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Dr Choong May Ling, Mimi, CEO of Singaporeâ??s Health Sciences Authority (HSA), one of the leading regulatory bodies in the Asia-Pacific region, outlines the impact of Singaporeâ??s status as a life sciences hub, the launch of novel priority review avenues, and how the authority is adjusting to the new industry paradigm that data and AI is helping create.

Could you begin, by giving us a quick introduction to the Health Sciences Authority (HSA)â??s mandate within Singapore?

The Health Sciences Authority (HSA) is a statutory board formed under Singaporeâ??s Ministry of Health on 1 April 2001. HSA applies medical, pharmaceutical and scientific expertise through its three professional groups â?? Health Products Regulation, Blood Services and Applied Sciences, to protect and advance national health and safety.

HSA is a multidisciplinary authority. It serves as the national regulator for health products, ensuring they are wisely regulated to meet standards of safety, quality and efficacy. As the national blood service, it is responsible for providing a safe and adequate blood supply for all patients in Singapore. It also applies specialised scientific, forensic, investigative and analytical capabilities in serving the administration of justice and public health.

Singapore stands as one of the most important pharma/biopharma and medical devices hubs both regionally and globally. What impact does this hub status have for HSA as a regulator?

As a small country, we are fortunate to be well located to reach markets in the region and beyond. Singaporeâ??s regional and global connectivity, pro-business environment and strong talent pool, coupled with its well-regarded healthcare infrastructure, have created a strong value proposition to attract and anchor healthcare and life sciences companies in Singapore. As a regulator, we are seeing more companies keen to set up and license pharma and MD manufacturing plants and apply for marketing authorisation for their health products here.

Collaboration has always been critical, and our connectivity has enabled us to build strong partnerships to achieve mutually beneficial outcomes. With the rapid growth in scientific and technological developments, it is important to learn from each other to build new capabilities, share and transfer new knowledge, and wherever possible, collaborate on common projects to increase the efficiency and effectiveness of global regulatory work.

Over the years, we have partnered with overseas regulators to exchange information in areas such as the evaluation of therapeutic products and safety assessments for novel ingredients for complementary health products. Such partnerships increase the efficiency and robustness of the evaluation process, enabling safe, high quality and effective health products to reach the market faster. Together with our partners, we continue to monitor the safety profiles of these products and promptly pick up safety signals to protect public health and safety. An example of this would be how we have been working proactively with our overseas counterparts to manage the risk of unexpected nitrosamine contamination in the manufacture of losartan medicines. Open sharing of information and investigation findings enabled us to expedite testing and promptly recall affected medicines from the market.

We also participate in many international and regional networks and workgroups to stay ahead of latest developments and steer discussions for greater standardisation and alignment among regulatory bodies. Some of these include the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, International Medical Device Regulators Forum, International Coalition of Medicines Regulatory Authorities, Asian Forensic Sciences Network, and the ASEAN Product Working Group for Traditional Medicines and Health Supplements.

Regulators are increasingly being scrutinized for their performance and how diligently they can process market approvals with solid scientific evidence. How would you characterise HSAâ??s performance over the last few years?

Despite our small market, HSA has done well in facilitating the entry of critical, as well as novel, therapeutics and medical devices into Singapore. We have taken a stakeholder-centric, fit-for-purpose and least burdensome regulatory approach. Such an approach enables us to achieve regulatory efficiency and enable patientsâ?? timely access to important health products while ensuring regulatory rigour. We constantly review our existing regulatory frameworks and engage industry stakeholders for feedback to ensure that our regulations remain relevant. We also work and closely consult industry to develop new regulatory frameworks for new product categories, so that we are well positioned when such products come to market.

For example, in 2017, we implemented priority review routes to enhance our efforts on reviewing new and emerging medical devices designed and validated for unmet clinical needs in any of five

focused healthcare areas of cancer, diabetes, ophthalmic, cardiovascular or infectious diseases. This enabled faster registration and market entry of these products. GASTROClear, a first-in-world test developed in Singapore for early detection of gastric cancer, was one such product that benefitted from this priority review route in 2019.

We also expedited the review and approval of Dengvaxia, the first dengue vaccine in the world, within six months. We were the sole regulator recommending sero-testing to identify patients who had never had a previous dengue infection, as they would be at higher risk of severe dengue if vaccinated. Eighteen months post-approval, new data from the company confirmed this assessment, and sero-testing was subsequently recommended by the company in all countries where the vaccine had been approved.

Are there metrics you are intending to work on to ensure that HSA remains fit for purpose?

As part of our efforts to better serve our stakeholders and ensure we remain fit-for-purpose, relevant and effective in discharging our responsibilities, we developed a comprehensive Transformation Roadmap in 2019. This is organised into four broad pillars that focus on stakeholder-centric products and services, process transformation, strong partnerships and people transformation. We also have key workgroups that cover the areas of digitalisation, data analytics, behavioural insights, and future sensing to support our transformation initiatives to bring HSA forward.

What are the changes within science, technology and society that strike you the most and which are the ones that you feel will have the most impact on the mission of HSA?

Cell, tissue and gene therapy, precision medicine and pharmacogenomics are a few emerging areas to watch closely in the next few years. Rapid advancements in these areas have led to the development of more novel and innovative health products in the market. To support these innovations, we engage the companies at the product development stage to provide early scientific and regulatory advice. We also developed guidances to provide clarity to the developers on what is necessary to meet the regulatory requirements of the final products.

In the area of cell, tissue and gene therapy, we recently implemented the regulations for Cell, Tissue and Gene Therapy products (CTGTP) in Singapore. This significant milestone was years in the making â?? from the early days of policy conceptualisation and design, to public consultation of all relevant stakeholders, including researchers, industry, and healthcare professionals, and eventual refinement and drafting of the regulations. This new class of health products comprises stem cells, tissues and genetically modified organisms, which can be engineered to grow healthy and functional tissues to reconstruct, regenerate or repair damaged tissues or organs; or new genes introduced into the body to treat or cure diseases. It is an area of therapy that is developing rapidly and has the potential to transform the current practice of medicine and offer potential cures for chronic and debilitating diseases.

â??Breakthrough designationsâ?•, â??fast-track and conditional approvalsâ?•, â??orphan drug designationsâ?• and special status for â??regenerative medicinesâ?• are key parts of regulatorsâ?? toolboxes today to ensure that the latest innovations reach patients in a safe and efficacious manner. Are these tools part of the HSA reviewing process?

We recognise the importance of timely access to beneficial and critical health products. Aside from providing early scientific regulatory advice to stakeholders, we work closely with industry partners and research institutions and keep a close tab on emerging technologies and trends to help us in developing policies and guidance documents required for the industry.

With the ongoing COVID-19 pandemic, it is even more crucial to ensure access to critical health products that have been evaluated to meet the stipulated safety, efficacy and quality standards.

To mitigate the potential shortage of medical equipment, we expedited the approval of medical devices such as diagnostic test kits and ventilators via a new provisional authorisation route, which is based on a risk-calibrated review process to ensure essential safety and performance requirements are met. The healthcare system benefitted as we had sufficient diagnostic tests, even at the outset of the pandemic, and all were evaluated by HSA.

We also facilitated the rising import of surgical masks, particulate respirators and protective gear to ensure sufficient supply for healthcare workers and the general public. As there were many new industry players in this field, we provided scientific and regulatory advice to facilitate their development, testing and manufacturing. In addition, we conducted virtual inspections of local mask manufacturing sites to ensure they met good manufacturing and distributing standards.

In June 2020, we granted conditional approval for remdesivir in the treatment of adult patients with COVID-19 infection. The review of remdesivir was expedited given the urgent public health need. However, even before that, while new data from trials done in other countries was just emerging, we had facilitated the early access of remdesivir in clinical trials to COVID-19 patients in Singapore since March 2020. Singapore was among the earliest countries to grant an approval for remdesivir.

In December 2020, we introduced the Pandemic Special Access Route (PSAR) to facilitate early access to critical novel vaccines, medicines and medical devices during a pandemic, such as the current COVID-19 pandemic. Using PSAR, our evaluators are able to start reviewing the data of new vaccines, medicines and medical devices from the early stages of clinical studies, as and when real-time data is submitted by companies on a â??rollingâ?•, or staggered basis, instead of waiting for the full data set to be submitted before starting our evaluation. This gives us more time to review the submitted data while companies continue with further clinical trials and development concurrently. Such regulatory agility and flexibility allow for speedier development and evaluation. To-date, interim authorisation under PSAR was granted for Pfizer-BioNTech and Moderna COVID-19 vaccines in Dec 2020 and Feb 2021 respectively to support Singaporeâ??s fight against the COVID-19 pandemic. We were the first Asian country to authorise these vaccines.

Where is HSA well equipped and which novelties would you like to develop moving forward?

The diversity of functions we have as an organisation is our strength. Aside from regulating health products (medicines and medical devices), we have the national blood service, and the Applied Sciences Group (ASG), which covers forensic medicine, forensic science and analytical science. Having all these under one roof creates synergy that enables us to do our work better. Instead of looking for expertise outside when we need it, the regulatory group can find help within, such as in terms of technical or scientific advice.

This synergy was demonstrated when our Health Products Regulation Group (HPRG) and ASG worked closely together to promptly develop a system to identify and remove products contaminated with unacceptable levels of nitrosamine impurities from the market. As there was no test method available internationally to analyse for nitrosamine contamination, ASG proceeded to develop a new

testing methodology. We became the first regulator in the world to recall ranitidine and metformin products due to nitrosamine contamination in September and December 2019 respectively. We also worked closely with the Ministry of Health and the public healthcare family to coordinate the recalls, so that the recall and medicines exchange process would be smooth for our patients. Our strong ties and close working relationships ensured that the switch to alternative medicines for affected patients was smooth and seamless.

Our line of work also attracts individuals who are highly committed to our mission to secure national health and safety. Our staff are our greatest asset and are key to ensuring we continue to work towards HSAâ??s vision. We will carry on building our passionate and capable staff, and focus on retaining and upskilling them.

Data and AI are the current hot topics in the healthcare and life sciences field, with many claiming that they are going to be total game-changers for the industry. What is your point of view?

We are keeping a keen eye on smart technologies and digital skills as we look out for ways to improve processes and be more efficient. We are exploring artificial intelligence (AI), natural language processing, robotic process automation, digitalising and automating routine work processes across all work areas for greater efficiency. As a scientific organisation, it is essential that we are forward-looking, maintain a spirit of innovation, keep up-to-date and be curious about how we can leverage these technologies and skills in our various areas of work.

AI is a key enabler for healthcare innovation. It can analyse large amounts of health data to derive meaningful insights for improving medical care including diagnosis, disease management and treatment monitoring. Currently, one of the most common use of AI is in improving diagnosis from images generated using various imaging modalities (e.g. CT scans, MRI, X-ray images).

In 2017, we set up a pre-market consultation pathway where researchers and innovators could seek our scientific and regulatory advice in the early phases of medical device development. This facilitated regulatory compliance and enabled faster access to safe innovations for patients and healthcare providers. Over 40 percent of the consultation applications were for software and AI medical devices. Such medical devices, especially those that function by themselves without any hardware equipment (i.e. standalone software), have unique challenges. They undergo frequent upgrades and may need to continuously learn and change post deployment. Therefore, a fit-for-purpose regulatory approach that includes more process-based controls on top of the traditional product controls is necessary to be able to regulate these products effectively and efficiently.

In April 2020, we published comprehensive regulatory guidelines specifically for innovators of software medical devices. Aside from providing clarity on our regulatory requirements and licensing, it covered risk management topics such as cybersecurity, â??continual learningâ?• algorithms, as well as additional process controls and risks that should be carefully considered in designing and validating these medical devices. To date, we have evaluated and registered over 30 AI-based medical devices with a significant number of them being first-in-world approvals, including Selena+ deep learning system for eye screening, See-Mode Augmented Vascular Analysis software and Kronikare Wound Scanner. After receiving our scientific and regulatory advice during consultation and obtaining HSA regulatory approval, many of these devices have successfully gone on to receive regulatory approvals in other markets (e.g. EU, Australia, USA).

We are also collaborating with other local agencies to identify and monitor key adverse events in electronic healthcare records to make post-market drug safety surveillance more efficient and

informative. This is a step forward towards developing automated tools for detecting adverse drug reaction episodes.

Singapore is a member of the ACCESS Consortium along with Australia, Canada, Switzerland, and now the UK. What positive aspects would you like to highlight about participation in such an alliance?

Over the years, HSA has worked closely with the ACCESS Consortium. Through work-sharing initiatives, we have successfully sped up the approval of diagnostics, therapeutics and vaccines. HSA has reviewed and approved various therapeutic products through such work-sharing, and continues to receive a number of expressions of interest from companies intending to file simultaneously in Singapore and partner agencies through this collaboration pathway.

HSA is a relatively young agency, and the publication of the *Singapore Healthcare & Life Sciences Review 2021* will coincide with its 20th anniversary. What message would you like to share with other regulators and industry sponsors globally?

It takes global collective effort among industry and regulatory bodies to ensure that healthcare institutions, patients and the public have access to safe, good quality, effective and timely health products. Given our current dynamic operating environment and rapid scientific and technological advances, it is even more important now for regulatory bodies and the industry to work collaboratively. By strengthening trust and communications between different stakeholders, we can all work closely together to bring much needed health products to the market efficiently and effectively to achieve better health outcomes for all.

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