MEMORANDUM FOR: Carl J. Paperiello, Director
Division of Industrial and Medical Nuclear Safety, NMSS

FROM: Barry A. Siegel, M.D., Chairman
Advisory Committee on the Medical Uses of Isotopes

SUBJECT: SUMMARY MINUTES FOR THE MEETING OF THE ADVISORY COMMITTEE ON MEDICAL USES OF ISOTOPES, NOVEMBER 17 AND 18, 1994

The Advisory Committee on Medical Uses of Isotopes (ACMUI) held its semiannual meeting on November 17 and 18, 1994.

ACMUI members present at the meeting were:

Judith Brown
Wil B. Nelp, M.D.
Barry A. Siegel, M.D., Chairman
Dennis P. Swanson, M.S., B.C.N.P.
David Woodbury. M.D., FDA
Daniel F. Flynn, M.D.
Robert M. Quillin, M.S.P.H., M.S.
Judith Anne Stitt, M.D.
Louis K. Wagner, Ph.D.

Also present: John E. Glenn, Ph.D., Nuclear Regulatory Commission (NRC), (Designated Federal Official for the panel); Carl J. Paperiello, Ph.D., Director, Division of Industrial and Medical Nuclear Safety, NRC; Larry W. Camper, Section Leader, Medical and Academic Section, NRC; John Graham (ACMUI member-designate, whose appointment to the ACMUI is not yet finalized, and who attended by invitation).

John E. Glenn, Ph.D. officially opened the meeting at 8:05 a.m., November 17, 1994. Dr. Glenn stated that he had reviewed the financial statements and employment interests of the ACMUI members and had determined that no member appeared to have a conflict of interest with respect to the agenda items, and that no member had submitted a petition for rulemaking involving any of the rulemaking items on the agenda. Dr. Glenn stated that if a member became aware of a conflict of interest during the meeting, he or she would be obligated to so inform him or the Chair of the Committee. Dr. Glenn then introduced the members of the Committee and the member-designate of the Committee.

Dr. Glenn indicated that he had not received notification from any members of the public requesting the opportunity to make a presentation during the public comment period of the meeting. Dr. Siegel indicated that the Chair reserved the right to recognize members of the public during the course of the meeting depending on the available time and the nature of the discussion.

The ACMUI discussed the issues and made the recommendations indicated below.

I. "Preparation, Transfer, and Use of Byproduct Material for Medical Use"

Dr. Glenn led a discussion of the rule regarding the "Preparation, Transfer, and Use of Byproduct Material for Medical Use" (also referred to as the "Radiopharmacy Rule"). This final rule was submitted to the Commission and affirmed on November 15, 1994, and will be effective January 1, 1995.

The Radiopharmacy Rule resolves many of the problems that have arisen, largely by omission, with previous regulations (predominantly in 10 CFR 35) and licensing procedures. The rule allows medical licensees flexibility to use, modify, or prepare radioactive drugs in accordance with the latitude afforded to practitioners by State boards of medicine and pharmacy and by the U.S. Food and Drug Administration (FDA). It clarifies the difference between a specific license of broad scope and a specific license of limited scope. The rule recognizes preparation of radioactive drugs by authorized-user physicians (AUPs) and authorized nuclear pharmacists (ANPs), sets criteria for training and experience of ANPs, provides for uses of byproduct material in research involving human subjects, permits licensee authorization of qualified physicians as AUPs and of qualified pharmacists as ANPs without a license amendment, and states exemptions regarding Type A specific licenses of broad scope.

Currently, 10 CFR 35.49 restricts radioactive drug preparation to materials or reagent kits manufactured, labeled, packaged and distributed in accordance with a license issued pursuant to Sections 32.72, 32.73, or 32.74 (or equivalent Agreement State regulations). The current regulations do not provide for preparation by the institution. The new Section 35.49 is silent on the preparation or the suppliers of drugs. Radioactive drugs now can be obtained from a manufacturer licensed pursuant to 10 CFR 32.72, or they can be prepared by an ANP or by an AUP (meeting certain training and experience requirements), or by individuals working under the supervision of either. The required training and experience for AUPs must be equivalent to that required for Section 35.200 uses.

Current regulations restrict use of radioactive drugs to those drugs covered by an Investigational New Drug (IND) exemption or by an approved New Drug Application (NDA), and further restrict licensees to adhere to the manufacturer's instructions for preparation and to labeled indications for therapeutic radiopharmaceuticals. (Certain exceptions to these restriction are permitted by the "Interim Final Rule"—which will expire on 31 December 1994—upon specific instruction by an AUP.) With the new rule, if use of the drug is permissible under FDA regulations, it can be used.

Dr. Woodbury and Florence Kaltovich (from the FDA Center for Biologics Evaluation and Research) questioned how NRC regulations will treat radiolabeled biologics distributed under approved Product License Applications (PLAs); these products are controlled by different FDA regulations than the IND or NDA regulations applicable to drugs. Dr. Glenn stated that, since the new NRC regulations are silent about specific classes of FDA approval, NRC will not restrict the use if allowed under FDA regulations.

Part 32, which is the regulation under which nuclear pharmacies are licensed, will have conforming changes. Currently, under Section 32.72, a radiopharmacy can only receive byproduct materials that are covered by an NDA, a PLA, or an

IND (or materials demonstrated to be not subject to FDA regulations). Section 32.73 restricts use by radiopharmacies of generators and reagent kits to FDA approved materials, unless the licensee can demonstrate that the product is not subject to FDA regulations. Under the new rule, generators will be included under radioactive drugs in Section 32.72, and Section 32.73 will be deleted. The new rule will grant distribution licenses for drugs and generators prepared by FDA- or State-licensed (or registered) manufacturers or pharmacies, or nuclear pharmacies within a Federal medical institution.

Labeling: A letter received from Dr. Carol Marcus and distributed to ACMUI members raised concerns with the proposed labeling requirements in the regulation. Dr. Glenn indicated that the new labeling requirements do not differ greatly from the current requirements. Currently, the following must be on the label: (1) radionuclide; (2) quantity of activity; (3) date of assay; and (4) Part 35 listed use. The required information on the container label may be combined with that required by FDA regulations.

The new rule also requires that the time of assay be included in the labeling. However, the rule, as approved by the Commission, has limited this to radionuclides with half-lives <100 days.

Dr. Nelp questioned why NRC would require labeling that is already required by current guidelines and FDA. Dr. Glenn indicated that this labeling is required so that medical use licensees will to be able to comply with NRC's radiation safety and misadministration requirements. This Part 32 requirement applies to a supplier shipping materials to a medical facility, not to an in-house radiopharmacy dispensing material directly for use in a patient.

Mr. Swanson questioned the need for inclusion of the Part 35 listed use on the label, since centralized nuclear pharmacies are restricted to distribute drugs to licensees that are appropriately licensed for the drugs. In addition, Part 35 licensees are restricted to receiving drugs from suppliers that are appropriately licensed for distribution. He expressed concern that, as more information is required on the label, it becomes more difficult to find the critical information, and this could have a bearing on misadministrations and safety.

Mr. Swanson raised a concern about requiring the clinical procedure, or the patient's or human subject's name, on the syringe label. For example, a syringe is labeled with a patient's name and is sent to a hospital for eventual administration. For some reason that patient's study is canceled. Often, a hospital will schedule another patient for that study, and use that dose. He suggested that this would be construed by NRC as a misadministration, since the syringe was originally labeled for another patient. Dr. Glenn stated that the "or" in the labeling requirement (for the clinical procedure or the patient's name) alleviates this problem. Licensees could list only the clinical procedure on the label.

Dr. Nelp stated that it was not routine practice for diagnostic or research uses to put the patient's name on the syringe. Dr. Siegel stated this would be done for other drugs — a prescription is filled for a specific patient use. Commercial nuclear pharmacies distribute radioactive drugs with implicit patients in mind without stating the identity of the patient. One can indicate Tc-99m MDP for a bone scan without listing the patient's name on the syringe. Further, the authorized user has the right to alter that prescription.

Mr. Swanson stated that the main difference between traditional pharmacy dispensing and nuclear pharmacy dispensing is that the traditional pharmacy dispenses the drug directly to the patient for the patient's own use. A nuclear pharmacy dispenses the drug to the nuclear medicine clinic for use in one or more patients under the direction of an AUP.

Mr. Swanson indicated that Part 35 requires licensees to label a syringe with the name of the patient, with the clinical procedure, or with the name of the radiopharmaceutical. The regulatory guide for Part 32 states that the pharmacy should label the syringe with the name of the patient or the clinical procedure. It does not specify that they also could label it with the name of the radiopharmaceutical. He believes that this needs to be modified to be consistent with Part 35.

Mr. Swanson also pointed out that the regulatory guide for Part 32 states that the labels for containers of radioactive drugs tagged with Tc-99m should specify the total activity or concentration of Mo-99. If the expiration time for the radiopharmaceutical is put on the label, as is currently done, why is this additional information needed? Dr. Glenn replied that Part 35 requires that medical-use licensees know the Mo-99 content of the dose that is delivered. The concentration is not specifically required to be on the label. This is in the guide as a "should," and is not an absolute requirement. This might be an issue raised by a license reviewer, i.e., how the pharmacy's customers will know the Mo-99 content of a drug. If this is not incorporated into the license it would not be an inspection item. Mr. Swanson stated his concern that NRC is getting involved in product labeling when in fact these issues are adequately regulated by State boards of pharmacy and by nuclear pharmacy practice standards. One of NRC's criteria for recognizing and authorizing nuclear pharmacies is board certification of the pharmacists. Labeling requirements are included in the examination for board certification. Dr. Glenn stressed that the labeling is to meet Part 20 requirements, and does not have the same objectives as FDA-required labeling. NRC requires a label on a container that permits the person using that container to use it safely.

Mr. Swanson requested the meaning of the requirement for including the Part 35 listed use on the label. Dr. Glenn clarified that this is a statement that the drug is intended for use under 35.100, 35.200, or 35.300. The actual

regulation states that the label or the leaflet/brochure that accompanies the radioactive drug must contain a statement that the NRC has approved distribution of the byproduct material to persons licensed to use byproduct material pursuant to 35.100, 35.200, or 35.300, as appropriate..." The Commission's labeling requirements are independent of requirements of the FDA. Mr. Swanson stated that distributors can only distribute to certain licensees, i.e., only to those authorized to receive that product, and that product brochures are not routinely distributed with unit doses of radiopharmaceuticals. This is an additional expense that must be borne by the centralized nuclear pharmacy and eventually the public. Dr. Glenn stated that this information is required because that is the licensing basis. This identifies the class of licensees that can receive the material.

Dr. Siegel stated it appears that if the drug is distributed without a "package insert," this would not be in compliance, and that this is a new requirement. Dr. Glenn stated that this has been in Part 32 all along, but, in the past, it has applied only to manufacturers. Now it also applies to nuclear pharmacies since they are permitted to be the original preparers of the material.

A question was raised by a member of the public (Ms. Kathy Seiffert of Syncor International) as to whether the package insert would then have to be given to the patient. Dr. Glenn stated that this is for licensee information only, and does not have to be given to the patient.

A question was asked if the package insert has to be included with each unit dose. The rule language does not imply every container, just every transfer. If the information accompanies the packing list with a shipment, that would be adequate.

Mr. Graham questioned whether the additional labeling requirements were going to improve the distribution process and reduce the number of errors. His belief was that this is additional information one will have to sort through to get to the more relevant information, and thus is redundant information. Mr. Camper stated that this concern was moot, since the final was rule approved, but that eliminating this requirement necessitated assumptions that the limited specific licensee understands the intended use of a particular shipment of product and further that the product has been distributed in accordance with a Part 32 license.

Ms. Seiffert, speaking as a member of the public, stated that the pharmacies she represents would be able to comply fairly easily; however, she agreed that the more information you put on the label (the more "noise" there is), the more chance there is for misadministrations. Syncor International tracks misadministrations that occur as a result of errors in the pharmacy as well as errors in the nuclear medicine department. The most common cause of misadministration is reading the label incorrectly; the more you have on the label, the more difficult it is to see exactly what is there.

Dr. Siegel summarized the ACMUI's concerns based on the discussion thus far as follows. It is appropriate for NRC to reconsider whether everything required on the label is absolutely essential for patient safety or is intended just to satisfy some legal requirement (so that NRC can insure that it has communicated appropriately with suppliers and medical licensees). It also was the consensus of the ACMUI that the syringe labeling requirements should be made consistent with the more flexible approach currently permitted by Part 35.

Several members raised the point that the rule was already approved, and there was nothing that could be done at this point. Mr. Camper interjected that for now, changes could not be made to the rule. However, the guidance documents are still in draft stage, and open for public comments. With regards to the rule language itself, there is a major revision to Part 35 planned in the near future, and these issues can be addressed in that process. If the issues are serious enough, and could be handled simply and quickly enough, there might be other ways of dealing with them prior to the major revision to Part 35.

Ms. Brown questioned why the Commission had approved the rule prior to the ACMUI meeting. NRC staff responded that the timing was important because the interim final rule is expiring on December 31, 1994. If this rule were not approved, there would have to be another rulemaking to keep the current "interim" rule in place or revert to the very restrictive past requirement to adhere entirely to the package insert. In addition, the rule has been reviewed with the ACMUI in several previous meetings. NRC has met with numerous representatives of the radiopharmaceutical industry and various workshops around the country. The labeling issues have not come up until now.

In further discussion of the draft regulatory guide, the ACMUI addressed whether or not the Mo-99 labeling needed to be on the label. The problem is whether a Part 35 licensee will be able to know it is in compliance with the requirement if something they get from a commercial pharmacy does not tell them that it is okay. Mr. Swanson indicated that, if the Part 32 licensee is following the rules, the expiration time of the drug addresses the problem.

Dr. Glenn stated that, during discussion of this rulemaking, the issue of Mo-99 content was a point of concern, since pharmacies will now be able to specify expiration times that differ from those indicated in the manufacturer's instructions. Dr. Siegel pointed out that expiration times would not be changed so as to be in violation of the Mo-99 requirement. Dr. Siegel further pointed out that Part 35 requires that a licensee may not administer to humans a radiopharmaceutical containing more than the authorized limit of Mo-99. If the licensee does not have this information, the licensee cannot know if it is acting in compliance with this requirement. Although compliance could be achieved by an understanding of the underlying procedures, it is more explicitly addressed by providing this information on the label.

Dr. Glenn stated that maybe the regulatory guide should just say that the pharmacy can have procedures to assure that the dose is used within the stated time that is put on the label. Mr. Swanson stated that the guide does say that. If the expiration time is on the label, there ought not to be a requirement that the pharmacy actually put the Mo-99 concentration on that label. If the shortest allowable expiration time were on the label, that would address the problem. The ACMUI recommended that this issue should be addressed by NRC when it revises the draft regulatory guide.

Authorized nuclear pharmacist: One can be an ANP if one is board certified as a nuclear pharmacist, named as an ANP on an NRC or Agreement State license authorizing nuclear pharmacy, or named as an ANP on a permit of a license of broad scope. Documentation of training for ANPs is current certification, or completion of a 700-hour structured program of didactic training and supervised experience, and a signed preceptor statement of competency, by an already approved ANP. A preceptor statement is not required for training received before the publication date of the rule. This will allow pharmacists working under a broad scope license, who have thus not been specifically listed on a license, to continue to work as ANPs.

Character: Dr. Siegel questioned the rationale for the discussion of "character" assessment as a basis for licensure as an ANP in the preamble to the rule, and how this assessment might be used by NRC. Dr. Glenn stated that the Atomic Energy Act provides for character assessment as a basis for licensing. In addition, a Deliberate Misconduct Rule, published in 1992, authorizes NRC to take actions against an individual who is responsible for providing false information or deliberately causing violations of NRC's requirements. Dr. Siegel asked if there have been applications of the character provision in the licensing process. Dr. Glenn indicated that there have been physicians and technologists who have been banned from NRC-licensed activities. Dr. Paperiello added that this is a very uncommon enforcement action and is done by Order, with guaranteed due process. The prohibition from NRC-licensed activities has generally been imposed for a specific period of time.

Human Research: Current Part 35 is silent on use of byproduct material in human subjects for research purposes. The new rule has multiple conforming changes so that requirements relating to such research uses in human subjects parallel the requirements for medical uses in patients. It also requires either that the research be conducted, funded, supported, or regulated by another Federal agency that has implemented the Federal Policy for the Protection of Human Subjects, or that the licensee obtain a specific license amendment to conduct the research with the further requirement that there will be approval of the research by an institutional review board (IRB) and informed consent will be obtained from the research subjects. NRC would not review and approve the IRB decisions, but will ensure that the process was used.

Dr. Siegel requested clarification regarding the following issue. There is a substantial amount of research done with byproduct material that is not funded or supported or directly regulated by another Federal agency. This research is, however, conducted at institutions that have filed General Assurances with the Department of Health and Human Services indicating that all human research performed within the institution will be conducted in accordance with the Federal Policy for the Protection of Human Subjects. How would NRC handle a situation where an inspector sees that a research project has been performed, but does not see direct evidence that there is Federal funding or that the research is regulated by another Federal agency? Dr. Glenn asked whether such institutions possess a document stating that the research would be conducted in accordance with the Federal Policy for the Protection of Human Subjects. Dr. Siegel responded that such documentation existed and is provided to DHHS by the institution. Dr. Glenn indicated that the inspection guidance might need to be clearer in addressing this issue.

Authorized Users: An amendment will no longer be required to add authorized users to a specific license if the AUP or the ANP is certified by one of the organizations listed in Subpart J of Part 35; is identified as an AUP or an ANP on an NRC or Agreement State license; or is identified as an AUP or an ANP on a permit issued by a NRC or Agreement State licensee of broad scope. However, the licensee must notify the NRC within 30 days of adding the individual as a user and must submit a copy of the basis document used by the licensee in determining the individual's qualifications This will eliminate the delay in allowing individuals to become authorized users and will save license amendment fees. The notification to NRC is required to keep the license file current with respect to authorized users.

For a Type-A broad-scope license, no amendment is required to name an AUP or an ANP, or to add or change areas of use at the authorized address of use. Further, no notification to NRC is required for AUP or ANP changes.

Misadministrations: The definitions of misadministrations were amended to include human subjects. Dr. Siegel questioned whether extension of the misadministration reporting requirements to human research with byproduct material would cause a problem in clinical radiation oncology practice where research to evaluate new treatment protocols is being conducted in parallel with patient care. Dr. Stitt replied that, in diagnostic research, the human subjects are not necessarily patients, whereas therapeutic research is directly linked to patient care. Dr. Glenn replied that the term "human subjects" refers to volunteers. Dr. Stitt stated that volunteers are not used in therapy. The treatment is considered innovative therapy, not experimental.

Certification: The rule newly recognizes the following certifications as satisfactory documentation of training and experience for the uses indicated: (1) American Osteopathic Board of Nuclear Medicine for 35.900. 35.910, and

35.920; (2) American Osteopathic Board of Radiology for 35.900, 35.930 after 1984, and (3) Royal College of Physicians and Surgeons of Canada for 35.900, 35.910, 35.920, and 35.930.

Dr. Flynn stated that, to his knowledge, the only two osteopathic training programs in radiation oncology have closed. He thus has a concern with acceptance of certification of the Osteopathic Board of Radiology as a basis for training and experience documentation, since this board examines and certifies individuals infrequently. Dr. Glenn responded that training and experience issues will be addressed with the major revision of Part 35, and the criteria will be evaluated for all training requirements. Mr. Camper indicated that the NRC soon plans to assess the adequacy of training programs and of the board certification process as a prelude to this revision of Part 35. Dr. Siegel stressed the greater importance of evaluating what training and experience is actually needed for protecting public health and safety, and to determine the best approach to achieve the desired qualifications to use radioactive material. This approach would be more efficient than looking at the current system to determine whether it is adequate.

Licensing issues: There will be more flexibility with regard to uses and forms of authorized radioactive material on various types of licenses. NRC will not be interpreting FDA labeling restricting uses. The licensing process will emphasize radiation safety. Two sample licenses, one for a supplier and one for an in-house nuclear pharmacy, were discussed to show how the licenses will list authorized radioactive material and the standard conditions that will be on the licenses.

The rule will be effective on January 1, 1995. The Agreement-State compatibility requirement for the rule has been classified as Division I for definitions and Division II for the requirements of the rule. NRC has volunteered to work with the Conference of Radiation Control Program Directors to develop model regulations for the Agreement States.

Pharmacy issues: For pharmacy licenses, only a pharmacist may be listed as an ANP. Pharmacists currently listed as users will qualify as ANPs, and board certified nuclear pharmacists are not required to be listed on the license.

Regulatory Guidance: There was a discussion of the draft regulatory guidance. Mr. Swanson noted that the quality assurance requirements for dose calibrators for pharmacies are more restrictive than those for Part 35 licensees. Dr. Glenn stated that this came from existing guidance, and would need to be evaluated. There is an ANSI standard which is very close to Part 35. Dr. Siegel noted that the regulatory guide states that orders for byproduct material must be placed by the ANP or the pharmacy's radiation safety officer (RSO). This appears literally to require that this individual will be the one who places the order and performs the administrative tasks associated with ordering. Dr. Glenn indicated that this is not what NRC intends, and the

wording of this section will be evaluated. In addition, it was noted that the limits given in the draft guide for Mo-99 breakthrough are incorrect. A member of the public questioned whether an ANP can qualify as the pharmacy's RSO. Dr. Glenn indicated that this was correct.

A requirement was added to measure the activity of alpha- or beta-emitting radionuclides. However, this is not applicable to unit doses received from a Part 32.72 supplier. The licensee may use a combination of measurements and calculations in order to determine the dose.

II. Status of Implementation of the Quality Management Rule

Sally Merchant, NMSS, presented a report on the status of the implementation of the Quality Management (QM) Rule. The contractor has completed the review of 1,700 Quality Management Plans (QMPs). There is a contract in place to perform misadministration-events analysis. NRC Regions sent letters to 35 licensees stating that their QMPs, as written, appear to meet the objectives listed in 10 CFR 35.32. Letters stating that the QMPs, as written, have weaknesses, but appear to meet the objectives listed in 10 CFR 35.32, were sent to 278 licensees. Letters were sent to 1,228 licensees stating that their QMPs failed to meet at least one of the QM objectives. The deficiencies varied significantly in safety significance. There were 168 declarations that radioactive drugs applicable to 10 CFR 35.32 are not being administered. The most common problems with the QMPs were incomplete written directives and procedures for periodic reviews. Positive and negative findings are entered into a database in order to track what parts of the rule are and are not being met.

Dr. Siegel emphatically stated that this experience indicates that a relatively simple prescriptive rule may be better than an ambiguous "performance-based" rule. He further stated that NRC's actions to date suggest that its approach to implementation is not performance based; rather, NRC is holding licensees to the smallest details specified in Section 35.32 and the accompanying regulatory guide. He recommended that NRC should consider reducing the QM rule to its simple prescriptive components at such time that it is evaluated for its effectiveness. Mr. Camper countered by stating that a performance-based rule, with a pilot program, was the recommendation of the ACMUI in the past before the current rule was drafted. (For the record, Dr. Siegel noted that the ACMUI was composed of different members at the time of that recommendation.).

Agreement States are required to implement the QM rule by January 25, 1995. However, it was pointed out by Mr. Quillin that many Agreement States do not have the resources to perform the reviews of the plans, as did the NRC, within the timelines required by individual State laws.

III. Re-examination of NRC Enforcement Policy

E. William Brach, NMSS, presented a report concerning the agency-wide effort to re-examine NRC's Enforcement Policy, which is set forth in Part 2, Appendix C. This policy applies to all NRC licensees—reactor, material, and fuel cycle. A task force was formed in July 1994. The objectives of the review are to: (1) determine whether the defined purposes of the enforcement program are appropriate; (2) determine whether the implemented program is consistent with the defined purpose; and (3) recommend changes. The purpose of the enforcement program is to promote and protect health and safety, the common defense and security, and the environment. There are four objectives to the program: (1) ensure compliance; (2) obtain prompt corrective action; (3) deter future violations; and (4) encourage improved performance. There are five specific areas that are being examined: (1) balance between deterrence and incentives; (2) appropriateness of NRC sanctions; (3) amount of civil penalties; (4) different policies and programs for large and small licensees (e.g., reactor vs. material licensee); and (5) open enforcement conferences. The fourth point is of importance to NMSS, since there is a wide variety in the size of the licensees.

The team is looking at three approaches in its review. First, the team is interested in learning what other Federal agencies do in the enforcement of their regulatory programs. Letters were sent to over 20 Federal agencies with questions and requested input on their enforcement programs. Second, the team is looking within the Agency, including both the regions and the program offices at Headquarters. Third, the team will solicit input from members of the public. A Federal Register notice was published in August 1994, with a 60-day comment period that closed in October 1994. Letters were sent to each NRC licensee, as well as to a large number of industry organizations, associations, public interest groups, and Agreement States.

NRC has received about 50 comments. Not all of the comments have been reviewed. A summary of some of the comments that have been reviewed follows. There were seven topics of particular importance to NMSS licensees. Regarding the purpose and objectives of the program, most comments were supportive. However, with regard to implementation of the program, commenters stated that NRC should focus more on safety aspects and less on the implementation of a rigid proceduralized type of program. Comments were generally supportive of the way in which severity levels are classified. However, there were requests that NRC provide more complete definitions and examples of the severity levels. Most comments from non-licensees were in favor of open enforcement conferences. Comments from licensees generally indicated that it is difficult to conduct an uninhibited exchange of information in an open forum. NRC's view of enforcement conferences are to learn more about the violation, the corrective actions taken by the licensee, and to convey the safety significance of the findings to licensee management. There were comments that it appeared that NRC came to an enforcement conference with a decision already

made, and that the enforcement conference was just a step in the process that had to be conducted. Regarding the use of Notices of Violation, and of Form 591 for minor violations, commenters stated that NRC should not always be so compliance oriented to keep licensees focused on safety. Some licensees liked the use of the Form 591; others did not. With regard to civil penalties, some commenters stated that civil penalties may not have much impact on large licensees, but they do have substantial impact on small companies. The consensus so far is that, with the exception of smaller licensees where the financial impact is significant, it is not so much the size of the civil penalty that is of importance, as it is the occurrence of a violation at a level requiring escalated action. Commenters supported continued use of adjustment factors. Of the comments reviewed thus far, NRC has not seen many comments regarding the timeliness of enforcement action.

Several comments or questions were presented by the Committee. Dr. Flynn stated that self-identification of violations should be a strong factor in mitigation. Dr. Wagner stated that with regard to the severity levels, responding to many "minor" violations resulted in excessive paperwork, which can be contrary to ALARA principles. Individuals are busy processing paperwork for severity level V violations rather than focusing on safety issues. He would suggest using a process with a minimum amount of required record-keeping for severity level IV and V violations.

Dr. Siegel asked whether there really was a scientifically valid way to determine whether an enforcement program is set at the right level. One suggestion would be to randomize enforcement interventions (i.e., to perform a controlled experiment) to determine what would happen if NRC deregulated or reduced enforcement for one group of licensees, and continued in the same way with the rest. The view has always been that one cannot reverse procedures, since history has shown that regulations keep getting increased (ratcheting). He encouraged NRC to consider gathering some real data about whether these enforcement programs really work in reducing violations and increasing safety. NRC is operating at an event frequency that is so low that NRC cannot prove statistically that its enforcement program is working.

Mr. Swanson stated that it would be helpful to the community if licensees got information regarding procedures and practices that work well at facilities with good compliance records, instead of just receiving negative information. The response to this comment was that NRC cannot place itself in the role of an advisor or a consultant, and cannot recommend how licensees should perform their work. Mr. Brach stated that NRC cannot recommend a "better way to do things" if what licensees are doing is in compliance with the requirements. To this comment, Dr. Siegel responded that it was only NRC's mind-set that made this so, and there might indeed be ways to improve the performance of licensees in a less adversarial manner.

IV. Institute of Medicine/National Academy of Sciences (IOM/NAS) Study

Dr. Patricia Rathbun, NMSS, presented an update of the study being conducted by the IOM/NAS Panel for Review and Evaluation of the Medical Use Program of the Nuclear Regulatory Commission. The Committee met July 10-12, 1994 and October 13-14, 1994. Dr. Siegel presented the views of the ACMUI during the meeting in July. The Chairman and the Commissioners of NRC spoke during the October meeting. The Commissioners encouraged the NAS to be fair and objective. They stated that NRC was looking not for specific answers, but for an overall evaluation of the Medical Use Program. There are four subcommittees looking at the following issues: (1) data/risk; (2) regulatory issues; (3) quality management; and (4) education and training. The subcommittees are preparing four papers on the following topics: (1) risk of low-level exposure to ionizing radiation; (2) cost of NRC regulation; (3) misadministrations; and (4) regulatory issues. There is a meeting scheduled in January 1995. This will be the last meeting before the panel begins preparing its draft paper and its recommendations, which will then undergo extensive peer review as do all NAS reports. At this time, the IOM/NAS panel is on schedule and within budget.

V. Brachytherapy Fractionation Issues

Patricia Holahan, NMSS, led a discussion on brachytherapy issues. Since the last ACMUI meeting, a program has been initiated to look at specific brachytherapy problems. Dr. Holahan discussed the trends in misadministration frequency since 1991. She noted that the reported misadministrations for remote afterloading brachytherapy do not include single-fraction errors in a course of high-dose-rate (HDR) treatment. Case summaries of recent misadministrations and other events not classified as misadministrations were presented to focus on some of the areas of current NRC concern and for which the staff is requesting ACMUI input. These events include errors in computer data entry and computer malfunctions triggered by licensee errors. Other issues are involved with treatment planning, misplaced sources, and dislodged sources. Misplaced sources are those that have actually been implanted in the wrong location or have fallen out of the applicator. Sources are considered to be dislodged if they are still within the treatment volume, but the applicator or ribbons have shifted slightly. There have been numerous cases of patient intervention resulting in source dislodgement. The sources become dislodged because of patient movement or because the patient has pulled the sources or ribbons out of the treatment site. There are also several types of human error involved, including incorrect data entry, improper loading of applicators, or selection of the wrong sources for treatment.

Dr. Holahan described a few recent cases. Dr. Stitt pointed out that in some cases, the "misadministrations" resulted in an increased dose that actually was in the appropriate therapeutic range (i.e., the prescription in these cases would actually be considered an underdose by comparison with the

standard of practice). In addition, she indicated that any new regulations should recognize the frequent combination of brachytherapy and teletherapy in the total prescribed treatment plan. She cautioned that the NRC should avoid regulating to such a minute level that there is no flexibility in treatment.

Dose fractionation is defined in Part 35 for teletherapy, but not for brachytherapy, radiopharmaceutical therapy, or gamma stereotactic radiosurgery. The staff published Federal Register notice on November 3, 1994, which contained a list of issues and questions focusing on dose fractionation, source calibration, source placement, and training and experience. The staff is evaluating several issues with brachytherapy. One is whether the existing regulations for brachytherapy are adequate. The staff is looking at the availability and adequacy of industrial standards and procedures, and whether there should be required quality assurance checks and calibrations for brachytherapy similar to those required for teletherapy. The staff is evaluating the need for a category of misadministrations for fractionated brachytherapy. The staff has prepared a Generic Letter that will be sent to licensees requiring them to report errors in administration of fractionated treatments so that NRC can evaluate how often such errors are occurring and thereby determine the need for additional regulations. This issue will also be discussed at professional society meetings, with manufacturers, and with members of the public. The staff will also evaluate the training and experience requirements for physicists and physicians involved with HDR therapy, computer treatment planning, and the definition of "treatment site." For radiopharmaceutical therapy, the staff will review the adequacy of training and experience requirements in 10 CFR 35.930, problems in the assay of doses of beta-emitting radiopharmaceuticals, and problems in fractionated radiopharmaceutical therapy.

Dr. Nelp observed that the number of misadministrations, as reported by Dr. Holahan, seems so low that any efforts to reduce this number further would be tantamount to attempting to eliminate human error. He further commented that the NRC should be pleased by the effectiveness of its regulatory program because the error rate is so low.

There was a discussion of the questionnaire that will be sent to licensees and professional societies. Several ACMUI members indicated that they would like to have reviewed the questionnaire prior to its use. Dr. Siegel emphasized that, even though the questionnaire had to be finalized by staff for use at an upcoming professional society meeting prior to the current ACMUI meeting, the individual ACMUI members are always available to provide their advice to the staff on such matters in their roles as NRC consultants.

During prolonged discussion of the draft Generic Letter, there was concern that the reporting of events to NRC could trigger reactive inspections. The ACMUI believed that, if at all possible, inspections should not be conducted as a result of information the licensee provided to NRC in accordance with the

Generic Letter. Dr. Siegel emphasized a fundamental problem that had been discussed by the ACMUI many times before: namely, there is a "disconnect" between NRC's legitimate need to gather data in order to allow for assessment of generic or systematic problems of public health significance and the fact that reporting (of misadministrations or other events) to NRC usually results in a series of "unpleasant" events for the licensee (large amounts of paperwork, referring physician and patient notifications, enforcement actions) even when there has been no injury to the patient.

The ACMUI agreed that a 20% difference from the prescribed brachytherapy fraction dose is an appropriate reporting threshold; this is the same threshold used to define a misadministration involving the total dose for brachytherapy, and radiopharmaceutical therapy. However, it also was suggested that use of this percentage difference along with a dose threshold (e.g., the fraction dose differs by > 20% from that prescribed AND is > 200 rads) would be a medically sensible modification.

Mr. Quillin stated, and the ACMUI agreed, that this new reporting requirement should not be of indefinite duration; rather, a finite time period should be selected. If the information gathered during this period was insufficient to evaluate the magnitude of the problem, an extension should be sought.

There was general agreement of ACMUI members that the Generic Letter was much too long and needs to be simplified. The ACMUI strongly believed that the Generic Letter did not clearly indicate that its purpose was information gathering regarding fractionated brachytherapy errors.

There was a major discussion concerning the definitions of treatment site and wrong treatment site in brachytherapy. Written directives do not usually specify the treatment volume with detailed isodose curves. If a source becomes dislodged and the dose is delivered within a volume that may have been included in the original isodose profile, is that still the treatment site? The problem is that the definition of a misadministration to the wrong site does not have a dose threshold. Dr. Holahan indicated that NRC would like the ACMUI's views on the definition of "treatment site." Dr. Stitt strongly suggested that NRC not attempt to define the "treatment site" per se. It is too difficult due to the differences in treatment planning across facilities. It might be more efficient to define "wrong treatment site" for purposes of determining when a recordable event or misadministration has occurred. Based on early responses to the questionnaire and preliminary discussions in professional organizations, individuals are suggesting the use of a wrong-site definition that incorporates both reference to the dose that would have occurred if the treatment had proceeded as prescribed (e.g., differing by greater than 20%) and a dose threshold (e.g., greater than 200 rads). NRC will develop a working model and submit it to the ACMUI for review. Definitions from the International Commission of Radiological Units were discussed and will be used in developing the definition of treatment site.

The ACMUI was asked if it is appropriate for NRC to proceed with expedited rulemaking to address HDR issues, quality assurance for brachytherapy, modification of 10 CFR 35.400 (use of sealed sources for brachytherapy), and any revision of brachytherapy definitions. The ACMUI believed that there should be additional regulations for these issues rather than continuing the requirements under license condition as is presently being done. The ACMUI stated that the modifications to Section 35.400 should allow for greater flexibility in use of sources for therapeutic purposes not specifically defined in Section 35.400 (because therapeutic needs frequently warrant novel uses of existing sources, but manufacturers are unlikely to obtain approval for these new applications). In addition, brachytherapy quality assurance should be addressed now, rather than waiting for the major revision to Part 35. The definitions also should be revised.

The ACMUI did not recommend incorporation of additional questions or issues in the questionnaire that is designed to identify the need for additional regulations or guidance, nor did the ACMUI believe that additional issues needed to be addressed in the draft Generic Letter.

The future direction of this effort will be involved with the major revision of Part 35, will incorporate industry standards, will include public meetings to discuss regulatory criteria to address changing technologies, and will include input from the IOM/NAS study. Several workshops are scheduled. The objectives are to: (1) identify and evaluate therapy errors to include fractionated therapy doses; (2) discuss current standards or industry practice; (3) discuss the need for quality assurance checks and calibrations for brachytherapy; and (4) discuss the need to modify current regulations to incorporate licensing guidance on remote afterloaders.

VI. Status of Abnormal Occurrence Criteria Revisions

Robert Prato, Office of Analysis and Evaluation of Operational Data (AEOD), presented a discussion of the status of the revised abnormal occurrence (AO) reporting criteria. He indicated that the information he provided is predecisional, and that the proposed revisions are currently with the Commissioners for their review and approval. AEOD received 12 comments from Agreement States, which have been incorporated into the revisions. These comments were received after the ACMUI members received the August 1994 draft revisions. Mr. Prato provided a brief background on the AO process. In May 1994, a Staff Requirements Memorandum from the Commission directed the staff to initiate an effort to revise the AO criteria, with attention to three specific areas: (1) medical misadministrations, including overexposures; (2). the revised Part 20 requirements; and (3) the criteria for lost, stolen, or abandoned sources.

The previous overexposure criteria have been combined into a single criterion for members of the general public, occupational workers, or wrong patients.

In addition, a criterion of 5 rem total effective dose equivalent was established for minors, fetuses, and embryos. This is lower than for other overexposures because of the increased radiosensitivity of this group.

The AO reporting criteria for misadministrations will be changed such that the threshold dose is 100 rads to a critical organ, or 1,000 rads to any other organ. In addition, the event has to involve a dose exceeding the prescribed dose by greater than 50%, the wrong radiopharmaceutical, the wrong route of administration, the wrong treatment site, the wrong treatment mode, or a leaking source.

The revisions should be published within the next two weeks, with a 90-day public review comment period. There will be 120 days to review the comments and make any appropriate changes to the revised criteria. At that time, the revisions will be resubmitted to the Commission for review and approval. The revised criteria should become policy in the early summer of 1995.

Dr. Siegel commented that the revised AO reporting criteria now appeared to be straightforward and were vastly improved by comparison with the draft the ACMUI had reviewed at its meeting in May 1992.

VII. Administration of Radioactive Material to Individuals

Steve McGuire, Office of Research, NRC, presented a discussion on the administration of radioactive material to the "wrong patient." Mr. McGuire provided general background as to how the issue had evolved. Recommendations were sent by the staff to the Commission. The Commission ruled that a medical administration to a "wrong patient", even where no administration was intended, is governed by Part 35 rather than Part 20. This does not, however, affect the classification of other exposures, such as inadvertent exposure of nurses to gamma-rays or X-rays. Part 20 will now exclude doses "due to any medical administration that an individual has received. The term "individual rather than "patient" is used to avoid having to define the latter under those circumstances where no administration was intended. The proposed rule will be submitted to the Commission after this meeting. The ACMUI unanimously recommended that the proposed rule be submitted to the Commission as it stands.

The meeting was adjourned for the day at 4:40 p.m.

November 18, 1994

The meeting was reconvened at 8:00 a.m. on November 18, 1994.

The meeting opened with a brief follow-up discussion of treatment site. A proposed definition of "irradiated volume" was presented. Dr. Flynn stated that licensees prescribe brachytherapy dose by one of several methods: (1)

dose to a reference point (or points) such as "Point A"; (2) milligram-hours; or (3) dose to a volume, e.g., as recommended by ICRU Report No. 38 for LDR intracavitary implants. However most licensees do not use the approach recommended by ICRU Report No. 38. About two years ago, a working group of physicians and physicists recommended that NRC not be overly prescriptive in the brachytherapy section of the QM rule. The final QM rule allows licensees flexibility in defining brachytherapy dose. Dr. Stitt agreed and added that the concept of mg-hours in LDR implants is not applicable to HDR implants where most licensees currently prescribe dose to a reference point (or points). Dr. Siegel stated that NRC's concern should focus on a site that is irradiated that would not have been expected to be irradiated if the treatment had been performed as prescribed. Thus, NRC should try to avoid defining treatment site since it is so difficult to define. Dr. Siegel stated that workshops should be conducted to develop a professional consensus on this issue. He emphasized that the staff should start the procedure to select a therapy physicist to serve on the ACMUI as soon as possible, in order to help NRC deal with this problem area.

VIII. "Release of Patients Containing Radiopharmaceuticals or Permanent Implants," 10 CFR 35.75

Kitty Dragonette, Office of Research, provided a discussion on the "Release of Patients Containing Radiopharmaceuticals or Permanent Implants." This issue has been discussed with the ACMUI during previous meetings. Three members of the ACMUI (Drs. Siegel and Wagner and Mr. Quillin) met with staff informally in October 1994 and discussed several items pertaining to the proposed rule and the public comments received. At that meeting, it was proposed that the argument for moving from the 100-mrem limit in Part 20 to the 500-mrem limit (which is the implicit basis of current 35.75) must be based on cost/benefit considerations. It was further suggested that the activities affected by this issue should be those that are currently tied to a written directive so that diagnostic imaging radiopharmaceutical doses used in nuclear medicine (other than doses of I-131 or I-125 iodide >30 μCi) would not be affected. There is a particular problem with respect to the breast-fed infant as a member of the general public and diagnostic nuclear medicine procedures. Dealing with this could become very complicated for licensees and involve a substantial allocation of resources for investigation and documentation of breast-feeding status in all women in the right age range who are referred for nuclear medicine examinations.

The proposed rule was published in June 1994, and the public comment period ended August 29, 1994. There are two major components of the proposed rule. First, the proposed rule would exclude from 10 CFR 20.1301(a)(1) and (2) the dose received by members of the general public from patients released under the provisions of 10 CFR 35.75. Second, Section 35.75 would be modified to specify a 500-mrem annual limit of total effective dose equivalent (TEDE) for

the individual likely to receive the greatest dose. The final rule and regulatory guide are due to the Commission in the summer of 1995.

The comments received on the rule were discussed. The strongest opposition to the proposed rule related to the proposed recordkeeping requirement for doses >100 mrem to the individual likely to receive the greatest dose. Commenters asserted that this would result in excessive costs to find previous administration records, and that NRC underestimated the cost of record generation and retrieval. One option being considered by the staff is to eliminate the recordkeeping requirement in the rule, and allow licensees to develop their own procedures to demonstrate compliance with the rule (possible approaches, including means to keep track of multiple administrations, would be addressed in the regulatory guide). Another option is to require records for only those releases based on case-specific calculations rather than use of general tables providing guidance for patient release. Dr. Wagner raised a concern about guidance to cover multiple administrations during a year at different hospitals. Ms. Dragonette stated that the major concern with multiple administrations would be with therapies. The diagnostic studies were well below the 100-mrem limit. Dr. Siegel questioned whether anything was needed between the 100- and 500-mrem limits.

There was a brief discussion concerning the basis of dose limits to provide Ms. Brown with background information in response to her questions regarding how to make a judgment between a 100- and a 500-mrem limit. Several ACMUI members pointed out that the 100-mrem limit is a population limit, and is less than the average dose individuals receive as background radiation and of the same order of magnitude as additional doses received from such specific activities as living in Denver or frequent flying. Ms. Brown expressed the concern that none of the comments appeared to be from consumer-based groups, health research groups, etc. All of the comments appeared to be from groups with cost/benefit interests in addition to patient-care interests. Ms. Brown stated that there were distinctions between risks an individual chooses to take vs. risks that are imposed by the activities of others. She expressed a concern about the consequences of something done to a person that may have an effect on family members when the risks are not adequately explained to that individual or to other members of the family. Dr. Siegel stated that one has to think about the high anxiety level created in the patient who gets instructions about risks that are not present. People should receive instructions and understand what is being done. However, people should not be inundated with information about hazards that do not exist. Dr. Paperiello discussed the international and national groups that have established the standards that NRC must incorporate into its regulations.

Several comments to the Federal Register notice were received regarding the proposed requirement to provide written instructions to released patients. Commenters stated that oral instructions should be sufficient. A major health maintenance organization strongly supported the requirement that the

instructions be written. Most believed that a sizable fraction of patients will not behave as instructed. Options being considered are to provide oral instruction only or to provide written instructions as proposed, and address degree of patient compliance in the regulatory guide. The last option would entail more detail in the guide about explaining things and walking a patient through the directions and the assumptions on the behavior used in releasing the patient. The physician would not be responsible if the patient intentionally did not follow the instructions. Ms. Brown stated that written instructions should be given. Dr. Siegel agreed that written instructions should be given to the patient, but elaborated that written instructions alone were not sufficient. The working group had suggested changing the wording in the rule to indicate that the licensee must "....provide the patient with instructions, including written instructions,..." Thus, the licensee is obligated to explain the instructions, and not to just hand the patient a piece of paper. Again, it was suggested that this requirement should be tied specifically to those procedures requiring written directives.

The issue of exposure to a breast-fed infant/child was discussed. The 500-mrem per year limit might be exceeded if breast-feeding continued after some diagnostic tests. One commenter stated that the breast-fed infant/child should be viewed as a special case and should not be considered in complying with the annual limit. One commenter stated that the breast-fed infant/child should be addressed as a part of patient-physician decision to conduct the procedure. Ms. Dragonette indicated that from the standpoint of a general radiation protection policy, one should provide for consistent protection of individuals. From a patient-physician standpoint, the focus should be on balancing all factors and providing maximum flexibility.

The rationale for treating the infant/child as an individual is that the infant/child is physically separate from the mother, unlike the embryo/fetus. Some infants may never be breast-fed, so there is an inequitable protection. There is not a clear age-related break point, since breast-feeding times vary over a wide range. The available options include the following: (1) having the mother express milk and store it for feeding before the study or (2) interrupting or discontinuing breast-feeding; both options are used in standard medical practice when radioactive drugs and certain nonradioactive drugs are prescribed to the mother.

There are several problems with the proposed rule if the breast-feeding infant/child is considered an individual. The proposed rule does not include provisions for preventive action before administration. It is very difficult to estimate doses to breast-fed infants, because only limited data are available about the secretion of many radiopharmaceuticals into breast-milk. The proposed rule could limit certain medical-care decisions by physician and patient. There is a potential for patient confinement being required in many more cases (for diagnostic procedures) than at present. Options being considered are: (1) not changing the proposed rule; (2) expanding the

regulatory guidance to include a discussion of preventive measures, but not delineating such measures as requirements; (3) limiting considerations relating to nursing to specific dosage levels of specific radiopharmaceuticals and providing tables showing acceptable times to resume nursing; or (4) clarifying that licensee reliance on instructions to breast-feeding women provided in the regulatory guide is an acceptable approach to demonstrate compliance.

Dr. Siegel suggested that the staff should seek advice from ACMUI members during the preparation of the guidance tables on breast-feeding. He further suggested that the regulatory guide should also contain information on breast doses resulting from administration of radiopharmaceuticals (particularly I-131 iodide) to lactating women, and the need to discontinue breast-feeding days to weeks before the administration in order to allow breast uptake to return to basal conditions.

Near the end of the discussion, Dr. Siegel stated that it still was not clear to him how the staff is now proposing to address potential exposures between 100 and 500 mrem. Ms. Dragonette stated that these circumstances would require instruction of patients to maintain exposures to others ALARA. It would be left to the physician either to determine from tables (without creation of specific records) that multiple administrations will maintain potential exposures below the 500-mrem limit or to use more detailed recordkeeping and case-by-case calculations, outside of the parameters in the tables, in order to demonstrate compliance with the 500-mrem annual dose limit.

The consensus of the ACMUI was that the wording regarding instructions should be modified as indicated above, and that the proposed recordkeeping requirements in 35.75(b)(2) should be dropped (unless this section is rewritten so that it is linked only to extraordinary circumstances where calculations are used to show that specific patients released with high activity levels will not cause exposures exceeding the 500-mrem limit). The ACMUI otherwise found no problems with the proposed rule.

IX. Discussion of Advanced Notice of Proposed Rulemaking for Part 35

Janet Schlueter, NMSS, presented a discussion of the Advanced Notice of Proposed Rulemaking (ANPR) for Part 35. There is a five-year management plan for the medical use regulatory program, referred to as the Medical Management Plan. The plan has 90 action items, the major one being a major revision to Part 35. The revision would encompass issues that need to be clarified or revised for one reason or another. These issues have become apparent through inspections and also as a result of implementing the current rule for the last seven years. In addition, there are emerging technologies that need to be addressed. The results of the IOM/NAS study and subsequent Commission direction will also impact the issuance of the ANPR and the revision to

Part 35.

The current schedule is to publish the ANPR in March 1995 and to identify key areas for discussion and the issues under consideration. Numerous workshops are being scheduled within the medical community, with Agreement States, with professional societies, and with manufacturers for the Summer and Fall of 1995. The proposed rule should be published in late 1996, with the rule becoming final in 1997. The revision will address training and experience criteria for physicians, RSOs, physicists, and the need for training and experience documentation for other allied health personnel, such as dosimetrists and technologists. The staff currently uses licensing guidance for many of the new and emerging technologies and this information needs to be incorporated by rulemaking into Part 35. Quality assurance/quality control procedures for devices need to be incorporated into Part 35, as well as minimum radiation safety requirements for devices. There are several areas of brachytherapy that warrant evaluation. The staff is looking at areas where industry standards can be utilized.

X. Misadministrations - Follow-up, NRC Consultants, etc.

Larry Camper, NMSS, presented a discussion on patient notification issues. Patient notification issues have been discussed in previous ACMUI meetings. Background information was provided for newer members and the public. In reviewing misadministrations between 1990 and 1992, the staff learned that a large fraction of patients were not notified orally, and an even larger fraction of patients did not receive written notification. An Information Notice was published that brought to licensees' attention the requirement for notification under Section 35.33. The staff then evaluated the notification requirements in Section 35.33. Items that appeared to warrant re-evaluation were submitted to the Office of the General Counsel (OGC) for comment. OGC determined that the notification requirements were already covered explicitly in Section 35.33. Therefore, the staff needed to make this clear to licensees. A second Information Notice was discussed with the ACMUI at its last meeting. The ACMUI stated that the issues addressed were closely associated with the practice of medicine, and that the clarification in the Information Notice went beyond what licensees had previously understood. Specifically, if NRC's intent was that someone had to be notified even if it would be harmful to inform the patient, the regulations should state that explicitly. The term "responsible relative" was not clear, and the term "relative" should be used. In addition, since informing a relative may, in fact, lead to the patient being informed, limited immunity from liability for breach of confidentiality should be provided to physicians who follow this NRC requirement. The staff then decided to issue a Generic Letter that will require licensees to look at their past misadministrations and ensure that proper notifications have been made. Also, since this is a policy issue, the staff plans to obtain the Commission's concurrence.

There are four options under consideration by the staff variably involving the use of a Generic Letter, Information Notice, or rulemaking. Option 1 is to issue the Generic Letter, and re-affirm the Commission's intent regarding patient notification. Option 2 is to publish an Information Notice and initiate rulemaking to revise Section 35.33, including the provision that, if it is deemed harmful to notify the patient, no further notification is required. Option 3 is the same as Option 2, except that a relative would have to be notified if it were deemed harmful to inform the patient. Option 4 is the same as Option 2, except that, regardless of potential harm to the patient, the patient (or guardian, if the patient is a minor) must be notified. Dr. Siegel reiterated that an immunity clause would need to be included to address potential liability for breach of confidentiality.

Dr. Siegel then proposed a fifth option, namely to revise Section 35.33 in accordance with the original concept proposed by the Commission nearly 20 years ago requiring notification of the patient only when there is a likelihood of harm as a result of the misadministration. If there is harm or probable harm to the patient, the patient has the right to know. (This approach also has the advantage of uncoupling the NRC's need to gather information about both incidents that cause harm and those that do not from the added sequence of events related to misadministration reporting, as was discussed previously.) Dr. Stitt also added that in the vast majority of misadministrations, there are no medical consequence and certainly there is no injury. The cases are actually technical misadministrations. The real issue is that if a dose is wrong (e.g., an IV dose, medication dose, radiation dose), the patient and family must be involved because one has to make medical decisions and continue with proper medical treatment. She believes the options presented by the staff are paper trails more than anything, and do not have anything to do with the care of the patients. She emphasized that it is important to remember emotional harm, which is the basis being used by physicians in not informing patients. If NRC focuses on medical consequences, this can be avoided.

Dr. Flynn brought up the problem wherein the radiation oncologist informs the referring physician, who is not regulated by NRC, and the referring physician decides it would cause anxiety if the patient were notified, and would be of no benefit to the patient. This puts the radiation oncologist in an awkward position. He thought another option might be considered wherein the AUP is simply responsible for notifying the referring physician. This is a way to remove the AUP from a possible conflict of interest, in light of Ms. Brown's concern that some person, other than the one who administered the radiation, should be made aware of the misadministration.

Another option suggested is for use of an NRC medical consultant to make an independent judgment of whether or not there is the potential for harm.

Ms. Brown expressed the concern that more people are trying to become well-

informed patients, and they should be provided with the maximum amount of information concerning their care. There was subsequent discussion regarding the availability of second opinions to make informed decisions about the use of services of various professionals. Ms. Brown argued that radiation medicine is an arcane area, making it more difficult for individuals to know whether a mistake in treatment has been made. Dr. Siegel and other ACMUI members strongly disagreed with Ms. Brown's belief that the risks of radiation exposure are uniquely more dangerous and the adverse effects less visible than in other types of medical care, and thus radiation medicine should be regulated more stringently.

Dr. Paperiello stated that the notification requirement has been in Part 35 for a long time, and the recent OGC interpretations are compelling him to address a current set of problems. The intent of the Generic Letter is to offer the Commission the opportunity to determine that this is in fact what it intends. Whether there should or should not be notification is not the issue.

Cathy Haney, NMSS, presented a discussion on patient follow-up. An internal management directive entitled "NRC Medical Event Assessment Program" was issued in July 1994. It sets forth the policy for NRC's follow-up and investigation into medical events, primarily misadministration events. As a result of two recent misadministrations, NRC is re-evaluating two items in the management directive. First, NRC will continue to obtain follow-up on patients until any expected deterministic effects have been observed, in the opinion of the medical consultant. Second, if the medical consultant believes that the patient should be followed beyond the initial review period, he or she would so recommend to NRC. NRC management would then determine if follow-up is necessary.

The ACMUI was asked for its response to several questions. First, "What is the appropriate role of NRC and the medical consultant in long-term patient follow-up, when long-term follow-up has been recommended by the NRC medical consultant?" Dr. Siegel stated that there are two potential goals for the NRC's interest in long-term follow-up. One is to gather information about the consequences of the events as part of a scientific database. As discussed in the past by the ACMUI, the frequency of such events is so low that they are not adding significantly to the scientific literature regarding the thresholds for deterministic effects. Another goal is ensuring that the patient gets appropriate medical care. The ACMUI in the past had indicated that the NRC-mandated responsibility for informing the patient about the event and its potential consequences should be a sufficient endpoint for NRC intervention.

Dr. Flynn stated that, when he reviewed a case as an NRC consultant, he always conferred with the referring physician to ensure that he or she understood the misadministration and to determine whether the referring physician intended to maintain follow-up of the patient. This is a question asked of the medical consultants by NRC. Ms. Haney asked what NRC should do if the medical

consultant states that the patient will not be receiving adequate follow-up care. Dr. Siegel stated that NRC medical consultants are not allowed to participate in the process as medical practitioners and NRC cannot control the actions of referring physicians. Moreover, the patient may no longer have any medical relationship with the licensee. Accordingly, there was some confusion as to NRC's intent. Ms Haney clarified that NRC is concerned with long-term care given after the initial assessment and care of the patient primarily to ensure that the patient is getting adequate medical care. Several members of the ACMUI believed this was legislating adequate medical care, that NRC would be inappropriately making a determination as to what is, and is not, adequate medical care. FDA does not take continuing responsibility for ensuring that patients injured by drugs or devices are getting adequate follow-up medical care. Dr. Siegel suggested, however, that (legal constraints notwithstanding) affording NRC medical consultants with the flexibility to guide licensees and referring physicians in their management of an injured patient would be one positive thing that NRC could do in this arena.

Second, "Should NRC determine whether the patient will consent to follow-up care if the medical consultant recommends long-term follow-up?" The ACMUI was unable to perceive how NRC would use such information. Ms. Haney stated that referring physicians, authorized users and patients are becoming more aware of a program at Oak Ridge to follow-up patients.

Finally, "In those cases where the referring physician has informed the licensee that, in his medical judgment, notifying the patient would be harmful, what is the role of NRC when the medical consultant indicates long-term patient follow-up is appropriate?" The ACMUI felt that NRC's role in such circumstances clearly is limited. Dr. Flynn also noted that it was quite unlikely that no medical care would be provided when there was actual injury or a reasonable chance of future harm.

XI. Administrative Matters

A. ACMUI Bylaws

The bylaws were discussed in detail and revised accordingly during the May 1994 meeting. The Commission subsequently approved the draft bylaws as they were presented. The ACMUI unanimously approved the adoption of the bylaws.

B. Report on October 20, 1994 Commission Briefing

Dr. Siegel presented a brief report on the Commission Briefing he had given along with Drs. Stitt and Wagner and Mr. Quillin. All ACMUI members had been provided with the background material used at the briefing and the transcript of the briefing. The three major areas discussed were patient notification, brachytherapy, and training and experience criteria. NRC has been discussing the training and experience criteria for several years, and the ACMUI strongly

recommended that NRC should start re-evaluating the criteria and making decisions. The ACMUI also stated that there is a need for a more congenial working relationship with OGC. There has been a reluctance for OGC to discuss issues in a public forum. However, it is crucial for the ACMUI to be able to interact with OGC early in the process of rulemakings so that the ACMUI can be optimally effective in providing advice and guidance to NRC.

C. General Issues

Second Medical Physicist Position: The Commission has approved the re-establishment on ACMUI of the second medical physicist position. The individual will be a specialist in radiation therapy physics.

Visiting Medical Fellow: A Federal Register notice was recently published calling for nominations for the position of Medical Visiting Fellow. NRC is seeking an individual with expertise in radiation oncology or radiation therapy physics to join the agency during 1995. The current Medical Visiting Fellow is scheduled to complete his term in December 1995.

Radiation Therapy Dosimetrist/Medical Dosimetrist Position: Eleven nominations for this position were received. A screening panel is being established to review the nominations. The screening panel will meet within the next few weeks and make its recommendation to the Commission.

Scheduling of Next Commission Briefing: The ACMUI bylaws state that the Committee will provide an annual Commission briefing in the first or second quarter of each year. Dr. Siegel indicated that, since a briefing had just been given in October, he preferred to delay the next Commission briefing until after the May 1995 meeting. Giving the briefing in conjunction with the annual medical-program briefing by the NRC staff appeared to be quite effective this year. Dr. Paperiello indicated that he had no objections to continuing this dual effort. The staff will consult with the Office of the Secretary to determine whether this is acceptable.

Dr. Glenn officially closed the meeting at 12:06 p.m.

Barry A. Siegel M.D.
Barry A. Siegel, M.D., Chairman

12/21/94
Date