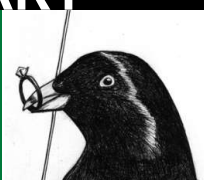

LETTERS

edited by Jennifer Sills

The Status of Atlantic Bluefin Tuna

WE ARE CONCERNED BY SOME STATEMENTS IN THE LETTER "THE FATE of Atlantic bluefin tuna" by tuna scientist J.-M. Fromentin (12 March, p. 1325). Fromentin's comments reflect widespread misconceptions used to argue against the inclusion of Atlantic bluefin tuna (BFT) in Appendix I of the Convention on International Trade in Endangered Species (CITES).

Fromentin's statement that current scientific knowledge does not unequivocally support a BFT listing under Appendix I doesn't serve the debate. Very rarely does fisheries science unequivocally support any conclusion; rather, it expresses a high probability of a given scenario being met. Fromentin omits the fact that the International Commission for the Conservation of Atlantic Tunas (ICCAT) Scientific Committee concluded (*1*) that there was a 95% probability that BFT had declined to the extent that it would qualify for an Appendix I listing. This conclusion was endorsed by the majority of the FAO Panel (*2*), the International Union for Conservation of Nature (IUCN) (*3*), and the CITES Secretariat (*4*).

Although CITES decided not to list the Atlantic BFT on Appendix I, it is not true that it would have been the first commercially exploited marine species so listed. Most of the great whales, all marine turtles, all but one sawfish species, and two sturgeon species are listed on CITES Appendix I.

We regret that many governments and individuals continue to be more concerned about future CITES listings of other marine species than about the very reasons why those may be eligible: the dire state of many fish stocks. Nothing indicates, as Fromentin suggests, that the listing of BFT could lead to CITES implicitly assuming management of fisheries. Such a statement is absurd. CITES deals specifically with international trade only, and its mandate is therefore completely different from fisheries organizations. In cases where international trade drives overfishing, fisheries organizations and CITES working together offers the best possible chance of ensuring sustainability.

SEBASTIAN LOSADA,[1]* SUSAN LIEBERMAN,[2] CARLOS DREWS,[3] MICHAEL HIRSHFIELD[4]

[1]Greenpeace International, San Bernardo, 107, Madrid 28015, Spain. [2]The Pew Environment Group, 901 E Street, NW, Washington, DC 20004, USA. [3]WWF International, Avenue du Mont Blanc, Gland 1196, Switzerland. [4]Oceana, 1350 Connecticut Avenue, NW, Washington, DC 20036, USA.

*To whom correspondence should be addressed. E-mail: slosada@greenpeace.org

References

1. ICCAT, "Extension of the 2009 SCRS meeting to consider the status of Atlantic bluefin tuna populations with respect to CITES biological listing criteria" (ICCAT, Madrid, 2009).
2. FAO, *Report of the Third FAO Expert Advisory Panel for the Assessment of Proposals to Amend Appendices I and II of CITES Concerning Commercially-Exploited Aquatic Species* (FAO Fisheries Report No. 925, Rome, 2010).
3. IUCN/TRAFFIC, *Analyses of the Proposals to Amend the CITES Appendices* (Information document CoP15, Inf. 18A, CITES, 2010).
4. CITES, *Comments from the Parties and Comments and Recommendations from the Secretariat* (Working document CoP 15, Doc 68, Annex 2, CITES, 2010).

CREDIT: PHOTOS.COM

Response

LOSADA *ET AL*. EXPRESSED CONCERN ABOUT the level of scientific evidence that supports listing bluefin tuna in Appendix I. It is a fact that there are great uncertainties in determining whether the current stock status of bluefin tuna (BFT) really meets the CITES biological listing criteria. The scientific committee of ICCAT, the group of international experts that is responsible for assessing BFT and had made the original diagnosis of overexploitation, was solicited to perform this analysis (*1*). Although two CITES criteria were not relevant for BFT, a third one—"a marked decline"—could be. However, evaluating this criterion necessitated the estimation of key parameters that are currently highly uncertain, particularly the reference biomass level. Therefore, two historical baselines were considered: (i) the highest observed historical level and (ii) the virgin biomass (the biomass that would be expected without fishing). There is only a 21 to 30% probability that the former meets the CITES criterion, whereas there is more than a 92% probability in the case of the latter (*1*). There was no scientific consensus as to which of the two options to choose as the reference level. This critical scientific uncertainty, which was also reported by the FAO panel, was absent from the public debate, as in Losada *et al*.'s response.

Regarding the possible precedent, I should have been more specific. It is correct that BFT would not have been the first commercially exploited marine species to be listed on Appendix I, but it would be the first commercially exploited marine bony fish species to be so listed.

Regarding the role of CITES, I agree that fisheries organizations and CITES could work together (as CITES and FAO do), but this is a challenging task (*2*). The poor performance of the fisheries organizations has been thoroughly analyzed and transparently reported [e.g., (*3*)]. It has led to 100 fish species (or more) that are as overfished or even more overfished than BFT (*4*, *5*). Therefore, I reckon that the same process could logically lead to the listing of these 100 species, which raises the question: Would CITES do better? In the specific case of BFT, Appendix I would

Published by AAAS

ban most of the legal fishing but may have little impact on illegal fishing. As with many CITES-listed species of high value, a lucrative black market is likely to develop. Therefore, the fishing pressure could remain at a substantial, but unknown, level. Meanwhile, the Appendix I listing will also impair future scientific advice because the ban of most legal fishing fleets will curtail the flow of adequate information on which BFT stock assessment is based.

Unfortunately, the debate around BFT has become too political and, thus, too black and white. In such an arena, the scientific advice is truncated, sometimes distorted, while the inherent complexity and uncertainties are simply ignored. Stakeholders and fisheries lobbies have played this game for decades, leading to the severe overfishing of BFT. It is more than timely to have an open-minded and dispassionate debate and crucial to separate science and political issues.

JEAN-MARC FROMENTIN

IFREMER, Centre de Recherche Halieutique Méditerranéenne et Tropicale, avenue Jean Monnet, BP 171, 34203 Sète cedex, France. E-mail: jean.marc.fromentin@ifremer.fr

References

1. ICCAT, "Extension of the 2009 SCRS meeting to consider the status of Atlantic bluefin tuna populations with respect to CITES biological listing criteria" (ICCAT, Madrid, 2009).
2. P. Doukakis *et al.*, *Conserv. Biol.* **23**, 841 (2008).
3. S. Garcia, J. R. Grainger, *Philos. Trans. R. Soc. London Ser. B* **360**, 21 (2005).
4. FAO, *The State of the World Fisheries and Aquaculture 2008* (FAO Fisheries and Aquaculture Department, Rome, 2009).
5. B. Worm *et al.*, *Science* **325**, 578 (2009).

Protect Pharmaceutical Innovation

IN HER POLICY FORUM "FIXING THE LEGAL framework for pharmaceutical research" (26 February, p. 1083, published online 11 February), GlaxoSmithKline attorney S. M. Knowles contends that the Hatch-Waxman Act should be altered to increase data exclusivity from 5 to 14 years. If implemented, this disturbing change would likely narrow the drug development pipeline and certainly increase drug prices.

Knowles reports the average R&D costs per drug in 2008 to be $1.2 billion. However, when the analysis accounts for tax deductions given to the pharmaceutical industry and removes opportunity costs from the expenses column, the results show an estimate of one-seventh the cost (including drug failures) (*1*) of Knowles' industry-funded analysis. Knowles claims that the inadequate patent system does not allow for cost recovery, yet pharmaceutical companies have garnered three times the profit of the average Fortune 500 company over the past decade (*2*). Knowles also suggests that the federal government should pay for the use of innovator safety and efficacy data by generic competitors, but she fails to acknowledge that worldwide, government and nonprofits already fund the majority of the health R&D that generates these discoveries (*3*).

Since its inception in 1984, the Hatch-Waxman Act has saved the U.S. $734 billion by providing an effective conduit for lower-priced, generic pharmacotherapies to come to market. Generic drugs now make up 70% of prescriptions dispensed and account for only 20% of dollars spent on medications in the United States (*4*). Hatch-Waxman has been preserving the precarious balance between public welfare and industry incentive for drug innovation by providing affordable medicines.

We agree with Knowles on one point: Hatch-Waxman requires reform to widen the R&D pipeline. Congress must ban brand-name pharmaceutical firms' unethical "pay-for-delay" agreements with generic competitors. In doing so, it would create a paradigm shift, disincentivizing compensatory agreements and, instead, refocusing brand-name companies on constructing novel therapies that may address presently unmet medical needs.

LAURA W. MUSSELWHITE[1]* AND JANE ANDREWS[2]

[1]Duke University School of Medicine, Durham, NC 27710, USA. [2]Johns Hopkins School of Medicine and School of Public Health, Baltimore, MD 21205, USA.

*To whom correspondence should be addressed. E-mail: laura.musselwhite@duke.edu

References

1. B. Young, M. Surrusco, "Rx R&D myths: The case against the drug industry's R&D 'scare card,'" *Public Citizen* (July 2001).
2. The Henry J. Kaiser Family Foundation, "Profitability of pharmaceutical manufacturers" (16 September 2009).
3. Global Forum for Health Research, "Monitoring financial flows for health research" (2006).
4. A. B. Engelberg *et al.*, *N. Engl. J. Med.* **361**, 1917 (2009).

Response

MUSSELWHITE AND ANDREWS MAKE THE unsupported argument that increased incentives (through longer exclusivity periods) will lead to decreased innovation or numbers of new pipeline drugs. On the contrary, a National Academies study recommends extending the data exclusivity period to 12 to 14 years to avoid competitive disadvantage in the United States "given the complexity and length of drug development today" [p. 190 in (*1*); (*2*)].

Musselwhite and Andrews' statement that generic drugs now make up about 70% of pharmaceutical prescriptions and account for about 20% of consumer spending on drugs strongly supports my conclusion that the rate of new innovator drugs is not keeping pace with the loss of innovator pharmaceutical markets. This trend is confirmed by a recent report of the Congressional Budget Office (*3*), which documents that introductions of innovative new molecular entities spiked in the mid- to late 1990s and have been decreasing since 2000, in most years, to levels not seen since the mid-1980s. The Congressional Budget Office also notes that production of new molecular entities that provide a "significant therapeutic or health advance" has decreased from an average of 13 per year in the 1990s to 10 per year in the 2000s (*3*). New drug launches have been correlated with increased longevity and quality of life (*4*).

Musselwhite and Andrews assert that the true cost of drug discovery and development is about one-seventh of that found by DiMasi, citing an earlier study done by Ralph Nader's Public Citizen group. The Public Citizen publication is non–peer-reviewed economic analysis. The Public Citizen study contends that the actual out-of-pocket cost per drug is between about $57 and 110 million, including the cost of failures. As such, it concludes that pharma R&D is less risky than it appears. If this were true, common sense tells us that there would be many more drugs on the market today.

The statistics in the Kaiser Permanente report—that pharmaceutical companies have received three times the level of profits of the average Fortune 500 companies over the past 10 years—cannot be clearly interpreted because they lack definitions for inclusion and include confounding issues (*5*). One unambiguous and objectively measurable metric is share price: Since 2000, the share prices of many of the largest global pharmaceutical companies have declined dramatically, several by roughly 60% or more (*6*). Unexpected losses of U.S. market exclusivity under Hatch-Waxman have contributed substantially to this downward view of the

CORRECTIONS AND CLARIFICATIONS

Reports: "Erosion of lizard diversity by climate change and altered thermal niches" by B. Sinervo *et al.* (14 May, p. 894). In note 32, FONDYCET should have been FONDECYT.

Review: "Arguing to learn in science: The role of collaborative, critical discourse" by J. Osborne (23 April, p. 463). The credit for Fig. 2 did not appear in print; it is RYAN MCVAY/PHOTODISC/GETTY IMAGES.

Published by AAAS

sector by the investment community.

Musselwhite and Andrews suggest that government and nonprofits already fund the majority of the R&D that generates pharma innovation. In fact, valuable NIH-funded R&D complements and supports private R&D, typically through pre-innovation basic research—far removed from commercial development and not appropriate for private investment—and certain clinical trials. It is wholly incorrect to suggest that public grants and investments fund the bulk of private pharma R&D. Increased public spending stimulates and in some cases may be necessary, but is not a substitute for private spending (*3*).

Innovator and generic pharmaceutical companies are required to file all patent litigation settlement agreements with the Federal Trade Commission (FTC) (*3*). Since 2004, approximately 152 final settlement agreements have been received by the FTC (*7*). The FTC has chosen to challenge only a very small number of these settlements and, of those challenged, has lost more than it has won in appellate courts before experienced judges [e.g., (*8*)]. The misnomer "pay-for-delay settlements" does not reflect the reality that the overwhelming number of settlements are pro-competitive and not objectionable even to the FTC. Furthermore, the settlement rate for pharmaceutical/generic patent litigation is less than that for patent settlements across all industries, which includes medical devices, biopharmaceutical products, consumer healthcare, important electronics, and software (*9*–*12*).

SHERRY M. KNOWLES

Chief Patent Counsel, GlaxoSmithKline, King of Prussia, PA 19406, USA. E-mail: sherry.m.knowles@gsk.com

References and Notes

1. Committee on Science, Engineering, and Public Policy, *Rising Above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future* (National Academies Press, Washington, DC, 2007), pp. 185–92.
2. The Patient Protection and Affordable Health Care Act of 2010, signed by President Obama on 21 March 2010, provides 12 years of data protection for follow-on biologics.
3. Congressional Budget Office, "Pharmaceutical R&D and the evolving market for prescription drugs" (October 2009).
4. Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub. L. No. 108-173, Title XI, §1112, 117 Stat. 2066 (8 December 2003) ("MMA").
5. Several sectors in the overall Fortune 500 have had very significant issues that could have dramatically influenced the overall average profit (e.g., AIG, Fannie Mae, Freddie Mac, automotive companies, and airlines). Furthermore, sometimes companies classified too broadly as pharmaceutical companies generate a significant portion of their profits from other health care sectors such as consumer products (OTC medicines, oral care products), medical imaging, diagnostics testing, and medical devices such as heart stents.
6. Cumulative Stock Price Performance from 1 January 2000 through 28 February 2010 collected from Bloomberg Financial News: Pfizer –62%, Merck –58%, BMS –65%, and Eli Lilly –63%.
7. Federal Trade Commission, Pharmaceutical Agreement Filings (www.ftc.gov/bc/healthcare/drug/index.htm).
8. *Schering-Plough Corp.* v. *FTC*, 402 F.3d 1056 (11th Cir. 2005).
9. Of 370 Hatch-Waxman cases studied in 2000–2010: 47% settled, 7% were dropped, the generic lost 24%, and the innovator lost 22%.
10. RBC Capital Markets Report, "Pharmaceutical-analyzing litigation success rates," 15 January 2010.
11. J. P. Kesan, G. G. Ball, *Wash. U. Law. Rev.* **237**, 259 (2006).
12. The Health Care Reform Bill, H.R. 3590, passed by the House of Representatives on March 22, 2010, correctly omitted the proposed Hatch-Waxman patent settlements provision, based on S. 369 introduced by Senator Kohl on February 2009.

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 3 months or issues of general interest. They can be submitted through the Web (www.submit2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

Published by AAAS