on prisoners follow the states that permit such research by accepting the view that prisoners can consent to be subjects so long as adequate safeguards are provided. The proposals published for public comment by DHEW (November 16, 1973) include such safeguards as a required certification by a review committee that there are no undue inducements to participation by prisoners, taking into account the comparability of the earnings otherwise offered; a requirement that no reduction in sentence or parole in return for participation in research be offered unless it is comparable to what is offered in return for other activities; and a provision for accreditation by DHEW of prisons in which research is to be supported or conducted. A subsequent DHEW Notice of Proposed Rulemaking (August 23, 1974) adds a requirement that the review committee also take into account whether living conditions, medical care, etc. would be better for participants than those generally available to prisoners, but deletes the provision for accreditation by DHEW.

The report by the Center for Law and Health Sciences concludes with the following recommendations: that provision for accreditation by DHEW should be made, to ensure that research will not be conducted under such circumstances that participation is the only way for a prisoner to obtain minimally decent living conditions; that the rewards for participation should not be such that they provide the only way for a prisoner to maintain his health and personal hygiene, or induce a person to incur great personal risks; that parole or a

reduction in sentence should never be offered in return for participation in research; that there should be some provision for the protective role of an independent counselor; that full information about the research should be given the prospective participant, and that he should not be asked to waive his rights against anyone for injuries that he might sustain. If these safeguards are adopted, the law generally will recognize the informed consent of a prisoner to participation in research.

Chapter 11. Alternatives and Foreign Practices

Alternatives employed in the United States and foreign countries to the conduct of biomedical research in prisons were examined by the Commission. A paper on alternative populations for conducting phase 1 drug studies was prepared by Dr. John Arnold. Information on two programs using normal volunteers as alternatives to prisoners, one for vaccine testing and one for general physiologic testing, was provided by staff reports. An additional staff report was prepared on the use of prisoners in a research program located in a hospital outside of the prison. Practices in foreign countries related to development and testing of new pharmacologic agents were surveyed and reported to the Commission by Mr. C. Stewart Snoddy and Dr. Marvin E. Jaffe, Clinical Research International, Merck Sharp & Dohme.

The Quincy Research Center, Dr. John Arnold, Director, is an innovative phase 1 drug testing program using cloistered, normal volunteers. It was recently established in Kansas City, Missouri. Dr. Arnold, an investigator with 29 years of experience in drug testing in prisons, highlights some of the practical and ethical problems associated with the use of such a research population, and explains the reasons he now believes that the use of prison inmates as research subjects should be phased out. He identifies limitations imposed by the prison system on the optimal conduct of such studies, and his reasons for believing that the use of nonprisoner volunteers for them is preferable. Cloistering, he says, is necessary to enable the researcher to strictl control the medications received, to intensively monitor subjects for signs of adverse effects, and to identify drug properties with greater confidence. In

contrast with research facilities designed exclusively for the cloistering of free-world volunteers for phase 1 studies, however, prisons are neither built nor operated around the needs of medical research. The prison environment may be poorly controlled, particularly with regard to the presence of contraband drugs that may seriously influence the result of a clinical trial. Further, the dropout rate for his free-world studies has been about 1.5 percent, a lower rate than he experienced in a prison setting.

Dr. Arnold suggests that the behavioral problems associated with cloistering volunteers are the greatest barrier to the development of alternative populations and require sensitivity with regard to volunteer selection, adequate preparation for the experience of complete control of life-style, and physical facilities that are attractive and interesting. The second largest problem is the cost. While lodging and food contribute to this expense, the single largest increment stems from the greater degree of supervision and closer medical control required for volunteers in a nonprison setting.

Despite the problems, Dr. Arnold believes the advantages make the use of nonprisoners preferable. One advantage he cites relates to compensation for injury, which the consent form should address. While an indemnification plan similar to those governing other occupational hazards can be arranged for nonprisoner volunteers, it cannot necessarily be done for prisoners. Rates for the Quincy workman's compensation insurance are based on data that show the risks for participants in phase 1 drug research to be only slightly greater than the occupational risks for office secretaries, one-seventh of those for window washers, and one-ninth of the risks for miners. The problem of rendering

long-term follow-up and extended care, because prisoners are not likely to return to prison for follow-up examinations or medical attention, is also reduced by using a free-living population.

Dr. Arnold believes that three advantages of the free-world volunteer system will eventually lead to its exclusive use: (1) paid stipends can be comparable to wages paid for other services, (2) indemnification can be offered under plans similar to workman's compensation, and (3) volunteers may choose medical research against other forms of limited employment without any special coercive force.

Dr. Arnold described characteristics of the population attracted to his nonprisoner volunteer program, based on the last 150 subjects at the Quincy Research Center. The men were 80% white, 15% black, and 5% other racial background. Age group was 50% age 20-30, 40% age 30-40, and 10% age 40-55. Ninety percent were recently or seasonally unemployed, 8% steadily unemployed, and 2% were college students. Most had completed 8th grade, 60% had completed 12th grade, 2% were college students, and 0.5% were college graduates. Approximately 60% of the subjects were former prisoners; 5 to 10% had been subjects in Dr. Arnold's earlier studies in prisons.

The Clinical Research Center for Vaccine Development (CRCVD) was developed to provide an alternative to the use of prisoners in infectious disease research. It was established in 1974 under a contract with the National Institute of Allergy and Infectious Diseases (NIAID), the primary inpetus being NIAID's desire to develop a dependable source of healthy, adult volunteers that would circumvent many of the problems plaguing its prison-based research and allow

infectious disease research to continue. A contract was awarded to the University of Maryland School of Medicine to demonstrate the feasibility of recruiting adult volunteers from the community for research in which live attenuated vaccines for respiratory viruses and mycoplasma are administered to subjects to test infectious capability, symptoms produced, ability to induce immunity, and contagiosity.

The CRCVD is under the direct supervision of two physician-researchers who conduct the protocols developed by NIAID. They are assisted by two part-time recruiters, a consulting psychologist, and support staff. The facility is part of the University of Maryland School of Medicine complex in Baltimore; its major unit is a self-contained, limited access, air-sealed isolation ward, where volunteers reside for the duration of the study.

Recruiting procedures have focused on attracting young, intelligent and healthy adults, to minimize problems with informed consent and adjustment to the dormitory-like setting of the isolation ward. College students were selected as the free-world population most likely to meet these requirements. Recruiters present information on the program at college campuses; interested students subsequently meet with the recruiters so that a blood sample may be drawn. Those volunteers who pass this initial screening procedure are contacted by the recruiters and offered the opportunity to participate as subjects.

Most of the studies conducted by the CRCVD last between 15 and 30 days. During a two-day acclimation period on the unit, there are intensive educational presentations concerning vaccine development and the upcoming study, preliminary medical and psychological screening procedures are conducted, and

the volunteers become acquainted with the isolation ward environment and staff. The researchers reserve the right to dismiss volunteers prior to inoculation, but thereafter only the subject may choose to withdraw from a study. To supplement the consent form, an examination is administered prior to inoculation, to assess and document the participant's comprehension of the research protocol. Each volunteer must pass this exam before being permitted to participate in a study.

The volunteers earn $20 per day on the isolation ward, based on what the average college student might earn in a summer job. Volunteers who withdraw from the study are paid up to the point they drop out, whether or not a public health quarantine has been imposed, requiring every subject to remain on the ward until completion of the study. The consent forms note that any medical problems that may arise will be treated at the CRCVD's expense.

As of June 1975, 70 volunteers had participated in nine studies, and the subject pool consisted of 547 people. The age range is between 18 and 50. Of the 70 people who have completed studies, there were 4 with less than four years of high school, 30 high school graduates, 19 college undergraduates, 12 college graduates, and 5 with advanced degrees; 84% were white, 7% were former prisoners.

The Normal Volunteer Patient Program of the Clinical Center, National Institutes of Health, was established in 1954 and represents one of the earliest efforts to involve members of the community in experimental studies. Volunteers participate in research designed primarily to measure the parameters

of normal body functions. Most of the subjects are members of certain religious sects which view participation in this program as part of their public service commitment (e.g., Church of the Brethren, Mennonites, Mormons) and college students. While the volunteers in both categories receive little in terms of financial compensation (usually restricted to transportation and living expenses), the student volunteers, who reside at the Clinical Center for up to three months on "career development internships," are offered an opportunity to study with NIH scientists in many of the research laboratories. Hence, the program appeals primarily to students interested in careers in the health sciences and related fields.

Recruitment of many of the volunteers for the program is done by colleges under contract with the NIH. The contractor college or university is responsible for handling all the local recruitment details, transporting the volunteers to and from the Clinical Center, and providing any transportation required for follow-up procedures. In return, the contractor receives a fixed fee for each volunteer (to cover the cost of round trip air fare and ground transportation to and from the airport) plus a certain amount for each day of the volunteers' time and inconvenience.

Prospective participants in the program are advised of its purposes and the restrictions in life-style they may experience during their sojourn at the Clinical Center. Studies in which they are asked to participate include, for example, studies of normal physiology (awake, asleep and during exercise), psychological studies (reaction time, attention), dietary manipulation, studies involving drugs, hormones or tracer doses or radioisotope administered either

orally or by injection, and exposure to viruses or biochemical products derived from viruses or bacteria.

The Eli Lilly Company Research Unit located at Wishard Memorial Hospital, Indianapolis, Indiana, employs prisoner and nonprisoner normal volunteers in phase 1 drug studies. The prisoners come to the hospital unit from Pendleton State Reformatory 30 miles away; most of them have previously participated in pharmaceutical studies in the Lilly unit at the prison. All studies involving the initial administration of an agent to humans, use of radioisotopes, or tests requiring complex monitoring equipment are done at the hospital unit rather than at the prison unit.

Prisoner volunteers, in order to qualify for participation in the Lilly hospital research program, generally must meet the basic work-release requirements: a date set for parole or for a parole hearing, and one year of good behavior. In addition, specific permission from the warden is required. These restrictions are imposed to make escape less likely. Other work-release choices, when available, generally offer better pay and more freedom of movement. A prisoner participates at the hospital only once and returns to the prison afterward. The stay at the hospital may be as long as three months. While at the hospital, prisoners are required to remain on the research ward. They have limited recreation facilities but may have visitors daily. No special security precautions are taken, but escapes from the unit have been rare.

Two hospital wings adjoining the prisoner research unit are used for phase 2 studies in patients and phase 1 studies in nonprisoner normal volunteers. The later are generally men off the streets, chronically unemployed,

who know of the program and request on their own, often repeatedly, to participate in drug studies. Prisoners and nonprisoners usually are not involved in the same protocol, although the types of studies are the same. Nonprisoners are paid $7 a day; the prisoners receive $3 a day (the rate established as the maximum by the prison).

Advantages of the hospital as the setting for research of this type are the availability of excellent emergency care (although no serious adverse reactions requiring it have occurred in 10 years of operation), the ease of access of the investigator to the subjects, and surroundings that are pleasant in comparison with the prison. Disadvantages are the limited number of prisoners who can qualify for the program and the boredom of the research. The main reason men drop out of a study is that they become bored and ask to return to their friends and activities at the prison.

Human studies in pharmaceutical research and development in other countries. The survey* conducted on practices of foreign countries regarding use of prisoners and other groups in the development and testing of new pharmaceutical agents included seven European nations, five English speaking countries, four Latin American nations and Japan. In all the countries surveyed, clinical pharmacology studies (pharmacokinetic and dose-ranging studies) can be conducted in normal subjects. Almost uniformly, these countries do not permit such studies to be conducted in prisoners. In theory, prisoner studies could be done in the United Kingdom, but in practice no such research is conducted in prisoners out-

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* Provided to the Commission by Marvin E. Jaffe, M.D. and C. Stewart Snoddy, Merck Sharp & Dohme Research Laboratories.

side the United States. In most countries volunteers, when used, are students, civil servants (military, police and firemen), and medical and paramedical personnel.

In general, clinical pharmacology studies conducted abroad involve patients with the disease which the drug is intended to treat, rather than normals. The use of patients with other diseases is not uniformly approved, but may be permitted if data relevant to the primary indication can be obtained. The requirement for specific governmental approval (IND or clinical trials certificate) to conduct clinical pharmacology studies in normal subjects or patients also varies among countries. In all the countries surveyed, human pharmacokinetic and pharmacodynamic data are "helpful" to support new drug registration. In about half the countries, such data are mandatory. Only France and Japan require that such data be generated in the indigenous population; other countries accept foreign data.

With the exception of Italy, no country requires long-term (1-3 months) controlled safety studies in volunteers before initiating studies in patients. For registration purposes, however, Belgium, Italy, Canada, and in some cases the United Kingdom require such data. Since prisoners are not used in those countries for such studies, it is assumed that such data often are generated elsewhere. In most countries, longer term studies to determine the safety of a new drug entity are done in the patient population which the drug is intended to treat. This provides a measure of how the drug may be expected to behave in clinical practice under the more usual conditions of use and when combined with the usual concomitant therapies. The subjects of such studies receive the presumed benefits of therapy with the new agent to balance its unknown risks.

Although prisoners have not been subjects in phase 1 drug testing in other countries, they have been subjects of nontherapeutic research. For example, prisoners in a number of countries, including Australia, Canada, Denmark, England, Germany, Greece, Ireland, Mexico, Poland and Japan, have been surveyed to determine the incidence of the XYY chromosome anomaly.

Chapter 12. Survey of Review Procedures, Investigators and Prisoners

Data on research in prisons were presented by the Survey Research Center, University of Michigan, in a preliminary report to the Commission on a study of institutional review procedures, research on human subjects, and informed consent. Data were presented from interviews done in early 1976 with investigators in 41 studies and representatives of review committees in five prisons, with 181 prisoner-subjects in four of these prisons, and with 45 prisoner-non-subjects in two of these prisons. The subjects had all participated in research since July 1, 1974. No individuals or institutions were identified in the report.

The research. As described by principal investigators in the five prisons, their research was predominantly pharmaceutical research, mostly phase 1 testing. In most of the studies, drugs were administered orally and blood and urine samples were analyzed. Very few of the experiments, according to investigators, were intended to benefit subjects, although researchers felt that a medical or psychological benefit might occur in some cases. The research also entailed some medical and psychological risk according to investigators, although they estimated the probability of serious risk to be very low or nonexistent. All investigators reported the existence of procedures for treating subjects who might suffer harmful effects of the research.

Review procedures. The Survey Research Center found that the structure of the review process differed among the five prisons. In some places it included Institutional Review Boards (IRB's) established in compliance with DHEW regulations on protection of human subjects; in others it included review committees

appointed by the state department of corrections, by prison authorities, or by university officials. The review process at some prisons included committees created by drug companies. Biomedical and legal consultants and prisoner representatives played a role in some review procedures. At all prisons, the review was conducted in stages involving different combinations of the above mechanisms. Membership on review committees was reported as being very stable.

While few proposals are rejected in the review process, it was reported that few are approved as submitted. Most frequent changes are in consent procedures, though modifications were also reported in research design. The process was said to work smoothly, at least in part because of long-standing relations between review committees and investigators, and awareness of mutual expectations. Little monitoring of the actual conduct of research was reported, although most members of review committees were said to have visited the prison or research facilities at some time.

The prisoner subjects. The interviews with prisoner subjects revealed them to be generally supportive of biomedical research in prisons. The near concensus of favorable attitude among subjects occurred in all four institutions where prisoners were interviewed. Practically all of these subjects said that the information they received in advance of the experiment was understandable and correct, that the researchers were willing to answer subjects' questions, and that participation was voluntary. About one-third of the subjects indicated that they expected the research would involve some risk. A few subjects nonetheless felt that they had experienced specific difficulties as a result of the

experiments that they did not fully expect. Subjects offered a number of reasons for participating in research, the most prevalent being financial. About 90% of them said that they would be willing to participate in future experiments.

Consent forms. The Survey Research Center's analysis of consent forms provided by investigators indicated that almost all described the purpose of the experiment, and all described the procedures. About 85% mentioned and listed risks. An analysis of the reading ease of consent forms indicated that a large proportion were at a difficult reading level. The difficulty did not appear to be solely attributable to the use of medical and technical terminology; some of the difficulty was related to the complexity of sentence structure and the nature of many of the nontechnical terms that were employed. Reading difficulty appeared to be greater for consent forms associated with projects that investigators estimated to entail relatively higher risks. The explanations provided in the consent forms, however, were supplemented in all cases by oral explanations.

Nonsubject prisoners. Prisoners who have never participated in research projects, or whose participation was not recent, were less favorable, on the average, toward research in prisons than were the current subjects. Differences of opinion about research were more apparent within the group of nonsubjects than within the group of subjects. Some nonsubjects were strongly opposed to research in prisons. Prisoners offered a number of explanations for not participating, including assertions that they had not been asked, that they feared the possibility of serious harmful effects, that they mistrusted research or

researchers, or that they were opposed to the idea of research in general. Some said that they would participate if they were asked and/or if the benefits to themselves were more substantial. Nonsubjects who were interviewed had a slightly lower level of formal education than did the subjects, and the former were less likely to have prison jobs. Furthermore, for those inmates who held jobs, the number of hours worked per week was slightly lower for nonsubjects than for subjects.

Suggestions from respondents. Relatively few prisoners offered suggestions about how studies on human beings might be improved. Increased payment, better facilities (e.g., rooms to be used exclusively for research purposes), more complete explanation of possible harmful effects (e.g., pamphlets or written materials explaining projects), and better treatment (e.g., taking more time with subjects and exercising more care) were among the suggestions of prisoners. Some nonsubject prisoners suggested abolishing the research program.

Principal investigators also offered few suggestions. Some proposed that rules and review procedures be simplified and made less rigid. Others suggested that larger review committees be established, that committee members should have experience in dealing with prisoner volunteers, and that the committee procedure be made less susceptible to the biases of individual members.

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