

Makina Kato

is a research associate at the Graduate School of Biostudies, Kyoto University. She earned her B.Sc. and Ph.D. in bioethics from the University of Tsukuba. Her current research focuses on bioethics and public communication in biotechnology companies.

Darryl Macer

is Regional Advisor on Social and Human Sciences in Asia and the Pacific, at RUSHSAP, UNESCO Bangkok, Thailand. He is also an affiliated professor in bioethics at United Nations University Institute of Advanced Studies; and Director, Eubios Ethics Institute, Japan, New Zealand and Thailand. (<http://www2.unesco-bkk.org/eubios/index.htm>). He taught bioethics at the University of Tsukuba, Japan from 1990–2005, during which time this research was conducted. He is a member of the International Union of Biological Sciences (IUBS) Bioethics Committee and HUGO Ethics Committee, a Board Member of the International Association of Bioethics, and Secretary of the Asian Bioethics Association.

Keywords: *bioethics, business ethics, biotechnology, education, ethics committees*

Makina Kato, PhD
Department of Biostudies and Society,
Graduate School of Biostudies,
Kyoto University,
Yoshida-Honmachi, Sakyo-ku,
Kyoto 606–8501, Japan

Tel: +81 75 753 9244
Fax: +81 75 753 9245
E-mail: makina@lif.kyoto-u.ac.jp

Bioethical concerns in Japanese biotechnology companies

Makina Kato and Darryl Macer

Date received (in revised form): 16th March, 2006

Abstract

Analysis of responses from a 2003 survey of 304 Japanese biotechnology companies found that 93 per cent responded that they had never had a bioethical problem related to biotechnology in their company but 31 per cent did expect to have some kind of problem in the future while 26 per cent already had systems in place to deal with these issues. The open responses to all these questions are presented and discussed. Specific issues raised by the companies concerned problems related to dealing with human samples, clinical trials, animal experiments and public reaction to their research/business. Concerns about future problems relating to intellectual property rights (IPRs) were not raised by any of the companies. A number of different systems were in place to deal with bioethical issues although some companies said they did not need any specific system to deal with any problems which might arise.

INTRODUCTION

Although new biotechnology applications can prove a great boon to society, a variety of bioethical issues have been raised as there is often an underlying feeling, particularly among consumers, that profits come before ethics in the companies that are developing and selling these applications. There have been a number of surveys in a range of countries which have shown that consumers do not trust product safety information when it comes from the company making or selling the product.^{1,2}

It is therefore of interest to examine how aware companies are of possible bioethical issues and what actions they have taken, if any, to deal with these issues. This paper details the results of a survey, conducted in 2003, of Japanese companies that were in some way related to the biotechnology industry and follows on from a similar international study.³

SAMPLING OF 'COMPANIES RELATED TO BIOTECHNOLOGY'

For the purpose of this study, 'the companies related to biotechnology' were

defined broadly as companies that operated business activities in connection with biotechnology either directly or indirectly but did not include companies that only invest money in biotechnology, financial institutions, publishing companies or clinical research organisations (CROs).

Companies were initially identified from the 'Nikkei Bio Yearbook 2003',⁴ from member lists of industrial organisations and by searching the internet, while surveys and market research reports were also consulted to include venture companies. After excluding the companies that did not fall into our broad definition, the list comprised 1,556 companies. Of the companies which could be contacted by telephone, 769 consented to receive the survey. Only 39 per cent (304) of the companies completed the survey while 17 per cent responded but declined to complete the survey. The remaining 44 per cent of companies did not respond at all to the survey. The first telephone call was on 16th January, 2003, and the last response was received on 17th June, 2003. To maintain company privacy,

during the initial telephone conversation and in the subsequent questionnaire all companies were told that their responses would be anonymised and that no mention of individual company names would be made in subsequent reporting of the study.

Basically the same questionnaire format (Table 1) as that used in the international survey³ was employed. Results of this yes/no (Y/N) questionnaire demonstrate that only 6 per cent of the 304 companies which responded to the survey had had bioethical problems in the past but a third expected to encounter problems in the future.

ATTRIBUTES OF THE COMPANIES AND METHOD OF ANALYSIS

There was little difference between the composition of the whole survey population and that of the valid responses when companies were categorised by industry type (Table 2).

To analyse the data obtained, the following methods were used:

- Quantitative analysis of Y/N answers.
- Cross-tabulation of Y/N answer and attributes of the companies (type of industry, main field of biotechnology, amount of capital, volume of sales and number of employees).
- Cross-tabulation between the answers to each question.
- Qualitative analysis of comments by

KJ method (or Card Work method).

- Secondary analysis of responses received in different questions.

The KJ method⁵⁻⁷ was employed to analyse qualitative data. It is an established method to summarise the free opinions of respondents in a comprehensive manner. In this method all of the responses are grouped and stratified based on their similarity to the other responses. For details, refer to our previous paper.³

Have you had bioethical problems in your company?

In response to the initial question, only 6 per cent (17 of 304 companies) said they had encountered problems in the past, while 29 companies made specific comments to this question. These comments were resolved into 32 different elements (irrespective of a yes or no answer) using the KJ method (three companies gave responses that were resolved into two different elements). These elements were then grouped by their similarity and classified into four groups as follows (the numbers in parentheses indicate the number of elements, and the number of companies):

- Group 1 Have had specific problems (23,20).
- Group 2 Have not had such problems (4,4).
- Group 3 Have nothing to do with such problems (3,3).

Methods used for data analysis

Table 1: Results of the questionnaire survey (Y/N answer)

Question	% of valid responses		
	Yes	No	N/A
Have you ever had a bioethical problem related to biotechnology occur in your company? If so, what kind of problem was it?	6	93	1
Do you think in the future you could have a bioethical problem related to biotechnology in your company?	31	67	2
Do you have any special measures or systems in your company to deal with bioethical issues related to biotechnology? If so, please tell me what they are.	26	73	1

Table 2: Results of survey categorised by industry type comparing total survey population with valid responses, and proportion of those valid responses who indicated that they expected future bioethical problems and whether they currently had systems in place to deal with such problems

Industry type	Examples	% of total by industry type		Proportion of companies who answered yes to the question (%)	
		Whole survey population	Valid responses	Do you have future concerns?	Do you have current systems?
R&D, contract research & non-clinical tests	Research, contracted research/experiment/analysis, non-clinical test, R&D type venture, development and breeding of experimental animals, synthesis of DNA/proteins for research	21.5	23.0	21.5	28.8
Pharmaceutical	Pharmaceuticals, therapeutics, therapeutic enzyme, vaccines, generics	13.8	9.9	14.0	18.8
Trading & wholesaling	Trading, wholesaling, sales, energy, petroleum	13.3	12.5	10.8	1.3
Chemical manufacturing	Quasi-drugs, materials/intermediates for pharmaceutical/agrochemicals, insecticide for home use, textile, ceramic, glass, cosmetics, fermentation, synthetic resin, leather, industrial enzymes, agrichemical, fertiliser	12.5	14.8	10.8	16.3
Research instrument and reagent manufacturing	Equipment/instrument/reagent for research/non-clinical tests, laboratory apparatus, measuring device for research/experiment, analytical instrument	7.8	9.5	11.8	7.5
Food manufacturing	Food, beverage, health food, nutritional supplement, food processing	7.7	9.9	7.5	10.0
Medical/clinical instrument & reagent manufacturing	Medical equipment/instrument, instrument/reagent for clinical test/diagnosis, diagnostics, contact lenses	6.1	5.3	8.6	8.8
Medical/clinical service	Clinical tests, contracted pathological test/diagnosis, storage of samples for therapeutic purposes	3.9	1.0	2.2	3.8
Other service	Service other than medical service, design, real estate, telecommunication, software (not for research), DNA identification, preservation of DNA without immediate medical purpose	3.9	3.3	3.3	1.3
Machine manufacturing	Electronic machine, equipment/instrument not for research/clinical purpose, heavy industry, electronic cable	3.6	4.6	5.4	2.5
Agriculture/veterinary	Agricultural/agriculture-related products, dairy, horticulture, animal feed, drugs/vaccines for animals	3.3	2.6	2.2	1.3
Construction and engineering	Construction, engineering, plant, environmental clean-up operation/system	2.7	3.6	2.2	0

- Group 4 The question is not very clear (2,2).

Of the 20 companies in group 1, 4 said that they had received enquiries or criticisms from external sources. This group was further divided based on the specific problems which had been encountered. Handling of biological samples and problems relating to the environment were the most reported

problems. Some illustrative examples are shown below for each subgroup of group 1.

- 1–1 Had problems/concerns about handling biological samples (8,7).
‘Issue of how to deal with samples derived from humans (including genetic information) and the associated personal information’

- 1–2 Had problems/concerns about animal experimentation (4,4).
‘The method used to euthanase experimental animals’
- 1–3 Had problems/concerns about genetically modified materials (3,3).
‘Receiving inquiries from customers about the effects of genetically modified ingredients on the human body’
- 1–4 Had problems/concerns about influence on the environment (7,6).
‘Influence on the environment and living organisms, from using recombinant DNA techniques’
- 1–5 Had problems/concerns about clinical development (1,1).
‘Ethical protection in clinical development’

Although comments in groups 2 and 3 were that they had not had any problems, some in group 3 did give their reasons for not having had any problems, for example, ‘We always adjust to the standard which is considered as most appropriate in academic society and industry.’ The two comments grouped under group 4 were general criticisms that the area covered by bioethics is unclear.

Do you have future concerns about bioethical problems?

Almost one-third of companies (31 per cent, 96 companies) indicated that they had future concerns about bioethical problems in the company, significantly more than those who said they had experienced a problem in the past. Looking at the distribution of responses by industry (Table 2), there was a slightly higher proportion of ‘Pharmaceutical’ and ‘Medical/clinical instrument and reagent manufacturing’ companies that responded ‘Yes’ to this question than in the distribution of total valid responses, suggesting that the risks of bioethical

problems were recognised more often by these groups of companies. Interestingly, none of the ‘Pharmaceutical’ companies, which had the second highest proportion for this question, had said they had encountered problems in the past.

Some 114 companies made comments in response to this question, which were resolved into 126 elements and subsequently into six groups based on their similarity as follows:

- Group 1 Have (possible) concerns of facing specific problems (96,85).
- Group 2 Have concerns in broad perspective over genetic manipulation (4,3).
- Group 3 Do not have any problems at the moment but have problems might occur depending on our future business (8,8).
- Group 4 Although we do not have problems at the moment we cannot say we definitely will not have problems in the future (6,6).
- Group 5 Will not have problems in the future (9,9).
- Group 6 Do not know (3,3).

Some 83 per cent of the 102 companies who gave comments (groups 1–4) had specific concerns of some kind. This group was further divided into 13 subgroups based on the specific issues mentioned. The most frequently reported concerns were those over handling biological samples and handling personal/genetic information. It is also interesting to note that eight companies expressed their concerns that they could face problems indirectly through customers or users. Sample comments are shown below for each subgroup of group 1.

- 1–1 Have concerns about problems on the handling of biological samples (22,19).

Future concerns about bioethical problems

- ‘About the research use of patients’ samples in development of diagnostics’
- 1–2 Have concerns about problems on informed consent (3,3).
- ‘Informed consent in the use of samples for genetic analysis’
- 1–3 Have concerns about problems on the handling of personal/genetic information (14,14).
- ‘Individual information management of sample donors in research’
- 1–4 Have concerns about problems on the security of information (5,5).
- ‘Case of individual information leak in development of gene analysis technology/equipment or in gene analytical service, which might violate human rights’
- 1–5 Have concerns about problems on the application of technology to humans (7,7).
- ‘Application of technology to, for example, culture of *in-vitro* fertilised egg or xenotransplantation’
- 1–6 Have concerns about problems on adverse event/clinical accident (8,8).
- ‘In the development of medicine, there is always the possibility that adverse effects might occur’
- 1–7 Have concerns about problems on genetic diagnosis (2,2).
- ‘In selling DNA chips for diagnosis, there may be a disease for which there is no treatment or the possibility of diagnosis influencing a person’s insurance’
- 1–8 Have concerns about problems on handling experimental material (2,2).
- ‘Control over the natural materials which have particular physiological activities, for example, toxic agents’
- 1–9 Have concerns about problems on animal experiments (9,9).
- ‘We might have problems with regard to animal protection, since we use rabbits and mice for antibody production’
- 1–10 Have concerns about problems on the influence on the environment (6,6).
- ‘In the case that we apply the technology with microorganisms to accelerate cleanup process of pollutant in environment’
- 1–11 Have concerns about problems on social/consumer acceptance (6,5).
- ‘Consumers’ understanding about the safety of genetically modified organisms (GMOs)’
- 1–12 Have concerns about problems on the views of social norms or regulation (4,4).
- ‘Problems could occur in the future if we overlook ethical values and standards/regulations of society. We carefully observe and consider future trends but do not think it’s an infallible measure’
- 1–13 Have concerns about facing problems indirectly (8,8).
- ‘How to respond to the request to build equipment for companies which have bioethical problems’
- The comments in group 2 referred to the awareness of the ethical aspects of genetic technology in a broader social sense rather than concerns over the possible problems in one company. For example:
- As an extension of gene analysis of livestock, there are some issues of genetic modification of livestock and

the issues of human gene analysis, but we have not yet discussed in-depth to such issues at the moment.

The comments in the group 5 showed various reasons not to have the concern. Only one company said that they did not have any concerns about future bioethical issues since they already had systems in place to deal with any such problems.

Do you have any systems in place for dealing with any bioethical problems?

Despite a significant proportion of the companies having had a problem or expecting to encounter a problem, only 26 per cent (80 companies) said they had some special measure/system in place to deal with potential problems.

Looking at the distribution of responses by industry (Table 2), 'Pharmaceutical' and 'R&D, Contract research and Non-clinical tests' companies were more positively answered to this question. Strikingly, however, significantly fewer of the 'Trading and wholesaling' companies had systems in place despite their concerns about encountering problems in the future.

The largest companies (by capital) were much more likely to have systems in place compared to medium and small companies (Table 3) and this tendency was similar when comparing data by sales and the number of employees.

Some 100 companies made comments to this question and were grouped as follows:

- Group 1 Have several measures to deal with the issues (23,23).
- Group 2 Have an ethics committee (26,26).
- Group 3 Have a committee/examination organisation (16,16).
- Group 4 Have guidelines/standards/norms (3,3).
- Group 5 Deal with the issues in other form than internal system (7,7).
- Group 6 Have no system or code but try to deal with the issues in some way (11,11).
- Group 7 Company is currently considering which system/s to employ (10,10).
- Group 8 Do not have any measures/systems and do not deal with the issues (4,4).

Of the 23 companies in group 1, 20 said some form of committee made up part of their overall strategy. The comments referring to the committees with the word 'ethics' were separately grouped into the group 2. This group was subdivided into three subgroups as follows. The first subgroup 2-1 was composed of the comments that did not mention specific content or subject of the committees.

- 2-1 Have an ethics committee/

Systems in place for dealing with bioethical problems

Table 3: Total valid responses and companies which said they had systems in place to deal with bioethical problems categorised by company size (capital)

Size of company by capital	Proportion of all valid responses (%)	Companies that have systems in place (%)
Large (¥1bn or more)	35.9	58.8
Medium (between ¥100m and ¥1bn)	28.6	20.0
Small (less than ¥100m)	34.2	20.0
Unknown	1.3	1.3

Results clearly show presence of bioethical issues related to biotechnology

research ethics committee (16,16).

- 2–2 Have an ethics committee on gene/biological samples (9,9).
- 2–3 Have an ethics committee for animal experiments (1,1).

Group 3 was subdivided into five subgroups according to the subject of the committee/organisation:

- 3–1 Have a committee on recombinant DNA (7,7).
- 3–2 Have an organisation on clinical trial (3,3).
- 3–3 Have an organisation on quality control/quality assurance (2,2).
- 3–4 Have an organisation on safety control (1,1).
- 3–5 Have a committee/organisation of some kind (3,3).

Group 4 included three companies that said they had written protocols to address any issues. Group 5 consisted of seven companies (all small) that said they depended on an external guidance to deal with any problems:

- 5–1 Apply criterion of judgment by outsider/external institution (5,5).
- 5–2 Have committee at parent company (2,2).

Group 6 was composed of 11 companies (medium and small sized) with no specific system but who dealt with problems in some. This group included three subgroups:

- 6–1 Deal with the issues company-wide (3,3).
- 6–2 Consider on the side of management (2,2).

- 6–3 Have alternative means (6,6).

The companies in groups 7 and 8 had no systems in place to deal with any problems although those in group 7 implied the possibility of developing some measures in the future.

DISCUSSION

The results of the survey clearly show the presence of some bioethical issues related to biotechnology in the companies that responded. Although the majority of respondents said they had not faced bioethical problems in the past, it is possible that they had actually faced problems, given their concerns about facing potential problems in the future. Despite the promise of anonymity, it is possible that companies did not answer truthfully when asked if they had encountered problems in the past so as not to negatively impact on the public perception. It is also possible that those completing the survey might not have known about any existing problems within their company.

Some specific problems were indicated, such as handling human samples, clinical trials, animal experimentation and public backlash. Despite some strong concerns seen in public debates, no companies mentioned intellectual property rights (IPRs) as a past bioethical problem (nor as a future concern). IPRs are very important in biotechnology and any problems over IPRs may be discussed more as an institutional obstacle or an inevitable factor for competitiveness, rather than as specific bioethical issues.

About one-third of the companies answered that they saw the possibility of future bioethical problems, although it is not possible to judge from this survey how acute and urgent these concerns are, but it is clear from the survey that some companies were very worried that their companies might encounter bioethical problems at some time in the future. Past and/or future 'problems' included not only actual events such as discontinuation of experiments or recall of products, but

also difficult inquiries from customers, and dilemmas in decision making.

It is also noteworthy that some companies thought they might be involved in bioethical issues indirectly. Although this kind of concern has been documented previously, it reflects the fact that the activity of one company can be directly and/or indirectly affected by another, particularly as the spread of biotechnology businesses widens. For example there have been cases involving the recall of food which unknowingly contained genetically modified organisms (GMOs) where companies that did not directly deal with biotechnology were still economically affected.

The survey also showed that a variety of systems were employed by the companies surveyed to deal with any bioethical issues which might occur. Some companies have multiple systems to deal with these issues and others indicated that they did not need any measures. The survey also revealed that bioethical issues were not always dealt with separately but sometimes in conjunction with systems such as crisis management and health and safety. The results also suggested that the companies with the greatest concerns about encountering problems in the future also tended to be the ones that took/were taking positive actions to make sure systems were in place to deal with those potential problems.

According to a survey by the Japan Registered Clinical Laboratories Association in 2000,⁸ 80 per cent of the laboratories that conducted human genetic testing had or were setting up ethics committees. Compared with the results of the present survey where only 20 per cent of all companies indicated that they had some internal organisations to deal with the potential issues, it is clear that the specific industry greatly influences a company's attitude toward setting up such committees.

Although they fell within our broad definition of 'companies associated with biotechnology', many of the companies

that we contacted explicitly stated that they had nothing to do with bioethics, and that their activities were irrelevant to the issues, and this included companies that did not participate as well as some that did.

Furthermore, although there were some comments that suggested that only companies that were involved in genetics or handling human tissues would be concerned with bioethical issues, it is clear that many more companies will need to be aware of these issues in the future. Insurance companies, for example, are likely to be very interested if they can have the results from genetic testing for disease susceptibility. Oliver⁹ argues in his book 'The Coming Biotech Age' that every industry, company and all kinds of organisations will have to be concerned with biotechnology. Concerns about bioethical issues surrounding biotechnological applications may not be limited to only the companies related to biotechnology.

References

1. Macer, D. R. J. (1994), 'Bioethics for the People by the People', Eubios Ethics Institute, Christchurch, New Zealand.
2. Macer, D. R. J. (2001), 'Bioethics; perceptions of biotechnology and policy implications', *Int. J. Biotechnol.*, Vol. 3, pp. 116–133.
3. Kato, M. and Macer, D. R. J. (2003), 'How companies respond to bioethical issues', *J. Comm. Biotechnol.*, Vol. 9, pp. 153–162.
4. Nikkei Biotech and Nikkei Biobusiness, ed. (2002), 'Nikkei Bio Yearbook 2003', Nikkei BP, Tokyo (in Japanese).
5. Kawakita, J. (1967), 'Method of ideas: for inspire creativity', Chuokoron-sha, Tokyo (in Japanese).
6. Kawakita, J. (1970), 'Method of ideas 2: Development and application of KJ method', Chuokoron-sha, Tokyo (in Japanese).
7. Kawakita, J. (1986), 'KJ Method: Let chaos speak', Chuokoron-sha, Tokyo (in Japanese).
8. Japan Registered Clinical Laboratories Association (2001), 'Ethical Guidelines on Human Contract Genetic Testing', Tokyo, Japan.
9. Oliver, R. W. (2000), 'The Coming Biotech Age', McGraw-Hill, Columbus, OH.

A variety of systems were employed to deal with bioethical issues