

Interview with **Dr. Leeza Osipenko**, Head of NICE Scientific Advice

HTA Scientific Advice – Is it Becoming More Important?

Dr. Susanne Michel, Vice President and Practice Lead, Market Access Consulting, of Evidera recently spoke with Dr. Leeza Osipenko, Head of NICE Scientific Advice, about the evolution and importance of HTA Scientific Advice.

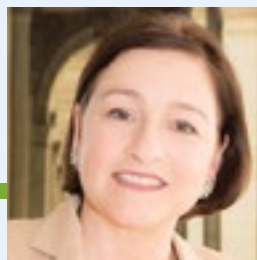
How has the process of working with manufactures to provide scientific advice evolved over the past five years?

There is now a greater acceptance of a dialogue between manufacturers and Health Technology Assessment (HTA) bodies. This is a very welcome development, however, there is still a lot of room to grow and to make sure that sponsors see the value in generating evidence relevant to patients and clinical practice and are not simply trying to fulfil minimal requirements set by the Food and Drug Administration (FDA). At NICE, we have significantly expanded our services and in addition to providing advice in parallel with the European Medicines Agency (EMA) and European HTA agencies, we offer an express service for the national advice, an abridged service for Small and Medium Enterprises (SMEs), advice for developers of devices and diagnostics, and quality assurance and sense checking of economic models. We are currently developing links with our North American colleagues and starting a project with the Canadian Agency for Drugs and

Technologies in Health (CADTH) as well as running pilots with organisations in the U.S. Our team continues to deliver educational seminars and conduct site visits to companies. Such a diversity of activities has increased the awareness and uptake of scientific advice. Overall, as we hear from the NICE committees, the quality of sponsors’ submissions is becoming better. There is still a lot of variation but more companies now make attempts to collect quality of life and longer-term outcomes data.

From our experience manufacturers most often seek scientific advice due to specific data or trial design uncertainties, do you agree? What are the other motivations for seeking NICE scientific advice? Have these motivations shifted or changed over the last years?

This is a question for manufacturers not for NICE. I suppose motivations range widely and in big companies they can often be political rather than methodological. Sometimes we receive genuinely interesting methodological questions and sometimes companies come for a check-box exercise. The latter is something NICE does not provide as we always



Susanne Michel

This interview was conducted in conjunction with ongoing efforts by Evidera’s Market Access Center of Excellence, currently led by Katie Gardner, Senior Director, Market Access Communications, to provide relevant and up-to-date information to help support our clients’ needs for product access.



take a critical view of the proposed plans and scrutinise them to ensure methodological rigour. We never endorse a company's plans but focus on explaining outcomes of different options and approaches.

What specific data and trial design uncertainties do you see being brought forward repeatedly in scientific advice sessions? Is that in specific indications?

Whilst there are some examples of innovative trial designs that are of interest, overall our experience is that the quality of clinical trials is going down, and this is very worrying. The regulatory bar for approval is falling lower and we see more and more single arm trials, surrogate endpoints, trials stopped for efficacy reasons, etc. This is in addition to the just generally poor scientific rigour of many clinical trials. There are clear situations where randomised trials are not possible and where powering on overall survival is not feasible, but unfortunately there is a strong push for suboptimal trial designs and trial durations. This is a potentially dangerous practice which can put patients at risk of being exposed to products licensed on a very weak evidence base. For the manufacturers, it is a disadvantage as well, because once they bring their products to NICE with weak clinical evidence, they are forced to make much greater discounts to mitigate uncertainty. The latter is a massive problem in oncology but for other indications we see many instances of inadequate quality of life data collection, and inability to define treatment stopping rules and to appropriately select clinically relevant endpoints. There is currently a lot of effort going into the design of new patient-reported outcomes (PRO) instruments but validation of these is a problem. We also receive many questions about real-world evidence (RWE) and unfortunately there is a strong move to start using RWE in place of, rather than in addition to, properly collected and analysed data which are needed to establish relative clinical effectiveness of the intervention. RWE often produces more noise than clinically relevant information.

We are aware of the new EMA/EUnetHTA advice scheme called Post-Licensing Efficacy Generation (PLEG), focusing specifically on post-launch data generation. How much is the post-launch development of data an issue for the scientific advice delivered by NICE?

Dr. Osipenko joined the National Institute for Health and Care Excellence (NICE) in 2012 and has been leading the Scientific Advice (SA) service since 2014. She works closely with EMA, MHRA, and European HTA agencies. She chairs most of the national, international, and parallel scientific advice meetings for medical device and pharmaceutical product developers. She also signs off key deliverables produced by NICE SA and is responsible for the team's operations and performance. Dr. Osipenko's research interests focus on methodologies of trial design, evidence generation for economic modelling, and policy implications of HTA.

Sometimes we receive questions on post-authorisation data collection and I wish these questions accompanied every project. With an increase in CMA (conditional marketing authorisation), PLEG becomes more and more favoured. Unfortunately, PLEG is poorly enforced by the regulators and many companies either do not produce these data or present them with significant delays. These data are crucial, but often, even when available, they rarely prompt the initial decision review or translate to changes in clinical practice. It is also important to remember that the quality of the PLEG data is paramount but rarely do we see PLEG data being generated up to required scientific standards. Reforms are needed at the regulatory level and in the HTA field to enforce PLEG, ensure its quality, and then to act on its results.

What is the role of Advanced Therapy Medicines Products (ATMPs) in scientific advice? Do you see these technologies being increasingly the subject of scientific advice submissions? Are the questions in scientific/rationale for seeking scientific advice somewhat different? If so how? Can you explain?

We've had a significant increase in requests for scientific advice on ATMPs. To date we have given advice on 19 products. Usually such projects are very interesting and they bring along many methodological questions and issues that neither regulators or HTA agencies have seen before. At NICE, we commend companies coming to us to discuss their plans and enhance learning of the changing drug development landscape for all stakeholders. However, frequently companies think that because they are developing ATMPs this gives them an option of disregarding methodology of clinical trial conduct and proper evidence generation. While for many indications, where ATMPs are currently being developed, the populations are small and trials are challenging, scientific rigour is of utmost importance. These products are likely to carry a hefty price tag and risky side effects. The developers of these products must produce clinical evidence according to the highest standards of clinical research. ■

Advice requests on ATMPs pose questions on managed access agreements. This is a welcome discussion which we encourage companies to have before appraisal through NICE's Office for Market Access.

She holds an Honorary Fellow post at the University of Warwick Medical School, Senior Visiting Fellow post at London School of Economics, and represents NICE as a Chief Analyst at the Department of Health Appraisal Alignment Working Group. She is also a reviewer of a number of academic journals.

After completing a PhD in Systems Engineering, Dr. Osipenko was Senior Research Fellow at the University of Warwick and between 2010 and 2012, she worked as Principal Economist at a public sector consultancy, Optimity Matrix.