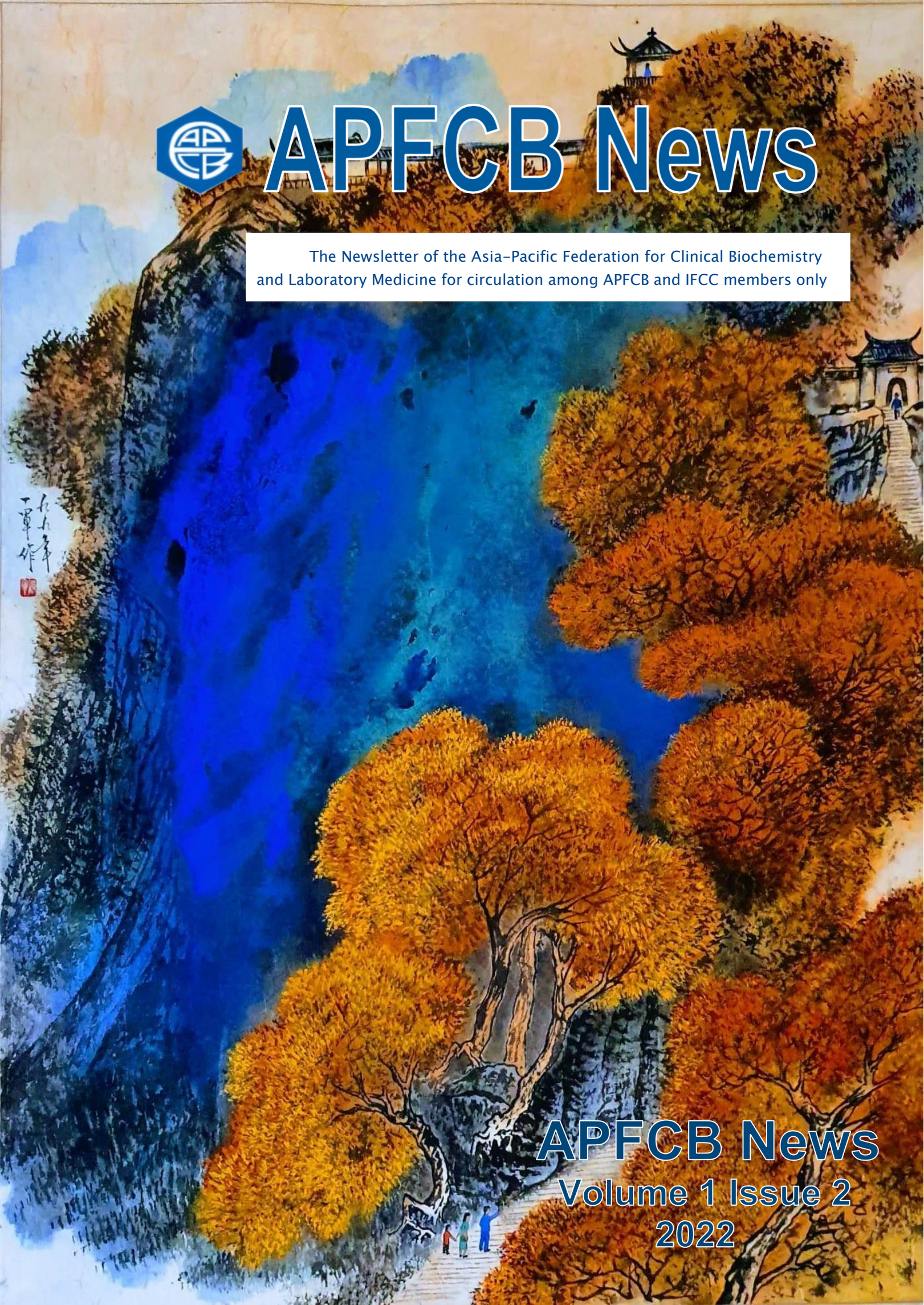

APFCB News

The Newsletter of the Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine for circulation among APFCB and IFCC members only

APFCB News

Volume 1 Issue 2
2022

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APFCB Executive Board and Chairmen Of Committees, Elected December, 2020-2022

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Submissions

The APFCB News welcomes suitable contributions for publication. These should be sent electronically to the Chief Editor. Statements of opinions are those of the contributors and are not to be construed as official statements, evaluations or endorsements by the APFCB or its official bodies.
Contact email: afpcbofficial@apfcb.org

Cover page:"In Autumn, when the sky is Blue and weather is sunny and cool"
Contributed by Dr. Tan It Koon
Founding and Past President APFCB

Address

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APFCB, c/o Solid Track Management Pte Ltd. 150 Cecil Street, #10-06, Singapore

Contents

From the desk of Chief Editor

Dear friends and colleagues,

It is with great pleasure that we bring to you the second issue of the APFCB News 2022.

I am pleased that for this issue we received reports from seven national societies. I thank national society representatives for their support and would like to encourage more national societies to contribute to the APFCB News and make the newsletter a platform for sharing the activities that are carried out in their respective countries.

I take this opportunity to thank Professor Khosrow Adeli and IFCC for contributing a report on the activities of the IFCC and for their continuous support. A special thank you to Dr. Graham White for contributing an article entitled "Hitchhikers Guide to Measurement Uncertainty in Medical Laboratories" and to Dr Graham Jones for his opinion paper entitled "eGFR – 10 years on from the KDIGO Global Recommendations". These papers will serve as useful guides to medical lab professionals.

I would also like to thank Prof Nader for sharing a special report on Adaptive Learning Courses in Laboratory Medicine. The AACC Learning Lab is a cloud-based program which consists of over 100 courses, covering topics span across all disciplines of laboratory medicine. Members are encouraged to make use of the program as it is now available without a subscription fee for individual users.

Also included in this issue are reports on the various activities of the APFCB. The committees will see a change in chairs and membership in early 2023. To create awareness and encourage a culture of sustainability in the medical laboratories, a new Green Patch section has been added to this issue. My thanks to all contributors as well as to corporate members and those who have contributed educational articles. My sincere thank you also goes to Dr Tan It Koon who has generously shared his painting for the cover of the APFCB News all these years.

As this is the last issue with me as Chief Editor, I would like to express my gratitude to everyone who had rendered their kind support and assistance towards making the publication of the APFCB news from 2020 to 2022 possible. I take this opportunity to also thank the editorial board and the C-CP team for their dedication and hard work throughout the whole three years.

Thank you once again and may 2023 be a good year for everyone!

My vest wishes to all,

Dr. Raja Elina Raja Aziddin,

Chief Editor, APFCB News

Message from APFCB President

From the desk of the APFCB President, October 2022

Dear APFCB family,

I am very pleased to learn that this second issue of the APFCB News in 2022 is ready to be shared, in the early month of the second semester.

A lot has happened during the last couple of months. We are grateful that the 16th APFCB Congress which was jointly organised with the IFCC Worldlab in Seoul, was successful thanks to the positive developments of the pandemic and the hard work of the organisers. Although not all of us could join the event in-person, but the event was well attended.

The APFCB had its most important triennial meeting, which is the Council meeting, in Seoul, conducted in hybrid mode. It was attended by almost all council members and affiliate members. The new elected Executive Board which will be starting its office on 1 st of January 2023 was announced during this meeting. We congratulate and welcome Dr Tony Badrick as elected President, Dr Sam Vasikaran as Vice-President, Dr Praveen Sharma as Secretary, Dr Raja Elina Raja Azzidin as Treasurer and Dr Douglas Chung as Corporate Representative, and wish them a productive two years in office. This also marks the end of term of office of the current Executive Board which will end on 31 December 2022.

The 16th APFCB Congress was the last triennial APFCB Congress, as the next congress will be held in Sydney, Australia, in 2024, as the first biennial congress. From then on, all APFCB congresses will be conducted biennially.

A new APFCB News Editor will also come on board following the change of the Committee Chairs. Dr Raja Elina has certainly been successful in producing the APFCB News with high quality and in a timely manner. I would like to take this opportunity to thank her and her team for their continuous commitment during these past three years.

Lastly, I hope you will enjoy reading this last issue of 2022.

My best wishes always

Prof Sunil Sethi

President, APFCB

SK Sethi

Prof. Sunil Sethi
President, APFCB

IFCC Activities 2022: Latest Developments & Future Ahead

Prof Khosrow Adeli, President, IFCC

IFCC has had a successful first half of 2022, making significant strides towards "advancing excellence in laboratory medicine for better healthcare worldwide". Indeed, we saw the return of large in-person scientific meetings, launch of global initiatives and first-ever forums, as well as so much more!

In April, we gathered in the beautiful city of Munich for EuroMedLab 2022 following a long wait due to the COVID-19 pandemic. The conference was a huge success, with over 4,100 attendees who traveled from countries all around the world to participate in an excellent scientific program featuring innovative and diverse education opportunities that incorporated the best of clinical laboratory medicine and in vitro diagnostics. Other highlights included the lively industry exhibit with interactive booths, educational workshops, poster presentations, as well as social and networking opportunities.

To kick off the EuroMedLab, IFCC officially launched Global Med Lab Week (GLMW), which is an initiative aimed at promoting and celebrating the value of laboratory medicine and laboratory professionals in both public health and patient care. Creating global awareness among various stakeholders will increase the visibility of laboratory medicine as well as help to increase funding to support innovation and sustainability, thereby improving both public health and patient care. This year, we celebrated the "Laboratory's Vital Role in the Global Fight against the COVID-19 Pandemic" from April 18-24. Together, many Regional Federations,

National Societies, and over 30,000 lab professionals joined our social media campaign in support of this important initiative, and we can't wait to celebrate again for GLMW 2023.

In June, we visited the vibrant city of Seoul for WorldLab 2022, which garnered international participation in excellent scientific and social programs from over 3,000 attendees. Key highlights include the President and Speaker's dinner, during which 10 awards were presented in an IFCC Award Ceremony, as well as the first-ever Young Scientists Forum, where young scientists can present and discuss their activities in laboratory medicine and build on career skills. A total of 40 scholarships were provided to trainees in developing countries to present at this forum and attend the WorldLab meeting. Given the success of this forum,

IFCC plans to make this an annual event, providing opportunities for new young scientists to take part each year.Behind the scenes, IFCC Task Forces continue to make progress toward IFCC's goals to become the largest provider of free distance learning in the field of laboratory medicine, contribute to global lab quality, aid in the fight against the COVID-19 pandemic, as well as impact healthcare delivery and patient outcomes. Additionally, IFCC has been working to upgrade the current IFCC website to improve community experience and develop a virtual platform to support future conference activities for years to come.

As we reflect on the first half of 2022, it is exciting to see the great productivity of the IFCC organization. Now, IFCC is looking forward to upcoming events, including the 2022 IFCC General Conference, which will be held in Brussels, Belgium, from October 25-30, 2022. Not only will this meeting allow IFCC to foster collaboration between our regions and divisions, but it will also be the perfect occasion to celebrate the 70th Anniversary of IFCC. Moving forward, let us all recognize 70 years of global leadership in laboratory medicine, celebrate our contributions to advancing excellence in laboratory medicine, and continue to strive for improving healthcare worldwide!

APFCB Congress 2022

Reported by Endang Hoyaranda

After being delayed due to the pandemic, the 16th APFCB Congress was conducted in collaboration with the IFCC World lab in Seoul, 26-30 June 2022.

The event took place at the COEX Seoul, and was well attended despite the uncertain situation which caused cancelled travel plans due to participants or speakers getting unwell, visas not granted, or any other unexpected situation. All scientific sessions were fortunately arranged as hybrid meetings courteously provided by the organisers, allowing virtual attendance by participants who had limitations to attend in-person. Those facilities became very convenient for the speakers as well, as several key speakers were not able to travel, mostly due to the pandemic situation. The APFCB had several business meetings arranged during the event, the most important one being the APFCB Council Meeting which was held before the opening of the congress. APFCB President, Dr Sunil Sethi, could not attend the meeting due to health issues, but attendance by members at the Council Meeting was encouraging with 20 member associations, council and affiliates, from the total 23, present in-person or virtually.

Photo 1: APFCB Council meeting in Seoul, Korea

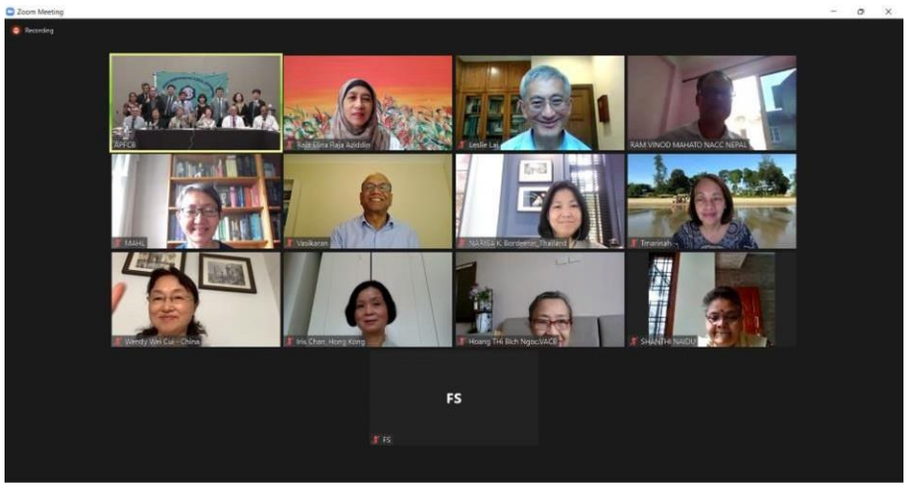


Photo 2: Virtual attendees at the APFCB Council meeting

A new Executive Board for the term of office 2023-2024 was announced as result of the elections held electronically several months before, as follows: Dr Tony Badrick was elected as President, Dr Sam Vasikaran as Vice President, Prof Dr Praveen Sharma as Secretary, Dr Raja Elina Raja Azziddin as Treasurer, Dr Douglas Chung as Corporate Representative. Two Auditors were also elected, namely Dr July Kumalawati and Dr Hassan Bayat. The only outgoing member of the Executive Board, who will stay in office, according to the constitution, will be the Immediate-Past President.

Photo 4: Joint APFCB EB and IFCC EB Meeting

The outgoing and incoming EB had another meeting to discuss future strategic issues, and another joint meeting with the IFCC EB, discussing future collaborations between the APFCB and IFCC.

Education and Laboratory Management Committee Report

Chair: Dr Tony Badrick

The successful candidates for the Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine Young Scientists Award Competition are listed below with their project titles. These candidates attended the WorldLab Seoul 2022 – 24th International Congress of Clinical Chemistry and Laboratory Medicine 16th Asia-Pacific Congress of Clinical Biochemistry and the IFCC Young Scientist Forum. The Young Scientist Forum ran over two days and focussed on the following themes: "Laboratory Management, Leadership & Teamwork" and "Empowering Evidence Base Medicine thought Clinical laboratory Research - Best Practices for Today's Laboratory Scientists".

Name	Country	Title
Fauqa Arinil Aulia	Indonesia	Specific Serological Patterns of Anti-SARS-CoV-2 in Mild and Moderate Illness of COVID-19 Patients Using Qualitative SARS-CoV-2 IgM/IgG Testing
Victoria Indah Mayasari	Indonesia	Analysis of Adrenocorticotropic Hormone and Cortisol Levels Before and After Corticosteroid Treatment in Covid-19 Patients with Acute Respiratory Distress Syndrome
Sushant Pokhrel	Nepal	MPV as an indicator of vascular complication in poor control Diabetic Population
Julie Sherfan	Australia	Morning spot urine is a suitable matrix for measurement of copeptin
Malavika L	India	Relationship between BDNF, Serotonin and Lead in Indian School Children

Shruti Gupta	India	Assessment of gene expression and serum Interleukin-22 levels in Tuberculosis patients of North western India
Prasenjit Mitra	India	Assessment of miR-146a, miR-222 and miR-210 expression and their relationship with immune-regulatory cytokines in workers occupationally exposed to Cadmium
Smriti Suri	India	'Relationship of circulating miRNA-198 expression with DNA repair genes XRCC1 and OGG1 in patients with New Onset Type 2 Diabetes Mellitus (T2DM)
Kay Weng Choy	Australia	Pilot Quality Assurance Program for 14C-Urea Breath Testing
P.Padmavathi	India	Atherogenic risk in premature canities among college students-India
Saswati Das	India	Evaluation of pre analytical and post-analytical errors in a clinical chemistry laboratory using Sigma Metrics
Mark Raymund G. Nava	Philippines	Nanosilver-Bentonite Composite for Possible Hydrogel Applications: Synthesis, Characterization, and Antibacterial Investigations

Report of IFCC WorldLab and APFCB Congress 2022 -Young Scientist Award Winner

Thursday, 7 July 2022

This was the first time I have the opportunity to be an awardee of a travel scholarship from APFCB. I was so glad to attend IFCC Worldlab Seoul and Young Scientist Forum 2022. It was a new experience that opened insight and knowledge for me. Seoul is a very beautiful developed city. All access is very easy to reach by foreign tourists who come. The event took place very well, exciting, and impressive. Visit session to GC Labs provided experience about the advancement of medical laboratory technology. GC Labs provides many inspections with sophisticated tools. Visit session to Seoul National University Bundang Hospital provided experience about the important role of the laboratory in the progress of service in hospitals. The scientific session provided a new insight about the latest discussions that needed to be considered for the progress of the world of laboratory medicine. The sponsor booth was presented with an interesting. I got many new young researcher friends. All of these new experiences will be applied to where I work in Surabaya, Indonesia. It can bring enthusiasm to be more advanced in my laboratory. Hopefully one day I can get the opportunity to learn and get new experiences again. Thank you very much, APFCB!

Regards,

Fauqa Arinil Aulia, MD., Clinical Pathologist

Surabaya, Indonesia

Report of IFCC WorldLab and APFCB Congress 2022 -Young Scientist Award Winner

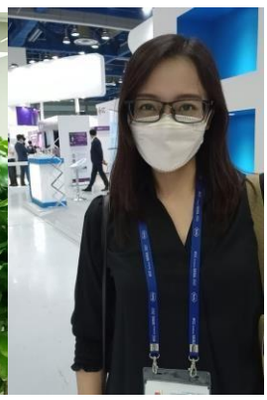
Victoria Indah Mayasari (Indonesia)

It is an honour for me to be the recipient of the Young Scientist Award held by APFCB so that I could attend the IFCC WorldLab 2022 as well as the IFCC Forum for Young Scientists in Seoul. IFCC Worldlab 2022 provided an interesting and informative scientific program. I learned a lot and got information about the latest laboratory developments in terms of technology applications in laboratory management, application of evidence-based guidelines, quality control, evaluation of laboratory examination methods, standardization of laboratory examinations, and ethical issues, all of which aim to increase clinical effectiveness in laboratory medicine.

The lab tour to GC Lab and SNHU that we participated in during the IFCC Forum for Young Scientists provided valuable knowledge. I could see how the settings and sophistication of the technology are not yet in my hospital laboratory. Those can provide an overview for the development of the laboratory at my place

Event IFCC WorldLab 2022 followed by many countries allowed me to meet many people from different countries and made a friendship with them. We shared experiences and ideas, not only about laboratory medicine but also about the culture of our country.

Thanks to APFCB for this amazing experience. I hope I will be able to have an opportunity to join in APFCB congress 2024 in Sydney.



Report of IFCC WorldLab and APFCB Congress 2022 -Young Scientist Award Winner

Julie Sherfan, (Australia)

I had the opportunity to attend the 24th IFCC and 16th APFCB Congress in Seoul at the end of June, thanks to the APFCB Young Scientist Travel Scholarship.

The IFCC Young Scientist forum held on the weekend was a prelude to the congress, and it brought together young aspiring scientists from around the world in thoughtful discussions about harmonization of curriculums, the impact of digital healthcare, and the importance of mentorship in clinical and diagnostic research.

The group was treated to a lab tour to the Green Cross Laboratory and Seoul National University Bundang Hospital and our Korean hosts at both labs were kind, generous and honest in sharing information about their workflow processes, assay methodologies, and test count numbers. I was particularly intrigued by the configuration of their automated chemistry track systems. In Australia, large chemistry track systems are configured in a closed loop, however, at GC laboratories, there are 4 individual subunits with their own independent tracks. This configuration has demonstrated to be more efficient than closed loop systems and I found this insightful as my own organization is in the process of updating our system.

The Congress offered an array of interesting topics. I found the symposium on best laboratory practices for kidney disease thought provoking, particularly the recent changes to the estimated eGFR based on a racially neutral formula presented by Graham Jones (Australia) and the evidence to support the clinical utility of acute kidney injury biomarkers by Joe El-Khoury.

Fred Apple (USA) presented data on the Siemens Atellica VTLi point of care instrument for high sensitive troponin in the emergency was promising. However, the greatest benefit I gained from this congress was an opportunity to meet with Dr David Sacks (USA) and hear his lunchtime presentation on measurement of HbA1c by capillary electrophoresis. An added bonus was I got to have a casual chat with Dr Sacks about the complexities and ethical dilemma of HbA1c reporting in the presence of a haemoglobin variants.

I am grateful to the APFCB for giving me this opportunity to connect with my peers and progressing my knowledge.

By Julie Sherfan

NSW Health Pathology, Sydney, Australia

Date: 9/7/2022

Report of IFCC WorldLab and APFCB Congress 2022 -Young Scientist Award Winner

Smriti Suri (India)

I am Smriti Suri, PhD student from Department of Biochemistry, Postgraduate Institute of Medical Education & Research, Chandigarh, India. I am very thankful to the selection committee and all the organizers for selecting me as a recipient of APFCB Young Scientist Travel Award. I feel delighted to a part of IFCC Worldlab- APFCB Congress 2022. The conference was a great opportunity for young researchers like us to meet renowned scientist and learn from them.Talks and symposiums from esteemed researchers gave us an interface to know about them, talk to them and learn from them. To meet eminent scientist from around the globe and know about their journey and experiences was a dream come true. This was definitely an experience that I will cherish forever.

Report of IFCC WorldLab and APFCB Congress 2022 -Young Scientist Award Winner

Kay Weng Choy, (Australia)

I am thankful to APFCB for the opportunity to attend the IFCC WorldLab – APFCB Congress in June 2022.

On Sunday, the conference started on a high note with an opening lecture by Dr. Hawoong Jeong, a statistical/computational physicist, with a reminder message at the conclusion of the lecture "Don't forget the power of data and network. But connect them wisely." This was timely as conference continued on Monday with a talk on machine learning in laboratory medicine by Dr. Thomas Durant. In the same session, Dr. Tony Badrick provided an up-to-date and practical summary on patient based real-time quality control. We were reminded that quality control has become in many laboratories a poorly understood and practiced process relying on compliance rather than based on risk. Patient based real-time quality control promises better detection of error in real time at low cost. It is time to consider tools such as machine learning to automate quality control. As we consider the future of laboratory medicine, we were reminded of the important roles of mass spectrometry-based assays. This was nicely demonstrated by Dr. Mari De Marco using an intact ACTH LC-MS/MS assay as an arbiter of clinically discordant immunoassay results. As immunoassays continue to have their place in routine laboratory medicine, there was a great talk by Dr Cynthia Papendick, an emergency department physician in Australia. Some important messages included high sensitivity troponin in use with the European Society of Cardiology 0/1-hour algorithm now has robust, real-world evidence to support its use. The assessment of acute coronary syndrome in the emergency department has become increasingly complicated and efforts to simplify the process with new strategies including decision support need to be clarified. I am always excited to hear first-hand perspectives from practising physicians using laboratory tests. Dr. Yong Mong Bee, an endocrinologist from Singapore, discussed the role of NT-proBNP in the management of patients with type 2 diabetes. Cardiovascular disease risk stratification for patients with type 2 diabetes is important for reducing disease burden and associated healthcare costs. There is evidence that NT-proBNP can predict risk of cardiovascular complications in patients with type 2 diabetes and may help with optimisation of cardioprotective treatment. NT-proBNP may help identify patients with type 2 diabetes who may benefit the most from treatment with SGLT2 inhibitors – glucose lowering agents that improve cardiovascular outcomes in patients with or without type 2 diabetes.

A conference on laboratory medicine is not complete without a session on external quality assurance. We listened to the great work by Dr. Finlay Mackenzie from UK NEQAS, Dr. David Alter from the College of American Pathologists and Dr. Tony Badrick from RCPAQAP. It was encouraging to be reminded that external quality assurance programmes are intended to be "aspirational" and for "quality.

On Tuesday, Dr. Philippe Gillery presented a great summary of the challenges in assay standardisation, including analytical concerns and priority strategies, scientific improvement", ultimately for quality patient results in the interest of patient care.concepts and clinical attitudes, economical aspects and marketing strategies, and regulatory frameworks. There is a need for a global approach involving regulators, national measurement institutes, professional/scientific societies, IFCC executive board and scientific division, and last but not least, individual laboratory professionals. Haemoglobin A1c was used as an example of a success story in standardisation. We were reminded that "The standardisation adventure is still in progress". In a talk on the importance of commutability for metrological traceability in standardisation and harmonisation by Dr. Greg Miller, important lessons included procedures to assess commutability and assessing the status of harmonisation using commutable EQA samples. In his presentation on the evidence of analytical performance specifications, Dr. Sverre Sandberg reminded us that estimated of biological variation are evidence-based and greatly improved. Furthermore, database on biological variation estimates is now established, which includes calculations of performance specifications.

In a lecture on laboratory testing in the screening and management of non-alcoholic fatty liver disease, Dr. Elisabeth Powell discussed the need for clear protocols for non-alcoholic fatty liver disease with guidance for assessment of liver disease severity to aid primary care clinicians and ensure people with advanced fibrosis correctly referred for specialist care. The ELF test has a clear role in this process but further studies are required. On Wednesday, as I continued my journey learning about the utility of laboratory tests in the management of patients with chronic diseases, Dr. Eric Kilpatrick presented on the utility of both HbA1c and complementary tests (e.g., fructosamine, glycated albumin, 1, 5-anhydroglucitol) as markers of microvascular risk, cardiovascular risk and risk of developing diabetes; each is not without its limitations and their limitations are not the same. On the theme of laboratory testing in monoclonal gammopathy, Dr. Ronald Booth discussed the Canadian Society of Clinical Chemists recommendations for protein electrophoresis reporting. This was followed by Dr. David Keren who summarised the College of American Pathologists recommendations on the initial detection and measurement of monoclonal protein. Dr. Peter Mollee presented an update on protein electrophoresis reporting in Australia and New Zealand. Dr. David Murray from the United States posed a timely question on the role of mass-spectrometry in laboratory testing for monoclonal gammopathy.

On the last day of the conference (Thursday), it was great to hear again from Dr. Greg Miller on commutability issues in standardisation and harmonisation of clinical laboratory results. We were reminded that equivalent results are important for medical decisions. Commutable reference materials are required for metrological traceability of results for patient's samples. Suitable procedures are available to assess commutability. Equivalence of results can be assessed using commutable EQA samples.

Congratulations to the organising committee for IFCC WorldLab – APFCB Congress 2022.

Yours sincerely,

Kay Weng Choy

Report of IFCC WorldLab and APFCB Congress 2022 -Young Scientist Award Winner

P.Padmavathi

I am so glad that I have selected for APFCB young scientists travel scholarship. Unfortunately, due to some issue in visa processing I couldn't able to attend the conference in person however the organizing committee kindly accepted my request allowed me to attend the virtual conference.

June 25th the day started with 'IFCC young scientist forum' due to the time difference in India I have enrolled in second session global survey results and Harmonization in education curriculum are very interesting to listen. The data's of the survey are so amazed me. In the next day young scientist career, research and networking enlightened the pathway of the young scientist like me who is struggling to understand the value of research among laboratory professions.

The advantage of attending the virtual conference is I can easily move from one seminar room to another without spending much of time. On 27th I have attended best laboratory practice for kidney disease. Current status of accreditation gave me the knowledge and idea of where the world and India stands in accreditation. I have also understood the importance of the accreditation in clinical laboratory.

The golden age of the clinical lab as we transition from volume to value fascinated the laboratory practice. HbA1c in the monitoring, diagnosis and screening of diabetes: views on quality requirements in relation to its clinical use gave the broad knowledge of HbA1c in screening and diagnosis. Novel HbA1c enzymatic microslide dry chemistry assay impressed to know further in detail

I am also happy to know that this time India is a part of UNIVANTS Award. Next day Traceability in the laboratory medicine thought me the importance of traceability in laboratoty. At last Standardization and harmonization of clinical laboratory results showed the importance of standardizing the laboratory results. I thank Tony Badrick and APFCB for providing the opportunity to young scientist.

Thanks and regards
P.Padmavathi

Report of IFCC WorldLab and APFCB Congress 2022 -Young Scientist Award Winner

Saswati Das, (India)

This summer, I had the wonderful opportunity of attending Worldlab Seoul 2022 Congress as APFCB Young Investigator Awardee, held at Coex, Seoul, Korea from June 26-30, 2022, and was co-hosted by Asia Pacific Federation of Laboratory Medicine, Korean Society of Clinical Chemistry and the International Federation of Clinical Chemistry.

After a hiatus of more than two years, it was a welcome change to attend the IFCC WorldLab Seoul in person. Despite the fact that I continued to learn during the pandemic era, I missed being able to network in person. The Congress was held in a hybrid format with many national and international participants joining virtually. I especially cherish attending the plenary lectures on cutting edge technologies in Clinical Chemistry. I enjoyed all the sessions especially the sessions on laboratory management and cardio biochemistry. In the current scenario where the whole world is struggling in the midst of a pandemic, several sessions with focus on COVID-19 were included in the programme. Being an APFCB Young Scientist Awardee, I could attend the first IFCC Young Scientist Forum. This forum was organized by a team of young scientists and included presentations focussed on time management, leadership skills and sustainable laboratory practices. As a part of the YS Forum program we visited a laboratory in Seoul wherein we got a glimpse of the technologically efficient laboratory system in South Korea.

During the Congress, it was discussed how a well-organized system of continuing medical education might help to globalize medical knowledge in the areas of clinical chemistry and laboratory medicine. Educational workshops and poster presentations were essential components part of the engaging scientific sessions during the meeting. My presentation was focused on women's health. During the conference, I could present my work with the help of my poster to all the attendees of the conference and receive constructive feedback on my research.

Being recognised and honoured on such an esteemed platform was invaluable. During the many scientific sessions of the conference, I had the opportunity to speak with the local organising team representing different South Korean medical institutes. I had the opportunity to share my findings with world-class experts in clinical chemistry and laboratory medicine thanks to IFCC Worldlab 2022. It was an honour to present my findings to such a distinguished group of people. I'm grateful that I was given the opportunity to present my work on being chosen as an APFCB Young Investigator Awardee. Many ideas were sparked and many scientific minds were motivated by the conference talks. I'm looking forward to working with the colleagues I met at the conference and attend future IFCC & APFCB scientific sessions.

Report of IFCC WorldLab and APFCB Congress 2022 -Young Scientist Award Winner

I, Dr. Shruti Gupta, (Senior Resident in the Department of Biochemistry at All India Institute of Medical Sciences (AIIMS), Jodhpur, India), would like to sincerely thank Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine (APFCB) for awarding me the prestigious APFCB -YOUNG SCIENTIST TRAVEL AWARD to participate in the IFCC World lab - APFCB Congress at Seoul, Republic of Korea from 25th to 30th of June 2022. It was a tremendous honour to be acknowledged by such an esteemed and prestigious organization. All the scientific sessions were enriched with knowledge and gave an exposure beyond the daily practices that are being followed in a developing country like mine. The experience was remarkable, providing me with a future vision for my academic work. The platform gave me an opportunity to interact with many learned people from the field of clinical chemistry across the world that helped broaden my perspective. I am extremely grateful to have received this award and I am sure it will add tremendously to my scientific career. The travel fellowship awards are a great initiative from APFCB, making it possible for the young scientists to participate in such global conferences, motivating them to move beyond their comfort zones and exposing them to a wide array of possibilities in our field. Once again, I would like to extend my heartfelt gratitude to the entire organization for giving me this opportunity.

APFCB Communications and Publications Committee Report (C-CP)

Chair: Raja Elina

Members of the committee for this term 2020-2022 are as follows:
Dr. Raja Elina Raja Aziddin (Chair)
Dr. Purvi Purohit (Web Editor)
Dr. Rojeet Shrestha (Media Coordinator)
Dr. Pradeep Dabla
Will Greene (Corporate -Roche) and
Lim Ai Tin (Corporate -Siemens)

A new member was co-opted in 2022 to replace Will Green (Roche)

The APFCB Communications and Publications Committee (C-CP) has been responsible for the development and management of the APFCB website and coordination of the online activities of the APFCB as well as for the online publication of APFCB news. Throughout the term, the C-CP has kept active communication and promoted the activities of the APFCB via electronic means not only to its member societies in the Asia Pacific region but also to countries under the IFCC.

1. APFCB website development, maintenance and management

The C-CP is responsible for the development, maintenance and management of the APFCB website. The APFCB website has been frequently updated with the latest information on webinars, online courses, virtual conferences of the APFCB, its member societies and international professional bodies. Also available are scientific publications, guidelines, recorded and live webinars on various topics of interest. The C-CP also oversees the management of the website which has been awarded to a third party, Ubitech Solutions.

The COVID-19 pandemic which dramatically accelerated the trend towards working remotely and pushed more and more activities online saw shortcomings and limitations of the APFCB website. In view of this, the C-CP is working on developing a new and improved mobile dynamic APFCB website. Work on the new design began in May 2022 and is expected to be completed before the end of 2022.

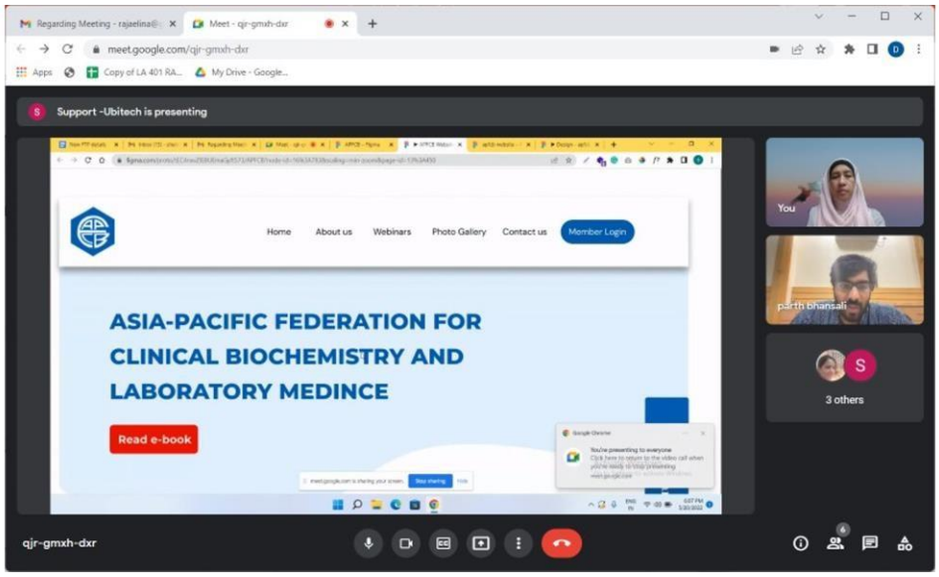


Photo 1: Meeting on web design on 19 May, 2022

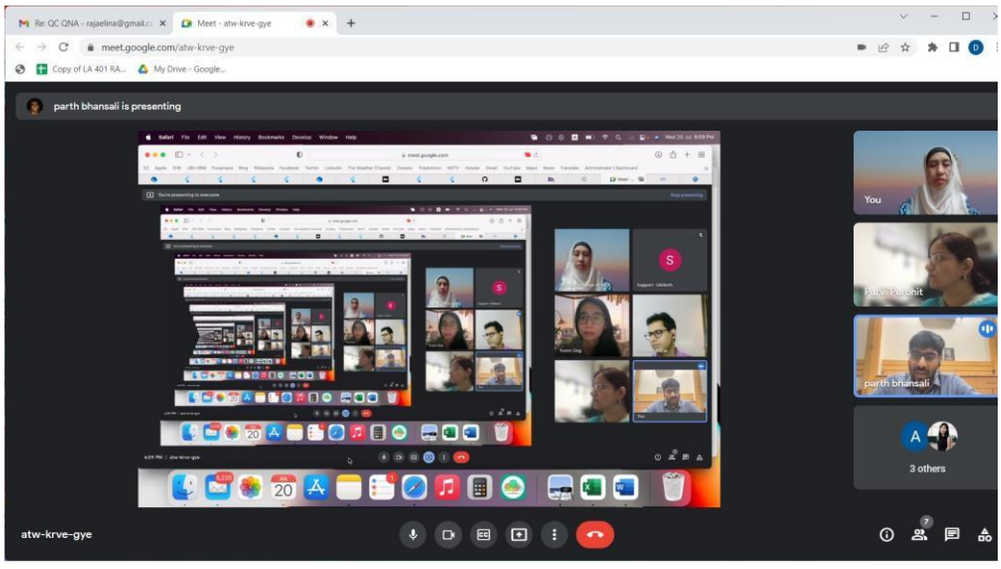


Photo 2: Meeting on web-design on 20 July, 2022

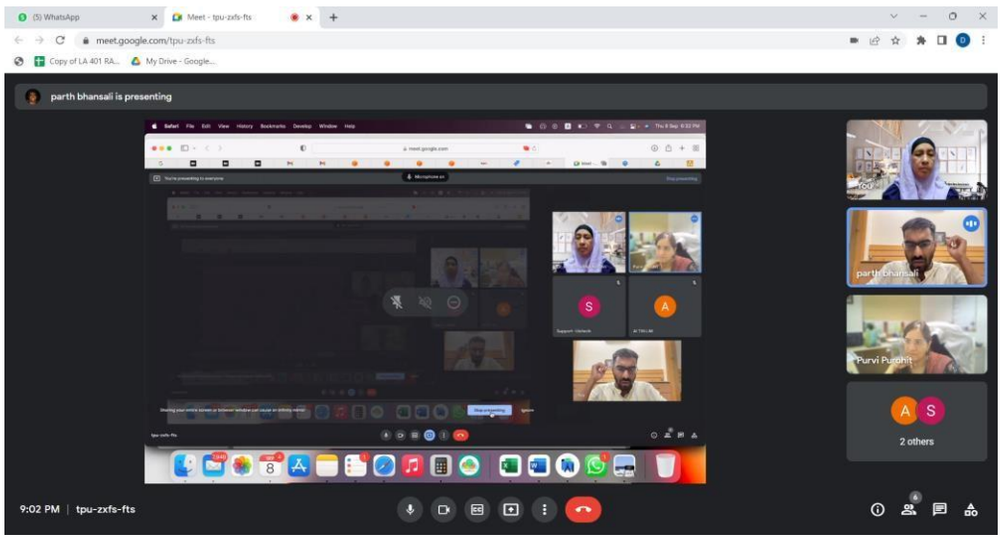


Photo 3: Meeting on web design on 8 September, 2022

2. APFCB social media development and management

For effective communication and distribution of news and updates of APFCB's activities among the national societies and clinical laboratory professionals, the C-CP has created social media accounts for the APFCB. Since August 2020, the APFCB is officially available on Facebook, Twitter, LinkedIn, Instagram and YouTube. Since then, the C-CP has been actively using social media to communicate and disseminate news and information on APFCB's recent activities which includes publications, congress and events, nominations and awards as well as promoting various e-learning activities and materials produced by the APFCB.

Links to the APFCB social media pages are as follows –
Facebook Page: https://www.facebook.com/APFCB/
Twitter: https://twitter.com/APFCB_LM
Instagram: https://www.instagram.com/apfcb_lm/
LinkedIn https://www.linkedin.com/company/apfcb/
YouTube: https://www.youtube.com/channel/UCoiicTsnVX-COjklgZHQ54Q

3. Publication of online activities, educational material and resources

The application of the virtual platform for educational and training purposes accelerated with the onset of the Covid-19 pandemic. Information on Covid-19, such as scientific publications, guidelines, recorded and live webinars on COVID-19 are made available on the website. Since August 2020, with the assistance of the APFCB Education and Lab Management Committee (C-ELM) and corporate members, additional educational and training material on other topics of interest were uploaded on the APFCB website so as to provide its members easy access to education and training.

The C-CP team also collaborated with other committees such as the C-ELM, Scientific and C-CC as well the corporate sector to coordinate the APFCB online activities. Announcements of upcoming events such as the APFCB Masterclass webinars on Interpretative Commenting, webinars under the APFCB auspices, IFCC webinars, APFCB Congress, IFCC Townhall event, conferences of the APFCB member societies were made available on the homepage of the APFCB website https://www.apfcb.org/index.html. Also available on the homepage is the APFCB virtual workshop on Complete Guide on Laboratory Testing of COVID-19.

To date, recordings and slides of past APFCB Masterclass Webinars on Interpretative Commenting have been uploaded on the webinars page of the APFCB website at https://www.apfcb.org/webinars.html. Also available on the webinars page are the IFCC webinars. Links to past webinars organised by the APFCB corporate members under the auspices of the APFCB are listed under the Congress and Conferences Committee page at https://www.apfcb.org/conferences.html. Links to these events have also been made available on APFCB social media which are listed at the footnote on the APFCB website homepage.

4. Promotional Activities

All upcoming events of the APFCB are promoted on the APFCB website homepage as well as on social media. In addition, the C-CP also sends out blast email invitations to members and reminders on upcoming events. The C-CP is continuously expanding the list of members in its database.

5. Publication of APFCB News

The C-CP is also responsible for the online publication of APFCB News. The chair of the C-CP is also Chief Editor of the APFCB News. The newsletter is published twice yearly and is available on the APFCB website as an e-book and can be downloaded as a pdf copy. The APFCB News is an important publication of the APFCB as it contains reports of APFCB activities under the various committees, report on IFCC activities as well as reports from member societies.

To standardise article submissions, the C-CP team drew up a Guideline for the submission of reports, articles and advertisements to the APFCB News in May 2021. This guideline is available on the APFCB website via this link: https://www.apfcb.org/Submission%20Guidelines%20APFCB%20News%20050721.pdf.

In following with tradition, the cover of the APFCB newsletter features paintings of Dr Tan It Koon, founder and past President of APFCB.

In line with the C-CP efforts to provide members access to educational material, educational articles have been included in the APFCB news from 2020 Issue 2 onwards. Since then, the response for educational article submission has been very encouraging. To further strengthen the educational content of the APFCB newsletter, opinion papers from experts have also been published in the newsletter since 2020 Issue 2. With this addition, the C-CP hopes to make the APFCB News a useful platform not only for sharing information on the activities carried out in the Asia Pacific region but also to make it a useful resource for knowledge sharing.

To encourage more participation and involvement of corporate members, a section called industry voice was introduced in 2020 Issue 1. This section contains reports of corporate member activities related to the APFCB such as reports on webinars under the auspices of the APFCB. In early 2021, rates for advertisements in the APFCB News were revised to make it more attractive to corporate members. Corporate members responded positively to the revised rates and the APFCB newsletter has since published advertisements in the newsletter from APFCB News 2021 Issue 1 onwards. Another exciting feature added to APFCB News 2022 issue 1 is a quiz section which is a new feature of the newsletter. Questions in this section are based on the APFCB webinars which were organized in 2020-2021 and which are still available on the APFCB website.

To date, 5 newsletters have been published:


READ THE LATEST NEWS
Get a copy of the APFCB News
@ https://www.apfcb.org/apfcb-news.html
APFCB News
2021
2022
ASIA PACIFIC FEDERATION FOR CLINICAL BIOCHEMISTRY AND LABORATORY MEDICINE

APFCB Scientific Committee Report

Chair: Samuel Vasikaran,

Members:

1. Tze Ping Loh, Chair of Harmonization of Reference Intervals WG
2. Ronda Greaves, Chair of Mass Spectrometry Harmonisation WG
3. Mohamed Saleem, Chair of Laboratory Data for Improving Diagnostics WG
4. Mithu Banerjee, Chair of Diabetes Testing Harmonisation WG
5. Pavai Sthaneswar, Chair of APFCB / WASPaLM Task Force on CKD

1. Reference Intervals WG

The Harmonization of Reference Intervals WG has examined and compared indirect methods for the derivation of reference intervals using data from laboratories within the Asia-Pacific region. The results of these studies have resulted in three publications.

Publications:

Comparison of two (data mining) indirect approaches for between-subject biological variation determination.
Tan RZ, Markus C, Vasikaran S, Loh TP; APFCB Harmonization of Reference Intervals Working Group. Clin Biochem 2022 Apr 27. doi: 10.1016/j.clinbiochem.2022.04.015. Online ahead of print.

Comparison of 8 methods for univariate statistical exclusion of pathological subpopulations for indirect reference intervals and biological variation studies. Tan RZ, Markus C, Vasikaran S, Loh TP; APFCB Harmonization of Reference Intervals Working Group. Clin Biochem 2022; 103:16-24.

Comparison of four indirect (data mining) approaches to derive within-subject biological variation. Tan RZ, Markus C, Vasikaran S, Loh TP; APFCB Harmonization of Reference Intervals Working Group. Clin Chem Lab Med 2022; 60(4):636-44.

2. Mass Spectrometry Harmonisation WG

A multicentre study of the influence of internal standard on the analysis of 17-hydroxyprogesterone by LCMSMS was completed in association with RCPAQAP – AACB and IFCC ETD Pediatric Hormonics Working Group.

A study of patients presenting to the National Children's Hospital in Vietnam with 5α-reductase type 2 deficiency detected by GC-MS analysis of the urinary steroid metabolome was conducted. The additional aim of this study was to determine the sensitivity and specificity of urinary steroid metabolite ratios in the diagnosis of 5α-reductase type 2 deficiency

Publications:

- Validation of steroid ratios for random urine by mass spectrometry to detect 5α-reductase deficiency in Vietnamese children. Tran TCM, Tran TNA, Le HBN, Nguyen VH, Tran MD, Vu CD, Greaves RF. Clin Chem Lab Med 2022 May 24. doi: 10.1515/cclm-2022-0272. Online ahead of print.

3. Laboratory data for improving Diagnostics WG

The WG has Analysed Laboratory Data for Improving Diagnostics and produced data on the reporting of critical results in Asian laboratories and Quality indicators in Chinese Laboratories. These survey reports will be used to support healthcare goals for improved disease management in the region. The support of Roche Diagnostics for this activity is acknowledged.

Publications:

A current analysis of quality indicators in Chinese clinical Laboratories. Saleem M, Wong W, Huang XZ and Badrick T. J Lab Precis Med 2021; 6:16

Turnaround times and modes of reporting critical results in Asian laboratories. Badrick T, Saleem M, Wong W. Annals of Clinical Biochemistry 2021:58(3):247-50.

4. Diabetes Testing Harmonisation WG

The WG has expanded its survey of diabetes testing and reporting practices in the region. Results of surveys conducted in the Philippines, Sri Lanka and Singapore have been analysed and will be presented as a poster at the AACB Annual Scientific Conference in Perth, Australia in October 2022. Results confirm that whilst most laboratories follow recommended practices, there is some lag in laboratory practices in some areas which could benefit from activities to harmonize and update practice.

5. APFCB-WASPaLM TF-CKD

The WG has undertaken a survey of testing and reporting practices for CKD related laboratory indices in India in order to ascertain concordance of reporting practices with current guidelines and industry standards. The results have been analysed and will be presented as a poster at the AACB Annual Scientific Conference in Perth, Australia in October 2022. It is hoped that the findings would lead to activities to harmonize testing and reporting practices according to current recommendations throughout the region.

6. Masterclass webinars: Interpretative commenting on clinical chemistry reports.

Webinars to discuss and analyse interpretative comments and to educate laboratory professionals on the addition of interpretative commenting have continued through the first half of 2022 with wide participation from the region. The resource material and the recordings of these webinars are available on the APFCB Youtube channel: https://www.youtube.com/channel/UCoiicTsnVX-COjklgZHQ54Q/videos

Future webinars are planned on a monthly basis. The support and the excellent organisation of the webinars by Dr Pearline Teo, Siemens Healthcare Pte Ltd is acknowledged.

APFCB Masterclass on Interpretative Commenting Webinar series

Drs. Sam Vasikaran, Raja Elina and Pearline Teo

Since August 2020, the APFCB Scientific Committee has organized a monthly webinar series on Interpretative Commenting.

In this series, chemical pathology experts discuss the interpretation of laboratory test results and recommend comments that may be suitable to provide in the laboratory report. The format of the webinars is generally a discussion of case reports for 45 minutes followed by question and answer session for about 15 minutes.

The series continues to enjoy excellent support from invited experts and the APFCB community.

The past and upcoming topics since our last report in December 2021 are as follows:

Month	Topic	Speaker
February 2022	Hyperandrogenism in Females	Dr. Melissa Gillett
March 2022	Serum protein electrophoresis Part 2 & Free Light Chains	Dr. Nilika Wijeratne
April 2022	Anemia testing	A/Prof. Ken Sikaris
May 2022	Bone markers	Dr. Sam Vasikaran
August 2022	Renal function and eGFR	A/Prof. Graham Jones
September 2022	** Lab Quality “Ask the Experts” Q&A	A/Prof. Tony Badrick & Dr. Tze Ping Loh

In September 2022, we will have a special collaboration with the APFCB Education Committee to hold an “Ask the Experts” session on Laboratory Quality.
Recordings and slides of past webinars are available via the APFCB website and youtube channel, while registration links for future webinars are posted on Eventbrite.

https://www.apfcb.org/webinars.html
https://www.youtube.com/channel/UCoiicTsnVX-COjklgZHQ54Q/videos
http://APFCB.eventbrite.com

We thank the speakers for volunteering their time and effort to support this educational initiative. Their depth of knowledge and experience are clearly appreciated by our webinar participants. Participant feedback continue to be overwhelmingly positive: >95% of responders “agree” or “strongly agree” that the session had been useful to them, and that they would recommend it to others.

We thank the participants for their attendance and lively discussion during the Q&A sessions. Many participants are consistent supporters of the series and have provided valuable suggestions and feedback.

Last but not least, we thank the APFCB Communications team, for their support in publicizing each event, and making the slides and recordings available online.
We invite all interested laboratory professionals to participate in future webinars.

Chinese Association for Clinical Biochemistry (CACB-Taiwan)

CACB participated in the 36th Joint Annual Conference of Biomedical Science (JACBS) (Photo 1). The 36th JACBS was held in hybrid format on 26-27 March 2022. The Conference venue was at the National Yangming Jiaotong University, Yangming Campus, Taipei. CACB planned for a scientific symposium focusing on "Precision Laboratory Medicine and Sustainable Healthcare". Four speakers were invited to present the progress on identifying novel biomarkers and therapeutic targets for various diseases. The speakers include Dr. Khosrow Adeli, IFCC President and Professor at The Hospital for Sick Children/University of Toronto, gave a keynote speech on "Value and Impact of Lab Medicine in Healthcare and Public Health" (Photo 2); Dr. Wen-Chien Chou, Director of the Department of Laboratory Medicine at National Taiwan University Hospital, presented "Precision Medicine- from blood cancers"; Dr. Sui-Yuan Chang, Professor of Clinical Laboratory Sciences and Medical Biotechnology, National Taiwan University, shared their latest findings on "Inhibition of SARS-CoV-2 infection including the Omicron variant by a broad-spectrum siRNA"; Dr. Wen-Hui Ku, CEO of Taipei Institute of Pathology, presented "Precision Medicine: the utility of LC-MS" (Photo 3). CACB also held competitions for poster and oral presentation (Photo 4). Overall, the two-day conference was successful and truly an enjoyable academic gathering for the attending members of CACB.

This year, CACB marks it 40th year. A scientific symposium followed by celebration was held on July 9th at the Department of Clinical Laboratory Sciences and Medical Biotechnology, National Taiwan University. Past and current presidents, board members and friends of CACB reunited to honor the past and celebrate the future of CACB (Photo 5). A traditional Chinese edition of "The chronicle and commemorative photographs of Chinese Association for Clinical Biochemistry 1982-2022" was also published and distributed to CACB members (Photo 6).

Photo 1 CACB board members at the 36th Joint Annual Conference of Biomedical Science (JACBS).

Photo 2 Keynote Speaker, Dr. Khosrow Adeli and CACB Executive Director, Dr. Woei-horng Fang at the 36th JACBS.

Photo 3 CACB board members and the invited speakers at the 36th JACBS.

Photo 4 CACB oral presentation competition at the 36th JACBS. Front: judges (CACB president and board members) Back: contestants.

Photo 5 CACB 40th anniversary.

Hong Kong Society of Clinical Chemistry

The year started with the newly elected office bearers elected at the Annual General Meeting (AGM) of the Hong Kong Society of Clinical Chemistry held on 22 January 2022, taking up their office. The office bearers elected were:

President	Dr Iris HS CHAN
Vice President	Dr Sammy PL CHEN
Immediate Past President	Dr Jeffery SS KWOK
Secretary	Ms Cybil TY WONG
Treasurer	Mr Emmett WK LAW
Council Members	Prof YM Dennis LO
	Prof Allen CK CHAN
	Dr Lydia CW LIT
	Mr Yun Chuen LO
	Ms Judy PS LAI
	Dr Doris CK CHING
	Dr Felix CK WONG
	Dr Toby PY LAU
	Dr Stella MT LEUNG
	Dr Richard KT KAM

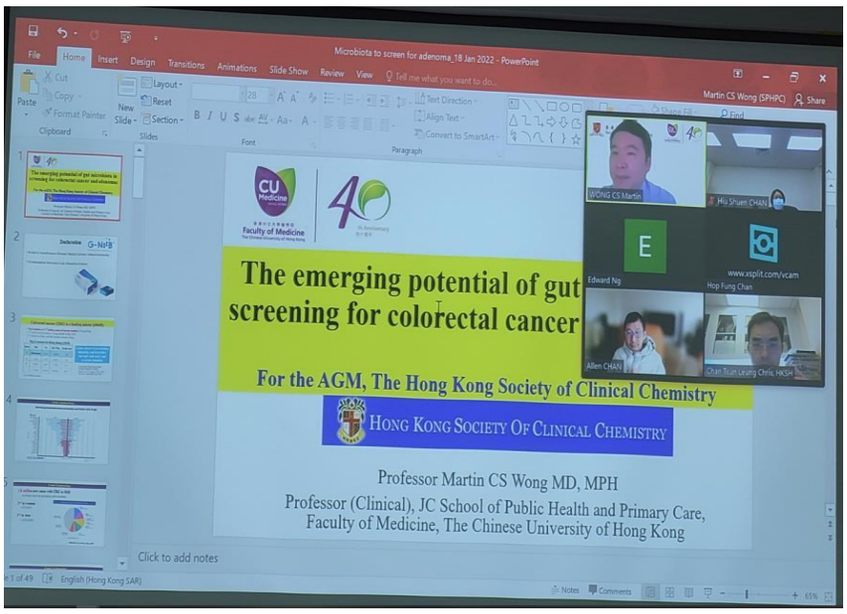
National Representative to IFCC	Dr Iris HS CHAN
National Representative to APFCB	Dr Iris HS CHAN
Representative to FMSHK	Ms Judy PS LAI

Council 2022 – 2023

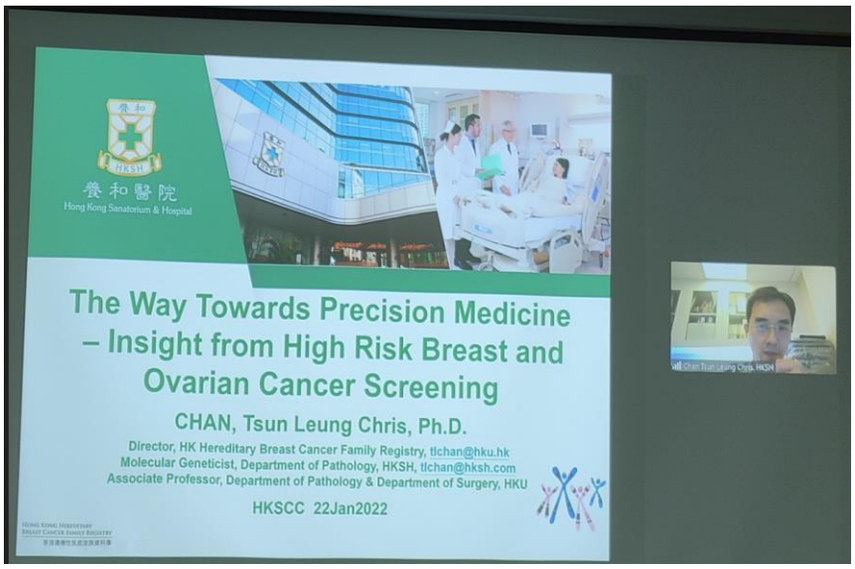
The 2022 Annual Scientific Meeting (ASM) was held on the same day in hybrid mode and the theme this year was “Biomarkers in Oncology: Current Practice and Development in Hong Kong”. There were two presentations from invited speakers:

(1) "The Emerging Potential of Gut Microbiota in Screening for Colorectal Cancer and Adenomas" by Professor Martin CW WONG, Director, The Jockey Club Bowel Cancer Education Centre, The Chinese University of Hong Kong; and (2) "The Way Towards Precision Medicine – Insight from High Risk Breast and Ovarian Cancer Screening" by Dr Chris TL CHAN, Molecular Geneticist, Supervisor, Division of Molecular Pathology, Department of Pathology, Hong Kong Sanatorium & Hospital. The ASM was attended by 71 members and guests.

ASM 2022 (22 Jan 2022): Prof Martin CW WONG

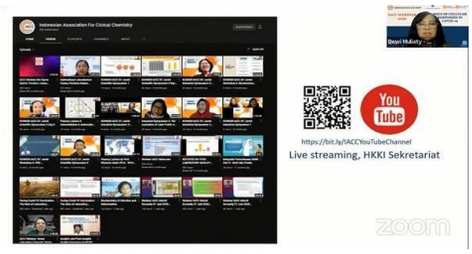


ASM 2022 (22 Jan 2022): Dr Chris TL CHAN



Report of Indonesian Society of Clinical Chemistry (IACC)

PERKUMPULAN KESEMINATAN KIMIA KLINIK DAN LABORATORIUM INDONESIA
INDONESIAN ASSOCIATION FOR CLINICAL CHEMISTRY



IACC has been involved in the fight against the COVID-19 pandemic since it began. This year in the period time to prepare for a new normal, IACC still conducts and produces webinars for the training and education of laboratory professionals.

Role of cellular responses in covid-19

COVID-19 Opening the year 2022, IACC held COVID19 Webinar series collaborated with UBC Medical Indonesia. Webinar attended by around 500 participants. Live webinar broadcasted through zoom and IACC's YouTube channel.

Topic	Speaker
Opening	
Newborn screening test: what is the importance & what is the problem	Prof. Dr. dr. Aman B. Pulungan, SpA(K), FAAP, FRCPI (Hon.)
Diskusi topik Prof Aman	
How to assure qualified dried blood spot for newborn screening test	dr. Thyrza L. Darmadi, SpPK
Interpretation of newborn screening test results (rekaman presentasi)	Dr. dr.Ina S. Timan, SpPK(K), MARS
Product Presentation	Sponsor
Discussion	All speakers, kecuali Prof. Aman
Quiz & Closing	

Qualified dried blood spot for newborn screening test & its interpretation

Most countries, including Indonesia, have established newborn screening as a national program. It is routinely performed by using a few drops of blood from the newborn's heels and placing them into a cards. There must be an appropriate techniques to collect, handles, store, and ship the dried blood spot to assure its integrity and quality before the blood is measured in the instrument. THis webinar was attended by 700 participants.

Thyroid seminar – pre congress event

The Role of laboratory in Managing Thyroid Health as a theme of Seminar held in Borobudur Hotel Jakarta on July 2022. This is the first offline meeting for IACC after pandemic. Participants were 200 people,

IACC branches

Biomarkers for sepsis

Webinar was held by IACC Jambi lead by Dr. dr. Sotianingsih, SpPK(K)

Management of dengue & sars cov2 mutation

Webinar was held by IACC Malang lead by Dr. Hani Susianti, SpPK(K). During the pandemic era, management of dengue quite challenging.

Updates on laboratory testing & management of diabetes mellitus

an hybrid event held by IACC Surabaya lead by dr. Ferdy R. Marpaung SpPK(K

Management & monitoring in critical care patient

Webinar was held by IACC Makasar lead by Dr. Darwati Muhadi SpPK(K).

Regional & International Events

External Quality Assurance

IACC delightedly join an External Quality Assurance Survey program from IFCC's global initiative to enhance clinical laboratories' quality in developing countries cooperated with One World Accuracy

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IFCC YOUNG SCIENTIST

Young Scientists (YS) are the future of laboratory medicine and comprise the major workforce of laboratory professionals. IACC YS participated in The IFCC is pleased to announce the IFCC FORUM for YoungScientists that took a place on 25 and 26 June 2022 in conjunction with the IFCC WorldLab Congress 2022 in Seoul, South Korea

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IFCC WORLDLAB CONGRESS 2022

IACC delegation attended IC World Lab Congress 2022 in Seoul, South Korea. It is great opportunity meet up and gathered Lab Scientist from all of the world

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Korean Society of Clinical Chemistry (KSCC)

1. IFCC World Lab Seoul 2022

1) Overview

The 24th International Congress of Clinical Chemistry and Laboratory Medicine & 16th Asia-Pacific Congress of Clinical Biochemistry (24th IFCC World lab & 16th APFCB) co-hosted by KSCC, IFCC, and APFCB were successfully held at COEX in Seoul, Korea from June 26th to 30th.

Title	24th International Congress of Clinical Chemistry and Laboratory Medicine & 16th Asia-Pacific Congress of Clinical Biochemistry
Date	June 26-30, 2022
Venue	Coex, Seoul, Korea
Hosts	IFCC, APFCB, KSCC
Website	www.seoul2022.org
Registrations	1,157 Delegates, 230 Hybrid Delegates, 1,150 Visitors from 97 Countries
Scientific Program	4 Plenary lectures, 34 Symposia, 25 Education workshops, 3 Korean Students Sessions, 1 Satellite Meeting

Meeting	21 Meetings
Sponsors & Exhibition	2 Platinum Sponsors, 5 Gold Sponsors, 1 Silver Sponsor, 9 Bronze Sponsors and 27 Exhibitors
Social Program	Sunday, 26 June 2022: Opening Ceremony and Welcome Reception Monday, 27 June 2022: Presidents' and Speakers' Dinner Thursday, 30 June 2022: Closing Ceremony

2) Scientific Program & Social Program

Congress Timetable

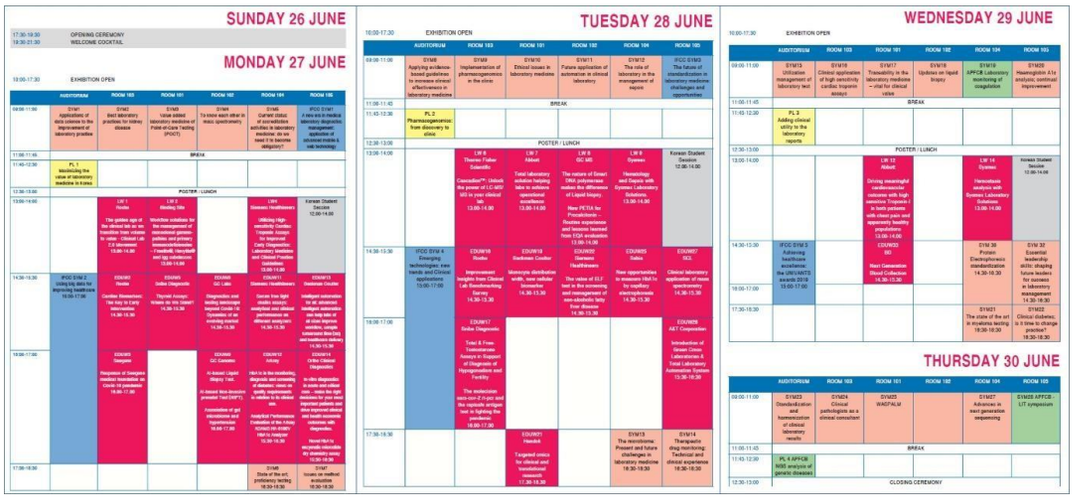


Fig.2

Fig.3

3) Abstracts

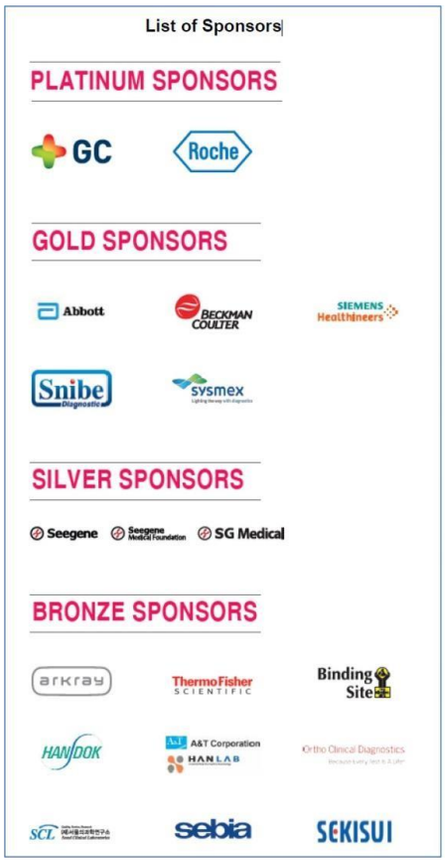
- Abstract Submission

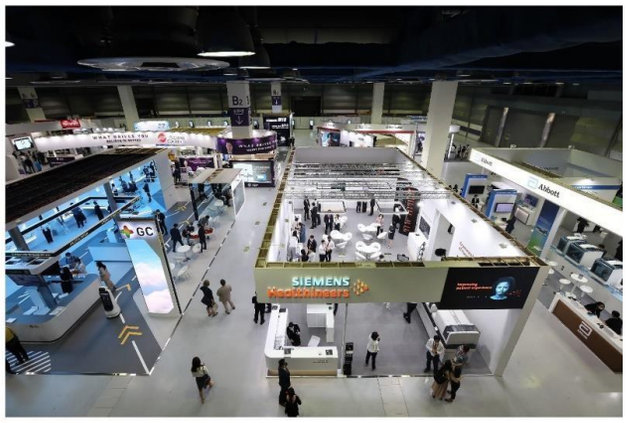
The Congress Organising Committee decided to fix the last deadline to submit the abstracts on January 15th, 2022. The final number of accepted abstracts was 886.

- Abstract review

46 reviewers were recruited and a schedule was made to give each reviewer the topic(s) of expertise. The total number of submissions when the congress was planned in 2020 was 826, of which 757 were accepted. After abstracts system new re-opening, 220 new abstracts were evaluated. For the first time in IFCC conferences posters were displayed in electronic

4) Sponsors & Exhibition





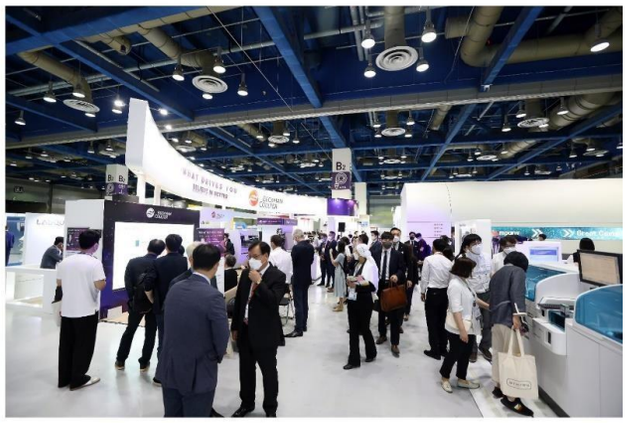


Fig.4

List of Exhibitors

ARK Diagnostics	LABQUALITY
BD	LG Chem
BOM MEDICAL	NOVA BIOMEDICAL
BÜHLMANN Laboratories	QIAGEN
COLLEGE OF AMERICAN PATHOLOGISTS	QUIDEL
EONE Laboratories	RADIOMETER
EUROIMMUN	SAMKWANG LABTREE
EUROSPITAL	SAMKWANG MEDICAL LABORATOIRES
EXIAS Medical	SCL
GENESYSTEM	SD BIOSENSOR
GREINER Bio-One	SEKISUI
HUVAROS	SHINYANG
IMPROVE MEDICAL	WEQAS
	WERFEN

5) Committees

Congress President

Prof. Won-Ki Min

Congress Organizing Committee

Prof. Junghan Song, Organizing Committee Chairman

Prof. Yeo-Min Yun, Secretary General

Prof. Sail Chun, Scientific Program Chairman

Prof. Jehoon Lee, President of KSCC

Prof. Sang Hoon Song, Secretary of KSLM

2. KSCC Satellite Meeting

To commemorate the 24th IFCC Worldlab & 16th APFCB, the Korean Society of Clinical Chemistry organized a Satellite Meeting, as follows:

Title: COVID-19 Diagnosis and Quarantine

Date: June 25 (Sat), 2022 14:00~20:00

Venue: Orchid Room, Grand Intercontinental Seoul Parnas

Sponsor: SD BIOSENSOR

Fig.5

Fig.6

More than 50 participants from Korea and abroad attended KSCC satellite meeting to share the unprecedented COVID-19 pandemic and the experience and research results of overcoming the COVID-19 crisis in the Asia-Pacific region to completely overcome it, and it became a meaningful place to prepare for the remaining challenges.

Malaysian Association of Clinical Biochemists

Dr. Raja Elina Raja Aziddin, President, MACB

1. Project on Measurably Better Healthcare Performance

This project was launched in December 2021 and is supported by Abbott Laboratories. Five (5) project submissions were received from two (2) institutions, two (2) from Hospital Selayang and three (3) from Pantai Premier Pathology. Due to limited funds, one project from each institution was selected in March 2022. The study is currently ongoing.

2. Workshop

The MACB Scientific Committee has to date conducted three (3) physical workshops in 2022. All workshops were carried out in collaboration with Department of Standards Malaysia.

i) Method Verification for Qualitative Tests – Two Workshops

The first workshop on Method Verification for Qualitative Tests was held on 21st March 2022. This workshop was organised as a follow-up to the lecture that was held at the pre-AGM scientific program in 2021 on a similar topic.

Photo 1: Participants at the MACB Method Verification for Qualitative Tests Workshop 1 in March 2022

In consideration to the situation of the Covid-19 pandemic, the number of participants had to be limited and only 56 participants were allowed to participate. This one-day hands-on workshop was very well received and 95 % found the workshop relevant and useful. Topics covered include precision, verification of cut-off value and comparison studies for qualitative tests.

Due to requests from participants who were unsuccessful in their registration to the first workshop, a second workshop on Method Verification for Qualitative Tests was caried out on 2 August, 2022. This workshop had 87 participants and more than 97% found the workshop relevant and useful for their job.

Photo 2: Participants at the MACB Method Verification for Qualitative Tests Workshop 2 in August, 2022

ii) Approach to Method Verification for Quantitative Tests to Fulfil ISO 15189 Requirements

This 2-day workshop was held on 18-19th July 2022 and had 83 participants. Topics include quality specifications, imprecision, method comparison, linearity, reportable range, detection limit, functional sensitivity, verification of reference interval and how to prepare a method verification report.

Photo 3: Organising Committee of the Workshop on Approach to Method Verification for Quantitative Tests to Fulfil ISO 15189 Requirements

Photo 4: Participants at the Workshop on Approach to Method Verification for Quantitative Tests to Fulfil ISO 15189 Requirements

Participants found this hands-on workshop very relevant and useful and due to the high demand a second workshop on the same topic will be carried out in October 2022.Participants feedback is presented below:

3. Collaboration with other professional societies

The Malaysian Association of Clinical Biochemist (MACB) organised a discussion on the topic of Non-alcoholic Fatty Liver Disease (NAFLD) with Prof Dr. Rosmawati Mohamed, Consultant Hepatologist, University of Malaya and medical lab representatives from various hospitals on Tuesday, 14 June, 2022 @12 noon.

Agenda of the discussion were as follows:

1. Background on NAFLD disease burden and impact
2. Background and rationale of liver disease screening and risk stratification at the primary care level
3. Potential for reflex fibrosis-4 (FIB-4) scoring algorithm and consensus workflow for liver disease screening and risk stratification.

The objective of the discussion was to create better awareness among medical lab professional on NAFLD and to formulate an algorithm on lab testing for better detection and management of NAFLD in hospitals and public health labs in the country.

4. MACB Annual Conference

The 32nd MACB Conference will be held from 11-13 September, 2022. A pre-conference which will focus on Point of Care Testing (POCT) will be held on 11 September 2022 followed by a 2-day conference. The theme of the virtual conference is "Integrated Approach in Medical Laboratory: Challenges and Opportunities". Various topics of interest such as integrated diagnostics, updates on eGFR reporting, personalised medicine and quality management.

Photo 5: Announcement on the 32nd MACB Conference 2022

For the first time ever, MACB held a Young Scientist Awards Competition. Five winners were selected and they will be presenting at a special oral session during the conference. Four winners were locals while the fifth winner is from India.

Philippine Council for Quality Assurance in Clinical Laboratories (PCQACL) National Report

Author: Dr. Sarah Jane L. Datay-Lim, PCQACL President
Email: sarahdataylim@gmail.com

1. Educational activities

Back in 2021, we launched the free online webinars dubbed as "P.O.W.E.R." which stands for "PCQACL Online Webinar Educational series", aimed to adapt to the challenges of the pandemic and support laboratory professionals by providing free continuing medical education and updates. The online platform was integrated into the revamped and improved website, with automatic certificate generation and provision of the CPD points needed by professionals for their license renewal. It was made possible through partnership with diagnostic companies who shared PCQACL's vision of providing free quality education in the time of pandemic. From four episodes in 2021, the series will be finishing off with six episodes until the end of the year (POWER 5 to 10) covering timely and relevant topics in laboratory medicine. The 2022 series started last April, successfully garnering more than 1000+ participants each episode (See Image 1).

Image 1: POWER (PCQACL free Online Webinar seRies) 5 to 8 episodes.
L to R (POWER5- Philippines' cell morphology day with Sysmex, April 21, 2022; POWER6- Transitioning into the new normal with JARC group, May 31, 2022; POWER7- Taking a leap towards urinalysis standardization and quality improvement with Mindray, June 30, 2022; POWER8- Philippines in the battle against Tuberculosis with Lab mate, August 25, 2022)

PCQACL Academy online Certificate and Training program or P.A.C.T. on the other hand is another online educational tool available in our website that provides a more in-depth training for laboratory professionals. Speakers are experts in the field and enrollees can learn at their own pace and convenience using their devices, with the certificate given to those who will pass the final exam. It is designed to improve competencies, knowledge and skills of laboratory professionals and bridge the gap in trainings during the pandemic and beyond. See Image 2 for the PACT courses.

Image 2: PACT (PCQACL Academy online Certificate and Training program) course offerings.

L to R: Peripheral Blood Smear training: Standardization, Updates and Morphology Review launched last year and Point of Care Testing Certificate program new offering for 2022)

There was also collaboration with diagnostic companies in terms of supporting their scientific activities such as webinars especially in assistance for CPD points for laboratory professionals. Collaborations with Sysmex for 2022 are as follows: Using Expanded CBC Parameters in Clinical Practice: Quick and Relevant Lab Data (March 3, 2022); Routine and regular testing to avert and early detect heart disease (March 11, 2022); North Luzon Sysmex User's Group meeting 2022 (June 15, 2022); National Capital Region Sysmex User's Group Meeting 2022 (July 20, 2022); and The Interconnection between the Heart-Kidney-Diabetes and Anemia from Pathophysiology to Management (August 5, 2022).

2. Website improvements

The Information Communication and Technology Systems (ICTS) Committee in partnership with Progressive Productivity Solutions (PPS) improved the look, functionality and information on the PCQACL website: www.pcqacl.org. Aside from consolidation and hosting of the online educational programs and membership management, the new section of the website features PCQACL Bulletin which aims to give not just updates about the organization activities but also features laboratory medicine news and important developments or announcements. Contributions come from members and everything is also synchronized with our social media account. See Figure 3 for PCQACL Bulletin.

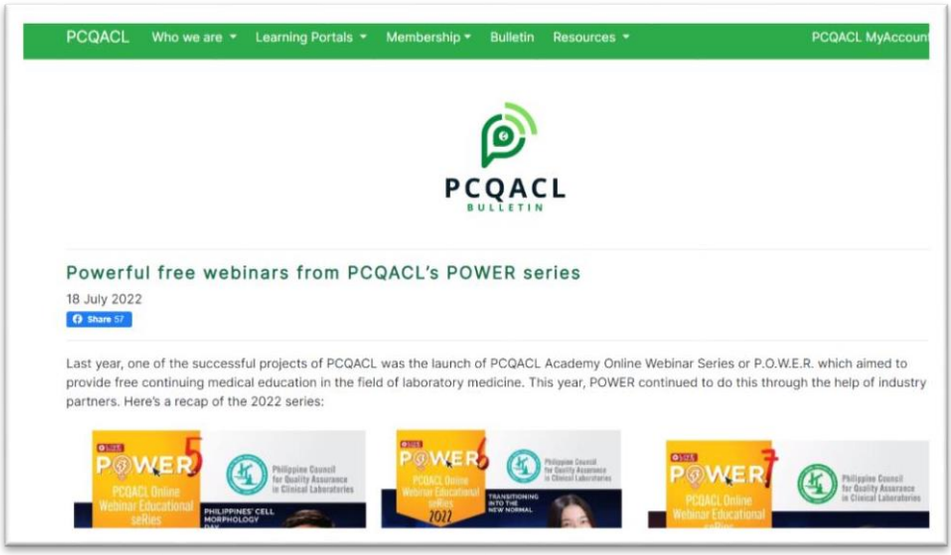


Image 3. PCQACL Bulletin featuring updates on organization activities, news and announcements in the field of laboratory medicine.

3. Meetings

Monthly board meetings continued this year starting January 2022, mostly virtually done due to the unpredictable COVID-19 situation and other threats of emerging infectious diseases here in the Philippines. Among the projects developed aside from POWER, PACT and the annual convention are the following: launching of Research project PCQACL P.A.S.S.I.O.N. "Philippine laboratory Advancements through Survey and reSearch for Improvement and innovatiONs" (first project is about Philippines' laboratory quality indicators), update of CBC standardization monograph (2nd edition) in collaboration with hematologists through their society, Philippine Society of Hematology and Blood Transfusion (PSHBT) and planning for urinalysis standardization monograph. Last June 18, 2022, with the significant drop in the number of cases and lifting of restrictions, we had our first face to face board meeting for the annual convention organizational meeting and photoshoot at Sofitel, Manila.

Image 4: PCQACL's first face to face board meeting and photoshoot for annual convention held at Sofitel, Manila.

4. Upcoming event

For this year, we will be having hybrid pre-convention (face to face and virtual) and a full virtual Annual Convention. It shall be held this September 7-10, 2022 with the theme: "Redefining Global Challenges into Quality Laboratory Standards".

Image 5: First announcement PCQACL Annual Convention

Philippine Association of Medical Technologists, Inc. (PAMET)

PAMET-PASMETH Awards DLSMHSI-CMLS for Bagging First place in Annual National Quiz Show

Jino Paolo G. Perlas

DASMARIÑAS, CAVITE - On September 17, 2021, the joint PAMET-PASMETH (Philippine Association of Medical Technologists, Inc. - Philippine Association of Schools of Medical Technology and Public Health) held their annual, nationwide medical technology quiz bee for college students. It was only last March 26, 2022, when the PAMET officials awarded the quiz bee participants from the De La Salle Medical and Health Sciences Institute College of Medical Laboratory Science (DLSMHSI-CMLS). The DLSMHSI-CMLS bagged the first place out of the 54 participating schools nationwide, which was live streamed via Facebook Live.

The PAMET National President Rommel F. Saceda, RMT, MBA and PAMET National Executive Secretary Mark Raymund G. Nava, RMT, MPA, MSMT, personally awarded the trophies and medals to the 4 winners who tenaciously represented their university: Patricia Nicole Magsino, Maria Veronica Cabubas, Beatriz Allysa Maranan, and Athene Guevarra who was awarded the Most Valuable Player.

Each of the participants received individual trophies and medals, while the university received a trophy, plaque, and a Key to Academic Excellence.

The participants' mentors, Amapola D. Puaso, RMT, MSMT and Jenny S. Gayondato, RMT, MSMT, were also present during the awarding in order to be recognized as well as to hand out their speeches for the participants and the CMLS body.

CMLS professor Michael John Dacela, RMT hosted the event and CMLS Dean Rolando M. Reyes, RMT, MD, MHPEd, FPCS, FPSGS, FPALES was also present to thank and congratulate the participants in person.

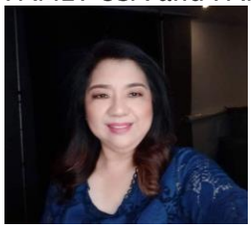
The PAMET-PASMETH Inter-School Medical Technology Quiz Bee is an annual quiz bee that has been running for 40 years as of present date. This is the second time in its history that the quiz bee was hosted online due to the COVID-19 pandemic and its restrictions


CONGRATULATIONS


CONGRATULATIONS


Welcome!
DE LA SALLE
ROMMEL F. SACEDA, RMT, MBA
PAMET National President
MARK RAYMUND G. NAVA, RMT, MPA, MSMT
PAMET National Executive Secretary
Awarding of PAMET-PASMETH Quiz Show
Championship Trophy
De La Salle Medical and Health Sciences Institute
College of Medical Laboratory Science
Champion 2021

PAMET USA and PAMET National: Teamed-up for a Medical Mission



Sanita A. Vistal

The Philippine Association of Medical Technologists (PAMET) – USA, Inc. headed by Mr. Dan Dominguez, CLS and PAMET National, headed by Mr. Rommel F. Saceda, RMT, MBA organized a Medical Mission in partnership with Civitan International, last April 30 and May 14 in Botolan, Zambales and Abucay, Bataan respectively. Dubbed as "PAMETatag ng panahon, PAMETagumpay sa darating na mga hamon". The program aimed to reach out to the underprivileged citizens as well as to offer medical and laboratory services that are unavailable to them.

This medical mission was able to provide medical screenings, blood laboratory tests such as blood chemistry and complete blood count, urinalysis services, and eye reading tests. Additionally, distribution of reading glasses, medicines, and supplements along with hygiene goods were offered.

The Zambales medical mission was held at the Baquilan Resettlement School II, Malomboy, Botolan, Zambales, while the Bataan medical mission was held in Mabatang Elementary School, Mabatang, Bataan which both reached more than 200 beneficiaries.

This event was made possible by the overwhelming support and collaboration of PAMET USA and PAMET National delegates, together with PAMET Olongapo-Zambales Chapter, headed by Ms. Jean Balquin, PAMET Bataan Chapter lead by Ms. Norayda Alim the Committee on Outreach of PAMET National through the leadership of Ms. Sanita Vistal, and the Committee on Laboratory Management of PAMET National directed by Ms. Myra F. Maceda.

Different diagnostic partners paved the way to make the event possible namely, Mindray Philippines, Sysmex Philippines, Zafire Distributors, Biosite Medical Instruments, Labmate Pharma, and the P&G Philippines for the donated goods.

Over-all, the team-up of PAMET USA and PAMET Philippines in a medical mission was a success. The continuous community outreach in various communities despite challenges proves that we are PAMET, "PAMETatag ng panahon, PAMETagumpay sa darating na mga hamon".

BATAAN


Philippine Association of Medical Technologists, Inc.
PAMET Bataan Chapter
Medical Mission
"PAMETatag ng panahon,
PAMETagumpay
sa daratinng mga hamon"

Zambales


CIVITAN CLUB
CIVITAN INTERNATIONAL
EPP
MAPEH


Medical Mission


Medical Mission

PAMET and P&G: Extending Joint-Hands to Reach Communities

haris Maye T. Nacario

Battling this pandemic have highlighted the need to maintain proper health and hygiene. More people became cautious about keeping their hands clean as well as maintaining a healthy habit, which has increased the need for hygiene kits and comprehensive health education to successfully combat the virus. However, less fortunate communities may need additional support.

Given this, the Philippine Association of Medical Technologists, Inc. (PAMET) and Proctor & Gamble Philippines (P&G) have joint-hands to reach various communities during the last quarter of 2021 and earlier this year. It has been more than 30 years since the partnership between PAMET and P&G started, where they conduct different community outreach activities such as medical missions, hygiene kit distribution and handwashing activities. The continuous collaboration of P&G and PAMET in extending their hands to reach communities have been successfully conducted despite the current pandemic situation. With P&G sharing their resources, and PAMET being the reaching arm, the community programs of the two organizations are in full swing and are always in success.

As to date, PAMET and P&G aims to unceasingly conduct countless outreach programs offered to deserving communities and to the less fortunate.

Here are some of the Outreach Programs highlighted during last quarter of 2021 and earlier this year.

PAMET CEBU Chapter
February 19, 2022
Barangay Nangka, Consolacion, Cebu
Handwashing Advocacy & Busog Lusog Program

PAMET Agusan del Norte – Butuan Chapter

February 14, 2022

Remedios T. Romualdez, Agusan del Norte

Handwashing Activity & Medical Mission

PAMET Bataan Chapter

December 11, 2021

Aeta Community, Banawang, Bagac, Bataan

Handwashing Activity & Gift-Giving

PAMET Kalinga-Apayao Chapter
Tabuk, Kalinga
Handwashing Program

PAMET Davao del Sur Chapter
Badjao Community, Digos, Davao del Sur
Handwashing Activity & Gift-Giving

PAMET Quirino Chapter

February 20, 2022

Aeta Community, Pulang-lupa, Nagtipunan, Quirino

Handwashing & Distribution of Hand Hygiene, Slippers and Gift Pack

PAMET Quezon Chapter

September 2021 and March 2022 Lucena City, Quezon

Medical Mission and Hygiene Kit Distribution

PAMET Nueva Ecija Chapter

Bahay ni San Jose, San Antonio, Nueva Ecija Home for the Girls, Palayan City, Nueva Ecija Indigenous Community, Gabaldon, Nueva Ecija Outreach Programs

PAMET Rizal Chapter

September 2021 and March 2022

Lucena City, Quezon

Handwashing Activity & Distribution of Hygiene Kits to Medical Frontliners

PAMET Tarlac Chapter

Continuing program

Handwashing Activity & Gift-Giving

PAMET Iloilo Chapter

Feliciana Java Kelly Elementeray School, Calahunan, Mandurriao

March 5-7, 2022

Support for Limited Face-to-face Classes

PAMET North Cotabato Chapter
Distribution of Hygiene Kits to Frontliners

PAMET SOCSKSARGEN Chapter
Tambler, General Santos City
March 25, 2022
Handwashing and Hygiene Kit Distribution

PAMET Zamboanga del Sur – Pagadian Chapter
Pagadian City, Zamboanga del Sur
Outreach Program

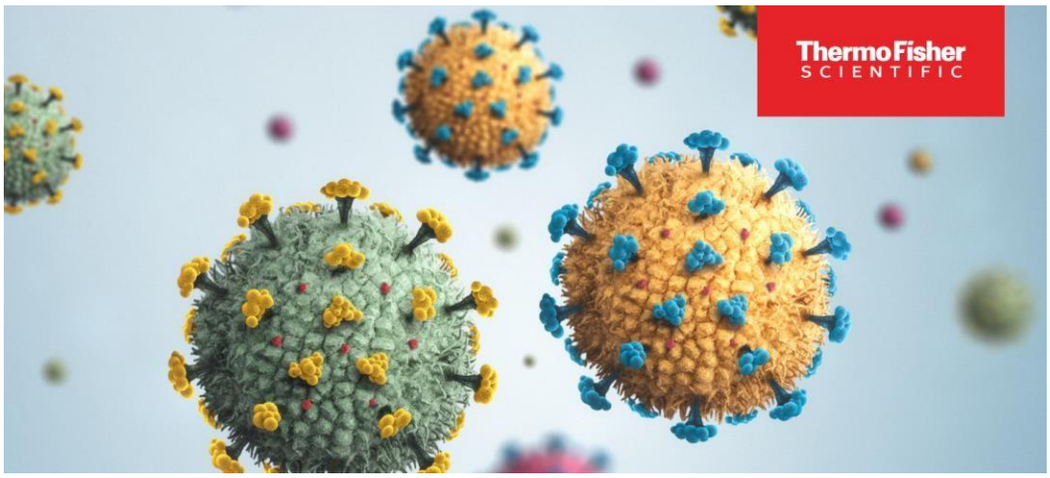
PAMET Davao Chapter

Mount Karilongan, Brgy. Carmen, Baguio District, Davao City March 26, 2022

Outreach Program

A report on Molecular Diagnostics QC webinar: Webinar on Molecular Diagnostics and Quality Control

By
MEL CHENG
Product Manager



Webinar on Molecular Diagnostics and Quality Control
Conducted by
Dr. July Kumalawati

Immediate past president, Indonesian Association for Clinical Chemistry

And

Dr. Chen, Chi- Kuan

Chief Secretary, Taiwan Precision Medicine Society

During the era of dealing with the COVID-19 pandemic, the interest of implementing 3rd party quality controls in clinical molecular diagnostics tests increased quickly. At the same time, the demand of molecular methods-based Laboratory Developed Tests (LDT) is getting more obvious. How we support solid clinical demand with affordable solutions with by monitoring with appropriate 3rd party quality controls practices will become the key focus of clinical laboratories.

With the auspices of APFCB and Thermo Fisher Scientific sponsorship, a molecular diagnostics quality control webinar was held from 14:00-15:00 (SGP Time) on 20 Jan 2022 using the ON24 online meeting platform to reflect this situation. We were happy to be able to invite Dr. July Kumalawati, immediate past president of Indonesian Association for Clinical Chemistry, to share her experiences and insights on the topic "The Future Role of Molecular Diagnostics in Clinical Laboratories". Our next speaker was Dr. Chen, Chi- Kuan, the Chief Secretary of Taiwan Precision Medicine Society, who is well-versed on the updates of COVID-19 diagnostic testing and QC and has been conducting many talks for Molecular Diagnostics Tests and Quality Control. He provided a sharing about "Why is quality control crucial in managing molecular diagnostics testing?"

During this webinar, Dr. July provided her advice and observations on what clinical laboratories should do to prepare for SARS CoV-2 molecular diagnostic testing, including capability and capacity, to ensure that labs are able to account for large patient volumes with low turnover time. She also introduced the concept that infrastructure used in molecular testing of SARS CoV-2 can also be used to test for other infectious diseases, malignancies, genetic disorders, metabolic syndromes and other conditions. Dr. Chen focused on the application of 3rd party quality controls for molecular diagnostics testing and shared his experience with recommendation of best practices. He emphasized the importance of using reliable 3rd party quality controls to monitor and validate molecular testing performance.

In total, there were 486 registrants of which 359 attended the webinar. 22 participants provided their feedback while 73% responded that this webinar was good. 5 participants felt the content was relevant while 3 hoped that this webinar could be allocated more minutes to discuss on more details such as Westgard rules and 6 sigma rules in Molecular Genetics and Cytogenetics.

It was great to see the high engagement levels from the partcipants in this webinar and the feedback shared by audience were generally positive. The topics related to molecular diagnostics and quality control can be considered practical to clinical laboratories. With the slowdown of the pandemic, it will be interesting to explore more applications of molecular diagnostics with quality control concept in the near future including oncology research, infectious disease diagnostics as well as SARS-CoV-2 diagnostics.

Ultra-low Temperature Freezers – Why so cold?

Most laboratories would not think twice about how much energy their Ultra-low temperature (ULT) freezers are using. However, when set at -80°C, ULT-freezers may use up to 20kWh per day. This is as much as entire households and accounts for >US$900 in electricity costs per annum. Older ULT freezers do use more than the newer models (perhaps three times as much energy), but many laboratories have banks of these freezers, many quite old but still working. Energy usage is also influenced by capacity, how often the door is opened, ice buildup, dust on the condensers and the space between specimen boxes on the shelves.

But perhaps a more fundamental question needs to be asked about the use of ULFs.

Why do we run them at the temperatures that we do?

In the 1980s and 1990s ULT-freezers used to be set at -65°C or -70°C. Using lower temperatures was largely manufacturer driven, despite that extra 10 degrees increasing the energy usage by as much as 30%! Furthermore, there is no evidence that lower temperatures improved sample stability or recovery. The crystallization (freezing) point of water (0°C), the 1st re-crystallization (-60 to -63°C) and 2nd re-crystallization point (-130 to -135°C) are critical temperatures for long-term storage of samples; -80°C, however, is not a critical temperature.

There are other issues that are important to consider. One is the impact of freeze-thaw cycles and how these may effect samples. If there is a power cut, running an ULF at -80 only provides an additional 35 minutes compared to -70!

In terms of sample stability Genomic DNA is stable at -20°C or -70°C; similar stability and viability of fungal isolates was achieved after 8-year storage at - 70°C and -130°C; plasma antibodies against HIV, HCV and HbsAg were stable for over 15 years at -20°C 10, and cardiac troponin T plasma concentrations are stable for over 8 years when stored at -70°C.

Thousands of scientists around the world compete in the International Laboratory Freezer Challenge each year to learn how to be more energy efficient with their lab's cold storage, improve sample accessibility, reduce risk, and save costs for their institutions. Second only to fume hoods, your lab's cold storage (refrigerators, freezers, cold rooms) is likely the next biggest category of energy consumers in your lab space. Ready to do something about that?

This fun, free program is a partnership between My Green lab (https://www.mygreenlab.org/) and the International Institute for Sustainable Laboratories (https://www.i2sl.org/), two nonprofits working within the laboratory sustainability space. No other international competition engages more laboratories in sustainability than the Freezer Challenge. Read on to learn more, and don't forget to register your lab to join in the fun! (https://www.freezerchallenge.org/the-challenge.html accessed 7 July 2022)

Now is the time to review in your laboratory the ULF temperatures. This is an easy way to reduce energy costs and usage, and the carbon footprint!

Acknowledgement: This article was based on "-70 is the new -80", written and compiled by Teun Bousema (Radboud university medical center, Nijmegen, The Netherlands) for the Radboud Green Office, in collaboration with Allison Hunter (Imperial College, UK), Kathryn Ramirez-Aguilar (University of Colorado, US), Martin Farley (LEAF - UCL, King's College London labs), Jeroen Dobbelaere (Climate@MaxPerutzLabs, Vienna, Austria) and Christina Greever (mygreenlab.org) (accessed 7 July 2022).

Hitchhikers Guide to Measurement Uncertainty in Medical Laboratories

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The recently updated formal definition of Uncertainty in Measurement (MU) is doubt about the true value of the measurand that remains after making a measurement. This means that the true result for a measurand cannot be exactly known.

This paper discusses important aspects of estimating measurement uncertainty (MU) for scientists and technical staff working in medical laboratories. Measurement uncertainty is not concerned with total measurement error. MU is concerned only with the uncertainties introduced by the measuring process itself, for example it starts with primary tube sampling or sample preparation through to result output. MU focuses on defining a range of results that could be obtained for an analyte if a sample was measured repeatedly, providing a quantitative estimate of where the true value of a measured analyte is believed by the laboratory to lie, with a stated confidence level.

A medical laboratory's knowledge of the MU of their reported results provides them with a valuable quality tool. An estimate of the measurement uncertainty of a test result provides a quantitative measure of the reliability of the reported result to demonstrate that the laboratory is meeting, exceeding or failing the reliability performance required by clinical users.

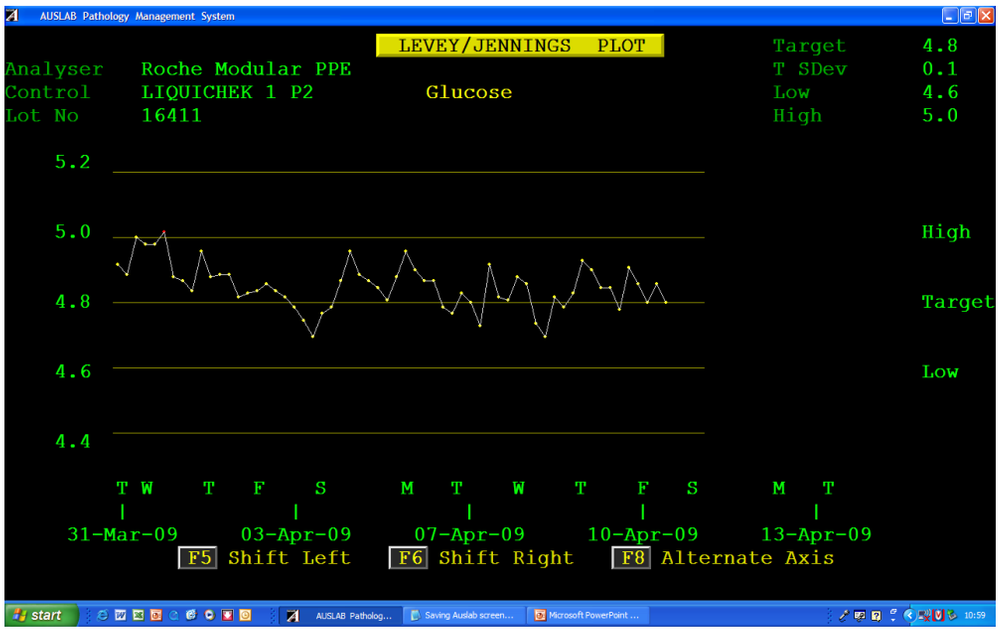
The MU estimate can also assist with identifying technical steps in the measurement procedure which significantly contribute to the uncertainty of the measurement procedure's results. This may also provide the laboratory with the opportunity to reduce the MU for that measurement procedure by modifying or replacing the technical step.

Measurement Uncertainty Can be visualised

Internal quality control (IQC) charts plotted using data collected for a month or more illustrates measurement uncertainty (Figure 1). If the IQC material for a given measurand is stable, correctly stored and prepared for the measurement procedure, laboratories can assume that the concentration of the measurand will not change. However, even rapid repeat measurements of an IQC sample will produce different values for the measurand. Medical laboratories can also assume that multiple repeat measurements of the same patient sample will produce a similar pattern of different values.

This pattern of measurement results is termed Random Variation, which means the next measurement result cannot be predicted from the previous result (Figure 1).

Figure 1: Plasma Glucose Quality Control results over time



Mean ± 2SD: 4.8 ± 0.2 mmol/L

Visualisation of MU for glucose measurement by single MP

Causes of Measurement Uncertainty

Major potential contributors are:

- Instrument sampling
- Sample dilution
- Sample inhomogeneity
- Reconstitution procedures for lyophilised materials
- Uncertainty of calibrator values
- Reagent and calibrator instability
- Reagent and calibrator lot-to-lot variability
- Re-calibrations
- Reagent dispensing

- Differences between reagent batches
- Electro/mechanical fluctuations of measuring devices
- Performance changes in measuring devices following routine maintenance
- Differences between operators of measuring devices
- Fluctuations in laboratory environment
- The algorithms used by measuring devices for rounding raw results to reported results

For certain types of manual measurement methods, changes of operator can have a significant impact on random variation (Figure 2).

Figure 2

Urine 2

Technician	WBC/µl
1	250
2	153
3	137
4	348
5	290
6	360
7	180
8	304
9	230
10	240
11	280
12	248
13	297

It is important to be aware that no matter how sophisticated the measuring device, results produced by all types of measurement has uncertainty. This means all measurement results are estimates of the true value of the measurand.

Therefore there is a need to ensure measurement results are meaningful to the user.

Making measurements are essential to everyday life in households, shops, industry, health services, science and research. It is important to ensure measurement results are sufficiently accurate for the purpose to which they will be applied. This is particularly critical for removing costly roadblocks to international trade. For example, a stated weight of wheat shipped to another country can be trusted by the receiver and not require re-weighing, or a patient's stated serum glucose concentration is meaningful and trusted by global health services.

To assist this, the science of measurement (Metrology) was developed.

Also essential has been the standardisation of measurement units, known as the SI system. An international organisation, the International Bureau of Weights and Measures (BIPM) is responsible for developing and maintaining the SI system, the world clock, the metre, mass and other constants of nature. It is also responsible for developing and publishing Guides in Uncertainty in Measurement (GUM) and for developing a standard International Vocabulary for Metrology (VIM). The GUM and its Supplements are the primary references for estimating uncertainty in measurements.

Terminology in Metrology

It is useful to know some of the terms used in Metrology because they can be difficult to understand:

Accuracy	closeness of agreement between a measured value and a true quantity value of a measurand
Indication	numerical result produced by a measuring instrument
Measurand	quantity intended to be measured
Quantity	the property of a substance that has a magnitude that can be expressed as a number and measurement unit
Property	attribute of a substance, for example colour, nucleotide sequence, length, mass, light emission wavelength
Metrological traceability	property of a measurement result whereby it can be related to a primary reference through a chain of calibrations, each step contributing to the MU of the patient's result
Measurement method	generic description such that it cannot be used to perform a measurement, for example, spectrophotometry
Measurement procedure	detailed description of the measurement procedure that can be used by an experienced individual to perform a reliable measurement

Measurement Uncertainty Disappears

This occurs if the measurement procedure is very insensitive. For example, if a weighing machine reports weights to the nearest 10 kg, it is unlikely to show measurement uncertainty with repeated measurements of the same weight, whereas if the weighing machine is more sensitive and reports to the nearest gram (g), it will show measurement uncertainty for repeated measurements of the same object.

Concept of Measurement Uncertainty in Medical Laboratories

The GUM approach to estimating MU is not suitable for use by medical laboratories because it requires using very high-level statistics and mathematics. However, some basic GUM principles can be used to develop an approach to estimating MU in medical laboratories:

- Definition of the quantity being measured (measurand)
- Recognition that a measured value is an estimate because of the effects of imprecision and bias
- Expressing measurement uncertainties as a standard deviation or relative standard deviation (CV)
- Systematic and random uncertainties are statistically treated in the same way
- An estimate of MU allows definition of a set of possible values for the measurand that is believed by the laboratory to include, with a stated probability, the true value of the measurand
- The measured value accompanied by its stated MU is considered to be the best estimate of the true value

Estimating Measurement Uncertainty in Medical Laboratories

There are two approaches to estimating MU. The first method is termed Bottom Up which is not recommended for medical laboratories. Top Down is the much preferred approach whereby measurement data is used in calculating MU estimates.

For routine quantitative measurements of patient samples using automated instrumentation, a single measurement of each analyte is usually made. To generate sufficient data to calculate measurement uncertainty, internal quality control (IQC) measurement results are used because over time the effect of many changes in operating conditions are recorded. Data from external quality assurance programmes are not recommended because they do not provide such comprehensive coverage of changing measurement conditions.

Definition of a Measurand

Requires at least three pieces of information:

- System containing the analyte
  For example, venous whole blood, urine, red blood cells, renal stone
- Identity of the analyte
  For example, rubella antibody, digoxin, subunit of hCG, HIV-1 RNA, CCG tri-nucleotide
- Quantity
  For example, amount of substance concentration, number, mass concentration, number concentration, number fraction, amount of substance rate concentration

An example would be the number concentration of white blood cells in whole venous blood.

Biological analytes can be complex (isoforms, fragments) and/or poorly defined, and therefore definition of a measurand may additionally depend on the specific measurement procedure used. For example, the catalytic activity concentration of a plasma enzyme can be affected by changes in the temperature, pH and co-factors used in performing the measurement.

Another example is the different epitope selectivity of antibodies used by different commercial measurement procedures to measure the 'same' glycoprotein hormone, for example, different antibodlies may recognise different isoforms, or bind them to different extents. In such cases, identification of the measurement procedure must be included in the measurand definition.

For example:

- Enzyme X: catalytic activity concentration by IFCC reference measurement procedure
- Protein hormone Z: reagent kit manufacturer Y
- Tumour marker B: reagent kit manufacturer A

Although not part of the formal definition of a measurand, it is usual practice to identify the measurement unit.

What do Medical Laboratories Measure?

Measurands are rarely directly measured. For example, the serum concentration of total calcium is not routinely directly measured by counting the number of calcium atoms per litre of serum.

Serum total calcium is routinely measured using a surrogate marker. For example, the measurement of the colour intensity produced when the serum sample reacts with a chromogen.

The measurement result is calculated using the value obtained for the calcium calibrator and an algorithm in the instrument software. Another example is the change in electrical resistance when red blood cells pass through an electronic gate in a blood cell counter.

Uncertainties can be introduced by the defined measurand:

- Incomplete definition of the measurand
- May not be fully measured because of inadequate analytical specificity
- Analytical interferences
- Analyte not fully available to measurement system, for example caused by protein binding

Measurement Uncertainty Targets

Before estimating the MU of an analyte it is important to set a target value that is clinically acceptable for making good decisions for patient care. International expert panels may already have set MU targets for some analytes, for example plasma cholesterol. Setting other targets will require discussion with local clinical experts or professional organisations, for example international sports bodies setting upper limits for banned drug use.

Data Required for Estimating Measurement Uncertainty

Calibrator and reference material values are assigned by making measurements, and therefore the calibrator reference values themselves have an uncertainty, which is stated in the reference material certificate. It should be noted that WHO biological standards

are not metrologically traceable back to an SI measurement Unit, for example the Mole. WHO reference materials are purified, bioactivity checked and allocated an International Unit (IU). International Units are therefore arbitrary and cannot be compared with other WHO reference materials.

Reporting Patient Results

It is recommended not to report measurement uncertainties to clinicians and other healthcare professionals unless specifically requested. They may be requested from medical laboratories that are providing test results to pharmaceutical companies undertaking clinical trials of new drugs.

How to Perform Estimates of Measurement Uncertainty

For detailed practical guidance on how to perform estimations of MU, readers are recommended to refer to Reference 1. This reference provides worked examples of calculating MU estimates for a wide range of routine analytes, for example parathyroid hormone, Anion Gap, urine calcium/creatinine ratio, number concentration of white blood cells, INR, human immunodeficiency virus type 1 viral load, BCR-ABL gene transcript measurements, Rubella IgG antibody measurements, hepatitis B surface antigen measurements. It also addresses problems such as medical laboratories using multiple analysers across an organisation.MU estimates expressed as SDs cannot be added together, they must be expressed as variances, where SD2 = variance. This is very useful for laboratories that have multiple measuring devices where an average MU is required because a patient specimen could be measured on any of the devices. For example, (SD2 + SD2)/X = average variance for X instruments. Square root of the variance provides the average SD across all the devices.

Initially 30 or so IQC values would be adequate for a reasonable estimate of MU for a single measuring device. One SD is the parameter of MU (standard measurement uncertainty, symbol u). Since ± 1 SD would cover approximately 68 % of the dispersion of obtained QC values. This is of limited practical application, so the uncertainty is widened by applying a coverage factor (k) to provide an expanded measurement uncertainty (symbol U). If 2 is chosen for k, then coverage is a more useful approximately 95.5 % of the dispersion of possible results.

Expressing Measurement Uncertainty Estimates

It is recommended to express MU estimates as Expanded MU (2 x MU) which provides approximately 95.5 % confidence that the true value is included in the expression: result value ± 2 x MU.

Measurement Bias

Bias cannot be eliminated, but significant bias should be minimised using recalibration or by applying an adjustment factor to the raw results. The residual bias will be small relative to the uncertainty of the imprecision. A rule of thumb is that if an SD is <25 % of the largest MU, it can be ignored when combining SDs (u).

Rule of Thumb: If two results on the same patient differ by >3 x MU they are measurably different.

Biological Variation

An advantage of using measurement uncertainty is that important uncertainties that arise from non-technical sources can easily be included in the calculation of the estimate. For example, within-individual and within-group biological variations. Such data is freely available from the website of the European Federation of Clinical and Laboratory Medicine (EFLM) Biological Variation Database. The relevant CV must be expressed as a variance then added into the estimate calculation. Including biological variation is not always physiologically appropriate, for example hCG in pregnancy, urine sodium.

Laboratory Quality Records

It is recommended that laboratories retain their MU estimates and the method used to obtain them is retained in the laboratory quality records, including the required frequency of re-estimation. MU estimates should also be regularly re-estimated if technical steps are changed.

Laboratory Value of Estimating Measurement Uncertainty

- Quantitative expression of the reliability of the test result
- Demonstrates the results meet clinical requirements
- Use of internal quality control data for estimating uncertainties
- Does not require additional work to gather data
- Estimates can assist interpretations if results are close to clinical decision values
- Estimates can be used to define grey zones for interpretation
- No need to separately determine bias and imprecision as used in the Total Error Concept
- Ability to include non-technical uncertainties, for example biological variation
- Is essential for meaningful comparison of results with reference values, with previous results, with results from other health systems and clinical research
- Can provide insights as to which technical steps might be open to improvement, thereby reducing overall MU
- Is an essential component for achieving standardised and harmonized measurement results for which there is increasing global demand

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eGFR – 10 years on from the KDIGO Global Recommendations

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Opinion Piece

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Introduction

In 2012, the key international kidney guideline group KDIGO (Kidney Disease – Improving Global Outcomes), released the document "Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (CKD)". It is not an understatement to say this this guideline changed the world of renal practice and the role of the routine laboratory in this field.

The definition and classification of CKD in this guideline have been widely accepted around the world and used for research, epidemiology, clinical practice and education providing uniform criteria for CKD worldwide (figure 1). An additional use of the classification, for example by Kidney Health Australia, is to link the staging directly to clinical management guidelines with "colour coded" plans linked to the categories in figure 1. The diagnosis and classification are based on glomerular filtration rate (GFR) and urine albumin. These two key measurements are dependent on pathology testing, therefore placing the chemical pathology laboratory in the centre of the process. Perhaps unusually for clinical guidelines the KDIGO document provides important information on laboratory practice in this field relevant to the pre-analytical, analytical and post analytical phases of testing. Implementation of the guidelines has also stimulated close collaboration between clinicians and laboratories at local and national levels.

What is GFR?

The GFR is the amount of fluid passing through the combined 2 million nephrons in a person's kidneys in a period of time. A typical value in a healthy young person is about 100 ml/min which equates to about 144 L per day, of which about 99% is resorbed in the tubules, the remaining excreted as urine. The kidney has many homeostatic functions including waste removal, endocrine, water, electrolyte and acid-base balance and red cell production, and disorders related to these functions are seen as kidneys become damaged. The detection of these signs of CKD (usually by other laboratory tests) however are not used to diagnose or grade kidney function. GFR by contrast provides a single excellent measure of kidney function, irrespective of the cause of the kidney damage, and, importantly, reduction in GFR can be identified at the pre-clinical stage, with the aim of preventing or reducing further damage. GFR also provides a tool to monitor progress and predict possible need for dialysis. An additional vital use for GFR is for drug dosing decisions for renally excreted medications.

GFR can be measured directly, often referred to as a formal GFR test. This type of testing involves intravenous injection, collection of multiple urine or serum samples over several hours, specific analytical techniques (eg measurement of radioactivity for radiolabelled markers) and experience in performing the test. While an estimate of GFR (eGFR, see below) is used almost universally in place of a formal GFR measurement, formal GFR testing is the gold standard for assessing GFR and has an important role for some patients when an accurate measurement is required and eGFR does not suffice, e.g. extremes of body composition, some drug dosing decision (eg some cytotoxic medications), kidney replacement therapy living kidney donors.

What is eGFR?

As GFR is so hard to measure in routine practice there have been developed many equations to estimate GFR in simple practical ways. Historically the Cockcroft and Gault equation, from a single study in 1979, was widely used. .The KDIGO guidelines recommend the use of the CKD-EPI creatinine equation developed in 2009 (CKD-EPI (Cr, 2009)). Alternate equations should only be used if they have been shown to improve accuracy compared with this equation.

Like most eGFR equations, CKD-EPI (Cr, 2009) has the inputs of serum creatinine, patient age and sex. Additionally there are versions for African Americans and non-African Americans. With the exception of the race variable a major benefit of this equation is that the inputs are known by the testing laboratory and the formula can be calculated and, as recommended by KDIGO, should be routine reported along with serum creatinine in adults.

Limitations of eGFR

All eGFR equations have limitations. A common assessment of these equations is the percent of eGFR results which are within +/- 30% of a simultaneously measured formal GFR (P30). The best performance that can be expected is a P30 of about 85% ie that for more than 15% the equation may be wrong by more than +/- 30%. In addition, there are factors in the patient and factors in the creatinine measurement that can make the estimate more likely to be wrong. In the patient these can include extremes of muscularity (high or low), pregnancy, dialysis, diet (cooked meat) and sex change. In the creatinine measurement these include assay bias, imprecision and interferences.

Laboratories and eGFR

It is important for laboratories to provide high quality creatinine assays. The key factor to avoid assay bias is traceability to agreed reference standards, usually summarised as IDMS (isotope dilution mass spectrometry) traceability.

A more specific statement would be traceability to reference materials through a reference method in a reference measurement service with all of these components listed on the Joint Committee for Traceability in Laboratory medicine (JCTLM) database. This traceability must be provided through manufacturers to ensure the accuracy of results in laboratori4es using their assays. The other practical factor is the use of enzymatic assays rather than Jaffe assays if possible. This reduces interferences and generally has lower bias and imprecision.

Laboratories must also select the eGFR equation to use and most importantly should work with other local or regional laboratories to report in the same way to avoid patients getting difference diagnoses at different laboratories.

The Race-Neutral CKD-EPI equation

Recent work in the United States has challenged the use of race as a health determinant. This is due to poor definitions of race, the risk of race-based discrimination as well as recognising that the concept of race as a social concept not a physical standard. With this in mind, the original CKD-EPI (Cr, 2009) equation was revised in 2021, using the original data, but without a race factor. Using this equation, known as the CKD-EPI(Cr,2021), or race-neutral equation, subjects previously tested using the non-African American equation will have higher eGFR values, by about 5% on average, and those previously assessed with the African American version will have lower results with the new equation.

The National Kidney Foundation in the USA has recommended the immediate uptake of the CKD-EPI (Cr, 2021) equation in the United States. It is unclear what action will be taken in other countries. For individual patients current using the non-African American equation, a 5% increase in eGFR is not highly significant against a background uncertainty of the equation of +/- 30%. There would however be a reduction in the number of people with a diagnosis of CKD, especially in the elderly. There may also be some changes in drug dosing decisions and changes seen when monitoring patients over time. A personal opinion would be that each country should consider this issue and decide for or against changing and ensure uniformity amongst testing laboratories.

Cystatin C

Creatinine based eGFR equations are by far the most widely used globally in clinical practice with creatinine assays being widely available and amongst the cheapest chemistry tests. A limitation to creatinine is that it is produced from muscle and thus differences in the amount of muscle between subjects is a confounding factor. Cystatin C is produced from all cells and thus does not have the same relationship to muscularity that is seen with creatinine. It has also shown less variation between African-Americans and non-African-Americans in the CKD-EPI data. The CKD-EPI (2012, cystatin C) equation does not include a race factor, and its use is being specifically promoted in the USA to avoid the possible effect of race in that setting.

The use of this equation, rather than the CKD-EPI(Cr,2021) race neutral equation increased the P30 from 86% to 89%. An improvement, but not a solution to the wide variability seen with GFR estimating equations. The costs of cystatin assays remain very high compared with creatinine assays and, again as a personal opinion, I think the first action for laboratories is accurate creatinine assays before considering introduction of cystatin C assays.

Drug dosing decisions

This is a vital aspect of the use of eGFR results as many renally-excreted drugs require reduced doses in kidney disease. The best equation for GFR estimation for this purpose has been widely debated over the last 15 years, with the key players being the Cockcroft and Gault equation (C&G) and eGFR, initially with the MDRD equation and now with CKD-EPI. A key factor in this debate is the units used for these tests and the meaning for the difference. C&G is reported in mL/min and CKD-EPI is reported in mL/min/1.73m2. The "1.73m2" factor is an adjustment for a standardised body surface area (BSA). The use of the BSA normalised result is clearly useful for CKD diagnosis and staging, as kidney size, and therefore GFR, is related to the size of the person. Without the BSA normalisation, smaller people (with lower GFRs in mL/min) would be diagnosed with CKD more frequently than larger people, and vice versa. By contrast, for drug dosing, the rate at which a drug is lost from the body in urine depends on the actual amount of fluid passing through the glomerulus (mL/min) rather than a value adjusted for body size.

While C&G reports in mL/min and was widely used in original pharmacological studies, it was developed in only a small number of subjects most of whom were male, using a creatinine assay which is no longer available. Use of this equation also requires the doctor to obtain the patient's weight and remember to perform the calculation to determine the effect on drug dosing. By contrast the CKD-EPI equations correlate better with the gold standard of measured GFR, and can be readily available on the pathology report. It may however be necessary to remove the inbuilt BSA normalisation, at least in patients markedly larger or smaller than average.

The future

There is ongoing research to try and improve GFR estimating equations. Multiple factors have been considered including measures of body size and composition. While it makes sense, especially for creatinine-based equations, that inclusion of factors related to muscle mass would be an advantage, the improvements have generally been small. Importantly, the difference between research and clinical practice must be recognised and any possible revised equation must be tested in a wide range of subjects (age, body composition, size, diet, physical activity etc) before being considered for use.

While this commentary focusses on eGFR, the need for accurate and widely available assays for urine albumin and creatinine is also required for best implementation of CKD testing.

As well as seeking improvements in what is possible with new assays or new equations, the full implementation of current best practice in all laboratories remains an important goal with standardised creatinine assays, use of the same GFR equations and supportive education developed together with renal physicians being vital for patient care. In short, 10 years later, the 2012 KDIGO guidelines remain highly relevant for laboratory management of CKD.

Selected additional reading

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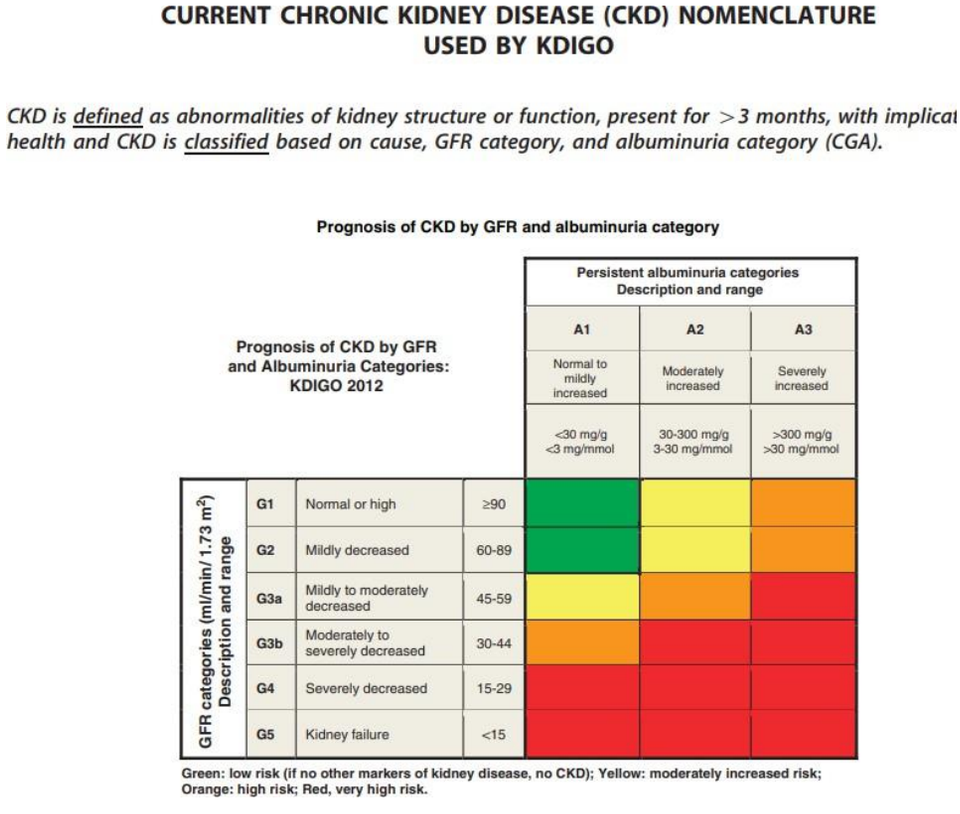

Figure 1. The criteria for diagnosis and classification of CKD (KDIGO 2012)

Adaptive Learning Courses in Laboratory Medicine Are Now Available without A Subscription Fee!

Nader Rifai

In order to increase utility and eliminate financial barriers, AACC Learning Lab for Laboratory Medicine on NEJM Knowledge+ program is now available without a subscription fee for individual users (previously $89/year). This cloud-based program consists of over 100 courses, covering topics span across all disciplines of laboratory medicine (https://area9lyceum.com/laboratorymedicine/course/). The courses are based on the concept of adaptive learning, the closest to personalized education.

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Autoverification in Clinical Biochemistry in an Indian Cancer care set up: Implementation and achievements.

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Introduction

Auto verification (AV) is the validation of results from a clinical chemistry analyzer without manual check [1]. Verification of results is the final and vital step before it becomes visible to the requester (clinical colleagues). This provides an opportunity to check for any errors that has slipped in the earlier stages and also initiate a discussion with the clinics about the pathological values. Switching from manual to auto validation of results, therefore, requires a great deal of planning and routine inspection. This concept, though 20 years old [2], is currently being adopted in Indian laboratories in the last four to five years. The AUTO10-a document from the CSLI gives an overarching guideline [3]. Implementation requires a preplanning stage, formation of dedicated teams, development of computer logic, validation and verification of the system, maintenance of the AV system, risk management protocols, and regular audits. Here, we describe the implementation and achievements in our hospital-based laboratory.

ISO 15189 (2012) [4] and the 112 documents from the National Accreditation board for Laboratories (NABL) provide an overarching and very broad set of rules. The AUTO10-A (CSLI) adds some specificity and defines Boolean logic and algorithm development in some details [3]. There is, however, a void of guidelines on the specifics of auto verification. This task is daunting if not impossible because the requirements of each hospital or stand-alone laboratory is different. Our laboratory is different in demographics and medical characteristics as it caters to a cancer population in a tertiary set up.

Preplanning

In preplanning, we deeply introspected our need for an AV system. Our management was convinced of the need for an AV system. The goal was uniformity in result evaluation, role-based access to staff, reduced fatigue across all levels of personnel, reduced manual record keeping, improved turnaround times (TAT), better utilization of staff, and reduction of laboratory errors.

Vendors for AV systems should be carefully selected to meet the required goals. They should train personnel and provide maintenance and support services. We selected Instrument Manager® (IM) from Ortho Clinical Diagnostics (Ortho) as our AV system.

This could directly link with the in-house laboratory informatics system (LIS) and connect to the XT-7600 analysers (Ortho). A primary and a back-up computer were provided for the task. Agreements were made with the vendor in securing the goals. Both parties agreed that rules would be developed in-house and the medicolegal onus of the rules will lie with the laboratory.

Team Building

The information technology (IT) team, the laboratory technical team, and a team of the signatories were organized. They were primed to initiate, implement, and maintain the AV system. The IT team collaborated with Ortho for procuring and structuring the hardware and software systems. The technicians' team were trained in a phased manner to accustom to them to the IM and wean off their total dependence on the LIS system of seven years. The signatories' team were entrusted to build the algorithms and chalk out the validation and verification of the systems as per the ISO (Clause 5.9) and NABL guidelines. Figure 1 shows an algorithm of serum sodium validation for both outpatients and hospitalized patients.

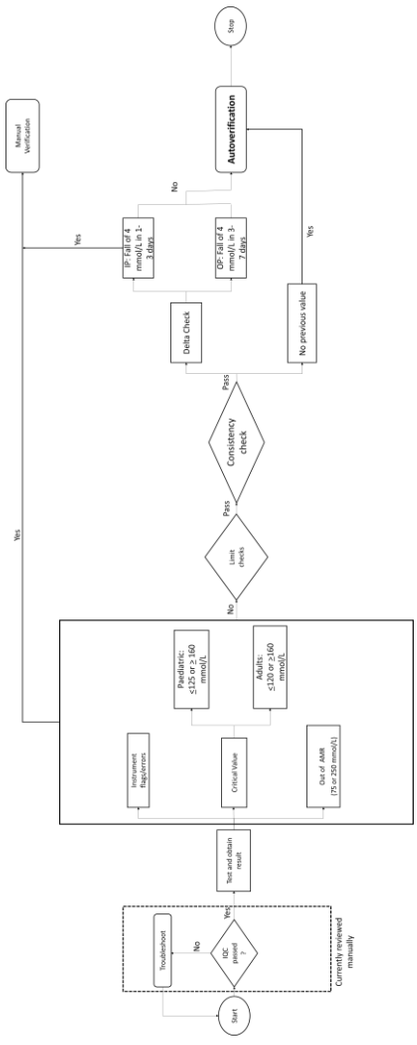

Figure 1: A simplified auto verification algorithm for serum sodium in our tertiary care cancer hospital

Development of computer logic

The computer Boolean logic was based on instruments flags and warnings, delta value checks, stochastic derivation of limit checks (review intervals), critical values, consistency checks, and other customized checks (gender and age). Internal quality controls (IQC) were deliberately kept in manual review as non-departmental staff were also involved in running IQC due to their involvement in shift and holiday duties. A detailed guide can be found in the paper by Randel ET. Al [5].

Validation and verification were carried out in the IM itself as it had two distinct segments for rules – "testing" and "go-live" environments. The rules were first tested on simulated data and then real patient data in the testing environment. Records were kept as per the guidelines.

Risk management for the AV system

A risk management strategy was developed wherein the back-up computer could function as the primary computer or an entire shift to the LIS system in case of breakdown. Several trials were given by shutting off the primary computer during off-peak hours. Caution needs to be exercised in routine AV operations. The rules are of if-then-else type and cannot always predict errors in complex situations. Some rules may inadvertently interact with others. Software upgrades must need a fresh set of validation or verification. It is difficult to pre-judge all such scenarios beforehand. So, the learning curve on an AV system is continuous and daily supervision is a must.

Results

We went live with AV in October 2017 with the metabolic panels after prior intimation to our clinicians. We actively sought inputs to abnormal results. Auto validated reports were marked as "Auto verified". Intensive audits which were performed to check for outliers and inadvertent auto validated results for three consecutive months. The audits are currently performed on ten random samples a day. A provision has been kept to increase the number of audits if test methods or the AV rules change.

The AV system along with the track system (from Ortho) proved to be a game-changer. 78% of the metabolic panel tests are currently auto validated (Fig 2). Manual tasks were reduced by 50.2% for the technologists. Unnecessary repeat blood draws were avoided in up to 7% of the samples due to visible hemolysis, turbidity, or icterus. Pre-analytical errors could be detected in up to 10% of the samples. This group could now focus on communication of critical results, writing operating procedures and so on. Thus, this led to better staff utilization. TAT which were fixed at three hours after sample receipt in the laboratory were reduced by 50-60% (Fig. 3). Now, we can deliver results within 1.5 hours for general patients and 52-58 minutes for the intensive care and day-care chemotherapy sections. Signatories could now focus on the absolutely critical results and subsequent discussions and communications to clinicians.

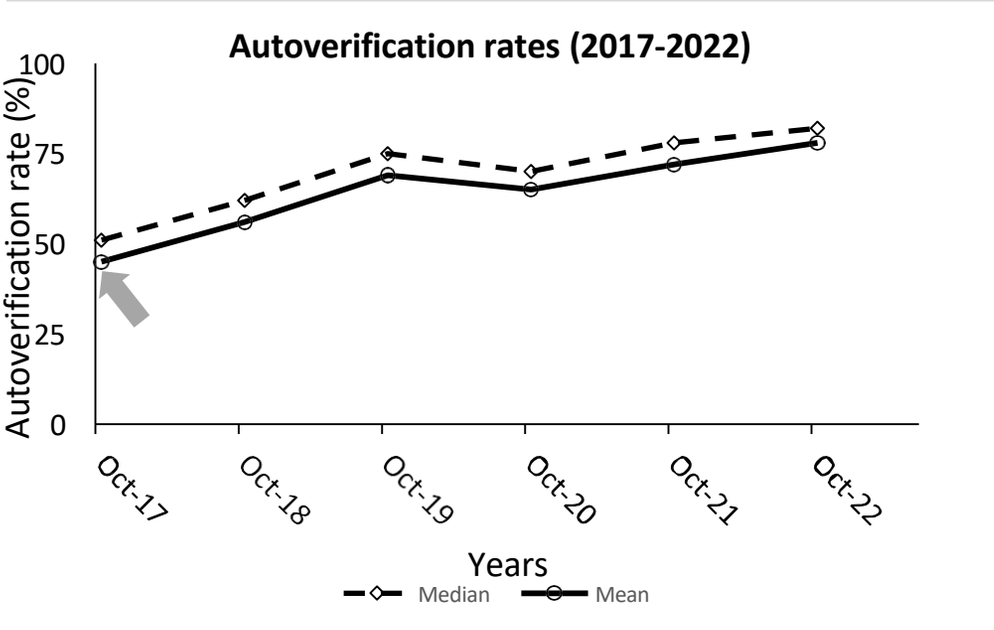

Figure 2: Increase in the rate of auto verification from 2017-2022.

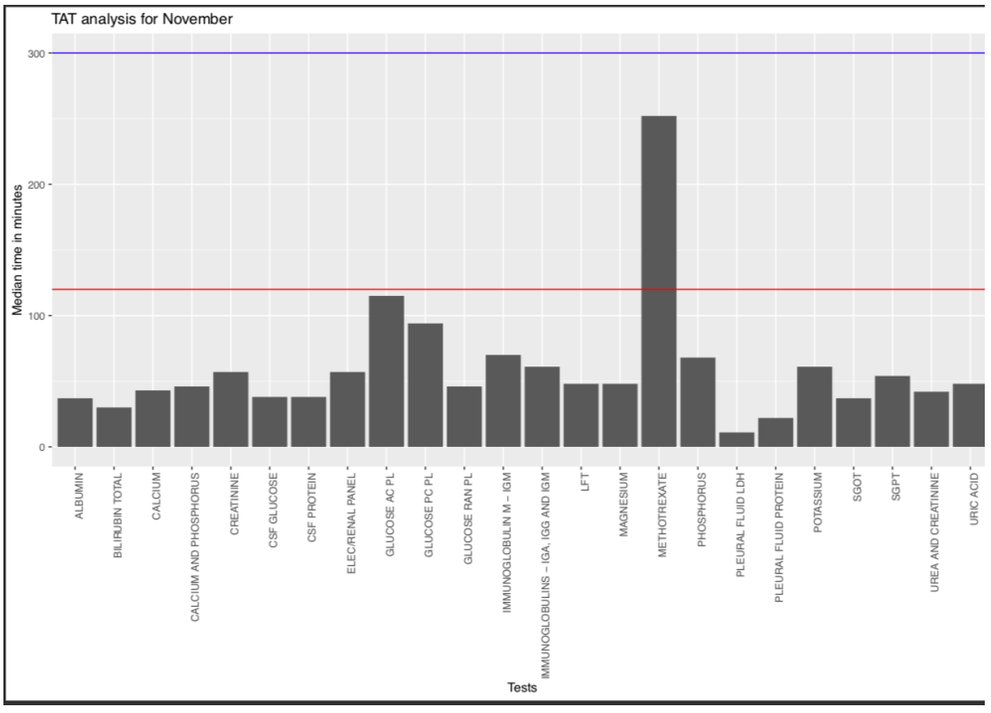

Figure 3: Current median TAT for different metabolic panel analytes for outpatients. Most of it has been reduced by more than half from the original bench mark of 180 minutes (three hours). The only exception is methotrexate which is omitted from the auto verification system.

Conclusion and future directions

Our future plans are pivoted on specialty-based reports such as those of surgical oncology, haemato-oncology, medical oncology, or paediatric oncology. We also intend to use the moving averages for selected parameters and incorporate daily IQC runs as a part of AV. Overall, we and our clinical colleagues are satisfied with the operation of the system in place. Rarely, there has been a complaint on the AV system that has come to our notice. Most problems (98%) have been identified to have arisen in the pre-preanalytical and pre- analytical phase and are out of direct control of the laboratory.

To summarize, implementation of the system requires forethought and scrupulous planning, developing logic, frequent audits, clinical communications and collaborations, and daily monitoring. It is indeed satisfying to have an AV system in place for a busy 24 x 7 hospital based laboratory.

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Hemoglobin A1c: Summary of Existing Test Methods and Introduction of a Novel Assay Design

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Introduction

Diabetes mellitus is caused by impairment in insulin secretion (type 1 diabetes) or poor response to insulin with subsequent impairment in insulin regulation and production (type 2 diabetes), which contribute to chronic hyperglycemia..1 Elevated blood glucose is associated with microvascular and macrovascular damage that can lead to debilitating conditions, including heart disease, chronic kidney disease, diabetic neuropathy, and retinopathy. Globally, there are 537 million adults living with diabetes, of whom 90 million are in Southeast Asia and 206 million in the Western Pacific.2 Approximately half of all diabetes cases are undiagnosed, leaving millions of people unaware that they are at risk of developing life-threatening complications from a disease that was the 9th leading cause of death globally in 2019.2, 3

Chronic hyperglycaemia results in a greater abundance of circulating glycated proteins, which play an important role in the pathophysiology of diabetes.4 Of particular importance is glycated hemoglobin A1c (HbA1c), which is an indicator of average blood glucose concentration over the previous 3 months.5,6 In the 1990s, two landmark clinical trials, the Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS) demonstrated that controlling hyperglycemia, as assessed by serum HbA1c, led to a reduction in diabetes complications.7–10 As a result, HbA1c measurement has become the gold standard for diabetes diagnosis and monitoring.5, 11

Here we review diabetes diagnosis and monitoring, the pathological impact of chronic hyperglycemia, and the molecular features of HbA1c relevant to diabetes pathophysiology and HbA1c measurement. We also highlight international efforts to standardize HbA1c measurement, as well as current HbA1c testing methods, including a new and innovative Dry Slide HbA1c assay.

Diabetes Disease Burden

Epidemiology

Diabetes is a major cause of morbidity and mortality worldwide.2 In a large cohort study including >1 million individuals from 7 Asian countries, those with diabetes had a nearly 2-fold risk of all-cause mortality compared with those who did not have diabetes.12

individuals with diabetes worldwide is projected to increase from 537 million adults in 2021 to 783 million by 2045.2 This increase will be largely driven by an increase in type 2 diabetes due to higher rates of obesity and more sedentary lifestyles. Over the same time period, the worldwide direct costs of diabetes—currently 11.5% of total healthcare costs—are estimated to increase from $966 million to $1.05 trillion USD.2 Clinical pathology

The term diabetes refers to a class of metabolic disorders that is usually divided into two main categories.1 Type 1 diabetes makes up a small percentage of diabetes cases (5%–10%) and is caused by autoimmune destruction of pancreatic β cells that impairs insulin production and secretion. The vast majority of diabetes cases, however, are type 2 diabetes (90%–95%), which is characterized by insulin resistance rather than insulin insufficiency. Whereas individuals with type 1 diabetes require daily insulin injections to manage their hyperglycemia, those with type 2 diabetes generally do not, at least initially.1 Management of type 2 diabetes instead usually consists of lifestyle modifications, including healthy diet and exercise, with an emphasis on maintaining a healthy weight, although medications may also be used if lifestyle change alone is not enough to control the hyperglycaemia.

More than 80% of end-stage renal disease is caused by diabetes, hypertension, or a combination of the two.13 One systematic literature review concluded that the prevalence of cardiovascular disease in patients with type 2 diabetes was 32%, and that cardiovascular disease caused approximately half of the deaths observed in the studies reviewed.14 In a separate pooled analysis of data from 22,896 diabetic individuals, the prevalence of diabetic retinopathy was 35%, and the prevalence of vision-threatening diabetic retinopathy was 10%.15 Another, smaller study found a prevalence of 26% for painful diabetic peripheral neuropathy.16 These and other data highlight the significant burden of diabetes-related complications on individuals with the disease.

Multiple pathophysiological mechanisms contribute to the development of diabetes complications.1 Perhaps chief among these is oxidative stress.[4,17,18] The term glycoxidative state has been used to describe the persistent environment of oxidative stress due to chronic hyperglycemia that underlies many of the pathological effects of diabetes.[4,17] Oxidative stress contributes to damage and dysfunction of the vascular endothelium through multiple mechanisms and is thus associated with both the macrovascular (coronary artery disease, peripheral arterial disease, and stroke) and microvascular (diabetic nephropathy, neuropathy, and retinopathy) complications.[10, 13,18]

Higher levels of protein glycation under hyperglycemic conditions contribute to the increase in oxidative stress by promoting formation of early and advanced glycation end products (AGEs), leading to the generation of free radicals and oxidants.4 HbA1c is not only an indicator of average blood glucose levels over the long term, it is also an early glycated protein that can undergo further chemical modification to generate hemoglobin-AGE, which may contribute to vascular endothelial dysfunction by blocking nitric oxide production. HbA1c itself may enhance oxidative stress, since the glycated protein is more susceptible to digestion by endogenous proteases, a process that releases heme, ferrous iron, and free radicals.4

Clinical Use of HbA1c Testing

Why and when to measure HbA1c

Undiagnosed diabetes is of particular concern as chronic hyperglycemia can lead to microvascular and macrovascular damage, causing more severe complications and a higher risk of death the longer the condition goes untreated.[1,2] Early diagnosis of prediabetes and diabetes, followed by aggressive lifestyle modifications, medical treatment, and close monitoring is key to improving quality of life and reducing mortality risk.[2,19]

The American Diabetes Association (ADA) recommends routine screening of low-risk individuals every 3 years starting at age 45 and more frequent screening for high-risk asymptomatic individuals (e.g., smokers and those suffering from obesity or hypertension) and patients with prediabetes.[1] Patients with diabetes should have their glycemic status monitored using HbA1c at least twice a year if they are meeting their glycemic goals and at least every 3 months if those goals are not being met or if there has been a change in therapy.[19]

Current diagnostic criteria for diabetes

According to ADA guidelines, diabetes may be diagnosed either by measuring HbA1c or plasma glucose.[1] Acceptable diagnostic criteria include one of the following:

1. HbA1c ≥6.5% measured by a National Glycohemoglobin Standardization Program (NGSP)-certified method standardized to the DCCT assay
2. Fasting plasma glucose ≥126 mg/dL (≥8 hours fasting)
3. Oral glucose tolerance test (OGTT) ≥200 mg/dL (2-hour plasma glucose)
4. Random plasma glucose ≥200 mg/dL with symptoms of hyperglycemia/hyperglycemic crisis

Unless the patient is exhibiting classic symptoms of hyperglycemia or is experiencing a hyperglycemic crisis, an abnormal screening result based on criteria 1–3 must be confirmed with a second test, either using the same or a different testing method.

Advantages of HbA1c testing compared with fasting plasma glucose include greater patient convenience with no need for fasting, better preanalytical sample stability, less short-term variability in marker levels, and assay standardization.[1] Disadvantages of HbA1c testing include a higher cost compared with plasma glucose measurement and potentially limited availability in the developing world, although access continues to improve. In addition, HbA1c should not be used for certain patient populations, including those with conditions that affect the red blood cell (RBC) lifespan (normally ~120 days) such as pregnancy, recent blood transfusions, or HIV treatment.[20] It should also not be used with patients who have interfering levels of genetic hemoglobin variants or chemically modified hemoglobin derivatives.[5,6,20–22] In these cases, alternative methods should be considered, such as plasma glucose testing or measurement of fructosamine, glycated serum protein, or glycated albumin. The glycated protein tests provide a shorter glycemic view of 2–3 weeks compared with 3 months for HbA1c testing, which can also be beneficial when monitoring the impact of changes in treatment.[5,6]

Monitoring glycemic control

As mentioned above, patients with diabetes require routine monitoring of glycemic status to assess therapeutic effectiveness and determine if there is a need for further intervention.[19] When setting HbA1c target goals, the physician should consider individualized needs based on patient lifestyle and health risks (such as diet and exercise, patient's age, disease duration, or existing comorbidities). While HbA1c <7% is a suitable goal for many, a lower cut-off may be appropriate if it is safely achievable for the patient.[19] Alternatively, a higher cut-off may be necessary for patients with certain medical conditions or whose HbA1c remains somewhat elevated despite receiving standard of care disease management. Other vascular and metabolic parameters such as blood pressure and serum lipids should be monitored to assess treatment efficacy and determine if any changes are required. In addition to routine laboratory HbA1c measurement, it may be desirable for the patient to frequently self-monitor glucose levels to adjust behavior and daily insulin levels. Recent advances in technology such as continuous glucose monitoring (CGMs) have made blood glucose monitoring simpler and more informative.[19]

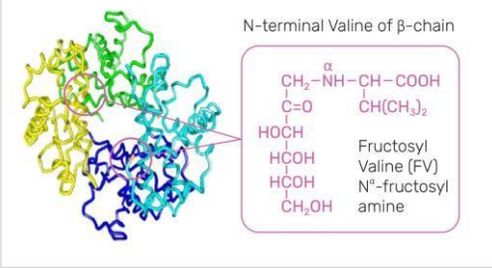
HbA1c Structural Biology

Chemical structure and glycation reaction

Haemoglobin A (HbA) is the primary form of haemoglobin in adults, accounting for approximately 97% of circulating hemoglobin.[11] HbA is a heterotetramer consisting of two identical α chains and two identical β chains; each of the four chains has a globular structure that surrounds a heme group containing a single iron atom. The main function of HbA and other forms of haemoglobin is to transport oxygen through the body.[23]

Although there are multiple forms of glycated HbA, HbA1c, in which glucose is added to the N-terminal valine residue of the HbA β subunit to form fructosyl valine, accounts for approximately 80% of glycated HbA in the human bloodstream (Figure 1).[11] HbA1c is formed nonenzymatically through a Maillard reaction in which a glucose molecule forms a Schiff base with the valine residue.[24] The Schiff base then undergoes an Amadori rearrangement, creating a nonreversible covalent bond. The stability of the HbA1c protein-glucose adduct makes it a useful indicator of average blood glucose levels over time, given that HbA1c levels are directly correlated with average blood glucose concentrations.[5,11] Hemoglobin is found in RBCs, which normally have an average lifespan of 90 days; thus, HbA1c levels reflect blood glucose levels over the previous 3 months.[5,6]

Figure 1: Glycated Haemoglobin Structure Featuring Fructosyl Valine at β-Chain N-Terminus.



In addition to the other, less plentiful forms of glycated HbA, glucose can also glycate other serum proteins, including albumin.4 Therefore, measuring other glycated proteins may be a suitable alternative to HbA1c testing in patients who have altered RBC lifespan or hemoglobin variants.

Sources of HbA1c measurement interference

As with any clinical laboratory test, HbA1c measurement is subject to multiple types of interference, including hemoglobin variants.[5] Structural variants of HbA are caused by point mutations in the genes encoding the protein's subunits, resulting in amino acid substitutions that can alter hemoglobin structure and, potentially, function.2[5] When individuals are homozygous for a genetic hemoglobin variant, they may develop a symptomatic disease, e.g., sickle cell anemia in HbS homozygotes. HbA1c testing is not appropriate for these patients.[5] On the other hand, individuals who are heterozygous for a hemoglobin variant may not be phenotypically different from individuals who are homozygous for HbA (non-variant hemoglobin). HbA1c testing may be appropriate for patients who are heterozygous for a hemoglobin variant, depending on the testing method.[5,6,21]

The worldwide prevalence of hemoglobin variants is 5%–7%, with four single amino acid substitution variants, namely HbS, HbE, HbC, and HbD, being the most common.[25] Position 1 on the HbA β chain is the N-terminal valine residue that is the glycation site targeted by a number of HbA1c assay methods.[5,25]

HbS, the hemoglobin variant that causes sickle-cell anemia, has an amino acid substitution (valine for glutamic acid) at position 6 on the β chain, whereas the variant HbC has a different substitution (lysine for glutamic acid) at the same position. HbE has a lysine for glutamic acid substitution at position [26,] and HBD has a glutamine for glutamic acid substitution at position 121.[25]

The prevalence of hemoglobin genetic variants can vary by geography.5 For example, approximately 300 million people worldwide are heterozygous for HbS, with parts of Africa, the Middle East, and India having HbS allele frequencies >5%.[5,26] The highest prevalence of HbC, 40% – 50%, is seen is parts of West Africa.[27] HbD is most prevalent (2% – 3%) among Sikhs in the Punjab region of India and is also found in many individuals in Northwest India, Pakistan, and China.[28] HbE is particularly prevalent in South-East Asia, being present in 30% – 40% of the population in some regions.[29] For patients with these hemoglobin variants, an HbA1c testing method that is unaffected by hemoglobin variants is recommended.[25]

Elevated fetal hemoglobin (HbF) can interfere with some HbA1c assays.[25] Although HbF is the major hemoglobin species in fetuses, it usually accounts for <1% of circulating hemoglobin in adults. Some individuals, however, are genetically predisposed to persistently elevated HbF levels in adulthood, a condition that is asymptomatic in many cases. Elevated HbF is also associated with certain medical conditions, such as multiple myeloma.[25]

In contrast to the physiological interference associated with anemia caused by hemoglobinopathies and other conditions, analytical interference can be caused by structural/biochemical changes due to amino acid substitutions.[11] Substitutions that change the net ionic charge of HbA may cause interference with methods that separate molecules based on charge differences, such as ion-exchange high-performance liquid chromatography (HPLC) or capillary electrophoresis.[25] Some immunoassay methods may have interference depending on where the detection epitope it targets is located.[5] If it is near an amino acid substitution or if the amino acid substitution results in a protein conformation that inhibits access to the epitope, it may interfere in the test measurement. Additionally, mutations at the glycation site may alter the glycation rate, thus affecting the results of immunoassays or boronate affinity HPLC measurement methods.[30] Although some HPLC methods do not separate HbF from HbA1c or HbA1, others can separate even elevated levels of HbF from the HbA peaks.[25] The N-terminal residue of HbF γ chains (analogous to HbA β chains) is glycine instead of valine, which is likely glycated at a lower rate. Boronate affinity methods, which measure the ratio of glycated to non-glycated hemoglobin, will give an HbA1c result lower than the actual value in patients with elevated HbF.[25]

Laboratories need to consider the impact of hemoglobin variants on their HbA1c testing methods, particularly when serving patient populations where specific variants are more prevalent.[25] As the majority of hemoglobin variants are genetic in origin, they may only need to screen new patients using methods capable of detecting variants and then use easier, higher-throughput testing methods for subsequent HbA1c measurements. Clinicians should also be aware of the limitations of HbA1c testing for patients with specific variants and order tests for variants when they suspect hemoglobinopathy or note discordance between a patient's HbA1c measurements and his or her self-monitored blood glucose levels.[19]

Chemical derivates of hemoglobin can also affect the accuracy of HbA1c measurement.[11] One such derivative created by labile carbamylation of the N-terminal valine is common in uremic patients. Carbamyl-hemoglobin may interfere with results based on charge, since the two forms of hemoglobin have similar isoelectric points, increasing the reported amount of HbA1c. Schiff-base hemoglobin (an intermediate in HbA1c formation) is another possible source of interference.[11]

Standardization of HbA1c Measurement

Use of HbA1c as a biomarker of glycemic control was proposed in the early 1990s, spurred in part by results from the DCCT, which demonstrated that controlling HbA1c levels in patients with type 1

diabetes reduced microvascular complications, including diabetic retinopathy, nephropathy, and neuropathy.9 The DCCT was followed by the UKPDS, which demonstrated that lowering HbA1c decreased microvascular and macrovascular (i.e., cardiovascular disease-related) complications in patients with type 2 diabetes, further supporting the use of HbA1c as a marker for diabetes management.[7] However, implementation of HbA1c testing was hampered at the time by the high variability in test results.[31]

To address this variability, two different initiatives were established to standardize HbA1c measurements across testing methods: the International Federation of Clinical Chemistry (IFCC) Working Group on Hemoglobin A1c Standardization and the National Glycohemoglobin Standardization Program (NGSP).[32,33]

The IFCC Working Group established reference methods for HbA1c analysis to ensure accuracy-based results using primary reference materials made of HbA1c and HbA0 (non-glycated hemoglobin), which are first isolated by cation exchange and affinity chromatography.[6,32,34,35] After the proteins are digested by proteolysis, the glycated and non-glycated N-terminal peptides of the hemoglobin β chain are then quantified by either mass spectrometry or capillary electrophoresis.[35] The IFCC has a network of approved laboratories and offers calibrators to manufacturers, as well as bimonthly monitoring to ensure traceability back to the IFCC standard.[33]

The NGSP was established with the goal of standardizing HbA1c test results to those of the DCCT and UKPDS, "which established the direct relationships between HbA1c levels and outcome risks in patients with diabetes."[36] To that end, the NGSP and its network of laboratories work with manufacturers to establish calibration settings for their HbA1c tests, provides annual certification for manufacturers and laboratories, and performs proficiency testing of routine clinical laboratories (Figure 2).[33,36]

Figure 2. NGSP Network Overview.

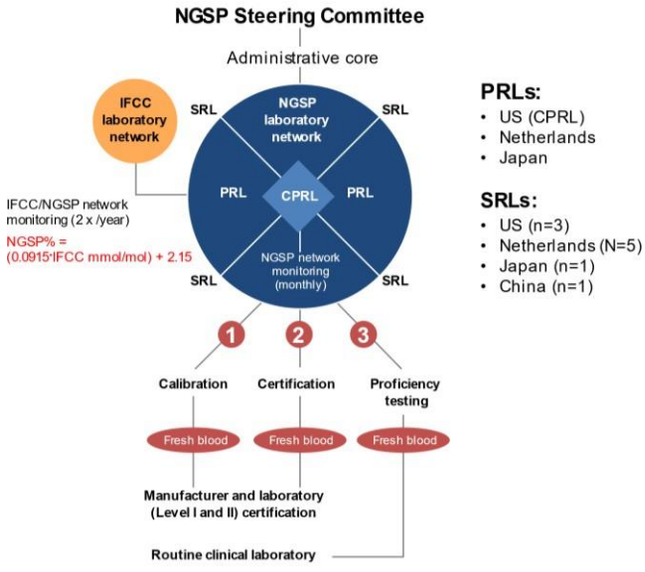
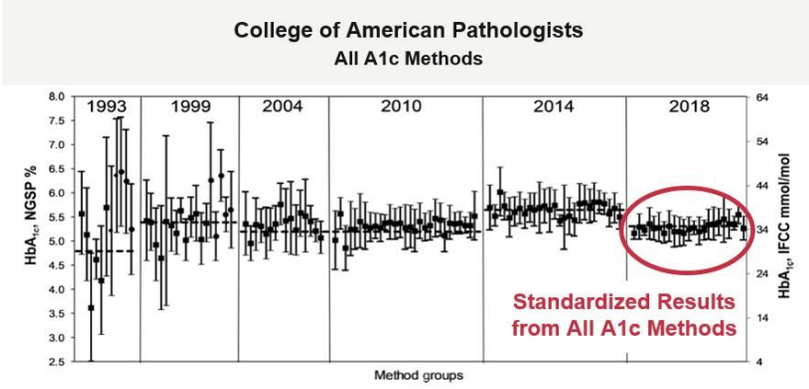


Figure adapted from Little et al. Clin Chem. 2019;65(7):839-848. CPRL: central primary reference laboratory; IFCC: International Federation of Clinical Chemistry; NGSP: National Glycohemoglobin Standardization Program; PRL: primary reference laboratory; SRL: secondary reference laboratory.

Calibration ensures that HbA1c measurements—regardless of method or equipment used—are comparable to DCCT results.[33] To achieve this goal, the NGSP provides support to HbA1c test manufacturers for initially calibrating their methods and then confirming that calibration.

NGSP certification, which is valid for 1 year, requires a manufacturer to demonstrate that its method meets specific criteria, which have become more stringent over time (Figure 3). Since 2019, manufacturer certification requires that results from 36 of 40 individual whole blood samples be within ±5% of results for the same samples from a secondary reference laboratory, in a blinded comparison.[33,37] To monitor HbA1c values in clinical laboratories, the NGSP assesses the College of American Pathologists (CAP) HbA1c proficiency surveys that use pooled whole human blood.[33]

Figure 3. CAP Proficiency Demonstrating Standardization Over Time and NGSP Certification Requirements.



NGSP Certification Requirements: 1996 – Today			
Precision	**Precision**	**37 out of 40 results within**	**36 out of 40 results within**
1996-1998: < 5%	1999-2002: ≤ 5% 2002-2012: ≤ 4%	2013-2014: ± 7% 2014-2018: ± 6%	2019-Today: ± 5%

Figure adapted from Little et al. Clin Chem. 2019;65(7):839-848. CAP: College of American Pathologists; DCCT: Diabetes Control and Complications Trial; GHB: glycated hemoglobin; HbA1c: hemoglobin A1c; IFCC: International Federation of Clinical Chemistry; NGSP: National Glycohemoglobin Standardization Program; SD: standard deviation.

Because the IFCC method uses purified standards, it is considered a higher order method, in contrast to the designated comparison method used by the NGSP, which is based on measurements from blood samples and is not completely specific for HbA1c.[33] The NGSP and IFCC use different measurement units: %HbA1c for NGSP and mmol HbA1c/mol Hb for IFCC. For this reason, a master equation has been developed that describes the relationship between the two standardization systems: NGSP = [0.09148 * IFCC] + 2.152.[32] The rigorous work of the NGSP and IFCC provides confidence in HbA1c result standardization, which has contributed to reduced variability of clinical HbA1c measurements over time (Figure 3), thus enabling better diabetes care based on more accurate test results.[33]

HbA1c Testing Methods

A variety of HbA1c testing methods have been developed over the years, as advances in technology have minimized HbA1c hemoglobin variant interference, increased throughput, and provided other operational advantages.

High-performance liquid chromatography (HPLC)

HPLC methods measure HbA1c by either ion-exchange or boron ate affinity. Ion-exchange chromatography separates different forms of hemoglobin according to ionic charge.[11] The proteins form ionic bonds with the charge solid phase of the chromatography column and are then eluted based on charge using buffers of increasing ionic strength, which disrupt the binding between the protein and solid phase.6 As proteins are eluted from the column, they are detected, and a chromatogram is generated showing peaks corresponding to each eluted protein species. The concentration of HbA1c is calculated based on these peaks.[11] Examining the chromatogram can reveal potential interferences and allow detection of hemoglobin variants, assuming those variants don't co-elute with either HbA1c or HbA based on charge.[25,31] For example, HbF co-elutes with HbA1c using older ion-exchange HPLC methods; newer ion-exchange methods produce a separate peak for normal levels of HbF, but only some of these can also separate peaks for elevated levels of HbF.[25] Methods that use high-resolution chromatography decrease the interference from hemoglobin variants and derivatives but also take longer than lower resolution methods, so the tradeoff between more accurate variant detection and time/throughput needs to be considered when choosing a method.[5,11]

Another HPLC-based method for HbA1c measurement is boronate affinity chromatography.[5,11,30] In this method, the column contains a gel bonded to m-aminophenylboronic acid, which forms a complex with the cis-diol groups of hemoglobin-bound glucose. The glycated hemoglobin is then eluted from the column by adding sorbitol. Because all glycated hemoglobins are detected, this method is largely unaffected by interference from hemoglobin variants. However, this method cannot detect the presence of hemoglobin variants.[5]

Capillary electrophoresis

Capillary electrophoresis separates molecules by charge—like ion-exchange HPLC—and also by mass.5 This allows identification of hemoglobin variants and other interferences by displaying separated peaks on an electropherogram.[30(p49)] Given the effective separation of molecules by mass and charge, the most common variants do not produce analytical interference affecting the HbA1c measurements.5 This method can characterize and diagnose hemoglobin variant type for clinicians who are interested in this information.[5,30]

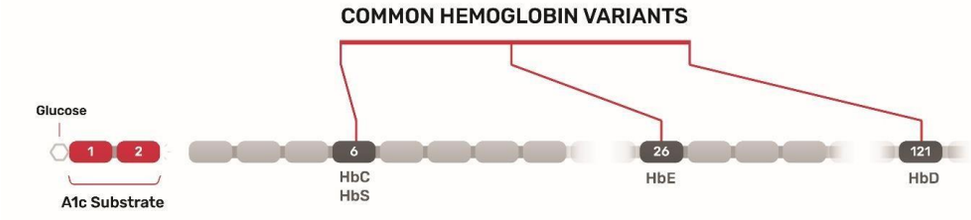
Immunoassays

Immunoassays are antibody-based methods that bind a targeted epitope on the hemoglobin β chain.[5,25] Typically these antibodies bind the first 4-10 amino acids of the β chain, and can be subject to interference from the HbS and HbC variants, since the sixth amino acid is substituted and prohibits access due to a structural change in the hemoglobin.[5] Downstream amino acid substitutions found in HbD and HbE are further away from the N-terminus and, thus, the epitope can be recognized by the antibody, resulting in little to no interference. The antibodies used in HbA1c immunoassays do not recognize chemically modified hemoglobin derivatives.[11] Immunoassays are easy to implement in routine clinical laboratories and are not affected by ionic charge differences in hemoglobin variants or derivatives.[38] However, this method cannot detect the presence of hemoglobin variants.

Enzymatic HbA1c testing

Newer HbA1c measurement methods are based on enzymatic detection. In these methods, proteolytic digestion of lysed whole blood results in fragmentation of the HbA1c β chain and release of its N-terminal fructosyl valine, which is detected via a horseradish peroxidase-catalyzed reaction with a chromogen.[39,40] Enzymatic methods are not very sensitive to interference from hemoglobin variants because the most common variants are upstream on the HbA1c β chain (Figure 4). However, this method cannot detect the presence of hemoglobin variants.[5]

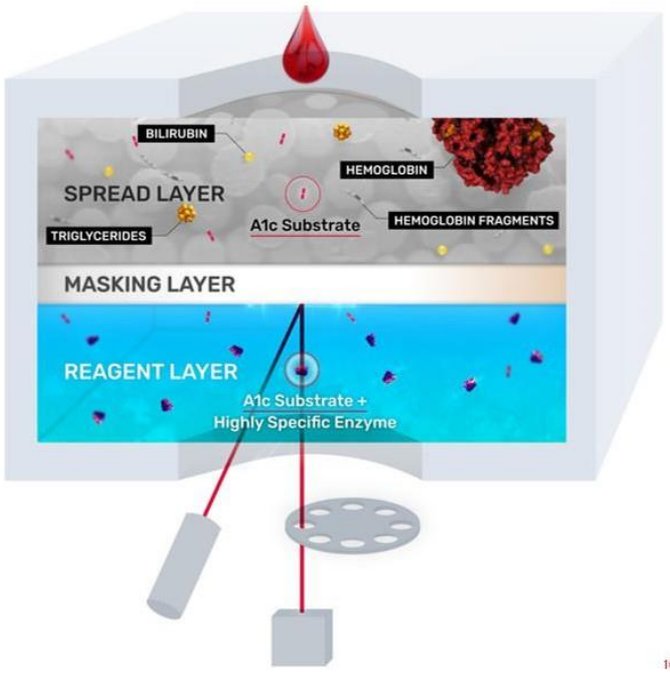
Figure 4. Cleavage Site for Hba1c Enzymatic Assay Substrate Relative to Locations of Common Hemoglobin Variant Amino Acid Substitutions. Figure 4. Cleavage Site for Hba1c Enzymatic Assay Substrate Relative to Locations of Common Hemoglobin Variant Amino Acid Substitutions.



HbC, HbD, HbE, and HbS represent the most common genetic hemoglobin variants. Recently, a Dry Slide method for enzymatic HbA1c testing has been developed: VITROS® Chemistry Products A1c Slides (Figure 5).[41(p1)] This dry and multilayer slide system features reagents applied to a clear polyester support base cut to the size of a postage stamp. This testing method uses a single drop of neat whole blood that is placed on the top spread layer. The spread layer filters out interferences such as hemoglobin, turbidity, and paraproteins. In this test design, the slide contains two surfactants and a protease. The first surfactant lyses the RBCs, while the second surfactant denatures the glycated hemoglobin released from the cell. The protease cleavage site on the hemoglobin molecule is accessible after denaturation, allowing the protease to cleave a two-peptide fructosyl-alpha-valyl-histidine fragment from the N-terminus of HbA1c. Larger hemoglobin fragments and other filtered interferences remain trapped in the spread layer, while the smaller hemoglobin fragments filter through the masking layer until it reaches the reagent layer. In the reagent

layer, the dipeptide substrate is oxidized by a highly specific fructosyl amino acid oxidase to produce hydrogen peroxide, which triggers oxidation of a leuco dye by horseradish peroxidase, producing a colorimetric signal directly proportional to the concentration of glycated hemoglobin. This reaction is detected by reflectance spectroscopy. The masking layer minimizes optical interference to enable accurate results.[41(p1)]

Figure 5. VITROS® A1c Slides Schematic Showing the Three Functional Reagent Layers.



VITROS® A1c Slides are tested on VITROS® Integrated or Chemistry Systems along with other routine and esoteric tests that can optimize lab workflow on a consolidated testing platform.41 With up to 180 tests per hour, this method simplifies whole-blood management with less hands-on time, directs primary test tube sampling, and is compatible with the VITROS Automation Solutions track.

VITROS® A1c Slides have excellent performance standardized to the NGSP Tosoh G8 method and are NGSP certified as required by ADA guidelines.[1,41,42] As an enzymatic method is used, no clinically significant interference is seen with common haemoglobin variants (HbS, HbC, HbD, and HbE). The Dry Slide format is impervious to reagent degradation and has excellent performance stability and calibration stability up to 20 weeks.

Comparing HbA1c testing methods

Each of the available HbA1c testing methodologies has its advantages and challenges (Table 1). Test selection should be based on laboratory objectives and testing needs, including need for a diagnostic claim and identification of hemoglobin variants, or avoidance of hemoglobin variant interference. The patient population being tested should also be considered, since hemoglobin variant prevalence differs by geography as well as by racial/ethnic composition. High-throughput platforms may be more suitable for high-volume testing, and multi-test platforms offer operational efficiencies that single-test platforms do not.

Table 1. Advantages and Challenges of HbA1c Testing Methods.

Method	Principle	Advantages	Challenges
Enzymatic	Measures HbA1c using an enzyme that specifically targets the N-terminus of the β chain	No analytical interference from Hb variants	Unable to detect Hb variants
Immunoassay	Uses antibody targeted against the glycated N-terminus of the β chain	No analytical interference from the most common Hb variants using newer-generation assays	Unable to detect Hb variants; newer-generation antibodies still susceptible to interference from rar Hb variants
Boronate affinity	Glycohemoglobin binds affinity resin, while nonglycated Hb species pass through the column	Minimal analytical interference from Hb variants	Measures all glycated Hb, not just HbA1c; unable to detect Hb variants; throughput
Ion-exchange HPLC	Separates Hb species based on charge	Able to detect the most common Hb variants	Prone to interference by Hb variant that co-elute with peaks of interest; throughput
Capillary electrophoresis	Separates Hb species based on charge and hydrodynamic volume	High chromatographic resolution and resulting ability to detect many Hb variants	Throughput

Hb: hemoglobin; HbA1c: hemoglobin A1c; HPLC: high-performance liquid chromatography.

Conclusion

The reliability of HbA1c measurements across various assay technologies is ensured by the standardization work of the NGSP and IFCC.33 This standardization links HbA1c measurements to clinical outcomes from early landmark trials demonstrating the relationship between controlling HbA1c levels and the reduction of diabetes-related complications. Easy, accurate, and fast measurement of HbA1c promotes better diabetes care through the assessment of average blood glucose levels over time, enabling diabetes diagnosis and monitoring of glycemic control. Laboratories should consider their own testing objectives (i.e., detection or avoidance of hemoglobin variant interference, test volumes, ease of use) in the selection of HbA1c testing methods. The novel, enzymatic VITROS® A1c Slides assay offers simplified and integrated workflows on a consolidated testing platform with high throughput for routing testing.41 The assay has no clinically significant interference from common hemoglobin variants.

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Leveraging technology and innovation to improve operational and environmental sustainability of clinical laboratory operations

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Introduction

While environmental sustainability has become an area of growing global awareness and concern, the Covid-19 pandemic has caused great disruption to countries and societies around the world over the last few years. Recently, the United Nations Economic and Social Commission for Asia and the Pacific (ESCAP) reported [1] that the Asia-Pacific region is falling behind on the 2030 sustainability targets. It now appears that these targets will not be reachable until 2065 [2] -- for us in laboratory medicine, there is an increasing need to re-energise our efforts, do more and move beyond "business as usual" to improve our environmental sustainability.

Before the pandemic, APFCB and experts in our region had already initiated some discourse in this area. An earlier publication by Lopez et al. [3] had earlier identified four main ways in which healthcare (and laboratory operations) impacts the environment. These are: (1) generation of large quantities of waste; (2) usage of hazardous or toxic substances that may cause harm to the environment; (3) consuming large amounts of energy and contributing to greenhouse gas emissions; and (4) consuming copious amounts of water. Some of the helpful recommendations included basic behavioural changes that do not impose financial burden on the laboratory's budget, such as an end-of-day walkthrough to ensure that unnecessary devices are switched off, consolidating tests and equipment, encouraging staff to carpool or commute via bicycle, etc.

While such peripheral behavioural changes can be easily implemented, the core function of the laboratory remains firmly rooted in well-defined, validated, and regulated analytical processes, which are pre-determined by the manufacturers of the analyzer systems. Therefore, it is important for laboratorians to understand the technological and performance characteristics of different analyzers in the selection stage. The decision on one particular analyser system over another can lead to significant downstream impact on laboratory operations and environmental sustainability, as demonstrated in publications [3].

This article focuses on the clinical chemistry and immunoassay core laboratory where the majority of the routine clinical workload is performed, introducing some of the specific technologies and innovations that can be leveraged to achieve more efficient and environmentally sustainable laboratory operations.

Waste Reduction

First, in the area of waste reduction we begin by looking at clinical chemistry analysers. Many systems utilise plastic cuvettes that require monthly replacement. By selecting a system that utilises permanent quartz cuvettes, there are both operational and environmental benefits: on one hand the laboratory can reduce its hidden costs of plastic consumables and waste disposal, while on the other hand reducing its plastic waste.

Also In clinical chemistry, samples often have analyte concentrations above the measuring range of the assay, thus requiring dilutions and reruns. This is particularly challenging for enzyme assays where the substrate can be exhausted rapidly before the rate measurement is completed. Some clinical chemistry analysers employ an extra Flex read window earlier in the reaction before the main measurement time, thereby achieving much higher upper measuring intervals even at very high enzyme levels with excellent precision [4]. This allows the laboratory to report reliable results in the first pass with less need for dilutions, less additional workload for analysers and staff, and less unexpected delays in the turnaround time, while reducing the materials and costs of such dilutions and reruns and lessening its environmental impact.

Next, let us examine the issue of sample-to-sample carryover. On sensitive immunoassays, carryover can potentially lead to sample contamination and incorrect results. To avoid this problem, most immunoassay systems require single-use plastic pipette tips for each test and recommend complex aliquoting workflows into additional tubes. For a typical laboratory that performs millions of tests per year, this translates to a significant environmental impact with millions of pipette tips and tubes being dumped into landfills and floating in the oceans. Fortunately, there are some systems which utilise a unique SmartWash technology which can prevent clinically significant sample-to-sample carryover (0.1 ppm or below) [5, 6], eliminating the need for plastic pipette tips and enabling more streamlined integrated workflows with both clinical chemistry and immunoassay tests aspirated from the same sample tube. This leads to reduced environmental impact, as well as lower hidden costs on plastic consumables, lower waste disposal costs as well as much more simplified workflow for the operators.

Beyond advanced analytical technologies, smart and efficient product design can also contribute towards waste reduction. For example, some systems have multiple reagent packing size configurations and powerful informatics capabilities that allow the same reagent cartridge to be shared and tracked between different modules. This allows laboratories to optimise inventory management, decrease the number of plastic reagent cartridges being used, reduce the amount of manual operation loading and unloading used cartridges, and lessen the carbon impact of the supply chain, while minimising waste and saving valuable refrigerator storage space.

Hazardous substances

Most diagnostics manufacturers are now moving towards compliance with the REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) regulations under the European Chemicals Agency and removing Substances of Very High Concern SVHCs) from their products. This also contributes towards a safer working (environment for laboratory staff and reduce the impact to the environment, while offering new

opportunities to enhance product ease-of-use to operators.An example of this change comes from Abbott's reformulation of the pre-trigger solution used across its chemiluminescence immunoassays. The formulation has now been updated to replace Triton X-100 with Tergitol 15-S-9 which is a readily biodegradable and more environmentally friendly compound. Furthermore, while the previous product required refrigerated storage (2 to 8°C) the new formulation can now be stored at room temperature (2 to 30°C) allowing the laboratory to free up valuable refrigerator or cold room space and simplify inventory storage.

Electricity and water consumption

It has been well documented that laboratory operations require very high consumption of water and electricity. Per unit surface area, the typical laboratory uses 3 to 6 times more than office space. Furthermore, research [7] has shown that equipment such as ultra-low temperature freezers and immunoassay analysers are amongst the most energy intensive devices in the laboratory. The utility consumption of different laboratory equipment should, therefore, be considered in the selection and procurement process, as it is related to the long-term operating expense and Total Cost of Ownership. Water and electricity requirements across different systems can be compared easily, since such information is usually published and readily found in promotional brochures and operator manuals. A recent case study from a laboratory in Vietnam [8] has shown that switching to a more efficient analyser enabled a reduction in electricity consumption rate by 51.1% and water consumption rate by 2.9%.

Conclusion

There are many technologies and innovations that can enable laboratory operations to be environmentally sustainable (via the reduction of wastes, hazardous substances, or utilities consumption) while at the same time delivering on operational and economic benefits (such as streamlined workflows, lower repeats and hidden costs, simplified sample and reagent management, decreased utilities and waste disposal expenses, etc.). While a few of these technologies are introduced in this article, there are certainly many more out there that can be considered and incorporated into procurement criteria to help laboratories to identify and select the right solution for their needs.

Organisations around the region are now beginning to incorporate sustainability implications into procurement and tender decisions [9]. Additionally, the environmental efforts of vendors and suppliers can also be assessed and endorsed by credible, independent third parties. For example, the Dow Jones Sustainability Index (DJSI) calculates an annual sustainability score for the top companies across 61 industry sectors. For the last nine years, Abbott has been ranked number one with the highest score in the health care equipment industry [10], and its corporate sustainability report [11] has shown that it has outperformed its 2020 goals of reducing normalised carbon emissions by 40% and water intake by 30% versus the 2010 baseline. Such industry awards and assessments are not only for publicity purposes, but also serves as powerful indicators of the company's investment and

track record in environmental sustainability that can inform laboratorians and administrators in the vendor selection process.

Finally, implementing new technologies often involve significant transformation of laboratory processes and operations. It is, therefore, vital for laboratorians to understand the tangible and intangible benefits and the impact on overt and hidden costs. Demonstrating that environmental sustainability can also contribute towards operational and economic improvements will help to secure buy-in and support from senior leaders, employees, shareholders and other important stakeholders. Moreover, continuing education and training are important to drive deeper fundamental culture change across the organisation and instill a long-term sustainability mindset. Environmental sustainability is not only good for the environment, it can also help laboratories to succeed in gaining competitive advantage and drive long-term growth [3].

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    https://dam.abbott.com/en-us/docume

Quiz Section!!

Refer to our Adrenal Testing webinar, or the next APFCB newsletter for the answers.
Endocrine Part 1 (adrenal tests):
https://www.youtube.com/watch?v=azqnGXoD0kY&t=1s
https://www.apfcb.org/webinars.html

Question 1: (Case 2)
Patient: 29-year-old Female
Clinical information: Addison's?
Time: 6:30 am

Analyte (Plasma/serum)	Result	Ref. Range
Cortisol	<30 nmol/L	(150-700)
ACTH	331 pmol/L	(2.0 - 10.0)
Renin	1310 mU/L	(3 - 40)

Which of the following is the most likely interpretation?

a) Untreated primary adrenal insufficiency
b) Treated primary adrenal insufficiency
c) Secondary adrenal insufficiency
d) Renal disease

Question 2: (Case 3)
Patient: 34-year-old Female
Clinical information: Hyponatremia. Exclude Addison's
Time: 7:30 pm

Analyte (Plasma/serum)	Result	Ref. Range
Cortisol	110 nmol/L	(150-700)
ACTH	2.4 pmol/L	(2.0 - 10.0)

Which of the following suggestions is most useful?

a) Diagnose secondary adrenal insufficiency
b) Suggest repeat blood draw and measurements in the morning
c) Suggest Synacthen stimulation test
d) Suggest 24 hour urine cortisol

Question 3: (Case 5)
Patient: 73-year-old Female
Location: Ward
Clinical information: Pneumonia, raised serum cortisol
Time: 8:05 am

Analyte (Plasma/serum)	Result	Ref. Range
Cortisol	1800 nmol/L	(150-700)
ACTH	3.6 pmol/L	(2.0 - 10.0)

Which of the following is not appropriate?

a) Exclude extraneous glucocorticoid (eg. Hydrocortisone)
b) Consider 24hr urine cortisol, overnight dexamethasone suppression test and/or midnight salivary cortisol to investigate Cushing's syndrome
c) Consider pituitary MRI
d) Suggest test for anti-adrenal antibodies (eg. 21-hydroxylase antibody test)

Question 4: (Case 7)

Patient: 53-year-old Female

Clinical information: Hypertension

Time: 8:15 am

Posture: Erect

Analyte (Plasma/serum)	Result	Ref. Range
Aldosterone	207 pmol/L	Erect: (60 – 980)
Renin	4.3 mU/L	Erect: (4 – 46)
Aldosterone/ Renin ratio	N/A	(<50)
Sodium	142 mmol/L	(134 – 146)
Potassium	2.2 mmol/L	(3.4 – 5.3)
Bicarbonate	31 mmol/L	(22 – 31)
Urea	5.2 mmol/L	(3.0 – 8.0)
Creatinine	90 umol/L	(60 – 105)

Which of the following is most useful?

a) Rule out primary aldosteronism
b) Suggest to repeat aldosterone and renin with patient in supine position for 30 minutes
c) Suggest to repeat aldosterone and renin when serum potassium has normalized above 3.5 mmol/L
d) Suggest to check for beta blockers, methyldopa and clonidine

Question 5: (Case 9)

Patient: 58-year-old Male

Clinical information: Hypertension

Time: 8:30 am

Posture: Not recorded

Analyte (Serum)	Result	Ref. Range
Aldosterone	2610 pmol/L	Erect: (60 – 980) Supine: (<650)
Renin	26.7 mU/L	Erect: (4 – 46) Supine: (3 – 40)
Aldosterone/ Renin ratio	98	(<50)

Which of the following is least likely?

a) Primary aldosteronism
b) Secondary aldosteronism
c) Spironolactone/ diuretic therapy
d) Renal artery stenosis

Question 6: (Case 14)

Patient: 57-year-old Female

Clinical information: (adrenal) incidentaloma

Analyte (Plasma)	Result	Ref. Range
Normetanephrine (free)	960 pmol/L	(< 750)
Metanephrine (free)	270 pmol/L	(< 300)

Which of the following is least helpful?

a) Suggest to check for beta blockers, tricyclic antidepressants, phenoxybenzamine
b) Suggest clonidine suppression test
c) Suggest endocrine referral for further investigation (20% of phaeochromocytoma have borderline elevated metadrenaline)
d) Suggest to repeat plasma metanephrines in 12 months

Adrenal Testing Quiz Answers:

1. a
2. b
3. d
4. c
5. a
6. d

Climbing Up a High Mountain in Golden Autumn

Dr. Tan It Koon

Founding President of APFCB and SACB

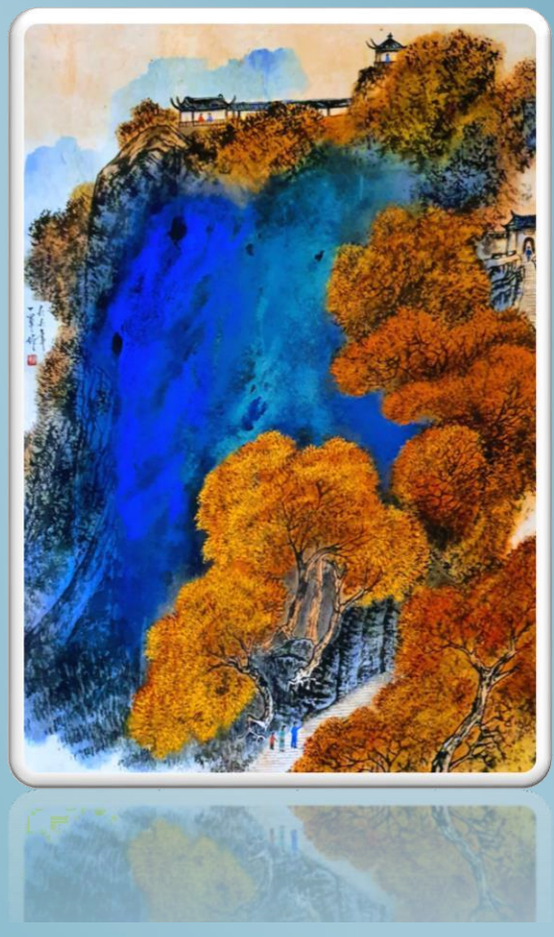
During the times when I had extended stays in China after participating in congresses and conducting training courses or lectures, I often made arrangements with friends to make full use of my vacation. We would take full-day trips or make visits to museums, art galleries, scenic places, mountains and waterfalls, famous parks and gardens, as well as enjoy cruises on lakes and rivers. In autumn, when the weather is often fine and the air, cool and crispy, it is particularly suitable for outdoor physical activities. This painting 《Climbing Up a High Mountain in Golden Autumn》 is inspired by my trips to high mountains with friends and expresses the sentiments of the following poem that I composed:

"In Autumn, when the sky is blue and weather is sunny and cool;

Trees at the mountain forests have changed to a golden brown;

Let us take this opportunity to visit a majestic mountain;

Get together, enjoy a pleasant picnic, cordial fellowship and hearty conversations at its summited Earth.



The painting shows a family of 3 standing at that bottom of a mountain about to take an arduous climb up the high mountain. On the extreme right of the artwork is a stone stairway hewn out of limestone rock of the mountain, with an initial gradual incline and progressing to a steep slope. It ends at an entrance gate with typical Chinese structure, which leads to a spacious pavilion and lookout station with unique roof structure for visitors to enjoy the beautiful scenery around and have their picnic meals. A couple dressed in red and blue are already at the pavilion waiting for their friends from below to join them.

For the more energetic, there is a covered walkway leading to a pagoda further up at the summit which provides an even more spectacular and magnificent panoramic view over a large area. Much of the mountain is covered with trees that have turned golden brown in late autumn and provides a most glorious sight.

Below is my poem in Chinese entitled《金秋时节登高山》written in the ancient Tang Dynasty style of 4 sentences, with each comprising 7 words, and with the last words of sentences 1, 2 and 4 in rhyme when recited:

秋日晴空天气爽，
满山树林换彩装，
趁此上山远足去，
好友欢聚话家常。

With Best Wishes
IK Tan