The Life Sciences Research Office
by
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In the development of new research thrusts, in the conduct of scientific programs, and in the applications of research to public health and welfare, federal agency administrators have specific questions and problems that require prompt answers. Only a few organizations are available to undertake tasks of unbiased objective scientific evaluation and analysis. Having access to organizations such as the National Research Council (NRC) and FASEB's Life Sciences Research Office (LSRO), capable of providing unbiased advice and counsel, provides research program administrators with alternate sources of information and guidance. The recognition of these factors was one of the reasons for organizing the LSRO.

Early History
As early as 1955, the FASEB Board responded to requests for reviews of research areas and evaluation of scientific issues from the National Science Foundation, the National Institutes of Health (NIH), and the NRC. These included evaluation of such topics as usefulness of the germ-free animal in biomedical research, prediction of personnel needs in the basic health sciences, and training needs for use of data processing in research studies. Reports were prepared by committees appointed by the Federation Board.

In July 1962, the Army Research Office, Office of the Chief of Research and Development, formally requested FASEB's assistance in analyzing specific problems confronting the military in biology and medicine. To meet this request, M. O. Lee, Executive Director, with the approval of the FASEB Executive Board, established the LSRO. The Office, under the leadership of W. H. Griffith, former Professor and Chairman of Physiological Chemistry at UCLA Medical School, expertly evaluated and appraised scientific problems using ad hoc reviews by qualified scientists actively engaged in research. Written reports prepared by the LSRO scientific staff analyzed and interpreted available scientific data, outlined research opportunities, and included specific recommendations based on the opinions of the biological scientists who contributed to these analytical reviews. This concept of ad hoc review and evaluation by expert scientists has been the hallmark of the LSRO's approach to various topics in biology and medicine over the past 27 years.

From 1962 to 1967, the LSRO conducted several studies for the Department of the Army. One notable contribution was the review entitled "A Study of the Biomedical Problems Related to the Requirements of Troops at Terrestrial Altitudes of 10,000 Feet or Above." Completed in 1963, this LSRO report formed the scientific basis for a major acceleration of the Environmental Medical Research Program, Office of the Surgeon General of the Army, by documenting the needs for increased research funding in environmental physiology. A 1965 LSRO report presented to the Joint Committee on Atomic Energy of Congress led to major revisions of the Army Food Irradiation Program.

Developmental Period
In 1967, C. Jelleff Carr, noted pharmacologist, assumed the position of LSRO Director. Under his leadership the scope of activities grew as the value of LSRO studies became recognized. Numerous expert scientific panels were convened to evaluate research topics for various agencies including the Office of the Chief of Research and Development, and the Office of the Surgeon General, Department of the Army; the Bureau of Radiological Health, U.S. Public Health Service; NIH; the Health Services and Mental Health...
Administration; and the Food and Drug Administration (FDA).

Studies conducted by the LSRO played a prominent role in the development of new life sciences research programs of several federal agencies during this period. Research administrators found the reports useful in identifying promising areas in the biological sciences for future emphasis and as a basis for reaching decisions on issues related to health and environmental safety. One such effort was "A Study of New Methods of Measuring Cerebral Circulation," funded and sponsored by NIH in early 1970. The LSRO report, based on a meeting that brought physicists and engineers together with medical scientists, emphasized the possibility of applying emerging principles of electronics and nuclear physics to the complex problem of detecting and measuring brain blood flow in ways that would be painless and without risk to the patient. A major outgrowth of this LSRO study was the establishment of centers for the study of cerebrovascular disorders and measuring brain blood dynamics by NIH.

In 1972, at the request of the FDA, LSRO initiated a review and evaluation of the safety of the Generally Recognized as Safe (GRAS) food ingredients. The panel, designated the Select Committee on GRAS Substances (SCOGS), evaluated the available scientific information on over 400 GRAS Substances (Fig. 1). The Select Committee's evaluations spanned 10 years and resulted in 150 reports. Their reviews and analyses were made independently of guidelines provided by FDA or any other group, governmental or nongovernmental. A unique feature of this effort involved making the tentative reports on each substance available to the public. Interested persons could appear before the SCOGS at a public meeting to present data, information, and views on the substances covered by the reports. The data, information, and views presented at these meetings were considered by the SCOGS in reaching its final conclusions. Final reports were approved by the LSRO Director, and subsequently by the LSRO Advisory Committee and the FASEB Executive Director. The Committee's evaluation report on each GRAS substance provided FDA with an analysis of all relevant scientific data, expressed as a conclusion with regard to the strength or absence of evidence of health effects.

The Select Committee's deliberations focused on a scientific evaluation of potential health hazards posed by each GRAS substance for normal individuals. Since 1972, the FDA has been revising regulations with respect to each GRAS substance, using the SCOGS reports as one factor in their decision-making process. Patricia R. Harris, then Secretary of the Department of Health and Human Services commended the Select Committee, LSRO, and FASEB for their outstanding performance of a difficult task and took note of the high credibility accorded the work by the scientific community, the regulated industry, and the general public. Dr. Harris also cited the Select Committee's reports as the largest, most comprehensive, and authoritative review of food safety ever conducted.

**1977 to Present**

In 1977, Dr. Carr was appointed Director Emeritus and Kenneth D. Fisher became the LSRO's third Director. During this period, the LSRO expanded its studies in nutrition and biochemistry to include analyses of problems and research opportunities associated with manned space flight for the National Aeronautics and Space Administration as well as assessment of the usefulness of several electronic databases for the National Library of Medicine. In addition, scientific reviews were conducted for other federal agencies and organizations including the U.S. Department of Agriculture, the Office of Disease Prevention and Health Promotion, Department of Health and Human Services; the Office of Naval Research, Department of the Navy; the Federal Aviation Administration; the Department of Education; the National Dairy Council; Research Triangle Institute; and Universities Associated for Research and Education in Pathology, Inc.

In recent years, topics identified by sponsors have become increasingly detailed and complex. Whereas studies in previous years required only one or two meetings of a panel, a current study by the Expert Panel on Nutrition Monitoring has required eight meetings and 21 months to complete, (Fig. 2). A major reason for the increased time and effort in this case has been the quantity of data reviewed and evaluated.
Current Policies and Procedures

Study techniques

Approaches to the conduct of an LSRO study are flexible and depend on the scope of the study, the time constraints for response, and the particular needs of the sponsor. For issues of limited scope, LSRO staff contact knowledgeable scientists directly. When rapid responses are requested, direct contacts are supplemented by meetings with individual scientists. Depending on sponsor requirements, LSRO can organize workshops, conferences, or ad hoc group meetings.

A typical LSRO study involves the organization of a panel of expert scientists. Key scientists are invited to participate in preliminary conferences with the LSRO staff. These meetings identify specific topics that may be explored by the ad hoc scientific review group. These activities are critical to the development of a balance among divergent views and expertise on the scientific review group.

A working paper may be prepared by LSRO staff and key scientists. The working paper identifies the specific aims of the study, the topics to be reviewed, a critical summary of the scientific issues with journal references as appropriate, and a proposed plan of study. This background material forms the basis of the agenda for the ad hoc scientific review group meetings.

Panel activities typically involve one or more 2-day conferences, structured to permit active participation by the 7 to 15 invited scientific participants. Formal presentations are not expected; rather, participants are asked to discuss informally interpretations and implications of relevant research. Participants have adequate time to discuss their own and other relevant research, opportunities for research, and future research needs. The panel discussions are the basis of a summary report prepared by the LSRO scientific staff. The report includes the background discussions and suggested areas for future research. In some cases, an extensive annotated bibliography is prepared. Drafts of the reports are sent to the ad hoc panel members for their comments, corrections, and critical evaluation. The final copy of the report is written in a style that offers factual scientific information with adequate, less technical summaries. Concerted effort is made to have reports scientifically accurate and organized in an easily read format.

The Advisory Committee

In 1968 the LSRO activities included several projects for Department of Defense agencies in addition to the Army Research Office. That these studies were being conducted came to the attention of the Federation Board, who, in 1971, convened a special committee to review and evaluate the role and scope of LSRO within the Federation. This group, known as the Kinney Committee, recommended that the LSRO be retained as a key department of the Federation. The Committee also recommended that an LSRO Advisory Committee be established as a Standing Committee of the Federation. The Advisory Committee would be responsible for reviewing activities of LSRO and reporting to the Federation Executive Committee of the Federation Board. The Kinney Committee also noted that the responsibility for the organization of studies and reports should continue to rest with the LSRO Director.

Recommendations of the Kinney Committee were accepted by the Federation Board and the LSRO Advisory Committee was organized in 1971. Since February 1, 1972, the Advisory Committee has met one to four times a year to review activities, suggest guidelines on activities as appropriate, recommend acceptance of grants or contracts, and report on activities, which are then reviewed by the Federation Executive Committee.

In 1981 the LSRO Advisory Committee developed three fundamental criteria for the appropriateness of LSRO studies. These criteria were approved by the Federation Board in April 1983 and have guided LSRO since then:

1. The first criterion for the willingness of the Federation to conduct an LSRO study is that the subject or area to be reviewed (or evaluated) have scientific merit with respect to basic research, have potential value in the context of dissemination of scientific knowledge, or involve the timely application of basic research to a topical area in biology or medicine. Furthermore, the subject for review must be associated with the disciplinary expertise of the membership of the scientific societies that constitute, or are affiliated with, the Federation.

2. The second criterion demands that the topics for LSRO studies be timely and related to public health
and welfare. The final product of an LSRO study is a publicized, readily available report that is widely disseminated to the scientific community and the general public. When appropriate, reports or synopses of reports are published in peer-reviewed scientific journals. Copies of reports or reprints are available gratis or at cost to all requestors, with first priority to members of the FASEB Constituent Societies.

3. The third criterion specifies that the LSRO may respond to requests from both public and private organizations whose inquiries meet the first two criteria. Public organizations include federal governmental agencies, departments, institutes, offices, or administrators; analogous state agencies; other scientific societies; and nonprofit foundations supporting basic research in biology and medicine. Private organizations include other nonprofit foundations supporting basic research in biology and medicine; other nonprofit organizations, such as industrial, trade, or consumer associations; or nongovernmental organizations, such as industrial firms or commercial associations.

Although the scope of the LSRO activities has expanded within this framework developed by the Advisory Committee, the primary function of the LSRO has remained consistent with its original goals.

Advantages

FASEB, through its LSRO, provides sponsors with a mechanism of scientific review and evaluation with several distinct advantages. First, LSRO studies are guided by the criteria developed by the LSRO Advisory Committee. Potential sponsors who seek guidance or evaluation on topics or issues outside basic research in the life sciences, its application, or its dissemination and issues related to public policy when the science base is inadequate are referred to other sources.

Diversity of scientific opinion is sought, and the resultant deliberations of the expert panel include alternative approaches as well as suggestions for future research. Unless requested, no consensus or priorities for programmatic emphasis are identified. Thus, research administrators have the freedom of choice and the flexibility of action to implement any of the suggestions made by an LSRO expert panel. These administrators must weigh not only the scientific opportunities identified by the LSRO report, but also the financial, political, and other factors that impinge on the creation or conduct of major research programs.

The use of the ad hoc approach offers additional advantages both to the sponsoring agency and to FASEB. To identify and avoid problems that may result from real or possible conflicts of interest, LSRO study techniques are based on ad hoc, self-terminating approaches, minimizing bias, avoiding quasi-permanent committees, and avoiding vested interests. Since 1976, the LSRO has formalized its procedures concerning conflict of interest regarding specific contracts and cooperative agreements if and when such techniques are determined necessary or desirable. This determination is made by the LSRO Director with the concurrence of the LSRO Advisory Committee. It may or may not be requested by the sponsoring agency; in either case, the decision to implement a conflict of interest review rests with the LSRO Advisory Committee.

Research administrators recognize and appreciate the way FASEB's LSRO can rapidly assemble ad hoc committees to review a subject and prepare a report. The tempo of biomedical research requires relatively rapid responses by research program administrators and federal agencies; thus, reports on specific research topics must be timely. The LSRO, along with the agencies using its services, benefits from the ready availability of over 30,000 experts who make up the membership of the FASEB Constituent Societies. As a general rule, LSRO ad hoc review groups are convened within 2 to 3 months after a study is started and the final report is delivered to the sponsor within 9 to 12 months. The ability of the LSRO to respond promptly requires that study sponsors be precise in formulating the initial scope of work. This, in turn, leads to early clarification of questions to be addressed by the expert scientists. A secondary benefit of prompt responses is containment of study costs.

Because LSRO studies take less time and are usually focused on discrete topics, the requirements for funding are less than those of studies with larger scopes. In an atmosphere of limited resources to support an ever-expanding universe of life sciences research, LSRO studies provide a cost-effective approach to evaluating biomedical research programs, topics, and needs.

Funding

Financial support for LSRO studies is obtained by grants, contracts, and cooperative agreements between sponsoring agencies and FASEB. Since its modest beginnings in 1962, the LSRO has conducted between $0.7 and 1.3 million business annually, in recent years (Fig. 3).

Grants, contracts, and cooperative agreements negotiated on behalf of LSRO are administered and managed by the FASEB Comptroller. Funds obtained for LSRO studies cover all direct expenses of LSRO including consultants' travel and fees, meeting costs, supplies, equipment, and staff salaries. FASEB collects a modest overhead to cover costs of space used, administrative and maintenance services, and bookkeeping. FASEB also collects a fixed fee, which provides funds for furniture, major equipment purchases, and other expenses not covered by contracts as direct or indirect expenses. For example, in 1988, total income of LSRO was $778,953. Direct costs (consultant expenses and fees, meeting expenses, staff salaries) were $574,682. Indirect costs (income to the Federation) were $162,339 and the fixed fee was $41,932.

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3A list of LSRO reports is available on request.
as a FASEB activity. For the past 27 years the LSRO's rapport with the scientific body has been remarkable, and many outstanding scientists have given generously of their time and talents by participating in these studies. LSRO conferences have brought approximately 2000 scientists, 75 percent of whom are members of one of the Constituent Societies, to the Beaumont campus, an activity that has frequently elicited expressions of approval of LSRO's study techniques.

It has been the policy of the LSRO to publish reports in the scientific literature and to give wide publicity to these studies. The public dissemination of the reports is acknowledged in the contractual agreements with the sponsors, and no classified or proprietary studies have been undertaken. Consistent with the policies of the LSRO Advisory Committee, staff scientists are acknowledged as editors of LSRO reports. Each report contains a foreword that recognizes the assistance of the ad hoc review group participants and other investigators who have contributed to the study and preparation of the report. All participating scientists are listed in each report.

Figure 3. LSRO income and expenses of LSRO: 1962-1989. Direct costs include expenses associated with operation of the office. Indirect costs represent FASEB charges against LSRO income for services. Total income of LSRO covers direct and indirect expenses.

Benefits to FASEB

One immediate benefit of LSRO activities is the income to FASEB. In addition to supporting LSRO's direct costs, the indirect charges of FASEB (as overhead on contracts) are a source of income to the Federation. For example, LSRO activities generated $204,271 income to FASEB in 1988. This income contributes to funding the operating costs of FASEB and helps reduce the assessment on the Constituent Societies.

In addition, LSRO activities have brought substantial intangible benefits to FASEB. Along with the Office of Public Affairs, the LSRO has helped develop an appreciation of the scientific resources of FASEB and its Constituent Societies in the biomedical community as well as throughout the legislative and executive branches of the federal government.

LSRO studies and the ad hoc approach have established a mechanism for exchanging current scientific information among the members of the biomedical community. Ideas developed by ad hoc scientific panels have led to development of new research concepts and programs. LSRO studies have been used in justifying increased support for research on motion sickness, immunological aspects of weightlessness, noninvasive techniques for measurement of cerebral blood flow, the role of dietary fiber in health and disease, and methods for estimating exposures to substances in foods. Regulatory agencies such as the Food and Drug Administration, the Environmental Protection Agency, and the Federal Aviation Administration have benefited from guidance in applying research results and in identifying future research directions and needs.

The numerous laudatory comments received from sponsors and ad hoc reviewers suggest that the LSRO studies reflect favorably on FASEB. The ability of the office to involve able scientists in the biological and medical disciplines to take part in these review sessions is a measure of the scientist's recognition of the LSRO

Future Activities

Events of the past several decades reveal that resources to support the ever-increasing scope of research in the life sciences are limited. Research administrators, both in federal agencies and outside the government, are faced with the need to reach decisions about or set priorities for the increased or decreased support of various programs. These are not easy choices nor should they be decisions reached in the absence of knowledge and objective assessment.

Within the past several years, an increasing number of requests for LSRO studies have been received from various federal agencies and other organizations. More and more, the LSRO approaches to review and evaluation of scientific issues are being recognized as useful and appropriate to vexing problems in the environmental and life sciences. Some requests are consistent with Advisory Committee guidelines; others are not. In some cases, research programs administrators actively solicit extramural guidance and evaluation. In other cases, requests for LSRO studies are attempts to obtain the imprimatur of FASEB on administrative decisions made without benefit to scientific input. The LSRO Advisory Committee has the responsibility to recommend to the Board what studies are undertaken. Balancing the requirements for continued high scientific quality and integrity of studies with the obligation to maintain a steady or increasing level of indirect cost reimbursement to FASEB is an enduring facet of LSRO Advisory Committee discussions and LSRO activities.

The continued success of LSRO can be ensured only by maintained the high quality of the studies it conducts. The organization of ad hoc review group meetings has required imagination and diplomacy and a considerable degree of finesse in conducting the sessions. Maintaining high goals requires an unusually
competent scientific and professional staff. As suggested by the changes in annual total income in Figure 3, the size of the LSRO staff is directly related to the number of requests for LSRO studies. The LSRO's core cadre of highly qualified scientific and professional people has allowed the size of its staff to expand and contract as work demands fluctuate. Using Constituent Society members on sabbatical as well as postdoctoral and retired scientists as LSRO staff scientists adds an important dimension to this flexibility.

The Federation must continue to assess its future role in the analysis of scientific problems for federal agencies and other funding agencies as programmatic reviews and new initiatives develop in the biological sciences. Prudence dictates that cautious growth with due regard to scientific objectivity should be maintained. In any event, the LSRO Advisory Committee continues to assess the role and scope of LSRO's activities in order to develop the most appropriate actions that reflect the thinking of the Executive Committee and FASEB Board, the Member Society Councils, and the membership of the Constituent Societies.

In conclusion, the LSRO is FASEB's arm in marshalling resources of the scientific community to address specific questions in biology and medicine. In the final analysis, solutions to these increasingly complex issues require that scientists knowledgeable in these disciplines be available in a forum where research results can be applied openly, objectively, and without bias to issues of national and international public health and welfare. The LSRO brings scientific expertise to bear on these issues. FASEB and other responsible components of the scientific community should continue to provide the expert advice and counsel necessary to ensure that self-serving sources of information are not used to the detriment of biomedical research, science in general, and the public that willingly supports biological research.

Next month: The Office of Public Affairs by Gar Kaganowich, Director.