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(Applause.)

DR. KENAGA: Now, we come to that point in our morning where we are peeking at our famous speakers. We have all famous speakers this morning, of course, but today we have with us Dr. Joshua Lederberg who was educated at Columbia where he received his bachelor's of art and Yale University where he received his PHD in microbiology. He received his honorary doctorate degrees from both of those alma maters as well as several other universities. He has taught and chaired departments of genetics and medicine at the University of Wisconsin, Stanford University, is now President of Rockefeller University in New York.

While at Yale where he received his PHD in 1947 he discovered the mechanism of genetic recombination in bacteria, demonstrating for the first time that a form of sexual reproduction occurs in these microorganisms. Prior to this discovery scientists had known little about bacterial genetics, and many had even doubted that bacteria possessed a genetic mechanism similar to that of higher organisms.

Because of their simple structure and rapid growth, bacteria now afford geneticists a field for study. Later at the University of Wisconsin Dr. Lederberg and his then student Dr. Norton Zinder, now a professor at the Rockefeller University showed that bacterial genetic material was exchanged not only by conjugation when the entire complement of chromosomes is then transferred from one bacterial cell to another but, also, by transduction where only fragments are transferred.

They did this by introducing bits of genetic material into the bacterial body and found that they became part of the genetic material of the bacterial cell, thereby altering its constitution.

This was among the first demonstrations of the manipulation of an organism's genetic material. Eleven years later at the age of 33, he was named co-recipient with Dr. Edward L. Tatum and George Beetle of the Nobel Prize in Physiology and Medicine for his work in bacterial genetics.

In addition to being an outstanding research scientist, Dr. Lederberg has been active in numerous govermnet and advisory boards dealing with problems of mental health and retardation, a member and chairman of the

President's Cancer Panel, played an active role in the Mariner and Viking missions to Mars sponsored by NSA, was a consultant to the Arm Control and Disarmament Agency during the successful negotiation of the treaty in biological weapons disarmament, as a Director of the Center for Advanced Study in Behavioral Sciences at Stanford and the Institute for Scientific Information at Philadelphia.

He is especially interested in comparative toxicology and hopefully in organizations like SETAC.

His continuing interest in improving communication amongst scientists, the general public and government policy makers has led Dr. Lederberg to write extensively for lay audiences and includes a seriesof columns distributed by the Washington Post syndicate on the social impact of scientific programs.

If I continued to list his many achievements and events of his illustrious career, I will be encroaching on the time allotted for his message which we are all anxiously awaiting to hear today, entitled Comparative Toxicology, Environmental Health and National Productivity. I am pleased to present to you as our founding lecturer Dr. Joshua Lederberg.

DR. LEDERBERG: Thank you, Dr. Kenaga. I noticed walking in the room that the placement of the lecturn on one side was making it rather difficult for people to see and perhaps even to hear down at that end, although the latter does not make much sense.

I must confess that when Eugene Kenaga first approached me about attending this first meeting of SETAC I was more than a little bit skeptical. My first question was who needs it? Did we really need another scientific society? Would we end up contributing not only some further pollution along the lines of hot air, as well as the depletion of those important natural resources like airplane fuel and human energy? Did we need another clarion call to action and further rationality in public affairs based on scientific and technical judgments?

To be very frank with you, I did not fully appreciate the unique thrust of the society until just a few days ago when I carefully scanned the program and the titles of the papers that were being presented here and then the full impact of what it is that you are trying to accomplish finally did reach me, and in my observation from that program of the combination of deep concern for environmental conservation and rigor of scientific analysis in reaching conclusions in that field, I am certainly a firm convert to both the uniqueness and the necessity of this kind of organization.

It is, if anything, long overdue, and I certainly wish you all success in that enterprise. Yes, there is a need.

In my own perspective on toxicology, it has been founded more on the specific threats to human health that are embraced by human toxicology, and so in my observation of your program I was led to reflect on a couple of elements by which these perspectives might be contrasted and what it was that was really especially unique about this meeting. These may be platitudes to you, but one person's platitude is another person's illumination, and let me share some of that with you.

First of all, the ramification of ecosystem responses which is your immediate preoccupation seems to me to embrace even deeper complexities and uncertainties and perplexities than asking specific questions about the encounter of one particular species, the human with defined quantities of a particular environmental exposure.

The ecosystems are, if anything, more intricate than the physiology of the single organism. You must be vulnerable to issues of balance amongst competing species in a given niche. You must be concerned not only with toxins, but with nutrients, alterations of habitat, the actions of other species, and they may be prey or predators or parasites and these, of course, must lead an outsider, and I do not count myself a professional ecologist, to wonder at the audacity of establishing a theoretical system in which not merely to understand and explain observed phenomena but to attempt some prior prediction as to what the consequences for the evolution of an environmental system will be on the introduction of a new substance.

Secondly, ecosystems, if they, in fact, can survive other natural perturbations must already have some degree of adaptive robustness. Therefore, there is certainly a threshold of environmental insult that such systems can tolerate, a non-linearity of response which is far less controversial than is true at the present time in human toxicity, but this is a double-edged sword.

On the one hand it does offer some latitude with respect to what may be regarded as insignificant exploitation of the environment but may, also, be beguiling because most systems are far too complex for us to anticipate the consequences of human intervention before the fact. The ease with which a biocommunity responds to our taking, let us say, 1000 tons per year of a given species of fish may delude us into believing that 100,000 tons will be likewise acceptable and when the fisherie collapses we may not then know whether it was a pesticide runoff or over-fishing or some even more complex interactions that were responsible. So, whilst there is some comfort in the view that yes, indeed, there must be insignificant levels of insight that can be applied to something as huge and as diffuse and sometimes as self-protecting as the biosphere. It may, also, deprive us of advance indicators of major collapses of those systems. It is my own belief as an outsider that ways to detect indicators of major collapse may be one of the most important challenges, both at a practical level and in the development of the theory of environmental toxicology.

The other branch of your preoccupation and especially today is an explicit concern for risk hazard and how it is perceived by various communities. The last 30 years has seen the maturation, perhaps even the decadence of an environmental movement of major proportions. What was an exciting awakening of public consciousness after a very long era of neglect and indifference has now become itself one of our major industries, contributing its own pollution as a side effect of some of its activities and invoking the clamor of public attention to compete for power with the technocratic sector of our society, and a system that was strongly out of balance 30 years ago on one side has in the perception of many, many people, swung far in the direction of paralyzing almost every initiative on the technological side.

This has two hazards; one, and the most material is that the invocation of delay, delay in every project that one can see as the last ditch resort of resistance in the confrontation of these groups has left everyone far poorer and highly frustrated. The environmentalists on the one hand see continued encroachment on the environment, can have little optimism that there will be significant improvement over the next decade or two decades over the present status. They can speak in many areas at best to having held up the initiation of this, that or another project but from their prospective that they are always in a losing battle, that the major interests, the strength, the financial and advertising and public relations and sometimes political strength of industry will, in the end, override them, and on the other side we have the exasperation and frustration that we have run out of alternatives, that whereas from a broad national perspective it did not matter much to give in on one pesticide on the abrogation of one food coloring, on the delay of one particular drug in its introduction, in the construction of one powerplant in a particular area, in the exploitation of one particular form of energy supply we have reached the point where these are not vulnerable merely point by point but are in a totally pervasive network of confrontation and opposition to where there is scarcely an industrial project of any magnitude and particularly one of any innovation that does not have to anticipate public confrontation and considerable delay in its further implementation, and plainly something has to give in this context. Besides the immediate and obvious economic costs that are involved in this phenomenon, there is in my view even the more serious one of the stultification of initiative. In many areas people have given up trying to develop or to introduce technological innovations regardless of their merits, because they know there will be such a long struggle before they can, in fact, be introduced that the likelihood of the original investment, both in dollars and in human initiative and in individual careers and that whole texture ultimately founded on individual greed but tempered by the mandates of the social contract begins to falter in efforts at initiative, and I am afraid this is not too far from being a description of the tenor of society today. But the other cost which could be even more serious is the backlash which I believe we are seeing emerging in full swing against regulation of every kind and if one could contemplate the extension of the public psychology that has led to the legitimation of Laetrile and in other areas beginning to emerge very strongly and perhaps some element of the testimony of the last election is really all I need to remind you of very sudden and rapid swings of public concern on major issues not unrelated to what we are now facing.

So, I think there is a real sense in which the concern for environment of the eighties must take stock, must look for realistic objectives and above all must find ways for the more constructive conciliation of these motifs, of the very necessary concern for the protection of environmental amenities, environmental necessities, both from the standpoint of public health and for our ability to enjoy life as we would like to see it in this country and that if we do not find better ways to reach some sensible accommodation, important values on both sides are very seriously at risk and the best that we can hope for will be a variety of highly irrational, often mutually contradictory and inconsistent decisions that are likely to leave us all far worse off than we are today.

There are some indications that there is still a residue of accommodative thinking in the public will as expressed both by the Congress and by some elements of the Executive, although these are often no more consistent here than they are in other spheres of national life. One way to offer the statement of what we must achieve may seem like a brutal one, but I think it better than we confront the necessity of certain facts than shilly shally about them, and that is that we must embrace ways to identify and then accomplish some optimal level of environmental pollution and to understand that this optimum is often not zero.

This may appear to be like some new diabolistic ritual, maybe appear to be embracing the devil. We all hate pollution in some form or another as it appears to our lives, and the notion that we will find some optimal level of being sure that our environment is contaminated with such and such dosages of various toxins or other insults to us may seem bizarre and the difficulty of understanding that there is an optimum of evil in a world that has to run along some practical principles is one of the chief difficulties that we face, not only in our own understanding of the problem, and I think an audience like this is sufficiently sophisticated that one can at least discuss it, but even more so in trying to reach what is all too often a highly confused public.

It may end up putting people in the posture of being proud of having found mechanisms whereby they can guarantee that a certain number of people will die, but for the benefit of socially distributed goals which should, also, guarantee that a larger number will be protected, and this can sometimes be expressed in direct trade-offs with respect to health opportunities and sometimes through the vehicle of other economic advantage.

One wishes one lived in the world that it was impossible to discuss trading off lives for dollars, but that is not the world that we live in today. We are constantly making decisions where we reach some limit with respect to the expenditure of public funds, with respect to our own personal investments, in protecting our safety as against some statistical expectation of a reduction of death hazard having come to an equilibrium with the level of social or personal investment in that sphere.

How many of you have guaranteed the electrical safety of your home by investing some few thousands of dollars in a ground fold interrupter circuit? That gives you a particular example. How many of you have installed filters in your air ventilation system to guarantee against the dissemination of potentially infectious microorganisms as against other chemical insults?

We all draw the line at some point on matters that we do know might afford some level of protection with respect to our personal health. I don't feel that in this audience I need to argue the point, but it is one that one needs to have some illustration of.

But this is a rather brutal confrontation not only to have to express but to have to internalize. It is a very uncomfortable position to be in, to be even thinking about these kinds of trade-offs, and if there were ever any way to evade the moral dilemmas that are involved in that kind of trade-off, I think we would eagerly seak them.

I do not believe they are evaded by the asserted doctrine that there can be no trade-off, that risks must be reduced to zero, that no matter what the cost, chemical or physical pollution of an environment that might bear some hazard to human health should be driven down to zero. That is simply looking at a problem in a very narrow sphere, examining only the single transaction that is at issue at that point and failing to recognize the spillover of the invocation of those costs into every other sector of our economy and the immediate health consequences that will flow from that neglect, to the extent that after a fair consideration of the overall framework in which such trade-offs occur we can verify that we can reach zero pollution as not only an optimum, not merely an optimum but even an acceptable level of investment which is fair to the competing demands for health, as well as for other purposes in other spheres, then that zero level might be acceptable in a rational framework. I am not aware that that can ever be done.

Those who deny it, those who look for zero pollution are in my view living in a world I would like to inhabit myself but which I believe is one of fantasy. Above all it denies Avogadro's number. It suggest that this is a small finite indenture, that we can obtain absolutely pure preparations of materials that we take in that can guarantee that there are zero molecules of undesired pollutants in them.

To a degree it denies that the natural world itself is already free of predators, of toxins, of infectious microbes and other hazards which require measures that have environmental costs of their own in order to provide our protection against them. One need only invoke the trade-offs that are involved in both public and private policy with respect to the use of vaccines to illustrate that point. There is no vaccine which is totally free of risk and if one were to invoke that as a principle for the introduction of a health saving measure in that sphere the human cost would be absolutely enormous and sometimes has been.

Once one accepts that zero pollution is a fantasy at least from the standpoint of the informed chemist who knows about Avogadro's number, then it is plain that some kind of quantitative standard must be set by some principle in the regulation of affairs that may influence the entry of a substance into the environment.

Once one has done that, once one has agreed that a standard is what must be applied because zero is an undefinable in chemical terms as against Avogadro's number, then the question is no longer whether a trade-off analysis is going to be done, but the procedure by which it is accomplished, and I would submit that every decision that has mandated a standard, even those where the number zero was used but in a real world where analytical methods are capable sometimes of identifying only a few molecules of a given substance and that that has been used as the standard of application that there has been some kind of implicit trade-off analysis made in the mind of that administrator, and our main purpose in speaking for cost/benefit/risk analysis, it seems to me must be to attempt to expose in detail, to lay out on the table for public examination the full process of reasoning by which any such conclusion is made, and I will make the rather harsh statement that in the present state of the art I do not believe this can be done by a rigorous mechanism of cost-risk/benefit analysis as it is commonly put on, but there is someplace in between in which the mind of the regulator must not allow to be a black box, must not allow to be insulated from examination and criticism where the arguments must be exposed and exposed in some kind of technically sensible, quantitative rationale. There will still be an extraordinary latitude of judgment that must be invoked at a time when almost none of the variables that are involved in an explicit cost risk/benefit analysis can in fact be stated with any high degree of precision.

We have seen circumstances where predicted costs of environmental improvement have failed to materialize sometimes very drastically. I can think of by factors of 100 in either direction, where engineering improvements that were asserted to be very difficult to apply have resulted in fact, in savings and other circumstances where engineering improvements that were mandated on industry have proven to be essentially impossible to achieve regardless of any reasonable degree of investment that would be mandated. One certainly wants to encourage a deeper examination of what the costs of an initiative will be than is likely to be conducted in the absence of pressure from a regulator to accomplish a given aim, but here in the one area which should be the hardest, the soundest of the numbers that could be attributed to an analysis we find that there are already grave difficulties.

Risks of environmental pollution are, of course, the very meat of the scientific concerns that we have at a meeting of this sort, and I would acknowledge that they are far more difficult in your sphere of concern in terms of the complex responses of complicated ecosystems than they would be even on their intersection with and their involvement with the health of human individuals. Benefits must embrace health improvements, environmental amenities, other elements of production, conservation of resources for future use and those resources include in very large measure that environmental sink which is the place we have to go when we want to get rid of something and which is a very finite number.

The estimation of those benefits since they are not fungible; they are not readily translated into dollars is not only a technical exercise of great complexity, but is probably the main focus and legitimate one of value controversies; precisely what trade-offs should there be between having a clear atmosphere around a city and the costs of improvement of its factories? That is not something that can be settled for the rest of the community inside of this room. That is something where the basic issues have to be presented for public determination on a far broader sphere, but they must be presented far more clearly than they have been up to the present time.

One the risk side, we know we face many dilemmas, and here I am going to speak mainly from the perspective of the human toxicologist. The question of linearity of response, the absence of tresholds of human responses to toxic substances remains and will long remain one of the most controversial issues that we have to face. The fact is there are theoretical arguments that would allow for any of the numerous models that are proposed abstractly in this sphere; as against the notion of mandating a threshold one could invoke sunlight, one of the best proven carcinogens. Would we suggest that exposures to this carcinogenic entity be subject to governmental regulation in order to reduce the risk to zero? And while we may wish to refrain from interfering with the personal preferences of recreational sunbathers and believe some protection of privacy with respect to large-scale exposure might, in fact, be something that is a personal privilege, there are, of course, many people who have no recourse but to expose themselves to sun. A considerable fraction of our population not only lives but works out of doors, enjoys it; should we mandate engineering controls in order to minimize their exposure to ultraviolet light which can be guaranteed to cause a certain incidence of skin cancers, and while many of them are quite innocuous, one cannot dismiss the melanomas that will, also, be some fraction of that exposure.

For other chemical substances there is a wide range of theoretical argument with respect to threshold. I do not think one can adopt the general and generalized view that since there are indeed repair mechanisms and there are indeed metabolic mechanisms that can dispose of a certain fraction of the insults induced by a particular molecular species that this has anything whatever to do with the existence of a threshold.

For either metabolism or repair to be relevant to the question of linearity one must know more about the chemical kinetics of those mechanisms. If there is a cup that can be filled, and only the spillover is toxic, then of course there will be a threshold, but is that the mechanism by which either repair or metabolism of toxic substances occurs? The answer is probably not, in most of the specific circumstances that one can invoke as applications of those particular notions.

To the best of my knowledge, and this has been investigated quantitatively only in bacterial systems repair of DNA damage is not a saturating phenomenon but is one which is proportional at every level of the insult. One does have repair of ultraviolet induced injury, chemically reduced injury, but at least in these bacterial systems it is a constant fraction of the primary insults that are subject to repair; a constant fraction even at the lowest doses escapes and under those circumstances one changes the slope of the dose response curve but not its shape, and one will still have a linear response for which no absolute threshold can be determined.

These are matters that could be studied experimentally in tissue culture, for example, even with human cells. To my knowledge that has not been done. So, I am asserting a rather, I think, soundly based theoretical proposition in this sphere. If one relies on the metabolic capacity of the organism to provide that cup that can be filled without injuring the rest of it, one faces even greater perplexities. There again, it is difficult for me to invoke systems where I am aware that they are saturated with respect to the toxic substances with which we are most concerned.

In fact, for highly toxic materials it is rather unlikely that that will be the case because it would imply that you are titrating out the enzyme molecules responsible for that metabolic conversion, and if we are dealing with toxins that are active at fairly low concentrations, it is rather unlikely that that will ever be the case in practice. There may well be exceptions. There certainly can be differences in the metabolic handling of large quantities of a toxic substance compared to small ones, and I do have some sympathy for those people who are working in bladder cancer and are aware that feeding of very large amounts of particular substances can result in crystallurias and in the formation of stones where this is indeed an example of spillover, where the ability of the urine to remove a given quantity of solute does reach saturation on super saturation and in a very literal sense you have the formation of precipitants and there in principle the possibility of local toxic actions which would be highly dose dependent.

These are very interesting theoretical propositions. None of them has been carried to the point of experimental corroboration in ways that they would be useful for regulatory purposes. I just wanted to give one or a few examples where it would be possible for those people who are most deeply concerned about what they would call the premature application of general principles of limited rationality like the linear response to dose, really do have an opportunity to offer up some concrete and relevant evidence to the contrary. One might be quite optimistic that one will discover exceptions to the linear rule, but they have not as yet been forthcoming, and I think that there is a gap that can only be filled by further scientific investigation.

We do, of course, suffer in many, many ways from the historical development of toxicology as an orphan science. It is a field which until very recently was neither a very great public or national importance, nor one that had achieved a considerable degree of academic respectability.

I think we are all very pleased that this situation is changing, changing quite rapidly at the present time on both counts.

It was not helped by the fact that for the past 15 years the market for toxicologists has been dominated by the demand of the regulatory agencies to perform tests that had to be, I stress had to be conducted in the most routine way imaginable because they were testing protocols for safety of materials that in the way the bureaucracies must run had to be applied fairhandedly to all comers, had to be written down in a book in advance and had to be applied without favor or exception or reasonable accommodation or any approach to the acceptance of real scientific insight to a given problem in order to meet the regulatory demand.

No wonder a profession, the market for whose product was dominated by the need to staff laboratories to perform these very routine tasks that went contrary to common sense, as well as scientific reason for so many years had great difficulty in establishing itself as an attractive setting for the most aggressive, energetic and enthusiastic of young minds and even when they would go into it would find themselves in circumstances where, guess what, they had to kill 10,000 mice next week in order to meet their quota.

This is something that must change, and it must change in the direction of bringing toxicology firmly into the mainstream of modern biology.

There are a number of ways in which this can and must be done. The relationship of toxins to the general evolution of ecosystems which is the main focus, I believe, of the scientific interest of this organization is an exciting illustration of how to build a bridge to a major arena of modern biology, and it is not only in this field that in fact I think we will find that not only does that modern biology offer a good deal to toxicology but that the converse may be true even more deeply.

There were dozens of papers in the program that I looked at today that involved close analytical examination of the responses of an ecosystem to an intended or inadvertent but in any event manmade intervention that involved experiments with the environment that could never have been done and would never have been analyzed were it not for the toxicological framework of that examination. I believe that in general principles the physiology of individual organisms and the responses of communities are going to profit enormously not only from the general attention and support but from the provocation of the findings of these kinds of experiments that can bring that field as well to a state of development and excitement that it would be unlikely to have achieved in its absence.

In fact, I rather suspect that by far the major effort that goes on in ecological analysis during the next decade is going to be in the context of environmental toxicology.

The same is true of other aspects of biology. One route that would be of particular pertinence would be to try to generate more excitement for toxicology about the application of the comparative method which is one of the fundamental routes of biological analysis. It is one that runs so deep in my own consciousness and the way that I think about how to ever design experiments or to look for general principles in biology. I guess it was mentioned that I was on the Mars Viking team, and of course, that had no other motivation than an attempt to go beyond the bounds of our own terrestrial biosphere to see if there were something else that that rather limited evolutionary framework that we had here could be compared with. So far it looks as if the answer is negative, but that has been far from exhausted as a matter of examination.

This runs so deep that I was rather startled to find that to my own knowledge there really has not been a careful historical examination of the way in which comparative thinking has pervaded biology since its roots. So, I can offer a few observations only as an amateur in my examination of the history of ideas in this field.

I was quite intrigued to see how deeply Aristotle used judgments based on comparisons of a range of organisms to make a wide variety of generalizations about what was and was not pertinent, what kinds of correlations would be available, animals that had more teeth in their lower jaw had certain properties compared to animals who had more teeth in their upper jaw and so on and so forth. I am sorry I did not bring the text to read to you on these matters, but it is plain that from the very beginnings of the scientific examination of living forms that the variety with which these forms present themselves was the most immediate provocation to the development of theories of life, of its nature in general, obviously the segregation of living organisms from other aspects of the organization of matter and in much greater detail.

We find in 1628 the founder of physiology, the founder of physiology, William Harvey, conducted his examination of the function of the heart by the most meticulous and detailed comparison of the circulatory systems of a variety of species and that this set of comparisons comparing hearts with two chambers with those of four chambers and so forth was of crucial importance in his development of the physiological theory of circulation, and he must have been very much on the defensive for looking at organisms other than man. He apologizes for this at many places in his discussion and in particular he inveighs strongly against those who feel that the only sphere of observation relative to humanity is the examination of the dead human being. That must sound a little bit familiar in today's context.

The comparative approach is, of course, fundamental to our understanding of the evolution of life. We have a framework of what we generally now believe the monophyletic origin of all living forms based on that kind of comparison and through the mechanisms that Darwin and the neo-Darwin in evolutionary theory has dwelled upon in very great detail.

More recently comparative biochemistry which reached its culmination, I would say, in Beetle and Tatum's work on the laboratory production of specific genetic alterations that then have specific biochemical consequences has been absolutely invaluable in the analysis of biochemical pathways.

One wants to reflect a little bit why that tool has been so important. I think it can be summarized in large measure to the very complexity of the individual biological organism. This is so complicated that it is until the point when one knows the pathway and can isolate the enzymes hard to grasp in all of its detail. One has two organisms that differ in respect to one gene, therefore one primary function. It is far easier to dissect out the specific differences between two complex systems which are highly circumscribed and which then cast out a lot of the commonality as being totally irrelevant.

If you have one form of an organism that makes no pigment, is white and another form that makes a yellow pigment, you find in trying to chase out the pathways that there are some enzymes that differ between these two strains and others that are common. You can discard the common elements immediately as being irrelevant to the difference in pigment formation and therefore like to be immaterial to that pathway. It is a method that has been used over and over and over again, and it may be one of our most powerful ways of dealing with systems as complex as the organism. You use it as well in your ecological studies. It is far more difficult to do there, to form two bions that differ in only a limited number of initial conditions from which to then try to dissect what the consequences of those will be.

I would like to invoke that history of comparative biology as being one of the most powerful potential tools that we have for working out the mechanisms of toxicity of new substances. There are several paradoxes about that. First of all, in the way that toxicology has been mandated to develop as a regulatory discipline the discovery of the toxicity in a single species out of a panel that may be prescribed is usually not the starting point for an investigation of why one species differs from another one but the closure of development of that particular substance, because there is a prima facie argument that if a substance is toxic in any species whatever, that it is likely to be toxic in man. This is sometimes rebuttable, sometimes in practice not but almost always makes the game hardly worth the candle for the further development of that particular chemical and from the standpoint of the developer and producer it is likely to be more economical to abandon one's efforts at the study of a particular substance once it exhibits toxicity in any interesting species that might be thought of as a model for man than to pursue the question of why it kills rats and not mice and try to go on from there for whether it is likely to be a good predictor of its behavior in the human.

So, I am convinced, and I have been told that there is, in fact, a vast amount of information on differential responses of different species to potentially toxic substances which has never been followed up, which has never been published. It was in no one's apparent interest to do so, and therefore those kinds of anomalies, those kinds of surprises or discrepancies or paradoxes that are the very meat of scientific inquiry in the academic laboratory are the closure of further developmental study in the industrial laboratory, and we must find some way in which that can be broken out.

The other side of comparative toxicology is that in fact it is the theory of prediction as far as human risk is concerned.

The one way we do not wish to become the canonical method of determination of human toxicity is by the explicit discovery of human injury after a substance has been introduced into the environment. In order to prevent that from happening, in order to keep our environmental introductions from making unwitting guinea pigs and in the real sense that people have been injured for lack of adequate foresight, we, of course, must develop far more robust and reliable methods of prediction based on laboratory assays on a variety of other species and so on, but there unlike the circumstance in clinical medicine where the final test of a new drug is a clinical trial in which human beings are empirically exposed to a substance that has had some prior testing, some prior validation but where your decisions about its value, positive or negative are based on human exposure, we are obliged to try to prevent those tests from being done where there will be significant physiological responses of humans to a substance.

Therefore in environmental affairs, far more even than in therapeutics we need a robust theory of prediction. We need a set of principles, of validated procedures, of methods of analysis and extrapolation upon which we can place some faith and reliance so that when we do these studies in the laboratory we can make confident predictions as to the nature of the human response.

That puts a load on comparative biology, including the biology of the human and that of the other test systems far greater than it has had to bear in any sphere up to the present time, but I believe it is one of the greatest challenges both to toxicology as an applied science and to toxicology as a mainstream element of the development of general biological theory that we can look forward to at the present time.

At stake in this is not only some straightening out of our national posture in this respect but I must say even to the credibility of our scientific effort itself. I do not know how long the public is going to stand for the uncertainty to which it is subjected, the assaults which it hears, statements that something may be risky, but we really don't know on the one hand and demands for the continued support of basic science for its own sake on the other.

I think there is going to be an increasing demand to scientists in the basic biological disciplines to put up or shut up, to provide some effective contribution to what is becoming an ever more urgent confrontation between scientific uncertainty and the needs of public policy.

I congratulate the organization of this group for what I believe is a major step towards the bringing about of a dialogue and a forum for critical inquiry of the discipline of scientific investigation criticism and comment in a field that needs it ever so badly.

I wish you well.

(Applause.)

DR. KENAGA: Please don't leave the podium. Dr. Herbert Ward has proposed an award of our society, a single award for your being our very first lecturer and our first award, and he has a citation here which we want to present to you in honor of this occasion. It is a very nicely lettered document which says, "The Society of Environmental Toxicology and Chemistry awards this to you as our founder lecturer," and you can maybe find a place on your wall amongst all the rest of your awards for that, and we thank you very much.

(Applause.)

DR. LEDERBERG: Thank you. It is really my privilege.

DR. TUCKER: You are all anxious to go to lunch I know. Just one brief announcement.

(Administrative announcement.)

(Thereupon, at 12:20 p.m., a recess was taken until 1:30 p.m., the same day.)