IUPAC Division VII. Chemistry and Human Health

Council Report: 2003-2005

I. Executive Summary

The merger of the former Medicinal Chemistry and Clinical Chemistry/Toxicology Sections into the Division of Chemistry and Human Health (VII) has proven to be an effective way for the IUPAC to oversee and allocate funding to each of these areas while using a condensed administrative infrastructure. To promote the core of expertise required to support the technical diversity afforded by these areas, Division VII, in turn, maintains three, standing Subcommittees led by appointed Chairpersons who are recognized internationally within each of their fields. These Subcommittees (and their respective Chairpersons) are: (i) Medicinal Chemistry and Drug Development (MC; C. Robin Ganellin); (ii) Nomenclature, Properties and Units in Laboratory Medicine (C-NPU; Urban Forsum); and, (iii) Toxicology and Risk Assessment (TOX; John Duffus). A fourth subcommittee, also led by an appointed Chairperson (Tom Perun), has additionally been organized to deal with the IUPAC nomination and election processes for the Division. While a few members of each Subcommittee also sit on the Division Committee, the majority of the technical Subcommittee members are drawn as volunteers from each of these fields, respectively. The Election Committee has representation from all three technical areas.

The Subcommittees hold independent meetings on a regular basis and each Chairperson provides an update about their activities by either personally attending or forwarding a written report to the Division meetings which, in turn, are held twice each year. This focus of expertise coupled with the broader perspectives afforded during the Division meetings, has proven to be an effective way to encourage and initiate the evaluation of new IUPAC Project submissions, as well as to provide for assessments of ongoing projects and their subsequent impact. Final approval of new projects and additional tracking of ongoing projects, occur at the Divisional level wherein an equitable balance across all activities and the Division VII's IUPAC-allocated funds is sought among all three Subcommittees. Presently, Division VII is carrying 24 projects and has 16 projects undergoing review. It can be additionally noted that these same demarcations of expertise are also used advantageously when projects reach completion wherein final reports, recommendations or other publications then typically require review and/or extensive editing. In this regard, each Chairperson ultimately assumes final responsibility for assuring the quality of products derived from their particular area of expertise.

A representative highlight from each of Division VII's three technical areas follows. One of the most exciting developments within the MC Subcommittee is the recent formation of the 'IUPAC-Richter Prize in Medicinal Chemistry.' Funded by a generous donation from Richter Pharmaceuticals, Ltd. (Budapest, Hungary), this program will recognize one scientist every two years whose work has made a significant contribution to medicinal chemistry within the context of drug discovery and development. Awardees will receive

a $10,000.00 cash prize at an IUPAC-associated scientific meeting wherein they will be expected to deliver a lecture about their work. Funding has been allocated for five of such awards across ten years. A noteworthy development within the clinical arena is that the C-NPU database (http://dior.imt.liu.se/cnpu) has been upgraded with codes for the most common properties associated with clinical chemistry using mass concentrations along with identifiers for clinical molecular biology, transfusion medicine and immunoheamatology. The database is published on the IFCC homepage (Scientific Division) and on the IUPAC homepage (Division VII) with a link to the server Dior. Both the IFCC and IUPAC are owners of the property (intellectual content and the physical database). Finally, a noteworthy development for the TOX Subcommittee is the nearly completed second edition of the popular text entitled 'Fundamental Toxicology for Chemists.' All existing chapters have been revised and a number of new chapters have been added including *'Pharmaceutical Toxicology,' 'Toxicology in the Clinical Laboratory,'* and *'Pathways and Behavior of Chemicals in the Environment.'* The new edition will soon be published by the Royal Society of Chemistry.

II. Activities Organized by the Six Goals of the IUPAC Strategic Plan

1. Provide leadership as a worldwide scientific organization that objectively addresses global issues involving the chemical sciences.

Division VII's organization into three subcommittees allows this objective, as well as all of the other strategic objectives, to be focused within the specific contexts of Clinical Chemistry, Medicinal Chemistry and Toxicological Chemistry. Each Subcommittee brings together a group of experts from around the globe to discuss items relevant to their area. For example, through such discussions, the Medicinal Chemistry group has determined that the global harmonization of patent laws impacting upon the pharmaceutical industry would benefit from a broad consideration of several issues. Toward that end, a project proposal has been drafted to objectively address these issues by starting with a general survey that will be administered globally to a variety of scientists, practitioners and administrators for whom patents are an important aspect of their work. Already approved at the Division level, it is anticipated that a final version of this project proposal will be delivered to the Secretariat during third-quarter 2005.

2. Facilitate the advancement of research in the chemical sciences through the tools that it provides for international standardization and scientific discussion.

All three of Division VII's Subcommittees remain extremely active in producing glossaries and recommendations for standardization of terms within their respective areas. A quick scan down the list of completed, ongoing and proposed projects indicates our numerous activities in this area (see Section IV. Tabular Material).

Another type of tool that Division VII has effectively deployed is that of the Internet accessible database. The C-NPU database has already been described in the highlights of the Executive Summary (Section I). Similarly, but this time in conjunction with the IUPHAR and the latter's initial funding supplied by the ICSU, Division VII is

constructing an Internet database that will contain human drug metabolism data and will, in turn, be made available to users across the globe via a non-profit basis. With an emphasis on the chemical structures for both the parent drug or xenobiotic and the various metabolic biotransformation products, the Human Drug Metabolism Database (hDMdb) will be extremely useful to both the medicinal and toxicological chemistry arenas. The importance of such projects within the chemical community is only just now beginning to be fully appreciated. For example, statements quoted in a C&E News (June 28, 2004 pages 37-41) article that highlighted an international conference dedicated to 'Charting Chemical Space: Finding New Tools To Explore Biology" indicate that one of the 'grand challenges' elaborated by these well-recognized scientists was an outright appeal for the production of open databases having chemical structures connected to biological properties.

3. Assist the chemistry-related industry in its contribution to sustainable development, wealth creation, and improvement in the quality of life.

Moving forward from one of its earlier publications ('Medicinal Chemistry in the Development of Societies: Biodiversity and Natural Products,' Eur. J. Med. Chem., **32**, 2000, pages 1121-1125) which specifically addresses the critical role that the pharmaceutical industry can play in developing nations, Division VII is now undertaking follow-up projects that intend to bring workshops on this topic to such countries. Our initial program will target the pharmaceutical industry in India which has heretofore been able to establish strengths in process (scale-up) chemistry but not in the earlier stages of drug discovery and invention, despite their long history with natural product-based remedies and herbal medicines. This undertaking may also be applicable to China and many other Eastern countries. Even less developed nations are being targeted in a somewhat different manner (see Strategic Goal 4.)

4. Foster communication among individual chemists and scientific organizations, with special emphasis on the needs of chemists in developing countries.

The aforementioned hDMdb project is also applicable to this goal. For example, during a poster presentation about this project at the recent International Society for the Study of Xenobiotics (ISSX) meeting (Vancouver, September, 2004), its 'free-access-for-all' principle was applauded by several scientists from less developed nations who happened to have become engaged in a broader discourse with scientists from some advanced countries who wanted to know if the database might be able to be commercialized so as to generate funding that could move its development along at a faster pace (but with the inherent principle then falling into place that the db would thus be made available only to those who could afford to purchase it).

Continuing from Strategic Goal 3, we have determined that the best follow-up to our earlier publications for countries which are in the very early stages of development in that they completely lack any type of sophisticated chemical industry infrastructure, needs to be approached at a more fundamental level, i.e. by educational programs directed through their budding academic institutions rather than at the industrial level. Division VII's

ongoing projects on basic clinical/medicinal/toxicological chemistry education within the Latin America region represents an initiative along these lines. Also in this regard and similar to all of the other Divisions, Division VII repeatedly votes in favor of IUPAC sponsorship of meetings and conferences applicable to our area whenever they are to be organized or hosted by less developed nations and wherein the caliber of the related chemical technologies is to be held in the highest regard. During the period of this report, Division VII has favorably reacted to about two of such requests for IUPAC sponsorship each quarter.

Finally, along this same theme it can be noted that several members of the MC Subcommittee participated without remuneration in the Brazilian 'XI Summer School in Medicinal Chemistry' (held February 14-18 in Rio de Janeiro) by delivering several lectures to an enthusiastic group of graduated students who attended from various South American countries.

5. Utilize the IUPAC's global perspective and network to contribute to the enhancement of chemistry education, the career development of young chemical scientists, and the public appreciation of chemistry.

Ongoing chemical education initiatives pertinent to human health have been described above for audiences in industry (Strategic Goal 3) and academia (Strategic Goal 4). For the public at large, one additional initiative deserves mention. As a follow-up to our prior, somewhat technical article ('Natural and Non-natural Substances Related to Human Health,' PAC, **74**, 2002, pages 1957-1985) Division VII produced a summary version which compares the attributes of synthesized drug versus natural sources for chemical compounds in laypersons terms. Subsequent to publication of the latter in CI, this has now been picked-up within the lay press with translations being effected by other countries as evidenced by the entries noted on the Web-based, Eureka Alert Service.

6. Broaden national membership base and seek the maximum feasible diversity in membership of IUPAC bodies in terms of geography, gender and age.

One of the new project criteria that Division VII has laid in place from the onset during the Subcommittee meetings and then further reinforces at the Division level, is that the proposed project participants list reflects the exact spirit conveyed by this final IUPAC strategic goal. That these participants might then become future members in various IUPAC bodies provides a grass-roots technical approach toward accomplishing this end. Exemplifying this scenario is the fact that the current President of Division VII first became involved with the IUPAC via an invitation to participate on a project about ten years ago and has gradually become more and more active. The same philosophy has been applied to the Subcommittee charged with the Division VII-related nomination and election processes, although in this case there is the possibility that a new member might become immediately involved at a higher administrative level within the IUPAC infrastructure.

In terms of seeking younger members (also applicable to Strategic Goal 5.), Division VII had the pleasant experience of hosting a 'Young Observer' during the Ottawa meeting. To further support this program, Division VII subsequently encouraged this individual to seek IUPAC sponsorship for a symposium that he was trying to set-up in his country. This has all occurred favorably and a full set of proceeding papers covering the symposium's cutting-edge chemistry in the area of nuclear delivery and functional modification by small molecules was recently published in PAC. It is hoped that through such mentoring, this young and rising investigator will gradually become more and more active within the IUPAC as well. Finally, as a US-based scientist, the Division VII President has also become involved with the US National Academy of Sciences IUPAC Relations Committee wherein young observers from the US are selected and mentored. From this relationship, Division VII is scheduled to assist in mentoring two of such young observers during the Beijing meetings.

III. Other Information

After favorable and supportive discussions in Bled, Division VII is beginning to move forward with its plan to raise money to enhance its various activities and meetings associated with its IUPAC endeavors. The fund-raising plan is as follows:

1. Subcommittee member/team proposes a fund-raising effort on behalf of his/her/their subcommittee activities and/or project(s).
2. Subcommittee Chairperson submits summary to the Division about how funds are to be sought and specifies how the money will be spent in a non-profit manner to enhance the Subcommittee's activities and/or to further support its ongoing projects.
3. Division provides approval for Subcommittee to initiate fund-raising effort and forwards the summary to the Secretariat.
4. Incoming money is deposited directly into general IUPAC account(s) via Secretariat.
5. Secretariat sets-up a "Fund Project" using its Project System mechanism specifying the Subcommittee Chairperson as the Project Leader who can then spend the money via the same expense submission process used for any other projects. No "cuts" will be excised by either the Secretariat or the Division, i.e. 100% of the funds that are raised will be returned to the Subcommittee.

The same process may be undertaken on behalf of the Division wherein the President then becomes designated as the "Fund Project" Leader. Depending upon various goals of the fund-raising effort, other spending scenarios may be able to be set-up by the Secretariat as well. For example, a self-sustaining sum of ca. $5 K per year could be established by "banking" ca. $ 100 K of raised funds into an IUPAC account so as to produce such a level of annual interest income in a perpetual fashion. The latter, in turn, might then be used to support some initiative that the Subcommittee or Division wants to maintain in an ongoing manner for several years, such as a continuing IUPAC poster award at some regular conference that is specifically relevant to the Subcommittee's or the Divisions' technical area.

Likewise, Division VII is in the process of adopting a more formal 'project tracking system' for our projects in a format that would go out to all Project Leaders on a regularly scheduled basis, e.g. just prior to our DC meetings or at least on an annual basis. Based upon the form already being used by Division V, the Division VII form requests the following information:

1. IUPAC Project # and Title:
2. Project Leader:
3. E-Mail, Telephone # and FAX#:
4. Project Start Date:
   Amount budgeted:
   Recorded Completion Date:
5. Estimate Completion Percentage:
   Amount Spent:
   Anticipated Completion Date:
   What Will Be Delivered First:
6. List of changes in the Project Team's membership (provide complete contact information for any new members):

IV. Tabular Material (2003-2005)

Publications

1. R. Dybkaer. Units For Quantities Of Dimension One. Metrologia **41**, 69-73 (2004).
2. R. Dybkaer. An Ontology On Property For Physical, Chemical And Biological Systems. APPMIS Supplement 117, **112** (2004).
3. P.S. de Araujo, B. Zingales, P. Alia-Ramos, et al. Properties And Units In The Clinical Laboratory Sciences – Part XVIII. Properties And Units In Clinical Molecular Biology. PAC, **76,** 1799-1807 (2004).
4. M. Nordberg, J.H. Duffus and D.M. Templeton. Glossary of Terms used in Toxicokinetics. PAC, **76**, 1033-1082 (2004).
5. M. Nordberg. Glossary of Terms Used in Toxicokinetics. Chemistry International, **26**, No 5, 21 (2004).
6. M. Nordberg, Explanatory Dictionary of Concepts in Toxicokinetics. Chemistry International, **26**, No 4, 23-24 (2004).
7. D.M. Templeton. Mechanisms of Immunosensitization to Metals. PAC, **76**, 1255-1268 (2004).
8. R. Klein, M. Schwenk, R. Heinrich-Ramm, D.M. Templeton. Diagnostic Relevance of the Lymphocyte Transformation Test for Sensitization to Beryllium and Other Metals. PAC, **76**, 1269-1281 (2004).
9. J. Duffus, et al. Exposure Assessment and Decision Rules in compliance Testing for Implementation of Exposure Limits. Published.
10. Natural and Unnatural Substances Related to Human Health initially published in PAC with follow-up summary in CI by T. Perun and P. Erhardt, and which then prompted several lay press publications during this report period.
11. D.M. Templeton et al. Properties and Unites for Transfusion Medicine and Immunohaematology. Published.

Current Projects (all project numbers end in -700)

1999-047-1- Immunochemistry of Metal Sensitization.
2000-009-1- Drug Metabolism Terms.
2000-010-1- Human Drug Metabolism Database.
2000-014-1- Recommendations for the Use of Nanotechnology in Clinical Laboratories.
2001-048-2- Research and Training in Medicinal Chemistry in India, Pakistan and Sri Lanka.
2001-049-2- Glossary of Terms Used in Process Chemistry/Manufacturing of Active Pharmaceutical Ingredients, and Pharmaceutics.
2001-050-2- Chemical, Pharmacological Aspects of Natural Products with Medicinal and Nutritive Value.
2001-053-2- Fundamental Toxicology for Chemists.
2001-058-1- Concepts and Structure for Requests in Clinical Laboratories.
2001-066-1- Global Use of the C-NPU Concept System for Properties in Toxicology.
2001-067-1- Properties and Units for Function Examinations.
2001-068-1- Properties and Units in Medical Molecular Biology.
2001-070-1- Properties and Units for Urinary Calculi.
2002-001-1- Compendium of Terms Associated With Drug Discovery and Development.
2002-051-1- Analogue-Based Drug Discovery.
2003-001-2- Explanatory Dictionary of Concepts in Toxicokinetics.
2003-028-1- Glossary for Chemists of Terms Used in Toxicology: Revision and Updating.
2003-044-1- Glossary of Terms Used in Combinatorial Chemistry.
2003-059-1- Quantifying the Effects of Compound Combinations.
2004-019-3- Glossary of Terms Used in Biomolecular Screening.
2004-023-1- Internationally Agreed Terminology for Observations in Scientific Communication.
2004-025-1- Compendium of Targets of the Top 100 Commercially Important Drugs.
2004-028-1- Practical Studies for Medicinal Chemistry: An Integrating Approach for Developing Countries.
2004-045-01 Training of School children on Pesticides and Health

Projects Undergoing IUPAC Review

2001-069-1- C-NPU Concepts and Traceability of Measurements.
2003-016-1- Integrating Environmental Exposure Pathways for Medicinal Products.

Projects Undergoing Divisional Discussion

1. Bioinformatics: Prototype Analysis Of Molecular Biomarkers Of Diseases.

2. Prototype Analysis Of Glossary Terms To Establish Biological Context By Text Data-Mining.
3. IUPAC Survey And Discussion Group On Present Trends In Patenting Drug-Related Technologies.
4. Nutraceuticals Derived From Plant Sources Of South America.
5. Nutraceuticals Derived From Marine Sources.
6. Prediction Of Storage Stability Of Drugs And Compound Libraries.
7. Introduction Of The NPU-Database Into The Russian System.
8. Revision Of The Silver Book.
9. Extension Of The SCNPU-System To Imaging.
10. Problems Of Metrology Dealing With Uncertainty.
11. Educational Material / ToxLearn.
12. Joint Project Clinical And Medicinal Chemistry: Validated Targets of Individual Drugs and Analogues.
13. Kids In Life Science.
14. Properties And Units In CD Markers.