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Book reviews

Law, Medicine and Socially Responsible Research: A symposium. Published in the American Journal of Law and Medicine, XXIV, Nr 2 and 3, 1998. American Society of Law, Medicine and Ethics, Boston, MA, USA.

Those who do not normally see the serial publications of the American Society of Law, Medicine and Ethics should make a special effort to secure issue 2/3 of its *Journal*. The bulk of it is devoted to a group of seven distinguished contributions on themes related to socially defensible medical research. Norman Frost tackles the difficult question of when and how consent to medical research can validly be waived by those involved. The background to his review is a recent revision of the US federal rules for the waiver of consent in research, particularly introducing new standards with respect to "experimental" treatment in certain emergency situations where consent cannot be sought or obtained yet where use of an unproven therapy seems to offer the only hope of survival. Kathleen Boozang looks at the increasingly positive attitude of western medicine to alternative therapies, and provides helpful rules of thumb for the practitioner in deciding when and how he should accede to a patient's request to seek alternative treatment. Leonard Glantz considers how policy has evolved (and might well evolve further) as regards research in children. George Annas looks at the history of consent as it applies to the use of investigational drugs and vaccines in combat, developing a theme which he introduced in the *New England J. Medicine* in 1992. Dorothy Nelkin and Lori Andrews review the emergent standards for research on cadaver material – one of their case histories relating to the post-mortem study of Albert Einstein's brain despite his known request that his body not be used for investigational purposes; some such cases have causes much mental anguish to the families of the deceased. Jesse Goldner provides a competent overview of the endless struggle to establish legal barriers to scientific misconduct; several of the cases discussed illustrate the manner in which falsified scientific data can result in risk to the community.

This collection of papers is competently pulled together in an introductory essay by Rebecca Holmes-Fairley and Michael Grodin, who consider how physicians, other scientists, lawyers and government have become involved in ensuring that medical research is conducted in a proper manner. The symposium as a whole is heavily orientated towards the situation in the United States but many of its elements are equally applicable elsewhere in the world.

C. Smit, A. Kent and I. Poortman, *Biomedical Research and Orphan Medicinal Products*, 1998. Published by the European Platform for Patients' Organisations, Science and Industry in collaboration with Fontein b.v., Baarn, the Netherlands. ISBN 90 261 1412 5, price not indicated.

In September 1997, the European Commission convened a one-day meeting at Brussels to consider the further development of its policies with respect to "orphan drugs" and the treatment of rare diseases. The concept of "orphan drugs" has various definitions; the meeting, the proceedings of which are reflected in the present book, dealt almost entirely with drugs which are needed for the treatment of such small patient groups that the sales prospects render it highly unattractive to the pharmaceutical industry to identify, develop, register and market them. Cystic fibrosis is one case in point: Gaucher's disease is another. Several hundred conditions can be regarded as falling into this category. The massive problem of developing better and safer drugs for the treatment of tropical diseases is analogous, but understandably it fell largely outside the scope of this European consultation.

It is entirely logical that national authorities (or, in this case the European Community) should try to identify solutions to the problem of developing orphan drugs. The authorities in the United States set a good example as earlier as 1983 and others (notably in Japan and Australia) have followed. Among other things there is a need to bring together aetiological and therapeutic knowledge (which tends to be scattered over many centres and countries) and to co-ordinate research efforts. A related issue, which receives much attention in this book, is that of developing reasonable incentives for the drug industry to undertake more work in this direction. It is this latter issue which needs to be considered carefully when one is concerned with safety in medicine.

One major element in existing national legislation on "orphan drugs" is that the procedure for securing marketing licences shall be simplified and accelerated; costs will then be reduced and the drug will reach potential users more rapidly than would otherwise be possible. This approach is also adopted in the proposed European regulation, a draft of which is appended to the main text of this book. The manufacturer of such a drug will be exempt from the new product approval fee, currently 200,000 ECU, but will also enjoy what could be a simpler and faster approval procedure involving a "Committee on Orphan Medical Products"; after marketing, he will enjoy a number of years of exclusivity in order to earn a reasonable return on his investment. It is primarily the prospect of facilitating new drug approval which must cause some concern. Drug registration is not merely the bureaucratic formality which some would claim. A fair proportion of new drugs are still rejected, at least provisionally, because they have been submitted for approval before there was sufficient evidence of their efficacy or their safety. As US experience shows, the more "sympathetic" one attempts to be as regards the approval of a deserving drug for a deserving population, the greater the risk that one will cut corners and thereby leave important questions unanswered. If, either in regulation or practice, drugs for rare diseases are given easier and more rapid access to the market, other safeguards have to be provided, particularly in the form of post-marketing studies and surveillance. If the drug in question remains a financially marginal one, the public authorities might well consider providing support to such follow-up work. However, one might well bear in mind that some "orphan drugs" which have sailed through the US approval procedure have subsequently become very profitable indeed. A speaker at this meeting from the US "National Association for Rare Disorders" pointed, for example, to the case of Ceredase, developed in the US for the treatment of Gaucher's Disease, and used by less than 2,000 Americans a year. Currently, the drug is highly profitable, since the price has been set at such a level that a year's course of treatment can exceed $350,000 per patient, and it is also being used at this price in more common indications. In such a situation at that the responsibility for continuing safety studies should surely lie with the manufacturer.

At the time of writing the European Parliament and Council's "Regulation on orphan medicinal products" has proceeded further than sixth draft as printed in Annex V to this book, but it is still amenable to revision. Up to the present, however, it does not seem to have been enriched with any clauses covering the post-marketing safety issue. It is a matter which deserves close attention if what is essentially a well-intentioned approach to the orphan drugs problem is not to introduce new risks for the very patient groups which it is intended to assist.

Douglas Powell and William Leiss, *Mad Cows and Mother's Milk. The Perils of Poor Risk Communication*, McGill-Queen's University Press, Montreal and Kingston, 1997, 308 pp. ISBN 0.7735-1618-2, £29.95.

The science establishment has been slow to accept what business people have always known: *the customer is always right*. The present, very readable book is all about the perils inherent in overlooking

this business rule of thumb when scientists, and governmental users of science, try to communicate with the public and address their apprehensions in a risk situation.

The book is in itself a good piece of communication, from the title, which makes many readers curious, through the cover, where a large, moist cow's eye looks quizzically at you from the night-table, to the organising of the material, which is didactically well done and clear.

The authors have chosen to illustrate their points through a series of examples of complex and controversial risk situations that are globally well known: mad cow disease, dioxin, *E. coli* O157 : H7, silicone breast implants, recombinant bovine somatotropin, "escape" of bioengineered genes, and PCBs. In each case the problem is laid out for the reader in a neutral fashion, the history and development of risk communication management in each case is described, and conclusions are drawn that demonstrate what went wrong, why, and what could have been done differently.

This is a book with a mission. Its main message is that risk communication is serious business, and failures are costly. Risk communication is the responsibility of those who possess the power to do something about the situation: the industry that may have created the risk situation in the first place, and governmental regulatory authorities. If they fail to recognise and respect the customer's (or public's, or problem-owner's) concerns, be they scientifically justified or not, a "risk information vacuum" may grow and fester, and spoon speculation, fantasies and vested interests alike. Leaving it to be filled by these monsters, those who eventually try to assuage public opinion or provide better-founded information may find that the monsters are impossible to root out.

The book concludes with ten lessons that have been learnt from past mistakes; these are worth quoting *in extenso*:

1. A risk information vacuum is a primary factor in the social amplification of risk.
2. Regulators are responsible for effective risk communication.
3. Industry is responsible for effective risk communication.
4. If you are responsible, act early and often.
5. There is always more to a risk issue than what science says.
6. Always put the science in a policy context.
7. "Educating the public" about science is no substitute for good risk communication practice.
8. Banish "no risk" messages.
9. Risk messages should address directly the "contest of opinion" in society.
10. Communicating well has benefits for good risk management.

These lessons are very convincingly argued in the book, simultaneously providing well documented insight into some of the big public health controversies of our times. Obligatory reading for those responsible for good risk communication, fascinating and entertaining reading for all others.

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