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WHO Vision for Safety of Medicinal Products
No country left behind: worldwide pharmacovigilance for safer medicinal products, safer patients

The aim of the newsletter is to disseminate regulatory information on the safety of medicinal products, based on communications received from our network of national pharmacovigilance centres and other sources such as specialized bulletins and journals, as well as partners in WHO.

The information is produced in the form of résumés in English, full texts of which may be obtained on request from:

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This newsletter is also available at:
https://www.who.int/teams/regulation-prequalification

The WHO pharmaceuticals newsletter provides you with the latest information on the safety of medicinal products and regulatory actions taken by authorities around the world.

In addition, this edition includes a summary of Pharmacovigilance Partners' Meeting held in New Delhi, India on 13 October 2024 with a synopsis of WHO Global Smart Pharmacovigilance Strategy.

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All the previous issues of the WHO pharmaceuticals newsletter can be accessed from our website. For request of addition in the mailing list of this newsletter, please contact us at: pvsupport@who.int

Fluconazole

Potential risk of abnormal pregnancy outcomes

Ireland. The Health Products Regulatory Authority (HPRA) has announced that the product information for fluconazole has been updated to reflect available data on abnormal pregnancy outcomes (spontaneous abortion, cardiac malformations and other birth defects) as well as new advice on use in women of childbearing potential.

Fluconazole is a potent and specific inhibitor of fungal sterol synthesis and is indicated in the treatment and prophylaxis of a wide range of fungal infections.

Based on the review of available data on adverse pregnancy outcomes, the EMA's PRAC has recommended new advice on use of fluconazole in women of childbearing potential:

- Before initiating treatment in women of childbearing potential, inform the patient of the potential risks to the foetus.
- After single dose treatment, a washout period of one week is recommended before pregnancy.
- For longer courses of treatment, contraception may be considered, as appropriate, in women of childbearing potential throughout the treatment period and for one week after the final dose.

Reference:
HPRA drug safety newsletter, HPRA, 29 November 2024 (link to the source within www.hpra.ie)
(See also WHO pharmaceuticals newsletter No.1, 2021: Fluconazole and potential risk of spontaneous abortion and cardiac septal closure anomalies from New Zealand)

Mebendazole

Risk of fever

Kingdom of the Netherlands. The Netherlands (Kingdom of the) Pharmacovigilance Centre has announced that the product information for mebendazole will be updated to include the risk of fever.

Mebendazole is an anthelmintic and is indicated for the treatment of infections by worms, such as pinworm and common roundworm.

The Lareb received and reviewed 23 reports of fever following the use of mebendazole. Based on the review of reports and other source of information, the relation between mebendazole and pyrexia was deemed plausible.

The Lareb informed the Dutch Medicines Evaluation Board (MEB) about the reports, and the MEB asked the marketing authorization holders to add fever to the product information of mebendazole.

Reference:
Safety updates, Lareb, 24 October 2024 (link to the source within www.lareb.nl)

Medroxyprogesterone

Risk of meningioma

Europe. The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) has recommended measures to minimise the risk of meningioma, a type of brain tumour, with medroxyprogesterone acetate.

Medroxyprogesterone acetate is used for gynaecological (including contraception and endometriosis) and oncological indications.

The committee's recommendations followed a review of data showing an increased risk of meningioma in people taking high doses of medroxyprogesterone acetate (injectables and ≥100 mg tablets) for several years. Although the relative risk of meningioma is significantly increased with the use of high-dose medroxyprogesterone acetate, the absolute risk is very small.

The PRAC recommended that:

- In patients who have a meningioma or have had one in the past, high-dose medroxyprogesterone acetate must not be used, unless it is needed for the treatment of an oncological indication.
- Patients taking high doses of medroxyprogesterone acetate should be monitored for symptoms of meningioma.
- If a patient treated for a non-oncological indication is diagnosed with meningioma, treatment with high-dose medroxy-progesterone acetate must be stopped.
- If a patient treated for an

oncological indication is diagnosed with meningioma, the need for further treatment with high-dose medroxy-progesterone acetate should be carefully considered, on a case-by-case basis, taking into account individual benefits and risks.

Reference:
Patients and carers, EMA, 6 September 2024 (link to the source within www.ema.europa.eu)

Metamizole

Measures to minimise serious outcomes of agranulocytosis

Europe. The PRAC of the EMA has recommended measures to minimise the serious outcomes of agranulocytosis, a known side effect caused by metamizole. Agranulocytosis involves a sudden and sharp decrease in granulocytes that can lead to serious or even fatal infections.

Metamizole, also named as dipyrone or sulpyrine (i.e., the same active substance), is painkiller and indicated for the treatment of moderate-to severe pain and fever.

After reviewing data on the risk of agranulocytosis for metamizole, the PRAC concluded that the existing warnings in the product information need to be updated to increase awareness of this serious side effect and facilitate its early detection and diagnosis.

The updates include:

- Health-care professionals must inform patients to stop taking these medicines and seek immediate medical attention if they develop symptoms of agranulocytosis.
- If patients develop symptoms of agranulocytosis, a test to measure their levels of blood cells, including the levels of different types of white blood cells, must be done immediately. Treatment must be stopped while awaiting the results.
- Metamizole must not be used in patients who are at increased risk of, or susceptible to, agranulocytosis.

Reference:
Patients and carers, EMA, 6 September 2024 (link to the source within www.ema.europa.eu)

Metronidazole, tetracycline

Risk of fixed drug eruption

India. The Signal Review Panel of Pharmacovigilance Programme of India (PvPI), Indian Pharmacopoeia Commission (IPC) has confirmed fixed drug eruption associated with the use of metronidazole and tetracycline, respectively.

The NCC-PvPI, IPC has received and reviewed individual case safety reports (ICSRs) for fixed drug eruption with the use of metronidazole or tetracycline, and found causal relationships between the event and each medicine.

The National Coordination Centre (NCC)-PvPI, IPC has recommended to the Central Drugs Standard Control Organization (CDSCO) to include fixed drug eruption as an adverse drug reaction in the product information for metronidazole and tetracycline.

Reference:
Recommendations of Signal Review Panel, IPC, 30 October 2024 (link to the source within www.ipc.gov.in)

Obeticholic acid

Risk of liver injury in patients without cirrhosis

United States. The US FDA identified cases of serious liver injury among patients being treated for primary biliary cholangitis (PBC) with obeticholic acid (Ocaliva®) who did not have cirrhosis of the liver.

The US FDA previously communicated about the risk of serious liver injury associated with obeticholic acid in May 2021 in PBC patients with advanced cirrhosis.

FDA evaluated liver safety in the post-market clinical trial in patients who were appropriate for obeticholic acid treatment based on the approved indication in the prescribing information. Among these patients, the risk of both liver transplant and death were higher in patients receiving obeticholic acid compared with those receiving placebo.

FDA is notifying health-care professionals and patients of this new safety information, and that frequent liver test monitoring is necessary to identify worsening liver function and ensure appropriate discontinuation of obeticholic acid.

Reference:
MedWatch, FDA, 12 December 2024 (link to the source within www.fda.gov)

(See also WHO pharmaceuticals newsletter No.3, 2021: Obeticholic acid and risk of serious liver injury from United States)

Olanzapine

Potential risk of syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

Canada. Health Canada has updated the product information for olanzapine to include the potential risk of syndrome of inappropriate secretion of antidiuretic hormone (SIADH). SIADH is a condition in which too much antidiuretic hormone causes more water to be held in the body and commonly leads to hyponatremia, which could be life-threatening or fatal consequences.

Olanzapine is indicated for the treatment of schizophrenia and related psychotic disorders, and bipolar disorder.

While a definitive link could not be confirmed, Health Canada's review of the available information could not rule out a possible link between olanzapine and the risks of SIADH and hyponatremia. Despite the limited available evidence, the extensive use of olanzapine in Canada and vulnerability of the patient population who could be prescribed the drug warranted a precautionary approach for these risks.

Reference:
Health Product InfoWatch, Health Canada, October 2024 (link to the source within www.hc-sc.gc.ca)

Thiopurines

Potential risk of intrahepatic cholestasis of pregnancy (ICP)

Saudi Arabia. The Saudi Food & Drug Authority (SFDA) has announced that the product information for thiopurines, including azathioprine and mercaptopurine, will be updated to include the potential risk of intrahepatic cholestasis of pregnancy (ICP). ICP, also known as obstetric cholestasis, is a liver disorder that occurs during pregnancy, characterized by intense itching and elevated bile acid levels.

Azathioprine is indicated for the treatment of inflammatory bowel disease and rheumatoid arthritis, and mercaptopurine is for acute lymphoblastic leukaemia (ALL). Thiopurines have been already labelled for the risk of hepatotoxicity and foetal harm with use during pregnancy, and should not be given to patients who are pregnant or likely to become pregnant without careful assessment of risks versus benefit.

The SFDA advises health-care professionals to closely monitor pregnant patients using thiopurines and educate patients to seek a medical help if they develop signs and symptoms of ICP such as itching, dark urine and pale stools.

Reference:
Safety communication, SFDA, 13 June 2024 (link to the source within www.sfda.gov.sa)

Triamcinolone acetonide (ophthalmic injection)

Risks of endophthalmitis and infective scleritis

Japan. The Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA) have announced that the product information for triamcinolone acetonide (ophthalmic injection) should be updated to include the risks of endophthalmitis and infective scleritis.

Triamcinolone acetonide is a synthetic glucocorticoid corticosteroid with anti-inflammatory action, and its ophthalmic injection is intended for the visualization of the vitreous body during vitreous surgery and the treatment of alleviation of macular oedema associated with diabetes.

The MHLW/PMDA reviewed several reported cases of endophthalmitis or infective scleritis, for which a causal relationship between the medicine and event was reasonably possible.

Health-care professionals should monitor patients closely after administration of this medicine and instruct

the patients to immediately consult physicians if any abnormalities occur.

Reference:
Pharmaceuticals and Medical Devices Safety Information, MHLW/PMDA, December 2024 (link to the source within www.pmda.go.jp)

Vancomycin

Risk of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome

India. The Signal Review Panel of PvPI, IPC has confirmed drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome associated with the use of vancomycin.

The NCC-PvPI, IPC has received and reviewed ICSRs for DRESS syndrome with the use of vancomycin, and found a causal relationship between them.

The NCC-PvPI, IPC has recommended to the CDSCO to include DRESS syndrome as an adverse drug reaction in the product information for vancomycin.

Reference:
Recommendations of Signal Review Panel, IPC, 30 October 2024 (link to the source within www.ipc.gov.in)

Varicella-zoster virus gE vaccine

Rare risk of Guillain-Barré Syndrome (GBS)

Australia. The Therapeutic Goods Administration (TGA) has updated the product information on varicella-zoster virus glycoprotein E (gE) vaccine (Shingrix®) recognising that Guillain-Barré Syndrome (GBS) is a very rare adverse event.

Shingrix® is a non-live vaccine based on the varicella-zoster virus gE, which is indicated for the prevention of herpes zoster and post-herpetic neuralgia in adults. Its preexisting warning about GBS described the findings of an observational study which showed an increased risk of GBS observed during the 6 weeks following vaccination although the evidence was insufficient to determine a causal relationship.

The TGA conducted an investigation into the possible association between Shingrix® and GBS after receiving two reports detailing this adverse event, and recommended that GBS be included in the adverse event section of the product information.

Health-care professionals should be aware of GBS cases following vaccination with Shingrix®. Patients should be warned of this possible but very rare risk and encouraged to seek medical attention if they experience symptoms.

Reference:
Safety updates, TGA, 29 October 2024 (link to the source within www.tga.gov.au)

Voxelotor

Suspension of marketing authorisation

1. Europe. The Committee for Medicinal Products for Human Use (CHMP) of the EMA has recommended suspending the marketing authorisation for the sickle cell disease medicine, voxelotor (Oxbryta®). This measure is taken as a precaution while a review of emerging data is ongoing.

Voxelotor is indicated for the treatment of haemolytic anaemia (excess breakdown of red blood cells) in patients aged 12 years and older who have sickle cell disease.

The recommendation follows emerging safety data from two registry-based studies, which indicate that patients in the studies had a higher occurrence of vaso-occlusive crises (VOC) during treatment with voxelotor than they did before starting the medicine. VOC are among the most common complications of sickle cell disease; they involve episodes of acute pain and can lead to further health complications, such as arthritis, kidney failure and stroke.

These new safety data emerged while EMA was already reviewing the benefits and risks of voxelotor as part of an ongoing review started in July 2024. This was triggered as data from a clinical trial showed that a higher number of deaths occurred with voxelotor than with placebo and another trial showed the total number of deaths was higher than anticipated.

The CHMP recommended that the authorisation, marketing and supply of the medicine be suspended until

all the available data have been assessed in the ongoing review.

Reference:
Patients and carers, EMA, 26 September 2024 (link to the source within www.ema.europa.eu)

2. United States. The US FDA has alerted patients, caregivers, and health-care professionals that voxelotor is being voluntarily withdrawn from the market by the manufacturer due to safety concerns.

The manufacturer of voxelotor has announced it is voluntarily withdrawing the medication from the market, ceasing distribution, and discontinuing all active clinical trials and expanded access programs for voxelotor because recent data indicate the benefit of voxelotor does not outweigh the risks for the sickle cell patient population.

Reference:
Drug Safety and Availability, FDA, 26 September 2024 (link to the source within www.fda.gov)

Call for submissions

We are very keen to make this newsletter even more useful to all our readers. We are calling out to all national medical products regulatory authorities to send us the latest information on safety and regulatory actions on medicinal products from their countries.

We also welcome short reports on any recent events or achievements in pharmacovigilance in your country.

All submissions will be reviewed for relevance and subject to the WHO internal selection, editorial review, and clearance process.

Please send your submissions or questions to: pvsupport@who.int

Bromocriptine

Need for blood pressure monitoring

United Kingdom. The Medicines and Healthcare Products Regulatory Agency (MHRA) has announced that blood pressure monitoring of patients prescribed with bromocriptine is essential especially during the first days of treatment.

Bromocriptine is a dopamine agonist and is indicated for the prevention or suppression of post-partum physiological lactation only where medically indicated.

The MHRA has received a Yellow Card report which highlighted the need for blood pressure monitoring during bromocriptine treatment, especially during the first days of therapy.

Health-care professionals should, when prescribing bromocriptine for any of its indications, carefully monitor for an increase in blood pressure, especially during the first days of therapy and with any subsequent dose increases. If patients prescribed bromocriptine present with signs and symptoms of hypertension, treatment should be discontinued, and the patient evaluated promptly.

Reference:
Drug Safety Update, MHRA, 24 October 2024 (link to the source within www.gov.uk/mhra)

Doxycycline

Risk of suicidality not supported

Europe. The PRAC of the EMA has concluded that the currently available evidence is not sufficient to establish a causal relationship between doxycycline and the risk of suicidality.

Doxycycline is a broad-spectrum antibiotic, widely used to treat a wide range of infections caused by bacteria.

A safety signal on the risk of suicidality, suicidal thoughts or actions with doxycycline was raised based on cases reported and the medical literature.

After reviewing all available evidence from spontaneous reports, the literature, the discussion on possible mechanisms and the study performed via DARWIN EU (Data Analysis and Real World Interrogation Network), the PRAC considered that the evidence is not sufficient to establish a causal relationship and that no update to the product information of doxycycline is warranted.

Reference:
Patients and carers, EMA, 29 November 2024 (link to the source within www.ema.europa.eu)

Finasteride, dutasteride

Review of risks of suicidal thoughts and behaviours started

Europe. The EMA has started a review of finasteride and dutasteride following concerns regarding suicidal ideation and behaviours.

Finasteride (oral 1 mg tablet and skin solution) is used to treat the early stages of androgenic alopecia in men aged 18 to 41 years. Finasteride (oral 5 mg tablet) and dutasteride (0.5 mg capsules) are used to treat men with benign prostatic hyperplasia (BPH).

Finasteride and dutasteride taken by mouth have a known risk of psychiatric side effects, including depression. Suicidal ideation has also recently been added as a possible side effect of unknown frequency in the product information for Propecia® and Proscar®.

To minimise the risks, measures are already in place for finasteride, including warnings in the product information for health-care professionals to monitor patients for psychiatric symptoms, stop treatment if symptoms occur, and recommendations for patients to seek medical advice if they experience psychiatric symptoms.

Reference:
Patients and carers, EMA, 4 October 2024 (link to the source within www.ema.europa.eu)

(See also WHO pharmaceuticals newsletter No.3, 2024: Finasteride and risk of mood alterations in Canada, No.1, 2024: Finasteride and risk of suicide-related events in Japan, Article on drug-induced suicidality by Swissmedic)

Levofloxacin

Medication error: incorrect drug administration rate

Egypt. The Egyptian Pharmacovigilance Center (EPVC), Egyptian Drug Authority (EDA) has alerted health-care professionals of incidents of incorrect drug administration rate as medication error with use of levofloxacin intravenous infusion.

Levofloxacin is a fluoroquinolone antibiotic used to treat infections caused by susceptible bacteria.

The EPVC received and reviewed a case series reports of levofloxacin intravenous infusion with incorrect drug administration rates, which resulted in complications including hypotension, dyspnea, hypersensitivity, anaphylactic reactions, rash and headache.

Health-care professionals are advised to follow the precautions for administration of levofloxacin intravenous infusion including: slow rate of infusion over 60 minutes for 250 to 500 mg and over 90 minutes for 750 mg; route by intravenous infusion only and not by bolus; and to avoid using solution containing multivalent cations (i.e. magnesium, calcium).

Reference:
Newsletter, EDA, October 2024 (*link to the source within www.edaegypt.gov.eg*)

Oral anticoagulants

Potential risk of mood changes

New Zealand. The Medsafe is reviewing the risk of mood changes in individuals taking direct acting oral anticoagulant medicines following receiving a small number of reports of psychiatric changes associated with rivaroxaban use.

Oral anticoagulants (apixaban, dabigatran and rivaroxaban) are referred to as 'blood thinners' and are prescribed to treat and/or prevent blood clots.

Medsafe is encouraging further reporting to obtain more information on this potential safety signal. Although the signal was identified with rivaroxaban, reporting of mood disorders with other direct acting oral anticoagulants is also encouraged.

Reference:
Safety information, Medsafe, 8 August 2024 (link to the source within www.medsafe.govt.nz)

Valproate

Potential risk of neurodevelopmental disorder in children from paternal exposure

1. United Kingdom. The MHRA has provided new advice on the use of valproate (INN: valproic acid, and the sodium salt, sodium valproate) in male patients in addition to the measures announced in January 2024.

Valproate is authorised for the treatment of epilepsy and bipolar disorder.

A retrospective observational study, combining analyses of electronic medical records in Norway, Denmark and Sweden, has indicated a possible association between valproate use by men around the time of conception and an increased risk of neurodevelopmental disorders in their children; however, the causal role of valproate is not confirmed.

As a precaution, health-care professionals should recommend that male patients use effective contraception (condoms, plus contraception used by the female sexual partner) throughout the valproate treatment period and for 3 months after stopping valproate, to allow for one completed sperm cycle not exposed to valproate.

Reference:
Drug safety updates, MHRA, 5 September 2024 (link to the source within www.gov.uk)

(See also WHO pharmaceuticals newsletter No.3, 2024: Valproate and potential increased risk of neurodevelopmental disorders in children from Europe and United Kingdom.)

2. Japan. The MHLW and the PMDA have announced that the product information for valproate should be revised to inform health-care professionals of the two reports with and without a statistically significant increased risk of neurodevelopmental disorder in infants/children with paternal exposure to valproate.

First study is as described in the previous article from United Kingdom. Second study is a cohort study using health register and social register data in Denmark, where no significantly increased risk of neurodevelopmental disorder was observed in children exposed to valproate.

Considering the results of the two studies, the MHLW/PMDA concluded that the possibility of occurrence of neuro-developmental disorder in infants/children with paternal exposure to valproate cannot be ruled out, although it has not been fully evaluated - regarding the first study, performing a new study for further investigation has been required by the EMA's PRAC taking the study's limitations into consideration.

Reference:

Pharmaceuticals and Medical Devices Safety Information, MHLW/PMDA, September 2024 (link1 to the source and link2 to the text to be added in the product information within www.pmda.go.jp)

WHO Pharmacovigilance Partners' Meeting
New Delhi, India, 13 October 2024

A WHO Pharmacovigilance Partners' Meeting was organized on 13 October 2024 in New Delhi, India on the margins of the 19th International Conference of Drug Regulatory Authorities (ICDRA). 147 people from 68 countries participated in this face-to-face meeting, to review the WHO Global Smart Pharmacovigilance Strategy. A synopsis of the draft Strategy is as below. The revised Strategy will be available in the coming months.

WHO Pharmacovigilance Partners' Meeting/©WHO

WHO Global Smart Pharmacovigilance Strategy: synopsis

Background

When faced with competing health priorities, countries will have to invest their limited resources judiciously, by focusing pharmacovigilance efforts on priority products and adopting approaches that are relevant to their settings, by relying on the work of other countries when possible and building national competence for those activities that cannot be delegated. This is Smart Pharmacovigilance.

A Global Smart Pharmacovigilance Strategy is proposed as an approach that can help establish robust, proactive, safety monitoring and risk management systems that leverage existing infrastructure but consider the specific constraints and requirements of the healthcare settings. The objective is to build on the learnings from the Smart Safety Surveillance (3S) pilot projects[1], the Global Vaccine Safety Blueprint (GVSB)[2] and the COVID-19 pandemic experiences[3], to develop a comprehensive and sustainable safety monitoring and risk management practice as an integral part of healthcare and regulatory system, enabling quick, adequate and sustainable responses to potential safety risks with priority medicinal products in all Member States. A key aspect of the 'Smart' approach lies in the fact that not all products would be monitored the same way, and not all countries would need to do everything. Instead, the focus would be on a development strategy that best serves the priority pharmacovigilance needs of the country while utilizing the information and leveraging the resources in other countries, to mutual benefit.

[1] N. Iessa et al. Drug Saf. 2021 Oct;44(10):1085-1098. doi: 10.1007/s40264-021-01100-z. Epub 2021 Jul 31. Smart Safety Surveillance (3S): Multi-Country Experience of Implementing the 3S Concepts and Principles.
[2] WHO. Global vaccine safety blueprint 2.0 (GVSB2.0) 2021-2023. 2022 February 21. https://www.who.int/publications/i/item/9789240036963
[3] R Chandler et al. BMJ Glob Health. 2024 Mar 7;9(3):e014544. doi: 10.1136/bmjgh-2023-014544. Collaboration within the global vaccine safety surveillance ecosystem during the COVID-19 pandemic: lessons learnt and key recommendations from the COVAX Vaccine Safety Working Group

Four key principles underpin the strategy: 1) Previous pharmacovigilance efforts and lessons learnt; 2) risk-based (approach to prioritize) pharmacovigilance activities; 3) work-sharing and reliance in pharmacovigilance; 4) pharmacovigilance as part of stepwise regulatory system strengthening efforts.

1) **Previous pharmacovigilance efforts and lessons learnt**: Pharmacovigilance has come a long way since the establishment of the WHO Programme for International Drug Monitoring (PIDM) in 1968, and it is important to learn from and build on previous accomplishments. Successes can be observed at national, regional, and global levels. Tailored approaches are taken in different settings according to assessed needs and functionality.

2) **Risk-based approach and prioritization:** This consists of focusing PV efforts on priority products: 1) Products that are exclusive to their settings, introduced to address a disease of limited geographic prevalence, data for which will not be available or forthcoming from the rest of the world; 2) Products with limited clinical data, receiving accelerated approvals for several reasons and to be introduced simultaneously in high income- and low- and middle-income countries (LMICs), with little global experience that LMICs can rely-on.

3) **Work-sharing and Reliance:** The overarching vision for the WHO General Programme of Work (GPW14) is to promote, provide and protect the health and well-being of all people everywhere. This strategy recognizes variation in health systems, some with fragile health systems on one end of the spectrum and more mature health systems on the other end. It is proposed that the focus and prioritization of PV consider available resources and regulatory system capacity. The principles of work-sharing and reliance would be key considerations.

4) **Pharmacovigilance as part of stepwise regulatory system strengthening efforts:** Pharmacovigilance needs to be embedded into a regulatory framework for sustainability. Relevant legal frameworks empower regulatory agencies in the implementation and oversight of safety monitoring and related activities. The WHO Global Benchmarking Tool (GBT)[4] helps to benchmark and assess the maturity of an entire national regulatory system. It consists of a set of indicators categorized into nine regulatory functions, including PV. Following a benchmarking exercise, gaps or areas where the PV system can be improved are incorporated into an institutional development plan (IDP) providing a roadmap to stepwise system strengthening approach.

In view of some of the common processes and requirements between medicines and vaccines' safety surveillance, the strategy advocates the use of data tools and methods, and regulatory framework across the two product types. It promotes the use of existing networks and platforms such as the WHO Programme for International Drug Monitoring (PIDM), the African Medicines Regulatory Harmonization (AMRH), South East Asia Regulatory Network (SEARN), Association of South East Asian Nations (ASEAN), the Regional Pharmacovigilance Network of the Americas and Caribbean Sub-regional Network (VigiCarib), the Western Pacific Regional Alliance of National Regulatory Authorities and the Coalition of Interested Parties (CIP), to name a few.

Medicine and vaccine safety communication is necessary throughout the life cycle of a product and is addressed as a cross-cutting component throughout the strategy. Methods to enhance communication are provided.

A few hypothetical scenarios of the introduction of medicines and vaccines in different settings and the application of the above concepts are also described, to help countries draft their own pharmacovigilance development strategies and plans.

The strategy's success can be measured by the number of countries adopting it and stakeholders contributing to its implementation. Several measures of impact are proposed, for example, changes in maturity of PV system measured by the Global Benchmarking tool, improvements in key performance indicators and others.

[4] WHO Global Benchmarking Tools (GBT) for evaluation of national regulatory systems of Medical Products - Revision VI. 2021 May 10. https://www.who.int/publications/i/item/9789240020245