EAPM Autumn Presidency Conference

Redefining the Unmet needs in Healthcare and the Regulatory Challenge

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European Alliance for Personalised Medicine

Foreword

Through the distinct prisms of diagnostics, data, medicines and cancer, the EAPM Autumn Presidency Conference examined how impending regulatory change could help transform prospects for the health of Europe's citizens.

This was the third Presidency conference that EAPM held during 2021 – a demonstration in itself of how closely EAPM is tuned into the current strategic discussions of healthcare in the EU. The conference grasped a moment when the opportunities and the challenges for better healthcare are expanding – both in the wake of Covid, and on the brink of a major review of European Union legislation on medicines. And as is EAPM's tradition, it attracted speakers and attendees from across the worlds of medicine, research, patients, industry, and payers to ensure a broad perspective that offers the chance of finding common solutions.

The central themes to emerge were that the resilience and sustainability that Europe is now seeking for its healthcare systems depend heavily on bringing innovation into practice. Recognising that the many stakeholders involved have different perspectives, EAPM addressed how innovation can provide value to patients, to society and to the developers of effective new approaches, in both the public and private sector, and how regulators can bring much-needed certainty to all constituencies.

Working sessions addressed how to maintain and develop diagnostic testing as new EU rules come into place next year, how legislation on pharmaceuticals can best be updated to seize the advantages of innovation, what potential the emergence of digital Europe is bringing to creating a personalised, predictive, preventive, and participatory health system, and which amendments to Europe's cancer strategy will make it deliver most effectively for patients and for society.

The principal conclusion that emerged was that integrating personalised medicine into clinical practice in Europe will allow unmet needs to be more effectively tackled – but only if a more comprehensive implementation strategy can be forged, focused on patients, and involving national decision makers, regulators, healthcare professionals and all stakeholders in the healthcare arena. With its assessment of obstacles and its exploration of solutions, this conference advanced towards that process.

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In vitro diagnostics regulation

The new in vitro diagnostics regulation adopted in 2017 is due to enter into application on May 26, 2022 – but there are serious risks that this deadline risks major disruption to the supply of current diagnostics, and imperils the development of newer testing techniques – including the emerging opportunities in genomics. This session pinpointed the principal challenges and outlined possible solutions.

As **Olga Tkachenko** *of the European Commission* spelled out, the new legislation overhauls the diagnostic regulatory framework in the EU, to bring higher standards of evidence, more transparency and traceability, and more alignment among actors. It also takes account of technological progress digital personalise medicines and a dynamic market. But in 2021 it became apparent that readiness was insufficient – across the regulatory framework and within the diagnostics and healthcare sector. The capacity of the responsible notified bodies is in question since they will have to cover about 80% of the market - a big jump from the 8% that they covered under the old rules. Readiness of industry is an issue, since several thousand certificates will need to be issued by notified bodies, and obtaining the necessary conformity assessment for products takes about a year. And in healthcare institutions that use and often develop their own diagnostics, awareness of the new requirements, especially for in-house devices, is low. Other gaps include implementing acts guidance documents that are still in preparation, EU reference laboratories that are still being established, and monitoring and contingency planning that is still underway. To prevent disruption in supply, the Commission has proposed amending legislation to provide for a progressive rollout with extended transitional provisions, and is now awaiting the response of the Council and European Parliament. "But legislative action on its own is not enough and continued engagement is needed from all sides," she said.

Petra Zoellner *of MedTech Europe* listed the challenges – and the severity of the risks - as seen by industry. She said 53% of manufacturers report that they are unable to sign with a notified body to certify their quality management systems and IVDs, and the current best-case scenario is that only 61% of today's IVDs will be certified by 26 May 2022, with a worst-case

scenario where only 24% will. “Solution needs to be decided and communicated as soon as possible,” she stressed. “All eyes are at the moment on the Parliament and the Council to see what they will do, and if they will in fact address the urgent situation and provide a solution.”

While accepting that a problem existed, **Marta Carnielli** *of TÜV SÜD* pointed out that efforts were being made to provide a remedy: “Six is a small number of notified bodies to be in operation, but it should be noted that all six have increased their capacities,” she said, with hiring more people and qualifying experts to conduct the necessary new reviews. “It takes time, but we need to ensure that our experts have the appropriate experience and qualification,” she said. Additional notified bodies “are in the pipeline,” she added - 11 notified body applications have been made for designation and are now in process.

Particular difficulties are anticipated for companion diagnostics on the market, since none of the available regulatory routes seem to work if manufacturers want to make changes to their products after May 2022. Tkachenko said the Commission is insisting with the authorities that they are under an obligation to process these applications and should put the appropriate processes and infrastructure in place. “We hope also that the European Medicines Agency could accept the applications for consultation as soon as possible even if the full processes are not yet in place, because it is important for those products to get on the market.”

Bastiaan Tops, *from the Prinses Máxima Centrum diagnostic laboratory,* expressed concern over the likely loss of speciality tests and a loss of innovation. He said measures such as additional accreditation requirements for use of laboratory-developed tests was “over-regulation”, and could lead to “the end of LDTs as we know them.”

Another unresolved concern is that the use of next-generation sequencing technology for genetic profiling of tumour cells to improve access to innovative cancer diagnosis and treatment - as envisaged in the EU’s cancer plan, could be compromised by the new requirements. It is not clear how to apply substantial amendments to next generation sequencing to keep pace with science in the case of newly identified gene alterations causing cancer.

The Pharmaceutical Strategy

The EU has made clear that its ambition with its Pharmaceutical Strategy, on which formal legislative proposals are expected by the end of 2022, is to create a future-proof regulatory framework supporting industry in promoting research and technologies that actually reach patients in order to fulfil their therapeutic needs while addressing market failures, and to take into account the weaknesses exposed by the coronavirus pandemic and take appropriate actions to strengthen the system. From a broad perspective, this EAPM conference examined the likely prospects, highlighting the points of view of patients, researchers and industry, to discern how best the pharmaceutical strategy could bringing innovation into healthcare systems. As Denis put it, how can the regulatory system best adapt to translate knowledge and insight into value and bring this value to patients, to society, and also in a broader return on the investment that innovation can presuppose. The conclusions from the session were that, pre-eminently, patients need secure supplies of safe, efficacious and high quality medicines. They also need them at an affordable price. And for this, legislation needs to keep up with the rapidly changing technological environment, and businesses need to operate in a system that fosters innovation.

UK patient advocate Alastair Kent insisted on availability. “Patients want access to safe affordable high quality medicines that will address unmet health needs, and authorization is not enough. We also need a framework that makes sure that they’re available, access is equitable and it’s sustainable over time”. New scientific understanding at a molecular level opens ways that research can intervene to develop disease-modifying therapies that will improve both the quality and quantity of lives. But unresolved fault-lines between the EU and the member states create uncertainties over access, geographically and in terms of equity. His demands were for incentives for research and development for treating small populations with complex diseases to be accompanied by more flexible regulatory approaches to innovative trials that take more account of patient experience, and to be complemented by measures that ensure timely access for patients.

Frédéric Destrebecq *of the European Brain Council* stressed that patients are still faced with huge unmet needs, with still no cure for most brain disorders, making it necessary to focus on risk reduction, addressing stigma, prevention and early detection. More research and the pharmaceutical strategy represented a window of opportunity. He urged prioritization of brain health and wider international collaboration in the field, to deliver novel therapies that can show improvements in outcomes. It was essential to implement an integrated approach, he emphasized – and to recognize the negative impact of Covid. His views were strongly endorsed by **Joanna Chorostowska** *of the European Respiratory Society,* who focused on the importance of revising the definition of unmet medical needs,which she depicted as too narrow and rigid, and over-reliant on the criterion of non-availability of alternative treatments. "We don't have the treatments that are able to modify disease. We just treat the symptoms," she said, calling for the pharmaceutical strategy to be "more solution-oriented." She urged greater emphasis to the real world data and observational trials, more flexibility to adaptive procedures, and a bigger role for academic research

From the industry perspective, **Ivana Cattaneo** *from Novartis* depicted the pharmaceutical strategy as the chance for a shared vision for a healthier future for Europe, with valuable initiatives in terms of anti-microbial resistance, data management, regulation and future protection against health threats. But she signalled points of caution in terms of potential risks for orphan medicine development in Europe and treatments for children, and health technology assessment. The industry is constantly innovating – but it is an industrial sector, and needs a strategy responsive to that, in terms of the regulatory environment, the scope for using healthcare data, protection of IP, and support for sustainable manufacturing.

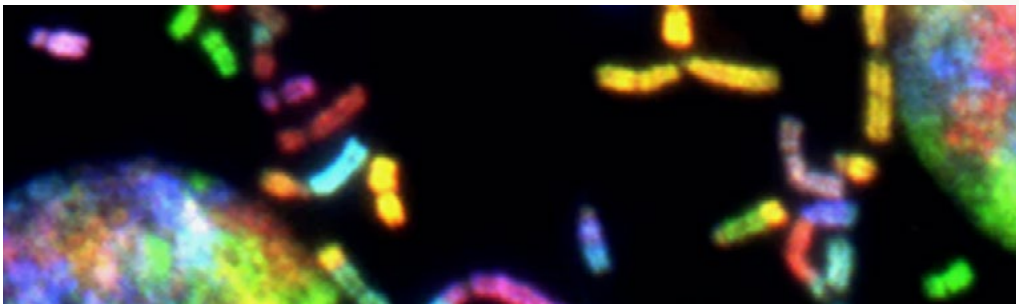
For her, the common goal should be serving patients whilst keeping EU at the forefront of innovation. EMA could do more to encourage the use of new types of clinical trials to help new medicines get to patients faster, accelerate the use and acceptance of real-world evidence in regulatory decision making, strengthen dialogue between industry and regulators throughout the development process, and simplify the regulation of combination products. And timelines between marketing authorisation and patient access should be shortened to save lives and avoid unnecessary economic damage. Right now, she said, the EU is losing ground internationally in the development of new treatments and in investment in research and development.

Philip Van Kerrebroeck *of the European Association of Urology* confirmed from his perspective the needs of patients across Europe for safe, efficacious and high quality medicines available equitably at an affordable

price. But his patients had problems where non-oncological indications (such as for overactive bladder or benign prostate problems) are considered ‘lifestyle problems’, or where better alternatives to broad spectrum antibiotics are not reimbursed. He also pointed to reimbursement problems causing uneven availability of authorized products at national level, or persistence of older medicines although more efficient or safer pharmaceutical equivalent are available.

Conclusions from the session included emphasis on the importance of some more structured dialogue to support the implementation of the pharmaceutical strategy to take account of the broader patient and citizen perspective, and adaptation of the regulatory framework to be fit for purpose, able notably to take account of the contribution now increasingly being made by the use of biomarker testing. Increased interconnection across EU policies on health and medical research should also be linked to the practical issues of access to treatment.

Digital health and data space for genomics in Europe



The dramatic improvements in genomic sequencing are increasingly enabling the shift to a personalised, predictive, preventive, and participatory health system by providing the right information and treatment to the right people at the right time. Genomics has also been a game-changer for clinical and translational research, transforming drug discovery and development and even stimulating economic return. Developing personalised medicine depends on creating a framework that makes the right use of medical data silos and genomic and m-health data silos, combining them effectively. The European Commission promises that its upcoming Digital Europe Programme will reinforce critical EU digital capacities with a focus on developing and deploying artificial intelligence, cybersecurity, advanced computing, data infrastructure, governance and processing. The session explored the elements that should guide policy makers as they put these programmes in place.

Veli Stroetmann *of empirica* presented the conclusions of Digital Health Europe, an EU project to advance priorities for the digital transformation of health and care in the context of the upcoming European Health Data Space. The focus on citizens' access to their own health data, better data, and citizens' empowerment led to recommendations for supporting responsible health data sharing and use, including setting up a multi-stakeholder forum for co-creating and sharing valuable and proven business models for secondary use of diverse kinds of health data, and a European digital health hub or knowledge centre to bring together knowledge and resources to collect, assess, consolidate resources and expert guidance and facilitate wide access to the EHDS assets. It also urged exploring models for incentivising data integration into EHRs and health systems from consumer devices, with interoperability standards and data quality rules

Mark Lawler *of Queen's University Belfast* suggested developing a blueprint for sharing of cancer data, since no single institution can go it alone and the future lies in embracing a new data-enabled research cooperative involving patients/citizens in the co-creation of health data science resources and the delivery of patient benefit/impact. It should also provide a framework for

responsible sharing of genomic and health-related data for research, linking longitudinal clinical, epidemiological, genomic, and health economic data and facilitating accelerated data analytics. He championed the development of a citizen-focussed data sharing culture, moving from a closed and selfish silo mentality to an open source collaborative culture. At the same time, it was essential to establish and maintain public trust in the use of big data. Among the initiatives he highlighted were a Meta-Knowledgebase, which aggregates all known information about gene mutations and variants of uncertain significance into a single searchable resource for the cancer community, should be developed – with the aid of an effective data translator, the DATA-CAN vision of facilitating data to enhance cancer care, and a national cancer trusted research environment platform.

Collaboration was a powerful theme through much of the discussion of data, with **Benjamin Horbach** *of Hoffmann-La Roche* strongly endorsing joint work with public and the private sector on commitments to the implementation of innovation. He underlined the need for a comprehensive approach, following the science but also the implementation of innovation into clinical routine on high quality testing, digital health and targeted therapies, so that patients get the best access to health care and improved patient outcomes. Other speakers reinforced the call for action to promote data enabled innovations, to improve the fragmented data infrastructure and tackle uneven interoperability and standards on quality, content and access, and to generate trust in data-enabled healthcare systems. Ultimately, only this would satisfactorily demonstrate the potential and raise the awareness needed to influence policymakers, so as to feed into the regulatory and HTA decisions that can support adequate reimbursement and funding. **Volker Liebenberg** *of Illumina* underlined the important role that the right frameworks for genomics data will play in the future of science and health, providing the space where the data is organized and structured, and where interaction is promoted between all stakeholders - patients and citizens, industry, and public health authorities and players. Gary Saunders of EATRIS highlighted how sustainable genomics data management needs strong incentivisation of standardization, which must be led by policy makers with funding strategies, mandating of standard use. He advocated federation of genomics data management as the model to be promoted, and urged collaboration between research infrastructures and policy makers to define and drive these incentives. And **Fabrizia Galli** *of aBRCAdaBRA*, speaking from the perspective of cancer patients, put in a plea for greater deployment of genomics across Europe to advance personalized medicine, reducing suffering and saving money for society.

Beating cancer – and unmet medical need

Against the background of the emerging EU Beating Cancer Plan, and the imminent European Parliament report on its orientations, this session explored how Europe and its member states are – and are not – developing effective actions against cancer, how more EU-level harmonisation might be generated, and crucially, how current discussions on the definition of unmet medical need hold much of the key to how Europe will be able to respond to the challenges not just of cancer but of health in general. Much attention was also devoted to the highly topical issue of unmet medical need – for which the definition is currently the subject of intense reflection in Europe as the orphan and paediatric drug incentive schemes are reviewed.

Ivica Belina *of the Croatian Coalition of Healthcare Associations* insisted that cancer care in Europe had to become comprehensive and tailored to the needs of patients and carers, and that it has a much broader scope than diagnostics, treatment and supportive care. It must be accessible, affordable, sustainable, providing for an active role for patients and carers, partnership with HCPs, and taking full account of social inclusion and quality of life. **Tit Albreht,** *Coordinator of the Joint Action Innovative Partnership For Action Against Cancer,* highlighted the need for multidisciplinary approaches, the use of registries, more effective links with ERNs. These could help overcome uneven provision and indifferent quality of cancer care that had for long been evident across Europe. And **Ken Mastris** *of ECPC* spoke of his organisation's efforts to shape the European and national political agenda so as to tackle inequalities between and within member states. Europe's diversity in hospitals and health care systems means that harmonisation at European level is all the more difficult because of roadblocks at individual country level – and there is still little provision for effective EU audit or quality control at national level. There are still conspicuous delays in diagnosis and gaps between diagnosis and treatment, delays in access to some treatments across Europe, and gaps between richer and poorer member states. Among the many recommendations put forward were the development of more focused EU-wide research programmes, more effective cancer prevention strategies and policies, optimised screening programmes and the development of novel approaches for early detection, and policy support to improve the quality of life of

cancer patients and their entourage.

Medical need should have a wider definition, in Belica's view. It should, he said, take account of prevention of disease, timely diagnostics and treatment, the development of clear patient pathways, and treatment options. Unmet needs extend into the realm of co-decision making, prediction of the disease, creation of personalized cancer care plans and levels of support, and research for new genetic mutations in different disease areas. Other key unmet needs are in prevention of disability and retention of working ability, and rehabilitation on all levels.

Christine Mayer-Nicolai *of Merck* saw the definition of unmet medical need as a hallmark defining the speed of innovation in Europe, since at stake was the future of public and private investments, the speed of R&D and the capability to improve patient outcomes. It was essential, she said, to avoid narrowing the principle to merely considering that the availability of one treatment meant there was no more medical need. That would be to disconnect Europe's regulation from scientific evolution. Her alternative was a definition of conditions based on evolving science and current practice in modern oncology, where typically tumor agnostic approvals cover a set of conditions rather than the vertically defined conditions for which a pivotal root cause has been established. In her view, if the EU wishes to accelerate innovation it must develop a broad and flexible definition based on principles defined with all stakeholders, working together in stronger public-private partnerships and in a transparent and predictable regulatory framework. The new definition should combine conditions based on signs and symptoms and on root causes, as supported by science. A condition should be defined as any deviation from the normal structure of the body or function, as manifested by a characteristic set of signs and symptoms including, where identified, the pivotal cause or root cause of such deviation: a typically recognised, distinct disease or a syndrome or as characterised by its potential to constitute the pivotal root cause or root cause of multiple characteristic sets of signs and symptoms affecting different parts or subsystems of the body, including where sufficiently identified, a set of such signs and symptoms.

Luzia Travado *of the International Psycho-Oncology Society* urged recognition of a standard for quality cancer care psychosocial cancer, with distress accepted as a vital sign. This should be a universal human right, since psychological suffering impacts on clinical outcomes, and adequate resources and funding should be provided for it in national cancer plans.

Policy inertia and the gap between plans and implementation were themes that arose repeatedly. As Belina recounted, in Croatia, it took years to develop a national strategy, and even when it was accepted by the national

parliament, nothing happened to put it into effect. The economic crisis and Covid have frustrated many plans, he recognized. The difficulty of winning support from policymakers was highlighted over and over again, with calls for intercession from the European Parliament to pressure reluctant national governments. “We have not been sufficiently influential without national politicians to have these recommendations applied,” said Travado, and “we need to know how to open this door.” Delays in action because of national budget approval processes or elections resulted in frequent disappointments, as a “roller coaster that never gets old.” Cooperation too was signalled as an important factor in influence. **Lydia E Makaroff** *of Fight Bladder Cancer* related how until 2019, there was not a single organisation to speak as the global voice for people living with bladder cancer, but that in response to the obvious need, the World Bladder Cancer Patient Coalition now brings together representatives of national bladder cancer organisations to foster an international community.

The tone of the session was exemplified by remarks from Albreht warning against any complacency: “Don’t assume agreement in principle at EU level means action at national level,” he said. Mastris echoed the view: “Ultimately it’s all down to delivery at local level”, so it is vital, he said to ensure that cancer remains on the political agenda.

Conclusions

Integrating personalised medicine into clinical practice in Europe will allow unmet needs to be more effectively tackled – but only if a more comprehensive implementation strategy can be forged, focused on patients, and involving national decision makers, regulators, healthcare professionals and all stakeholders in the healthcare arena. There are responsibilities at all levels to be met by all stakeholders, and a wider readiness to engage in more meaningful collaboration will be crucial to success. The hope is that this meeting will feed into the many other activities supporting the goal of better use of personalized medicine for the benefit of patients and wider society.

Recommendations

A series of bold recommendations were put before the conference, as follows.

- Launch the European Initiative to Understand Cancer, UNCAN.eu
- Develop an EU-wide research programme to identify (poly-) genic risk scores
- Support the development and implementation of effective cancer prevention strategies and policies within Member States and the EU
- Optimise existing screening programmes and develop novel approaches for screening and early detection
- Advance and implement personalised medicine approaches for all cancer patients in Europe
- Develop an EU-wide research programme on early diagnostic and minimally invasive treatment/ technologies
- Develop an EU-wide research programme and policy support to improve the quality of life of cancer patients and survivors, family members and carers, and all persons with an increased risk of cancer
- Create a European Cancer Patient Digital Centre where cancer patients and survivors can deposit and share their data for personalised care
- Achieve Cancer Health Equity in the EU across the continuum of the disease
- Set up a network of Comprehensive Cancer Infrastructures within and across all EU Member States to increase quality of research and care
- Childhood cancers and cancers in adolescents and young adults: cure more and cure better
- Accelerate innovation and implementation of new technologies and create Oncology-focused Living Labs to conquer cancer
- Transform cancer culture, communication and capacity building

Participants in the conference

Chair

Denis Horgan, *Executive Director, European Alliance for Personalised Medicine*

IVDR

Olga Tkachenko, *Policy Officer, DG for Health and Food Safety, European Commission*
Petra Zoellner, *Industrial Policies, Senior Manager In Vitro Diagnostics, Medtech Europe*
Marta Carnielli, *IVD Technical Officer – TÜV SÜD*
Bastiaan Tops, *Head of Diagnostic Laboratory, Prinses Máxima Centrum, Utrecht, Netherlands*

Pharmaceutical strategy

Alastair Kent, *Former Director, Genetic Alliance UK*
Frédéric Destrebecq, *Executive Director, European Brain Council*
Joanna Chorostowska, *Secretary General of the European Respiratory Society, Head of Department of Genetics and Clinical Immunolog, National Institute of Tuberculosisy and Lung Diseases, Warsaw, Poland*
Ivana Cattaneo, *Executive Director, Oncology Policy & Healthcare Systems, Novartis Oncology Region Europe*
Philip Van Kerrebroeck, *EAU Policy Office Chairman, Maastricht, Netherlands.*

Data and genomics

Veli Stroetmann, *Director empirica, Bonn, Germany*
Mark Lawler, *Queen's University Belfast, Faculty of Medicine, Health & Life Sciences*
Benjamin M. Horbach, *Global Policy Leader, F. Hoffmann-La Roche Ltd.*
Volker Liebenberg, Director Medical Affairs EMEA, Illumina
Gary Saunders, *Data Director at EATRIS*
Fabrizia Galli, *Vice-President, aBRCAdaBRA*

Beating Cancer

Luzia Travado, *President-Emeritus, International Psycho-Oncology Society (IPOS) And Clinician & Researcher Of Psycho-Oncology, Champalimaud Foundation, Lisbon, Portugal*
Ivica Belina, *President, Coalition of Healthcare Association*
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About EAPM

The European Alliance for Personalised Medicine brings together Europe's leading healthcare experts and patient advocates to improve patient care by accelerating the development, delivery and uptake of personalised medicine and diagnostics.