The Health Products Regulation Group ensures that health products in Singapore meet internationally benchmarked standards of safety, efficacy and quality. We have implemented a robust and risk-based framework that enables safe and timely access to health products, while taking into account industry needs for greater transparency and flexibility.

Faced with the ongoing evolution of the regulatory landscape, we strive to remain at the forefront of global trends and technological advances with regard to drugs and devices. We are constantly looking to redefine our processes and helping to define new regulatory frameworks, as well as pursuing new areas of research. In this way, our growing capabilities enable us to face the challenges of health product regulations.

Through our strong partnerships with local and overseas agencies, we strive to develop sound regulatory policies that could make a positive impact on public health and safety both in Singapore and beyond our borders. By leveraging our strengths to deepen integration across different disciplines, we will continue to sharpen our operating synergies to translate our strategic vision into tangible outcomes for our stakeholders.
TOWARDS SMARTER REGULATION

The past year saw new requirements under the Health Products Act (HPA) coming into effect for medical devices as part of the phased regulatory roll-out. The HPA, which was passed in 2007, serves to amalgamate existing controls under the Medicines Act and Poisons Act, as well as regulates new product groups not covered under the earlier legislation.

Medical devices were the first group of health products to be regulated under the HPA, followed by cosmetic products, with the implementation of the ASEAN Cosmetic Directive in 2008.

Product registration for Class C and Class D medical devices and dealer licensing for all medical devices were implemented in August 2010. Medical device dealers will be required to comply with the Quality Management System criteria for manufacturing and importing or supplying products. A transition list for Class C and Class D medical devices was published to allow the continued supply of products that met prescribed criteria in order to avoid disrupting patient needs. We further implemented six authorisation routes to allow novel and unregistered high-risk medical devices to be imported and supplied locally.

We are currently preparing for the product registration of Class A and Class B medical devices, which we are aiming to roll out in January 2012. The full legislative controls for medical devices will be in place with the completion of this final phase, with a total of over 15,000 products expected to be registered in Singapore. On-site regulatory audits of medical device dealers will also be carried out under the Good Distribution Practice for Medical Devices inspection scheme.

In the year ahead, we will be working to transfer the regulatory controls for the various product groups related to manufacturers, importers and dealers from the Medicines Act to the Health Products Act.

To help ensure a smooth transition for industry stakeholders in light of recent and upcoming developments, we organised briefings, focus group sessions and workshops to keep them well informed and engaged regarding the various regulatory changes taking place. A revised Guidance on Medicinal Product Registration was implemented on 1 April 2011 to reflect HSA’s current regulatory processes following industry consultations on the drafted guidance in October 2010. In August 2010, we also revised the HSA Guidance Notes on Good Distribution Practice in response to industry feedback seeking greater clarity regarding the guidelines for the management and control of cold chain products.
Elevating Safety Standards

A new verification evaluation route was introduced on 1 January 2011 for the registration of Generic Drug Applications (GDAs) to facilitate market entry of generic products that have been evaluated and approved by at least one of HSA’s reference agencies. This new route offers a shorter processing time and facilitates public access to generic medicines.

As a measure of enhancing public safety and meeting the growing needs of the public for wanting to know more about medicinal products, package inserts for new medicinal products will now require listing of the product’s non-active ingredients and/or materials with allergenic potential.

Looking ahead, other key priorities include the implementing of a risk-based approach to regulate new therapeutic products. We also aim to strengthen the enforcement action taken against errant dealers while continuing to engage our stakeholders with regard to the development of our regulatory framework.

Work is also currently underway to consolidate existing regulations for Chinese Proprietary Medicines (CPMs), traditional medicines and health supplements under the Complementary Health Products regulatory framework. We have implemented new initiatives related to CPMs and health supplements, such as allowing the use of vitamin K in health supplements under stipulated conditions and offering exemptions from CPM product listing requirements for locally manufactured CPMs produced solely for export.

We are also in consultation with the Ministry of Health (MOH) to develop a regulatory framework for the regulation of Cell and Tissue Therapies (CTTs) for both high-risk and lower-risk CTT products.

The existing regulatory framework for clinical trials is being revised and will be introduced in 2012 as the Health Products (Clinical Trials) Regulations. We conducted focus group consultation sessions with industry players and other stakeholders as part of the review process. Several new initiatives will be introduced to reduce the burden of regulatory processes without compromising the safety standards for conducting clinical trials.
QUICK DETECTION, PROMPT PREVENTION

Post-marketing surveillance remains a significant part of our ongoing efforts to ensure that the safety and efficacy of health products are optimised for patients and the general public. Singapore was ranked 2nd, up six spots from the 8th position in 2009, in a ranking of Adverse Drug Reaction (ADR) report submissions by the World Health Organization (WHO) Collaborating Centre for International Drug Monitoring at the Uppsala Monitoring Centre (UMC) in Sweden. In addition to the active contributions by our healthcare professionals to ADR reporting, the Critical Medical Information Store (CMIS) system, an electronic repository of patients’ medical records and drug allergies, has also significantly contributed to the high reporting rate.

In April 2010, we significantly enhanced our Product Quality Surveillance (PQS) initiatives to include involvement from pre-market and post-market groups in planning the selection of products for sampling, determining the class and level of recalls, and deciding upon the regulatory actions to be taken.

We developed a local risk management programme with the product license holder for restricted use of products containing rosiglitazone (Avandia®, Avandamet®). This step was taken in light of international concerns regarding cardiovascular safety issues associated with the use of these products.

Public Safety: Our Top Priority

In consultation with the MOH and its Expert Committee on Immunisation, we conducted an in-depth benefit-risk assessment on rotavirus vaccines in light of the discovery of DNA fragments of porcine circovirus 1 (PCV1) in Rotarix® and PCV1 and porcine circovirus 2 (PCV2) DNA fragments in Rotateq®. This assessment resulted in the issuance of a Dear Healthcare Professional Letter regarding recommendations on the use of rotavirus vaccines, as well as two product safety updates to provide information on the findings and outcome of our review.

We also conducted risk assessments for nine unregistered products arising from PQS and recommended regulatory actions that included retail level recalls and the issuance of press releases.

Several precautionary steps were taken over the course of the year to minimise consumers’ access to potentially harmful products. A total of 214 risk assessments on health products were carried out during the year, which led to regulatory changes such as the strengthening of package inserts; the issuance of Dear Healthcare Professional Letters and press releases; and the publication of ADR News Bulletin articles. The sales and product licences of sibutramine products (e.g. Ectiva®, Reductil®, Reduxade® and Slenfig®) were suspended due to an unfavourable benefit-to-risk ratio.
During the year, we took steps to strengthen our risk communication for medical devices through various communication channels. This included the issuance of a press release for the recall of Johnson & Johnson Acuvue contact lenses; a Dear Healthcare Professional Letter regarding Baxter Colleague Infusion Pumps; and an article in the ADR News Bulletin announcing the recall of the DePuy ASR™ Hip Resurfacing System and DePuy ASR™ XL Acetabular.

Several illegal traditional medicines found to be adulterated by Western medicinal ingredients were detected and withdrawn from the market. These included “Te Xiao Huo Luo Jing” [特效活络金], “Jianbu HuQian Wan” [健步虎潜丸] and “HorKut Chooi Foong Hor Lok Tan” [虎骨追风活络丹].

Other recalled items included Beijing 101 hair growth products detected to contain minoxidil, and non-compliant nail polish products that contained benzene, dibutyl phthalate or diethylhexyl phthalate, which are prohibited ingredients under the ASEAN Cosmetic Directive. Following the detection of B Cepacia contamination in Oral Guard Antiseptic-Antiplaque Mouthwash and Care Wipes, two other mouthwash products found to be similarly contaminated were also taken off the market.

Due to the increased popularity of Traditional Chinese Medicine (TCM), it is important to enhance our vigilance over traditional medicines in Singapore. As part of our ongoing efforts, we will continue to work with TCM practitioners to review the Adverse Event (AE) reports that we receive and to increase awareness of AE reporting. We are working in collaboration with our healthcare colleagues in the hospitals to enhance the safety monitoring of AEs related to TCM.

Maximising the quality, safety and efficacy of vaccines is recognised as an essential component of a successful immunisation programme. HSA is collaborating with KK Women’s and Children’s Hospital (KKH) on a project known as HK-InSpire (HSA-KKH Inpatient Surveillance of Post-Immunisation Reactions). It was developed to monitor pandemic influenza vaccines, with KKH serving as a sentinel site for intensive inpatient surveillance for Vaccine Adverse Events (VAEs).
The project was expanded in March 2010 to study VAEs following childhood immunisations. From the period November 2009 to December 2010, KKH has screened 15,458 children for VAEs and 636 cases with suspected VAEs were further evaluated. Of these, 93 were deemed to be serious cases.

As medical AE reporting has the potential to improve patient safety, we have also conducted outreach programmes to encourage healthcare professionals to submit AE reports for health products. As part of these efforts, we are also developing plans to establish a common vigilance function to strengthen post-marketing surveillance of health products in Singapore. We aim to coordinate follow-up actions to address identified risks to the public by enabling vigilance information to be shared across departments and allowing coordinated operations related to post-market surveillance activities to be carried out.

**Venturing into New Ground**

We further expanded our capabilities in pharmacogenomics through training workshops for staff as well as research collaborations with hospitals and institutions in the area of serious skin reactions and drug-induced liver injuries. Review of pharmacogenomic data was incorporated as part of risk assessments for certain drugs. Important associations such as irinotecan-induced severe neutropenia in individuals carrying certain UGT1A1 polymorphisms were communicated to healthcare professionals through regulatory label changes and communication tools.

New research in the area of pharmacoeconomics was also initiated to critically evaluate the cost and benefit of various strategies for incorporating pharmacogenetic knowledge in clinical practice aimed at reducing the incidence of ADRs. Collaborations have begun with bioinformatic scientists and statisticians to develop tools to measure the extent of differentiation in genes important for the mechanism of action, metabolism and transport of drugs among the three major ethnic groups in Singapore and populations in the International HapMap project. This will assist regulators in understanding the potential for an altered benefit-risk profile when examining clinical trial data from populations that differ from those in Singapore.

Looking ahead, we will expand our pharmacogenomics research capacity through various initiatives. These include establishing the necessary infrastructure and frameworks to reduce the risk of ADRs through the identification and validation of genetic associations. Ultimately, we aim to translate research findings into clinical practice in order to benefit patients.
TAKING A FIRM STANCE

We stepped up our enforcement efforts this year against syndicates involved in the illegal sale of codeine cough mixtures. Some of these enforcement operations and raids were conducted jointly with the Singapore Police Force, Singapore Customs, and the Immigration and Checkpoints Authority of Singapore.

Due to the borderless nature of the Internet and the ease of purchasing illegal health products online, we are constantly on the lookout for illegal health products in cyberspace. In October 2010, we represented Singapore in Operation Pangea III, an effort involving drug regulatory authorities from 44 countries. Besides increasing public awareness of the risks of buying health products from unregulated websites, the operation sought to close down illegal websites and take action against offenders. About 5,000 units of illegal items including hair loss products, slimming drugs and contraceptives were seized during the operation.

Our fight against illegal health products involves collaboration on a global scale with various international partners and agencies. We were appointed as one of six Vice-Chairs in the WHO Working Group of Member States on Substandard/Spurious/Falsely-Labelled/Falsified/Counterfeit Medical Products, which examined WHO’s role in the prevention and control of medical products of compromised quality and safety.

Going forward, we will strengthen our proactive enforcement measures by creating a framework for processing intelligence information using different types of analysis from tactical, operational and strategic perspectives. To tackle the rise in online distribution of health products, we will also be enhancing our capacity and capabilities in carrying out cyber-surveillance and cyber-crime investigations.

Strengthening Tobacco Control

In support of the National Tobacco Control Programme to curb underage smoking, we collaborated with the Health Promotion Board (HPB) to curb the supply and demand of tobacco products among youths. This included increasing the composition fine for underage smokers and penalties on errant retailers and licensees in December 2010. In addition, together with the policy makers at the MOH and HPB, we enhanced and renamed the parent Act to the Tobacco (Control of Advertisements and Sale) Act. This revised Act took effect on 1 September 2010.

We have ongoing initiatives to leverage community involvement and trade engagement to encourage compliance with tobacco control measures. These include setting up a tobacco licensing consultative panel in April 2011 to seek advice on contentious tobacco licence applications by retailers selling health-related or youth-centric products. We will also be holding trade briefings to ensure that retailers understand the new regulatory measures that will be rolled out over the next two years.
Recognising the competitive and challenging business environment faced by industry players, we strive to provide a positive experience by refining our policies and practices to meet business needs while ensuring that no sacrifices are made regarding health and safety. With this in mind, we have established a Service Management Office staffed by a cross-functional team to drive service-related initiatives and activities aimed at enhancing communication with industry and streamlining query-handling processes.

Maintaining an open communication channel with our stakeholders and industry partners has helped to facilitate the understanding of existing and upcoming regulatory requirements. Over the course of the year, we held numerous meetings, focus group discussions and dialogues to explain new regulatory policies and seek feedback on upcoming plans.

These included the inaugural Health Products Regulation Group (HPRG) Joint Regulatory Workshop held from 17 to 20 January 2011 for 700 industry and HSA participants, covering a wide range of topics including clinical practice, drug registration updates, analysis of Good Manufacturing Practice (GMP) inspection findings and GMP documentation. In addition, dialogue sessions were held with health product dealers to discuss new pro-enterprise initiatives and enhancements.

We keep industry stakeholders updated on the regulatory and administrative changes and the availability of services through our industry newsletter, HSA Connects. To complement this, we organised training sessions during the year to familiarise businesses with regulatory requirements and implementation timelines. These sessions helped industry members to discuss and clarify their doubts regarding product registration and regulatory processes, reducing uncertainty about the steps they need to take for product submissions.
Smother Transactions

Besides improving communication with industry, we also established an integrated product enquiry handling workflow. Enquiry forms from the various HSA branches were consolidated into one form to streamline the query handling process.

To improve our customers’ experience when transacting with us electronically, we have made enhancements to our online licensing system, PRISM, by implementing new application modules for the following:

- Licence to Import Controlled Drugs
- Licence to Export Controlled Drugs
- Licence to Export Psychotropic Substances
- Authorisation to Import Psychotropic Substances
- Authorisation to Import Restricted Substances

Under the enhanced system, users can also submit up to three major variation applications at any one time. Other improvements include the ability to view contraindications of herbal ingredients used in CPMs and the updated Anatomical Therapeutic Chemical Code in registered medicinal products.

External stakeholders and the public can also stay abreast of medical developments, such as information on approved new medicinal products, through the HSA website.
We brought our expertise in health product regulation to a global level throughout the year by sharing our insights and lessons learnt with international colleagues and stakeholders. Our participation in various meetings, working groups and committees provided valuable opportunities for the exchange of resources and knowledge.

We not only represented Singapore in the WHO Copenhagen Assessment Meetings No. 55 and 56, and contributed in the evaluation of Chemistry, Manufacturing and Controls, as a member of the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S), we also aim to share our expertise in GMP standards by cooperating and networking with international organisations. HSA is currently an Alternate Member in the PIC/S Executive Bureau, which provides us with a platform for creating a significant impact at the global level. We will also be co-hosting the PIC/S Expert Circle on Active Pharmaceutical Ingredients in Singapore in October 2011.

Besides being involved in PIC/S meetings and expert circles, we also chaired the ASEAN Sectoral Mutual Recognition Agreement for GMP Inspection. In June 2010, we were appointed Chair of the ASEAN Cosmetic Scientific Body for a term of three years. In August 2010, we were also appointed Chair of the ASEAN Traditional Medicines Health Supplements Product Working Group for three years.

Other achievements include our participation in the 8th Standing Committee Meeting and the 4th Symposium of the Western Pacific Regional Forum for the Harmonisation of Herbal Medicines. The presentations included updates on the surveillance of herbal medicines and Complementary Health Products in Singapore.
Together with the WHO and UMC, we hosted a 5-day Basic Pharmacovigilance Training Course from 31 May to 4 June 2010. The purpose of the course was to equip participants from ASEAN countries with the necessary skills to strengthen pharmacovigilance capabilities in their respective countries. The event featured local and international pharmacovigilance experts and offered a curriculum that included the management of traditional medicines and ADR reporting.

We have also organised a 3-day training workshop on Bioequivalence (BE) Trial Inspection in May 2010, which was attended by regulators from Hong Kong, Indonesia, Malaysia and Saudi Arabia. An experienced inspector from AFSSAPS (Agence française de sécurité sanitaire des produits de santé), the French Agency for the Safety of Health Products, shared the relevant knowledge to ensure that BE studies are conducted in compliance with the International Conference on Harmonisation (ICH)’s Good Clinical Practice and Good Laboratory Practice standards.

From 27 September to 1 October 2010, we also organised the inaugural annual basic training in Health Products Regulation in Singapore for overseas regulators, which was attended by regulators from Korea, Malaysia, Macau, Qatar and Saudi Arabia. We will continue to share and learn practices with other regulators.

We also hosted study visits throughout the year for delegates from regulatory authorities in Brunei, India, Macau, Hong Kong and China, introducing them to the roles and responsibilities of HSA, as well as the regulatory controls undertaken to ensure the supply of safe health products. These initiatives promote the exchange of information and help to identify future opportunities for collaboration.

We recognise that the challenges facing regulatory authorities are best addressed through joint efforts, rather than by individual organisations working in isolation. We therefore value opportunities that allow us to learn from others and apply international best practices in our regulatory processes.

We co-hosted the 14th International Conference of Drug Regulatory Authorities (ICDRA) held from 30 November to 3 December 2010 together with the WHO. The year marked the 30th anniversary since the inauguration of this important gathering, and we were honoured to receive close to 400 members from over 90 countries, the highest rate of participation for the ICDRA to date. We were also very encouraged by the positive feedback received from the WHO and participants in the 4-day programme, which provided regulators the opportunity to share and discuss current and topical issues of global concern. These included access to quality medicines, counterfeit medicines, pharmacovigilance, clinical trials and lessons learned from the H1N1 pandemic.
Our ongoing efforts to broaden our global network and strengthen cooperation with international regulators included the signing of several Memoranda of Understanding (MOUs) during the year with the following entities:

- Pharmaceutical and Food Safety Bureau of the Ministry of Health, Labour and Welfare and Pharmaceuticals and Medical Devices Agency, Japan
- Korea Food and Drug Administration, Republic of Korea
- Irish Medicines Board, Ireland
- New Zealand Medicines and Medical Devices Safety Authority
- Paul-Ehrlich Institute, Germany

These MOUs strengthen our strategic alliances and create opportunities for us to leverage the expertise of other authorities to contribute to the effectiveness of our regulatory decision-making.

Our work-sharing consortium with four agencies – Health Canada, Australia’s Therapeutic Goods Administration, Swissmedic, and New Zealand’s Medsafe – was strengthened as we tackled challenges in the field of GMP inspections. Through this consortium, we participated in three joint audits with our regulatory partners.
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<tr>
<th>Key Statistics</th>
<th>Number</th>
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<tbody>
<tr>
<td>New Product Licences Issued</td>
<td>161</td>
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<tr>
<td>Registered Medicinal Products</td>
<td>5,358</td>
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<tr>
<td>Medical Device Product Registration Applications (Class A, B, C &amp; D)</td>
<td>2,860</td>
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<tr>
<td>Medical Device Product Registration Applications by Product Models (Class A, B, C &amp; D)</td>
<td>3,659</td>
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<td>Medical Device Product Models Approved</td>
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<td>Approved Products on the Singapore Medical Device Register (SMDR)</td>
<td>6,570</td>
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<td>Chinese Proprietary Medicines Listed</td>
<td>9,066</td>
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<td>Cosmetic Products Notified under the ASEAN Cosmetic Directive (ACD)</td>
<td>144,900</td>
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<td>Clinical Trials Certificates Granted</td>
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<td>Medical Advertisement Permits Issued</td>
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<td>Site Audits Conducted for Good Manufacturing &amp; Good Distribution Practices</td>
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<td>Premises, Dealers and Importers &amp; Exporters of Health Products Licensed/Certified</td>
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<td>Authorisation Letters for Travellers Bringing Personal Medication into Singapore</td>
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<td>Spontaneous Adverse Drug Reaction Reports Received</td>
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<tr>
<td>Units (tablets/capsules/liquids/creams) Seized</td>
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<td>Tobacco Retail Outlets Licensed</td>
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<td>Underage Youth Smokers Caught</td>
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