KEEPING UP OUR VIGILANCE

Health Products Regulation Group

We strike a fine balance between facilitating access to safe and efficacious health products, and developing regulations that support innovation.



COVID-18 VACCINE MONIA

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COVID-19 RELATED WORK

HSA continued to support the nation in its fight against COVID-19.

AUTHORISATION OF COVID-19 VACCINES AND THERAPEUTICS

Over the past year, we granted interim authorisation under the Pandemic Special Access Route (PSAR) for the following:



We also granted product registration for a paediatric vaccine (Pfizer-BioNTech Comirnaty 3mcg/dose).

FACILITATION OF ACCESS TO MEDICAL DEVICES FOR COVID-19

As of March 2023, 323 COVID-19 diagnostic tests were granted interim authorisation under the PSAR.



ENHANCED SAFETY MONITORING OF COVID-19 VACCINES

From the start of the pandemic, we have been conducting enhanced safety surveillance of COVID-19 vaccines through:

- Expedited reporting of serious adverse events (SAE) by healthcare professionals
- Consumer self-reporting of adverse events (AE)
- Implementing an active surveillance system which utilises real-world data for signal detection

As the vaccination strategy expanded to include new COVID-19 vaccines, booster doses, bivalent vaccines, and vaccination for children, so did the scope of our surveillance activities. We promptly evaluated AE reports of COVID-19 vaccines to identify new safety concerns, as well as held consultations with clinical expert panels in different disciplines to discuss the SAE reports received after vaccination.

We also communicated the latest safety findings to keep the public apprised on latest developments. These included topics such as the safety profile of the Nuvaxovid COVID-19 vaccine, as well as the incidence of AEs for the bivalent mRNA vaccines and paediatric vaccinations.

REGULATORY UPDATES AND REVIEWS

Our role as a regulator is to ensure that health and medical products remain safe for consumers in Singapore.

IMPLEMENTATION OF HEALTH PRODUCTS (COSMETIC PRODUCTS - ASEAN COSMETIC **DIRECTIVE) (AMENDMENT) REGULATIONS 2023**

In February 2023, HSA made several key amendments including:

- Prohibition of wholesale and retail supply of cosmetic products that are not notified with HSA
- Deletion of obsolete provisions on existing cosmetic products
- Updates to the list of regulated cosmetic ingredients (in accordance with the ASEAN cosmetic ingredient list)



REGULATORY UPDATES FOR THERAPEUTIC PRODUCT REGISTRATION

- **e** Revised Checklists for Post-approval Minor Variations (MIV-1 and MIV-2):
 - MIV-1: Clarified eligible conditions and documentary requirements
 - MIV-2: Re-categorised a list of chemistry, manufacturing & controls (CMC) variations from "MIV-2 Notification" to "Do-and-Tell"
 - MIV-2: Introduced new "Do-and-Tell" checklists

The expansion of the "Do-and-Tell" changes aims to reduce regulatory submission burden and enable timely implementation of administrative and minor CMC changes that do not have any impact on the product's safety, efficacy and quality.

• Extension of Verification Evaluation Route to Biological Products

We extended the verification evaluation route to biological and biosimilar products to enable greater reliance on reference agencies' assessments and to minimise duplication of efforts.

LAUNCH OF PHASE 1 OF VOLUNTARY NOTIFICATION SYSTEM FOR COMPLEMENTARY HEALTH PRODUCTS

As of August 2022, companies dealing with commonly purchased complementary health products (e.g., vitamin and mineral supplements) and products at higher risk of adulteration (e.g., weight loss, pain relief and male vitality products) can voluntarily submit their notifications.

The Voluntary Notification System aims to establish a local database of reliable complementary health products for consumers to refer to when making their purchases, and facilitates traceability and regulatory actions by HSA when there are safety or quality issues.

Companies that participate in this initiative are required to submit relevant documents to demonstrate that their products meet the necessary safety and quality standards. Only products that are compliant with these standards will be published on the HSA database.



ACTIVE SURVEILLANCE SYSTEM FOR ADVERSE REACTIONS TO MEDICINES AND VACCINES (ASAR)

HSA has developed the first nation-wide application - ASAR - that analyses structured healthcare data and unstructured clinical notes from all public acute hospitals. This real-world data is then used to detect and quantify the risk of AEs of interest, as well as determine the overall benefit-risk balance of medicines and vaccines used in Singapore.

ASAR pools millions of de-identified patient records from multiple sources of diagnoses, medications, vaccination records, laboratory test results and AE reports, and applies them to epidemiological studies to confirm or refute safety concerns relating to medicines and vaccines.

ASAR has enabled HSA to detect early safety signals and implement timely risk mitigation measures. The evidence generated through these analyses have also been used to inform MOH's COVID-19 vaccination policies, relevant regulatory actions and public communications aimed at safeguarding public health.



ENFORCEMENT ACTIVITIES

We worked together with local enforcement agencies to crack down on illegal health products and tobacco-related activities.

ENFORCEMENT ACTIONS AGAINST ILLEGAL HEALTH PRODUCTS IN GEYLANG

We worked closely with different agencies including the Criminal Investigation Department (CID) of the Singapore Police Force (SPF), Central Narcotics Bureau (CNB), Immigration & Checkpoints Authority (ICA), Singapore Customs, Ministry of Manpower (MOM) and Singapore Food Agency (SFA) to conduct multi-agency enforcement operations in targeted areas such as Geylang.





163 joint operations



6 months

Seized an estimated \$456,000 worth of illegal health products



Prosecuted and sentenced 10 peddlers to imprisonment terms of up to



COMBATTING CYBERCRIME TO SAFEGUARD PUBLIC HEALTH

Through the deployment of robotic process automation technology and collaboration with various stakeholders, HSA has been able to enhance the detection and removal of illegal product listings on local e-commerce platforms.

In FY22/23:







OPERATION PANGEA

In June 2022, we participated in Operation Pangea, an annual exercise coordinated by the International Criminal Police Organisation (INTERPOL) to target the online sale of illegal health products, such as prescription medications, adulterated sexual enhancement products and unregistered medical devices.

HSA has participated in **15** Operation Pangea for 15 consecutive

years.

4 countries
ok part in Operation



9 too Pangea 2022

products were removed

ENFORCING THE ILLEGAL SALE OF ELECTRONIC VAPORISERS

1

Raid on Supplier

In June 2022, together with SPF officers from Geylang Neighbourhood Police Centre, we nabbed a seller of e-vaporisers in a mobile shop in Geylang. This allowed us to gain information which led to a larger raid on the supplier.



Prohibited products with a street value of more than

\$50,000 were seized.

Nabbing E-vaporiser Seller who Sold to Students

In January 2023, acting on a tip-off about a seller who allegedly sold e-vaporisers to students, HSA conducted a raid at a retail store in a shopping centre in the west.

This led to an arrest of the seller, and the discovery of:

More than

400 e-vaporisers and 350 related components in the seller's home and store

These were worth a total market value of more than \$11,000.



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CHEWING TOBACCO SEIZED IN LITTLE INDIA

In April 2022, HSA conducted a joint raid with the SPF and CNB at Little India. A total of six premises were raided, of which four were found to contain prohibited tobacco products. This is the largest-ever chewing tobacco haul in a Little India raid.



32







A total of 660kg of chewing tobacco, worth a street value of around \$130,000 were seized.

STAYING VIGILANT

Ensuring the health and safety of the public is one of our priorities.

LOCAL THERAPEUTIC PRODUCT DEFECT CASES





HSA worked with the associated companies to ensure that appropriate corrective and preventive actions were taken to ensure the safety and quality of the defective products as well as their future batches.

27

Types of regulatory action taken:



Issuance of registration (e.g. variation submission) release)





SINGAPORE-SPECIFIC RISK MANAGEMENT PLANS (RMP)



29 RMPs

were evaluated as part of the registration of therapeutic products and cell, tissue and gene therapy products (CTGTP).



and submission of

(PBRER) were

implemented.

SAFETY SIGNALS

• Therapeutic Products and CTGTPs

- 238 safety signals were assessed as part of post-market pharmacovigilance activities
- Notable regulatory actions taken included:
- Publication of an article in HSA's Adverse Drug Reaction (ADR) News Bulletin to remind healthcare professionals on the risk of suicidality associated with selective serotonin reuptake inhibitors
- Issuance of a DHCPL and publication in HSA's ADR News Bulletin on the risk of major cardiovascular events, malignancies, thrombosis, and death associated with Janus Kinase (JAK) inhibitors, identified from a large post-authorisation clinical study
- We also amended local package inserts to include newly emerging safety warnings, and communicated product safety information to healthcare professionals through safety alerts on HSA's website.

Evolving COVID-19 Vaccines

• Reviewed 4 PBRERs



educational materials,

periodic benefit-risk evaluations reports

The new RMPs included 1 enhanced RMP

for a CTGTP (Yescarta[®]), which required the product registrant to implement a controlled distribution programme, and submit long-term safety studies to manage the safety of this novel class of products.

In light of the evolving safety profile of COVID-19 vaccines, we:

• Reviewed 18 monthly and bimonthly safety summary reports

$\bullet \bullet$ **Adulterated Health Products**

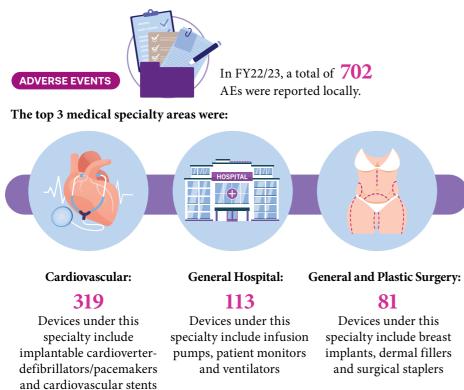
• 6 risk assessments were conducted on adulterated products detected through post-marketing surveillance

Subsequently, press releases were issued to warn the public about these products.

ADVISORIES ISSUED

- Issued 12 press releases, covering safety advisories on 16 products
- Reviewed 9 company DHCPLs
- Issued 2 DHCPLs
- Disseminated 3 HSA ADR news bulletins to registered healthcare professionals
- Published 3 Safety Updates on the HSA website

MEDICAL DEVICE POST-MARKET SURVEILLANCE AND **VIGILANCE SYSTEM**



FIELD SAFETY CORRECTIVE ACTION (FSCA)

HSA also worked with companies to ensure that appropriate corrective and preventive actions were taken to ensure the safety and quality of current and future batches of medical devices.





192 Safety corrective actions

286 Dissemination of additional safety information



JCTS REGULATION HEALTH 37

STREAMLINING OUR PROCESSES

By optimising our work processes, we can achieve higher efficiency and deliver greater value to stakeholders.

REGULATORY GUIDELINES AND FRAMEWORK (PRODUCTS)

• Revised Guidelines for Standalone Medical Mobile Applications and Clinical Decision Support Software

We came up with new guidelines to provide clarity on:

- Risk classification of standalone medical mobile applications based on:
- Significance of information provided to healthcare decision - State of healthcare situation or condition
- Qualification of Clinical Decision Support Software (CDSS) as a medical device

●● Guidelines for Software Medical Devices – A Life Cycle Approach

The guideline for software medical devices was refined to include evolving developments in cybersecurity considerations, software functionalities and artificial intelligence (AI) features.

• Strengthening of Regulatory Oversight on High-risk **Unregistered Medical Devices Intended for Local Clinical Use**

The Special Access Routes (SAR) allow qualified practitioners and local medical facilities to bring in unregistered medical devices. As of April 2022, to further protect patient health and safety, applications from public healthcare institutions that have Class D implants and new technologies or state-of-the-art medical devices are now required to have their clinical justifications reviewed by the Ministry of Health.

●● Unique Device Identification (UDI) Framework

We published the 2nd edition of the UDI guideline, which included instructions (via video guide and FAQ) on how to submit UDI information for registered devices under MEDICS.

Subsequently, in November 2022, Singapore implemented Phase 1 of the UDI framework, which seeks to enhance patient safety by increasing the efficiency of tracking and identifying high-risk implantable medical devices such as coronary stents, orthopaedic joint replacement implants and intraocular lenses.

●● Regulatory Guidelines for Laboratory Developed Tests (LDTs)

We published new guidelines to provide an overview of the scope of LDTs and the regulatory requirements for local clinical laboratories, covering product, quality and post-market controls.

More Seamless Change Notification (CN) Submission Process in MEDICS

To make the MEDICS CN submission process more seamless, a separate Safety and Performance declaration documentation is no longer required for submissions from March 2023.

REGULATORY GUIDELINES AND FRAMEWORK (DEALERS)

Reverting to Standard Regulatory Controls

At the start of the COVID-19 pandemic, we implemented an Exemption Order to allow access to low-risk medical devices such as surgical masks. As Singapore embarked on the endemic phase, we revoked the Order and resumed standard regulatory controls.

New Approach for Local Standalone Dental Laboratories ••

We adopted a simplified risk-calibrated approach that continues to ensure quality oversight for dental laboratories that manufacture custom-made Class A or Class B dental devices. As of January 2023, manufacturers of these lowmoderate risk custom-made devices no longer require HSA Manufacturer's Licences, and will only be required to:



 Have a Quality Management System in place for their manufacturing site (no certification required) • Submit a notification to HSA on their activities (no fees imposed)



TECHNOLOGY AND INFRASTRUCTURE

We constantly adopt new technologies to improve our service and enhance our overall productivity.

PRE-SUBMISSION CONSULTATION MECHANISMS

We added the following industry self-help mechanisms on our website:

- Therapeutic Product Classification Tool and Post-approval Variation Classification Tool
- Guidance for Therapeutic Products Registration
- Frequently Asked Questions (FAQs)

If specific issues cannot be addressed by the selfhelp mechanisms, procedures for email or meeting consultations are available.

ENHANCING REGULATORY TRANSPARENCY BY
PUBLISHING REGULATORY ACTIONS

We published a comprehensive range of information on regulatory actions relating to therapeutic products on our website to enhance transparency and accessibility to regulatory updates. Actions covered include New Approvals, Reclassifications, Transfers and Cancellation of Product Registrations, and Product Recalls.

AUTOMATING THE APPLICATION AND PROCESSING OF FREE SALE CERTIFICATES FOR MEDICINAL PRODUCTS

Previously, requests from companies for free sale documentation as evidence of their regulatory status for exempted medicinal products were received via email and manually processed.

In March 2023, to improve efficiency, we set up a new end-to-end digital process leveraging technological tools such as FormSG and GovTech (Digital) Workflow to streamline the internal processing and facilitate communication across branches for product verification.

Industry stakeholders can now enjoy a more expedient application process for export of such medicinal products by following a set of simplified instructions on FormSG.

ENHANCED SURVEILLANCE AND MANAGEMENT OF THERAPEUTIC PRODUCT DEFECTS USING DIGITAL TOOLS

We developed and implemented digital tools for managing therapeutic product defects:

- An automated web-scraping programme that uses machine learning to extract alerts relating to product defects and recalls from overseas drug regulatory agency websites
- A filtering algorithm based on machine learning and keyword-based approach to identify alerts relating to substandard medicines
- A combined machine learning algorithm with keyword-based model to classify quality issues using text relating to substandard medicines (CISTERM)
- A risk classification model for prioritising management of product defects (Regulatory Risk Impact Prioritisation Model for Product Defects - RISMED and stat-RISMED)

We shared our experience at the following local and international conferences:

- July 2022 Singapore Pharmacy Congress
- November 2022 11th Asia Regulatory Conference
- February 2023 DIA Middle East Conference



SHARING OUR KNOWLEDGE

We strive to raise the overall standard of health products regulation in Singapore through continuous knowledge sharing.

GUIDANCE FOR LOCAL RETAIL PHARMACIES

In August 2022, we published a set of FAQs for e-pharmacy operators on our webpage. The FAQs assist the industry in understanding the regulatory requirements when setting up an e-pharmacy service, including the need for a closed loop computerised system to ensure proper transmission of information from the prescriber to the e-pharmacy.

STAKEHOLDER ENGAGEMENT SESSION ON NEW ACTIVE PHARMACEUTICAL INGREDIENTS (API) REGULATIONS

In March 2023, we held industry stakeholders' engagement sessions to share updates on the new regulations for API, including the transition approach for existing API manufacturers and dealers.

At the sessions, stakeholders were able to provide feedback on issues such as the helpfulness of the proposed API licensing regime towards managing manufacturing risk, and dealing with API.



PHARMACOVIGILANCE AND MEDICAL DEVICES **EDUCATION INITIATIVES**

We collaborated actively with local and international working groups and organisations.

- September 2022 Facilitated group discussions on the Fundamentals of Health Products Regulation for Graduate Certificate in Health Products Regulation, Duke-NUS CoRE
- September 2022 Engaged professionals on "Translating Regulatory Agility into Actions in a Post Pandemic APAC" at the APACMED MedTech Forum
- October 2022 Represented in panel for the CoRE Annual Scientific Conference, in the session "Communication in Safety and Healthcare Delivery"
- November 2022 Facilitated discussions on the Regulation of IVD Devices for Executive Certificate and Graduate Certificate in Health Products Regulation, Duke-NUS CoRE
- November 2022 Engaged professionals on "Navigating the Pathway to Commercialisation" at the AI Health Summit, Singapore
- November 2022 Engaged healthcare professionals on "Safety assessment of COVID-19 vaccines and ART kits" during a toxicology webinar organised by the Toxicology Society of Singapore (TOXSSIN)
- February 2023 Engaged healthcare professionals on "Detection of adulterants in complementary health products" during an annual scientific meeting organised by the Society for Emergency Medicine Singapore (SEMS)

SUSTAINING EDUCATIONAL OUTREACH TO SINGHEALTH **PROFESSIONALS THROUGH DIGITALISATION**

In July 2022, we collaborated with SingHealth Pharmacy & Therapeutics Council Office to reach out to healthcare professionals for continuous education. This comprised a virtual lecture for healthcare professionals on the importance of pharmacovigilance and AE reporting, and the development of an e-module on AE reporting in SingHealth's e-learning system.



The lecture was attended by:

280 participants coming from 4 hospitals, 5 specialist centres, 3 community hospitals and 9 polyclinics.

INTERNATIONAL COLLABORATIONS

Beyond our shores, we also collaborated with global counterparts to widen our knowledge base.

INTERNATIONAL MEDICAL DEVICE REGULATORS FORUM (IMDRF)

●● AE Working Group

In the second year as Chair of the IMDRF AE Terminology Maintenance Working Group, we continued to improve, harmonise and expand the terminology used to code information relating to medical device AEs.



●● Good Regulatory Review Practices (GRRP) Working Group

The GRRP Working Group develops good review practices for regulatory authorities and their conformity assessment bodies. As co-chair, we reviewed and published a report relating to preparing medical device regulatory review reports, such as the collection of key information and documents that can improve the pre-marketing review process.

RECOGNISED BY AUSTRALIA AS A COMPARABLE OVERSEAS REGULATOR (COR) FOR MEDICAL DEVICES

In September 2022, Australia's Therapeutic Goods Administration (TGA) recognised HSA as a COR for the review of medical devices. With this recognition, companies can leverage HSA's medical devices approvals for faster entry into Australia. Singapore joins the European Union, United States of America, Canada and Japan as one of five listed TGA COR regulators.



GLOBAL HARMONIZATION WORKING PARTY MEETING

In February 2023, we were invited to speak at the 26th Annual Meeting on "Benefits of Regulatory Reliance". We shared with fellow regulators and regulatory professionals about our experience in regulatory reliance (using WHO's Good Reliance Practice model), steps towards regulatory convergence and resource optimisation.



ASEAN JOINT SECTORAL COMMITTEE ON GMP (GOOD MANUFACTURING PRACTICES) INSPECTION OF MANUFACTURERS OF MEDICINAL PRODUCTS MUTUAL **RECOGNITION AGREEMENT (JSC GMP MRA)**

In November 2022, we were appointed as Vice Chair of the ASEAN JSC GMP MRA. A key focus area of this committee is on expanding the scope of MRA beyond pharmaceutical products in finished dosage form to include biopharmaceuticals and APIs.

PROJECT ORBIS

We continued our collaborations with US FDA Oncology Centre of Excellence (OCE), ANVISA, Health Canada, Israel Ministry of Health, Swissmedic, TGA and UK MHRA through Project Orbis. Project Orbis provides a framework for concurrent submission and review of oncology products among international regulatory health authorities.





Over the past year, HSA has issued regulatory approvals for 10 applications

through Project Orbis.

ACCESS CONSORTIUM

Access Consortium is a coalition of regulatory authorities that aim to provide patients with timely access to high quality, safe and effective therapeutic products in the member countries.

Providing Timely Access to Safe and Efficacious Therapeutic Products

Over the past year, HSA has completed six therapeutic products applications through Access Consortium.

Collaborations to Assess New COVID-19 Safety Issues

As part of our COVID-19 safety monitoring efforts on vaccines and therapeutics, we actively collaborated with Access Consortium COVID-19 Vaccine & Therapeutics Working Group via participation in the Pharmacovigilance Subgroup Meetings.

Statement on GMP Inspections Reliance and Recognition

A collective statement was issued by the Access Heads of Agencies to solidify the Consortium's commitment to demonstrate greater inspection reliance and acceptance of one another's GMP inspection outcomes.

By relying on the review of inspection reports for GMP inspections conducted by Access members within their territories, it reduces the regulatory burden on stakeholders, and facilitates consumer access to high-quality, safe and effective pharmaceutical products.

HSA RECOGNISED BY WHO AS A STRINGENT **REGULATORY AUTHORITY (SRA)**

HSA has been recognised by the World Health Organization (WHO) as an SRA for high risk in vitro diagnostic medical devices (IVDs). With this recognition, any high risk (Class C or Class D) IVD registered with HSA will qualify for the abridged prequalification assessment by WHO. Manufacturers of such IVDs can now leverage HSA's SRA status to obtain expedited listing under the WHO prequalification programme, and gain access to various markets beyond Singapore. This recognition places Singapore alongside the United States of America, European Union, Canada, Australia and Japan as one of the six WHO SRAs for IVDs.



OUR INVOLVEMENT IN PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME (PIC/S)

Joint PIC/S-EMA-WHO Working Group HSA participated in the Joint PIC/S-EMA-WHO Working Group on Revised Annex 1 GMP Guide on the manufacture of sterile products which will enter into force in August 2023.

What the Future Holds for Industry and PIC/S

In October 2022, we chaired Session 3 of the 50th Anniversary Symposium. This session consisted of two presentations followed by a panel discussion on "Ensuring GMP inspections are fit for purpose in the 21st Century".



We were involved in developing the PIC/S Aide-Memoire on the "Inspection of Good Distribution Practice (GDP) for Medicinal Products in the Supply Chain", and the Q&A document regarding the PIC/S GDP Guide. Both documents were published in February 2023.

COLLABORATION WITH HUNGARIAN SUPERVISORY AUTHORITY FOR REGULATORY AFFAIRS (SARA)

In March 2023, HSA hosted Dr Marcell Bíró, Chairman of SARA, together with Her Excellency Ms Judit Pach, Ambassador of Hungary to Singapore. During the meeting, we talked about collaborations with SARA to foster twoway cooperation and sharing of best practices on tobacco control.



Co-ordinating Committee of the PIC/S Expert Circle on GDP

NEW AWARDS AND ACCREDITATIONS

We received the following awards and achievements for our commitment to serving the public and stakeholders.

PUBLIC SECTOR TRANSFORMATION (PST) AWARDS 2022

The PST Awards is a Whole-of-Government (WOG) pinnacle platform to recognise and reward public officers and public agencies for excellence in their work and organisational practices.

This year, we were awarded:

The Dare to Do Award, for HSA's contribution, alongside A*STAR, to the assay development of COVID-19 vaccines.

The Exemplary Leader Award, for Group Director of the Health Products Regulation Group, Associate Professor Chan Cheng Leng's outstanding leadership in driving excellence, innovation and agility in health products regulation.





RE-CERTIFICATION OF ISO 9001:2015

In March 2023, the Enforcement Branch (EB), Vigilance & Compliance Branch (VCB) and Tobacco Regulation Branch (TRB) successfully completed the re-certification audit, a testament to our commitment to high standards.

OPENGOV ASIA RECOGNITION OF EXCELLENCE AWARD 2023

HSA's VCB and Integrated Health Information Systems jointly received this award for building ASAR in Singapore. Specifically, their efforts included enhancing the AE monitoring programme for COVID-19 vaccines, and shifting pharmacovigilance in Singapore towards a significantly more proactive paradigm.





●● Ministry of Home Affairs (MHA) Team Award ●● Community Policing Appreciation (CPA) Award Certificate of Appreciation by Minister of Home

Affairs & Law

MHA OPERATIONAL EXCELLENCE AWARD

In January 2023, TRB together with ICA were awarded:



MINISTRY OF MANPOWER (MOM) CERTIFICATE OF APPRECIATION

In March 2023, TRB was awarded the MOM Certificate of Appreciation for its participation in International Migrants Day.





This was for their efforts in detecting substantial amounts of chewing tobacco and e-vaporisers and their components at the checkpoints.