

## Research without Borders: The Origins of the Declaration of Helsinki

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In June 1964 the eighteenth assembly of the World Medical Association endorsed a series of recommendations for the conduct of human experimentation. The Declaration of Helsinki, named for the city where the assembly was held, has been hailed as the “most influential international ethics document governing the conduct of clinical research.” (Weijer and Anderson, 2001: 19). The first international set of guidelines for human experimentation, the Declaration reflected the longstanding interest of the World Medical Association (WMA) in issues of medical ethics and the enduring shadow of the Nazi medical war crimes. But the road to the Helsinki Declaration was neither straight nor smooth; the development of the recommendations for human experimentation required more than a decade of active discussion and debate among WMA members before the Declaration was brought to the General Assembly for formal adoption in 1964.

The prolonged period of disagreement and discussion, noted Ronald Winton, an Australian physician-delegate to the WMA and a one-time president of the organization, was not “due to procrastination or lack of concern on the part of the Council of the WMA or of its Committee on Medical Ethics, but to the desire to produce a truly useful and practical document.” (Winton, 1976:59). This prolonged period resulted from more than philosophical differences and practical concerns. The Declaration reflected the organizational politics and financial structure of the World Medical Association. Although the ostensible product of an international medical association, the Declaration of Helsinki, like the Nuremberg Code which it followed, bore a sturdy American stamp.

This paper examines the winding road to the Declaration of Helsinki and the American issues that shaped its ultimate form in 1964.

### The Founding of the World Medical Association

In 1946, physicians representing 32 national medical organizations met in London to discuss an international association of doctors and national medical societies.

Prompted by the suggestion of Polish physician George de Swiet, president of the Polish Medical Association in Great Britain, the 1946 meeting took place in London. Hosted by the British Medical Association in conjunction with the Association Professionnelle Internationale des Médecins (APIM), the assembled physicians sought to promote international medical relations and the advancement of medicine and its social and cultural aspects. Physicians from the recently defeated nations of Germany and Japan did not take part in the meeting. More surprising perhaps, American physicians declined to participate, although the American Medical Association asked two British doctors to act as observers on its behalf. (Pridham, 1951)

Representatives from the American Medical Association were among those present at the first meeting in 1947 of the newly established World Medical Association. The assembled physicians unanimously adopted a series of explicit policy objectives, ranging from the professional to the universal. These objectives included maintaining the honor and protecting the interests of the medical profession, assisting the people of the world to attain the highest possible level of health, and the promotion of world peace. In addition, delegates to the assembly unanimously agreed to establish relations with, and to

represent the views of their profession, to the World Health Organization, UNESCO, and other international bodies. (Howard-Jones 1981; Lee 1997).

The first meeting of the new organization was held in Paris in September 1947, only one month after judgments had been rendered in the trial of 23 Nazi medical personnel (the case known as United States of America v. Karl Brandt et al or the Nuremberg Doctors' Trial). (Weindling 2001) The "betrayal of medicine by German doctors" cast a lengthy shadow over virtually all activities of the WMA. (War Crimes and Medicine. 1949:8).

One of the first acts of the fledgling association was the adoption of a statement about the dedication of the physician to his profession. In 1948 the General Assembly of the WMA formally endorsed the Declaration of Geneva or the Physician's Oath. The association recommended the oath to physicians of all nations, especially young physicians embarking on their professional career. The framers of the declaration self-consciously modified the Oath of Hippocrates, described by one representative as "obviously developed for physicians of Greece in the period of the School of Hippocrates . . . and not especially suited to such conditions as prevail today." (Dedication 1949:4) All references to the deity or deities were omitted, as well as the Hippocratic injunctions against surgery, abortion, and euthanasia. The physician who adopted the Declaration pledged not to allow considerations of nationality, race, party politics, and social class to interfere with the professional responsibility for the patient's welfare. (Ummel 1991)

In 1949, the WMA proposed an International Code of Medical Ethics, which incorporated the Declaration of Geneva and other professional commitments of the physician. Finding appropriate language to reflect different national traditions created

some discord among the delegates. When the Irish delegate to the WMA, for example, objected to the proposed clause regarding therapeutic abortion in the Code, the committee formed to reconsider the offending paragraph recommended that the code be altered. Whereas the original draft read, "A doctor must always bear in mind the importance of preserving human life from the time of conception. Therapeutic abortion may only be performed if the conscience of the doctor and the national laws permit." The revised version read "A doctor must always bear in mind the importance of preserving life from conception until death." (Minutes, 1949: 9).

In the early 1950s the WMA continued to revisit issues of medical ethics. The General Assembly passed in 1950 a resolution against euthanasia as contrary to the public interest and to medical ethical principles. (Resolutions, 1950:134.) In 1951 at the request of the United Nations the WMA cooperated with the World Health Organization to ascertain the "number, location and condition of the survivors of Concentration Camps, who, under the Nazi regime, were victims of so-called scientific experiments." (Victims 1951: 241-2) Noting that the victims of experiments were scattered in many countries, the WMA requested that member organizations ask these individuals about their willingness to have their names and addresses reported provided they were safeguarded from publicity and that they were assured of satisfactory compensation for their disabilities." The WMA asked member nations to collect the names and address of "Victims of Nazi medical Experimentation" and to forward this information to the World Health Organization in preparation for compensation (Annual Report 1952)

One pressing issue that confronted the WMA Council in the late 1940s was the rehabilitation of the German medical profession. In October 1949 council members of

the WMA had arranged to meet privately with leading members of the Arbeitsgemeinschaft Westdeutscher Aerztekammern (AWA). Drs. Otto Leuch (Switzerland) and Dag Knutson (Sweden) representing the WMA met with AWA doctors Hans Neuffer and Dobler in January 1950. (Report 1950) The four physicians agreed that no minutes of the meeting be recorded and together decided that nothing about the conference should be published in the medical press. The WMA delegates were charged with inviting the German representatives into closer relations with WMA doctors with an eye to electing the Germans to membership. One obstacle to this invitation for the WMA was the AWA's employment of Dr. Karl Haedenkamp, a physician known to have connections to the Nazi party in the years between 1934 and 1939. "The employment of Dr. Haedenkamp has been deemed irreconcilable with the principles and views, expressed in the said declaration, which categorically disclaims all connections with Nazi ideology and condemns those members of the German medical profession, who took part in or tolerated acts against the noble tradition of medical men." For their part, the German physicians argued that Haedenkamp's services were indispensable to their professional organization. They defended his moral character by "repeatedly stressing" that even those with prominent positions in the Nazi regime knew little about what was going on—the Nazi leaders, the two German physicians claimed, were "past-masters in the art of drawing iron curtains." (Report on Conference in Stuttgart 1950) After extensive discussion and negotiation, the German medical association prepared a statement acknowledging the numerous acts of cruelty and oppression perpetrated by some German doctors during the Third Reich and solemnly promising to do everything to prevent such a future betrayal of medicine by German doctors. (Leuch 1949) The AWA

noted, for example, how since June 14, 1947 every physician who obtained his medical license was required to take the Hippocratic Oath as revised by the WMA (the Declaration of Geneva). In 1951 when the Secretary-General of the WMA canvassed member nations about admitting West Germany and Japanese physicians, thirty of the thirty-one national medical associations who responded voted in favor of admitting Japan; twenty-eight voted in favor of admitting Germany. The General Assembly of the WMA subsequently authorized the Council to accept the Japanese and West German medical associations as members. (Memorandum 1951).

These early difficulties with the Nazi affiliations of some prominent German participants in the WMA continued to trouble the organization. In 1993 German physician and WMA president-elect Hans Joachim Sewering resigned his position following revelations that he had sent a 14-year-old girl with epilepsy to a "healing clinic" in 1943 where he knew she would be killed. A one-time member of the Nazi party and the Nazi SS, Sewering first joined the WMA in 1959 and had served as treasurer of the organization for twenty years. In the face of calls from individual German physicians and from Canadian, American and Israeli medical associations for Sewering to resign, the WMA, which owed much of its financial backing to German medical interests, continued to defend Sewering's selection as president. (Seidelman 1996; White 1996).

### The Problem of Human Experimentation

In 1953, the Royal Netherlands Medical Association asked the WMA to consider the use of human subjects in scientific experiments. L. A. Hulst, the Dutch medical

delegate, proposed that the WMA request that editors of medical journals around the world consider the importance of protecting “test persons” and to develop guidelines to judge whether subject protection was adequate. (Experiments on human beings 1953) The issue of clinical research was already under review in France, where in 1952 the French National Academy of Medicine had reviewed some features of experiments on human beings. (Human Experimentation 1952) In their deliberations, French doctors distinguished between the use of new methods intended to benefit an individual patient and experiments performed to benefit others. Whereas experiments on patients were regarded as “not only the right but the duty of the physician,” the Academy ruled that experiments for science could only be performed on “informed volunteers free to accept or reject” the intervention. (Frenkel, 1978: 131-32).

Dr. Paul Cibrie, a French physician-delegate to the WMA, chaired the WMA’s committee on medical ethics, which was asked to evaluate issues regarding human experimentation. From the start, Cibrie sought to dissociate the WMA’s considerations of human experimentation from the “scientific crimes” of Nazi medicine. The Nazi medical atrocities, he noted, could be eliminated as “true monstrosities, the commission of which ought always to result in merciless justice.” (Report 1952) Under his guidance, the WMA committee on medical ethics formulated four regulations to serve as a framework for consideration in discussions of human experimentation. The four conditions for ethical human experimentation included: the scientific and ethical qualification of the experimenters; caution and discretion in the publication of early results; the distinction between experiments applied to sick and healthy subjects; and the requirement that subjects undergoing experimentation fully recognized the risks involved.

Thus, under Ciprie's direction, the recommendations for ethical human experimentation reprised the French Academy's 1952 guidelines. In a supplemental report, Cibrie separated the requirements for experimentation on the sick and on the healthy to bring the number of regulations to five. (Report 1952)

Differences over the practice of human experimentation in different national settings became quickly apparent. When the Council of the WMA considered the report in October 1954, the American Austin Smith, one of Cibrie's fellow committee members (the other member of the committee on medical ethics was Spanish physician Lorenzo Garcia-Tornel) protested that the requirement that healthy human subjects be fully informed about an experiment would seriously undermine research in the United States. Smith had long been associated with the American Medical Association. He served as secretary of its longstanding Council on Pharmacy and Chemistry, and in 1949 he succeeded Morris Fishbein as editor of its influential journal, a position he held until 1958. Smith's reservations about informing healthy subjects stemmed from significant postwar changes in the organization and performance of clinical trials. Placebos were becoming integral to the efforts on the part of elite researchers to impose rigorous criteria for the evaluation of new drugs and other therapies. (Kaptchuk, 1998; Nadav? In this volume) The introduction of new methodological constraints in the conduct of clinical trials directly conflicted with the attention in the post-Nuremberg period to insure that research subjects were fully informed.

Other representatives shared Smith's concerns. British physician Hugh Clegg and Danish physician Otto Rasmussen expressed similar reservations in light of the need for properly controlled (and blinded, although the word blinded was not used) scientific



studies. Seeking to defuse the issue, the Dutch delegate L.A. Hulst observed that the difficulty was created by the language used. In the case of an experimental vaccine, he noted, it was important for the individual to know whether or not he had received the vaccine. It would not be appropriate to allow someone to think that he had been vaccinated when there existed a 50% possibility that he had received a placebo injection. Because vaccination trials were rarely conducted in adults, however, Clegg moved that the example of vaccination be deleted from the document because children could not legally give their consent. Following the discussion about the need to inform healthy subjects and to have controlled and blinded studies, the WMA Council endorsed Smith's proposal that any mention of informing healthy subjects about their participation in a control group be deleted from the document sent to the General Assembly.

In October 1954 the eighth general assembly took up the Resolution on Human Experimentation and the Principles for Those in Research and Experimentation. Several delegates explored the regulation about the lay press and the danger of premature and sensational publication. Other delegates raised the issue of consent in the case of experimentation on mental cases and in children. The American delegate F.J.L. Blasingame requested that the requirement of written consent of the responsible individual or the written consent of the individual legally responsible for the subject be added. The General Assembly endorsed the resolution on human experimentation, including the requirement of written consent.

After the adoption of the Rome resolution, the issue of human experimentation continued to concern the WMA's committee on medical ethics and the Council. In 1959, when British physician Hugh Clegg was appointed chair of the committee on medical

ethics, he found the Council seriously divided about the need for a revised code of regulations for human experimentation and the form such a code should take. To begin the work, the British physician (and editor of the *British Medical Journal*) solicited eleven member nations (including the US, Germany, France, Britain, Israel, Japan, India, Turkey, and Chile) for representative general guiding principles for the WMA to use to create a code on "this complicated subject." (Special Reports 1960) To assist the medical societies in articulating their views about clinical research, Clegg identified five scenarios for which the Committee was interested in formulating regulations: the administration of drugs to medical students to test their effects; preventive inoculations using a control group not inoculated against whooping cough or tuberculosis; controlled therapeutic trials of a new drug; using inmates of prisons, penitentiaries, or mental institutions for controlled prophylactic or therapeutic trials, and investigations on hospital patients which had no relation to the condition which brought them to the hospital. (Report 1959)

Several months later, at the request of French physician Marcel Poumailloux, Clegg's committee added a sixth situation for which guidance from member nations would be welcome: experiments undertaken on women in several countries in order to produce sterility either temporarily or permanently. (Minutes 1959)

Clegg's committee report to the WMA Council in April 1960 prompted considerable discussion. Council members offered a variety of observations and suggestions for revising and clarifying the recommendations for human experimentation. Some council members expressed concern about the use of "captive subjects." The Indian delegate A. P. Mitra noted that a prisoner offered remission in his sentence for submitting to an experiment could not exercise "judgment and conscience in the true

sense of the word.” The Philippines delegate urged Clegg and his committee to explore ethical aspects of sending humans into outer space. Otto Rasmussen, the physician representative from Denmark, advised that religious aspects should not be introduced in a code of ethics for human experimentation; instead the code should be based on a “common denominator” acceptable to all religious faiths. In a similar vein, Jean Maystre, the official liaison officer and a Swiss physician, requested Clegg and his committee to obtain additional information from other cultural and ethnic groups, especially Moslem and Buddhist countries. Several members expressed the need to consider experiments that altered or changed personality. (Minutes 1960)

The minutes of the 38<sup>th</sup> council session in Madrid illustrate how the Nuremberg Code of permissible human experimentation shaped WMA discussions about guidelines for clinical research. As some commentators have noted, the WMA’s 1954 Rome Resolution and the drafts of what would become the Declaration of Helsinki did not explicitly mention the Nuremberg Code. In spite of this, nearly all commentators have concluded that the Declaration was greatly influenced by the Nuremberg Code, a conclusion which Sharon Perley and her colleagues have noted is “nowhere documented.” (Perley et al 1992: 158). The minutes of WMA committee and council meetings offer documentary evidence for the salience of the Nuremberg Code for their deliberations. In their discussions over universally applicable guidelines for human experimentation, the WMA Committee on medical ethics debated, and rejected in some cases as too restrictive, specific principles in the Nuremberg Code. At the 1960 Council meeting, for example, members expressed concern that the requirement that all human experimentation be preceded by prior experimentation on animals would bar important

research: "The third rule in the Nuremberg Code would seem to be too restrictive as it provides that no human experimentation should be undertaken without prior experiment on animals. Under certain condition it might provide impossible to try the experiment on animals." (Minutes 1960: 22).

In his September 1960 report of the Committee on Medical Ethics in West Berlin, Clegg informed the Council members that he and his colleagues had briefly considered adopting the Nuremberg Code, published in the American periodical *Science* in February 1953, as a guide. (Report of Medical Ethics Committee 1960) Clegg's committee quickly concluded that the Code was not a sufficient guide, and instead found it necessary to attempt "to draft a code which could serve at least as a guide to doctors working in different conditions and in different countries." (Report 1960) Even before this report, Clegg had suggested the inadequacies of the Nuremberg code for resolving the "doctor's dilemma." In a March 1960 article for the *World Medical Journal*, Clegg offered the story of B.C.G. vaccination as a cautionary tale. Although the vaccination for tuberculosis had been introduced in 1922, it was 1956 before the efficacy of the vaccine in preventing tuberculosis was definitively established. "If only a properly controlled trial of B.C.G. had been conducted in 1923, then thirty-four years of doubt and controversy would have been avoided, and millions of lives would have been saved. And at the end of the thirty-four years one is left with the gnawing doubt about the justification of withholding a prophylactic for which there was reasonable evidence of its efficacy." (Clegg 1960: 77). Given the complexities of modern medical science, Clegg questioned the wisdom of laying down "hard and fast" rules to constrain investigators and their research subjects, but called on research workers to be saturated with the

“Hippocratic ideal,” the physician’s commitment to provide “compassionate care for the sick person.” (Clegg 1960:79.)

Perhaps not surprising, by September 1960 Clegg acknowledged that preparing a code for human experimentation that would simultaneously protect research subjects and not constrain investigators would require considerable time. To speed the discussion, Clegg personally drafted a provisional statement subject to modification and improvement by the Council and his fellow committee members (Italian physician A. Spinelli and Indian delegate A.P. Mitra joined Clegg on the medical ethics committee).

Clegg’s draft code included several restrictions on experiments performed for acquiring knowledge. These included the stipulation that the subject of the experiment be in a mental, physical and legal state to exercise fully the power of choice in decisions to participate. In addition, Clegg expressed disapproval for research in which the subject was in a dependent relationship to the investigator (including the medical student to his teacher, a patient to his doctor, a technician to his laboratory supervisor). He insisted that prisoners of war should never be used as experimental subjects nor should the persons housed in prisons, penitentiaries, and reformatories—that is, captive groups—be used as subjects. Clegg also identified the inmates of mental hospitals and hospitals for mental defectives as undesirable subjects for experimentation. (Supplementary Report 1960)

The Committee on Medical Ethics continued to rework Clegg’s draft code on human experimentation. The 1961 draft divided experiments into the sick and the healthy. In the case of experiments conducted solely for the acquisition of new knowledge, the draft code explicitly banned experiments on prisoners of war, on civilians detained as a result of military invasions or occupation, on persons retained in prisons, on

mental hospitals, and on those incapable of giving consent because of age, mental incapacity, or being in a dependent position.

At the April 1961 council meeting, the proposal received additional scrutiny from Council members. The use of children as research subjects generated much discussion among the physicians who debated the legal right of parents and guardians to consent to experimentation on their children. Although some rejected outright the idea that parents might benefit financially as a result of consenting to experimentation on their child, some insisted that children should categorically be excluded as subjects of experimentation. The issue of prisoners as subjects in research received similar scrutiny. Even though prisoners in some cases volunteered to participate in research, both Clegg and Spinelli insisted that these subjects be excluded as a captive group. The issues raised by children and prisoners in research were not the only sources of conflict. Council members disagreed about the need for defining what constituted a human experiment and about how input from member nations could be solicited to inform the deliberations.

In 1961 Spinelli succeeded Clegg as chair of the Committee on Medical Ethics, and continued to oversee the status of the draft code on human experimentation. In 1962 two American delegates to the WMA Council Gerald Dorman and Austin Smith raised several concerns about the legal and public relations status of the draft code. In May 1962 Dorman questioned the statements in the draft code about the use of prisoners in experimentation. He asked that the draft code of ethics on human experimentation be returned to the committee for further discussion in light of disagreements between the English and French texts, the divisions among the council on the regulations of experiments conducted for the advancement of medical knowledge, and the need to have

public relations advice. Smith, who by 1962 had left his position as *JAMA* editor to become president of the Pharmaceutical Manufacturers Association, similarly warned that both legal experts and public relations experts should review the wording of the document in order to minimize misinterpretation on the part of laypersons. (Minutes 1962; Campion 1984: 492)

In October 1962 the *British Medical Journal* published the WMA's Draft Code of Ethics on Human Experimentation. A brief accompanying editorial note stressed that the code appeared as a service to British physicians and did not represent a final version: "some of the items in it will be re-ordered and modified, and that, in particular, it will eventually be prefaced by a general statement on the essential part played by research in medicine." (Draft Code 1962: 1119.) The draft code defined an experiment on a human being as "an act whereby the investigator deliberately changes the internal or external environment in order to observe the effects of such a change." The draft outlined conditions for acceptable human experiments and those that should not be undertaken, especially those involving "children in institutions and not under the care of relatives." The draft similarly excluded as subjects of experiments prisoners of war—military or civilian, political prisoners, and persons retained in prisons, penitentiaries, or reformatories, mental hospitals and hospitals for mental defectives. (Draft Code 1962: 1119)

Earlier that year, publication of an article by British physician Maurice H. Pappworth entitled "Human Guinea Pigs: A Warning" sparked widespread comment in the British national press. An editorial appearing in the same issue as the Draft Code provided another opportunity to advance Clegg's views that certain classes of human

beings required special protections. Rules for human research became necessary when “general exhortation, letters in the press, and questions in Parliament seem to have little restraining effect on those who cannot always understand the difference between guinea-pigs and human beings, especially when they are collected together in penitentiaries, reformatories, and institutions for the mentally defective.” (Experimental Medicine 1962: 1108.)

In 1962 Clegg was the editor of the *British Medical Journal*. (Bartrip 1990) The decision to publish the draft code as a service to British doctors simultaneously advanced his interests in publicizing his version of the draft guidelines for human experimentation. American reservations about the draft code, especially the bans on using institutionalized children and prisoners as research subjects, may explain why the 1962 draft code did not appear in American medical or scientific journals. Even though Smith had resigned his position as *JAMA* editor, American physicians did not lack on-going access to the AMA’s journals for publishing WMA news and documents. One American researcher took the opportunity to criticize the Draft Code and its provision forbidding the use of “captive subjects” in a review of the use of volunteers in virological research. In 1964 V. Knight rejected the Draft Code’s restriction on using prisoners as volunteers. “Prisoners in the present experiments,” he explained, “were not unduly influenced by the modest privileges and comforts offered, and that there was no duress, stated or implied, with respect to their decision to participate.” (Knight 1964: 18-19) Moreover, Knight, like other American defenders of prisoner research, identified the “positive rehabilitative benefits” that prisoners derived from their participation in medical research. (Knight 1964: 19)



## Resolving the Deadlock

Controversy over using children in institutions and the “captive-subjects” of mental hospitals, prisons, and reformatories continued to divide the WMA members. In 1963 the Committee on Medical Ethics (now composed of American Gerald Dorman, Spinelli, Jean Maystre, Ole Harlem of Norway, and U. Siirala from Finland) reported a deadlock. At Dorman’s suggestion, the Committee agreed to insert a “frank statement” about the failure to reach consensus over the clauses governing both the participation of children in institutions and prisoners in clinical research. (Summary Minutes and Report 1963) The issue of using institutionalized children as research subjects pitted the Americans and Canadians against the French and British who argued that this population should not be used in research. American physicians similarly argued against restrictions on the use of prisoners, insisting that if a prisoner understood and consented to an experiment that he should be permitted to participate in clinical research. In 1963 the draft guidelines were sent to all member nations for study and comments. By October 31, however, only Finland had registered its comments.

In 1964 the Chair of the Committee on Medical Ethics presented the Council with its final deliberations on the draft document “Ethical Principles guiding Doctors in Clinical Research.” The issue of using research subjects in a dependant relationship had not been determined. After lengthy debate, the Council agreed to resolve the issue by altering the name of the document to “Recommendations guiding doctors in clinical research.” (Minutes 1965) When the document came to the General Assembly for a vote,

no mention about using children in institutions or prisoners appeared in the text. In June the General Assembly unanimously endorsed the recommendations for clinical research. To emphasize the importance of the document, the WMA decided to identify the recommendations as the "Declaration of Helsinki." (XVIII World Medical Assembly 1964)

The 1964 Declaration of Helsinki shared some features of the Nuremberg Code's requirements for permissible human experiments. The Helsinki declaration followed the Nuremberg Code's insistence that animal and laboratory studies precede human studies and endorsed the requirement for scientifically qualified investigators. Both the Declaration and the Code stipulated the right of the subject to withdraw from research and the responsibility of the investigator to discontinue the trial if he or she foresaw injury to the research subject. Both called for the consent of the subject.

Unlike the Nuremberg Code, the Declaration of Helsinki distinguished clinical research combined with patient care and non-therapeutic human experimentation. First introduced by the French in 1952 and endorsed by the WMA in the 1954 Rome Resolution, this distinction introduced different consent requirements for ethical human experimentation. The WMA document specified written consent from a healthy subject adequately informed of the aims, methods, anticipated benefits, and potential hazards of the study and the discomfort that it may entail. By contrast, physicians who combined clinical research with professional care were not advised to obtain patient consent in writing. "If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient had been given a full explanation." (Human Experimentation 1964: 177). In another striking departure from the Nuremberg

Code, the Declaration permitted experimentation on individuals unable to exercise informed consent, including children, whose parents or legal guardians agreed to allow the participation in an experiment.

The Declaration of Helsinki was unanimously endorsed but not all participants were pleased by the outcome. Even before the formal ratification of the document, the *British Medical Journal* recorded its dissatisfaction about the compromise of ethical principles necessary to achieve consensus. In 1963 an editorial in the *BMJ* had warned about the insidious “American influence” at work in the revisions of the code. “I am disturbed to learn that the World Medical Association is now hedging on its clause about using—or not *using*—criminals as experimental material,” noted the unsigned editorial. “The American influence has been at work on its suspension.” Crediting the Americans for being the first to apply the terrible lessons of the Nuremberg Doctors Trial, the writer nonetheless rejected the American argument for a profound difference between experiments performed in American prisons and those conducted on the inmates at Auschwitz. “One of the nicest of the American medical scientists I know was heard to say ‘Criminals in our penitentiaries are fine experimental material—and much cheaper than chimpanzees.’ I hope the chimpanzees do not come to hear of this.” (Without Prejudice 1963: 1603). One month following the formal ratification of the Declaration of Helsinki, *BMJ* editorial sentiment remained skeptical about the changes wrought by American influences: “we welcome the revised code of the World Medical Association, while regretting that its revision has to some extent weakened it.” (Ethics of Human Experimentation 1964: 136.)

What was the nature and extent of this American influence on the Declaration of Helsinki? When asked nearly thirty years later about the “American influence” on the Declaration of Helsinki, Gerald Dorman, the sole American member of the WMA’s committee on Medical Ethics in the critical years 1963-1964, confirmed that he made the case to his fellow committee members for the ethical use of prisoners in research. “At the time of the development of the Helsinki Declaration,” he recalled in 1991, “the U.S. delegation did not wish to declare unethical such laws [permitting prison experimentation] per se. However, we did want to restrict and limit their usage by insuring that prisoners had full knowledge of the risks, mishaps or unforeseen immediate and longterm results of their decision to participate.” (Harkness 1996: 161).

George Annas, one of the most prominent contributors to the literature on research ethics, has suggested another American influence. The most important single event to push the final adoption of the 1964 Declaration of Helsinki, he has argued, was the United States Food and Drug Administration’s proposal to streamline and standardize the process for granting approval for experimental drugs. (Annas 1991) In the wake of the thalidomide tragedy, the large-scale trials of new drugs made it necessary, Annas claimed, to confront the issues of human experimentation in a context far removed from both the Nazi concentration camps and the Hippocratic doctor-patient relationship model. As Ruth Faden and Tom Beauchamp have argued, the Drug Amendments of 1962 enacted by the U. S. Congress called for fundamental and potentially far-reaching changes in governmental regulation of the drug industry, including the need to inform patients that they were receiving an experimental drug. The FDA responded with “poorly developed” consent provisions that “repeated the vague wording and broad exception in

the law.” (Faden and Beauchamp 1986: 204). Confusion over the FDA regulations persisted, until the agency clarified its policy with a new set of regulations issued in August 1966. The new regulations—“Consent for Use of Investigational New Drugs on Humans: Statement of Policy”—drew extensively on both the Nuremberg Code and the Declaration of Helsinki.

Drug development and the large-scale trials of new drugs may have played an even more important and immediate role in the formulation of the Declaration of Helsinki. Funding for the WMA and its activities depended on dues from members and other sources. Although the Americans had initially declined to participate in the 1946 meeting that resulted in the WMA, American financial support played a crucial role in the organization’s early years. In September 1947 the American Medical Association organized a luncheon for pharmaceutical manufacturers and their representatives. Already assured of interest on the part of drug makers about “the desirability from many angles of the W.M.A.,” those lunching at the Waldorf Astoria Hotel in New York City heard the president of Warner-Hudnut speak about the humanitarian aims of the WMA. (Irons 1947:3) Elmer Bobst emphasized that the “pharmaceutical industries are part of medicine and their contributions to this project are really a business expense, since funds are an essential factor.” (Irons 1947: 5) The American supporting committee, Canadian physician T.C. Routley, chair of the WMA council, acknowledged, “guaranteed to underwrite the cost of maintaining and operating the central office up to \$50,000 a year for five years.” (Routley 1949: 18)

In 1949, some 1200 American physicians each contributed \$10 to the United States Committee. (World Medical Association 1949) In addition to these individual

doctors, "interested business friends" comprised the leaders of major American pharmaceutical companies. Among the life members of the U. S. Committee were Bobst, L.D. Barney, president of Hoffman-LaRoche, DeWitt Clough, chair of the board of directors of Abbott Laboratories, Adam Fiske, a vice-president at Eli Lilly, Howard Fonda, senior vice-president at Burroughs-Wellcome, Willard Greenwald, scientific consultant for Philip Morris, John McKeen, president of Charles Pfizer and Company, Robert Lincoln, founder of McNeil Laboratories, and Carleton Palmer, chairman of the board of the American pharmaceutical company, E.R. Squibb. (Life Members 1951)

The financial support of the United States Committee was critical to the survival of the new organization. The U.S. Committee played an important role in the daily life of the WMA. The Committee required that the WMA maintain its headquarters in America; the offices for the WMA were located at the New York Academy of Medicine in New York City until 1974, shortly after the AMA resigned in protest over funding and voting arrangements. (Richards 1994). American physicians occupied prominent positions in the new organization. Louis Bauer, who served as the WMA's secretary-general, chaired the Board of Trustees of the American Medical Association. American surgeon Elmer Henderson, a member of the AMA's Board of Trustees, served on the WMA Council. Morris Fishbein, ousted in 1949 from his longtime position as editor of *JAMA*, served as the initial editor of the *WMA Bulletin*. (Fishbein 1969) Austin Smith, who succeeded Fishbein as JAMA editor, also assumed the role of executive editor of the *World Medical Journal*. Smith's editorship at JAMA represented a peak period in the development of new pharmaceutical products, especially antibiotics. At the *Journal*, annual advertising

revenues rose from \$2.7 million in 1951 to more than \$8 million in 1959. (Campion 1974: 491)

In 1958 Austin Smith left the AMA and WMA to become president of the Pharmaceutical Manufacturers of America, a trade group to promote the interests of American drug makers. (He later became chair and chief executive officer of Parke, Davis & Company, and vice chairman of the board of Warner-Lambert Company, two of America's preeminent pharmaceutical houses.) Even after his departure from the AMA and WMA, Smith's position as president of the U.S. Committee gave him a voice in the affairs of the WMA. In the late 1950s and early 1960s the U.S. Committee continued to finance "approximately one-third of WMA activities." (WMA, AMA Archives) In 1959, following the WMA meeting in Montreal, Smith warned that he would be unable to recommend the continued participation of the U.S. Committee in light of the administrative problems in the organization and its troubled finances. To address the concerns of the Americans, the AMA Board of Trustees in 1963 appointed a committee on AMA-WMA relations; this committee was asked to advise the Trustees about the activities of the WMA and its relationship to the U.S. Committee. Among the members of this committee was Dr. Gerald Dorman, the American delegate to the WMA Committee on Medical Ethics and the one who opposed any explicit restrictions on using prisoners and institutionalized children in experimentation. Shortly after the Declaration of Helsinki was adopted, in December 1965, the U.S. Committee to the World Medical Association was dissolved. (WMA, AMA Archives, p. 20)

Drug development in the United States relied extensively on the use of prisoners and reformatories. After the United States Congress passed amendments to the Food,

Drug and Cosmetic Act in 1963, prisoners became essential to the performance of the clinical trials of new drugs. By 1972, FDA officials estimated that more than 90 percent of all investigational drugs were tested initially on the inmates of American prisons. (Harkness 1996: 158) The AMA delegates to the World Medical Association, especially physicians like Austin Smith who worked closely with pharmaceutical company executives, recognized a potential threat to American drug development by restrictions on the use of prison inmates. Even before the Draft Code of Ethics of Human Experimentation was published in 1962, the minutes of the WMA's committee on medical ethics and the council demonstrate that an American influence was already at work to forestall any restrictions on the use of inmates of prisons and reformatories from the document that became the Declaration of Helsinki.

American pharmaceutical companies were similarly invested in the development and testing of new vaccines. As physicians recognized, vaccine testing necessarily involved children, and American researchers and the pharmaceutical companies that supported their research had depended on institutionalized children as the initial recipients for many of the vaccines developed in the 1950s and 1960s. Jonas Salk's polio vaccine, for example, developed in cooperation with the Parke, Davis pharmaceutical company was initially tested in homes for retarded children. (Smith 1990) Vaccines for measles were tested in women's prisons, which allowed young children to remain with their mothers and in group homes for retarded and crippled children. At the Willowbrook State School, pediatric infectious disease researcher Saul Krugman hoped to develop a vaccine against hepatitis using the population of severely retarded infants and children in that institution. (Rothman 1991). It is hardly surprising that the American delegates to



the WMA resisted restrictions on the use of these populations—institutionalized children—in the development of new drugs and vaccines.

American medical organizations quickly embraced the Declaration of Helsinki. Publication of the new recommendations produced almost immediate changes. By 1966 eight American biomedical organizations had endorsed the Declaration, including the American Medical Association, the American College of Physicians, the American College of Surgeons, and the American Academy of Pediatrics. (Human Experimentation 1966). Investigators who submitted abstracts for presentations at conventions for the American Federation of Clinical Research learned that they were now required to sign statements that their work had been conducted in accordance with the Helsinki Declaration. Authors who submitted articles to medical and scientific journals were similarly required to sign statements before publication. (Levine 1996: 242-43)

The Declaration of Helsinki has been hailed as one of the most successful efforts to redeem medical research from the shadow of the atrocities committed in the name of biomedical research in Nazi Germany. Struggling to reconcile protections for the human subjects of biomedical research with the needs and constraints of the emerging clinical sciences, physicians representing many nations found the process protracted and difficult. But the long and winding road to the Helsinki Declaration also suggests that the Declaration, like the Nuremberg Code that preceded it, reflected a strong American slant. In light of the professional commitments of American physicians and political and fiscal realities in the early years of the World Medical Association, America was first among equals on the world stage and in world medicine.



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