HEALTH PRODUCTS REGULATION GROUP

ENHANCING REGULATORY AGILITY

We adopt a forward-looking mindset towards developing regulations, ensuring flexibility and adaptability to safeguard public health and safety.

COVID-19 RELATED WORK

We do our part to fight COVID-19 through regulatory vigilance.

CESSATION OF PANDEMIC SPECIAL ACCESS ROUTE (PSAR)

With the COVID-19 situation in Singapore having moved towards an endemic norm, HSA ceased receiving applications for interim authorisation of vaccines under PSAR in March 2023.

Accordingly, six PSAR interim authorisations for vaccines and therapeutics, including Comirnaty, Spikevax, Nuvaxovid and Paxlovid were transitioned to full registrations.

Additionally, in response to the continued evolution of COVID-19 and the emergence of new variants, HSA introduced a new minor variation (MIV) submission category. This category facilitates the updating of COVID-19 vaccines to target new virus strains. COVID-19 vaccines that fell under this category included the updated Comirnaty and Spikevax vaccines, each comprising a monovalent component that corresponds to the Omicron XBB.1.5 variant. These were authorised in September 2023 and October 2023 respectively.

ENHANCED SAFETY MONITORING OF COVID-19 VACCINES

Since the onset of the pandemic, we have enhanced our safety surveillance of COVID-19 vaccines, using real-world data to detect and validate potential safety signals.

These included analysing for the risk of myocarditis and pericarditis, as well as eight adverse events of special interest for potential safety signals. These were subsequently published in peer-reviewed scientific journals, such as Vaccine: X and Singapore Medical Journal, underscoring the recognition and credibility of our work within the scientific community.

We also shared our work at the following platforms:

September 2023
Singapore Pharmacy Congress, Singapore

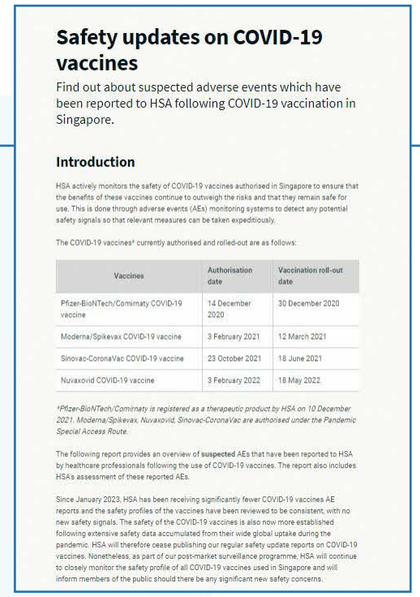
October 2023
15th Asian Conference on Pharmacoepidemiology, India

November 2023
International Society of Pharmacovigilance 22nd Annual Meeting, Bali, Indonesia

FINAL HSA COVID-19 VACCINE SAFETY UPDATE ISSUED

In July 2023, HSA issued its final regular public safety update relating to COVID-19 vaccines. HSA will continue to closely monitor the safety profiles of all COVID-19 vaccines used in Singapore and inform the public of any significant new safety concerns.

15 COVID-19 vaccine safety updates have been published since May 2021



Safety updates on COVID-19 vaccines

Find out about suspected adverse events which have been reported to HSA following COVID-19 vaccination in Singapore.

Introduction

HSA actively monitors the safety of COVID-19 vaccines authorised in Singapore to ensure that the benefits of these vaccines continue to outweigh the risks and that they remain safe for use. This is done through adverse events (AEs) monitoring systems to detect any potential safety signals so that relevant measures can be taken expeditiously.

The COVID-19 vaccines[a] currently authorised and rolled-out are as follows:

Vaccines	Authorisation date	Vaccination roll-out date
Pfizer-BioNTech/Comirnaty COVID-19 vaccine	14 December 2020	30 December 2020
Moderna/Spikevax COVID-19 vaccine	3 February 2021	12 March 2021
Sinovac-CoronaVac COVID-19 vaccine	29 October 2021	18 June 2021
Nuvaxovid COVID-19 vaccine	3 February 2022	18 May 2022

[a]Pfizer-BioNTech/Comirnaty is registered as a therapeutic product by HSA on 10 December 2021. Moderna/Spikevax, Nuvaxovid, Sinovac-CoronaVac are authorised under the Pandemic Special Access Route.

The following report provides an overview of **suspected** AEs that have been reported to HSA by healthcare professionals following the use of COVID-19 vaccines. The report also includes HSA's assessment of these reported AEs.

Since January 2023, HSA has been receiving significantly fewer COVID-19 vaccines AE reports and the safety profiles of the vaccines have been reviewed to be consistent, with no new safety signals. The safety of the COVID-19 vaccines is also now more established following extensive safety data accumulated from their wide global uptake during the pandemic. HSA will therefore cease publishing our regular safety update reports on COVID-19 vaccines. Nonetheless, as part of our post-market surveillance programme, HSA will continue to closely monitor the safety profile of all COVID-19 vaccines used in Singapore and will inform members of the public should there be any significant new safety concerns.

FACILITATION OF ACCESS FOR COVID-19 MEDICAL DEVICES

341 COVID-19 diagnostic tests have been granted marketing authorisation

PARTICIPATION IN COVID-19 VACCINES & THERAPEUTICS WORKING GROUP

As part of our efforts to monitor and assess new safety issues associated with COVID-19 vaccines and therapeutics, HSA has been actively involved in Access Consortium's Pharmacovigilance Subgroup Meetings.

REGULATORY UPDATES AND REVIEWS

We enhance our governance and compliance frameworks to ensure the safety of products throughout their lifecycle while streamlining regulatory obligations for the industry.

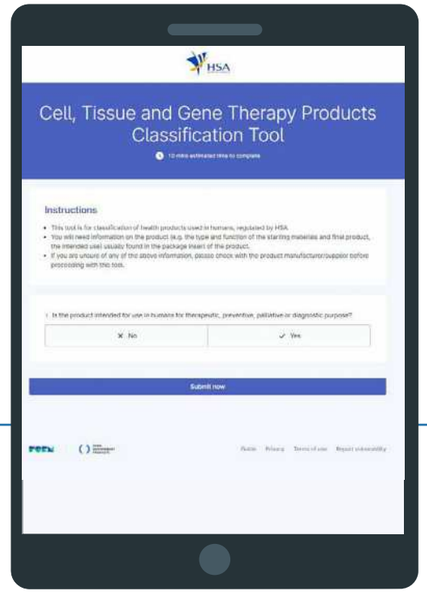
SUCCESSFUL IMPLEMENTATION OF HEALTH PRODUCTS (ACTIVE INGREDIENTS) REGULATIONS

In December 2023, we streamlined the regulation of active pharmaceutical ingredients into a single piece of subsidiary legislation to provide greater clarity on the legal requirements and regulatory controls for all active pharmaceutical ingredient manufacturers, importers and wholesalers.

This new fit-for-purpose, risk- and activity-based regulatory framework aligns with international standards and enhances mutual confidence among HSA and our overseas counterparts. This will pave the path for Singapore to be recognised as an EU equivalent Third Country with regulatory regime and Good Manufacturing Practices (GMP) standard for active pharmaceutical ingredients.

ONLINE SELF-HELP CELL, TISSUE AND GENE THERAPY PRODUCT (CTGTP) CLASSIFICATION TOOL

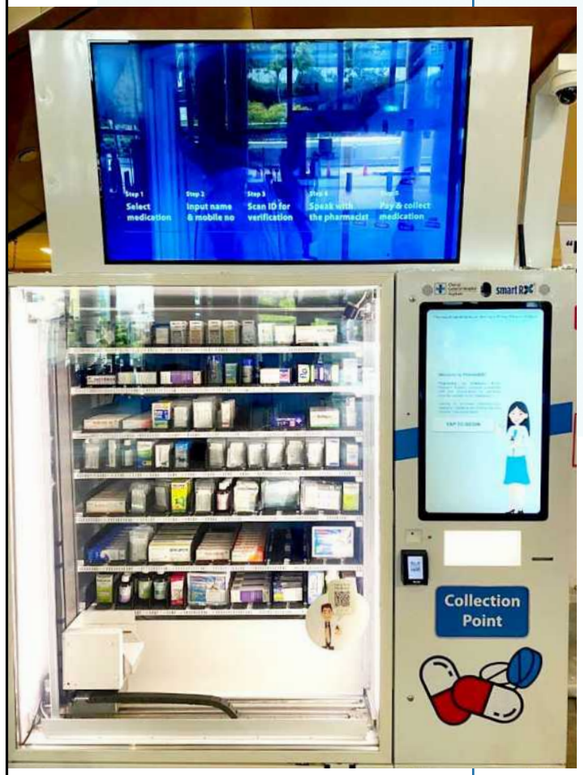
As part of our pro-enterprise initiative, we launched a new CTGTP Classification Tool on the HSA website in March 2024. This self-help tool assists stakeholders in determining if their product is a Class 1 or 2 CTGTP or a non-CTGTP.



PHASE 2 VOLUNTARY NOTIFICATION SYSTEM (VNS) INITIATIVE FOR COMPLEMENTARY HEALTH PRODUCTS (CHPs)

In August 2023, HSA launched Phase 2 of its VNS for CHPs to include products such as probiotics, medicated oils and balms, and medicated plasters. This follows Phase 1 which was launched in August 2022 for commonly purchased products (e.g. vitamin and mineral supplements) and products at higher risk of adulteration (e.g. products intended for weight loss, pain relief and male vitality).

This initiative aims to establish a reliable CHP database for consumers to refer to when making their purchases, and facilitates traceability and regulatory actions by HSA if there are safety or quality issues.



SUPPORTING PHARMACIES AND HOME DELIVERY SERVICES

This past year, HSA worked closely with Synapxe and Ministry of Health's (MOH) Chief Pharmacist's Office on the National Central Fill Pharmacy initiative, which seeks to ensure that pharmacies have in place robust processes for safeguarding the safety and quality of medicines being delivered to patients.

We also approved several innovative healthcare delivery services for retail pharmacies, including e-pharmacy, vending machines for Pharmacy Only Medicines (P), and medication delivery services to enhance patients' accessibility to medicines.

GUIDANCE NOTE PUBLISHED FOR MEDICINES VENDING MACHINES

In April 2023, HSA published a new guidance note on "Retail Supply of Registered Therapeutic Products – Pharmacy Only Medicines (P) and Prescription only Medicines (POM) via Vending Machines". This note guides retail pharmacies on the regulatory requirements and expectations for operating such vending machines in Singapore.

LAUNCH OF SINGAPORE HEALTH PRODUCT ACCESS AND REGULATORY E-SYSTEM (SHARE)

In January 2024, we launched the Singapore Health Product Access and Regulatory E-System (SHARE), a one-stop digital portal for Cell, Tissue and Gene Therapy Products (CTGTP) Dealer's Notice and Class 1 CTGTP Notification. This new portal is part of our ongoing efforts to streamline regulatory processes to achieve efficient transactions and enable closer collaboration among regulators, businesses, industry partners and the public, facilitating access to safe health products in Singapore. With the introduction of SHARE, applicants can now submit, check and update new dealer's notices and product notifications all in one system, resulting in enhanced process efficiency, regulation and compliance. SHARE will be progressively rolled out to other product types and eventually replace the Pharmaceutical Regulatory Information System (PRISM).

REGULATORY ENHANCEMENTS FOR MEDICAL DEVICES

We made the following updates to enhance regulatory processes and ensure alignment with global standards:

JANUARY 2023

Clarified the qualification criteria for immediate and expedited evaluation routes (IBR and ECR-1) to specify that devices must have a marketing history of at least three years in the jurisdiction of the approving regulatory agency

JULY 2023

Improved the risk classification for in vitro diagnostic medical devices and self-help tools through the expansion and clarification of specific risk class rules

SEPTEMBER 2023

Updated the "Medical Device Adverse Event Reporting for Medical Device Dealers" form to include unique device identifiers (UDI) and International Medical Device Regulators Forum (IMDRF) Adverse Event Reporting Terms and Codes

MARCH 2024

Highlighted the need to provide essential information such as the software development life cycle summary, software requirement specification (SRS) and traceability analysis during regulatory submission for software or programmable medical devices

TECHNOLOGY AND INFRASTRUCTURE

We leverage new technologies and build upon our existing infrastructure to raise productivity levels.

STREAMLINING THE ISSUANCE OF NOTICES OF COMPOSITION USING VaSER

In December 2023, we collaborated with the Ministry of Health (MOH) and Open Government Products (OGP) team to develop the Vaping System for Enforcement & Registry (VaSER). Leveraging open government products (FormSG, PaySG and Plumber), the system radically streamlines the process of issuing notices of composition, as well as provides a convenient payment platform for fines. It resulted in significant resource savings and expanded our Tobacco Regulation Branch's case handling capacity by 4.5 times.

ENHANCED SURVEILLANCE OF SAFETY SIGNALS

To enhance our surveillance of health products in Singapore, we used data preparation and visualisation software to improve our data preparation processes and increase the efficiency of generating adverse event statistics for trend analysis.

We also enhanced the way we analysed our electronic health records data by using natural language processing models and large language models, as well as new algorithms to identify and detect adverse drug reactions and facilitate safety signal evaluation.

THE POWER OF GOING DIGITAL – HSA ADVERSE DRUG REACTION (ADR) NEWS BULLETIN

The HSA ADR News Bulletin serves to communicate product safety information to healthcare professionals. Over the years, several key enhancements have been made:

- Redesigned bulletin format to facilitate easier picking up of safety information
- Introduction of digital copies to reduce printing and be more environmentally-friendly

Higher cost savings | **Wider reach** | **Increased readership**

STAYING VIGILANT

To ensure public health and safety, we endeavour to remain alert at all times.

SINGAPORE-SPECIFIC RISK MANAGEMENT PLANS (RMP) AND SAFETY SIGNALS

To ensure the safety of consumers in Singapore, we conduct regular surveillance activities on therapeutic products and cell, tissue and gene therapy products in the market.

144 *Safety signals assessed*

41 *Singapore-specific RMPs evaluated*

11 *New RMPs implemented*

This resulted in several notable regulatory actions being taken, including:

- Withdrawal of pholcodine-containing medicines due to the risk of perioperative anaphylaxis with use of neuromuscular blocking agents
- Reminder to healthcare professionals on the risk of psychiatric disorders and sexual dysfunction associated with isotretinoin

The following advisories were issued:

7 *Dear Healthcare Professional Letters (DHCPLs) issued by companies and HSA*

3 *Adverse Drug Reaction (ADR) news bulletins*

1 *Safety update*

ADULTERATED HEALTH PRODUCTS

Our post-marketing surveillance activities have enabled us to detect the presence of adulterated health products in Singapore. Advisories were issued to warn the public about such products.

9 press releases
issued including safety advisories on
22 products

DEFECTIVE LOCALLY REGISTERED THERAPEUTIC PRODUCTS

HSA received a total of **236 product defect cases** over this past year. HSA worked closely with the associated companies to ensure appropriate corrective actions were taken. These included:

29 *Communications issuances (e.g. DHCPLs, Dear Purchaser Letter, press release)*

25 *Amendments to product registration (e.g. variation submission)*

14 *Product recalls*

MEDICAL DEVICE POST-MARKET SURVEILLANCE AND VIGILANCE SYSTEM

Safety signals and risk management actions

3,952 *Safety signals assessed*

13 *Follow-up assessments conducted on device safety issues*

7 *Local product defect complaints investigated*

Device issues

Of the medical device defects reported, the top 5 problems were related to:

82 *Material integrity*

62 *Output*

55 *Electrical/electronic property*

48 *Infusion or flow*

43 *Patient device interaction*

Adverse events reported

We received a total of 763 reports of adverse events related to medical devices. The top 3 medical specialty areas from which the reports were received included:

311 **Cardiovascular** *(involving devices such as pacemakers, implantable heart valves and cardiovascular stents)*

164 **General hospital** *(involving devices such as infusion pumps, patient monitors and ventilators)*

87 **Ophthalmology** *(involving devices such as intraocular lens, contact lens and ophthalmic surgical systems)*

Field safety corrective actions and advisories

We undertook a total of 668 field safety corrective actions (FSCA) related to locally supplied devices. Top 2 categories of FSCA issues reported:

135 *Device operation*

70 *Physical property specifications issue*

HSA worked with companies to ensure that appropriate corrective and preventive actions (CAPA) were taken to mitigate the impact on the safety and quality of the defective medical devices as well as their future batches. The actions included:

437 *Communications pieces published on website*

350 *Issuances of additional safety information*

246 *Safety corrective actions*

89 *Change review submissions for implementing CAPA and mitigating risk*

72 *Product recalls*

Two noteworthy cases included ophthalmic products impacted by foreign particulate contamination, and defective medical devices illegally sold through overseas online platforms.

We also issued and reviewed the following advisories:

23 *DHCPLs issued by companies and HSA*

2 *Medical device safety updates*

2 *Medical device safety alerts*

2 *Consumer safety articles*

ENFORCEMENT

We continue to crack down on the sale of illegal health products and prohibited tobacco products.

ILLEGAL SALE OF HEALTH PRODUCTS

159 *Operations conducted*

43 *Suspects investigated*

23 *Prosecutions*

11,516 *Illegal product listings removed*

2,780 *Warnings issued*

Estimated value of seized items:

>1.4 million units
worth over $1 million

OPERATION PANGEA

Operation Pangea is an initiative by INTERPOL to target the online sale of illegal health products. Over the past year:

2 *Operations involving **89 countries** were conducted*

360 *Parcels were investigated, more than **7,000 illegal product listings removed** and **1,886 warnings issued***

PROHIBITED TOBACCO PRODUCTS

Together with our partner agencies, we continued to closely monitor the sale of illegal tobacco products in Singapore. A total of 22 raids were conducted, resulting in:

Total seizure value of smokeless tobacco and e-vaporisers:
>$7.3 million

Number of peddlers prosecuted:
53

Total number of notices of composition issued:
>9,000

Number of illegal tobacco product listings removed:
>6,000

NEW LOCAL PARTNERSHIPS

Our strong network of local partners enables us to bolster our efforts and advance our objectives.

STRENGTHENING ENGAGEMENT WITH OUR PUBLIC HEALTH INSTITUTIONS

We conducted meetings with partner hospitals and institutions such as National Cancer Centre, Changi General Hospital, Khoo Teck Puat Hospital and SingHealth to gather feedback on current clinical practices, systems and operational issues related to Adverse Event (AE) reporting.

This was followed up with educational engagement activities, where we shared clinical case studies which enhanced understanding of the value of AE reporting.

Through these exercises, we were able to reach out to healthcare professionals more effectively to improve AE reporting, and at the same time foster a more holistic approach for signal identification and safety assessments.

NEW OVERSEAS PARTNERSHIPS

Close collaborations with international partners are instrumental for fortifying our knowledge base.

MUTUAL RECOGNITION AGREEMENT (MRA) SIGNED WITH REPUBLIC OF KOREA'S MINISTRY OF FOOD AND DRUG SAFETY (MFDS)

In February 2024, HSA entered into a MRA with the Republic of Korea's MFDS to establish Good Manufacturing Practice (GMP) requirements for Medicinal Products. The agreement was signed by Dr Choong May Ling, Mimi, Chief Executive Officer of HSA, and Dr Oh Yu-Kyoung, Minister of MFDS.

This MRA allows for the reciprocal acceptance of GMP certificates and inspection results for pharmaceutical manufacturers located in Singapore and South Korea, and minimises duplicative on-site GMP inspections and assessment of manufacturing facilities. It will also enhance trade and improve the accessibility of medicinal products in Singapore and South Korea.

Photo credit: Ministry of Food and Drug Safety of the Republic of Korea

INVOLVEMENT IN PIC/S ACTIVITIES

In 2024, HSA was appointed by the Pharmaceutical Inspection Co-operation Scheme (PIC/S) Committee to be part of the re-assessment team to assess the Republic of Korea's Ministry of Food and Drug Safety.

HSA will serve as the Chair of PIC/S Sub-Committee on Training and as Member of the PIC/S Executive Bureau from 1 January 2023 to 31 December 2024.

MEMORANDUM OF UNDERSTANDING (MOU) SIGNED WITH POLAND'S NATIONAL REGULATORY AUTHORITY

In May 2023, HSA signed an MOU with Poland's Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL) to kickstart cooperation between the two regulatory authorities.

Both HSA and URPL are members of the International Medical Device Regulators Forum National Competent Authority Report (IMDRF NCAR) Exchange Programme, which facilitates the exchange of post-market safety information on medical devices of significant concerns or potential trends.

38th ASEAN COSMETIC COMMITTEE MEETING

From 20 to 23 November 2023, HSA hosted the 38th ASEAN Cosmetic Committee Meeting and its related meetings. This was the first in-person meeting since the COVID-19 pandemic.

The meeting provided a sharing platform for updates on the implementation of the ASEAN Cosmetic Directive, as well as harmonisation of the technical requirements and testing methods on cosmetic products.

ACCESS CONSORTIUM ESTABLISHES NEW WORKING GROUP

Access Consortium is a coalition of five regulatory authorities (Australia Therapeutic Goods Administration, Health Canada, Health Sciences Authority, Swissmedic, UK Medicines and Healthcare Products Regulatory Agency) that seeks to explore collaborative opportunities for optimising synergies among authorities and reducing duplicate efforts within industry.

A new working group for Advanced Therapy Medicinal Products was established in November 2023 to foster interdisciplinary scientific discussions on emerging innovative therapeutic concepts and technologies.

WORLD HEALTH ORGANIZATION (WHO) PILOT ASSESSMENT SESSIONS FOR NEW IN VITRO DIAGNOSTICS (IVD) PREQUALIFICATION MODEL

In June and December 2023, WHO's IVD Assessment Team organised joint sessions with invited assessors from various international agencies and institutions to pilot and trial new standardised assessment approaches for IVD prequalification.

HSA is a WHO-recognised Stringent Regulatory Authority for high-risk IVDs and four of our evaluators were invited to participate in these sessions. The sessions provided a good platform for enhancing assessment capacity and promoting knowledge sharing.

PERMANENT FORUM ON INTERNATIONAL PHARMACEUTICAL CRIME (PFIPC) AND INTERNATIONAL LABORATORY FORUM ON COUNTERFEIT MEDICINES (ILFCM)

From 25 to 29 September 2023, HSA hosted the PFIPC and ILFCM meetings in Singapore. These two events helped to forge closer ties between Singapore and global enforcement colleagues, as we work together to combat pharmaceutical crimes and safeguard public health.

HSA also took the opportunity to present on Singapore's regulatory framework of e-pharmacies and safeguards in place to ensure the safe supply of medicines.

INTERNATIONAL MEDICAL DEVICE REGULATORS FORUM (IMDRF) GOOD REGULATORY REVIEW PRACTICES (GRRP) WORKING GROUP

The IMDRF GRRP Working Group seeks to develop good review practices for regulatory authorities and their conformity assessment bodies.

In March 2024, the Working Group, co-chaired by US FDA and HSA, initiated an update of existing GRRP documents to achieve consistent terminology for development of a risk calibrated regulatory approach for innovations, and to harmonise pre-market review requirements for medical devices.

All **8 documents** that were tabled for updates were approved at the 25th IMDRF meeting.