



International Society for Enzymology (ISE)

Newsletter, February 2003

Editor: David M. Goldberg

A General Business Meeting of the Society had been convened for Saturday 19th October 2002 in the Convention Centre, Act City, Hamamatsu, Japan. Regrettably, a quorum could not be obtained and the Meeting did not take place, in lieu of which the Minutes of the Board Meeting preceding it, which would have formed the basis for information and discussion, are presented in this Newsletter. Further information, if desired, may be obtained on request to the Secretary, Dr. Eleftherios P. Diamandis (email: Secretary@ISEnzymology.org). Points of view and comments on any of the items in these Minutes are warmly welcome and should be addressed in the form of a Letter to the Editor Dr. David Goldberg (E-mail: PastPres@ISEnzymology.org).

The Editor prepared the Report on the Scientific Meeting that follows. It reflects his views and opinions only. The Board of ISE takes no responsibility for its contents.

Minutes of the Board Meeting

Present: Dr. E.P. Diamandis (Chair and Secretary),
Dr. D.M. Goldberg (Past President),
Dr. M. Plebani (Vice-President),
Dr. R. Rej (Councilor)

Regrets: Dr. F. Salvatore (President)
Dr. M.K. Schwartz (Treasurer)

Minutes of Previous Meetings

- General Business Meeting, May 24, 2000, Naples, Italy. Because of a lack of a quorum, the Minutes of the Board Meeting held in Naples had been published as a Newsletter after approval by the Board.
- Minutes of Conference Call, December, 21, 2001. These had been circulated and approved at the Conference Call below.
- Minutes of Conference Call, January 10, 2002. These have been circulated in draft form by the President. A list of corrections had been submitted by Dr. Goldberg. A revised version has not been circulated, pending which approval of these Minutes will be deferred.

Business Arising

- Status of Incorporation.* In view of the constitutional difficulties in meeting the requirements for incorporation in the USA, it was decided not to proceed.
- Board Meetings by Teleconference.* Two such meetings had been held quite successfully. The procedure works well for decision-making when all participants have previously considered the issues.
- Newsletter.* Difficulties have been experienced with Elsevier in terms of their long schedule for publication and the

dissemination of urgent information requiring action is not feasible with this instrument, for which purpose the website and direct electronic mail to members provide much better solutions. However, material that is not time-sensitive such as reports of meetings and minutes of General Meetings could be included in Newsletters to be published in *Clinica Chimica Acta* in order to keep our name in front of the readership. It had been agreed that the President would prepare a synopsis of Board Meetings for publication in this medium, but no action had yet been taken concerning the teleconference Board Meetings held in December 2001 or January 2002.

- Status of Councilors.* Dr. G. Ailhaud resigned from the position of Councilor approximately a year ago. After considerable discussion, it was agreed that the vacancy should not be filled pending identification of an outstanding candidate who could be groomed for a major role in our Society or who would take responsibility for a defined function, such as organization of a Scientific Meeting. It was noted that Dr. Robert Rej had been co-opted to the Board in place of Dr. C. Price.
- Meetings Committee.* No action had yet been taken on this matter. It was pointed out that this committee offered a unique opportunity to recruit individuals who could obtain experience of the working of the Society and could in turn be evaluated as potential Board Members. Dr. Plebani undertook to move forward with this proposal.
- Mario Werner Memorial.* The status of this item, which had been placed in the hands of Dr. Rej, was uncertain. The latter had previously spoken of a Special Issue of CCA, but information on how this is proceeding was not provided.

President's Report

None had been received.

Treasurer's Report

Dr. Schwartz had pre-circulated the detailed Treasurer's Report to the Board members and copies are available on request via email from the Secretary (Secretary@ISEnzymology.org). In summary, during the period 17 July 2000 to 17 July 2002, expenditures amounted to \$14,580. In actual fact these covered a real-time period from 3rd August 1999 to 2nd July 2002 and included all expenses for attending the 2000 Naples Meeting, a sum of \$6,435 in final settlement of the account for this meeting, \$2,890 in US taxes, \$2,450 in Financial Management Fees, \$2,293 to Dr. Goldberg for attendance at the Werner Service and compensation for the aborted Naples Meeting, and \$1,449 for Conference Calls. Income over this period from interest in the sum \$7,568 had been received. This had fallen dramatically over the 2-year period and was now running at around 2%. Our total assets comprised \$17,285 in a chequing account and \$116,697 in a 7-day CD Account with CitiBank, New York City, total assets being \$133,982.

The overall situation appeared to be satisfactory, but Dr. Schwartz had not yet made good on his attempt to place the funds in a secure long-term investment account that would earn a higher interest rate than the present account. Following these comments the Report was adopted.

Secretary's Report

- a) *Membership*: Dr. Diamandis stated that the membership list that he had received from Dr. Plebani included 403 names. Several attempts had been made to ascertain the status of these members. The most recent involved a circular sent out around four weeks ago seeking to know whether the individual would prefer to receive Society communications by direct e-mail, through the website or through personal mailing of hard copy. A printout of the membership information currently on-file was included in each member's package, and updated information was requested. As of the 17th of October a total of 51 responses had been received. Thirteen others were returned, of which three had died, two had retired, and the remainder had left their institutions for unknown addresses. It was resolved that a list of those who had not responded will be circulated to Board Members who might have personal information as to their whereabouts. It was not clear whether the number of responses included Annual Members as well as Life Members. It was resolved that the former should be requested to pay their due subscriptions starting from the current year.
- b) Several of those responding indicated that they were no longer interested in being active members. It was resolved to alter the Constitution to permit the resignation of Life Members who no longer wish to be active so that the Society had no further constitutional responsibility towards them.
- c) In response to an enquiry, the Secretary indicated that he was uncertain about the number of Associate (corresponding) members who had been recruited since a decision had been taken in Naples to create this category. Dr. Goldberg pointed out that a great opportunity had been missed since we were now more than two years through the 3-year trial that had been previously agreed, and that from discussions with Dr. Bromberg he was fairly confident that the numbers were very low.

Election of New Board.

A review of the Constitution revealed that the following timetable had to be adhered to:

- a) The Nominating Committee had to submit its Report by the 1st of August 2003.
- b) This list had to be circulated to all members by the 1st of September, 2003, inviting further nominations supported by at least 10 members of the Society in good standing and to be received by the 1st of October, 2003.
- c) In the event of such additional nominations, the Secretary will arrange for ballots to be mailed to all members together with biographical statements describing the candidates for any contested position by the 1st of November, 2003.

- d) All votes must be returned to the Secretary by the 1st of December, 2003, following which the results will be announced.
- e) Nominally the new Board is expected to take office from the 1st of January of the following year (2004) but it was recommended that the effective transition should take place in the coming instance during the meeting proposed by Dr. Salvatore if that goes ahead.

Website Report

Dr. Diamandis reported that this was now up and running and was proving to be a very useful resource. Suggestions for improvement were invited. Dr. Rej, who had indicated his interest in improving the site, had not yet offered any proposals nor had he made the trip to Toronto for which funds were authorized. It was very disappointing to report that several members of the Board had not yet submitted photographs and CVs for inclusion as requested two years ago.

Report on the Hamamatsu Meeting

Professor Masato Maekawa attended to present this report. He indicated that only six individuals had pre-registered. It was hoped that a number of on-site registrations would take place. Students and staff of Hamamatsu University would be allowed to attend. The University was taking responsibility for any financial deficit that could not be covered by sponsorship or registration funds. He asked that speakers from ISE be designated for the Opening and Closing addresses. Dr. Goldberg and Plebani were nominated for these respective responsibilities.

The question of holding the General Business Meeting as announced, following the Scientific Program, was discussed. Dr. Diamandis indicated that it would be difficult for him to stay for this meeting in view of his travel schedule; moreover, it was most unlikely that anything like the necessary quorum for a Business Meeting would be obtained. If this indeed proved to be so, the procedure adopted at the last Naples Meeting would be followed, *i.e.* no Meeting would be held, but the Minutes of this Board Meeting would be distributed to the full membership for approval which would be assumed if no objections were received within 4 weeks of circulation. Additionally, those members of the Board remaining at the conclusion of the Scientific Program would take the platform to answer questions and provide information to any members of the audience interested in the affairs of ISE.

It was noted that a very handsome Final Program was printed, including maps and other useful general information, as well as the abstracts of all presentations.

The Board thanked and congratulated Professor Maekawa for his work, especially the putting together of a very promising Scientific Program. The facilities provided were also superb. In due course he will inform the Board about the final number of registrants, but the financial details are not its concern.

Report on New York Meeting, 2003

[Editor's Note: Below is recorded the discussion that took place in Hamamatsu regarding the planned ISE meeting in New York City for spring of 2003. The reader should be aware, however, that the meeting was later cancelled.]

Dr. Rej referred to the e-mail that Dr. Schwartz had circulated indicating his health problems and his inability to contribute further to the organization of this meeting. He was not aware of any funds that had yet been raised, and his own status as a Government employee precluded his participation in such activities. The Auditorium at the Memorial Sloan Kettering Cancer Center was to have been reserved for the occasion, and he will confirm this with Dr. Schwartz at a meeting that they were to have shortly after his return. However, Dr. Rej was very pessimistic about the future of this meeting. Niagara Falls, New York, had already been ruled out, as had Toronto and its vicinity since IUBMB would not allow further satellites in this area. During the ensuing discussion, Dr. Diamandis strongly argued for continuing; Dr. Goldberg was enthusiastic about the meeting as well, but doubted that it could proceed without major efforts by Drs. Rej and Schwartz. Dr. Plebani was in favor of proceeding, even at considerable cost to the Society, on the grounds that if it did not play an active role in the organization of meetings then the Society had no further purpose left. It was resolved that:

- a) Dr. Rej would make one final attempt to persuade Dr. Schwartz to stay aboard. If this failed he would ask for his help in setting up a local committee that could take care of on-site arrangements. He would look after all other matters apart from Finance and the Scientific Program.
- b) Drs. Diamandis and Goldberg will continue their efforts to complete the Scientific Program.
- c) Dr. Diamandis presented a list of all speakers invited so far and their responses to the invitations. *[Note that this list will not be published because the meeting was later cancelled.]*
- d) Dr. Diamandis will attempt to raise some sponsorship money, but ISE funds will have to be utilized to fill any gap. All attempts will be made to trim the budget.
- e) Dr. Rej will attempt to bring about AACCC co-sponsorship with emphasis on the New York Metropolitan Section.
- f) Dr. Rej will report back to EPD and DMG the outcome of his discussions with MKS. If these are positive and if the three agree to proceed with the meeting, a Board Meeting will be held by Conference Call as soon thereafter as possible to confirm the proposed arrangements.

Report on Future Meetings, 2004

No information had been received from the President.

Future of the Society

A lively discussion on this issue ensued. Two contrary points of view were announced:

- a) The predominant view was that the Clinical Laboratory scenario is our real constituency and we should return to our original fold.
- b) A minority view was expressed by DMG who pointed out that the word "clinical" had been dropped from our title because of our failure of support from this source as witnessed by the turnout at the present meeting. No real attempt has been made to attract scientists from non-healthcare disciplines or to integrate with their activities.

It was resolved that all those present would contribute to the preparation of a Position Paper outlining the alternatives to secure the future of the Society over the next five years. This would be circulated to all Members and will form the basis of a "brain storming" session at the next Board Meeting. It was emphasized that this activity could not be conducted by a teleconference but required the physical presence and interaction of all those participating.

Adjournment

This was moved at 9:30 a.m. on Saturday, 19th October.

Report on Hamamatsu Meeting

The above Meeting, organized by Professor Masato Maekawa with the support of five local colleagues, took place in Hamamatsu, a city located in the middle of Honshu Island close to the halfway point of the bullet train line joining Tokyo with Kyoto. In Japan it is celebrated for its fine castle established 400 years ago by a local Shogun, and in the modern era as the centre of the motorcycle industry represented by such famous names as Honda, Yamaha and Suzuki as well as a company, Hamamatsu Photonics that produces 95% of the photomultipliers used in our present universe. The location was a magnificent space age complex, including a Congress Centre, hotel and shopping precinct known as Act City that stands adjacent to the main railway station.

The Meeting spanned a 24-hour period from early afternoon on Friday to noon on Saturday, so that the Scientific Program was comfortably divided into two Symposia flanked by Opening and Closing Lectures. The first, given by Dr. Eleftherios P. Diamandis of the University of Toronto, Canada, was a brilliant exposition of the work carried out by himself and his group, supplemented of course by that of many others in elucidating the role of kallikrein enzymes in cancer diagnosis and management. Thanks to these efforts, the complete genomic organization of the human kallikrein locus on chromosome 19q13.4 has been identified. The family includes 15 genes, its most celebrated product being prostate-specific antigen, which needs no introduction to this readership. However, three other kallikreins (hK6, hK10 and hK11) are increased in patients with ovarian cancer. Dr. Diamandis treated us to a fascinating dissertation on the molecular biological basis underlying the cancer-related changes in these enzymes and how they may be exploited for diagnostic purposes.

A Special Educational Lecture given by Dr. Steven Shoen-Lung Li of the National Sun Yat-Sen University, Taiwan followed this. He focused on the structure and function of human lactate dehydrogenase genes and their encoded isozymes (A, B, C).

Clearly a veteran of biomedical research, Dr. Li indulged the audience with much humour and several backward glances over a long and distinguished career with which Professor Maekawa had been strongly associated, in the course of which he outlined the structure and organization of the dominant LDH isozymes of muscle, heart and testis. In the course of their work, they had characterized many genetic mutations resulting in enzyme deficiency and electrophoretic variants. Surprisingly, these were not associated with overt clinical disease. The details of the catalytic reactions carried out by these isozymes were beautifully explained.

After a coffee break the first major Symposium — Heterogeneity of Serum Enzymes in Laboratory Medicine — commenced with a paper by our host, Professor Maekawa that provided an elegant link with Dr. Li's lecture. Entitled *An electrophoretic variant of a lactate dehydrogenase isozyme and selective promoter methylation of the LDHA gene in a human cancer cell line*, the speaker described his investigations on a 4-year old boy with metastatic hereditary retinoblastoma. An abnormal LDH band in the serum was accompanied by the presence of only LDH1 and the same abnormal band in a cell line established from the surgical retinoblastoma specimen. The absence of the A-isozyme in the tumor cells was traced to extensive methylation with consequent suppression of gene expression. In his presentation, Professor Maekawa demonstrated the scholarship that has won him an international reputation in this field.

In the next presentation Dr. T. Moriyama, Hokkaido University, Japan, described the importance of *sialyl salivary-type amylasemia* in the sera of six patients with multiple myeloma and ovarian cancer. He found the content of this abnormal amylase isozyme in the serum to be significantly related to the clinical course of the patient. Amylase featured once again in the review presented by Dr. M. Panteghini, who outlined the role of this enzyme in the diagnosis of patients with abdominal pain. In line with established thought, he advocated the substitution of pancreatic amylase for total amylase in that scenario.

A different enzyme, aminopeptidase N (APN), which catalytically behaves as a leucine aminopeptidase, was the subject of a brief presentation by Dr. M. Kawai from Tokyo Medical and Dental University. Three members of a family were found to have a very high activity without having any clinically apparent disease. The author elegantly described the structure of the normal gene product which, by cDNA analysis of the family members, seemed to be intact. However, a series of truncated APN isoforms were detected in their sera, often in high concentrations, suggesting that the abnormality was due to post-translational proteolytic cleavage.

The final presentation in this Session represented an update on a very old friend, mitochondrial aspartate aminotransferase, which has managed against the odds to survive into the Twenty-First Century. Dr. Robert Rej, who has done more than any other scientist to establish the physiological and clinical role of this enzyme, reviewed its history and his own important contributions. Despite Dr. Rej's eloquence, it is unlikely that this enzymatic Lazarus can be persuaded to rise from the dead.

That evening, a reception was held at a beer restaurant bearing the promising title "Mein Schloss". This was one of the jolliest

functions of its kind that I have attended. Staff dressed in typical Bavarian costumes handed out huge platters of sausages and other Germanic fare, accompanied by foaming tankards of several beer varieties all bearing the authentic taste of a Munich beer-garden. Professor Maekawa and other Japanese hosts delivered warm words of welcome, to which I responded on behalf of ISE. Authenticity took something of a somersault in the delightful interactions between drinkers and servers that characterized the beginning and the end of the occasion. As we arrived, a long line of female "Bavarians" gave us a huge smile, bowed politely, and in unison chanted "Auf Wiedersehen", while our departure was greeted in a similar manner by the chant of "Willkommen".

The final Session the following morning carried the title "Standardization and Enzyme Reference Materials". Nothing turns me off more than this topic, which I find tedious and repetitive, and this feeling was not allayed by the opening presentation given by Dr. George Ferard of the University of Strasburg, France, who described the general concept of standardization in clinical enzymology. This bureaucratic dissertation was followed by a similar lecture by Dr. Lothar Siekmann of the University of Bonn, Germany, but from that point onwards things improved dramatically and a spark of novelty illuminated the proceedings. The subject of the last two lectures was recombinant human enzymes as reference materials and the tone took a dramatic leap upwards from the mire of bureaucracy to the celestial heights of modern biotechnology. This is a field in which microbes are a help rather than a hindrance to man, and a wide range of chemical and biological skills are necessary to achieve optimal results. The first half was given by Dr. Ryouji Aoki of Asahi Kasei Corporation, and the second by Dr. Takayuki Uwajima of Fukui University, both of Japan. The country that gave the world the Honda motor car, the Cannon camera, the Hitachi television set and the Sony Walkman is on the threshold of world leadership in another industry, this time with enzymologists as the target market. May the Lord be praised!

The Closing Lecture delivered by Dr. Mario Plebani (Vice-President, ISE) from Padua, Italy, explored the pathogenesis of *Helicobacter pylori* infection and the genomic and enzymatic mechanisms underlying the virulence of this organism. It was a brilliant exposition in word and image, matching the quality and content of the Opening Lecture. In a topographical sense, the Hamamatsu Meeting could be described as a valley lying between two pinnacles, most of it fertile, but marred by a few barren areas. As a "view" of contemporary enzymology, it was far from comprehensive, nor could it be, given the time restraints within which it was confined. But there was much to admire and enjoy, and it provided a worthy portal of entry to the larger scientific panorama that lay ahead in Kyoto over the next five days.