DUAL-USE REVIEW POLICIES OF BIOMEDICAL RESEARCH JOURNALS

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To address biosecurity issues, government agencies, academic institutions, and professional societies have developed policies concerning the publication of “dual-use” biomedical research—that is, research that could be readily applied to cause significant harm to the public, the environment, or national security. We conducted an e-mail survey of life science journals to determine the percentage that have a dual-use policy. Of the 155 journals that responded to our survey (response rate 39%), only 7.7% stated that they had a written dual-use policy and only 5.8% said they had experience reviewing dual-use research in the past 5 years. Among the potential predictors we investigated, the one most highly associated with a journal having a written dual-use policy was membership in the Nature Publishing Group (positive association). When considered individually, both previous experience with reviewing dual-use research and the journal’s impact factor appeared to be positively associated with having a written dual-use policy, but only the former remained significant after adjusting for publishing group. Although preventing the misuse of scientific research for terrorist or criminal purposes is an important concern, few biomedical journals have dual-use review policies. Journals that are likely to review research that raises potential dual-use concerns should consider developing dual-use policies.

PREVENTING THE POTENTIAL MISUSE OF biotechnology for terrorist or criminal purposes has become a major public policy concern.^{1–5} To address biosecurity issues, government agencies, academic institutions, and professional societies have developed policies concerning the publication of “dual-use” biomedical research—that is, research that could be readily applied to cause significant harm to the public, the environment, or national security.^{1,3,4} Some scientific journals, such as *Science*, and some publishing groups, such as the Nature Publishing Group (NPG) and the American Society of Microbiology journal group, have developed dual-use review policies, but it is not known how many other journals or publishing groups have developed such policies.³ Van Aken and Hunger conducted a survey of 28 major life science journals that regularly publish research that may raise biosecurity issues and found that only 25% of these journals had dual-use review policies.⁶ Although their survey offers some important infor-

mation, it has limited utility because of the small sample size and the targeted (nonrandom) nature of the sample. The goals of our study were: (1) to conduct a larger, random survey of dual-use review policies of life science journals, and (2) to determine whether having a dual-use policy is associated with a journal’s impact factor, publisher, type of publisher (commercial versus noncommercial), country of origin, or editorial experience with reviewing papers that raise dual-use issues.

MATERIALS AND METHODS

A random sample of 400 life science journals likely to review research that may raise dual-use issues was drawn from the ISI Web of Knowledge Journal Citation Reports 2009 Edition. The journal categories included: biochemistry and molecular biology, biotechnology and applied

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microbiology, cell biology, biomedical engineering, genetics and heredity, immunology, infectious diseases, medical laboratory technology, medicine/general and internal, medicine/research and experimental, microbiology, parasitology, pharmacology and pharmacy, toxicology, tropical medicine, and virology. At the time of our study, these categories represented more than 1,200 journals.

We obtained contact information for the journals and sent the editors an e-mail asking them to provide information about dual-use policies and whether they had reviewed any manuscripts in the past 5 years that raised potential dual-use concerns. We defined a dual-use review policy as a written policy that required an additional level of review for submitted manuscripts whose results, if published, could be readily applied to cause significant harm to the public, the environment, or national security. We indicated in our e-mail that we considered a dual-use policy to be different from other ethics policies, such as misconduct policies. We sent a reminder e-mail within 7 days if we had no response and a second reminder after 14 days.

We also gathered data from Journal Citation Reports or the journal's website on impact factor, publisher, and country of origin. Impact factor is a measure of the average number of citations to a journal in a scientific field. Many view impact factor as an indicator of the importance or influence of a journal. Some studies have shown that impact factor is a positive predictor of journal policy development.⁷ The Office of Human Subjects Research at the National Institutes of Health (NIH) determined that our research was exempt from Institutional Review Board review.

We investigated the relationship between having a dual-use policy (yes, no) and 5 predictors: impact factor (continuous), experience with dual-use decisions (yes, no), commercial publisher (yes, no), nationality of publisher (U.S./Canada, Europe, Other), and publishing group (Elsevier, Wiley, Springer, Nature, BioMed Central, Taylor & Francis, Other). All analyses were performed with procedures from the SAS software package (version 9.2, SAS Institute, Inc., Cary, NC). We used the FREQ procedure to calculate exact 95% confidence intervals for the proportion of journals having a dual-use policy at each level of the categorical predictors. We also used FREQ to obtain a 2-sided *p*-value based on Fisher's exact test to compare the proportion of journals having a dual-use policy for 1 level of a categorical predictor versus all other levels combined. Finally, we used logistic regression (the LOGIST procedure) to assess the effects of individual and multiple predictors on the probability of having a dual-use policy. All tests were performed (and *p*-values calculated) at the nominal 0.05 significance level.

RESULTS

Of 400 journals randomly selected for contact, 155 responded to our survey (response rate 39%). Of the respondents, 12 (7.7%) said they had a written dual-use

review policy and 143 (92.3%) said they did not; the exact 95% confidence interval for the percent of respondents having a dual-use policy was (4.1%, 13.1%). The average impact factor was 3.8, with a standard deviation of 5.7 and a range from 0.3 to 47.1 (the median value was 2.5). Among the 12 journals with a dual-use policy, the average impact factor was 12.4 (median 5.7), compared with an average impact factor of 3.1 (median 2.4) among the 143 journals without a policy. As for reviewing dual-use research in the past 5 years, 112 journals (72.3%) said they had no experience, 9 (5.8%) said they had some experience, and 34 (21.9%) did not give a definite answer to this question (Table 1). Of the 155 journals that responded to our survey, 132 (85.2%) were published by commercial publishers and 23 (14.8%) were not. Regarding nationality, 85 journals (54.8%) were from Europe, 58 (37.4%) were from the U.S. or Canada, and 12 (7.7%) were from other countries. Journal publishing groups included: Elsevier, 29 (18.7%); Wiley, 23 (14.8%); Springer, 19 (12.3%); NPG, 9 (5.8%); BioMed Central, 7 (4.5%); Taylor & Francis, 4 (2.6%); and all others, 64 (41.3%). For a list of all 155 journals responding to our survey, see the Appendix.

The best predictor of a journal having a dual-use policy was membership in the Nature Publishing Group. All 9 NPG journals and only 3 of the remaining 146 journals had a dual-use policy, indicating a strong positive association between the NPG and having a policy ($p < 0.001$, Table 1). When considered individually, an impact factor above the median ($p = 0.017$) and experience with reviewing dual-use research ($p = 0.035$) also were positively associated with having a dual-use policy (Table 1). On the other hand, the odds of a journal having a dual-use policy were not significantly affected by publisher nationality, having a commercial publisher, or membership of the publisher in any of the other groups surveyed (Table 1). These results were based on Fisher's exact test, but similar results were obtained using logistic regression.

We also investigated which variables identified in the individual analyses remained influential when considered together. Membership in the NPG was clearly important, but we wanted to know whether impact factor or previous experience with dual-use decisions contributed additional information. To answer this question, we performed similar analyses on the 146 journals not in the NPG. Within this subset, previous experience with reviewing dual-use research was significantly (and positively) associated with having a dual-use policy ($p = 0.013$), but having an impact factor above the median was not (data not shown). The other variables still showed no effect on the odds of having a dual-use policy. Logistic regression gave similar results, whether including impact factor as a continuous predictor or creating a binary indicator based on the median.

Finally, we plotted the distribution of journals with and without a dual-use policy versus impact factor and membership in the NPG (Figure 1). As stated earlier, all 9 journals in the NPG had a dual-use policy. Of the

Table 1. Distribution of Dual-Use Policy Status Across Levels of Several Categorical Variables for Responding Journals

<i>Variable</i>	<i>Level</i>	<i>N</i>	<i>Number (%) with a Dual-Use Policy</i>	<i>Exact 95% C.I. for Percent with Dual-Use Policy</i>	<i>Exact p-Value^a</i>
Impact factor exceeds median ^b	Yes	77	10 (13.0%)	(6.4%, 22.6%)	0.017
	No	78	2 (2.6%)	(0.3%, 9.0%)	
Experience with dual-use decisions ^c	Yes	9	3 (33.3%)	(7.5%, 70.1%)	0.035
	No	112	8 (7.1%)	(3.1%, 13.6%)	
Commercial publisher	Yes	132	10 (7.6%)	(3.7%, 13.5%)	0.693
	No	23	2 (8.7%)	(1.1%, 28.0%)	
Nationality of publisher	U.S./Canada	58	6 (10.3%)	(3.9%, 21.2%)	0.140
	Europe	85	4 (4.7%)	(1.3%, 11.6%)	
	Other	12	2 (16.7%)	(2.1%, 48.4%)	
Publishing group	Elsevier	29	0 (0.0%)	(0.0%, 11.9%)	0.124
	Wiley	23	1 (4.4%)	(0.1%, 22.0%)	1.000
	Springer	19	0 (0.0%)	(0.0%, 17.7%)	0.363
	NPG	9	9 (100%)	(66.4%, 100%)	<0.001
	BioMed Central	7	0 (0.0%)	(0.0%, 41.0%)	1.000
	Taylor & Francis	4	0 (0.0%)	(0.0%, 60.2%)	1.000
	Other	64	2 (3.1%)	(0.4%, 10.8%)	0.124

Note: *N* = sample size; C.I. = confidence interval.

^aExact *p*-value is based on Fisher's exact test comparing current level with all other levels combined.

^bThe median value for impact factor was 2.496.

^cInformation on previous experience with dual-use decisions was not reported by 34 journals.

remaining 146 journals, there was no obvious association between the 3 journals with a dual-use policy and impact factor. Although 1 of the 3 had the second highest impact factor, the other 2 ranked 108th and 119th highest out of 146. Thus, our data did not provide any evidence that impact factor was significantly predictive of having a dual-use policy (at least among the survey respondents), after adjusting for information on membership in the NPG.

DISCUSSION

Our most important finding is that only 7.7% (95% confidence interval: 4.1%-13.1%) of the 155 responding journals indicated they had a dual-use review policy. Of the potential explanatory variables we examined, the best predictor of having a dual-use policy was membership in the NPG. All 9 NPG journals had a dual-use policy, whereas only 3 of the remaining 146 journals did. This suggests that the odds of having a dual-use policy depended more on a publisher's rules than on an individual journal's rules. Not surprisingly, among the journals outside the NPG, those with previous experience reviewing dual-use research were more likely to have a dual-use policy than those without experience. When considered individually, higher journal impact factors were associated with greater odds of having a dual-use policy, which is consistent with recent claims that impact factor was the only variable among several (such as publisher and country) that was significantly associated with having a misconduct policy.⁷ In our study, however, the significance of journal impact factor as a predictor of

having a dual-use policy disappeared after adjusting for publishing group membership.

The percentage of journals in our sample that had a dual-use policy (7.7%) was much lower than the percentage reported by van Aken and Hunger (25%).⁶ One likely explanation for the difference in results is that different populations were studied; they focused on top journals in biomedicine, which have high impact factors, while we did not limit our sample in this way. In their sample of 28 life science journals, van Aken and Hunger included 20 of the top journals in virology and biomedicine, which had an average impact factor of 16.7, as well as 5 Russian journals and 3 Chinese journals with no ratings for impact factor.⁶ In contrast, the average impact factor in our sample was 3.8. While it is important to understand how the top biomedical journals are responding to dual-use dilemmas in publication, it is also essential to have an understanding of how low- and mid-level journals are dealing with this issue, since these journals also review research that may pose a threat to biosecurity. Our research suggests that journals with high impact factors (ie, those in the top tier) are more likely to have dual-use policies than journals with low impact factors, though much of this may be explained by publishing group policies.

Nine journal editors described how they would respond if they encountered a paper that raised dual-use concerns, but our analysis did not count these journals as positive respondents because they did not have a formal (written) policy, and we decided to include only journals with formal policies. An interesting follow-up study would ask editors about their informal policies pertaining to dual-use research.

Figure 1. Distribution of Dual-Use Policy Status by Impact Factor and Publishing Group

The 9 diamonds denote journals in the Nature Publishing Group (NPG), all of which have a dual-use policy. The 146 open circles denote non-NPG journals, all but 3 of which do not have a dual-use policy.

None of the journal policies that the editors shared with us included criteria for determining whether research should be published, not published, or edited for potentially harmful content. The policies only described a procedure for applying an additional level of review for manuscripts identified as raising dual-use concerns. A follow-up study might ask editors about the criteria they would use in decision making, or whether they would make decisions on a case-by-case basis.

Several of the editors had interesting responses to our survey. One editor said that despite the fact that her journal had published several papers that had dual-use implications, she and her colleagues had never heard of the term “dual-use” and had never considered implementing a policy to address such manuscripts. Another editor immediately changed the journal’s policy to read, “All authors will conform to the National Science Advisory Board for Biosecurity (NSABB) guidelines for Dual-use Life Sciences Research.” Several editors stated that they would develop dual-use policies in the near future. Surprisingly, a few editors had negative reactions to the idea of a dual-use policy; in fact, one stated, “We do not employ two different tiers of peer review because of potential use of biotechnology by terrorists or criminals. This could be considered potentially as discrimination, bias or a political issue.” Another common reaction among editors was to state that it was unlikely their journals would ever receive a manuscript that would have dual-use implications and consequently there was no need to develop a dual-use policy.

These reactions from the editors suggest several reasons that so few biomedical journals have developed dual-use policies. First, many editors may simply not be aware

of the importance of biosecurity issues in scientific publishing. Second, some editors may be aware of biosecurity issues but do not feel that these issues are relevant to their journals because they have not reviewed dual-use research and they do not believe they are likely to do so in the near future. Third, some editors may understand the need for a dual-use review policy but have simply not taken the time to develop one. Fourth, some editors may view a dual-use policy as an inappropriate restriction on freedom of inquiry and the dissemination of scientific knowledge. Additional research could be conducted to explore journal editors’ ideas and attitudes concerning dual-use review and potential barriers to policy development.

A limitation of our study is the low response rate (39%). It is worth noting, however, that our response rate was not significantly lower than the response rates of other e-mail surveys, which tend to have lower response rates than telephone surveys.⁸ One possible explanation for our low response rate is that we conducted the study during the summer, when many academic institutions in the U.S. and Europe are on break. Some of the editors indicated that they would respond when they returned from vacation, but they never did. Another possible explanation for the low response rate is that some of our e-mails may have been rejected as spam or junk e-mail. Finally, editors may have been concerned about the potential legal liability implications of responding to our survey, although we stated in the e-mail that we would protect the confidentiality of the responses. We do not believe that any of the reasons for the low response rate undermined the validity of our data or biased our overall results.

CONCLUSION

Although preventing the misuse of scientific research for terrorist or criminal purposes is an important concern, few biomedical journals have dual-use review policies. Journals that are likely to review research that raises potential dual-use concerns should consider developing dual-use policies.

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Appendix: List of Responding Journals

1. Acta Clinica Belgica
2. Acta Crystallographica Section D-Biological
3. AIDS Research and Human Retroviruses
4. American Family Physician
5. American Journal of Human Biology
6. American Journal of Medical Genetics Part A
7. American Journal of Medical Genetics Part C
8. American Journal of Preventive Medicine
9. Annals of Biomedical Engineering
10. Annals of Clinical Biochemistry
11. Annals of Family Medicine
12. Annual Reviews
13. Antiviral Therapy
14. Aquatic Toxicology
15. Asian Biomedicine
16. Biochemical Genetics
17. Biochimica et Biophysica Acta—Molecular Cell Research
18. Bioessays
19. Biological Chemistry
20. Biologicals
21. Biomedical Chromatography
22. Biomedical Engineering Online
23. Biomedical Microdevices
24. Biomolecules and Therapeutics
25. BMC Genomics
26. BMC Medical Genetics
27. BMC Microbiology
28. BMC Molecular Biology
29. Bone Marrow Transplantation
30. Canadian Journal of Microbiology
31. Caryologia
32. Cell Communication and Adhesion
33. Cell Preservation Technology (Biopreservation and Biobanking)
34. Cell Stress and Chaperones
35. Chemical and Biochemical Engineering Quarterly
36. Clinical and Experimental Immunology
37. Clinical and Investigative Medicine
38. Clinical Chemistry and Laboratory Medicine
39. Clinical Toxicology
40. CNS Neuroscience and Therapeutics
41. Comparative Biochemistry and Physiology A—Molecular and Integrative Physiology
42. Computer Methods and Programs in Biomedicine
43. Connective Tissue Research
44. Croatian Medical Journal
45. Current Molecular Medicine
46. Current Opinion in Infectious Diseases
47. Current Opinion in Microbiology

48. Cytokine
49. Cytokine and Growth Factor Reviews
50. Development Genes and Evolution
51. DNA and Cell Biology
52. DNA Repair
53. Drug Safety
54. Drugs
55. Drugs of the Future
56. European Journal of Clinical Pharmacology
57. European Journal of Human Genetics
58. Experimental Hematology
59. FASEB Journal
60. FEBS Letters
61. FEMS Immunology and Medical Microbiology
62. Folia Histochemica et Cytobiologica
63. Folia Parasitologica
64. Food Biotechnology
65. Free Radical Biology & Medicine
66. Future Microbiology
67. Future Virology
68. Genes and Nutrition
69. Genetics
70. Genetics Selection Evolution
71. Human Genetics
72. Human Psychopharmacology—Clinical and Experimental
73. Immunology
74. Immunology and Cell Biology
75. Immunology Letters
76. Infectious Disease Clinics of North America
77. International Biodeterioration and Biodegradation
78. International Immunopharmacology
79. International Journal of Nanomedicine
80. Journal Biomedical Microdevices
81. Journal of Allergy and Clinical Immunology
82. Journal of Biological Chemistry
83. Journal of Biomaterials Applications
84. Journal of Biomedical Materials Research Part B—Applied Biomaterials
85. Journal of Biomolecular Structure and Dynamics
86. Journal of Cellular Biochemistry
87. Journal of Clinical Pharmacology
88. Journal of Family Practice
89. Journal of Genetic Counseling
90. Journal of Genetics and Genomics
91. Journal of Histochemistry and Cytochemistry
92. Journal of Histotechnology
93. Journal of Hospital Infection
94. Journal of Hospital Medicine
95. Journal of Human Genetics
96. Journal of Immunological Methods
97. Journal of Labelled Compounds and Radiopharmaceuticals
98. Journal of Leukocyte Biology
99. Journal of Microbiological Methods
100. Journal of Molecular Biology
101. Journal of Natural Medicines
102. Journal of Neural Engineering
103. Journal of Neurochemistry
104. Journal of Neuroimmune Pharmacology
105. Journal of Pharmacokinetics and Pharmacodynamics
106. Journal of the American Board of Family Medicine
107. Journal of the Mechanical Behavior of Biomedical Materials
108. Journal of Virological Methods
109. Korean Journal of Genetics
110. Lasers in Medical Science
111. Mammalian Genome
112. Melanoma Research
113. Microbiology and Molecular Biology Reviews
114. Molecular Breeding
115. Molecular Cancer
116. Molecular Vision
117. Mutagenesis
118. Mutation Research
119. Nature Biotechnology
120. Nature Genetics
121. Nature Immunology
122. Nature Medicine
123. New England Journal of Medicine
124. New Microbiologica
125. Oncogene
126. Perspectives in Biology and Medicine
127. Pharmaceutical Research
128. Pharmacoeconomics
129. Pharmacogenomics
130. Phytotherapy Research
131. Plant and Cell Physiology
132. Plant Biotechnology Journal
133. Platelets
134. PLoS Genetics
135. PLoS Pathogens
136. Postgraduate Medical Journal
137. Process Biochemistry
138. Progress in Lipid Research
139. Progress Neuro-Psychopharmacology Bio Psych
140. Protein and Peptide Letters
141. Protein Engineering Design & Selection
142. Protein Expression and Purification
143. Recent Patents on Anti-Cancer Drug Discovery
144. Sexually Transmitted Diseases
145. Statistics in Medicine
146. Stem Cell Reviews and Reports
147. Systematic Parasitology
148. Toxicology and Applied Pharmacology
149. Traffic
150. Transboundary and Emerging Diseases
151. Transgenic Research
152. Tropical Medicine and International Health
153. Undersea and Hyperbaric Medicine
154. Upsala Journal of Medical Sciences
155. Veterinary Immunology and Immunopathology