LETTERS

Recombinant DNA Research: Government Regulation

The following open letter to Congress represents a consensus of those who attended the 1977 Gordon Conference on Nucleic Acids. Discussions at the conference about the status of pending legislation proposed to regulate recombinant DNA research led to the formulation of this position, which was discussed and voted upon by the entire meeting. Subsequently, 137 individuals signed the letter, representing 86 percent of the members of the meeting. We are most concerned that the benefits to society, both practical and fundamental, that we foresee will not be forthcoming because legislation and regulation will stifle free inquiry. At the meeting this June, with a single exception, there was unanimous agreement that regulation beyond simple enforcement of the NIH Guidelines is unnecessary, and many expressed the view that less regulation would suffice to guard against any hypothesized dangers.

We are concerned that the benefits of recombinant DNA research will be denied to society by unnecessarily restrictive legislation.

Four years ago, the members of the 1973 Gordon Conference on Nucleic Acids were the first to draw public attention to possible hazards of recombinant DNA research. The discussions which started at that meeting resulted in the issuance in 1976 of the NIH Guidelines for the conduct of this research.

We, members of the 1977 Gordon Research Conference on Nucleic Acids, are now concerned that legislative measures now under consideration by Congressional, state and local authorities will set up additional regulatory machinery so unwieldy and unpredictable as to inhibit severely the further development of this field of research. We feel that much of the stimulus for this legislative activity derives from exaggerations of the hypothetical hazards of recombinant DNA research that go far beyond any reasoned assessment.

This meeting made apparent the dramatic emergence of new fundamental knowledge as a result of application of recombinant DNA methods. On the other hand, the experience of the last four years has not given any indication of actual hazard. Under these circumstances, an unprecedented introduction of prior restraints on scientific inquiry seems unwarranted.

We urge that Congress consider these views. Should legislation nevertheless be deemed necessary, it ought to prescribe uniform standards throughout the country and be carefully framed so as not to impede scientific progress.

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Sentence Length

R. Grantham's letter on sentence length and obscurantism (10 June, p. 1154) exploded upon my mind as one of those simple but forceful hypotheses which bring the light of rationality to bear on areas once dark and murky. It is a brilliant deductive leap to suggest that clarity of writing is inversely proportional to the incidence of grammatical periods. Grantham has done a great service to the art of literary criticism: by one simple test it has been reduced to an exact science. He has done for the study of English what Lowry did for the study of biochemistry.

Some of my initial researches on books hitherto considered to be among the foremost in the English language are summarized in Table 1. Like Grantham, I have determined the average sentence length of the first 32 sentences in the listed books. It is encouraging to note that, with minor exceptions, the clarity and lack of obscurantism of *Science*'s news writers exceeds that of some of the most highly regarded exponents of the art of English prose. Even Metz writes with only 83 percent of the obfuscation of George Eliot.

The strength of the method lies in its objectivity. Many of us had formerly thought that James's *The Golden Bowl* was rather an opaque text, but we can now see that, in fact, it is 5 percent more readable than *Martin Chuzzlewit*, and a staggering 84 percent more clear than *Tristram Shandy*, which I had always mistakenly assumed was a rollicking, roistering, and readable book. The increased critical insight yielded by this test is clearly demonstrated by an examination of Faulkner's works. *Light in August* has the amazing average sentence length of only 19 words, beating even the best of *Science*'s writers. Now we can see why he was the only author listed below to win the Nobel prize. He wrote the book in 1932. But see how decayed the older Faulkner became! Written in 1951, *Requiem for a Nun* at 116 words per sentence can hardly be considered literature at all.

Table 1.

Writer	Book	Words per sentence	
		M*	R†
Faulkner	*Light in August*	19	3–85
Fitzgerald	*Tender is the Night*	33	7–68
James	*The Golden Bowl*	37	6–107
Dickens	*Martin Chuzzlewit*	39	5–112
Eliot	*Middlemarch*	42	10–86
Boswell	*Life of Johnson*	64	14–168
Sterne	*Tristram Shandy*	68	5–292
Faulkner	*Requiem for a Nun*	116	4–476

*Mean. †Range.

The application of this tool extends beyond literature. As a pharmacologist, I was pleased to discover that counting words was a specific remedy for insomnia. Indeed, I fell asleep between sentences 16 and 17 of Boswell. I am now engaged in research as to the optimum number of sentences that should be counted to obtain the most satisfying sleep. (The average sentence length of this letter is 19.5 words, range 6–53.)

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Wine and Viral Diseases

I was dismayed by Thomas H. Maugh's brief article "Drinkers rejoice: A little wine may kill your virus" (Research News, 3 June, p. 1074). Maugh expands a report of an in vitro study showing potential virostatic properties of some wine polyphenols to an advisory to wine drinkers to rejoice in a viral disease cure (albeit facetiously), implying that 4 ounces of wine may be a preventative to gastric ailments of a viral etiology. I was further dismayed by the author's imputing to a U.S. government report that a glass of wine a day is a "good tonic" for several ailments and conditions. The material alluded to is apparently a chapter on "Alcohol and older persons" in the second special report to Congress on *Alcohol and Health* (*1*). The extrapolations in the *Science* article are overstatements of some comments contained in that report.

Maugh's article totally ignores the body of data currently accumulating in the scientific literature on the impairment of immunological mechanisms associated with alcohol use (*2*). While bacteriostatic properties of wine were observed as early as 1958 (*3*), no authors seem to have reported virostatic properties. However, many authors, including Koch, as early as 1884 (*4*), have demonstrated that ethanol can decrease resistance of both human and experimental animals to various bacterial infections. One such study, reported in 1965 by Brayton *et al.* (*5*), shows, additionally, the importance of observing pathogenic activity both in vitro and in vivo. In this study, doses of alcohol which could be fatal to humans were shown not to affect human ability to overcome staphylococci in vitro. However, the same inves-

tigators showed that small amounts of alcohol in humans significantly decreased the ability of the living organism to kill staphylococci.

It is apparent that, as more scientific evidence is accumulated concerning consumption of ethanol, very little if any of this evidence is giving drinkers cause to rejoice.

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Prostaglandin Research

We read with interest Jean L. Marx's review of the rapid advances and possible important clinical implications of recent research on the prostaglandin system in accelerating and inhibiting platelet aggregation and its role in thrombus formation (Research News, 3 June, p. 1072). We wish to respond to some omissions, errors, and misleading statements which concern the discovery of prostaglandin I_2 (PGX, prostacyclin). We reported preliminary findings of the chemical structure of PGI_2 and an isomer in 1970 and published detailed papers in 1971 (*1*).

At that time we presented chemical evidence of a structure identical to PGI_2 which we called 6(9)-oxy-11,-15-dihydroxyprosta-5,13-dienoic acid, or Compound II, abbreviated as 6(9)-oxy-Δ^5-$PGF_{1\alpha}$. The other isomer which was isolated in larger quantities had a double bond in the Δ^7 instead of the Δ^5 position. It was not possible to know the true stereochemistry of the Δ^5 double bond because of the limited supply of isolated material, so the *E* configuration was drawn for simplicity instead of the *Z* configuration, which Johnson *et al.* (*2*) recently proved through chemical synthesis. The prostaglandin X isolated by Moncada *et al.* (*3*) from microsomes of pig and rabbit aorta incubated with prostaglandin endoperoxides appears to be identical to one of the isomers isolated by us 6 years ago and now shown to be PGI_2 by Johnson *et al.* (*2*). The similarity in structure of these products with that of the primary prostaglandins suggested to us that they were derived from the prostaglandin endoperoxides which had not yet been isolated (*1*). Further work by Pace-Asciak demonstrated that purified endoperoxides are indeed converted into these products (*4*). He discovered that the major stable product in the enzymatic reaction was 6-keto-$PGF_{1\alpha}$, a structure previously unreported (*5*). The 6-keto-$PGF_{1\alpha}$ appears to be a hydration product of the Δ^5 cyclic ether (PGI_2) which is formed from the prostaglandin endoperoxides specifically by an enzyme termed 6(9)-oxycyclase. This enzyme is abundant in stomach tissue but also occurs in many other tissues (*6*). The early research on PGI_2 and the discovery of this terminal pathway of prostaglandin endoperoxide metabolism was carried out at the Montreal Neurological Institute of McGill University in Montreal. The statement in the article by Marx that the major breakdown product of prostacyclin, namely 6-keto-prostaglandin $F_{1\alpha}$, was discovered 6 years ago is incorrect. This new prostaglandin was first reported by Pace-Asciak at the Research Institute of the Hospital for Sick Children, University of Toronto, last year (*5*). Indeed, before the final stereochemical assignment of PGI_2 was known, Pace-Asciak demonstrated that 6-keto-prostaglandin $F_{1\alpha}$ was a major product from the prostaglandin endoperoxides, and he postulated its origin from the Δ^5 cyclic ether now called PGI_2.

As research in this field is advancing extremely rapidly and has considerable clinical relevance, we feel that a more accurate presentation of the course of events and the people involved is important.

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