



The International Society of Pharmacovigilance Vaccines Special Interest Group: Challenges and Opportunities

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1 Introduction

Over the course of only 2 years, severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), the virus that causes COVID-19, has shifted traditional paradigms in the areas of infectious disease epidemiology, outbreak response and scientific publishing. Many of the principles and infrastructures that were built and agreed upon in the pre-COVID era have been challenged and have adapted under the enormous pressure of political forces and public demands. Innovations in clinical vaccine development resulted in the approval of several vaccines from a diversified portfolio of vaccine technologies, compressing traditional development timelines of up to a decade to within one year after the beginning of the pandemic.

The emergence of a number of safety signals during the COVID-19 vaccination campaigns has been a reminder that even vaccines, one of our most important public health tools, may result in harm to individuals. A new syndrome called vaccine-induced thrombotic thrombocytopenia/thrombotic thrombocytopenia syndrome has emerged after vaccination with the adenovirus-based COVID-19 vaccines and exemplifies that serious harm, albeit rare, can occur and can have fatal outcomes [1, 2]. The observation of myocarditis in young males associated with the mRNA-platform COVID-19 vaccines has demonstrated that risks of harm may not be equal between different sexes or ages [3]. Furthermore, menstrual disorders after vaccination have been reported from thousands of women throughout the world [4–7] and a review was initiated by the European Medicines Agency in February 2022 [8], drawing attention to the importance of sex-specific and patient-reported outcomes in clinical trial designs.

It is within this background that the Vaccine Special Interest Group (SIG) has emerged, and it is looking to contribute to the growth of vaccine safety science.

2 Formation and Membership of the International Society of Pharmacovigilance Vaccine Special Interest Group

In 2019, the International Society of Pharmacovigilance (ISoP) Executive Committee encouraged the creation and development of a new SIG in ISoP dedicated to exploring issues relating to vaccine pharmacovigilance. A proposal that included a description of the aims and objectives for the SIG was presented and approved by the, and thus, the SIG was formally launched at the 19th annual meeting of ISoP in Bogotá in October 2019.

The overall aim of the SIG is to provide a focal point for ISoP members who are interested in vaccine safety to share and provide information on relevant issues and developments and to support vaccine pharmacovigilance.

The key objectives are:

- To provide bi-monthly news and information bulletins by email to VSIG members
- To organise a session at the ISoP annual meeting on the topic of vaccine safety
- To advise the ISoP Executive Committee, where required, on issues relating to vaccine safety
- To foster collaboration between national pharmacovigilance centres and national immunisation programmes
- To encourage collaboration with individuals working within the field of vaccinology to expand knowledge of how vaccines cause adverse reactions
- To develop and support improved approaches to communication regarding the benefits and risks of vaccines, in particular as our knowledge grows regarding the inter-

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individual variation in immune responses and the risk for adverse events following immunisation (AEFI)

Interest in the SIG grew significantly in late 2020 and early 2021. The Vaccine SIG currently includes 19 members with wide global representation, from industry, regulatory, consultancy and non-profit/non-governmental organisations. Given that its earliest days of existence coincided with the beginning of the pandemic, there was an initial effort to join various webinars on the development of COVID-19 vaccines and preparations for safety monitoring, such as those sponsored by the International Society for Vaccines and the Brighton Collaboration. The SIG designed an infographic “*Covid-19 Vaccine Safety: What you need to know and how you can help*” and co-hosted a 7-week webinar series “*Covid-19 vaccine vigilance*” with the ISoP Latin America and Israel Chapters in the spring of 2021. The SIG has most recently heard a presentation from Karina Top, a paediatric infectious diseases physician/epidemiologist from Dalhousie University, who is leading the formation of the International Network of Special Immunization Services (INSIS), a network whose aim is to collect data and clinical samples from a global pool to allow further research of risk factors for rare adverse events following immunisation.

3 Challenges and Opportunities

As the world enters a new phase of the COVID-19 pandemic, it is clear that challenges recognised prior to the arrival of SARS-CoV2 must be addressed in preparation for the next pandemic.

First, direct introduction of new vaccines into regions of the world vulnerable to emerging infectious diseases increases the demand on pharmacovigilance systems in countries with limited resources to monitor for serious and unexpected safety signals in the early post-licensure period. Previously, new vaccines, such as pneumococcal, human papilloma virus and rotavirus, were developed and used for a number of years in high-income countries (HIC) prior to being implemented into vaccination programmes in low- and middle-income countries (LMIC). During this time “vaccine pharmacovigilance” infrastructure developed in HIC with databases for passive surveillance for the identification of rare events and networks of electronic health data, which can be used to confirm signals and perform studies to estimate risk. “Potential risks” identified during clinical development are incorporated into risk management plans for further characterisation in post-authorisation safety studies. Central to this model is direct interaction and collaboration between national regulatory authorities (NRA) and vaccine developers/marketing authorisation holders. In contrast, an infrastructure with a focus on “vaccine safety”

was created in LMIC using the roadmap described in the first Global Vaccine Safety Blueprint [9]. Adverse events following immunisation (AEFI) collection forms and guidance and tools for AEFI causality assessment were created primarily to detect safety concerns related to vaccine quality issues and immunisation errors. Central to this model are national immunisation programmes (NIP). Going forward, it will be important to increase communication and collaboration between NRA and NIP to ensure sharing and pooling of reports of AEFI to improve the ability of LMIC to identify signals for serious, unexpected events. Furthermore, building enhanced capacity for active vaccine safety surveillance would allow for epidemiological studies to test signal hypotheses, moving LMIC into the practice of “vaccine pharmacovigilance”.

Second, progress in vaccine safety science has been hindered by the lack of a coordinated effort to pool cases of rare adverse events for characterisation of possible risk factors and elucidation of mechanisms. Several vaccine safety issues in the last decade (Pandemrix and narcolepsy, Dengvaxia and severe dengue) have suggested the presence of individual-level risk factors for the occurrence of these adverse outcomes [10, 11], and the field of “adversomics” has emerged as the study of vaccine adverse reactions using immunogenomics and systems biology approaches [12]. The vaccine safety community can learn lessons from the field of rare diseases, which requires pooling of cases from larger geographical regions for specialist care and research.

Third, conducted surveys have documented concerning decreases in public confidence in vaccine safety, and the WHO declared that vaccine hesitancy was one of the ten threats to global public health in 2019 [13]. The social unrest in many countries protesting vaccination passports and vaccine mandates suggest the need to re-address public confidence in vaccination programmes, particularly as mortality from the COVID-19 disease falls. Such complex issues require the engagement of professionals such as medical anthropologists, behavioural psychologists and ethicists.

The Vaccine SIG believes that it can play an important role in working within the greater vaccine ecosystem to address these challenges, by bringing greater awareness to the unique challenges in vaccine safety to the greater pharmacovigilance community and by cultivating an atmosphere of open discourse to allow progress in the field of vaccine safety science.

Declarations

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