

The Regulation of Carcinogenic Hazards

Gio Batta Gori

In earlier times economic development, an ethical imperative in the Western world, took precedence over concern for individual or collective safety. Rational audacity is a distinct human characteristic, and many have argued that too much regard for safety goes against human nature and happiness. But today new dangers of chronic illness and disability give new dimensions to fear, and there is a clear need to better define the odds involved.

Carcinogens have been recognized

latory issue (3), but in the United States regulation was born of the social dialectic of the turn of the century and retains some of the romantic intransigence of that movement. American laws do not give explicit directions for considering risk-benefit factors, and economic arguments usually are contested with the implicit assertion that health has a supreme value whose economic costs need not, should not, be measured.

Undeniably, for an individual life has transcendent value. But excessive regu-

Summary. In the United States, statutes for controlling carcinogens are largely motivated by the ideal of absolute safety at all costs. There is no requirement for risk-benefit assessment. Bias is inherent in the prescribed bioassays; test findings may have restricted meaning within the specific experiments but cannot be translated into quantitative assessment of human risk. Such data are improperly used in resolving regulatory questions case by case. It is suggested that a system of relative standards of utility be formulated which, paired to standards of tolerable risk or safety, would define a range of use restrictions. Substances intended for a certain use would then be regulated according to those standards.

since Percival Pott some 200 years ago (1), and regulatory initiatives have flourished for the last three decades, as anxieties gradually shifted from vanishing acute infections to chronic diseases made more prevalent by longevity gains (2), and in the wake of concern over ubiquitous industrialization.

The need for regulation of carcinogens in developed societies is undisputed, but the premises and practices of such regulation are not. In the United States we are experiencing a transitional period that reflects general trends of social evolution: regulatory agencies, which in accord with centuries-old traditions have been allowed to wield quasi-autonomous normative powers, find themselves increasingly at odds with expanding demands for due process in the resolution of uncertain perceptions and conflicting values.

In many countries the balance of tolerable risks and benefits is the central regu-

lation hampers technological development and thereby denies its fruits to the poor in our own society and elsewhere in the world. Public policy is fundamentally an economic exercise. It cannot evade the balancing of risks and benefits without incurring gross inequities.

Gradually, loftier views are giving way to a realism that expects regulation to improve the quality of life for the living, not merely to extend life expectancy. When it is accepted that absolute safety is not a reasonable goal, it becomes the business of regulation to define tolerable levels of risk; to this end, explicit procedures for benefit assessment need to be introduced into regulatory statutes. Also, revisions of current practices appear to be in order for a consistent approach to the determination of risk from potential carcinogens.

In general, normative regulation has relied on the definition of standards, usually of empirical origin but then upgraded

as use and newly acquired information suggests: the standards define reference compounds, testing procedures, process flows, as well as tolerable or permissible doses and levels.

In the late 1950's, in the heat of public concern over food additives and new pharmaceuticals, U.S. legislators sought the advice of science in the definition of carcinogen standards. Unfortunately, at that time understanding in this field was too problematic to produce even a suggestion of standards. Legislators were left with the alternatives of either intransigent policies, such as the Delaney amendment adopted at that time, or vague statements of intent, which have intrigued dialecticians ever since. It now appears that these legislative precedents have been largely responsible for the polarization and ambiguity which plague the regulation of carcinogens in this country, and for a climate of opinion that has discouraged intermediate solutions in favor of all-or-none pronouncements.

The public would be surprised to note that different potential hazards, documented with comparable scientific methods and data, are regulated by widely different criteria. The explanation is simple. There is an implicit necessity to tolerate certain conditions where intransigent regulation would mean a drastic alteration of traditional life-styles. There are many examples: exposure to sunlight; ingestion of fats, proteins, and excessive calories, or of foods containing natural and apparently unavoidable potential carcinogens such as aflatoxins; and the paradox of potential risk from the ingestion of our own saliva, at times very rich in nitrites, precursors of carcinogenic nitrosamines.

The need to tolerate such hazards has not been seriously challenged even by the most ardent proponents of regulation. But the absence of explicit statutory rules for risk and benefit assessment has led to a situation where each substance is considered separately, and widely disparate outcomes are influenced more by adversary emotions than by real values. Testing procedures have proliferated and become more complicated, logistic resources have been virtually exhausted, and testing as now envisioned may be precluded for the majority of environmentally significant substances.

Moreover, intrinsic uncertainties in current procedures make it impossible to prove safety beyond doubt; on this basis prognostications of doom have flour-

The author is Deputy Director, Division of Cancer Cause and Prevention, National Cancer Institute, Bethesda, Maryland 20205.

atom may take place. (iii) multiphoton free electron-free electron transitions (bremsstrahlung, inverse bremsstrahlung) can occur, and (iv) the close dynamics of the scattering process can be affected by n -photon transitions in the $(N + 1)$ -electron negative atom system. The theoretical treatment of these complex processes has been limited to special situations where one particular interaction dominates and the others can be neglected or treated as perturbations.

Experimental investigations in this area have been initiated only very recently and can be divided into two categories: (i) electron scattering by laser-excited species and (ii) free-free radiative transitions.

In the first category, tunable (low-power) dye lasers are utilized to excite the target atom and scattering by the excited species is studied. Here the interaction of the electromagnetic field with the target dominates and its interaction with the free electron can be neglected. Register *et al.* (33) excited the $(6p)$ 1P state of Ba with a wide-band laser (isotope and hyperfine levels unresolved) in a dense Ba beam (where multiple absorption and reemission cause all degenerate magnetic sublevels to be evenly populated). Electron scattering was then observed by the 1P Ba as well as cascade-populated 3P , 1D , and 3D Ba. Energy-loss spectra with the laser off and on are shown in Fig. 13. With the laser on, additional features are observed corresponding to superelastic scattering and to transitions from excited state to excited state. From this and similar spectra cross sections (averaged over isotope, hyperfine, and magnetic sublevels) were determined.

When a single-frequency dye laser is used, the energy resolution (10^{-4} eV) is good enough to selectively pump an individual hyperfine level of a specific isotope, and by selecting the proper polarization of the laser light the population of the magnetic sublevels can be controlled. In other words, a polarized target (aligned or oriented) can be prepared for electron scattering. These types of experiments make it possible to study electron scattering with an energy resolution of 10^{-4} eV and nuclear spin effects, and they yield scattering amplitudes for individual magnetic sublevel excitations. The excitation with polarized light and subsequent measurement of the superelastic electron scattering is equivalent to the time inverse electron-photon coincidence measurement (34).

Experiments in the second category have been concerned with free-free radiative transitions in strong electromagnetic fields. Here the photon energy is cho-

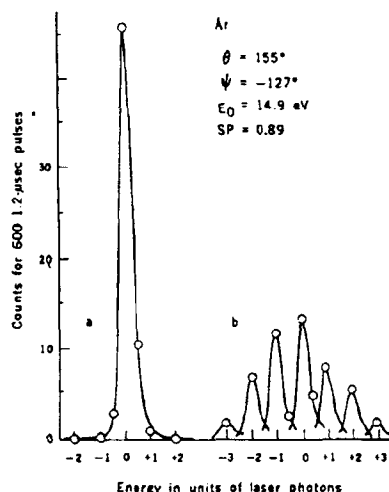


Fig. 14. Elastic scattering by Ar (a) without and (b) with a high-intensity CO_2 laser field.

sen to be far from resonance (even for multiphoton processes) and the major interaction occurs between the photon field and the free electron. The present situation in this area has been summarized by Gavrilu and Van der Wiel (35). Because of emission or absorption of photons by the scattering "free" electron (induced and inverse bremsstrahlung), the elastic (and inelastic) features appearing in energy-loss spectra have side lobes on both sides separated by an energy corresponding to the photon energy. Elastic scattering in a high-power pulsed CO_2 laser field has been studied by Weingartshofer *et al.* (36); an energy-loss spectrum for the laser off and laser on cases is shown in Fig. 14, a and b, respectively. The symbols θ , ψ , and E_0 in Fig. 14 refer to the electron scattering angle, the laser beam angle, and the electron impact energy, respectively. Here $SP = \epsilon K/2 k_0$, where ϵ is the laser beam polarization vector, K is the momentum transfer vector, and k_0 is the initial momentum of the electron.

Interesting situations concerning resonances can develop in connection with free-free radiative transitions. Resonances occur not only when the electron kinetic energy is proper but also when the photon energy or the electron-photon combined energy is appropriate. Such situations have been studied by Langhans (37) and Langendam and Van der Wiel (38).

I hope the examples of electron-atom (molecule) collision processes discussed in this article have given the reader a prospective view of this special, but very active, area of atomic and molecular physics. The investigations in this area yield information that is pertinent to our understanding of the basic laws of phys-

ics, and at the same time they are of considerable practical value for understanding the behavior of systems where free electrons are present.

References and Notes

1. S. Trajmar, *Acc. Chem. Res.*, in press.
2. H. S. W. Massey and E. H. S. Burhop, *Electronic and Ionic Impact Phenomena* (Clarendon, Oxford, 1969), vol. 1; H. S. W. Massey, *ibid.*, vol. 2.
3. S. Trajmar and A. Chutjian, unpublished results.
4. S. Trajmar and R. I. Hall, unpublished results.
5. S. F. Wong and G. J. Schulz, unpublished results; G. F. Schulz, in *Principles of Laser Plasmas*, G. Bekefy, Ed. (Wiley, New York, 1976), chap. 2.
6. D. F. Register, S. Trajmar, S. K. Srivastava, *Phys. Rev.*, in press.
7. S. K. Srivastava, A. Chutjian, S. Trajmar, *J. Chem. Phys.* **63**, 2659 (1975).
8. G. J. Schulz, *Phys. Rev. Lett.* **10**, 104 (1963).
9. For recent reviews see G. J. Schulz, *Rev. Mod. Phys.* **45**, 378 (1973); *ibid.*, p. 423; D. E. Golden, *Adv. At. Mol. Phys.* **14**, 1 (1978).
10. V. Fano, *Phys. Rev.* **124**, 1866 (1961); and J. W. Cooper, *Phys. Rev. A* **137**, 1364 (1965).
11. P. J. Chantry, in *Electronic and Atomic Collisions*, G. Watel, Ed. (North-Holland, Amsterdam, 1978), pp. 23-24.
12. S. Trajmar and R. I. Hall, *J. Phys. B* **7**, L458 (1974).
13. R. I. Hall, in *Electronic and Atomic Collisions*, G. Watel, Ed. (North-Holland, Amsterdam, 1978), pp. 25-41.
14. R. A. Bonham and M. Fink, *High-Energy Electron Scattering* (Van Nostrand Reinhold, New York, 1974); R. A. Bonham, in *Electron Spectroscopy: Theory, Techniques and Applications*, C. R. Brundle and A. D. Baker, Eds. (Academic Press, London, 1979), pp. 127-187.
15. H. A. Bethe, *Ann. Phys.* **5**, 323 (1930).
16. M. Inokuti, *Rev. Mod. Phys.* **43**, 297 (1971).
17. E. N. Lassettre, A. Skerbele, M. A. Dillon, *J. Chem. Phys.* **50**, 1829 (1969).
18. S. Trajmar, in *Electronic and Atomic Collisions*, G. Watel, Ed. (North-Holland, Amsterdam, 1978), pp. 113-128.
19. L. S. Vuskovic, S. K. Srivastava, S. Trajmar, D. Bozinis, *Cienc. Cult. (Sao Paulo)* **31**, 1018 (1979).
20. W. Williams, J. C. Cheeseborough, III, S. Trajmar, *J. Phys. B* **11**, 2031 (1978).
21. S. Trajmar, W. Williams, S. K. Srivastava, *ibid.* **10**, 3323 (1977).
22. W. Williams, S. Trajmar, D. G. Bozinis, *ibid.* **8**, L96 (1975).
23. S. Trajmar and W. Williams, unpublished results.
24. D. C. Cartwright, *et al.*, *Phys. Rev. A* **16**, 1013 (1977); *ibid.*, p. 1041; *ibid.*, p. 1052.
25. See, for example, J. P. Doering and J. H. Moore, Jr., *J. Chem. Phys.* **56**, 2176 (1972); J. P. Doering, *ibid.* **71**, 20 (1979).
26. See, for example, W. M. Flicker, O. A. Mosher, A. Kuppermann, *ibid.* **70**, 1986 (1979); *ibid.*, p. 2003.
27. R. H. Huebner, D. L. Bushnell, Jr., R. J. Celotta, S. R. Mielczarek, C. E. Kuyatt, *Nature (London)* **257**, 376 (1975).
28. H. Ehrhardt, K. H. Hasselbacher, K. Jung, K. Willman, *Case Stud. At. Phys.* **2**, 161 (1972).
29. I. E. McCarthy and E. Weigold, *Phys. Lett. C* **27**, 276 (1976).
30. R. E. Imhof and F. W. Read, *J. Phys. B* **4**, 450 (1971).
31. K. Blum and H. Kleinpoppen, *Phys. Rep.* **4**, 203 (1979).
32. M. J. Van der Wiel and G. Wiebes, *Physica (Utrecht)* **54**, 411 (1971).
33. D. R. Register, S. Trajmar, S. W. Jensen, R. T. Poe, *Phys. Rev. Lett.* **41**, 749 (1978).
34. I. V. Hertel and W. Stoll, *Adv. At. Mol. Phys.* **13**, 113 (1977).
35. M. Gavrilu and M. Van der Wiel, *Comments At. Mol. Phys.* **8**, 1 (1978).
36. A. Weingartshofer, E. M. Clarke, J. K. Holmes, C. Jung, *Phys. Rev. A* **19**, 2371 (1979). I am grateful to these authors for supplying a preprint of their paper and for permission to use their data in Fig. 14.
37. L. Langhans, *J. Phys. B* **11**, 2361 (1978).
38. P. J. K. Langendam and M. J. Van der Wiel, *ibid.*, p. 3603.
39. I wish to thank my collaborators whose work has been cited. This article represents the results of one phase of research conducted at the Jet Propulsion Laboratory under NASA contract NAS 7-100.

ished. Such prophecies fly in the face of a little-publicized circumstance, namely that in the United States and other advanced countries age-adjusted cancer rates in general have remained nearly stationary or have declined over the past several decades, except for some few cancers of recognized etiology (1, 4).

Yet, because regulation is an essential safeguard of civilized living, we must resolve the conflict between the need to improve living standards and the need to preserve health and the natural environment. We must find more rational and defensible regulatory options.

Of prime importance will be a reevaluation of the scientific framework for the appraisal of carcinogenic risks. For this purpose society needs to depend on the objectivity of scientists, free of political pressures in experimental choices, design, and interpretation (5). Today such pressures are not absent: scientists have often been forced to produce clear-cut statements that, however convenient for the regulator, may not have scientific justification.

Many of the debates on regulation of carcinogens have relied on the notion that animal tests can provide meaningful data for extrapolation of human risk, but evidence reviewed in this article suggests that this notion should be modified.

What Is a Carcinogen?

It is commonly observed that higher organisms are naturally affected by tumors. Because the information to determine their origins is lacking, it has been customary to define as baseline the natural rate of incidence of tumors in populations that have not been disturbed by known challenges. Thus, the current definition of carcinogens refers to insults that increase the incidence of all tumors or of certain tumors or that shorten their customary time of appearance (6-8). This teleologic definition identifies the biologic consequences of carcinogens but not the mechanisms of action involved, which at present are still unknown (9). Under such definition, overcrowding, noise, and circadian and other stresses (10) could come to be defined as carcinogens even though they may be merely modulating factors in the assay system used.

It has been argued that for regulatory purposes it does not matter that the definition is only teleologic, because it is the final outcome, increased cancer incidence, that regulation seeks to control. This would be true if simple and reproducible interactions existed within the

modulating factors and carcinogens that determine response in a given assay, but even in those instances where semi-quantitative outcomes can be experimentally reproduced, some artificial contrivance is necessary, such as the use of compounds that are strong carcinogens for the species or strain selected—but not necessarily for others—or the use of the maximum doses the test animals can tolerate. Both instances represent limiting situations, where the carcinogenic insult is artificially made to overpower other factors.

It is well known that general toxicity and carcinogenicity do not go hand in hand and that they vary from species to species and with the method of administration or intake: therefore, maximum tolerated doses—generally the highest intake that an animal can sustain for its lifetime without significant signs of acute or subchronic toxicity—will result in widely disparate testing levels, quite at odds with real-life conditions.

It is apparent that the current definition of carcinogens confines the validity of data to a specific experiment, restricts the opportunities for generalization, and makes it difficult to distinguish between direct carcinogens and modifying factors.

The Carcinogenesis Process

Essentially nothing is known of the ultimate molecular events that determine the transformation of normal cells into cancer cells (11, p. 7; 12). Tumors can originate spontaneously, thus suggesting a natural instability of the cell. Whether this is truly an intrinsic phenomenon has yet to be finally settled: more often transformation is observed after the application of an insult external to the cell.

Today it is generally believed that a carcinogen entering an animal may undergo various metabolic manipulations before reaching a target cell; there it may find various conditions of susceptibility, resistance, competition, or repair, and may be subject to additional modification before finding molecular receptors to determine, directly or not, transformation and the eventual appearance of a cancer cell (13), either as a single hit or after cumulation of progressive insults and damage. Not all cancer cells developed through this process have the opportunity of progressing to overt disease, because natural defenses may suppress the onset of asymptomatic cancer.

It is estimated (11, p. 11) that the potency of carcinogens in animal experiments can vary by a factor of 10^7 . Hu-

man exposure to environmental insults can vary by a factor of 10^4 (14). If one were to add the attenuations occurring between exposure and actual intake of a compound, it is conceivable that the range of effectiveness of a carcinogen could vary by several orders of magnitude, and the overall probability of a given molecule's being effective could become very small indeed.

As the outcome of cancer appears to be determined by the balance against the effectiveness of a single insult entity and the frequency of available entities, the regulatory process attempts to identify the quantity of insult to which man can be exposed without an unacceptable chance of developing cancer.

Because it would be unethical to conduct prospective testing in man, animal experimentation has been used as an alternative, with the implication that carcinogenesis data from animal experiments can be translated to human conditions.

Testing for Carcinogens in Animals

Using animals to test carcinogens has its roots in basic research where the principal concern was not and is not assessment of real-life risk but the study of the phenomenon of carcinogenesis. For that purpose negative results are unfruitful and there is understandable preoccupation with increasing the odds of inducing cancer. Hence, the practice developed of using maximum tolerated doses, and this in species and strains chosen for their susceptibility.

So it happens that current guidelines for carcinogen bioassay are replete with precise directions for the control of room temperature, air changes, humidity, and other easily controlled conditions but often suggest the introduction of deliberate bias into the experimental design (7, 15, 16), for example: "Both sexes of each of at least two species of animals should be used in the test throughout their lifespan. In most cases these species would be rats and mice. Hamsters and dogs might be suitable, but guinea pigs, for example, appear to be resistant to some known carcinogens" (17, p. 8) and presumably should not be used; and again "... considerations in selecting the proper species and strains should include ... sensitivity to tumor induction ..." (15, p. 4), or "Generally such decisions have been made on the basis of the most sensitive species tested" (16, p. 3).

Also, testing guidelines in general prescribe feeding whenever that is more

convenient than other modes of administration. Agents that in reality are absorbed by respiration or through the skin are thus subjected to abnormal metabolic processing and may impinge on cellular and organ systems that are not their natural targets; in general, feeding results in higher maximum-tolerated doses, because other routes offer less protected, more direct and rapid access to receptors that determine acute toxicity. Such recommendations are justified in the design of a research experiment of self-contained validity, but are difficult to reconcile with the need to obtain results of general value, particularly when other powerful obstacles exist.

For instance, it seems reasonable to conclude that, because the probability of developing cancer from natural exposure is related to the number of cells present in an animal and to the duration of its life, aged mice should have natural cancer incidences much lower than aged humans. In fact they have comparable incidences, which suggests that mice could be from 3×10^4 to 10^6 times more cancer-prone than humans (18, 19). The compelling power of such an argument cannot be dismissed simply because of its simplicity.

Further bias derives from the usual prescription of nearly toxic "maximum tolerated" doses. Although these may not appreciably affect the animal's visible condition during the experiment, they are known to cause metabolic overloads that may unpredictably promote or retard a carcinogenic process, with outcomes that differ from species to species. Disturbing questions on this issue have been raised by many reports and studies (11, 16, 17, 20-26) but usually go unanswered when actual recommendations for testing are made (7, 11, 15-17, 20, 23, 27).

Diet is likely to be a major source of experimental variation. Early observations (28) on the effect of caloric intake, of dietary fat and protein, have been followed by an even broader appreciation of the enzyme inducers and toxicants that may act, for example, on the immune system (29-31). Moreover, when the agent being tested is a promoter, the presence of carcinogenic contaminants in the diet may erroneously result in its classification as a carcinogen, with outcomes that may vary from species to species and from diet to diet.

Concern with dietary disturbances has been voiced in many reports: "... some natural constituents of the diet or even an essential nutrient, such as selenium, may constitute a carcinogenic risk. Clearly these substances cannot be com-

pletely excluded from the diet" (17, p. 5); or "What can be the significance of the incidence of ... tumors in susceptible strains when one is not certain about the presence of carcinogenic contaminants in the diet on which animals have been maintained?" (23, p. 427). The need to control diets, although frequently recognized (23), is still an unresolved problem in the official guidelines for carcinogenesis experiments (15).

Another source of difficulty is the translation of animal pathology into terms of human significance. Individual agents can produce different tumors in different species or only in certain species, thereby implying a variety of organotropisms probably related to widely different metabolic conditions and homeostatic mechanisms of cell proliferation and repair in different species. Hepatomas, for instance, are very frequent in rodent tests but remarkably rare in man, and the oncogenic viruses commonly infesting small rodents may be one reason for the unusually high frequency of lymphomas in these animals. The difficulties of comparison under these conditions are further complicated when tumors arise from tissues of different embryologic origin in different species. The biologic implication is that different agents may be carcinogenic for certain species or particular organs but relatively harmless for others, for reasons that are not yet apparent to science.

Kraybill (29) lists a number of other sources of quantitative uncertainty in animal testing, including inappropriate routes of administration, enhancement of susceptibility by deliberate immunosuppression or induced hormonal action, contaminants in the agents being tested, accumulation of a burden of the agent or other uncontrolled compounds in certain tissues, the theoretical and practical difficulties in matching duration of exposure in man and animals, and differences in the time required for tumor formation. One could add recent findings on the quantitative disturbances caused by various environmental and chemical stresses (10, 32), the use of rodent strains contaminated with endemic oncogenic viruses and of selected or inbred strains (23), and the effects of transient infectious contaminants (33).

In general, one can only conclude that current guidelines for the testing of carcinogens frequently introduce deliberate bias in order to enhance the probability of a positive response and that they ignore a number of sources of variability that cannot be controlled or are difficult to control with available technology. Under current testing a carcinogen may go

undetected in a particular test, but just as likely a positive result may be valid only for the particular species and test conditions utilized; current science cannot predict or explain the outcome.

Current Methods of Assessing

Human Risk

In present regulation, data from animal tests have been used, first, to define a particular hazard as a carcinogen—according to the general definition discussed above—and, second, as a basis for extrapolating to presumed conditions of human exposure.

The first use has been challenged because maximum tolerated doses may inhibit the appearance of tumors, as in the case of vinyl chloride (25) and other compounds, and because the metabolic overload created by such doses is likely to derange normal homeostasis and create physiologic conditions with no real-life counterpart (16, 17, 21, 23, 24, 26, 30, 34, 35). However, since false negatives are difficult to count, popular convention has it that current practices enhance the probability of detecting carcinogens in animals and prudence dictates that those detected should be deemed potential carcinogens for man. While the latter argument may be defensible (36), it does not provide scientific justification for the codified practice of using maximum tolerated doses (37, 38).

Of course, identification of an animal carcinogen is only a first step in the regulatory process, unless it happens to come under the provisions of the Delaney clause (39). In that case the regulatory verdict is unequivocal, because the law states that any substance against which there is evidence must be banned. This legislation has endured for over 20 years, but lately increased analytical sophistication and expanded testing activities have begun to raise public opinion in favor of a less intransigent approach.

Congressional action, and the temporary suspension of the Delaney requirement, in the case of saccharin is the most recent example of this trend (40). The real-life question in this case is whether the risk from exposure to artificial sweeteners is balanced by risks that users would incur without them from diabetes, excessive calorie intake, dental caries, and so on, or simply by hedonistic rewards.

Similar questions are likely to become a major issue of regulatory action in the near future, influenced by emerging attitudes toward no-effect thresholds and toward the limitations of animal test data.

The issue of no-effect thresholds will inevitably assume importance as smaller and smaller quantities of potentially hazardous compounds become identifiable through advances in chemical methods. Up to now, the probable occurrence of thresholds has usually been ignored, and some regulatory guidelines specifically prevent considering them (7, 15). Such an attitude largely results from avoiding the distinction between the practical and the theoretical. Difficulties in conceiving or measuring thresholds in cellular and molecular contexts have been taken as reason to question the reality of those practical levels below which adverse effects cannot be measured epidemiologically.

Tolerable limits of exposure (TLV) are a common concept in regulation, and while it is true that epidemiologic definition of practical thresholds has been difficult except in rare instances (41), their presence is suggested by much evidence (11, p. 10; 42, 43) which parallels universally accepted concepts in chemistry, physiology, and pharmacology. Deliberate laboratory and epidemiologic studies on this problem could supply information of direct significance to regulation.

Regarding the use of animal test data for human risk assessment, severe obstacles were recognized very early in several documents (6, 7, 11, 15, 17, 20-24, 27, 37-39), but the logical conclusions were not drawn: experimental practices quite valid in a basic research setting were adopted for regulatory purposes without a critical analysis of their limitations.

Once these practices were established, support was sought for them in several biometric models specifically developed to attempt a generalized quantification of human risk (7, 44, 45). These statistical exercises would be justified if the animal data used in their elaboration reflected generalized human risk conditions, but they do not: nor is there a basis for deciding in which direction their results should be adjusted. The situation was recognized by an expert panel of advisers to FDA (23, p. 433) a few years ago: "... it would be imprudent to place excessive reliance on mathematical sleight of hand, particularly when the dose-response curves used are largely empirical descriptions, lacking any theoretical, physical or chemical basis." Apparently statisticians have prudently competed with each other to produce methods that would give the most conservative estimates, as the same FDA panel of experts noted (23, p. 435): "Although it is possible in principle to estimate 'safe' levels of carcinogens, uncertainties involved in the downward extrapolation from test re-

sults will usually result in permissible levels that are the practical equivalent of zero." In a general appraisal of current procedures for human risk determination, a compelling statement has been recently advanced by Kraybill (29): "... the [carcinogenic] response ... is mediated and limited by certain biochemical, metabolic, and pharmacokinetic relationships. Such boundaries must not be exceeded in biological testing and assessment of carcinogens, lest irreconcilable implications are left with the scientific community and the public, which result, in the long run, in a waste of national resources in the interest of public health." The conclusion is that past and current testing practices do not unequivocally identify human carcinogens and do not yield quantitative information about conditions of human risk, and that biometric sophistication does not overcome the limitations of these data.

An impasse is being felt in debates about regulations (46), also reflected in confusion and contradiction at the international level (3) as regulatory guidelines are elaborated by several agencies empowered by recent statutory mandates (15, 47). Most of these attempts are based on the traditional assumption that animal tests allow reliable and generalized quantitation of real-life carcinogenic risk for man.

Over the last decades it has been fashionable to contrast the forthright simplicity of science with the apparent looseness of political debate. Scientific solutions are implicitly expected for many social difficulties: but science can draw valid conclusions only on the basis of proven theories, controlled methods, and consistent results, none of which are yet available in carcinogen testing. Ought scientists countenance the use of inconsistent data even for such worthy causes as human health and a wholesome environment (48, 49)? This question becomes yet more embarrassing if one considers that better safety might be achieved, with greater fairness, by an approach that explicitly recognized the sociopolitical nature of regulation and resisted the temptation to force arguments under scientific disguise.

Future Regulatory Directions

Discouraging as it may seem, it is not plausible that animal carcinogenesis experiments can be improved to the point where quantitative generalizations about human risk can be drawn from them. A multitude of disturbing variables is in-

involved. There are difficulties from a logistic and a design point of view. Even the expedient of large experiments is now regarded as an improbable solution, because background noise and sources of disturbance will increase with the number of animals. Nor will current proposals of more complicated testing procedures provide a solution (50), because the real issue is the fundamental biologic difficulty of resolving the inconsistency of chronic response in different species.

In vitro tests remain a possibility that is probably several years from practical application (51).

With current procedures, the assay capacity in the United States is limited to a few hundred compounds a year at best: the backlog of compounds that need to be tested and the new compounds that industry would like to have tested amount every year to several tens of thousands of individual items. The new Toxic Substance Control Act alone (52) is likely to create a crisis that could only be resolved by adopting new regulatory policies, expanding resources, and simplifying testing requirements.

The crisis would be exacerbated by the continuing pressures of a consumer society that is also environment-conscious. These could swell the outcry over what appears as an exorbitant or impossible regulatory burden, force the mitigation of current requirements for testing (34, 53, 54), and weaken enforcement of statutes (55). However, societal concern on environmental issues during the last decade indicates that a rollback to nonenforcement is not very probable (56), short of a profound economic crisis and depression.

It would seem desirable to think of an alternative scenario, one calling for official recognition that risk is an unavoidable element of life and the common welfare, that all human lives cannot be preserved at all costs, and that carcinogenicity tests in animals cannot be reliable quantitative models of human risk. Essential elements of such an approach have been identified and debated in a recent report of the National Academy of Sciences (57).

Today certainty in regulation is elusive, and it is likely to remain so until adequate science develops. At the same time, judgment in the face of uncertainty does not call for an apology. Indeed, the current regulatory process may be in disfavor because it is not honestly judgmental and, by insisting on inadequate science and intransigent ideals, produces results that are perceived at times as arbitrary, inconsistent, or unacceptable to the public at large. The central point of

procedural reform is that resolution of uncertainties must be attempted in an open sociopolitical context, because usefulness, benefit, tolerable hazard, and safety cannot be defined on the independent authority of scientific facts or statutory prerogative.

The diversity of real-life situations would seem to make this task impossible, but similar problems have been reconciled, traditionally, by flexible statutes that offer standards of reference, to be used in the fair and consistent resolution of individual situations.

For the regulatory process of our interest, two sets of references need to be defined: a standard of usefulness or benefit and a standard of safety or tolerable hazard. After this initial work, individual cases would be heard in open proceedings, much as in a judiciary process.

Initially, emphasis would be on identifying functional classes of products and uses considered necessary to sustain a modern society. Analysis and definition of a standard of need would have to be extensive only for each class of use. For a particular agent it would have only to be proved that it belongs to the class, and its standing would improve if it offered corollary benefits, such as additional therapeutic or nutritive properties. In other words, the analysis of benefits for individual agents could be largely settled by precedent.

The initial effort would eventually define standard categories of use, each being assigned a relative rank of usefulness. Primary items of need, such as basic foods, comforts, drugs, and fuels, and perhaps basic raw materials and chemical intermediates, would be ranked at the top, less-needed items receiving lesser ranking, depending on a sociopolitical judgment.

This task need not have prohibitive dimensions. It has ample precedents in the legislative process, and would appear to be a natural function for Congress, perhaps assisted by a systematic polling of public and expert opinion during the extensive activities necessary at the beginning, and for revisions thereafter.

Definitions and ranking would have to consider logistic, economic, hedonistic, esthetic, ethical, and other cultural issues. In principle these criteria would have at least equal weight in a final judgment. That man does not live by bread alone has never been so clear as in our time. The cultural mosaic of values that define happiness ought to be an important element in the definition of usefulness and benefits, even while we take into account the necessity of making choices among our desires.

Nevertheless, safety must remain an important objective, and in the process of ranking relative usefulness one could also identify a safety-standard agent representative of each class, and prescribe appropriate use restrictions or tolerable conditions of exposure. This could be based on the minimum human intake, or environmental load, compatible with the fulfillment of that use, and would also depend on the rank of usefulness of the particular category. The standard-of-need agent for each class would naturally become its standard of safety or tolerable hazard, and new agents aspiring to be classified for the same use would be compared for safety with that standard. For example, sucrose could be selected as the reference for sweeteners, because it is the most widely used substance for sweetening, and because a long record of chronic exposure in mankind suggests side effects that are either ignored or accepted as tolerable by the vast majority of users. The safety of another sweetener would then be compared with that of sucrose, at doses also including maximum conditions of exposure under intended human use.

Much research would still be necessary to improve our ability to predict the relative toxic potency of two different compounds in man, because the quantitative difficulties in translating results of chronic tests across species would persist. In fact, even the direct human evidence of epidemiologic studies is not always sufficient for a regulatory decision, because of apparent or suspected confounders.

Undoubtedly, complex assay protocols would be suggested: different routes of administration in different species, extensive dose-response kinetic studies, metabolic fate determinations, structure-activity inferences, chronic and acute toxicity tests, in vitro assays with human and animal tissues, and other approaches. The redundancy of these suggestions underlines their relative impotence, besides being incompatible with the limited testing resources now available.

All things considered, it would seem reasonable that until better methods for the definition of relative toxicity can be found, the role of science in regulation should be limited to those instances where nearly certain assessment of human risk is feasible and legitimate; at the same time more emphasis should be given to methodological and basic research for future application.

In this light, while carcinogenicity may not be measured reliably today, relative safety could be defined by a formula that would assign nearly equal weights to oth-

er forms of acute and chronic toxicity, the tests being selected when their generalization to real life is reasonable. The burden of proof would be left with the applicant, who could present the case to a jury of experts and users acting in a setting similar to a judicial proceeding to arrive at an opinion about the toxic potency of the substance in question relative to that of a reference agent. For the sweetener of our example, this judiciary proceeding might succeed in defining its rank relative to sucrose, based on its relative toxicity and the estimated dose from exposure under the intended conditions of use; and it could achieve the same rank as the reference if, for example, it were twice as toxic but its intended use resulted in only half the exposure.

Indeed, a safety judgment that is influenced by criteria of need would have to consider exposure as a prime determinant of hazard, and it may become necessary to develop more sophisticated approaches for determining human intake by various routes, under real-life conditions of an agent's proposed use (14).

The sum of regulatory restrictions would finally depend on the rank of need for the class of use, more necessary ones commanding fewer restrictions, and on the safety ranking of the agent considered, relative to the reference compound and the use restrictions applied to it; there might be a range of restrictions for special situations of exposure, such as pregnancy, young and old age, allergies, workplaces. Because of the uncertainties, precise numerical structures for reaching regulatory pronouncements are unlikely, even though the formulation of decision frameworks has been discussed and appears feasible (57).

But who shall make regulatory decisions? This question becomes important because the new scenario implies a shift from normative bureaucracy to an exercise in sociopolitical judgment. Society has repeatedly faced the challenge of regulators preoccupied with their own survival; and traditional normative mandates have come to be questioned as remnants of an autocratic past, particularly when situations are not clear-cut but defined by a range of judgment. The present regulatory system itself cannot avoid this situation, and in fact most of the important regulatory decisions are finally resolved by litigation.

It has been suggested (58) that it may become expedient to provide for an impartial and fair resolution of the uncertainties involved by instituting special courts independent of the regulatory agencies, the latter being left with the

task of proposing regulation and enforcing the courts' decisions by devising clear categories of restriction, easily understood and accepted by all consumers and special users alike (57). In this context, the ethical and operational incompetence of intransigent statutes might come to be viewed as an embarrassment to be rectified, and as inconsistent with the safeguards of due process that are at the philosophical core of a free society.

The proposed approach might also have important economic consequences, because of the attribution of rank to each compound within a class, and of use restrictions depending on rank. Clearly, a regulatory process that ranks efficacy and relative safety risks new dangers of intransigent interpretation. But when such a policy is exercised as social judgment, it could add a new incentive to develop increasingly better products (57).

The future of manufacturing may well be characterized by restraints and solutions unthinkable 10 years ago and only barely felt today, chiefly reflecting the inevitable depletion of raw commodities. In that context, a new regulatory posture of the general nature suggested becomes even more plausible, as it would provide incentives for a more farsighted utilization of diminishing resources while helping to preserve the values of enterprise.

References and Notes

- P. Pott, *Cancer Scroti: The Surgical Works of Percival Pott* (Clark & Collins, London, 1775), p. 734.
- Statistical Abstracts of the United States (Government Printing Office, Washington, D.C., 1959), table 3; *ibid.* (1960), table 71; *ibid.* (1977), table 104.
- R. Montesano and L. Tomatis, *Cancer Res.* 37, 310 (1977).
- R. Doll, *Proc. R. Soc. London, Ser. B* 205, 47 (1979).
- S. Epstein, in *Origins of Human Cancer*, H. H. Hiatt et al., Eds. (Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1977), 1727-1728.
- "Procedures for the Testing of Intentional Food Additives to Establish Their Safety for Use," *WHO Tech. Rep. Ser. No. 9* (1955).
- "Drinking Water and Health, Recommendations of the National Academy of Sciences," *Fed. Regist.* 42, 35764 (1977).
- Report of the Subcommittee on Environmental Carcinogenesis, National Cancer Advisory Board, *Criteria for Assessing the Evidence for Carcinogenicity of Chemical Substances* (National Cancer Institute, Bethesda, Md., 1976).
- Even current advances in mechanistic hypotheses, such as the experimentally justified multistage carcinogenesis theory, although they give useful insight into this matter, do not clarify the final molecular complexities of transformation (12, 19).
- V. Riley, *Science* 189, 465 (1975); _____ and D. Spackman, in *The Pigment Cell*, vol. 2, *Melanomas: Basic Properties and Clinical Behavior*, V. Riley, Ed. (Karger, Basel, 1976), pp. 163-173; *Lab. Anim.* 6, 16 (1977).
- "Assessment of the Carcinogenicity and Mutagenicity of Chemicals," *WHO Tech. Rep. Ser. No. 346* (1974).
- J. Cairns, in *Origins of Human Cancer*, H. H. Hiatt, J. D. Watson, J. A. Winsten, Eds. (Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1977), pp. 1813-1820.
- It is in this context that precursors and proximate or ultimate carcinogens are defined as well as initiators and promoters, acting genetically or epigenetically. It appears that cellular damage leading to higher cancer frequency does not necessarily have to be of direct mutagenic nature (18, 19). As such, the effectiveness of functional carcinogens could be modulated at any stage by other modifying factors which, although not carcinogenic per se, would appear to an experimenter who notices only the resulting cancer incidence.
- G. B. Gori, in *Air Pollution and Cancer in Man*, U. Mohr, D. Schmal, L. Tomatis, Eds. (International Agency for Research and Cancer, Lyon, 1977), pp. 99-111.
- Guidelines for Carcinogen Bioassay in Small Rodents (Carcinogenesis Program, National Cancer Institute, Bethesda, Md., 1976); "Scientific Bases for Identification of Potential Carcinogens and Estimation of Risk," *Fed. Regist.* 44, 39858 (1979).
- Committee for the Revision of Publication No. 1138, NAS Committee on Toxicology, *Principles and Procedures for Evaluating the Toxicity of Household Substances* (National Academy of Sciences-National Research Council, Washington, D.C., 1977).
- "Evaluation of the Carcinogenic Hazards of Food Additives," *FAO Nutr. Meetings Rep. Ser. No. 29* (1961).
- J. Cairns, *Cancer: Science and Society* (Freeman, San Francisco, 1978); R. Peto, *Proc. R. Soc. London, Ser. B* 205, 111 (1979).
- R. Peto, in *Origins of Human Cancer*, H. H. Hiatt, J. D. Watson, J. A. Winsten, Eds. (Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1977).
- "Procedures for Investigating Intentional and Unintentional Food Additives," *WHO Tech. Rep. Ser. No. 348* (1967).
- Drug Research Board NAS-NRC, *Clin. Pharmacol. Ther.* 5, 607 (1969).
- "Principles for the Testing and Evaluation of Drugs for Carcinogenicity," *WHO Tech. Rep. Ser. No. 426* (1969).
- Panel on Carcinogenesis Report on Cancer Testing in the Safety Evaluation of Food Additives and Pesticides, Food and Drug Administration Advisory Committee on Protocols for Safety Evaluation, *Toxicol. Appl. Pharmacol.* 20, 419 (1971).
- The Testing of Chemicals for Carcinogenicity, Mutagenicity and Teratogenicity* (Health and Welfare Department of Ottawa, Canada, 1973).
- C. Maltoni and G. Lefemine, *Environ. Res.* 7, 387 (1974).
- H. G. Smyth, *Food Cosmet. Toxicol.* 5, 51 (1967).
- Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics* (Association of Food and Drug Officials of the United States, Baltimore, Md., 1975), pp. 79-82.
- A. Tannenbaum, in *The Pathophysiology of Cancer*, F. Homburger, Ed. (Hoebner, New York, 1959), pp. 517-562.
- H. E. Kraybill, in *Human Epidemiology and Laboratory Correlations in Chemical Carcinogenesis*, F. Coulston and P. E. Shubik, Eds. (Ablex, Norwood, N.J., 1980).
- E. J. C. Roe and M. J. Tucker, *Proc. Eur. Soc. Study Drug Toxic.* 15, 171 (1974).
- H. F. Kraybill, *Clin. Pharmacol. Ther.* 4, 73 (1963).
- Some official guidelines for the care of experimental animals actually prescribe lighting conditions that are known to produce rapid blindness in rats commonly used in carcinogenesis experiments, with likely profound effects on the complex neurochemical functions of the pineal gland. Department of Health, Education, and Welfare, *Guide for the Care and Use of Laboratory Animals* (Government Printing Office, Publ. No. 7423, Washington, D.C., 1974); W. K. Noell, V. S. Walker, B. S. Kang, S. Berman, *Invest. Ophthalmol.* 5, 450 (1966); W. K. Noell and R. Albrecht, *Science* 172, 76 (1971); W. K. O'Steen, K. V. Anderson, C. R. Shear, *Invest. Ophthalmol.* 13, 334 (1974); K. V. Anderson, F. P. Coyle, W. K. O'Steen, *Exp. Neurol.* 35, 233 (1972); J. Axelrod, *Science* 184, 1341 (1974); R. J. Wurtman and M. A. Moskowitz, *N. Engl. J. Med.* 296, 1329 (1977).
- V. Riley et al., *Science* 200, 124 (1978).
- G. E. Moore, *ibid.* 199, 1157 (1978).
- A. C. Kolbye, *Oncology* 33, 90 (1976).
- The other often-advanced proposition that known human carcinogens, with notable exceptions such as arsenic, are also carcinogenic in animals, and therefore the reverse must also be true, is a generalization based on summarily matching less than two dozen recognized human carcinogens against some 2000 animal ones.
- E. I. Goldenthal, *Current Views on Safety Evaluation of Drugs*, *FDA Pap.* (May 1968), pp. 1-8.
- "Pesticide Residues in Food," *WHO Tech. Rep. Ser. No. 345* (1974).
- Federal Food, Drug and Cosmetic Act, as amended October 1976, Section 409(c)(3A) (Government Printing Office, Washington, D.C., 1976).
- Saccharin Study and Labelling Act, Public Law 95-203, 23 November 1967 (Government Printing Office, Washington, D.C., 1967).
- G. B. Gori, *Science* 194, 1243 (1976).
- G. E. Hutchinson, *Proc. Natl. Acad. Sci. U.S.A.* 51, 930 (1964); B. D. Dinman, *Science* 175, 495 (1972); G. I. Claus, K. Bolander, K. Bolander, *Food Cosmet. Toxicol.* 12, 737 (1975).
- Arsenic, for instance, otherwise a recognized human carcinogen, must have a nontoxic threshold because it is essential to the hematopoietic process and as a catalyst in phosphorylation. Similar considerations are valid for nickel, chromium, selenium, and other agents (26); and the presence of practical no-effect thresholds is clearly documented in smokers, not all of whom develop lung cancer or other smoking-dependent diseases (41). Organotropism of certain carcinogens also implies cellular and tissue thresholds; and the resistance of certain species to known carcinogens, even at maximum tolerated doses, ought to be taken as evidence that no-effect thresholds are a most common class of real-life phenomena. Moreover, because the carcinogenesis outcome is time- and dose-dependent, the finite lifespans of man and animals are bound to impose no-effect thresholds at some level of exposure (see H. Druckrey, in *Potential Carcinogenic Hazards from Drugs: Evaluation of Risk*, R. Truhaut, Ed. (Springer, Berlin, 1967), vol. 7, p. 60).
- M. A. Schneiderman, N. Mantel, C. C. Brown, *Ann. N.Y. Acad. Sci.* 246, 237 (1975).
- D. Hoel and N. Chand, in *Reliability and Biometry*, F. Proschan and R. J. Serfling, Eds. (Siam, Philadelphia, 1974), p. 382; J. Cornfield, *Science* 202, 1107 (1978).
- L. J. Carter, *Science* 204, 811 (1979).
- J. Walsh, *ibid.* 202, 598 (1978).
- C. Comar, *ibid.* 200, 1225 (1978).
- M. G. Morgan, *ibid.* 201, 971 (1978).
- R. J. Smith, *ibid.* 204, 1287 (1979).
- These tests are not yet fully developed; it is conceivable that they could yield useful data, particularly if they made use of normal human cells, tissues, and organs. Coupled with metabolic studies in man or human tissues, they might provide quantitative data more reliable for certain human extrapolations than those supplied by current animal testing (18).
- Toxic Substances Control Act, 11 October 1976, P.L. 94-469 (Government Printing Office, Washington, D.C., 1976); "General Provisions and Inventory Reporting Requirements, Supplemental Notice," *Fed. Regist.* 42, 19298 (1977); "General Provisions and Inventory Requirements," *ibid.*, p. 39182; "Notification of Substantial Risk Under Section 8(e)," *ibid.*, p. 45363; "Supplemental Notice to Proposed Inventory Reporting Requirement; Draft Reporting Forms," *ibid.*, p. 53804; "Inventory Reporting Requirements," *ibid.*, p. 64572; Office of Management and Budget, *Standard Industrial Classification Manual* (Government Printing Office, Washington, D.C., 1972); Office of Toxic Substances, Environmental Protection Agency, *Candidate List of Chemical Substances* (1977), vols. 1-3; *Addenda 1 and 2* (1978); *Activities of Federal Agencies Concerning Selected High Volume Chemicals* (1975).
- L. J. Carter, *Science* 202, 30 (1978).
- P. H. Abelson, *ibid.* 200, 487 (1978); *ibid.* 202, 473 (1978).
- B. J. Culliton, *ibid.* 201, 1198 (1978); R. J. Smith, *ibid.* 203, 28 (1979).
- Committee for a Study on Saccharin and Food Safety Policy, *Food Safety Policy: Scientific and Societal Considerations* (National Academy of Sciences, Washington, D.C., 1979), pt. 2.
- E. Marshall, *Science* 202, 949 (1978).
- D. L. Bazelon, *ibid.* 205, 277 (1979).

The Energy Impacts of Solar Heating

Chris Whipple

The attractions of solar energy are obvious: it is nondepletable, provides immunity to embargoes and fuel price increases, and is generally less damaging to the environment than conventional sources (1). Further, specific solar technologies (for example, water and space heating) have achieved or are approaching costs that are competitive with conventional sources in many regions of the country (2).

The purpose of this article is to examine the impact of a rapid implementation of active solar space heating and water

industrial demand is largely met with indigenous fuels—coal in the case of the steel industry, and coal, nuclear, and hydroelectrically produced electricity in the case of the aluminum industry—the effect of solar heating is both to substitute for depletable fuels and to cause a shift to domestic fuels. During the rest of the century, this shift may be more important than the net energy produced in helping the United States meet energy demand and reduce imports.

In discussing the impacts of solar heating I first consider the general case of net

Summary. The energy required to build and install solar space- and water-heating equipment is compared to the energy it saves under two solar growth paths corresponding to high and low rates of implementation projected by the Domestic Policy Review of Solar Energy. For the rapid growth case, the cumulative energy invested to the year 2000 is calculated to be $1/2$ to $1\frac{1}{2}$ times the amount saved. An impact of rapid solar heating implementation is to shift energy demand from premium heating fuels (natural gas and oil) to coal and nuclear power use in the industries that provide materials for solar equipment.

heating on the U.S. energy supply. The findings are considerably different from those of the recent Domestic Policy Review of Solar Energy (DPR) (1), a multi-agency analysis of the possible range of implementation of solar energy during the balance of the century. The difference is due to the fact that in calculating solar heating contributions, I include the energy required for construction of the solar facilities. When these energy inputs are considered, the energy saved by a rapidly expanding solar heating system becomes significantly less than if calculated without considering these factors. Offsetting this result is the very favorable effect of solar heating on the specific mix of fuels.

If solar heating is rapidly adopted, it will displace premium heating fuels (oil and gas). This conversion to solar heating will shift load from the residential and commercial sectors, in which the solar equipment will be used, to the industrial sector, and particularly to the steel and aluminum industries. Because this

energy analysis for an expanding supply system. Second, I review several estimates of the energy requirements of solar heating equipment and adapt them to the needs of this study. Third, I select two solar heating integration paths to represent low and high growth rate scenarios. The paths chosen were selected to represent, as far as possible, an exponential fit to high and low cases in the DPR. I then combine these results to estimate the net contribution of solar space and water heating (as contrasted with the more prevalent gross energy projections), and discuss the projected impact of solar energy implementation on fuel mix.

The Dynamics of Net Energy

It is possible for an expanding energy system to act as a substantial energy drain, because the consumption of energy for the creation of new production facilities for the system can exceed the

system's own energy production. The factors that increase the magnitude and duration of this drain are rapid growth rates of the energy systems, long times for single production units to achieve an energy payback, and long construction times. The interrelation between these system characteristics and their influence on net energy system outputs has been independently analyzed a number of times (3, 4). Further applications, usually to nuclear power systems, can be found for specific integration paths (5).

For solar heating technologies the net energy dynamics can be important because, relative to conventional energy sources, solar energy collectors and converters substitute an initial capital investment (frequently of energy-intensive materials) for a lifetime of fuel consumption. As such, the energy costs of solar facilities are front-end costs. As a contrast, the energy needed to provide coal and equipment for a coal-fired system is more evenly distributed over the operating life of the plant (6). An additional reason for examining the net energy dynamics of solar energy is the rapid rate of growth of solar energy use proposed for the remainder of the century.

As an illustration of the relative importance of net energy in a dynamic sense, the payback time (at which cumulative energy investments and outputs are equal) for a system expanding linearly in time is exactly twice the payback time for a single unit. For exponential growth paths, the system payback time is an increasing function of both the growth rate and single unit payback time.

For the analysis in this case, a number of simplifying assumptions have been made:

1) The time between solar heating equipment manufacture and operation is assumed to be zero. If this is not so, for example, because of slow inventory turnover in the industry, then this analysis overestimates the net energy output.

2) The energy requirements of the facilities required for solar equipment manufacture, or for associated industries, are not considered in either a static or dynamic sense, except to the extent that this energy has been amortized in the estimates of materials energy content. For example, if rapid expansion of glass manufacturing capacity accompanies the growth of solar collectors, the use of historically "average" energy intensity for glass will neglect the dynamics of its expanding system. Similarly,

The author is Technical Manager at the Energy Study Center, Electric Power Research Institute, Palo Alto, California 94304.

AP00024161