Regular Article

Evolution of Recombinant DNA Governance in Japan: Historical Insights and Implications for the Origins of Bioethics

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Abstract

This study analyzes historical documents related to the regulatory reform of recombinant DNA technology in Japan, reflecting the origins of bioethics in the country. Accordingly, the study examines deliberations conducted by committees independently established across multiple ministries and traces how these ministry-level discussions shaped a gradual shift in national guidelines away from mandatory biological and physical containment. The findings indicate that, in the early 1980s, government bodies relaxed containment standards set out in earlier recombinant DNA guidelines by drawing on advances in risk-assessment research. Around the same time, the foreign affairs ministry convened an expert meeting that included bioethicists from advanced industrial nations. These discussions confirmed that recombinant DNA techniques posed minimal risk when used under appropriate controls, and the meeting's statement recorded agreement on the need to establish ethical standards for research involving human subjects. However, participants refrained from promptly identifying specific principles related to individual dignity. In parallel, the ministry responsible for industrial policy participated in international deliberations that led to the establishment of a low-risk category, allowing existing facilities to be approved through case-by-case review—a framework that informed Japan's subsequent regulatory reforms in the late 1980s.

Keywords: Recombinant DNA governance; History of bioethics; International bioethics; Risk assessment; Asilomar Conference

1. Introduction

Recombinant DNA technology made it possible to introduce and stabilize DNA from different species in living organisms, although it also raised concerns about the potential escape of recombinant organisms from laboratory settings. In response, the scientific community called for a moratorium on recombinant DNA research. Following this pause, in February 1975, scientists from 16 countries convened at the International Conference on Recombinant DNA Molecules (the Asilomar Conference) in California to deliberate on the overall policy directions for regulating such experiments (Berg et al. 1975). After these discussions, the U.S. National Institutes of Health (NIH) issued the *Guidelines for Research Involving Recombinant DNA Molecules* in June 1976 (National Institutes of Health 1976). The primary regulatory mechanisms of these guidelines comprised two types of

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containment: (1) biological, which uses hosts that cannot survive outside specified culture conditions and vectors that rarely transfer to cells other than those used for experimentation, and (2) physical, through multiple safety levels to prevent recombinant organisms from escaping the laboratory. Requirements for facilities, design, and operational procedures were specified for each level.

The process by which recombinant DNA technology expanded from basic research to industrial application was well documented both in the United States and Europe (Krimsky 1982; Wright 1994; Gottweis 1998; Krimsky 2001; Jasanoff 2005). However, the involvement of bioethics in this field was not a major focus of scholarly inquiry. At the Asilomar Conference, Alexander M. Capron, a legal scholar and bioethicist from the University of Pennsylvania, together with other members associated with the Institute of Society, Ethics and the Life Sciences (the Hastings Center), participated in discussions. However, the primary emphasis remained on self-governance by the scientific community in these discussions. In Japan, the development of self-regulation for basic research in the 1970s was also examined (Nagai et al. 2009). The first Japanese guideline on recombinant DNA research was the *Guidelines for Recombinant DNA Experiments at Universities and Other Research Institutions*, issued by the Ministry of Education, Science and Culture (MESC) in March 1979 (Ministry of Education, Science and Culture 1979). These guidelines were modeled on the initial NIH guidelines. In August of the same year, the Science and Technology Agency (STA) issued the *Guidelines for Recombinant DNA Experiments* as an administrative directive based on recommendations from the Council for Science and Technology (CST), rather than formally on behalf of the prime minister, thereby extending administrative oversight to all domestic recombinant DNA research (Science and Technology Agency 1979). Although public deliberation on the social control of science was attempted during this period, it did not directly influence these guidelines.

The process of regulatory reform in Japan during the 1980s concerning the industrial application of recombinant DNA technology has been closely associated with the emergence of bioethics in the country, although its details remain insufficiently clarified. The Japan Association for Bioethics (JAB), which integrated medicine with the humanities and social sciences, was founded in 1988, preceding the American Society for Bioethics and Humanities (ASBH), founded in 1998. Some leading bioethicists, who were instrumental in the establishment of the JAB, later published historical retrospectives on the development of bioethics in Japan (Aoki 2007; Sakamoto 2007). According to these accounts, Japanese bioethical perspective began to take root when industry requested that the government establish unified national guidelines, as the industrial application of recombinant DNA emerged during the 1980s.

However, insufficient attention has been given to the Japanese academic community's substantial involvement in the initial creation of this technological innovation, as well as to the government's role in fostering a cooperative relationship with industry through administrative guidance operating within a soft-law framework. The catalyst for the world's first recombinant DNA experiment was the meeting of Stanford University geneticist Stanley N. Cohen and University of California, San Francisco, biochemist

Herbert W. Boyer at an international seminar on plasmid research in Hawaii as part of a U.S.–Japan scientific cooperation program (Lear 1978). The microbiologist Toshihiko Arai from the Japanese organizing team at Keio University attended the Asilomar Conference (Nagai et al. 2009, 6). Moreover, unlike the United States, where the academic community attempted to control commercialization of this technology through legislation but met resistance from industry, Japan operated under a framework often described as "Japan Inc.," in which the government guided industry through nonbinding administrative directives rather than legally enforceable regulations (Johnson 1982; Miwa & Ramseyer 2006).

If that is the case, certain consequences of international discussions on the social regulation of recombinant DNA technology that developed in the 1970s—triggered by the Asilomar Conference and the issuance of experimental guidelines—may have emerged within the context of regulatory reforms in Japan during the 1980s. Although historical research on bioethics has focused primarily on developments within the United States (Rothman 1991; Jonsen 1998; Stevens 2003; Evans 2012; Baker 2013), except for the work that examined the transmission of American bioethics to Europe (France) and Asia (Pakistan) (Fox & Swazey 2008), the field as a whole has not necessarily clarified the trajectory by which bioethical norms and practices expanded into an international domain. In the context following the convening of the Asilomar Conference—characterized by the pioneering contribution of Albert R. Jonsen, a theologian and bioethicist at the University of Washington, who described it as "a covert ethics conference" (Jonsen 1998, 184)—one may ask how ethical issues emerged. An empirical effort to examine this pathway also aligns with recent work that sought to grasp the historical development of bioethics on a global scale without resorting to either the mechanical application of American bioethics or the relativization of multiple cultures (Akabayashi 2020).

This article examines Japan's reform of its regulatory framework for recombinant DNA technology. The analysis examines public deliberations carried out by independent committees established across multiple ministries and traces the gradual shift in national guidelines away from the perspective of biological and physical containment. Preliminary findings indicate that Japanese ministries relaxed the containment standards articulated in the recombinant DNA guidelines issued by the U.S. NIH in the early 1980s, drawing on American research in risk assessment. Japan's Ministry of Foreign Affairs (MOFA) convened a "wise men conference," inviting representatives from G7 countries, including American bioethicists. The discussions confirmed that recombinant DNA technology posed minimal risk when used under appropriate controls, and the press statement released after the meeting recorded agreement on the need to establish ethical standards for research involving human subjects. However, the conference deliberately refrained from promptly identifying ethical principles representing individual dignity and rights. Furthermore, the Ministry of International Trade and Industry (MITI) contributed to deliberations within the Organization for Economic Cooperation and Development (OECD), which led to the creation of a low-risk category. This category allowed existing facilities to be authorized through case-by-case review and formed the basis for subsequent reform of Japan's regulatory framework in the late 1980s.

Table 1. Timeline of Japan's Revisions of Recombinant DNA Guidelines

Year/Month	MESC	STA	MOFA	MITI
1982/7	The Science Council proposed a revision of the guidelines, primarily relaxing biological containment requirements			
1982/8	Revised the *Guidelines for Recombinant DNA Experiments in Universities and Other Research Institutions*	Revised the *Guidelines for Recombinant DNA Experiments*		
1983/6		The Life Science Subcommittee of the CST reported a draft revision of the guidelines, primarily relaxing physical containment requirements		
1983/9		Revised the *Guidelines for Recombinant DNA Experiments*		
1984/3			The Conference on Life Sciences and Mankind issued a press statement asserting that risks of recombinant DNA are minimal under appropriate controls	
1986/5				The Chemical Products Council submitted a draft framework of guidelines introducing new categories not requiring mandatory biological or physical containment
1986/6				Issued the *Guidelines for Industrial Application of Recombinant DNA Technology*
1986/8		Revised the *Guidelines for Recombinant DNA Experiments*		

2. MESC and the Primary Relaxation of Biological Containment Requirements

In the early 1980s, as the United States and Japan sought to establish a cooperative framework for recombinant DNA risk-assessment research, the academic-led regulatory formation process that developed in the 1970s continued to shape the policy. In line with evolving risk-assessment practices at the NIH, the MESC relaxed biological containment requirements in its guidelines for basic research experiments, based on recommendations from its Science Council. This revision was subsequently extended to the broader regulatory framework of the STA.

In December 1978, the NIH issued revised experimental guidelines that rationalized biological containment requirements given accumulating evidence indicating that no serious safety problems had emerged despite advances in recombinant DNA research (National Institutes of Health 1978). In Japan, efforts were underway to establish U.S.–Japan cooperation in risk-assessment research. When NIH Director Donald S. Fredrickson visited Japan in November 1979, he met with the Science Council of the MESC and discussed how such research should address biological containment (Fredrickson 2001). During these meetings, Fredrickson proposed that the United States and Japan undertake joint research aimed at revising and easing regulations on recombinant organisms.

The Subcommittee on Recombinant DNA, established within the Special Committee for Promoting Specified Research Areas of the Science Council of the MESC, took up this proposal. Its core members included molecular biologist Itaru Watanabe of Keio University and geneticist Tetsuo Iino of the University of Tokyo. Following promulgation of the first version of the recombinant DNA experimental guidelines, the subcommittee created a Safety Review Committee to evaluate the conformity of research plans to the guidelines. Its members included Iino, along with molecular biologist Hisao Uchida and applied microbiologist Hiuga Saito, both of whom were also at the University of Tokyo. In the context of U.S.–Japan scientific cooperation, these scientists organized an international conference on recombinant DNA research in Hawaii in February 1981 (Japanese Planning Committee of U.S.–Japan Cooperative Program for Recombinant DNA Research 1988). At the conference, participants compared the two countries' progress in risk-assessment research, and Japan reaffirmed its commitment to adopting the U.S. framework, as it had done when drafting the first version of its experimental guidelines.

These developments influenced the Science Council to recommend primarily easing biological containment requirements in July 1982 (Ministry of Education, Science and Culture 1982). The following month, the MESC revised its *Guidelines for Recombinant DNA Experiments in Universities and Other Research Institutions* accordingly. This revision was also incorporated into STA guidelines, which cover all recombinant DNA experiments conducted in Japan (Science and Technology Agency 1982).

3. STA and the Primary Relaxation of Physical Containment Requirements

In 1983, the STA revised the national guidelines for recombinant DNA experiments based on a report by the Life Science Subcommittee of the CST, primarily relaxing requirements for physical containment. At this stage, in addition to scientists oriented toward applied

research, engineers from the fermentation and pharmaceutical industries also began to participate in the deliberations. However, these discussions remained confined to laboratory-scale experimentation and did not extend at that stage to large-scale industrial cultivation.

Demand for industrial applications of recombinant DNA technology expanded in Japan during the 1980s. In the fermentation and pharmaceutical industries, the utilization of recombinant DNA techniques became an important challenge in research and development. Consequently, calls for revising existing regulations intensified within academic research institutions and across the industrial sector. A survey conducted in September 1982 by the Japan Federation of Economic Organizations (Keidanren) found that 54 of 113 companies intended to conduct recombinant cultures exceeding 20 L, with 29 seeking early revision of the experimental guidelines (Japan Federation of Economic Organizations 1982).

In August 1980, the STA submitted the Opinion on the Promotion of Life Sciences to the Prime Minister through the CST (Council for Science and Technology 1980). This opinion called for revision of the experimental guidelines and emphasized the need to promote work involving recombinant DNA, artificial gene manipulation, and related areas of biological research. In response to growing domestic demand, the Life Science Subcommittee of the CST formed the Subcommittee on Recombinant DNA Technology, which examined revisions to the regulatory framework for these experiments. Itaru Watanabe, Hiuga Saito, and Hisao Uchida were among its core members and also played central roles in the earlier formation of the experimental guidelines.

Saito played a key role in linking developments across industry, government, and academia. He conducted research on applied microbiology and fermentation at the University of Tokyo's Institute of Applied Microbiology. Several engineers trained under him later became leading members of research teams conducting culture experiments using recombinant DNA technology at companies such as Kyowa Hakko Kogyo Co., Ltd. and Takeda Chemical Industries, Ltd (Tahara 1981). Saito maintained that if recombinant organisms posed sufficiently low risks, existing industrial fermentation facilities could be used with minimal modification (Saito et al. 1987). According to STA officials at the time, leading scientists such as Saito regularly participated in deliberative bodies convened by multiple ministries (Kaneichi et al. 2007).

In June 1983, the Life Science Subcommittee submitted a draft revision of the guidelines concerning large-scale (20 L or more) cultivation of recombinant organisms in experimental systems (Science and Technology Agency 1983, 74-87). The draft proposed allowing large-scale cultivation through a case-by-case review system for existing facilities. To address the potential release of recombinant organisms outside experimental apparatuses, the STA established a "special containment method." This method was less stringent than conventional measures, permitting the use of recombinant organisms confirmed to possess particularly high biological safety. This method was subject to individualized national review and guidance. In September of the same year, the then Prime Minister issued the revised *Guidelines for Recombinant DNA Experiments* in line with this report (Science and Technology Agency 1983, 1-54). However, this revision was limited to experimental systems and did not address

industrial-scale applications. Although it accommodated 20- to several-hundred-liter systems used in laboratory-based large-scale cultivation, facilities involving tens-of-tons tanks typical of industrial fermentation remained outside its scope.

4. MOFA and the International Consensus on the Low Risks of Recombinant DNA

In 1984, the MOFA organized the Conference on Life Sciences and Mankind, through which Japan contributed to establishing an international consensus on recombinant DNA technology. Proposed as part of Prime Minister Yasuhiro Nakasone's diplomatic initiative at the G7 Summit, the conference convened academic participants, including American bioethicists. The discussions confirmed that recombinant DNA posed minimal risk when used under appropriate controls, a conclusion reflected in the press statement issued after the meeting. The statement also recorded agreement on the growing need to establish ethical standards for research involving human subjects. However, consistent with broader transnational deliberations on recombinant DNA technology, the conference concluded that no specific ethical principles would be adopted at that stage, despite recognizing the importance of safeguarding individual dignity and rights.

In June 1982, at the Versailles Summit held in Paris, the potential for international cooperation in response to rapid advances in biotechnology was already under review. The leaders' communiqué noted that emerging scientific and technological fields—such as information technology, materials engineering, and biotechnology—were poised to shape the structural transformation of the global economy, and it emphasized the need for industrialized nations to cooperate in promoting research and development in these areas (G7 Summit 1982). However, for Nakasone, who became Prime Minister in November of that year, promotion of the life sciences and discussion of their ethical implications were understood to be inseparable components of the same policy agenda (Nakasone 2002).

Before the Williamsburg Summit of May 1983 in the United States, Nakasone delivered a lecture at Johns Hopkins University, where he emphasized the need to establish an international forum to discuss the ethical implications of advances in the life sciences for human dignity (Nakasone 1984). He argued that issues such as the creation of life through genetic manipulation and human intervention in the laws of nature were universal ethical concerns and proposed that the international community engage in comprehensive deliberation to protect human existence and dignity. Following the approval by the participating nations at the G7 Summit, Japan implemented the proposal by hosting an international conference. After returning to Japan, Nakasone instructed the MOFA to begin preparations for the conference. Around the same time, the STA established a Human Dignity Review Office within the Minister's Secretariat (Science and Technology Agency 1984) and publicly expressed its intention to contribute to convening the meeting (Nihon Keizai Shimbun 1983; Yomiuri Shimbun 1983). Although Nakasone served twice as Director-General of the STA, inter-ministerial consultation resulted in the MOFA assuming primary responsibility for organizing the conference (Ministry of Foreign Affairs 1983d).

Nakasone instructed the MOFA that the conference should not be limited to regulatory issues concerning specific biotechnologies such as recombinant DNA but

should instead address broader social implications of advances in the life sciences (Ministry of Foreign Affairs 1983a). In line with this policy, the MOFA held hearings with academic experts (Ministry of Foreign Affairs 1983b). In one session, Itaru Watanabe emphasized the need to "review the trajectory of developments in the natural sciences, from physics to the life sciences and then to the behavioral (or mental structure) sciences and to grasp their relationship to ethical issues from a broad perspective." Based on these consultations, the MOFA established what was provisionally titled the International Conference on the Development of Life Sciences and Human Dignity and, with involvement of the STA and cooperation of the MESC, the MITI, the Ministry of Health and Welfare (MHW), and the Ministry of Agriculture, Forestry and Fisheries (MAFF), advanced conference planning (Ministry of Foreign Affairs 1983c). Japanese participants were selected during preparatory meetings, and Watanabe was appointed a core member of the conference's advisory committee.

The first meeting of the conference, officially titled the Conference on Life Sciences and Mankind, was held in March 1984 in Tokyo and Hakone and brought together academic experts nominated by the heads of state of the G7 countries (Japan Foundation 1984). From the United States, participants included Paul Ramsey, a theologian and bioethicist from Princeton University, and Leon R. Kass, a physician and bioethicist from the University of Chicago; from the United Kingdom, Sydney Brenner, a molecular biologist from the Medical Research Council's Laboratory of Molecular Biology, also participated. Japan was represented by molecular biologist Setsuro Ebashi of the University of Tokyo, French literature scholar Takeo Kuwabara of Kyoto University, and psychologist Hayao Kawai, also of Kyoto University. Ebashi also served on the Council on Life and Ethics, established by the MHW in March 1983 (Ministry of Health and Welfare 1985). During the same period, Kuwabara and Kawai were among the intellectuals who, under Nakasone's auspices, sought to establish the International Research Center for Japanese Studies (Nichibunken) as a national hub for internationally oriented research on Japanese culture (Befu 2001).

In his keynote lecture, Kuwabara reflected on the 1975 Asilomar Conference and the subsequent formulation of NIH guidelines in the United States, characterizing this process as a model case of ethical conduct arising from scientists' self-reflection on technological practice. During the discussions, Kass also cited the scientists' moratorium on recombinant DNA research and development of NIH guidelines as a successful precedent, while stressing the need for broader ethical inquiry beyond responses to a single technology. These discussions similarly reaffirmed that recombinant DNA posed minimal risk when conducted under appropriate controls. According to officials at the MITI at the time, this conclusion was based on accumulated findings from many years of risk-assessment research, and it was following this meeting that Japan's domestic experimental guidelines were subsequently relaxed (Hosoya 1987).

Ultimately, the conference published a press statement affirming continuation of discussions among the G7 participants and indicating that future meetings would have a more specific focus (Japan Foundation 1984, 130-132). The document recorded agreement on the importance of addressing ethical considerations in biomedical research involving human subjects,

including the growing need to establish appropriate research ethics frameworks. However, the conference refrained from promptly identifying ethical principles representing the moral status of individuals. Two items were included:

> 12. Participants discussed ethical issues related to current developments in biomedical research. They concluded that experiments in the life sciences require a balance between the benefits to mankind in regard to health and welfare and the dignity and rights of individuals.
>
> 13. This raises the question of whether agreed normative principles are needed as preconditions for solving ethical problems. But it was concluded that no agreement on such specific norms could be attempted at present (Japan Foundation 1984, 131).

Item 12 affirmed respect for the trajectory by which U.S. policies for the protection of human subjects were formed, beginning with the National Research Act of 1974. The Department of Health, Education and Welfare (DHEW)—reorganized in 1980 into the Department of Health and Human Services (DHHS)—issued regulations for the protection of human subjects, formally codified as Title 45 of the Code of Federal Regulations Part 46 (45 CFR 46), and by 1981, the DHHS promulgated significant revisions of these regulations and encouraged other federal agencies to adopt them (Porter 1990). Item 13 indicated that, at that time, the conference did not adopt the contents of the Belmont Report, a foundational U.S. human subjects protection policy document that articulated three ethical principles: (1) Respect for Persons (honoring individual autonomy), (2) Beneficence (minimizing harm and maximizing benefits) and (3) Justice (ensuring fair distribution of burdens and benefits) (Nagai et al. 2022).

These international agreements on ethics concerning research involving human subjects may be viewed as reflecting the multicultural composition of the G7 countries, which consisted of three regions: Western Europe (the United Kingdom, France, West Germany, and Italy), North America (the United States and Canada), and East Asia (Japan). The three ethical principles established by law in the United States each had distinct origins: (1) Respect for Persons derived from Christian theological concepts and offered a comprehensive framework encompassing both respect for autonomy of competent subjects and protection for vulnerable individuals; (2) Beneficence was closely tied to professional ethics of those engaged in modern Western medicine; and (3) Justice incorporated conceptual analyses of distributive fairness developed primarily in North America. Even among countries in Western Europe and North America, these principles were interpreted and emphasized somewhat differently, reflecting variations in legal traditions, medical cultures, and philosophical foundations. As the host nation, Japan was all the more conscious of the distance between these ideas and its own intellectual traditions. In this context, the conference included a lecture by a Japanese Buddhist scholar on conceptions of life, establishing the meeting as a forum where ethical principles could be relativized in light of the cultural diversity of the G7 nations.

However, the ethical implications of agreement on items 12 and 13 for research involving human subjects extend beyond this and may also be understood considering developments within the United States. By 1991, the DHHS's regulations for the protection of

human research subjects had been harmonized with those of many other U.S. federal agencies. These regulations became known as the "Common Rule" (Porter & Koski 2008). Nevertheless, there is a lack of definitive evidence as to whether the three Belmont principles were consistently applied in the review of such research conducted under the jurisdiction of agencies other than the DHHS. In particular, it remains unclear whether agencies whose research primarily involved healthy adults accepted principles concerning the treatment of vulnerable individuals lacking decision-making capacity, such as minors. Thus, even in the United States, where ethical principles were introduced through law, it was not possible to apply these principles comprehensively across the spectrum from basic research to industrial applications, which fall under the jurisdiction of multiple agencies. Therefore, the G7 countries did not immediately adopt common ethical principles within the context of an international conference that also required diplomatic coordination.

Following the 1984 meeting, the conferences continued until all G7 countries hosted a session. The second meeting, renamed the International Conference on Bioethics, was hosted by the French government in April 1985 and focused on genetic engineering (International Conference on Bioethics 1985). The third meeting, held in West Germany in April 1986, addressed neuroscience and psychiatry (Opolka et al. 2012). This sequence of meetings may be seen as aligning, at least in part, with Watanabe's proposal to trace the developmental trajectory of the natural sciences, from physics to the life sciences and subsequently to the behavioral (or mental structure) sciences. Thereafter, meetings continued in rotation among the G7 countries, including the European Community (EC), and served as an international forum for public discourse on bioethics (Capron 1988; Bourdeau et al. 1990).

Building on this trajectory, Nakasone incorporated these developments into his broader diplomatic agenda, which sought to strengthen international cooperation in research and development in the life sciences. At the Venice Summit held in Italy in June 1987, Nakasone proposed the Human Frontier Science Program (HFSP) as an international initiative to promote cutting-edge research, particularly by fostering high-risk, high-gain, and interdisciplinary collaboration (International Human Frontier Science Program Organization n.d.). In October 1989, its administrative secretariat, the International Human Frontier Science Program Organization (HFSPO), was established in Strasbourg, France.

5. MITI and the Relativization of Biological and Physical Containment

In 1986, the MITI assumed a central role in linking international regulatory coordination with domestic administrative adjustment, marking a turning point in Japan's regulation of recombinant DNA technology. Through its participation in OECD deliberations, MITI contributed to the development of a regulatory approach that accommodated both the risk-assessment model employed by the U.S. NIH and the facility-based review method supported by Japan and the United Kingdom, thereby aligning emerging international consensus with domestic policy. At the national level, the MITI introduced guidelines for industrial applications based on recommendations of the Chemical Products Council (CPC), a subordinate advisory body under its jurisdiction, and extended the existing laboratory-based

regulatory framework to industrial use through administrative guidance.

In fiscal year 1981, the MITI launched the Research and Development Program for Basic Technologies for Future Industries, selecting "technologies for the industrial use of recombinant DNA" as one of its biotechnology-related themes (Hirato 1982). The program supported the development of microorganisms capable of efficiently producing substances using recombinant DNA technology. In 1983, the MITI formed the Subcommittee on Recombinant DNA Technology under the CPC to examine its application in industrial settings. Key members of this subcommittee included Hisao Uchida, applied microbiologist Kazuo Komagata of the University of Tokyo, and fermentation scientist Keiji Yano of the same university.

These domestic deliberations coincided with international regulatory discussions at the OECD. In 1983, the OECD Committee for Scientific and Technological Policy (CSTP) established the Group of National Experts on Safety in Biotechnology (GNE) to promote regulatory coordination. Japanese scientists and government officials, including Uchida and Itaru Watanabe, participated in these discussions (Ministry of International Trade and Industry 1985a). Japan and the United Kingdom emphasized that certain microorganisms used in fermentation and antibiotic production had a "long history of safe use." They proposed a facility-based, case-by-case review approach that would permit the use of existing facilities for cultivating recombinant organisms, underscoring that the two countries shared a pragmatic, experience-based orientation in contrast to the more theory-driven standards emerging from the U.S. NIH risk-assessment framework. According to Uchida, Japanese fermentation products and antibiotics accounted for more than 90 percent of the global market at the time (Uchida et al. 1995). Given this industrial dominance, the United Kingdom, already equipped with fermentation facilities, found common cause with Japan in promoting this facility-oriented approach, which differed from the prevailing U.S. model.

In 1985, Roger Nourish, the GNE chair and U.K. representative, visited Japan and delivered a lecture at the fifth meeting of the Subcommittee on Recombinant DNA Technology in March 1985, encouraging a facility-specific, case-by-case approach (Ministry of International Trade and Industry 1985b). At certain stages, the U.S. framework gained the upper hand, as when the draft OECD recommendation temporarily removed the case-by-case concept proposed by Japan and the United Kingdom. However, Uchida and other members of the MITI subcommittee traveled to France and continued coordination jointly with the U.K. representative (Ministry of International Trade and Industry 1985c). In July 1986, the OECD adopted the recommendation Good Industrial Large-Scale Practice (GILSP), known as the "Blue Book," which accepted a facility-based review approach and allowed use of existing equipment for relatively low-risk recombinant organisms (Organization for Economic Cooperation and Development 1986).

Rather than following the OECD recommendation only after adoption, the MITI moved in parallel to reflect this international agreement in domestic policy. In May 1986, the CPC submitted recommendations on industrial use of recombinant DNA technology (Ministry of International Trade and Industry 1986a), and in June, the Minister of International Trade and Industry issued the *Guidelines for Industrial*

Application of Recombinant DNA Technology (Ministry of International Trade and Industry 1986b). These guidelines introduced a flexible, five-category classification system and allowed the use of existing tanks, ultracentrifuges, and pipelines with minimal modification. The MITI's approach also influenced national-level regulation: in August, the STA revised its *Guidelines for Recombinant DNA Experiments* to incorporate the framework of the industrial guidelines (Science and Technology Agency 1986). In December of that year, formal review of corporate applications began, and 52 cases from 12 companies were approved (Tamaki 1987).

6. Limitations

This analysis focused on changes in the treatment of biological and physical containment within the regulatory formation process of recombinant DNA technology. The study has certain limitations, being confined to the stages leading up to the point when the regulatory framework proposed by the MITI began to influence national policy. Therefore, it did not examine the regulatory measures introduced by the MHW and MAFF from the late 1980s onward that controlled the use of this technology in clinical medicine and agriculture.

7. Conclusion

This study examined historical documents concerning the reform of Japan's regulatory framework for recombinant DNA technology. It identified public deliberations conducted through committees established by multiple ministries and traced the evolution of national guidelines as they shifted away from treating biological and physical containment as mandatory requirements. The analysis demonstrated that, in the early 1980s, government agencies eased the containment standards set out in earlier recombinant DNA guidelines, based on advances in risk assessment research. Simultaneously, the foreign affairs ministry convened a "wise men conference" that included bioethicists from several advanced industrial nations. The discussions confirmed that recombinant DNA techniques posed minimal risk when used under appropriate controls, and the meeting's statement recorded agreement on the need to establish ethical standards for research involving human subjects. However, participants deliberately refrained from promptly identifying specific principles related to individual dignity and rights. Meanwhile, the ministry responsible for industrial policy participated in international deliberations that resulted in the establishment of a low-risk category, under which existing facilities could be approved through individual review. This framework subsequently informed Japan's regulatory reform in the late 1980s.

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