ing panel discussion on Directions in Glycoscience was presented. It was chaired by Geert-Jan Boons (University of Georgia), with panelists Pamela Marino, NIH (USA); Serge Perez, European Union ; and Koichi Kato, National Institutes of Natural Sciences (Japan). A session on new technology for characterization of carbohydrates was presented by representatives of instrument manufacturers. The sustainability of processes and products at DuPont were described in another organized session. Both of those sessions were keynoted by university faculty members, however. The program was available in printed form, except for the abstracts of the contributed papers, which were available in the full program presented in various electronic formats, including a smart device app.

Nikolay Nifantiev and Amelia Rauter have volunteered to shepherd the various lectures to publication in *Pure and Applied Chemistry*. Peer review is currently underway. The next International Carbohydrate Symposium XXIX ICS (2018) will be held in Lisbon, Portugal, 15-19 July 2018, organized by Professor A. Rauter.

## Validation of Test Methods, Human Errors and Measurement Uncertainty of Results

### *by Ilya Kuselman*

The 3rd biannual international IUPAC/CITAC workshop on quality and metrology of chemical analytical results, organized with the participation of the Israel Analytical Chemistry Society (IACS) and the Israel Laboratory Accreditation Authority (ISRAC), was held 23 January 2017, in Kfar Maccabiah, Israel. The event was sponsored by Sigma-Aldrich Corporation (now a part of Merck) and arranged by Bioforum Ltd. Reports on the previous two workshops are available in *Chemistry International*. [1, 2]

The present workshop, titled, "Validation of Test Methods, Human Errors and Measurement Uncertainty of Results," was planned as a milestone of IUPAC project 2016-007-1-500. Validation of test (chemical analytical) methods is one of basic requirements for the competence of testing and calibration laboratories (ISO/IEC 17025) [3] and reference measurement laboratories in laboratory medicine (ISO 15195). [4] The same is required by national regulators, such as the U.S. Food and Drug Administration, the UK Medicines and Healthcare products Regulatory Agency, and others. There are also a number of guidelines in different industries and chemical analytical societies adapting these requirements for specific purposes and laboratories. The main aim of the workshop was to facilitate the discussion of the experience of chemists-analysts, metrologists, and quality specialists in method validation in pharmaceutical industry, food analysis, environmental analysis, and other fields. This discussion included the following topics:

- use of results of human error study at validation of an analytical method;
- evaluation of measurement uncertainty of the test (analytical) results as a part of the method validation task;
- evaluation of probabilities of false decisions at conformity assessment of test results obtained by the method under validation.

Opening remarks were given by Dr. Ilya Kuselman, Independent Consultant on Metrology, Israel, Chair of the Workshop International Advisory Committee. Dr. Bertil Magnusson, SP Technical Research Institute of Sweden, then delivered the keynote lecture "The fitness for purpose of analytical methods: a laboratory method validation and related topics", explaining the Eurachem guide. [5] Mr. Ilan Landsman, ISRAC, Israel, informed the workshop participants in his lecture about changes in requirements to method validation and verification at accreditation of measurement and testing laboratories in the new upcoming issue of ISO/IEC 17025, under voting now. The next lecture was on setting and using target uncertainty in chemical measurement by Prof. Ricardo J.N.B. da Silva, University of Lisbon, Portugal. It was dedicated to understanding the key concept of method validation "fit for purpose" or 'fit for intended use" in terms of measurement uncertainty and its target value, as in the Eurachem/CITAC guide. [6] Evaluation of probabilities of false decisions (risks) in conformity assessment of test results caused by measurement uncertainty was the subject of the lecture of Dr. Francesca Pennecchi, Istituto Nazionale di Ricerca Metrologica (INRIM), Italy. This lecture, based on the guidelines of JCGM 106, [7] Eurachem/CITAC, [8] and IUPAC/CITAC, [9] helped the participants to understand the metrological and mathematical background necessary for an evaluation of the risks. Dr. Pennecchi also announced the IUPAC task team's lecture on evaluating total risk of false decisions on conformity of a multicomponent material at

*A group of the lecturers in the Baha'i Gardens, Haifa. From left to right: Dr. Mikhail Zayats, Dr. Ilya Kuselman, Dr. Bertil Magnusson, Dr. Francesca Pennecchi. Mr. Ron Sinai (our local tour guide), Dr. Michela Sega, Prof. Ricardo J.N.B. da Silva, Dr. Markus Obkircher and Prof. Emil Bashkansky.*

the Isranalytica conference. [10]

In the lecture "Human error study as a part of method validation task", Dr. Kuselman proposed to use a method validation mapping possible human error scenarios according to the IUPAC/CITAC guide. [11] Results of such a study can be helpful in the correct formulation of the measurement uncertainty budget and the improvement of the standard operating procedure, as well as for training (how to avoid the errors) and for supervision. The map of the error scenarios, included in the validation report, may also be useful as a check list for prior assessment of an analyst before assigning the task, etc. Ms. Karen Ginsbury, PCI Pharmaceutical Consulting, Israel, talked in her lecture about the practical applications of risk management to analytical testing, paying attention mostly to human errors. She said that error prevention in analytical methods is possible by 1) investing in education and improving the technical writing skills of analytical personnel responsible for writing methods; 2) performing robust method validation after formal risk assessment; 3) monitoring the risk of method performance using control charts and continued methods (process) verification; 4) implementing corrective and preventive actions (CAPA), auditing, oversight, and feedback as risk communication; and 5) engaging management review for risk review and risk assessment updates.

After these lectures, Dr. Michela Sega, INRIM, Italy, moderated the round-table discussion, "Are there relationships between method validation, human errors and estimation of measurement uncertainty?" Dr. Kuselman presented a question on the treatment of bias for measurement uncertainty evaluation in legal metrology. In the recommendations of the International Organization for Legal Metrology (*e.g.*, OIML R111-1 [12] and OIML R126 [13]), bias is limited by comparison with 'maximum permissible error'. However, in addition, it is taken into account as a part of measurement uncertainty at conformity assessment of a measurement/test result, compared with the nominal value, *e.g.*, the weight or the alcohol content in a driver's breath relative to the national law. Dr. Magnusson supposed that in this way the level of confidence of the measurement/test results for legal metrology purposes is larger than the usual 95 %. Dr. Markus Obkircher, Merck, Switzerland, discussed the role of certified reference materials (CRMs) for bias evaluation at method validation, and described briefly the Sigma-Aldrich (Merck) activity in the field of CRMs.

The second half of the workshop day started with a lecture by Prof. Emil Bashkansky, ORT Braude College, Israel. This lecture was dedicated to the validation of qualitative methods: evaluation of repeatability and reproducibility. The applications of statistical methods, such as "Categorical Analysis of Variance" (CATANOVA) and "Ordinal Analysis of Variance" (ORDANOVA), to the analysis of test results of nominal and ordinal properties were discussed. A study of freshwater cultured pearls colour test results was demonstrated as an example.

Dr. Anneli Kruve, University of Tartu, Estonia, talked about handling different matrices in the validation of analytical methods based on LC/MS. Dr. Shulamit Levin, Waters (TC), Israel, reported on the use of peak purity and spectral matching during the validation of LC methods. The topic of the lecture by Dr. Bianca Avramovitch, Teva Pharmaceutical Industries Ltd., Israel, was "Analytical quality by design (AQbD) in practice: risk assessment based on failure mode and effects analysis (FMEA) methodology, applied for complex sample preparations and chromatographic impurities separation". As at the previous workshop, Dr. Orna Dreazen, Nextar Chempharma Solutions Ltd, Israel, summarized the day, asking the workshop participants in her lecture, "Can the theory (of method validation) work in reality?" Dr. Dreazen said that her experience in pharmaceutical industry indicates a number of problems. Validation design is affected by practical considerations, such as the availability of samples and their cost, the duration of the study, etc. Validation study may often detect imprecision, inaccuracy, requiring a return to the method development stage. Thus, it is important to understand that method validation is not a routine task.

The round-table discussion, "How can validation be planned to provide a method user with maximum information?" was moderated by Dr. Raphael Bar, BR Consulting, Israel. Dr. Kuselman informed the participants about method performance criteria in recently published AOAC International Guidelines. [14] Dr. Hellmuth Broda, PerkinElmer, Switzerland, reported on novel services of his company for analytical method validation and other method lifecycle activities. Dr. Mikhail Zayats, Institute of Plant Protection, Belarus, discussed challenges in the validation of a GC method.

More details about the workshop and presentations in pdf format are available at http://bioforumconf.com/satellite-event2017.

On the two days following the conference, 24-25 January, workshop participants took part in the Isranalytica 2017 Conference and Exhibition. A summary of these events is available at www.isranalytica.org.il.

**www.iupac.org/project/2016-007-1-500**

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