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# Alternatives in the 90's: What's Next?

Henry Spira

Animal Rights Coalitions

## ABSTRACT

The 80's was a decade of remarkable and innovative research and development of alternatives. We see the 90's as the decade of validation and implementation.

From an activist's perspective, the 80's was very encouraging,-- alternatives gained acceptance, legitimacy and credibility within the toxicology, corporate and regulatory communities. And The Center for Alternatives to Animal Testing (CAAT) at Johns Hopkins University played a significant role in making this acceptance possible.

But these new technologies have yet to realize their full potential; the focus to date has been on development more than on bringing these technologies into routine usage. And the public, including the more forward-looking sectors of the science community, is eager for results.

One way that activists in the 90's may promote alternatives is the development of a new "chic" in research, testing and education, in much the same way that anti-smoking groups have successfully turned around the image of smoking. With the support of pioneering groups, including the CAAT community, a trickle-down phenomenon can change the outlook and mind-set of future scientists. Starting with teenagers, we can turn around the tradition that sees animals as test tubes with whiskers towards the "chic" of Replacement, Reduction and Refinement as well as zero-based animal usage.

## ALTERNATIVES IN THE 90's: WHAT'S NEXT?

A sure sign of success in any movement is that it becomes self-sustaining. The size and diversity of this meeting testifies to the fact that the "Three R's" -- Reduction, Replacement and Refinement -- have a life of their own. Clearly, the concept of alternatives has gained legitimacy, become institutionalized and is moving into the scientific mainstream. But the pace needs to be accelerated.

There's a growing recognition that our treatment of animals merits serious consideration. Animal rights is recognized as a rapidly growing movement, with support across the entire spectrum, from young to old, from Right to Left, from rich to poor. It's one of three issues generating the largest amount of Congressional mail. It has made the covers of major publications and been the focus of national TV programs. It has rapidly gained credibility and legitimacy as a movement which has a rational foundation, has political clout, and is making real progress. The term animal rights is no longer belittled with quotation marks.

I believe that much of the movement's recent success can be traced to Peter Singer's 1975 manifesto, Animal Liberation. Singer provides a rational foundation for animal rights by framing it as a logical extension of earlier movements for human rights. He made it possible for social activists and professionals to rally to the cause. This new influx of talent has helped the movement gain widespread acceptance over the past decade.

## **DO PEOPLE CARE?**

Polls show that the public increasingly feels that the suffering of animals does matter. Doyle Dane Bernbach reported that nine out of ten people are concerned with protecting animals. To place this in a larger context, we need to remember that only fairly recently has it become generally accepted that all humans, regardless of sex, race, nationality, religious or political beliefs, abilities or popularity are entitled to equal consideration -- that they have the right to not be harmed. The next reasonable step, once all humans have been included in this "circle of concern," is to expand the circle to include non-human animals. In our view, animal rights will continue to gain public support, not as the latest fad vying for media attention, but as a natural progression, an additional ethical consideration, a matter of consistency, justice and fair play.

Still, many people perceive the movement for animal protection as negative and anti-science. To counteract this perception, we have continually accentuated the fact that members of the science community are part of the nine out of ten people concerned with protecting animals. We have attempted to turn walls into bridges by promoting the shared goals of better science, efficiency, economy and humanity.

Our role has been largely that of catalyst and amplifier. Members of the science community have been the first to note that humane science can also be better science. The "Three R's" had for some time been a quiet, pioneering enterprise; we encouraged proliferation of the concept within the corporate, regulatory, scientific, and educational sectors.

What is particularly encouraging is that within the past decade a whole new discipline of in-vitro toxicology has begun to enter the mainstream. There are now university centers, data bases, scientific journals, newsletters, books and professional associations devoted to alternatives. And the subject is routinely included in major scientific conferences, seminars, symposia and data bases.

## **HOW DID THESE EFFORTS GET UNDERWAY?**

In the old days, biological scientists and animal protectionists were usually to be found at each other's throats,-- each screaming that the other was immoral. This deplorable state of affairs, dependent on a black-and-white, saints-and-sinners way of looking at the issues, ruled the past century and did no good to anyone, including the animals.

Fortunately, early in the century, a small but rapidly growing cadre of visionary philosopher/scientists emerged. They conceived the possibility that the goals of science and of the animal protection movement need not be contradictory, that difficult as the idea might at first appear, humane science would be better science.

Individuals working within this framework produced a series of suggestions as to what was doable. In 1959, W. M. Russell and R. L. Burch published their ground-breaking study, The Principles of Humane Technique, which suggested that humane science can also be better science. They developed the concept of alternatives through the "Three R's" -- methods which (1) Replace the use of animals, (2)

Reduce the number of animals used, or which (3) Refine existing procedures so that animals are subject to less pain and suffering.

Then, in 1978, David Smyth, the late head of the British Research Defense Society, published Alternatives to Animal Experiments, which explored potential alternatives in biology. As Russell and Burch had done, Smyth attempted the difficult task of defining where alternatives were possible versus areas in which animal use, at the time, appeared essential. In 1984, Andrew Rowan's thoughtful assessment of the use of animals in research, Of Mice, Models, & Men, was, among other things, instrumental in changing the attitude within the science community from "if an alternative can be developed" to "when we develop an alternative."

And the movement toward alternatives gained energy from the traditional practise in science of questioning the usual ways of doing things and attempting to think through what is really necessary and sufficient for solving any problem.

### **HOW WE CAN "KICK THE HABIT"**

Since 1980, this theme was also promoted by our animal protection coalitions. We maintained that much unnecessary animal suffering is due to "creeping routinism," and suggested that this be countered by clear goals and questioning of methods. I use "we" rather than "I" to indicate that both the actions and the ideas described are the product of a loose network of organizations and individuals with a variety of expertise, meeting informally to develop and implement programs and campaigns.

One method of challenging "creeping routinism" is through the concept of "zero-based" animal use. This calls for an institution to examine its entire animal research program as if it had just begun, from ground zero, so that people do not mindlessly repeat what was done in previous years.

People and institutions tend to do tomorrow what they did yesterday. To counter this, we have suggested that before any laboratory animals are used, the review process must question: "Is this research/data really necessary?" "Can this information be obtained without using animals?" "With fewer animals?" "With less pain?" We feel that such a program can rapidly eliminate zeros from the more than 20,000,000 laboratory animals currently being used in the USA every year.

### **STARTING WITH THE DRAIZE**

Smyth was a pioneer of this concept and proposed replacing the Draize test. The Draize presumes to measure the potential for chemicals to damage the human eye based on the damage inflicted in the eyes of conscious rabbits. It clearly causes suffering and Smyth felt that the development of alternatives should not present any major scientific problems. We therefore decided to approach corporations involved in Draize testing, hoping to gain their collaboration in seeking alternatives. We began by attempting dialog with cosmetics industry leader, Revlon.

At first, Revlon refused to consider the potential of alternatives, perhaps "considering the source". But after more than two years of protests, Revlon responded with an historic initiative: multi-year funding of research at Rockefeller University to seek cell biological and other humane alternatives to the Draize test. Revlon launched a program that led to institutionalizing and carrying forward the seminal suggestions of Smyth and others.

This momentum and our negotiations with Avon, Bristol-Myers, Estee Lauder and other major corporations, all of whom were concerned with the image they were projecting, led to the creation of the Johns Hopkins Center for Alternatives to Animal Testing. CAAT distributed many small grants,

piggybacking the search for alternatives onto massive research projects already in progress. This resulted in established researchers becoming sensitized to emerging opportunities in new methods, and thereby expanding the alternatives loop. In addition, symposia and publications under the aegis of CAAT Director Alan Goldberg did much to promote networking among scientists developing new methods, as well as to legitimize the concept of alternatives.

As part of this initial thrust, the idea of giving alternatives a fair shake was furthered significantly by the trailblazing activities of a number of corporate toxicologists, including Ted Brenner, John Corbett, Pam Danneman, Yale Gressel, Jack Griffith, Myron Mehlman, Emil Pfitzer, Jim Russo, Bob Scala, Janice Teal, Alex Vongries, and John Yam; the initiatives of government scientists, including June Bradlaw, Gary Ellis, Ted Farber, Sid Green, Dick Hill, Kailash Gupta, John Moore, Gary Flamm, Victor Morgenroth and David Rall; and the work of science writers Jeannie Blake, Mary Brevnik, Ron Dagani, Barnaby Feder, Susan Fowler, Jane Gregory, Cathy Heinze, Constance Holden, Rex Rhein, Helen Smith, Nicholas Wade, and Jonathan Weiner, among others.

These initiatives were the "big bang,"-- an immense leap forward in establishing the legitimacy and promise of alternatives. They have generated new ideas and findings and spawned similar major programs elsewhere.

Meanwhile visionary high-tech entrepreneurs have begun to realize the great promise in alternatives. In addition to R&D they are aggressively marketing new methods: setting up laboratories, organizing workshops to familiarize technicians with the state of the art, and, most excitingly, joining forces with major multinational corporations.

## **ON TO THE LD50**

Similar progress has taken place in phasing down the 65-year-old classic LD50 test. The LD50 (Lethal Dose 50% Test) measures death slowly, painfully and badly. It generates, with meaningless precision, a number indicating how much of every product, per body weight, is needed to kill half of a group of lab animals.

Just ten years ago, the LD50 was considered the foundation of safety testing. Now, there's almost unanimous agreement that the LD50 is wasteful and unnecessary. And this change is due in large part to our amplifying the criticisms made by leading toxicologists, including Gerhard Zbinden, who in 1982 asserted that "clinical experience shows that the LD50 value determined in animals rarely bears a meaningful relation with the lethal dose in man." Zbinden suggested regulatory change from the LD50 to range-finding tests using one-tenth the number of animals with careful observation. Furthermore, Smyth had noted the incongruity of mortality being used as a test for morbidity, a lethal dose providing assurances about non-lethal toxicity.

A turning point in the campaign to phase out the LD50 was a letter from David P. Rall, then Director of the National Toxicology Program, who called the LD50 "an anachronism ... I do not think the LD50 test provides much useful information about the health hazards to humans from chemicals, the NTP does not use the LD50 ..."

## **THE EXPANDING LOOP**

Progress toward phasing out the LD50 and the Draize tests has been rapid. Ten years ago, replacing these tests appeared overwhelmingly difficult. But as events developed, it was the scientific objections to these tests, plus growing support for alternatives from sectors of the toxicology, corporate, and governmental communities that led to encouraging results.

Over the past decade, major corporations such as Avon, Bristol-Myers, Colgate, Hoffmann-La Roche, Johnson & Johnson, L'Oreal, Mobil, Procter & Gamble, Revlon, and Unilever, among others, have instituted structural changes to promote alternatives. Here are some examples:

- Hoffmann-La Roche has decreased its use of animals by 67% over a seven-year period. One of the techniques that made this possible is computer-assisted molecular modeling, which allows the shape and structure of an experimental compound to be visualized in a three-dimensional image on a computer screen; predictions of biological effects can then be made on the basis of similarities between the structure of molecules.
- In 1991 alone, Procter & Gamble spent over \$4.6 million on alternatives research and they are sharing these results with others to help advance scientific and governmental acceptance of alternative methods. P&G also publishes "Alternatives Alert," the first corporate newsletter devoted specifically to promoting alternatives. P&G researchers have published and presented more than one hundred papers on alternatives.
- Colgate-Palmolive has publicly committed itself to the long-term goal of completely replacing the use of animals with alternative methods. They have developed the CAM Test, which uses the membrane of a fertilized chicken egg to predict the potential of materials to cause eye irritation, and they are sharing the results.
- One of the most dramatic examples of a science-driven move toward alternatives is happening at the National Cancer Institute. NCI has developed a new in-vitro screen for testing potential anti-cancer compounds which has reduced their animal use from 6,000,000 to less than 300,000 annually, while improving the quality of research.

#### **WHERE DO WE GO FROM HERE?**

Now that the concept of alternatives has been legitimized and even institutionalized, the question becomes: Where do we go from here? Despite all the progress, energy and creativity, it's not clear where things are now, nor where it's all going. There are no timetables, no benchmarks and nobody has yet attempted to pull it all together. While each research project may well be brilliant and well organized, it's not necessarily linked to what others may be doing, nor to any overarching plan. If we keep pursuing the current trajectory, it's not at all clear what will be nailed down in any of our lifetimes. The potential is there to keep developing more and more candidates for alternatives when we need to focus serious energies on assessing, validating and implementing the most promising tests already developed.

It seems to us that we now need to shift gears, -- that what is now needed, in the common interest, is a blueprint.

To illustrate this concept, consider an orchestra. An orchestra can consist of brilliant, accomplished musicians, but if these musicians are not playing the same piece, if there is no agreed musical score nor even a conductor, then the many random sounds will not likely produce the coherent, harmonious music you are aiming for.

As another example, consider space exploration. Regardless of one's own sense of social priorities, NASA could never have met the challenge of putting people on the moon in the relatively short period of less than ten years without strong central direction, an absolute commitment to planning and coordination, and, above all, a strong conviction in their ability to succeed.

## **HOW DO WE GO ABOUT CONSTRUCTING A BLUEPRINT?**

The European community already recognizes that validation of potential alternatives is a key stumbling block in the application and use of alternatives. Accordingly, they are establishing the European Center for the Validation of Alternative Methods (ECVAM) in Ispra, Italy, whose primary focus will be to coordinate the validation of alternatives within the European Community. ECVAM will also serve as an information exchange on alternatives and promote dialogue among legislators, industry, biomedical scientists, consumer organizations and animal welfare groups.

Unlike the European Community, the USA has yet to establish a national center for the validation and implementation of alternatives.

Clearly, leadership is one of the first issues which will need to be addressed in the construction of a center and a plan. It has been suggested in several quarters that the National Toxicology Program/National Institute of Environmental Health Sciences (NTP/NIEHS) represents a natural setting for this initiative, and that its Director, Kenneth Olden, may well be the ideal person to pull it all together and set up a steering group.

It would be important that this steering group have representation from all the relevant sectors including industry, members of the Interagency Regulatory Alternatives Group (IRAG), academia, animal protectionists and consumer advocates such as perhaps the Council on Economic Priorities (CEP).

One of the first tasks that would need to be undertaken by this group is a "situation analysis" to summarize and assess where we are now, what's happened to date, the successes and obstacles to step by step implementation.

Upon completion, this "situation analysis" would form the basis for setting clear objectives, strategies and time-tables. In developing such a plan, it is crucial that there be guidance, input and participation from as many sectors as possible who will be affected by the outcome. And in the process of preparing the blueprint, additional ideas may well be generated.

We're not proposing a straitjacket, but rather a living, breathing, flexible plan, that is fine tuned as it progresses, a program that is modified and adapted on the basis of real world experience.

To ensure optimal progress, the Center's steering group should meet regularly to update progress and monitor implementation.

## **A PRACTICAL PLAN FOR CHANGE**

We're talking about a plan that leads to meaningful change. This is not wishful thinking since there are many initiatives that can be acted on immediately.

For example, the "zero-based" concept of animal use, while currently accepted by forward-looking researchers, needs to become the norm throughout the corporate, academic and governmental sectors.

In tandem with the "zero-based concept," corporate and government agencies need to adopt the "Three R's." The "Three R's" are methods which, as stated earlier, (1) Replace the use of animals, (2) Reduce the number of animals used, or (3) which Refine existing procedures so that animals are subject to less pain and suffering.

Practical application of these policies will lead to scrapping those animal tests that have no significant value in protecting the public or the environment and whose only justification appears to be "this is the

way we've always done it." Testing requirements should be science-driven, not based on historical baggage and check-lists.

Another thing a blueprint can do is to help avoid unnecessary and costly duplication by providing for a system of data sharing which also addresses concerns such as proprietary interests and compensation. A possible prototype: the FIFRA provisions used by the Registration Division of the EPA's Office of Pesticide Programs. This Office actively encourages data sharing, with the result that the majority of data submitted come from existing EPA files, not from needless duplication. Fair compensation is worked out between the submitter and user; if they cannot agree, the final determination is made by US Department of Labor arbitrators.

There's also the need to promote international regulatory acceptance of the most modern, most reliable and most humane methods. With commerce being global, international harmonization is crucial. Recently, there have been some encouraging agreements among officials from the FDA, the European Community and Japan to end the classic LD50, and to accept reproductive toxicology data that meet USA, EC or Japanese standards rather than duplicating the testing.

Finally, we need to address the issue of who will pay for this proposed undertaking which will be, in effect, a center for the validation and implementation of alternatives. One possibility is that this initiative be jointly funded by the corporate sector, government and the animal protection community.

## **THE NEED TO MONITOR PROGRESS**

It will be difficult to assess or quantify progress without a benchmark and tracking mechanism. It has been suggested that this can only be done with an Animal Utilization Survey, a basic tool which is used overseas but not yet in the USA. Such surveys provide a baseline against which to measure progress; they make it possible to prioritize goals and allocate resources on the basis of the numbers of animals, the opportunities for change and the pain involved.

Such a survey should be sufficiently detailed to make it possible to track animal usage in relation to objectives. Categories could include: drug discovery and development; data for regulatory purposes: education; production of biological products, etc.

Not least, an animal utilization survey can increase sensitivity. The research community and the public at large may well have the impression that nobody counts the numbers because the numbers don't count.

## **GETTING THE BALL ROLLING**

It has been suggested that closure for one specific animal test in one specific product category however narrow and specific, can provide a prototype to get the ball rolling. In this connection, the Draize eye irritancy test is most frequently mentioned.

The movement for new methods could be enormously energized were there a prototype for bringing a predetermined line of products to market without using traditional testing methods and without compromising consumer safety.

The first steps toward such a prototype are already underway: some of the largest household products companies are now working together to establish guidelines to identify shampoo formulations that would no longer require the traditional routine Draize animal tests. While developing a shampoo matrix might not appear of historic import, the matrix could in fact open the door to a revolution in toxicology. If carried to fruition, it could serve as a possible prototype for defining regulatory needs for other product lines.



But, in replacing the Draize test, as would be true for replacing other traditional tests, the point is not to daydream or "ivory tower" to the point of abstract perfection. Rather, let us seek methods that have practical application. And this is the audience that can make it happen.

To summarize, we've had a decade of brilliant development. What's needed now is a decade of aggressive implementation. As an engineering friend of mine told me, "there comes a point when you have to stop designing and start shipping."

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