Our position on
Pharmacovigilance

What is the issue?

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine or vaccine related problem.[i]

At GSK, we apply consistent pharmacovigilance principles across our entire product portfolio. By taking this approach, we aim to enhance patient care and safety in relation to the use of our marketed and investigational medicines and vaccines. We also look to support public health programmes by providing reliable, balanced information to inform on the overall benefits and risks of all GSK products.

This paper outlines the well-established and rigorous worldwide system that GSK has in place to monitor and review the safety of our products (e.g. medicines and vaccines) throughout clinical development and following their approval by regulatory authorities.

What is GSK's view?

- Patient safety is a fundamental principle for GSK. We comply with international regulations governing the reporting, analysis and communication of safety information. We have a governance framework and policies in place to help us detect and act on any side effects and other human safety information that may be associated with our products.

- We are committed to identifying and managing human safety information to help safeguard those who take our products or take part in our human subject research. All GSK employees and complementary workers across the world are trained on their responsibilities to report human safety information.

- We apply computerised statistical tools to support identification and evaluation of safety information; for example, the identification of new side effects or a change in the nature, frequency or severity of known side effects.

- GSK is committed to continuously evaluating the benefit/risk profile of our products. All products in development are assessed for their benefits versus risks at milestone reviews. Marketed products are regularly assessed throughout their lifecycles. We are committed to transparency in our evaluation and communication of these benefits and risks with patients, prescribers, payers and regulators.

- The science of pharmacovigilance is continuously evolving, and we are actively involved in working with industry, regulators, healthcare professionals (HCPs) and patients to enhance methodologies in this area.

Background

Product development and safety issues

Before evaluation of a potential new product in humans can begin, appropriate preclinical (or laboratory) research must be conducted. This research typically involves years of experiments including animals and human cells. If this stage of testing is successful, data is provided to regulatory authorities, requesting approval to begin evaluating the potential new product in humans. This evaluation is

conducted through interventional clinical trials, usually conducted in four main phases and governed by strict regulation:

Phase I

Phase I studies are primarily concerned with assessing the investigational product's safety usually in a small number of healthy human volunteers and are designed to determine what happens to the investigational product in the human body.

Phase II

An investigational product that passes Phase I testing then moves on to Phase II, which usually includes the "proof of concept" stage. Here, for the first time, it is administered to carefully selected patients suffering from the disease which the product will potentially address.

The main aim of these studies is to determine if the investigational product has a beneficial effect on the illness it is intended to target, as well as the amount and frequency of dosing that will achieve the optimal benefits for patients with the fewest side effects.

Phase III

In Phase III studies, the principle objectives are to demonstrate the safety and effectiveness of the investigational product in the typical patient likely to use it; to confirm effective dosing levels; to identify side effects or reasons why the treatment should not be given to people with another condition (known as 'contraindications'); and to build knowledge of the risks/ benefits of the product by comparing results with those achieved by existing treatments.

Phase IV

Trials of an investigational product may continue after it has been approved for marketing. Phase IV trials may further evaluate the effect of the product for the approved use, assess other potential uses or yield additional safety data. Regulatory agencies may require these trials to address specific questions.

Other types of clinical research, such as non-interventional research (using data collected during the provision of routine healthcare) and analyses of data that is combined from a number of clinical trials (e.g. meta-analyses), are increasingly seen as important evidence in the evaluation of the risks and benefits of products.

GSK's safety governance framework

We assess the benefit/risk profile of our products throughout their lifecycle, using a benefit/risk framework and appropriate analyses. When information is found that changes the benefit/risk balance in a negative direction, action is taken to characterise, communicate and minimise the risk.

Proposed actions are discussed with regulatory authorities and can include modifying the prescribing information (which includes the patient information leaflet), sending communications to HCPs and sometimes carrying out further clinical trials, epidemiological studies, post-authorisation safety studies and/or other risk management measures. In certain cases, it may be appropriate to stop clinical trials or to withdraw the medicine from the market.

GSK collects information on possible side effects of its products from multiple sources including:

- Clinical trials and clinical trial investigators
- Ad hoc (spontaneous) reports from HCPs and patients
- Regulatory authorities
- Interactive digital media, patient support programmes and market research studies
- Medical and scientific literature
- Newspapers and social media

It is GSK policy that staff are required to immediately report any issues relating to the safety or quality of our products. Our Global Safety department ensures that all safety information is collected, managed and reported in accordance with the requirements of regulatory authorities around the world.

Governance bodies

Our Chief Medical Officer (CMO) is accountable for the Patient Safety enterprise risk and human safety matters, in collaboration with the Head of Global Safety and Pharmacovigilance. A safety governance board oversees implementation of our control framework, and GSK's Global Safety Board ensures that human safety is addressed proactively throughout a product's lifecycle.

The GSK Global Safety Board proactively addresses human safety throughout each product's lifecycle and reviews the safety of GSK products. At designated milestones during the research and development stage, the Global Safety Board reviews the benefit/risk balance of pharmaceutical medicines, and the protection of patient welfare.

The Global Labelling Committee reviews and approves the prescribing and/or product information for GSK products, as well as updates when appropriate, and may refer labelling issues related to significant safety concerns to the Global Safety Board for advice and/or decision making. The Global Safety Board may direct teams to work with labelling committees to create or amend labelling related to safety issues.

Initiatives to enhance pharmacovigilance

Tools and processes used in pharmacovigilance are continually evolving. Effective use of these tools, along with improved reporting and communication, helps to ensure that human safety information can be better identified in investigational and marketed products. Initiatives to improve the pharmacovigilance framework focus on and include:

- **Improving reporting of human safety information by HCPs, patients and consumers:** Collection of data on rare side effects through company or regulatory agency databases serves as an important starting point for possible further action. GSK is an active participant in cross-industry initiatives to improve current practices.
- **Next generation pharmacovigilance:** GSK is working with other companies and third-party collaborators to further advance pharmacovigilance capabilities using the new and evolving technologies in data science and computing.
- **Strengthening education of medical students and HCPs in developing countries:** We have actively engaged with several low-and-middle income countries to facilitate the national

pharmacovigilance reporting system through a training and mentoring program of HCPs in these countries.

- **Ensuring compliance with the Identification of Medical Products (IDMP) Project:** IDMP is a set of international data standards for the unique identification of medicines. The standards allow for identification of a product, where individual components are sourced and where it is marketed, enabling consistent analysis of safety issues across products and manufacturers.
- **Using novel technologies:** Novel technologies such as real-life/real-time databases allow companies and regulators to access larger electronic health record information from anonymised data to help identify a potential association between a side effect and a particular medicine, or combination of medicines.
- **Pregnancy registries:** The creation of national or international pregnancy registries to gather information on medicines and vaccines received by a mother during pregnancy, together with the health outcome for the mother and baby which helps with the monitoring of safety of medicines and vaccines in pregnancy.

GSK supports all of these approaches to ensure that the benefits of our products continue to outweigh their risks. We are committed to collaborating with industry colleagues, regulators, healthcare providers, patients, consumers and patient advocacy groups and other interested parties to continually improve the science of benefit/risk evaluation and pharmacovigilance. We also invite continued dialogue with these stakeholders to improve communication about our products.

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[i] Regulation and Prequalification (who.int)