

## Proceedings from the International Radiopharmaceutical Education Consortium Workshop

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This supplementary issue of JPPS presents the deliberations of an international group of radiopharmaceutical scientists with academic, clinical and industrial backgrounds. Their common goal was to provide a philosophical basis from which a distance-learning template could be implemented. The end product of this exercise would be a multi-institutional distance-based didactic resource in the radiopharmaceutical sciences. This material would include both virtual classroom and laboratory settings in which the students could gain expertise in the practice of radiopharmacy. This computer database would also be designed to maximize the use of other resources available on the Internet. The magnitude of this project is such that an international expert collaboration is necessary in order to complete it in a timely, comprehensive and cost-effective way.

### Acknowledgements

We wish to thank the 21 delegates from 7 countries who attended the Workshop. Technical support was provided by scientific and technical members of the Tübingen PET Centre, and secretarial support was provided by Ms. Conny Daiker and Mr. Hans Jörg Rahm. We would also like to thank the management of the Hotel Germania in Bühl for their warm hospitality.

### Delegates

Hans-Jürgen Machulla (Germany); Georg Becker (Germany); Clyde Cole (United States); Peter Cox (Netherlands); Kara Duncan (United States); Peter Eu (Australia); Daniela Gündisch (Germany); Akli Hammadi (France); Bernd Johannsen (Germany); David Laven (United States); Steve J Mather (United Kingdom); Steve A McQuarrie (Canada); John Mercer, (Canada); Hans Jörg Rahm (Germany); Gerald Reischl (Germany); Frank Rösch (Germany); Stan Shaw (United States); Gerrit Westera (Switzerland); Leonard Wiebe Canada); Wolfgang Wiegrebe (Germany).

### Preface

H-Jürgen Machulla and Leonard I. Wiebe

The concept of developing computer-based resources to support didactic teaching of the radiopharmaceutical sciences outlined in this document originated from discussions among Prof. Peter Cox (Daniel den Hoed Clinic, Netherlands), Prof. Stan Shaw (Purdue U, USA) and Prof. Len Wiebe (U. Alberta, Canada) during recent international symposia<sup>1</sup>. Prof. Shaw visited

the University of Alberta in September, 1998, to explore methods of adapting and updating Purdue's nuclear pharmacy 'video-tape course material'. The Alberta group (Drs. McQuarrie, Mercer and Wiebe) consequently pursued the development of 'Web-based' tools in late 1998, focusing on presentation through a teaching platform called WebCT™. In 1999, Mr. Peter Eu (Peter MacCallum Cancer Institute, Australia) and Prof. Jürgen Machulla (U. Tübingen, Germany) joined this initiative, and by mid-1999, McQuarrie and Mercer had up-loaded a substantial amount of course material onto the WebCT™ platform<sup>2</sup>, including a virtual laboratory exercise<sup>3</sup> developed using Authorware (version 4, Macromedia Inc.).

At the time the Workshop was beginning to take shape, several independent international initiatives to develop Web- and/or CD-ROM - based course materials for teaching radiopharmacy and radiopharmaceutical chemistry were being planned or actively pursued by other groups. Discussions<sup>4</sup> among Cox, Machulla and Wiebe focused on pulling together an international working group to develop a comprehensive teaching 'database'.

<sup>1</sup> *Int. Symp. on Modern Trends in Radiopharmaceuticals for Diagnosis and Therapy*. IAEA Symp. Lisbon, Portugal, Mar 1998; *9<sup>th</sup> Europ. Symp. Radiopharm. Radiopharmaceuticals*, Lillehammer, Norway Mar 1999.

<sup>2</sup> J.R. Mercer and S.A. McQuarrie: Basic nuclear concepts, used in Pharmacy 443 (undergraduate course in radiopharmacy) and Pharmacy 601 (graduate course in tracer methodology).

<sup>3</sup> S.A. McQuarrie and J. R. Mercer: A Virtual GM Lab – Part 1: Half-life Determination.

<sup>4</sup> Eberhard-Karls Universität, Tübingen, Germany, 16 February 2000.

It was envisaged that materials to be included in the proposed database would eventually cover the full gamut of radiopharmaceutical sciences and selected clinical nuclear medicine materials, using didactic text with interactive graphics (including demonstration video clips), virtual interactive experiments, self-administered learning evaluation and testing capability, and on-line or e-mail access to international teaching faculty. Furthermore, although this material would in itself not constitute a formal course for practice licensing, it would be comprised of units which an instructor could 'bundle' to meet a given set of criteria. Each unit would contain didactic material presented in a standardized manner and on a common platform, utilizing either the Web and/or CD-ROM. Bundled database units would be accessible to subscribers (instructors, students, Institutions) on a license or user fee-basis, much as electronic textbooks are available on the Web today.

Initial objectives of the Workshop were to:

- develop a consensus for database content and associated publications,
- integrate available resources already developed by stakeholders, and
- assign responsibilities for the development or refinement of major subject-content units to Workshop delegates, based on their resources, enthusiasm and ability to provide materials within a specified timeframe.

The Workshop's opening 'working paper' (McQuarrie, Mercer and Wiebe) served as a basis upon which to develop the rationale and program for the 'Radiopharmaceutical Sciences Database Workshop'. Approximately 20 educator-scientists were invited to participate in the Workshop, ensuring broad subject coverage and regional input, yet limiting the group size so that productivity would be emphasized. The format chosen to achieve these goals included a review of the objectives of the exercise, and superficial examination of database content. Presentations of 'works in progress' by Workshop participants, followed by a break-out session to develop themes (theme groups), preceded the establishment of working interest groups (management, technology and content). Reports from each of these interest groups provided the basis for construction of a timetable for 'deliverables', and the identification of dates and venue(s) for future meetings.

## 1 INTRODUCTION: COMPUTER-BASED RESOURCES FOR THE RADIOPHARMACEUTICAL SCIENCES

*Leonard I. Wiebe*

This Workshop was convened by Professor Machulla, Tübingen University, with the encouragement and support of several members of the international radiopharmaceutical sciences community. The objectives are 1) to determine the level of support from within the community to develop a modern, computer-based knowledge base for both training and upgrading personnel engaged professionally in the field of radiopharmaceutical sciences, and 2) to establish working groups to develop issues of management, content and selection of electronic medium. These important questions must be addressed in order to rationalize a concerted, multi-national approach to this challenge.

The first question is 'why?'. There are several reasons to consider a computer-based data resource, including convenience and accessibility for both the educator and the student. In addition, computer material can be readily 'layered' to provide stepwise grading from the simple presentation of a subject, through to the most advanced level. This material can also be presented in dynamic fashion, not only creating interest for the student, but enabling the student to undertake a number of 'virtual' exercises such as the 'G-M lab' that has been developed by Drs. Mercer and McQuarrie (U. Alberta). Additionally, the tasks of editing and upgrading for both accuracy and currency are facile, compared to such changes to a hard-copy document. Finally, by working as a group, participants in the program would benefit from each others contributions and at the same time ensure that the materials would meet their own exacting standards of quality and detail.

**Who** would be the target audience? This material could be presented in a modular fashion with respect to both subject material and depth of knowledge within each subject module. As such, the material would be useful for not only radiopharmacists and radiochemists, but also for technical staff and medical staff. Furthermore, material could be selected from this modular database to meet the didactic needs for any interest group, be it an academic user preparing a 'credit' course' in a University or Technical School, or a professional /regulatory body offering courses for (practice) licensure.

**What** resources would be required? Clearly, the intellectual resources necessary to create a base of material (content) and a storage/distribution modality (platform) already lie within the assembled group, or are available for recruitment as deemed necessary. Questions such as internet *versus* CD-ROM, server site locations, access to programs (pass-word/license), and the development of teaching utilities (e.g. WebCT™ grading/record keeping/student chat rooms, etc.) associated with modules of the database, would need to be clarified.

**How** could this be achieved? The first step would be to establish a management structure to ensure orderly progression towards clearly identified goals. As an initial proposal, members of the Workshop could choose to join management, content or platform groups, to establish a temporary framework through which detailed tasks were to be identified and executed. Internal focus, together with adequate information exchange among these working groups allowed a plan to be developed, even within the short period that this Workshop was in session.

What are the **Workshop deliverables**? The establishment of a management structure, followed by initial discussions on organization, content and platform would form the basis for a *Planning Guide for the Development of Computer-based Resources for (teaching in) the Radiopharmaceutical Sciences*. It would seem appropriate for this Guide to be produced either in hard copy or in an accessible Internet file.

## 2 PRELIMINARY WORKSHOP AGENDA

**General themes** (Chair: L. I. Wiebe)

- H-J Machulla (Germany) and L. I. Wiebe (Canada): Statement of Workshop objectives and philosophy.
- S. Mather (UK): International market; issues of languages and national jurisdictions.
- D. Laven (USA): Target groups, including pharmacists, radiochemists, research support staff, technical support staff and others.
- S. Shaw (USA): Users of didactic database materials - undergraduate and postgraduate (degree) programs in universities, professional societies (post-degree certification), government regulatory/licensing bodies (post-degree certification), and industry.
- C. Coles (USA): Joint venture issues - ownership & copyright, rights to utilization, cost to users.
- P. Cox (Netherlands): Target venues, including University degree credit, University certification and certification by societies and government authorities.
- S. McQuarrie (Canada): Web-based Platforms - Java/C+, WebCT and others.

### Current status of training programs (Chair: J. Mercer)

- S. McQuarrie and J. Mercer - Canada
- P. Eu - Australasia
- S. Mather (UK) and G. Westera (Switzerland) - Europe
- S. Shaw and K. Duncan - USA

### Breakout interest groups

Three groups were organized, with membership by personal preference.

1. Scope and content of course materials (Secretary: J. Mercer). This group addressed definition of goals, assigning responsibilities for topics, graphics and publications, reviewing and editing, regional specialization and translations.
2. Media / platforms / software / hard copy (Secretary: S. Mather).
3. Identifying and contacting the audience, defining the scientific and industry stakeholders (Secretary: C. Coles).

## 3 CURRENT PROGRAMS AND STATUS

### 3.1 A European Post-Graduate Specialisation In Radiopharmacy

*Stephen J Mather, Imperial Cancer Research Fund, Dept. Nuclear Medicine, St. Bartholomen's Hospital, London, Great Britain*

- The EANM Radiopharmacy Committee has been working towards the establishment of a Europe-wide qualification in Radiopharmacy to help:
  1. set and maintain standards in the radiopharmaceutical sciences,
  2. provide a career structure for radiopharmaceutical scientists, and
  3. facilitate freedom of movement around the continent.

Under the auspices of the European School of Nuclear Medicine (ESNM), and in collaboration with several European Universities and Institutes, the Radiopharmacy Committee of the European Association of Nuclear Medicine (EANM) has established a European post-graduate specialisation certificate in Radiopharmacy. This certificate may be awarded to students, who, in the view of the ESNM Radiopharmacy Board, are suitably qualified, in that they have:

- a) acquired a university postgraduate diploma or attended other equivalent courses teaching the *theoretical* components of the radiopharmacy syllabus,
- b) completed a three-year period of experience during which they have completed the *practical* components of the syllabus,
- c) completed a nationally acceptable course on radiation hygiene.

### ***Status of the Certificate***

Award of this certificate means that, in the view of the EANM, the individual has acquired the theoretical knowledge and practical experience needed for them to assume responsibility for the small-scale production and quality control of radiopharmaceuticals. At the present time, this qualification carries no legal status but it is the hope of the Association that it will, in time, be recognised by the European Union and its member states as the appropriate qualification for those individuals managing radiopharmacy departments.

### ***Mechanism for award of the Certificate***

Students who have completed requirements (a - c) above and who wish to apply for the certificate should write to the Chairman of the ESNM Radiopharmacy Board enclosing the following documentary evidence of their studies and practical experience:

- certificates of attendance at the relevant courses
- a check list indicating when and where they have gained practical experience
- signed letters from the heads of departments in which they have gained this experience confirming this to be the case.

The Board will review the documents and, if they are found to be acceptable, then the Board will recommend the award of the certificate to the Dean of the European School of Nuclear Medicine. If necessary, arrangements will be made for the student to sit a

Board examination paper at a mutually convenient time and place.

### ***Radiopharmacy Courses***

In order to simplify the organisation of courses that teach the syllabus for this qualification, it has been divided into three modules or Blocks:

Block 1: Pharmacy;

Block 2: Radiopharmaceutical chemistry;

Block 3: Associated subjects.

At the present time the following courses have been presented or are planned:

- INSTN, Paris, (Block 2): November 2000
- ETH Zürich (Block 2): 19th Feb. - 2nd March 2001
- INSTN, Paris, (Block 3): spring 2001
- University of Frankfurt (Block 1): autumn 2001
- University of Leipzig (Block 3): spring 2002

### ***3.2 Purdue University Nuclear Pharmacy Training Programs***

*Kara Duncan, Purdue University, West Lafayette, Indiana, USA*

The Purdue University Nuclear Pharmacy Certificate Program (NPCP) was developed as a tool for training pharmacists for the practice of Nuclear Pharmacy. The program is a two-part training tool consisting of a videotape based distance-learning module as well as an intensive two-week on-campus session. The certificate program is designed to provide the fundamental background concepts essential to nuclear pharmacy practice. The NPCP, along with the undergraduate training program, the graduate research program and an advanced clinical clerkship for Pharm.D. students are integrated to meet the core nuclear education goals established by our department.

As part of the current revision process, the original program is being modified to better reflect present day practice and enhance the clinical skills necessary for daily practice in a nuclear pharmacy. The videotape portion of the program is being converted to a digital format to allow for current use as high quality video-

tape or for future modification to computer based or internet based delivery as technologic advances permit. The videotape material itself is being enhanced using digital editing techniques, digital graphics and practical real world examples. Clinical cases are used to supplement the learning process, as are practical lab scenarios.

With this revision, the Nuclear Pharmacy Certificate Program is moving toward the use of more technologically advanced teaching methods. In addition to the update of the videotaped material, the inclusion of internet based teaching resources like WebCT™ allow the students to more easily participate in the distance learning program. Internet testing with instant feedback has been established, as well as on-line chat rooms and discussion forums, all of which are designed to allow our trainees to interact easily with the faculty at Purdue, as well as with other trainees in the program. The site can also be used as a reference source and as a forum for future learning opportunities after the trainees have completed the program.

As a result of our current revision plans, the development of an internet-based database will lend itself well to incorporation in our program. The material developed will supplement our training process in an easily accessible manner. Together, the two formats can be used to greatly enhance the training of nuclear pharmacists.

### 3.3 Radiopharmaceutical Compounding and Dispensing in Australia

*Peter Eu, Peter MacCallum Cancer Institute, Melbourne, Australia*

The radiopharmaceutical regulatory affairs of Australia are governed by the Therapeutic Administration Act (TGA), which allows some professionals to compound and dispense radiopharmaceuticals under certain conditions. These professionals must have appropriate licenses to handle radioactive materials.

Nuclear Medicine Physicians are allowed to compound and dispense radiopharmaceuticals in their practice. For accreditation as a Nuclear Medicine Physician, the physician has to complete basic courses in the nuclear medicine sciences, including radiopharmacy. This radiopharmacy course is provided by the Australian

Nuclear Science and Technology Organization (ANSTO). It has a modular format that is taught on site, but course notes are provided before attendance at the course. Each module has prescribed learning outcomes, and the trainee is assessed by tests that include written short answer questions and multiple-choice questions. The Nuclear Medicine Physician trainee must receive practical training in an accredited Department and this training must involve the trainee in routine radiopharmacy procedures including quality assurance. The training Department is also required to have access to a radiopharmacist or radiochemist to discuss radiopharmaceutical sciences.

Nuclear Medicine Technologists are allowed to compound and dispense radiopharmaceuticals under the direct supervision of a Nuclear Medicine Physician. These technologists are usually taught Radiopharmacy practices for one and a half years in their senior years at a technical school. They then have to take a one-year internship post graduation in which radiopharmacy practice is part of the program.

Pharmacists are allowed to compound and dispense radiopharmaceuticals throughout Australia, depending on the conditions under which they practice. There is a very limited introduction to radiopharmacy in the undergraduate programs of pharmacy degree programs. Training to be a radiopharmacist can be obtained either on the job, or through a postgraduate certificate in radiopharmacy that is jointly offered by the Victorian College of Pharmacy, Monash University and the Society of Hospital Pharmacists of Australia. This certificate course is conducted via distance learning with tutorials and a minimum of two weeks full time residential practice at an approved radiopharmacy site.

Radiochemists are also allowed to compound and dispense radiopharmaceuticals in public hospitals within their State or Territory of practice. Their education in radiopharmacy can be obtained on the job or through the ANSTO course.

Other professions such as biomedical engineers and health physicists may be allowed to compound and dispense radiopharmaceuticals, depending on the circumstances of the facility in which they are employed. Their education and training are usually obtained on

the job and through courses offered by institutions such as ANSTO.

Several Universities in Australia are developing post-graduate courses leading to certificates, diplomas, and Master of Applied Science degrees, all with specialization in Medical Radiation Science and with Radiopharmacy as a major subject. These courses may not necessarily be involved with any pharmacy school at present. As the sciences component in radiopharmacy practice does not change anywhere in the world, a common background teaching course in radiopharmacy such as the one proposed in this workshop would be of value to the radiopharmacy practitioners including physicians, pharmacists, and nuclear medicine technologists in Australia. This will not only allow the principles of radiopharmaceutical sciences to be uniformly taught to the intending practitioners, but also serve as a reference resource to the current practitioners and interested professionals.

### 3.4 Radiopharmacy Training at the University of Alberta

*John Mercer, Steve McQuarrie and Len Wiebe, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta, Canada*

A high percentage of the senior practicing radiopharmacists in Canada were trained at the University of Alberta. The historical basis for this fact rests on more than three decades of radiopharmaceutical research in the Faculty of Pharmacy and Pharmaceutical Sciences at the University of Alberta. This provided an infrastructure and a highly trained and experienced faculty for student instruction. The faculty has had isotope production facilities, first through the installation of a Cockcroft-Walton Accelerator and later with the commissioning of a research reactor. This capability will be enhanced within the next year with the opening of a cyclotron/PET center at the University.

The core of radiopharmacist training is provided by a series of undergraduate and graduate courses offered in the Faculty of Pharmacy and Pharmaceutical Sciences. These include introductory and advanced radiopharmaceutical sciences, radiation biology, radiopharmaceutical chemistry and specialized courses in neutron activation as well as individualized research projects.

Internship training in Edmonton has been provided in conjunction with the Edmonton Radiopharmaceutical Center which is a centralized production facility providing products to local hospitals. The radiopharmacists graduate at the Masters of Science (M.Sc.) level with mentoring by established researchers and involvement with peer reviewed research projects. Many have achieved Ph.D. degrees with additional course and research work.

We have tested the concept of distance learning in a graduate course on radiotracer methodology in 1999, where a section of lectures on the physics of radioactive decay were provided over the Internet. A detailed description of this pilot project is discussed in Section 5.

## 4 TARGET GROUPS FOR COMPUTER/INTERNET-BASED, RADIOPHARMACY-ORIENTED COURSE MATERIALS (THE UNITED STATES PERSPECTIVE)

*David L. Laven, University of Kansas, Kansas City, Kansas, USA*

When considering radiopharmacy-oriented educational content for identified "target groups" (pharmacists, radiochemists, supportive personnel in clinical and research settings, etc.), we can prepare a basic core group outline of topic areas. Additionally, we can also develop the content of these topic areas with sufficient depth so as to meet the needs of more than one professional discipline. In terms of providing a "basic" knowledge base with global rather than limited applicability we must;

- provide information in such a way that individuals select those items they deem applicable to their respective professional areas of interest, or develop topic areas with varying degrees of depth so that a professional with extended content requirements will have all the information laid out before them.
- be aware of the "regulatory" attitudes that exists in various regions of the world.
- take into consideration any unique expectations in terms of education and training that must be satisfied.

The present faculty of the International Radiopharmaceutical Education Consortium (IREC) has the expertise to create a programme of instruction that will meet the varying needs of professionals regardless of where they reside and practice.

We will have the distinct opportunity to provide a harmonized approach to nuclear pharmacy education and training to various groups and organizations, academic and regulatory in nature. There are regions of the world where established expectations and requirements for nuclear pharmacy education and training already exist, and there will be others that are in more formative stage of development.

### *Nuclear Pharmacists and their Training*

In the United States many pharmacy students participate in a 6-year program that culminates in receiving a Doctor of Pharmacy degree (Pharm.D.) Formerly, a pharmacy student would participate in a 5-year program and earn a Bachelor of Science (B.S.) degree. The major difference between the Pharm.D. program and the conventional 5 year Bachelor of Science (B.Sc.) degree is an additional year of rotational "clerkship" learning experiences (non-paid, applied clinical) where pharmacy students spend one-month intervals in clinical areas such as internal medicine, pediatrics, geriatrics, oncology, drug information, and sometimes nuclear pharmacy. Internships, on the other hand, are often on-site training experiences (paid positions) that occur in one professional setting over longer periods of time (i.e. months) during a summer recess in-between academic years, or as an evening position during the school year. Typically, in 6-years of "traditional" didactic education in a pharmacy school, a student would encounter only 4 to 6 contact hours in nuclear pharmacy. During the upwards of 2000 contact hours of practical professional experience the trainee may receive only a one-month (approximately 160 hours) experience in a nuclear pharmacy setting. This is hardly a sufficient platform upon which to expect any pharmacy student to demonstrate a suitable appreciation for or interest in nuclear pharmacy.

In the United States there are a few pharmacy schools that offer expanded didactic and experiential opportunities in nuclear pharmacy. This is in part to satisfy the U.S. Nuclear Regulatory Commission (or individual state offices of radiation control) which requires any individual who handles and uses by-product (radioactive) materials to have completed 200-contact hours of didactic training and 500 hours of experiential training in nuclear pharmacy. Some of these extended programs exist at schools associated with the Universities of

Arkansas, Butler, Duquesne, Massachusetts, New Mexico, Ohio State, Purdue, and Temple. The number of students that matriculate from these programs may total no more than 50 to 60 individuals per year. There are at present only two post-graduate programs (the Medical University of South Carolina, and the U.S. Army) that offer a one-year residency or fellowship in nuclear pharmacy and they provide an additional 3 to 5 trained individuals per year. Few of the individuals participating in these nuclear pharmacy programs continue their studies to receive a Masters of Science (M.Sc.) or doctorate (Ph.D.) degree. Consequently, as academicians that are more senior approach retirement, the question of where to find qualified educators to replace them looms ever greater.

A booklet that contains a compilation of documents and articles pertinent to nuclear pharmacy education and training from various regions of the world has been circulated at this Workshop. These items can serve as a guide in our ensuing discussions and project development efforts for considering what already exists (or is being discussed – "draft form") in terms of nuclear pharmacy education and training, from an academic, professional (practice guidelines), and regulatory perspective. Many of these documents highlight issues that will be important to the planned effort. (Editor's note: these documents can be obtained by writing to Dr. Laven). One of these documents, entitled Nuclear Pharmacy Practice Guidelines, serves as the basis for the development of testing for Board-certification (and then re-certification 7 years later) in Nuclear Pharmacy by the Specialty Council on Nuclear Pharmacy of the Board of Pharmaceutical Sciences (BPS). In 1978, Nuclear Pharmacy was the first area recognized as a "specialty" in pharmacy by the Board of Pharmaceutical Specialties.

Another document, entitled Syllabus on Nuclear Pharmacy Training<sup>5</sup>, serves as a blueprint for developing the didactic and experiential content. Other documents, including the (proposed) Nuclear Pharmacy Compounding Guidelines<sup>5</sup>, serve as guidelines for addressing more specific topic areas in nuclear pharmacy.

<sup>5</sup> Contact David Laven for source documents.

In the United States before a pharmacy student can sit for the National Pharmacy Licensing Examination (NAPLEX), they must document having participated in 2000 hours of experiential training in recognized areas of pharmacy practice. Many state boards of pharmacy do not recognize undergraduate experiences in nuclear pharmacy as constituting acceptable pre-professional experience. Therefore they do not count towards the contact hours needed to sit for the NAPLEX. Out of the several hundred questions contained on the NAPLEX, there may be only 1 or 2 that address any issue relative to nuclear pharmacy practice and therefore most pharmacy schools and state boards of pharmacy view nuclear pharmacy as an area that is reserved for postgraduate learning situations.

Although several pharmacy schools continue to offer undergraduate programs for their students in nuclear pharmacy it has become fashionable and necessary to make available short-course, certificate-training programs in nuclear pharmacy. These programs range from 6-weeks to a few months and can be completed via on-site or through correspondence, home-study, or a combination of the two approaches. These programs are available to pharmacy students who attend schools where opportunity in nuclear pharmacy education doesn't exist, and help to re-train existing practicing pharmacists who desire a career change and enter nuclear pharmacy. Presently, Duquesne, Ohio State, and Purdue pharmacy schools offer a certificate-training program. Syncor International operates its own corporate short-course program which is accredited via liaison with Butler University.

### *Training Nuclear Pharmacy Technicians*

At present, basic training programs for pharmacy technicians are available through local (2-year) community or junior colleges or business-vocational schools, but none have any direct ties to existing pharmacy school programs. Additionally, there is no pharmacy technician training program today in the United States that can prepare an individual for a career in nuclear pharmacy. On-the-job training has been common in many pharmacy settings over the years, but this approach is falling from favor in order to stress more formal, structured educational approaches. There is obviously an opportunity for a well-prepared, broad ranging and structured education program to fill this void in

nuclear pharmacy technician training. For this reason, the project that we are undertaking, to develop a virtual, internet education program and text in nuclear pharmacy, becomes all that much more important. In fact, when one considers both the short- and long-term goals, this is an undertaking that will surely achieve critical acclaim.

### *Training Academic and Research Specialists*

The academic and research specialists who currently deal with the field of "nuclear pharmacy" or "radiopharmacy" are in general recruits from allied disciplines. They will have received a combination of formal and informal training and self-education in radiopharmaceutical sciences in order to reach their specialist status. These individuals have a wide diversity of backgrounds including pharmacy, chemistry, physics, medicine and biological sciences. Although a few universities may have the ability to provide this specialist training in radiopharmacy it is in general acquired in a less formal manner. This situation presents both an opportunity and a challenge since it should be possible to generate a database with sufficient content to meet the educational needs of technical personnel and also pharmacists, radiochemists, and perhaps even physicians who desire to specialize in the radiological sciences. In the end, the scope of this project could be broad enough to meet the needs of many different professional "target groups" the world over.

## **5 DEVELOPMENT OF A COURSE MATERIALS DATABASE TO SUPPORT RADIOPHARMACEUTICAL SCIENCE TRAINING**

*Steve McQuarrie, John Mercer and Len Wiebe, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta, Canada*

The information and demonstration module presented at the Tübingen-Bühl Workshop on Teaching Radiopharmacy was taken from the didactic radiopharmacy training program at the University of Alberta. One goal of this module was to provide a distance-based learning component to both undergraduate and graduate level course offerings. By providing some of the lectures in this manner, class time was made available for other uses such as a problem-based learning segment in which the students would tackle real-world problems using information received from our Internet material. This approach was tested in a graduate course on

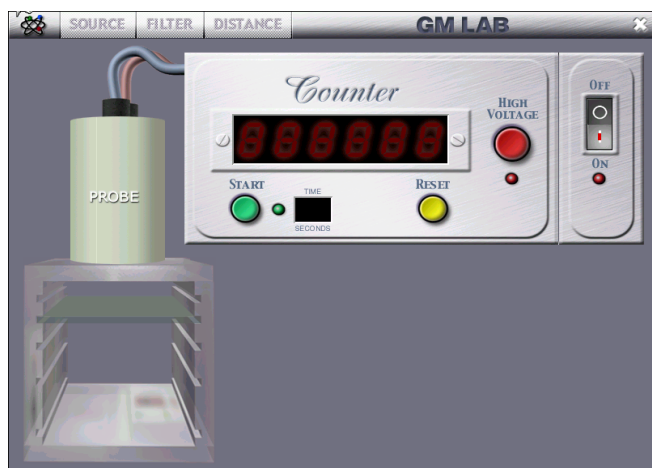
radiotracer methodology in 1999, where a section of lectures on the physics of radioactive decay were provided over the Internet.

Following consultations with the computer science group the University of Alberta, the software package, WebCT™, was selected as the host program to contain and manage our material. In addition to providing a mechanism to deliver text-based information, WebCT™ facilitates:

- inclusion in the text of figures, hot-links to internal/external web sites, animation and video,
- chat rooms for student-student and student-instructor discussions,
- assignment and automatic marking of problem sets and exams,
- maintenance of student records, and
- the capacity to perform virtual lab experiments.

A PowerPoint presentation may be viewed as a demonstration of the operation of our distance-learning approach.

[www.ualberta.ca/~csp/JPPS4\(2\)/S.McQuarrie/RadiopharmacyOnTheWeb.htm](http://www.ualberta.ca/~csp/JPPS4(2)/S.McQuarrie/RadiopharmacyOnTheWeb.htm)



**Figure 1: Graphical interface for the virtual GM lab.**

As part of this program, a virtual laboratory exercise was designed using Authorware™ (Macromedia). This lab involved the half-life determination of several unknown radionuclides, using a GM counter. All components were designed by a graphic artist under our direction to provide a life-like experience, including a “lab cleanup”. Help files were included to direct the student in the operation of the virtual detector, and outlined a set of experiments to be performed. A compressed time system was used to speed up data acquisition,

and student-selectable time points were used to collect activity data far into the future to determine half-lives of long-lived radionuclides, such as C-14. The graphic interface for this virtual lab is depicted in Figure 1. Readers interested in this program are referred to Steve McQuarrie. [smcquarrie@pharmacy.ualberta.ca](mailto:smcquarrie@pharmacy.ualberta.ca)

## 6 COPYRIGHT ISSUES IN DEVELOPING PUBLICLY-ACCESSIBLE COURSE MATERIALS

*Clyde Cole, Amersham, USA*

The International Radiopharmaceutical Education Consortium (IREC) proposed to develop educational programs that would provide consistency within the area of radiopharmaceutical education and training for interested individuals. IREC agreed on the program in principle. Questions then arose about protecting the intellectual property of the worldwide experts that composed IREC and the programs that were being developed. Investigation of the subject provided almost as many questions as it did answers. Discussion explored the aspect of protection of created programs and property with the idea in mind that the material would be available on the worldwide web.

### Copyright

Copyright protection generally means that certain uses of the work are lawful only if they are done with the authorization of the owner of the copyright. Included in the protection is the right to copy or otherwise reproduce any kind of work. “In the United States Constitution, copyright was intended as an incentive for scientific, artistic or other creative achievement. It allows the author of a work to retain the sole rights to copy or distribute that work for a certain period of time”<sup>6</sup>. The intent of the Copyright was not to restrict access to these works. The idea behind copyright was to allow authors retention of the rights to their work; hopefully stimulating them to create more works thereby increasing their creative effort.

“Existing copyright law recognizes the tension between the needs of society and the rights of creators by permitting a defense against charges of infringement for certain uses of copyrighted works as specified in sections 107-110 of the U.S. Copyright act of 1976. Among these uses are: the **fair use** of copyrighted

<sup>6</sup> Pfaff-Harris, K, Copyright issues on the Web (I-TESL-J)

works for teaching, scholarship or research, among other activities; the reproduction of copyrighted works by libraries and archives under certain conditions for specific purposes; and the performance or display of a work by instructors or pupils in the course of face-to-face instruction".<sup>7</sup>

It is generally accepted that for whatever purpose you are using the "copyrighted" information, you should get permission from the author if for no other reason than professional courtesy. Permission is considered essential.

Laws from "state to state", meaning political entities, vary significantly. In an effort to bring some consistency to the process and hopefully develop and maintain the protection of rights of authors, the World Intellectual Property Organization, WIPO, has amassed significant information pertaining to the subject of copyrighting. They have available on their website, the entire text of the "WIPO Copyright Treaty and the agreed statements of the Diplomatic Conference that adopted the Treaty and the provisions of the Bern Convention (1971) referred to in the Treaty (WIPO Copyright Treaty) (1996)".

### ***Copyright Registration***

The US Copyright Act protects the material created as soon as it is reduced to a tangible form. It is unnecessary to register. What registration does, however, is allow the creator the chance to 1) sue for damages; and 2) recover statutory damages. Even the fact that your work is protected upon fixation, you cannot sue someone until the work is registered with the Copyright office. Additionally if registration is done within 3 months of the first date of publication, or prior to the date of infringement, statutory damages can be collected. Should there be no registration only actual damages can be collected. Statutory damages can be awarded up to \$100,000 plus attorney fees and court costs.

Copyrighting essentially provides proprietary protection. Within that framework are several parameters including, but not limited to; cost to users, utilization rights and ownership. One of the problems with elec-

tronic availability is the ease with which an individual can plagiarize the original work.

Pfaff-Harris also points out "Many web browsers automatically copy every page to a cache on the user's hard drive, thus technically violating copyright. (The US has tentatively decided that this is not a violation of copyright, but that printing or 'WebWhacking' a site may be.) In general, viewing a website or printing a page from the site is acceptable, as long as the author is credited with the work".<sup>8</sup>

Plagiarism, the taking of someone's work and submitting as your own, is an easy project for the less than ambitious student and many times difficult to detect. Frequently the intent is to borrow a phrase or two or a paragraph or two and meld them into the treatise. What in fact happens is that more than the one or two paragraphs or statements are plagiarized and, in some cases whole pages and even documents, are incorporated without reference or permission.

Julie J.C.H Ryan, in her article "Student Plagiarism in an Online World"<sup>9</sup> addresses the fact that "Before the world was linked by the Internet, hard-to-detect plagiarism required ingenuity and skill. But today, with the click of a mouse, even technologically inept students have access to vast information resources in cyberspace without having to leave the comfort of their dorm rooms". She also notes "A few words typed into a Web search engine can lead a student to hundreds, sometimes even thousands, of relevant documents, making it easy to 'cut and paste' a few paragraphs from here and a few more from there until the student has an entire paper-length collection. Or a student can find a research paper published in one of the hundreds of new journals that have gone online over the past few years, copy the entire text, turn it into a new document, and then offer it up as an original work without having to type anything but a cover page. Even recycling efforts and ghost writers have gone global, with Web sites offering professionally or student-written papers for sale, some even with a money back guarantee against detection".

<sup>7</sup> National Humanities Alliance, Basic Principles for Managing Intellectual Property in the Digital Environment, Mar 1997, www.ninch.cni.org

<sup>8</sup> Pfaff-Harris, K, Copyright issues on the Web (I-TESL-J)

<sup>9</sup> Ryan, Julie, J.C.H, Student Plagiarism in and Online World, www.asee.org/prism/december

There are obviously many questions that arise when considering ownership of intellectual property in general. Those questions are even more complex when the worldwide web is the medium for the dissemination of that property. Among the questions are: Who owns it? How are the owners protected? Who gets the money? Administration and control of the material is essential if the authors are to be compensated for their efforts. Does this require an international license of some sort? Is there even such a license available? Do you need individual country licenses, or possibly a “national collaborative license? How will licensing fees be handled? With whom or where should the copyright be registered?

Utilization rights become an issue when there is a group of international experts responsible for creation of various parts of the program. When that occurs, how are utilization rights determined? How do the collaborators work together without competing when they are agents of separate organizations that naturally compete?

The area of fees raised even more questions. Will there be University fees that would be due to the Universities that many of the IREC participants were associated with? Would “private” user fees be possible to organizations such as independent training schools?

Commercial fees are another consideration as is how much “good will” availability will there be, if any? Further decisions concerning fees are related to how they will be levied. Per unit basis, per hour of use basis, per CE basis, per topic basis? And finally who gets what portion of the fee, or should there be a standardized remuneration?

Many of these questions can only be answered by the organizers, and while the issue of protection seems to be addressed by international organizations (like WIPO), there is still uncertainty in the globalization of that protection.

## 7 COMMITTEES TO BE ESTABLISHED

- Steering (Management) Committee
- Content group
- Technology group
- Finance committee (*to be appointed when appropriate*)

The Working-group should function as an international consortium (IREC). Matters to be discussed and approved relate to:

### *Licensing considerations*

- Fee is for access, payable annually
- License the using organization for the year
- Technology group to address access restriction aspects

### *Consortium composition*

- IREC membership would initially consist of those who were present at the Bühl 2000 Workshop.
- New contributors may be invited to participate.
- Maintain the status quo of the committee for a year and reevaluate at next year's Bühl meeting.
- Fair remuneration for contributors is to be decided by committee.

### *Action*

- Each workgroup is to produce a report on their activities before they leave Bühl. This should be presented as a one-page recapitulation of the committee's progress.
- All presenters were requested to turn in a text based abstract version of presentations and provide the presentation electronically to the recording secretary if possible.
- Participants were requested to provide any comments in electronic form.

## 8 STEERING (MANAGEMENT) COMMITTEE REPORT

Members:

Clyde Cole – Recording Secretary  
 Peter Cox  
 Peter Eu  
 Hans-Jürgen Machulla  
 Gerrit Westera  
 Leonard Wiebe

The committee identified issues important to the advancement of the project.

- Publication of the Workshop proceedings.
- The Management Group nominated Peter Cox to explore the possibilities for funding. The letter of solicitation would reflect sources of funding and

identify those contributed financial, technical and intellectual resources.

- The Technology Group will research and recommend the medium platform to be used for the educational programs. This group will also identify personnel resources to complete the initial phase of development.
- Funding allocation decisions will be made based on the financial resources acquired to fund the committee's short and long-term objectives.
- A number of management issues were identified, including formal recognition of editors and creators of units, the establishment of user-fees and budget planning.

## 9 REPORT OF TECHNOLOGY/MEDIA SUB-COMMITTEE

Members:

Georg Becker  
Kara Duncan  
Steve Mather – Recording Secretary  
Steve McQuarrie  
Hans Jörg Rahm

### *Distribution*

Universally compatible format will be developed to provide easy adaptation to the needs of individual course organisers and end-users.

Learning material will be distributed via a central server mirrored to (4-5) sites throughout the world but controlled through the central server. The need was identified to keep these mirror sites virus free. Likely / possible server sites could be in:

- Canada: Edmonton
- USA: Purdue
- Europe 1: Tübingen
- Europe 2: London
- Pacific: Australia

Individual chapters/sections should also be made available on CD-ROM. A companion workbook could be produced either internally by the group or by an external publisher. Local organisers could produce (electronic) logbooks.

### *Format*

This should be made compatible with current browsers such as Netscape and Internet Explorer. Microsoft "FrontPage" will be the recommended software package. A template will be developed containing:

- Title, subtitle, fonts, background (plain), format for graphs, images, equations and chemical structures, recommended plug-ins

### *Instruction to authors*

Detailed instructions will be developed to reduce the need for editorial input. Material must be supplied in a form compatible with the template. The authors will be encouraged to do as much as possible in terms of web page design. They should also identify topics that require professional graphic design/animation and include further supplementary material, exam questions/problems with answers, and reference/reading material. There will be a suggested limit of two screen lengths to limit the need for scrolling. Authors will have editorial access to final version before release.

### *Features of the material*

Several "core features" were identified to facilitate user interaction with the knowledge database. External data links will be limited to those with non-critical content and guaranteed continued access. Otherwise internal links will be preferred and other web publishers will be approached for permission to download their material. Different coloured text will be used for external and internal links. Printing capability could use PDF format or possibly text (rtf) format and will be included where appropriate. Material will contain a 'Watermark' or other copyright notice. Each topic should also include an email link to authors of that material.

### *Access*

*Security:* Users need to register (non optional) before access will be granted to the databases. Suggested user profiles would include name, password, position, institution (address and phone number) and/or email address.

*Registration:* Benefits will include notification of updates and formal recognition and certification following course completion.

*Access Fees:* Access may be sponsored by a local academic institution or may be purchased on-line. If access fees are a requirement, then a mechanism for charging must be developed.

### Resource Estimates

Some central resources have been identified and the committee recommends that these be located at the University of Alberta (Canada). Required personnel include one person with computer/secretarial skills full time (US \$20K) and 1-2 graphic artists/animators (US \$35K each) at an estimated total cost of US \$100,000/yr.

## 10 COURSE CONTENT SUBCOMMITTEE - INTERIM REPORT 21/JULY/00

### Committee Members:

Daniela Gündisch  
Akli Hammadi  
Bernd Johannsen  
David Laven  
John Mercer (Recording Secretary)  
Gerald Reischl  
Frank Rösch  
Stan Shaw (Chair)  
Wolfgang Wiegrebe

A number of general principals were adopted by the committee to provide a working base for discussion:

- Course material will be suitable for a wide rather than a narrow audience. This would include individuals who would work in a controlled and supervised environment (technicians) and others who would work with a high level of independence (developmental radiochemists and radiopharmacists).
- The content would be focused at an intermediate level of detail and difficulty.
- Additional content would be added to or linked to the intermediate level program to satisfy the needs of more advanced students.
- The requirements of the European and North American users are recognized to be different but overlapping. The European program would be most needed to educate students at a graduate level who had no background in pharmacy but would have a strong science education (chemistry). The North

American program would have the primary focus of educating pharmacists to become radiopharmacists (nuclear pharmacists).

- The majority of didactic material is immediately available from members of the workshop group. This material is in a variety of formats and on a variety of media (WEB based, electronic text, videotape, graphics etc.). The content subcommittee will be guided by the technical subcommittee in the preparation of these materials in a suitable style and format.
- The content subcommittee will rely on all members of the workshop group and not just members of the subcommittee in the preparation and organization of materials.
- Contacts and resources outside of the control of the workshop members will not generally be used in the preparation of course materials unless a clear need is identified.
- The content will include both practical information and theoretical background. This is regarded as important since the intent is to educate scientists as well as technicians.
- Some theoretical aspects of the course will be presented at an elementary level with links or references to more advanced and rigorous information. This allows a varied audience to be accommodated.
- Some topics will be presented in more than one location within the overall course material. This is required if the material is to maintain a modular character. For example a description of the ionizing ability of radiation would occur in a discussion of interaction of radiation with matter and again when the topic of radiation effects on biological systems was considered. In some instances this material could be linked while in others it might have to be organized or presented in a different manner.

The committee agreed to consider the document "Nuclear Pharmacy / Radiopharmacy Training Guidelines" as a starting point for discussion of content. This document outlines suggested content for a course in Nuclear Pharmacy. The material has been examined previously by the International Harmonization in Nuclear Pharmacy Committee on Education. During the subcommittee deliberations of this document a number of changes were suggested and implemented. The document which appears in Section 12 incorpo-

rates these changes and is recommended as the working document to guide the workshop members in the selection and organization of course materials. Several major alterations were incorporated into these guidelines based on the subcommittee discussions:

- An introduction section was added.
- Additional weight was suggested for the radiochemistry section to make it more appropriate for the European requirements.
- A section that deals with legal aspects and guidelines and adherence to regional Pharmacopeia would be added as a final section. This material would necessarily be generic but could be linked to specific national or regional information.
- A section was added which considered in vitro and in vivo analysis of new radiopharmaceuticals and the legislative aspects of bringing a new agent into clinical practice. Again this material would be generic with links to regional specific data.

Further discussion centered on the requirement for additional educational materials for students without formal education in pharmaceutical science. Professor Wiegrebe of Universität Regensburg presented the committee with a document entitled "Supplementary Education of Radiochemists in Pharmacy". This material was accepted as a model for the preparation of a supplementary package of educational material that could be developed to complete a program that would be more comprehensive in the European setting. This material would not be part of the initial development of course content but could be considered once other content has been completed.

#### ***Subcommittee goals:***

##### **Short term: 3 months.**

- Circulation of the detailed table of contents to workshop participants for final evaluation. The table of contents has been modified to conform with the wishes of the subcommittee as identified during the workshop and will be revised if additional issues are identified in the review process.
- Identification of existing resources and assignment of committee and other workshop members to areas of interest or expertise.
- Identification of sections of course material that would be applicable for three levels of users; (techni-

cian, intermediate and scientist).

#### **One-year goal.**

- Detailed preparation of one or more major sections of the required materials based on the format and design provided by the technical subcommittee. The aim will be to produce a module that is complete and adheres to all requirements identified by the technical committee.
- Assignment of responsibilities for further course material development.
- Presentation of a timeline for completion of the preparation of all remaining course materials.

### **11 EUROPEAN RADIOPHARMACY SYLLABUS (THEORY COMPONENTS)**

#### **Block 1:**

##### **Pharmacy**

- Pharmaceutical Technology
- Implications of Good Manufacturing Practice
- Sterile Manufacture
- Pharmaceutical microbiology
- Parenteral Products
- Formulation and Packaging

##### **Pharmaceutical Analysis**

- Pharmacopeial monographs
- Quality Assurance and Product Performance
- Quality Control Procedures
- Stability and Shelf Life
- Regulations and Legal Aspects
- Marketing Authorisations
- Responsibilities of Personnel

#### **Block 2:**

##### **Radiopharmaceutical chemistry**

- History of radiopharmaceutical chemistry
- Physics of radioactivity
- Properties of carrier-free substances, separation techniques
- Production of radionuclides in nuclear reactor and cyclotron
- Targetry, nuclear chemistry, generators
- Synthesis of labelled compounds

- Purity and stability of labelled compounds, radio-nuclidic and radiochemical purity
- Radionuclides in analytics, autoradiography
- The radiotracer principle
- Criteria for radiopharmaceuticals
- Production of radiopharmaceutically relevant radio-nuclides
- $^{99m}\text{Tc}$ -generator
- $^{99m}\text{Tc}$ -radiopharmaceuticals I, basics
- $^{99m}\text{Tc}$ -radiopharmaceuticals I, kit preparation
- Other radiometals
- Radioiodination
- Cell labelling
- PET-radiopharmaceuticals ( $^{18}\text{F}$ ,  $^{11}\text{C}$ ,  $^{13}\text{N}$ ,  $^{15}\text{O}$ )
- Animal models, animal protection regulations
- Radiotracer transport, pharmacokinetics, modeling

### Practical Components of the Radiopharmacy Syllabus

During a three-year period of work in a radiopharmacy department the student should gain a sufficient practical experience in the following areas as to be able to perform these duties independently and to be able to assume responsibility for supervising others undertaking these tasks in the future. If the student's own place of work is not able to provide the full-range of facilities necessary to gain this experience then either they or their supervisor should make arrangements to work for a period of time in another department of Radiopharmacy, Pharmacy or Nuclear Medicine where the necessary resources are available. Students should feel free to contact a member of the Radiopharmacy Board for advice if needed.

- Operation of a GMP facility** that provides full control of the environment, materials, procedures, equipment, and personnel involved in the preparation of radiopharmaceuticals.
  - Working in a sterile environment:**
    - aseptic-technique,
    - monitoring personal technique,
    - monitoring the environment
  - Design and application of a quality assurance programme.**
- Use of safe radiation practices,**
    - procedures for personal dose limitation and monitoring
    - contamination monitoring
    - accidents involving radioactivity
    - local and national regulations and procedures
    - radioactive waste disposal
  - Documentation of radiopharmaceutical procedures:**
    - Information should be provided on standard operating procedures, product and equipment specifications, records of radiopharmaceutical preparation, analysis and other processes.
  - Use, maintenance and calibration of equipment used:**
    - radioisotope calibrator (ionisation chamber): accuracy, constancy, linearity and geometry effects.
    - contamination monitors: efficiency, minimum detectable activity
    - (gamma) scintillation counters: efficiency, resolution, minimum detectable activity, counting statistics
    - liquid scintillation counter: efficiency and counting statistics
    - laminar flow hoods/radioisotope work-stations
    - centrifuges, autoclaves, balances
  - Procurement of radiopharmaceuticals**
    - Types and limits of radionuclide material that can be ordered
    - Ordering radiopharmaceuticals: consideration of purchase orders, suppliers, ordering schedules and times, precalibration times and record keeping, including familiarity with computer procedures.
    - Receipt of radiopharmaceuticals: delivery procedures, trace of delayed shipments, surveys, wipe tests, radioassay, packaging, disposal, storage requirements, and record keeping logs.
  - Radiopharmaceutical preparation:**
    - Elution of a  $^{99}\text{Mo}$ - $^{99m}\text{Tc}$  generator; quality control of eluates.
    - Preparation of  $^{99m}\text{Tc}$  radiopharmaceuticals using 'kits'.
    - Preparation of 'in-house' radiopharmaceuticals (non-kit).

- Labelling of red and white blood cells.
- Protein radio-iodination.
- Preparation of PET radiopharmaceuticals.

#### i) Quality control of radiopharmaceuticals

- Radionuclidic purity using gamma-ray spectroscopy.
- Radiochemical purity using absorption methods, thin-layer chromatography, solid-phase extraction and HPLC methods
- Chemical purity: pH
- Particle size of particulate radiopharmaceuticals: filtration, light microscopy
- Pharmaceutical acceptability: visual inspection, sterility, freedom from endotoxin (Limulus test)

#### j) Supply of radiopharmaceuticals:

Dispensing, labelling, allocation of control numbers and expiry dates, packaging, transport.

#### k) Participation in research and development projects

##### l) Presentation of work at an open scientific meeting

#### m) The student should also gain the following general experience:

- two weeks in a centre preparing PET radiopharmaceuticals or single-photon radiopharmaceuticals if this is not included in their three year experience
- two weeks in a clinical department of Nuclear Medicine including direct handling of patients, operation of imaging equipment, interpretation of images and quantitative data
- one week in a department performing radioimmunoassay

## 12 IREC PROPOSED CURRICULUM

The purpose of these guidelines is to describe basic fundamentals and concepts important to the assurance of quality radiopharmaceutical products and services to patients. The guidelines are relevant to radiochemists as well as nuclear pharmacists engaged in small-scale preparation and quality assurance of radiopharmaceuticals. They are not directed toward a person engaged in research and development of radiopharmaceuticals nor to an individual specializing in services in P.E.T. The knowledge and basic concepts listed may be obtained by formal lecture-laboratory exercises, directed self-

paced study or combinations of these approaches to education.

## INTRODUCTION

- I. History of Radiopharmaceuticals
- II. Radiotracer Principals
- III. Criteria for Selection of Tracers

## RADIATION PHYSICS AND INSTRUMENTATION

- I. Structure and Properties of Atoms
  - A. Atomic Models, Nomenclature
  - B. Nuclides and Radionuclides
    1. isotope, isobars, isotones, isomers
    2. chart of the nuclides
  - C. Orbital Energy Levels
    1. energy units: eV, keV, MeV
    2. electron shell binding energy, excitation and de-excitation
    3. characteristic X-rays, Auger electrons
  - D. Mass and Energy Intraconversion
  - E. Other Nuclear Considerations
- II. Radiation and Radioactive Decay
  - A. Radiation
    1. defined
    2. principal forms
  - B. Nuclear Stability and Radioactive Decay
  - C. Radioactive Decay Law and Equations
  - D. Units of Radioactivity
  - E. Half-life and Decay Constant
  - F. Types of Decay
    1. alpha
    2. negatron (beta minus)
    3. positron (beta plus)
    4. electron capture
    5. isomeric transition
    6. spontaneous fission
  - G. Consideration of Radioactive Decay Processes
    1. disposition of decay energy
    2. beta energy spectrum
    3. neutrinos
    4. beta only *vs.* beta-gamma emission
    5. annihilation reaction

6. characteristic X-rays
7. Auger electrons
8. isomeric transition
9. metastable states
10. internal conversion

### III. Decay Schemes of Radionuclides used in Nuclear Medicine

- A. Chart of the Nuclides
- B. Sequential Decay
- C. Growth of Radioactive Daughters
- D. Transient Equilibrium
- E. Secular Equilibrium

### IV. Interactions of Radiation with Matter

- A. Excitation and Ionization
- B. Positive Particle Interactions
  1. mechanism of excitation and ionization
  2. alpha particle, positron and heavy ion interactions
  3. specific ionization
  4. annihilation radiation
- C. Electron Interactions
  1. excitation and ionization
  2. Bremsstrahlung
- D. Neutron Interactions
- E. Photon Interactions
  1. photoelectric effect
  2. Compton scatter
  3. pair production

### V. Instruments for Radiation Detection and Measurement

- A. Ion Collection Methods (Cutie Pie, Pocket Dosimeters, Proportional Counters, Dose Calibrators, and G-M detectors)
  1. ionization chambers
  2. current-voltage relationships
    - a. simple ionization
    - b. primary and secondary ionization
    - c. proportional region
    - d. Geiger region
    - e. pulse vs. current
    - f. calibration
- B. Scintillation Detectors
  1. principles of operation

2. calibration
3. use
4. quality control
5. external solid crystals
6. internal liquid scintillation
7. pulse height analyzers
  - a. single channel
  - b. multichannel
  - c. gamma cameras, PET cameras

- C. Gamma Cameras, PET Cameras
- D. Film Emulsions
  1. film badges
  2. X-ray, radiological films
  3. autoradiography
- E. Thermoluminescent Detectors
- F. Solid State Detectors

### VI. Nuclear Reactions

- A. Accelerator/Cyclotron Production of Radionuclides
- B. Reactor Production of Radionuclides

## MATHEMATICS OF RADIOACTIVITY USE AND MEASUREMENT

### I. Radioactivity

- A. Radioactive Decay Law and Equations
- B. Units of Radioactivity
  1. traditional
  2. SI
- C. Half-life and Decay Constant
- D. Decay Tables (construction and use)
- E. Nuclear Counting Statistics and Measurement

### II. Health Physics Equations and Use

- A. Inverse Square Law
- B. Half Value Layer
- C. Linear Attenuation Coefficient
- D. Mass Attenuation Coefficient

### III. Radiopharmaceutical Preparation and Dispensing Calculations

- A. Activity
- B. Concentration
- C. Volume
- D. Pre- and Post-calibration Decay Tables

- E. Particle Number
  - F. Expiration Time
  - G. Specific Activity
- IV. Generator Operation and Use
- A. Calculations to Determine Parent Activity over Time
  - B. Calculations Using Transient and Secular Equilibrium Equations to Determine:
    1. daughter activity-time profiles following elution
    2. theoretical yields
    3. elution efficiency
    4. parent-daughter-granddaughter nuclide cascade
- V. Calculations Involved with Radioactivity Measurement and Counting Statistics
- A. Accuracy, Precision and Percentage Error of Radiopharmaceutical Dosage
  - B. Mean, Standard Deviation, Probable Error
  - C. Background Correction
  - D. Geometry Correction
- VI. Quality Assurance Calculations
- A. Radionuclidic, Radiochemical and Chemical Purity of Radiopharmaceuticals
  - B. Dose Calibrator Accuracy, Constancy, Linearity and Geometry
  - C. Scintillation Counter
    1. efficiency
    2. dead time
    3. resolving time
    4. precision
    5. minimum and maximum detectable activity
- VIII. Calculations Associated with the Quantitative Assessment of Radiopharmaceutical Absorption, Distribution, Metabolism and Excretion
- A. *In vivo* Function Studies
  - B. *In vitro* Studies
  - C. Kinetic Studies
- IX. Calculations Involved with Medical Decisions
- A. Sensitivity
  - B. Specificity

- C. Accuracy
  - D. Predictive Diagnostic Value
- X. Radiation Dosimetry Calculations
- A. MIRD Equation
  - B. Internal Dose Equivalents
  - C. External Dose
  - D. Bioassay

## RADIATION PROTECTION AND REGULATIONS

- I. Interactions of Radiation with Matter
- A. Excitation, Ionization, Energy Deposition
  - B. Specific Ionization; Linear Energy Transfer (LET)
    1. comparison of gamma radiation and particulate radiation
    2. range in matter
    3. relative hazard as external and internal sources
- II. Units of Radiation Measurement
- A. Roentgen (R)
  - B. Radiation Absorbed Dose (RAD)
  - C. Gray (Gy)
  - D. Radiation Biological Equivalent (RBE)
  - E. Radiation Equivalent Man (REM)
  - F. Quality Factors (QF) or Radiation Weighting Factor
  - G. Sievert (Sv)
  - H. External and Internal Dose Limits
- III. Occupational and Non-Occupational Exposure Radiation Protection Guides
- A. National Council on Radiation Protection and Measurements (NCRP)
  - B. International Commission on Radiological Protection (ICRP)
  - C. As Low as Reasonably Achievable (ALARA) Program
- IV. Principles of Radiation Protection
- A. Time of Exposure
  - B. Distance from Source (Inverse Square Law)
    1. specific gamma ray dose constant
    2. exposure dose calculations

- C. Shielding
    - 1. half-value layer and attenuation coefficients
    - 2. determination of shielding requirements
      - a. type of material
      - b. thickness needed
  - D. Automation/Remote Control
  - E. Quantity/Amount of Radiation (Radiation Accidents)
- V. Personnel Monitoring and Precautions
- A. ALARA
    - 1. concept, scope, and implementation
    - 2. exposure of the embryo/fetus
    - 3. exposure of the public
    - 4. occupational exposure limits
  - B. Restricted, Controlled and Unrestricted Areas
  - C. Effective Dose Equivalents
  - D. Monitoring Devices
    - 1. film badges
    - 2. ring badges
    - 3. thermoluminescent dosimeters (TLD's)
    - 4. pocket dosimeters
    - 5. other types of dosimeters
  - E. Bioassays
  - F. Precautionary Warning (Caution) Signs
  - G. Reports and Notices
- VI. Area Monitoring (Personnel and Work Environment)
- A. Surveys, Wipe Tests and Monitoring Intervals Required in Work Areas Where:
    - 1. radioactive material is stored or
    - 2. compounded, dispensed or administered
    - 3. unrestricted areas
  - B. Limits of Radiation Contamination and Exposure
    - 1. in work areas (restricted)
    - 2. unrestricted areas
  - C. Air Monitoring
    - 1. airflow velocity measurements - hood and room
    - 2. restricted and unrestricted areas
- VII. Radioactive Packages and Sources
- A. Procedures for Opening Radioactive Packages
- B. Requirements for Shipment of Radioactive Material (General Considerations)
    - 1. packaging
    - 2. labeling
    - 3. transport index
    - 4. shipping papers
    - 5. placarding of vehicles
    - 6. removable contamination survey
  - C. Monitoring Sealed Sources (Leak Tests)
- VIII. Radioactive and Biohazardous Waste Disposal Methods (General Considerations)
- A. Decay in Storage
  - B. Separation by Half-Life
  - C. Incineration
  - D. Sewer or Atmosphere
- IX. Radiation Safety
- A. Laboratory Techniques for Handling Radioactive Material Safely
  - B. Laboratory Design
    - 1. minimizes potential for radioactive contamination and radiation exposure
    - 2. proper placement of hoods and sinks
    - 3. location of storage, compounding, dispensing, quality control, and waste areas
  - C. Regulatory Agencies
  - D. Quality Management Plan
  - E. Radiation Safety Committee
  - F. Radiation Safety Officer
- X. Radiation Accidents
- A. Emergency Procedures
  - B. Major and Minor Spills
  - C. Industrial Accidents/Environmental Issues
  - D. Decontamination Procedures
    - 1. facility
    - 2. personnel
  - E. Incident Reporting
- RADIATION BIOLOGY**
- I. Interactions of Radiation with Emphasis on Biological Systems
    - A. General Concepts
    - B. Aqueous Systems

- C. Factors Affecting Reactions
    1. oxygen
    2. concentration
    3. LET
  - D. Application to Basic Compounds and Macromolecules
    1. types of molecules; enzymes, DNA, RNA
    2. structural changes
    3. influence of dose, dose rate, LET, and oxygen
- II. Cellular Response
- A. Effects on Cells
  - B. Sensitive Organelles
  - C. Concept of Radiosensitivity
  - D. Response to Increasing Radiation Dose
  - E. Factors Influencing Response
    1. dose rate and dose fractionation
    2. LET
    3. oxygen
    4. cell type and cell cycle
- III. Effects on Nucleic Acids
- A. Structural Changes
  - B. Synthesis and Replication
  - C. Mechanism(s) of Repair
  - D. Influence on Cell Cycle
- IV. Radiation Genetics (Hereditary Effects)
- A. Gene Effects
  - B. Chromosomal Effects
  - C. Assessment of Risk
- V. Effects of Ionizing Radiation on the Embryo and Fetus
- A. Mechanism and Consequences
  - B. Assessment of Risk (Teratogenic and Delayed Effects)
- VI. Whole-Body Effects of Ionizing Radiation
- A. Overview of Radiation Exposure of Tissues and Organs
  - B. Hematopoietic Tissue
  - C. Gastrointestinal Tract
  - D. Skin
  - E. Reproductive Organ

- F. Nervous System
- G. Respiratory System
- H. Circulatory System
- I. Urinary System
- J. Musculoskeletal System
- K. Endocrine Organs
- L. Sensory Organs

VII. Acute Effects of Ionizing Radiation

- A. Bone Marrow Syndrome
- B. Gastrointestinal Syndrome
- C. Cerebrovascular Syndrome
- D. Influencing Factors
  1. type of radiation and area of exposure
  2. dose, dose rate, and dose fractionation

VIII. Delayed Effects of Ionizing Radiation

- A. Occurrence, Risks and Types of Exposure
- B. Hereditary Effects (see also Radiation Genetics)
- C. Somatic Effects
  1. cancer induction
  2. life span shortening?
  3. organ fibrosis and degeneration

IX. Low Level (Low Dose) Exposure to Ionizing Radiation

- A. Sources
  1. medical
  2. natural background
  3. radon
- B. Significance
- C. Radiation Hormesis

**RADIOPHARMACEUTICAL CHEMISTRY**

- I. Introduction
- A. Distinction between Radionuclides, Radiochemicals and Radiopharmaceuticals
  - B. Criteria for Radiopharmaceuticals
    1. suitable radionuclides for diagnosis and therapy (nuclear physical properties, biological and effective half-life, metabolism, availability)
    2. design of radiopharmaceuticals
  - C. History of Radiopharmacy

- D. Legislation
1. principles and guidelines of good manufacturing practice for radiopharmaceuticals (encl. nuclear pharmacy practice guidelines)
  2. monographs for radiopharmaceuticals
- II. Production of Radiopharmaceutically Relevant Radionuclides
- A. Accelerator/Cyclotron Produced Radionuclides
1. nuclear reactions, activation equation
  2. targetry
  3. separation and purification
- B. Reactor Produced Radionuclides
1. nuclear reactions, activation equation
  2. targeting
  3. separation
- C. Radionuclide Generators
1. mathematical principles
  2. use and advantages
  3. applications
  4. quality assurance
- III. General Physicochemical Properties of Radioactive Compounds
- A. Physical Properties
1. decay mode
  2. photon energy
  3. particulate energy and range
  4. half-life
  5. chemistry
  6. *in vitro* stability
- B. Activity-Mass Relationship
- C. Tracer Concentration Expressions
1. specific activity
  2. concentration
- D. Carrier Concept/Designations (Carrier-Free, Carrier Added, No Carrier Added)
- E. Solution Chemistry of Tracer Radionuclide Metals
1. hydrolysis
  2. reduction-oxidation
  3. complexations reactions
  4. radiolytic decomposition
- IV. Types of Radiopharmaceuticals According to Their Mode of Distribution and Localization
- A. Introduction into Radiopharmacology
1. distribution
  2. metabolism
  3. excretion
  4. pharmacokinetics
- B. Cells, Particles and Colloids
1. capillary trapping
  2. phagocytosis and pinocytosis
  3. distribution volume, increased capillary permeability
- C. Radioimmunodiagnostic and Radioimmunotherapeutic Agents: Labeled Antibodies and Fragments, Peptides
- D. Biochemical Substrates and Ligands
1. enzyme substrates and inhibitors; metabolic trapping
  2. receptor-binding agents
- E. Small Nonspecific Molecules
1. distribution and diffusion
  2. compartmental space
  3. chemisorption
- V. Labeling
- A. Types of Labeling: Isotopic *vs.* Non-isotopic Labeling
- B. Labeling with Radiometals
1. small metal complexes
  2. kinetic and thermodynamic aspects of radiometal complex chemistry
  3. bifunctional chelators
- C. Radiohalogenation
1. strategies of fluorine-18 labeling
  2. methods of radioiodination
  3. radiobromine and Astatine-211 labeling
- D. Carbon-11 Chemistry
1. Preparation of precursors,
  2. C-11 -methylations and other methods
- E. Cell Labeling I
1. Direct labeling,
  2. Indirect labeling
- VI. Quality Control of Radiopharmaceuticals
- A. Radionuclidic Purity
1. gamma scintillation spectrometry

2. differential attenuation
  - B. Radiochemical Purity (*i.e.* Chromatographic and Other Separation Methods)
  - C. Chemical Purity (*i.e.* Chromatographic Methods)
  - D. Visual Inspection (*i.e.* Color, Clarity, Particle Size and Number of Particles)
  - E. pH Measurement
  - F. Sterility Testing
  - G. Endotoxin Testing
  - H. Cell Viability
  - I. Antigen-excess
- VII. Technetium-99m Radiopharmaceuticals
- A. Molybdenum Mo-99/Technetium Tc-99m Generator
    1. production schemes
    2. operation
    3. wet *vs.* dry column
    4. quality control
    5. generator physics
    6. specific activity
  - B. Technetium Chemistry
    1. oxidation states and coordination modes
    2. reduction methods
    3. technetium tin-ligand reactions in aqueous solution
      - a. hydrolysis
      - b. reoxidation
      - c. complexation
      - d. carrier effects
      - e. radiolytic decomposition
  - C. Technetium Kits (*i.e.* Preparation and Composition)
  - D. Specific Kits (*i.e.* Methods for Radiolabeling with Tc-99m)
    1. human serum albumin
    2. macroaggregates and microspheres
    3. phosphonates
    4. glucoheptonate
    5. HMPAO and ECD
    6. isonitriles, tetrofosmin
    7. MAG3 and EC
    8. DMSA
    9. antibodies
  - E. Other Tc-99m Radiopharmaceuticals
- VIII. Rhenium-186 and Rhenium-188 Radiopharmaceuticals
- A. Tungsten-188/Rhenium-188 Generator
    1. operation
    2. quality control
  - B. Specific Rhenium Radiopharmaceuticals
    1. Re(V)DMSA
    2. Re HEDP
    3. Re labeled antibodies and peptides
    4. Re loaded stents
- IX. Iodine Radiopharmaceuticals
- A. Radioiodine Isotopes for Radiopharmaceuticals: I-123, I-124, I-125, and I-131
  - B. Chemistry of Radioiodide
  - C. Specific Radioiodinated Radiopharmaceuticals
    1. sodium iodide
      1. radioiodinated albumin
      2. ortho-iodohippurate
      3. meta-iodobenzylguanidine (MIBG)
      4. iodocholesterol
      5. amphetamines
      6. proteins
      7. monoclonal antibodies
      8. peptides
      9. molecular recognition units (MRU's)
      10. neuro-transmitter ligands
  - D. Dosage Forms Available
  - E. Safety Techniques for Handling Radioiodine
- X. Fluorine-18 Radiopharmaceuticals
- A. Radionuclide Production
  - B. Remotely Controlled and Automated Radiosyntheses
  - C. Specific Fluorine-18 Radiopharmaceuticals
    1. fluoride
    2. fluorodeoxyglucose (FDG)
    3. L-6-fluoro-DOPA
    4. receptor ligands
- XI. Radiolabeled Blood Cells
- A. Methods for Blood Cell Separation Prior to Labeling
  - B. Tc-99m Red Blood Cells (*i.e. in vitro, in vivo* and Modified *in vivo* Methods of Labeling for

- Blood Pool Studies and Detection of Gastrointestinal Bleeding)
- C. Tc-99m Red Blood Cells (Heat Damaged) for Spleen Specific Imaging
- D. In-111 White Blood cells (*i.e.* Methods of Radiolabeling for Abscess Localization)
- E. Cr-51 Red Blood Cells (*i.e.* Methods of Radiolabeling for Blood Volume Measurement)
- F. In-111 Platelets (*i.e.* Methods for Radiolabeling)
- G. Tc-99m White Blood cells (*i.e.* Methods for Radiolabeling for Abscess or Inflammation Detection)
- H. Interaction with Drugs on Cell Labeling Procedures

### XII. Prepared Radiopharmaceuticals

- A. Thallium-201 Chloride
- B. Indium-111 DTPA, Labeled Peptides and Proteins
- C. Phosphorous-32 Sodium Phosphate
- D. Cobalt-57/58 Cyanocobalamin (Schilling test)
- E. Radioactive Gases (*i.e.* Xenon Xe-133, Xe-127, Krypton Kr-81m)
- F. Gallium-67 Citrate
- G. Strontium-89 Chloride
- H. Yttrium-90 Citrate, Labeled Antibodies and Peptides, Microspheres
- I. Stannous-117m DTPA
- J. Samarium-153 EDTMP
- K. Copper-64 and Copper 67 Labeled Biomolecules
- L. Miscellaneous

### XIII. Radiopharmaceutical Development

- A. Approaches and Trends
  1. empirical approaches to design
  2. rational approaches to design structure/distribution relationship
- B. Animal Models

## THE CLINICAL USE OF RADIOPHARMACEUTICALS

- I. Criteria for the Selection of the Appropriate Radiopharmaceutical
- II. *In Vivo* Kinetics of Radiopharmaceuticals

- A. Absorption, Distribution, Metabolism, Elimination
- B. Normal *vs.* Abnormal Kinetics
- C. Factors that Affect/Alter the Kinetics of Radiopharmaceuticals

### III. Specific Procedures Which Employ Radiopharmaceuticals

- A. Indications
- B. Optimal Diagnostic or Therapeutic Protocols
- C. Interventional Techniques Which Enhance the Procedure
- D. Interpretation of the Procedure Outcome, Its Effect on Patient Management, and Its Economic Implications
- E. Sensitivity, Specificity, and Predictive Value of Diagnostic Procedures
- F. Expected Benefits of Therapeutic Procedures

### IV. Preparation and Monitoring of Patients Who Receive Radiopharmaceuticals

- A. Patient Education and Preparation/Family Counseling
- B. Precautions and Considerations for Special Patient Populations
  1. pediatric patients
  2. pregnancy testing
  3. breast feeding
  4. others
- C. Dosage Adjustment Based on Age, Weight, Body Surface Area, Organ Function, Instrument Sensitivity, etc.
- D. Clinical Problems Associated with the Use of Radiopharmaceuticals
  1. adverse reactions/untoward effects
  2. misadministration/reportable events
  3. unusual or unanticipated images or therapeutic outcomes
    - a. artifacts
    - b. altered radiopharmaceutical biodistribution due to interference from drug therapy or surgical intervention; radiopharmaceutical formulation problems; improper administration techniques, etc.
    - c. variations in human anatomy

- E. Correlation Between the Results of Product Quality Control Testing and Clinical Outcome of the Procedure
- F. Use of Radiopharmaceuticals to Monitor the Safety and/or Efficacy of Specific Drug Therapy Regimens
- G. Drug Information Resources for Nuclear Medicine and Nuclear Pharmacy
- H. The Role of the Nuclear Pharmacist as Consultant and Provider of Patient Specific Information

IV. Introduction to Design of a Nuclear Pharmacy

- A. Facilities
- B. Organization
- C. Equipment

**LEGAL ASPECTS AND NATIONAL AND INTERNATIONAL GUIDELINES**

- I. Guidelines from United States Pharmacopeia and European Pharmacopeia
- II. *In Vitro* and *in vivo* Evaluation of New Radiopharmaceuticals
  - A. Biological Testing and Other Types of Evaluation
  - B. Legislative Aspects

**Research and development applications**

- I. Radiopharmacology (animal models, *in vitro* assays, tissue culture)
  - A. Introduction to the use of radiopharmaceuticals in research
  - B. The use of radiopharmaceuticals in research
  - C. Radioreceptor assays: Principle, Technology and Concepts
  - D. Tissue culture models
  - E. Animal models, animal protection Regulations
- II. Biopharmacy of radiopharmaceuticals
  - A. Formulation: Galenics of radiopharmaceuticals
  - B. Vectorisation of radiopharmaceuticals
- III. Toxicology

- A. Methods of toxicity assessment of the preparation of radiopharmaceuticals
- B. Meeting regulatory requirements

IV. New trends in radiopharmaceuticals

- A. Immunotherapy
- B. Aspects of biochemistry and molecular biology: Antisense technologies in diagnosis
- C. Developments on gene therapy
- D. Radiopharmaceuticals based on bioactive peptides (Detection of tumours, infection/inflammation and thrombus)
- E. New trends on targeted radiotherapy
- F. Therapy control using PET and nuclide pairs (I-124 PET, I-131 Therapy, 86Y PET, 90Y Therapy)

V. Clinical trials of radiopharmaceuticals

**13 CONCLUSION**

The second IREC workshop will be held in Rottenberg, Germany in June 2001 to finalize the plans for implementing a distance-based learning program in radiopharmaceutical sciences. An international appeal, to potential sponsors, is being launched to generate funding to finance specific projects within the programme.