JAPAN: CO-ORDINATED ACTION

If "regulation" has seemed to mean "free release" in North America and Europe, in Japan it means orderly development of industrial processes for pharmaceuticals and commodity chemicals.

As elsewhere, responsibility for regulating biotechnology is divided among several agencies: the Ministry of Education, the Science and Technology Agency (STA); the Ministry of International Trade and Industry (mighty MITI); the Ministry of Health and Welfare (MHW); and the Ministry of Agriculture, Forestry, and Fisheries (MAFF). (Table 1.)

As elsewhere, each agency has its own set of guidelines and its own mission: MITI's regulations tend to foster commercial applications; MHW's rules protect consumers and set standards for safety and efficacy in pharmaceuticals, biologicals, cosmetics, and medical devices. But beneath the differences lies a fundamental unity.

Regulatory activity is a fair index of scientific and industrial activity. In 1986 alone, Japanese researchers conducted some 4,600 experiments under regulatory guidelines. Universities accounted for the lion's share of these, some 72 percent. (Table 2.)

Since October of 1986, STA has signed off on 84 applications from nearly a score of companies. These requests involved recombinant production of reagents (63 percent of approvals), enzymes and biocatalysts (30 percent), and amino acids (7 percent).

In roughly the same period, pharmaceutical regulators approved 21 applications for clinical tests. In October and November, three companies—Nippon Roche, Takeda Chemical, and Schering-Plough—won final approval to market recombinant human alpha interferon. (Table 3.)

When it comes to biotechnology, only agriculture lies fallow.

Japanese regulators anticipate growing pains. An increasing volume of requests for permits for research and production, coupled with the regulatory policy of case-by-case evaluation and individual inspection, means far more work for regulators in the years ahead. The load looks especially burdensome in commercial-scale applications. Though the total volume may still be small, it is rising rapidly. And, because Japanese containment standards are said to be more stringent than those in the United States, requiring a more detailed review, the pressure on the regulatory apparatus is disproportionately increased.

Visitors see little popular opposition to biotechnology in Japan. Japanese point to the commercial appeal of cell-culture-derived shikonin (used in lipsticks) and the country's long familiarity with fermented foods. High-tech cachet and cultural familiarity far outweigh "Andromeda Strain" anxiety, they say. But there are exceptions: Community opposition, due at least in part to concern over the possible release of recombinant organisms, substantially delayed openings of two new biotech facilities—the new Protein Engineering Research Institute building near Osaka and the biosafety level 4 laboratory at Institute of Physical and Chemical Research (RIKEN) in Tsukuba.

Written by Douglas McCormick from material furnished by the editors of *Newton*, the Japanese graphic science magazine.

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1. RESPONSIBILITY FOR REGULATING BIOTECHNOLOGY IN JAPAN

University research
The Ministry of Education
Guidelines to Experiments in DNA Recombinations in Relation to University Research Organizations. March '79, rev. Aug. '82, amended Sep. '83, Aug. '85.

Research organizations excluding universities
The Science and Technology Agency
Guidelines to Experiments in DNA Recombination. August '79, rev. Aug. '82, amended Sep. '83, Aug. '85, Aug. '86, Sep. '87.

Industry
The Ministry of International Trade and Industry
Guidelines for Industrial Application of Recombinant DNA Technology. June '86. (Incorporates OECD drafts).

Pharmaceuticals
The Ministry of Health and Welfare
Guidelines to the Technical Adaptation of DNA Recombination in the Production of Pharmaceuticals. December '86, rev. May '87.

Agriculture
The Ministry of Agriculture, Forestry, and Fisheries
Guidelines to the Usage of Recombined Substances in the Fields of Agriculture, Forestry, and Fisheries. December '86.

2. JAPANESE rDNA EXPERIMENTS, FY 1986

Research performed by:	Total	Under 20 liters				Over 20 liters			
		EC	SC	BS	P/A	EC	SC	BS	P/A
National laboratories	151	121	10	3	17	—	—	—	—
Private laboratories	98	94	—	—	4	—	—	—	—
Public utilities	107	81	9	—	14	—	3	—	—
Special-status corporations	50	32	2	2	14	—	—	—	—
Private enterprises	875	611	69	36	115	35	4	2	3
University related	3324	2749	120	82	373	—	—	—	—
Total	4605	3688	210	123	537	35	7	2	3
Containment level: Percentage at P1/LS1		43%	77%	30%	28%	94%	100%	100%	33%

EC—*Escherichia coli*; SC—*Saccharomyces cerevesiae*; BS—*Bacillus subtilis*; P/A—Plant and animal cells.

3. CLINICAL APPROVALS IN 1987

April '87:
Pyruvic acid oxidase
Toyo Jozo
Erythropoietin
Kirin Brewery
Chugai Pharmaceutical
Tissue plasminogen activator
Toyobo Biotech

May '87:
Granulocyte colony stimulating factor
Chugai Pharmaceutical
Human beta interferon
Kyowa Hakko Kogyo
Human gamma interferon
Kyowa Hakko Kogyo
Meiji Milk Products
Tumor necrosis factor
Asahi Chemical Industry
Dainippon Pharmaceutical

August '87:
Hepatitis B vaccine (CHO)
Mitsubishi Chemical Industries

October '87:
Human alpha 2a interferon
*Takeda Chemical Industries**
*Nippon Roche**

*market approval

November '87:
Alpha 2 interferon
*Schering-Plough**

Other approvals:
Interferon 2
Takeda Chemical Industries
Human gamma interferon
Takeda Chemical Industries
Nippon Roche
Suntory
Somatomedin C
Fujisawa Pharmaceuticals
Human epidermal growth factor
Wakunaga Pharmaceuticals