

# Peer Consultation of NIEHS' Contribution to IARC Monograph Programme

By

Toxicology Excellence for  
Risk Assessment (*TERA*)

For

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## **Executive Summary**

Since 1992, National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP) have made an annual contribution of approximately \$90,000 to the IARC Monograph Programme. The IARC Monograph Programme has primarily used funds from the NIEHS to partially support one monograph meeting and one scientific meeting each year, with the scientific meeting representing the largest use of these funds. The NIEHS contribution covers the direct expenses of the meetings, honorariums for the panel members and printing the monographs. The NIEHS contribution does not support the salary or internal structure of the IARC Secretariat. The NIEHS asked TERA to conduct a peer consultation to help NIEHS/NTP management understand the scientific value the agency receives for its contribution.

The qualitative peer consultation of the NIEHS contribution to IARC took place on May 6 and 7 at the NIEHS facility in Research Triangle Park, North Carolina. The goal of the consultation was to help the NIEHS/NTP management understand the scientific value that the agency is receiving for its contribution to IARC and to make recommendations to NIEHS on the actions that organization can make to improve its support for IARC. An expert panel was convened to interview people knowledgeable about IARC and NTP and to make recommendations to NIEHS management. Approximately 20 interviews were scheduled during the two-day period. The interviews were intended to reveal a qualitative understanding of the scientific goals and needs of the NIEHS/NTP regarding the contribution to IARC. Interviewees were selected primarily from staff in management and scientific positions within NIEHS/NTP. Representatives from agencies and risk assessment groups involved with cancer hazard identification were also interviewed.

Issues discussed during the peer consultation involved the scientific quality and credibility of IARC monographs, a comparison of the monographs with similar reports, the accessibility of the monographs and the contribution of the monographs to agency mission. The consistent opinion of those interviewed was that the IARC monographs are based on the best possible science, are high quality, and make a significant contribution to the ability of NIEHS to carry out its mission. All interviewees felt that the NIEHS contribution to IARC should continue and many suggested that the dollar amount be increased. The panel agreed and recommended that if NIEHS does increase the funding for IARC, the agency should specify that the increased funding should be used to sponsor additional scientific issue meetings rather than agent-specific monographs. In any case, the independence of IARC is of primary importance.

Many people interviewed have heard criticisms that undue influence by special interest groups may have compromised the credibility of the judgments made in some of the monographs. This potential for undue influence has resulted from processes that IARC has used to select panel (conflict of interest issues) and conduct meetings (role of observers). However, interviewees also observed that IARC is aware of such criticism, and is actively taking steps to minimize these criticisms.

The panel recommended that the IARC funding be moved out of the office of the Director to a more traditional funding mechanism within NTP. The panel felt that a more traditional funding mechanism would provide more stability for IARC by building in cost of living increases in

funding, accommodating differences in the monetary exchange rate, and providing flexibility to accommodate special projects through easy modification. In addition, the use of a traditional vehicle would allow NIEHS to identify a person responsible for improving coordination between NIEHS and IARC, a role that is greatly needed.

While the panel recognized that the funding that NIEHS provides should be directed to IARC without any strings attached, it recommended that NIEHS/NTP should monitor how IARC uses the funding it receives and that NIEHS should have a role in IARC's priority setting. In order to implement this, the panel recognized that more direct coordination between IARC and NIEHS/NTP may be needed. The panel recommended that NIEHS appoint an IARC liaison who would serve as a point of contact within NTP. The liaison would be responsible for using a regular process of gathering input for IARC from NIEHS/NTP staff.

## **Introduction**

Since 1992, National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP) have made an annual contribution of approximately \$90,000 to the International Agency for Research on Cancer (IARC) Monograph Programme. The purpose of this peer consultation was to use an interview format to develop a tool that will help NIEHS/NTP management understand the scientific value the agency receives for its contribution. In addition, NIEHS/NTP management may use the peer consultation report to assess the project planning and management related to this contribution. The peer consultation report does not draw conclusions about IARC's process, procedures, or specific scientific conclusions in the monographs, nor does it make recommendations to IARC in any of these areas. Rather, the report evaluates the contribution that the Monograph Programme makes to NIEHS, other US agencies, and the US risk assessment community. The report makes recommendations to NIEHS on actions that organization can make to improve its collaboration with IARC through planning, communication, and mutual goal setting; it does not make recommendations to IARC.

## **Background Material on NTP and IARC programs**

### **National Toxicology Program**

The National Toxicology Program (NTP) is an interagency program headquartered within the U.S. Department of Health and Human Services at the National Institutes of Health's NIEHS. NTP was established in 1978 to coordinate toxicological testing programs within the Department, strengthen the science base in toxicology; develop and validate improved testing methods; and provide information about potentially toxic chemicals to health regulatory and research agencies, the scientific and medical communities, and the public.

NTP's mission is to evaluate agents of public health concern by developing and applying tools of modern toxicology and molecular biology. The NTP consists of relevant toxicology activities from several several different United States health and regulatory agencies including NIEHS, the Centers for Disease Control and Prevention's National Institute for Occupational Safety and Health (NIOSH), and the Food and Drug Administration's National Center for Toxicological Research (NCTR). Although, the NIH's National Cancer Institute was a charter agency, the NCI Carcinogenesis Bioassay Program was transferred to the NIEHS in 1981. However, the NCI remains active in NTP through membership on the NTP Executive Committee.

The NTP Program is administered by the NTP Director, who is also the Director of the NIEHS. Program oversight is provided by the NTP Executive Committee, composed of the heads of Federal health research and regulatory agencies. Scientific oversight is provided by the NTP Board of Scientific Counselors and its Technical Reports Review Subcommittee. The primary activities of the NTP are the chemical testing program and the annual Report on Carcinogens.

The Report on Carcinogens contains a list of substances that may pose a potential hazard to human health. The Reports are informational scientific and public health documents. They serve as meaningful compilations of 1) the cancer data available for the listed substances in humans and/or animals, 2) the potential for exposure to these substances, and 3) the regulations required

by Federal agencies to limit exposures to these substances or exposure circumstances. The Reports do not present risk assessments of cancer potential. The evaluation of substances listed in the Report is performed by scientists from the NTP, other Federal health research and regulatory agencies, and non government institutions. The listings in the Report identifies a substance or exposure circumstance as a known or reasonably anticipated human carcinogen.

### **International Agency for Research on Cancer – Monograph Programme**

IARC, a part of the World Health Organization, is a research organization that combines epidemiology and laboratory research programs under one roof for investigation of human cancer causation for purposes of informing cancer prevention strategies. IARC's mission is to coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer control. The Agency is involved in both epidemiological and laboratory research and disseminates scientific information through publications, meetings, courses, and fellowships. The IARC Monograph Programme is a document development and risk assessment unit within IARC. The Monograph Programme sponsors three types of meetings: monograph meetings, science meetings, and advisory meetings.

The program conducts three meetings each year to produce the monographs that present cancer assessments for a variety of agents and exposures that are known or suspected of causing cancer in humans. The monographs are written by Working Groups that are composed of international experts. The monographs support health ministries worldwide.

The IARC secretariat selects the members of each Working Group as well as the Working Group and subcommittee Chairs. The Working Group uses a consensus approach to make all decisions regarding the content and conclusions of the monographs. The panel considers mechanistic data to both upgrade and downgrade the classification of chemicals. All Working Group members write the part of the monograph draft that is their area of expertise. IARC secretariat usually does not do any initial writing; although members may help to revise or rewrite drafts if requested by the meeting chair or subgroup chairs. In addition, IARC secretariat carefully checks the documents for accuracy after the Working Group meetings. The IARC secretariat does provide the authors with instructions and writing guidelines. The secretariat members never participate as members of the panel. Their function at the meeting is to answer questions, participate in discussions and make sure that the panel addresses all issues. They do not vote at or chair the meetings.

In addition to the monograph meetings, the Monograph Programme conducts on average one science meeting each year to address general scientific and mechanistic issues related to cancer hazard assessment. For example, recent science meetings have addressed such issues such as how to evaluate peroxisome proliferation, the use of epidemiology data in carcinogen assessment, and how to assess rodent bladder, thyroid, and kidney tumors.

Finally, an Advisory Group of experts from many countries meet every five years to recommend priorities for agents and exposures nominated for future Monographs evaluations. The Advisory

Group is also asked to consider a number of questions concerning working procedures, public health issues and future developments of the IARC Monographs Programme.

### **Financial Background**

Since 1992, NIEHS/NTP has made an annual contribution of approximately \$90,000 to the IARC Monograph Programme. The NTP contribution to IARC has been made in the form of a “donation.” As such, there has been no government contract, Statement of Work or other formal mechanism specifying how the money is to be used. However, the transmittal letter that accompanies the contribution has provided some examples of appropriate use of the funds, including for meetings and travel.

The IARC Monograph Programme has primarily used funds from the NIEHS/NTP to partially support one monograph meeting and one science meeting each year, with the science meeting representing the largest use of these funds. The NIEHS/NTP contribution covers the direct expenses of the meetings, honoraria for the panel members, and printing of the monographs. The NIEHS/NTP contribution does not support the salary or internal structure of the IARC Secretariat. IARC makes sporadic, informal reports to NIEHS/NTP describing how its contribution was used; these reports are not quantitative. Detailed administrative IARC reports on the expenditure of NIEHS/NTP funds are also provided, on request, usually to accompany narrative reports on the projects for which these funds have been used. These reports are provided by the IARC Director for Administration and Finance, and are independent of the Monographs Program staff.

However, NIEHS/NTP is not the only, or even the largest, contributor to the IARC Monograph Programme. Other agencies in the U.S. and Europe provide significant support. The National Cancer Institute is largest single external contributor to the Monograph Programme with a yearly cooperative agreement of approximately \$700,000. The NCI cooperative agreement currently covers the salaries for six of the 10 Monograph Programme staff. In addition, the NCI cooperative agreement pays for 2 of the 3 yearly monograph meetings but none of scientific workshops or the advisory meetings. Therefore, the contribution from NIEHS is critical to the continuation of the scientific workshop series on key issues involving mechanisms of carcinogenesis.

The Monograph Programme also receives an annual grant of approximately 50,000 euros from the European Commission and a small annual contribution from the U.S. Environmental Protection Agency. Finally, the Monograph Programme receives funding from the IARC regular budget that support some of the staff (including the unit chief, unit secretary, a scientist serving as a monograph officer, and a support staff person), all disposable supplies and equipment, all computer-related expenses, and all travel except the relatively few travel expenses that are allowable from NCI or NIEHS funds.

### **Peer Consultation Methodology**

The qualitative peer consultation of the NIEHS contribution to IARC took place on May 6 and 7 at the NIEHS facility in Research Triangle Park, North Carolina. The goal of the consultation

was to help the NIEHS/NTP management understand the scientific value that the agency is receiving for its contribution to IARC and to make recommendations to NIEHS/NTP on actions that the organization can take to improve its collaboration with IARC.

An expert panel was convened to interview people knowledgeable about IARC Monographs and the NTP and to make recommendations to NIEHS/NTP management regarding the value that the organization is receiving for its contribution to IARC. Each panel member was selected for his/her experience in one or more of the following areas: cancer hazard characterization; cancer mechanisms of action; participation on or knowledge of IARC monograph working groups; NIEHS/NTP goals, products, or administration; and cancer science policy. Biographical information and statements regarding potential bias for the panel members is presented in Appendix A.

To guide the panel in its discussions, *TERA* developed an interview protocol (Appendix B) that formed the basis of the questions asked during the interviews. To develop the interview protocol, *TERA* met with the sponsors and helped them identify their goals for the consultation. In addition, *TERA* consulted guidance on how to conduct program reviews provided by the Fogarty International Center, an office in the National Institute of Health that specializes in evaluating health-related programs. The interview protocol was reviewed by management at NIEHS/NTP to ensure that it would provide them with the types of information that would be useful for making decisions regarding the contribution to IARC. The goal of the interview protocol was to focus 90% of the effort on the scientific usefulness of the IARC monograph program to NIEHS/NTP, other federal agencies, and the risk assessment community and 10% of the effort on issues related to the planning and management of the contribution. Only those interviewees knowledgeable about NIEHS planning and management were asked those questions.

*TERA* staff and Dr. Christopher Schonwalder, Senior Environmental Health Advisor to the Director, NIEHS met with most of the panel members the evening before the peer consultation. Panel members introduced themselves and discussed potential panel member conflict of interest or bias concerns. Dr. Schonwalder provided background on the NIEHS and IARC. *TERA* staff discussed proper interview techniques and the protocol or questions that would be used for the interviews. This discussion focused on the need for panel members to listen objectively to what the interviewees say and ask appropriate follow up questions to insure understanding. However, the panel was also encouraged to form their own opinions about the interview questions and to include their opinions in the peer consultation report. Panel members were reminded that the goal of the peer consultation was for the panel to objectively seek information and opinions from those being interviewed in order for the panel to make recommendations regarding the NIEHS/NTP contribution to IARC. *TERA* stressed that the panel was not making recommendations to IARC on how to improve the Monograph Programme.

The consultation session began on the morning of May 6 with presentations by Dr. Christopher Schonwalder and Dr. V. James Cogliano, Chief, Monograph Unit, IARC to the panel members. Dr. Schonwalder provided background information on NIEHS and its goals for the consultation. Dr. Cogliano described IARC's process and goals, particularly focusing on how IARC uses the contribution from NIEHS.



Approximately 20 individual interviews were then conducted by telephone over the two-day period. The panel formed 2 separate teams and interviewed approximately 10 individuals each. Additional interviews were conducted at a later date with some people who were not available during the two-day meeting. A list of the people interviewed is attached as Appendix C. *TERA* did not select interviewees using random sampling techniques, nor was the sample selected to allow for generation of statistically valid results. The interviews were intended to reveal a qualitative understanding of the scientific goals and needs of the NIEHS/NTP regarding the contribution to IARC. Therefore, interviewees were selected primarily from staff in management and scientific positions within NIEHS/NTP in order to answer these questions. *TERA*'s goal in selecting interviewees from NIEHS/NTP was to primarily include scientists active in developing the Report on Carcinogens or selecting chemicals for testing in the bioassay program as well as to include program managers. Because NIEHS/NTP serves other federal agencies and the risk assessment community, individuals from other agencies and risk assessment groups that are involved with cancer hazard identification were also interviewed. The list of interviewees was developed by *TERA* with input from NIEHS.

## **Interview Results: Scientific Contribution and Quality**

Below is a summary of the comments and opinions expressed during the interviews. The questions were open-ended and not all those interviewed answered every question. More than one person may have made specific comments. This summary notes if more than one interviewee expressed an opinion. However, the intent of this summary is to provide readers with a qualitative understanding of the opinions expressed, and not to present a quantitative or statistical assessment of the responses.

### **Quality of Monographs**

Overall, the interviewees and the panel noted that the data collection and reporting in the IARC monographs, including the exposure, mechanistic, epidemiology, and animal studies, is of high quality and credible. Generally, interviewees and panel members felt that IARC monographs are produced using the best possible science and that they incorporated mechanistic data appropriately.

Almost unanimously, participants indicated that IARC used the best possible science in developing the monographs and did a good job of incorporating mechanistic data into the monographs. Several interviewees noted that the science on mechanisms is progressing at an uneven pace and there will likely be disagreement on how the science of mechanisms should be interpreted for reaching conclusions regarding cancer classification. The important aspect of IARC is that there is a process in place to evaluate mechanism data. The working groups do give mechanism data serious analysis and incorporate mechanism data where appropriate.

One scientist mentioned that IARC's self-imposed restriction of using only published data may limit the monographs, because there are known animal carcinogens without published studies that may be missed in the evaluation. However, other interviewees thought that the peer-reviewed publication restriction greatly adds to the Monograph's credibility.

Many of the interviewees distinguished between the scientific data presentation in the documents and the judgments drawn by the working groups. While all interviewees agreed that the scientific presentations were of high quality, many people interviewed have heard criticisms that undue influence by special interest groups may have compromised the credibility of the judgments made in some of the monographs. This potential for undue influence has resulted from processes that IARC has used to select panel members (conflict of interest issues) and conduct meetings (role of observers). For example, several interviewees mentioned that at past meetings, people who they believed to have a conflict of interest had written parts of the document under discussion. Many interviewees mentioned hearing concerns that invited participants and observers (who were not members of Monograph Working Group) were not always clearly identified as such until the Working Group voted on issues. Therefore, these people may have had an undue influence on the working group discussion. However, interviewees also observed that IARC is currently taking steps to address these criticisms. For example, IARC is now conducting a more in-depth review of conflict of interest issues for the working group members and is more clearly distinguishing work group members from observers. Nevertheless, there is value in having a variety of groups involved with the monograph meetings.

### **Comparison of IARC monographs with similar reports**

Many of those interviewed noted that the IARC monographs are unique in that they are an internationally developed document and that they are produced for a non-regulatory purpose. Interviewees noted that the monographs bring an international credibility to the cancer hazard identification community by incorporating points of view and data from many countries. Participants indicated that U.S. regulatory efforts particularly benefit from the monographs because they incorporate data from the European community that the US scientists are not aware of. In addition, many participants appreciated that since IARC is a non-regulatory agency, the monographs can be scientific products with conclusions that are not influenced by cost/benefit considerations.

### **Accessibility of Monographs**

Interviewees noted that the monographs are excellent scientific resources that are incorporated primarily into larger risk assessment efforts in the US, but used directly in less developed countries. However, it was observed that the monographs are only accessible to people with enough expertise to understand them, but are not used by the general public. For example, the monographs are likely to be used by groups such as National Resources Defense Council or Environmental Defense Fund because these groups have the expertise to understand them. However, the monographs are not likely to be used by community groups. One interviewee noted that more members of the general public will be looking for information about cancer hazard with the Safe Drinking Water Act's provision for public notification regarding exposure. The fact that full documents are not available on the Internet makes them less accessible and makes it harder for NIEHS/NTP scientists to use the monographs.

## **Contribution of Monographs to NIEHS/NTP Work**

Interviewees mentioned that IARC monographs make valuable contribution to the work of NIEHS, as well as other agencies that conduct cancer assessments. NIEHS uses the monographs while preparing the Report on Carcinogens (ROC), including nomination of chemicals to the report and development of the background documents. For example, the NIEHS internal nomination committee for the ROC reviews recent IARC monographs when considering which chemicals should be nominated for the Report. The committee gives higher priority to chemicals that have been evaluated by IARC for the first time and a lower priority to chemicals whose classifications have been upgraded or downgraded.

The NTP bioassay program uses monographs to prioritize research needs and design chemical studies. For example, scientists in the NIEHS bioassay program will routinely review the monographs for chemicals that are in Group 3 (not classifiable as to carcinogenicity), to identify chemicals for new studies. They assume that if IARC has evaluated the chemical, then there is probably significant exposure to the chemical, and if the chemical lacks sufficient data to be classified (i.e., Group3), then it is a high priority for a new bioassay.

## **Interview Results: Planning and Management**

One important finding from this peer consultation is that among the NIEHS employees interviewed, most were not aware that the Agency contributed to IARC, let alone aware of the goals, or planning and management processes for that contribution. However, the all interviewees and panel indicated that the contribution is valuable. This opinion was best expressed by one person who said “I want to emphasize that the IARC monographs are extremely important to the toxicology effort, and NIEHS does not want to lose this. It is important to make sure that the program continues.”

Many interviewees and the all of the panel members noted that they thought the size of the contribution from NIEHS should be increased. Some suggested that an increase in funding should be used to provide increased support for IARC’s scientific workshops, rather than the agent-specific monograph meetings. While IARC should be accountable for the use of funds, its independence should be protected, and therefore, the funds should be given without strings attached. Nonetheless, most participants felt that it was appropriate for NTP to play a role in suggesting research priorities for IARC and in participating on IARC’s advisory committee. While some participants felt that there should be better tracking of the contribution to IARC, they did not want to impose an undue burden on IARC for such a small contribution.

Some of those interviewed identified instances where there is coordination between NIEHS and IARC, but they thought that this coordination could be improved. It was suggested that there should be more formal and sustained dialog between the two organizations. On the NIEHS side, one scientist suggested that NIEHS formally designate an IARC liaison that would be responsible for polling NIEHS staff to gather broad input on research needs. This input could then be communicated to IARC through its advisory group. Interviewees also suggested that increasing the interaction between the two agencies’ websites would help improve coordination. For example, NIEHS/NTP scientists in the bioassay program would like to be able to search

IARC's website to more easily identify which chemicals are currently under study somewhere in the world. Another suggestion was to include an assessment of data gaps or list of data needs in the monographs, which would help others, such as the NTP bioassay program, to prioritize agents for new studies.

## **Panel Conclusions and Recommendations to NIEHS**

The panel reached conclusions and formed recommendations based upon the results of the interviews and their own opinions. The panel concluded that it is appropriate for the NIEHS to fund IARC and that NIEHS and the scientific community receives a valuable benefit from this contribution. The panel made recommendations regarding how the NIEHS contribution might be internally managed, and also recommended that better coordination between the two organizations be established, with the NIEHS point of contact made more widely-known within NIEHS. In addition, the panel made several suggestions regarding best uses of the NIEHS contribution and how the benefits from the NIEHS contribution might be more fully realized.

The panel recommended that responsibility for the IARC funding be moved out of the Office of the Director and a more traditional funding mechanism be established within NTP. The panel was concerned that the non-traditional funding mechanism currently used allows for the perception that NIEHS is inappropriately influencing IARC. The panel felt that a more traditional funding mechanism could provide more stability for IARC if there were provisions for inflation increases of funding and accommodation of differences in the monetary exchange rate. It would assist NIEHS by providing flexibility to accommodate requests for special projects through easy modification. The panel did not want to recommend a specific type of vehicle for the funding, but suggested that NIEHS should base its decision on an analysis of what vehicle is the most appropriate for the circumstances. The panel noted that NCI and EPA provide similar types of funding to IARC and WHO, respectively, and recommended that NIEHS discuss potential funding mechanisms with the responsible people at those agencies (David Longfellow at NCI, and Karen Hammerstrom at EPA).

An overwhelming opinion among those interviewed and the panel members is that IARC must maintain its independence in the conduct of its reviews in order to be effective. The funding from NIEHS should be provided to IARC without any strings attached. However, the panel also recommended that NIEHS/NTP should monitor how IARC uses the funding and that NIEHS should have a role in IARC's priority setting. For example, since NIEHS/NTP benefits particularly from IARC's scientific issue meetings, NIEHS should recommend topics and agendas for these meetings to ensure that IARC's science issue meetings are relevant and timely for NTP. The panel encouraged NIEHS to continue to participate in IARC's 5-year advisory meetings, but recommends that there be more coordination within NIEHS prior to the meetings to provide broader-based NIEHS input to IARC in setting priorities for both chemicals to be evaluated and the science issues meetings.

In order to implement the above recommendation, the panel recognized that more direct coordination between IARC and NIEHS/NTP is needed. The panel recommended that NIEHS appoint an IARC liaison that would serve as a point of contact within NTP. It would be most efficient if this point of contact also be the one responsible for overseeing the NIEHS funding.

The liaison could be responsible for using a regular process of gathering input from NIEHS/NTP staff. Better coordination could result in better communication between the two groups that would help reduce duplication of efforts and maximize impact of efforts.

The panel concluded that although the monographs are accessible to agencies and public health officials, they are not readily accessible to the public. The panel recommended that NIEHS could maximize the benefit of its contribution to IARC by suggesting that IARC consider various options to increase public accessibility and understanding of IARC monographs. Suggestions included placing complete copies of monographs on the Internet and adding a plain language summary of the overall evaluation put it in a public health context.

Interviewees and panel members were aware of recent criticisms of the monograph process. The panel thought that certain practices used by IARC to conduct the monograph meetings (e.g., conflict of interest issues and participation by workgroup observers) have affected the credibility of the monograph conclusions for some users. This effect on credibility also affects NIEHS as it uses the monographs in its work. To maximize the benefit of its IARC contribution, NIEHS should encourage IARC to protect its credibility by continuing to increase transparency, openness, and balance of the process. Suggestions mentioned included establishing procedures to record votes and the reasons for disagreement in cases of mixed votes. In addition, NIEHS staff would find it useful and improve the perception of scientific integrity if IARC entertained public comments on monograph drafts to allow knowledgeable public parties to present their analyses and information. . The panel recognized that IARC has improved the process recently through better evaluation of conflict of interest in working group members and in the handling of meeting observers; the panel is encouraged by this trend and hopes these improvements continue.

The panel recommended that it would be valuable to the NIEHS mission if IARC were to implement a method to update older monographs in a timely manner. Several NIEHS/NTP scientists also suggested that if IARC updated older monographs with a summary of new literature that might affect an agent's classification, NIEHS would be able to improve its process for nominating chemicals for bioassays and capitalize on the IARC effort.

Most of the interviewees thought that NIEHS should consider increasing the funding for IARC, given the significance of the work that is done. The panel agreed that increased funding would be beneficial to NIEHS efforts. The panel thought that if NIEHS does increase the funding for IARC, the agency should specify that the increased funding should be used to sponsor additional scientific issue meetings, rather than agent-specific monographs.

## **Appendix A: Panel Bios and Bias Statements**

**Byron E. Butterworth, PhD.** Dr. Butterworth is currently the President of Butterworth Consulting. He is recognized for his experience in genetic toxicology, chemical carcinogenesis, and toxicology. For over 20 years, Dr. Butterworth was with the Chemical Industry Institute of Toxicology, where he headed Genetic Toxicology and Chemical Carcinogenesis programs. In these positions he guided research programs in reproductive toxicology, mutagenesis, cell transformation, cytogenetics, DNA repair, nongenotoxic mechanisms in carcinogenesis, chemically-induced cell proliferation, oncogene expression, use of transgenic animals in cancer research, mechanisms of carcinogenesis, and emerging technologies including gene arrays. In addition, he has collaborated with the National Toxicology Program to conduct chemical carcinogenesis research. Dr. Butterworth has published and presented extensively in the area of assessing mechanisms of chemical carcinogenesis.

**Gail Charnley, PhD.** Dr. Charnley is the Principal of HealthRisk Strategies and is an internationally recognized scientist specializing in environmental health risk assessment and risk management science and policy. She has over 20 years of experience in the biological, chemical, and social policy aspects of environmental and public health protection. She currently serves on a National Academy of Sciences committee convened to improve the regulation of low-level nuclear waste disposal. She has chaired or served on numerous peer review panels convened by the Environmental Protection Agency, the Food and Drug Administration, and Health and Welfare Canada. From 1994-1997 she was executive director of the Presidential/Congressional Commission on Risk Assessment and Risk Management, mandated by Congress to evaluate the roles that risk assessment and risk management play in federal regulatory programs. Dr. Charnley has also served as director of the Toxicology and Risk Assessment Program at the National Academy of Sciences/National Research Council and the Board of Scientific Counselors for the National Toxicology Program. She lectures frequently on science policy issues and has published in the areas of chemical carcinogenesis, risk assessment, and science policy.

**Anthony B. DeAngelo, PhD.** Dr. DeAngelo is a Research Toxicologist in the Cancer Biology Branch, U.S. EPA's Office of Research and Development, National Health and Environmental Effects Research Laboratory. Dr. DeAngelo has 30 years experience in the fields of cancer biology and chemical carcinogenesis. At EPA, he has conducted cancer bioassays, particularly for disinfection by-products, and conducted research into identifying modes of action for chemical carcinogens. Dr. DeAngelo has participated in the IARC workshop evaluating the carcinogenicity of disinfection by-products, and is currently collaborating with the National Toxicology Program on a research project evaluating gene expression in rat peritoneal mesotheliomas. Dr. DeAngelo has published extensively in the areas of chemical carcinogenesis and evaluating mechanisms of action for carcinogens.

**George W. Lucier, PhD.** Dr. Lucier is currently a consultant in toxicology and an Adjunct Senior Scientist for the Environmental Defense Fund. He retired from the National Institute of Environmental Health Sciences (NIEHS) in 2000, where he was Director of the Environmental Toxicology Program and Associate Director of the National Toxicology Program. In that capacity, Dr. Lucier was responsible for coordinating toxicology research and testing across

Federal agencies. Dr. Lucier was head of a research group in molecular epidemiology and risk assessment, where his research focused on the use of basic biology to reduce uncertainty in human risk assessments and to improve the tools used in exposure assessment. His work has made major contributions to risk assessments for dioxins, endocrine disrupters, and methyl mercury. Dr. Lucier has participated extensively in IARC workshops, including chairing the workshops evaluating the carcinogenicity of tamoxifen and dioxins. He chairs the Science Advisory Board for hazardous air pollutants for the State of North Carolina. Dr. Lucier has published extensively in many areas related to chemical carcinogenesis and risk assessment, including hormonal carcinogenesis, receptor-mediated carcinogenicity, and dioxin carcinogenesis. In addition, Dr. Lucier was the editor of the journal *Environmental Health Perspectives* for 28 years.

## **Appendix B: Interview Protocol**

NIEHS provides a significant annual contribution to the IARC monograph program. The goal of this review is to evaluate the value that NIEHS is receiving for its contribution. The interviews will primarily focus on defining the scientific quality and contribution of the IARC monograph program. Less emphasis will be placed on defining planning and management issues for the NIEHS/NTP – IARC partnership. A key to defining the scientific contribution of IARC monographs is understanding the opinion of scientists at NIEHS/NTP, other agencies, and the risk assessment community in general on the following issues:

- how IARC monographs contribute to agency mission and work.
- how IARC monographs contribute to public health protection
- the scientific quality of IARC monographs
- the degree that scientists understand the purpose and goals of IARC monographs and rely on them to complete their own work.

A key to defining planning and management issues for the NIEHS/NTP-IARC partnership is understanding the following issues:

- whether key staff understand the goals of NIEHS funding for IARC
- whether managers have concerns regarding management of the NIEHS funding for IARC
- whether NIEHS/NTP-IARC partnership adequately serves other NTP partners and the risk assessment community.

### **Questions about scientific contribution and quality:**

1. How would you describe the goals and mission of the IARC monograph program?
2. How do you and your organization use IARC monographs?
3. Do other organizations provide essentially the same service as IARC or does IARC play a unique and valuable role in gathering information into a cohesive review and in assessing cancer risk?
4. In your opinion are IARC monographs based on the best possible science? Are there valid criticisms of the monographs?
5. In your opinion how does the risk assessment community perceive the scientific integrity of IARC monographs?
6. To what degree do the IARC monographs provide a critical review of all information and present a realistic view of potential human cancer risk? How well do they incorporate mechanism of action studies in their risk assessments?
7. Do you have a view as to the public use and perception of the IARC monographs?
8. What contribution to meaningful cancer hazard characterization has the IARC monograph program made possible?



## **Questions about planning and management**

9. How would you describe the goals for NIEHS funding of the IARC monograph program?
10. How would you describe the planning process for defining these goals? If there is none, should there be a planning process?
11. Should NIEHS implement a more formal system for tracking and monitoring IARC's achievements and progress relative to the financial contribution from NIEHS?
12. What role, if any, does NTP play in helping the IARC monograph program set its research priorities? What role, if any, does IARC play in helping the NTP set its research priorities? Is this level of interaction appropriate? Why or why not?
13. What recommendations can you make to improve the NIEHS/NTP-IARC partnership?

## **Appendix C: Interviewees**

### **IARC**

Dr. Jim Cogliano, Current Director, IARC Monograph Program

Dr. Jerry Rice, Former Director, IARC Monograph Program

### **NIEHS/NTP**

Dr. Gary Boorman, Veterinary Medical Officer, Environmental Toxicology Program

Dr. John Bucher, Deputy Director, Environmental Toxicology Program

Dr. Bill Jameson, Head, Report on Carcinogens, NTP

Dr. Scott Masten, Head, Chemical Nomination Office, NTP

Dr. Ron Melnick, Environmental Toxicology Program, Office of Director

Dr. Chris Portier, Director, NTP

Dr. Joseph Roycroft, Environmental Toxicology Program, Toxicology Operations Branch

Dr. Ray Tennant, Chief, Laboratory for Environmental Carcinogenesis and Mutagenesis

Dr. Errol Zeiger, currently a consultant. Previously, Head of Chemical Nominations and Head of Environmental Mutagenesis, National Toxicology Program.

### **NCI**

Dr. Aaron Blair, Chief, Occupational Epidemiology Branch.

### **ATSDR**

Dr. Chris DeRosa, Director, Division of Toxicology

Dr. Bruce Fowler, Assistant Director for Science, Division of Toxicology

### **NIOSH**

Dr. Mark Toraason, Supervisory Scientist, Division of Applied Research and Technology

### **Risk Assessment Community**

Dr. Mike Gallo, Professor of Toxicology and Director of NIEHS Center for Excellence, Robert Wood Johnson Medical School.

Dr. Bernie Goldstein, Professor, Environmental and Occupational Health; Dean, Graduate School of Public Health, University of Pittsburgh

Dr. Steve Olin, ILSI

### **EPA**

Dr. Linda Birnbaum, Director, Experimental Toxicology Division, National Health and Environmental Effects Laboratory

Dr. Bill Farland, Acting Deputy Assistant Administrator for Science, Office of Research and Development

Dr. Gary Fourman, Toxicologist, National Center for Environmental Assessment

Dr. Joyce Donohue, Office of Water