

# Pharmacovigilance 2030 Invited Commentary for the January 2020 “Futures” Edition of *Clinical Pharmacology and Therapeutics*

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**A new healthcare system is emerging that encompasses systems approaches to biology and medicine, radically enhanced capabilities for collecting, integrating, storing, analyzing, and communicating data and information, and increasing numbers of networked and activated patients and consumers.**

Pharmacovigilance systems around the world have come a long way in the last 60 years. Systems have evolved from reliance on the individual case safety report (ICSR) of suspected adverse drug reactions (ADRs), through addition of the periodic safety update report, and risk management plan, to the current era where many stringent regulators have a pallet of regulatory tools and access to an ever increasing spectrum of data sources, real-world or otherwise. Modern systems also leverage the collaborative efforts of multiple stakeholders, notably the biopharmaceutical industry, regulators, healthcare professionals, patients, and academia.

Pharmacovigilance is well stocked with clairvoyants who have made many claims, sometimes wild, for the future, including that we will rely on artificial intelligence and robotics, that the ICSR is dead (or should be dead), or that mobile health holds the ultimate promise for increasing engagement and impact.<sup>1</sup> There is no doubt that technology

is advancing rapidly, that the accumulation of data is increasing logarithmically, and that society is changing, particularly the engagement of patients in healthcare decision making. However, some things stay the same. The ultimate goal remains to optimize the safe and effective use of medicines so patients can benefit in terms of health and quality of life while suffering the minimum of side-effects. The challenges to optimizing safe and effective use of medicines are common to all regulatory and healthcare systems: how to influence the behavior of patients and healthcare professionals based on robust evidence and sound decision making.

We make three predictions for pharmacovigilance in 2030. (1) Collection and reporting of ICSRs will be smarter. (2) Measurement of on-market performance of medicines will inform decision makers and users of medicines. (3) Improved engagement of patients and healthcare professionals will increase the impact of pharmacovigilance.

## PREDICTION 1: SMARTER COLLECTION AND REPORTING OF ICSRs

By the end of 2018 EudraVigilance, the European database of ICSRs held over 14 million case reports and Vigibase, the World Health Organization (WHO) database held over 20 million. Although only representing a snapshot in time, these are electronic health records and have the huge value of capturing a suspicion of a patient or health care professional that a medicine may have caused an adverse reaction. With the onset of the digitalization of health care, there is the opportunity to access more and better data and provide alternative approaches in pharmacovigilance, including both the detection and evaluation of ADRs. This means that we need to design our systems based on an abundance of data rather than a scarcity.<sup>2</sup> However, over recent years, the proportion of new drug safety issues detected from ICSRs has been high at around 55%,<sup>3</sup> and the number of product withdrawals based partly or wholly on ICSRs has also remained high.<sup>4</sup> These observations have occurred despite the increasing interest in other data sources for signal detection. The evidence suggests that ICSRs remain a very useful data source for detecting potential new safety issues, whereas electronic health records (EHRs) are more useful for evaluating the issues already detected. This is in line with the principle of hypothesis testing in a dataset separate from that in which the hypothesis was generated.

We do not question that there are opportunities to improve the collection and management of ICSRs,<sup>5</sup> and in the way such reports are submitted to regulators. We also acknowledge that the investment in the collection and management of ICSRs has been and continues to be high. However, we believe that by 2030 ICSR reporting

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will be much smarter. New technologies including e-Health apps, as well as the international collaboration between industry and regulators to revise International Conference on Harmonization (ICH) guideline E2D provide excellent opportunities to optimize data collection and management. The wider reach of the reformed ICH also provides the chance of a more global implementation of a harmonized approach. Our message is to protect and improve ICSRs, our main source of safety signals. The ICSR is far from dead but it can and should be improved. We do caution that future process improvements, including the update of processes based on artificial intelligence and robots, should be evidence based and the impact of changes should be monitored particularly in terms of data quality and signal detection.

### **PREDICTION 2: MEASUREMENT OF ON-MARKET PERFORMANCE OF MEDICINES**

In 2010, the proposition that healthcare is evolving from reactive disease care to care that is predictive, preventive, personalized, and participatory (the “4Ps”) was regarded as highly speculative. Today, the core elements of that vision are widely accepted.<sup>6</sup>

In parallel with the move to the 4Ps, opportunities have increased to leverage the exponential growth in real-world data, including data from EHRs, disease registries, claims data, mobile applications, and social media.<sup>7</sup> These sources, particularly EHRs and claims data, can provide new insights in health, disease, and, critically, the use and performance of medicines, including both benefits and risks.

In 2020, in the global world of medicines regulation, traditional barriers have started to come down, including the binary definition of a medicine to have preauthorization or postauthorization, for studies to use randomization or observation, and, importantly, for safety to be measured and evaluated separately from efficacy. Pharmacovigilance has made great progress in moving from a reactive activity driven by spontaneous reports of suspected ADRs to a more proactive activity with planning starting before the product is on the market.

By 2030, to move to the next level, we need the monitoring of medicines to encompass both safety and efficacy on the market

(performance) and for this to be planned well before market entry. If this is done well and representative data are available, data can be analyzed and fed into decision making by regulators and pharmaceutical companies for product labeling, to health technology assessment bodies for assessment of value, to payers for reimbursement decisions, and as health information to support individual decisions by healthcare professionals and patients (contributing to the realization of precision medicine).<sup>8</sup> Significant progress in accessing and analyzing real-world data has been made through initiatives, such as Sentinel in the United States, the Observational Health Data Sciences and Informatics (OHDSI) network, and harnessing the rich and diverse longitudinal healthcare data in the European Union. Challenges to accessing and analyzing real-world data continue<sup>9</sup> of which the methodological challenge to evaluating on-market efficacy is perhaps the greatest. Although acknowledging these challenges, we believe that by 2030, for targeted new medicines, a planned monitoring of performance on the market will take place with nearly real-time decision making by regulators to optimize the safe and effective use of medicines.

### **PREDICTION 3: IMPROVED ENGAGEMENT OF PATIENTS AND HEALTHCARE PROFESSIONALS**

New forms of participation by patients and healthcare professionals are key to delivering the vision for transformation of healthcare in the digitally networked era. One of our society's greatest assets is the increasing determination of healthcare consumers to better manage their own health using the internet to gather information and their ability to self-organize using social networking tools.<sup>10</sup> Therefore, our final prediction for 2030 is that regulators will engage patients and healthcare professionals much more intensively to maximize the positive impact of pharmacovigilance on the safe and effective use of medicine.

Both the Holy Grail and the Achilles Heel of pharmacovigilance are to change the behavior of patients and healthcare professionals based on information about a medicine's safety and efficacy (performance). Recent work conducted in the European Union on measuring the impact of pharmacovigilance<sup>1</sup> has found

sometimes disappointing results of regulatory action taken, a recent example being the 2013 review of pregnancy safety of valproate and the lack of impact of stringent warnings in product information in terms of prescribing practice.

Different regulatory authorities around the world have made major efforts to engage with healthcare professionals and patients and this represents a dramatic change compared with 20 years ago when regulation was fundamentally disengaged from the key stakeholders. However, there is much further to go if we are to be truly effective in responding to patients' needs and to enabling patients to use their medicines optimally. Opportunities include electronic product information updated in close to real-time supporting decision-support systems for the prescription, dispensing, or use of medicines, and fostering much closer relationships between regulators and patients and healthcare professional organizations. The latter means that, when there is a need for change and a call to arms goes out, stakeholders are ready to listen, to trust, and to change behavior. We believe that in 2030 much more of the regulators' time will be spent engaging with patients and healthcare professionals and ensuring that the information provided to them is effective in supporting the safe and effective use of medicines.

### **CONCLUSION**

The pace of change in pharmacovigilance is rapid. We must measure the impact of our work and ensure we make evidence-based process improvements. We should value what works and strive to meet the challenges and opportunities of our fast-changing world, a world of increasing openness, data collection, technological power, and patient engagement. We predict that smarter collection and reporting of ICSRs, of measurement of on-market performance of medicines, and of improved engagement of patients and healthcare professionals will be the most significant changes in pharmacovigilance by 2030. We also believe that these changes will enable faster access to life-saving treatments for patients around the world and for these treatments to be used more effectively and safely.

We look forward to seeing if our predictions come true, and we might just try to make them.

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**DISCLAIMER**

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