Position Paper on the European Union's New Pharmaceutical Regulation and Directive Pharmacovigilance and Patient Safety.

As an Alliance of Organisations representing the European health ecosystem, we wholeheartedly endorse the ongoing reform of the European pharmaceutical legislation for its commitment to patient safety by improving access to safe, effective medicines. The Proposal for a Regulation laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency and the Proposal for a Directive on the Union code relating to medicinal products for human use presents a **unique opportunity for the European Union to be a global leader in reducing harm from medication errors.**

This reform is more than a legislative update; it is a 'once-in-a-generation' opportunity to safeguard patient lives. However, the suggested reform introduces only limited changes to the current EU pharmacovigilance provisions. Startling statistics from the OECD reveal that as many as 1 in 5 inpatients experience medication-related harm during hospitalisation (OECD, 2022). In Europe, an alarming 80 million people have reported experiencing serious medication errors during a hospital stay. Patient harm can occur if medication is incorrectly stored, prescribed, dispensed, administered, or monitored insufficiently. To enhance patient safety and eliminate harm from unsafe medication practices, collective responsibility amongst all healthcare stakeholders is essential. Errors do not discriminate; they disproportionately affect vulnerable populations such as children, older adults, and patients in complex care settings. Tragically, medication errors can lead to fatal outcomes. With this position paper, we urge the European Union to **close gaps in the current EU pharmacovigilance by tackling downstream determinants of harm to better protect the health of European citizens from medication hazards in healthcare settings.**

THE CASE FOR WIDESPREAD ADOPTION OF MEDICATION TRACEABILITY IN EUROPE

At some point in our lives, many of us will need hospital care requiring medications to aid recovery and symptom management. Medication often plays a pivotal role in these processes, but it can also pose a risk to a patient's health and well-being. **In Europe, daily deaths from medication errors overshadow deaths from breast cancer, HIV or road traffic accidents (EHMA, 2022).** Implementing digitalisation in hospitals' medication management pathways is a crucial step to improve patient outcomes and the quality of care in hospitals. Digital tools have huge advantages. These advantages can only be fully realised when they are designed and implemented in partnership with end users – frontline healthcare professionals and pharmacists in hospital settings (Schiff et al, 2015).

Medication represents the primary therapeutic intervention in hospital settings. Individuals are often prescribed numerous medications during a single episode of care (Carroll & Richardson, 2019) in addition to any medications they are prescribed prior to admission. However, despite the ongoing digital revolution, healthcare professionals, including hospital pharmacists, continue to perform these critical tasks manually. Taking barcode medication administration (BCMA) as one example, a survey by ECAMET (2022) found that only 30% of 317 hospitals use this tool. Widespread evidence now exists demonstrating the value of BCMA for patient safety. For instance, the introduction of barcode scanning during medication dispensing can reduce medication error rates by up to 76% (Courtney, 2020).

In another study of closed-loop medication management systems over 80% of nurses considered the system helpful in preventing medication errors and ensuring patient safety (Shi, et al., 2018). In Denmark, for example, a 57% decrease in medication administration errors in a haematological ward was observed after the introduction of single-unit dose barcoding (EAHP, 2020).

A 2016 study for Dutch hospitals revealed that the countrywide usage of single-unit dose barcoding could lower healthcare spending by 21 million Euros per year (EAHP, 2020). It is no surprise then that the Netherlands is the sole European Member State with a national programme for BCMA (OECD, 2022). In the absence of digital tools, manual processes will persist to add to the burden of medication errors on healthcare systems. Children and older adults are most likely to be affected by a medication error. Up to 8 times more medication errors occur in neonatal ICUs than in ICUs for hospitalised adults (Reece, et al., 2016), (Cayot-Constantin, et al., 2010). In children, it is therefore essential to pay even more attention to the medication process than in adults as the characteristics of the paediatric population make children, and new-borns, particularly sensitive to the medication process, as the individual calculation of the correct dose based on body weight, for example, is very decisive (Healthcare Safety Investigation Branch I2020/26, 2022).

Electronic and other digital possibilities are readily available to prevent medication errors, however, their widespread implementation lags. In parallel to the widespread introduction of electronic prescribing systems, we urge the European Union to define quality and safety criteria for the design as well as correct use of electronic tools. Achieving widespread implementation of digital medication management systems can instil confidence in European citizens and healthcare professionals that modern healthcare provides a high degree of patient safety shielding them from medication harm.

MODERNISE HOSPITAL'S PHARMACEUTICAL PATHWAYS FOR PATIENT SAFETY AND HEALTH SYSTEM SUSTAINABILITY

Medication errors have serious health and economic consequences on health systems. They are the most common adverse event in hospitals in number, mortality, and morbidity (Elliott, et al., 2018). **15% of hospital activity is associated with patient harm equating to 3% of national healthcare budgets which could amount to €43 billion to the EU annually** (EHMA, 2022). 3 million avoidable hospital days, costing an annual total of $51 billion are associated with hospital-acquired medication harm in OECD member countries.

Only 5% of doctors escape close, or direct, involvement with adverse events during their entire careers. 33% of nurses involved in an adverse event require a 3-month absence from work to recover from the psycho-emotional consequences of being involved in an error (EBN, 2021). For families, parents and healthcare professionals involved in a fatal medication error, their lives, hopes, and dreams are fundamentally and indefinitely altered.

Quality management studies on medication-related errors place medication harm occurrences in the ‘never’ category, however, they are not a never occurrence. Therefore, to facilitate harm reduction and cost-benefit savings from medication errors hospitals' medication management should be modernised and follow the digital by-default principle. By doing so, financial losses associated with patient safety from medication errors in healthcare settings can be diminished supplementing efforts to ensure the long-term sustainability and resilience of health systems.

DO NO HARM – A PRIMARY OBLIGATION IN HEALTHCARE DELIVERY

"Primum non nocere" or "First, do no harm" underscores the primary duty of healthcare professionals to not cause harm to patients and to prioritise their well-being. However, it is crucial to recognise that medication safety and medication harm remain the most **underdiagnosed** and **under-appreciated sources of risk** in healthcare professionals' everyday practice.

To empower professionals to reduce harm from medication, **the new Pharmaceutical Directive must mandate that member states progressively introduce standardised single-unit dose barcodes, such as GS1 standards, on medication blister packs, vials, pre-prepared syringes, and ampoules.**

These standardised approaches will enable healthcare professionals to effectively prioritise patient safety and well-being, upholding the 5 Rights of Medication Use. Ireland's National Cancer Information System (NCIS) is an excellent example of how digitalisation supports professionals to uphold this principle. The NCIS, a clinical information system, supports the care of cancer patients with key functionalities including prescribing, electronic medication administration records, support for aseptic compounding, and medication management.

By embracing such digitalisation in combination with ISO-recommended standardised practices, including tall man lettering (TML) and drug syringe labelling (ISO, 2020) and the availability of ready-to-use medication doses in pre-prepared syringes (IHI, 2023), we can ensure that healthcare professionals are equipped to honour the core principle of "First, do no harm," and provide the highest level of care and safety to their patients.

LEGAL DEFINITIONS OF ADVERSE REACTIONS IN THE PHARMACEUTICAL LEGISLATION MUST INCORPORATE MEDICATION ERRORS

The proposal of the Regulation laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006 and the proposal for a Directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC maintain a robust legal framework to protect public health and guarantee the safety of medical products.

However, the legislation currently overlooks the harm that can arise during the everyday handling and administration of medicines to hospital patients. While current statistics are alarming, **the incidence of people harmed is expected to be the tip of the iceberg as reporting medication harm is not mandatory in all EU countries.** The key website for reporting medication errors at the European level is EudraVigilance. However, information collected by this website concerns suspected side effects of medication and not medication errors. Therefore, to identify and tackle the root cause of medication errors, we ask that **reports of adverse reactions arising from unintended medication errors be recorded and made available in the EudraVigilance database** so that corrective measures, procedures and/or protocols be implemented to prevent avoidable harm.

Furthermore, to support reliable reporting of adverse reactions from medication errors **we request that the reformed Regulation includes the Directive 2010/84/EU amended definition of 'adverse reaction' in Article two of the Regulation.**

Additionally, we recommend that definitions for adverse reactions in the reformed Directive correspond to the amended definition of 'adverse reaction' contained in Directive 2010/84/EU that includes medication errors rather than the current definitions from **Directive 2001/83/EC.** By updating the definition to reflect more recent legislative updates ambiguity of definitions is removed, and definitions are standardised for pharmacovigilance purposes which will improve accountability and reporting of adverse reactions including medication errors. Furthermore, we suggest that reports on medication errors in the EudraVigilance database should be produced and Competent Authorities of the Member States and Risk Assessment Committee and the Committee for Medicinal Products for Human Use review them to ascertain if corrective actions are needed to achieve high standards of medication safety in healthcare settings.

The reformed Pharmaceutical legislation presents a once-in-a-generation opportunity to standardise medication safety handling and administration processes within the Union. To address safety concerns about medication handling in clinical practice, it is necessary to ensure that hospital pharmacovigilance systems in the Union are continually adapted to make the best use of technological progress. The use of electronic and technological possibilities, including medication traceability systems can enhance workplace wellbeing while improving the safety of patients. By enhancing pharmacovigilance activities in hospitals, the reformed legislation will recognise the key role of hospitals and healthcare professionals to prevent and reduce harm to patients from medication. Therefore, we suggest the following recommendations to ensure that medication safety is prioritised in the reformed legislation:

1.Include the definition of adverse reaction which includes medication error from Directive 2010/84/EU in Article 2 of the proposed Regulation and in Article 4, subparagraph 59 of the proposed Directive.

2.Stimulate the progressive introduction of standardised single-unit dose barcodes, such as GS1 standards, on medication blister packs, vials, pre-prepared syringes, and ampoules.

3.Support countries and national ministries to facilitate harm reduction from medication errors in hospitals by following the digital by-default principle for medication handling and administration activities and invest in digitalisation.

4.Promote quality and safety improvements of medicinal products through the development and availability of hospital risk management and patient safety plans to reduce harm from medication errors.

The EPACT Alliance (AlliancE for the Digitalisation of HosPitAls' MediCation Management PaThways) was founded in February 2022, by the European Health Management Association . The Alliance consists of NGOs representing patient and healthcare professional organisations to advocate for the implementation and upscaling of digital medication management tools in hospitals' medication management pathways to enhance the quality of patient care, healthcare professionals' well-being and the long-term resilience and economic sustainability of European hospitals.

(1)The European Health Management Association is a non-profit membership organisation that focusses on enhancing the capacity and capability of health management to deliver high-quality healthcare.

MedTech Europe
from diagnosis to cure

European Alliance for
Access to Safe Medicines

EJD European Junior Doctors
Association

EUROPEAN PATIENT SAFETY FOUNDATION

ENSH
European Network for Safer Healthcare

ECAMET
European Collaborative Action on Medication Errors and Traceability

ECHO
European Children's Hospitals Organisation

european cancer ORGANISATION

International Alliance of Patients' Organizations
A global voice for patients

espnic
European Society of Paediatric and Neonatal Intensive Care

EUROPEAN ONCOLOGY NURSING SOCIETY

FEAM
Federation of European Academies of Medicine

ESN
EUROPEAN SPECIALIST NURSES ORGANISATION

E S A IC
European Society of Anaesthesiology and Intensive Care

All.Can

EUROPEAN UNION OF PRIVATE HOSPITALS
Uehp

European Cancer Patient Coalition

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

EACH
PROMOTING CHILDREN'S RIGHTS AND WELFARE IN HEALTHCARE

RSCN
REFERENCE SITE COLLABORATIVE NETWORK

HEALTH FIRST EUROPE

EFCNI
european foundation for the care of newborn infants

eahp
european association of hospital pharmacists

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Transparency Register Number: 352972410521-12)

ANNEX

Amendments to the proposal of the Regulation laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency

Chapter 1 Subject Matter, Scope & Definitions

Article 2 Definitions 16 (NEW)

ORIGINAL	ADMENDED
/	Adverse reaction means a response to a medical that is noxious and unintended and includes medication errors and uses outside of the terms of the marketing authorisation, including the misuse and abuse of the medication product

Observation:

Adverse reaction is not defined in the regulation although the term is used throughout. In comparison, three different definitions of 'adverse reaction' are defined in the revised Directive, which uses the definitions from Directive 2001/83/EC. None of these definitions include adverse reactions from medication errors which is contained in the amended definition from Directive 2010/84/EU.

Standardised terms of 'adverse reaction' are required in both pieces of the reformed pharmaceutical legislation to ensure consistency in the reporting and recording of adverse reactions with National Competent Authorities and for the EudraVigilance database.

Chapter VIII Pharmacovigilance

Article 101

ORIGINAL	ADMENDED
The Agency shall, in collaboration with the Member States and the Commission, set up and maintain a database and data processing network ('EudraVigilance database') to collate pharmacovigilance information regarding medicinal products authorised in the Union and to allow competent authorities to access that information simultaneously and to share it. In justified cases, the EudraVigilance database may include pharmacovigilance information with regard to medicinal products used under compassionate use referred to in Article 26 or early access schemes.	The Agency shall, in collaboration with the Member States and the Commission, set up and maintain a database and data processing network ('EudraVigilance database') to collate pharmacovigilance information regarding medicinal products authorised in the Union and to allow competent authorities to access that information simultaneously and to share it. In justified cases, the EudraVigilance database may include pharmacovigilance information with regard to medicinal products used under compassionate use referred to in Article 26 or early access schemes.

The EudraVigilance database shall contain information on suspected adverse reactions in human beings arising from use of the medicinal product within the terms of the marketing authorisation as well as from uses outside the terms of the marketing authorisation, and on those occurring in the course of post-authorisation studies with the medicinal product or associated with occupational exposure	The EudraVigilance database shall contain information on suspected adverse reactions in human beings arising from use of the medicinal product within the terms of the marketing authorisation as well as from uses outside the terms of the marketing authorisation, *including medication errors,* and on those occurring in the course of post-authorisation studies with the medicinal product or associated with occupational exposure

Justification:
To ensure standardisation of definitions and to increase the reporting of medication errors to the EudraVigilance database ambigiuity on whether to report a medication error to the database should be removed. This will allow more data on the number of medication errors that occur in Europe to be collected. The availability of consistent, reliable, data will support research and analysis on the root causes of medication errors which will contribute to evidence-based policy making on how to prevent medication harm in healthcare settings.

Article 111 Cooperation with Member States

ORIGINAL	ADMENDED
The Agency and the Member States shall cooperate to continuously develop pharmacovigilance systems capable of achieving high standards of public health protection for all medicinal products, regardless of the routes of marketing authorisation, including the use of collaborative approaches, to maximise use of resources available within the Union.	The Agency and the Member States shall cooperate to continuously develop pharmacovigilance systems, including those that record adverse events including medication errors, processes and standards for medication safety, and implement digital technologies in healthcare settings, capable of achieving high standards of public health protection for all medicinal products, regardless of the routes of marketing authorisation, including the use of collaborative approaches, to maximise use of resources available within the Union.

Justification:
80 million people in Europe have reported experiencing serious medication errors during hospitalisation. To **close gaps in the current EU pharmacovigilance policy and legislation tackling the downstream determinants of harm to better protect the health of European citizens from medication hazards in healthcare settings is required. Currently,** the Netherlands is the sole European Member State with the only national programme for barcode medication administration (OECD, 2022) which has been proven to reduce harm from medication errors associated with prescription, wrong time and administration.

A study by Jessrun, Hunfeld et al (2022) in Erasmus MC, University Medical Center Rotterdam, The Netherlands has shown that based on 2,260,870 administered medications in the entire hospital annually, a total of 102,210 MAEs and 59,830 potentially harmful MAEs were estimated to be avoided. The intervention was associated with an increased incremental cost of €1,808,600 annually. The cost-effectiveness ratio was €17.69 per avoided MAE and €30.23 per avoided potentially harmful MAE. https://doi.org/10.1016/j.sapharm.2022.07.006

Amendments for the proposal for a Directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use

Chapter I: Subject matter, scope and definitions

Article 1 (6)

ORIGINAL	ADMENDED
Medicinal products referred to paragraph 5, point (a), may be prepared in duly justified cases in advance by a pharmacy serving a hospital, on the basis of the estimated medical prescriptions within that hospital for the following seven days.	Medicinal products referred to paragraph 5, point (a), may be prepared in duly justified cases in advance by a pharmacy serving a hospital, on the basis of the estimated medical prescriptions within that hospital.

Observation:

Access to medicines is a key element of the fundamental right to health. A key objective of the current reform is to ensure access to and the continued supply of medical products, especially during times of crisis, thus the competencies of hospital pharmacists to step in and counteract shortages when they occur must be supported as a key element of patients right to access to medicines. During the COVID crisis, hospital pharmacies throughout Europe promptly prepared oral liquids and capsules including dexamethasone, remdesivir, and other potentially promising drugs prescribed off-label (Carvalho & Almeida, 2022). Thus, we strongly recommend that the time limit contained in Article 1, subparagraph 6 be deleted from the revised Directive to let compounders provide patients with the medicines they need and to ensure the continuity of care during times of crisis

Article 3 (1)

ORIGINAL	ADMENDED
1. A Member State may, in order to fulfil special needs, exclude from the scope of this Directive medicinal products supplied in response to a bona fide unsolicited order, prepared in accordance with the specifications of an authorised healthcare professional and for use by an individual patient under their direct personal responsibility. However, in such case Member States shall encourage healthcare professionals and patients to report data on the safety of the use of such products to the competent authority of the Member State in accordance with Article 97. For allergen medicinal products supplied in accordance with this paragraph, the competent authorities of the Member State may request the submission of relevant information in accordance with Annex II.	A Member State may, in order to fulfil special needs, exclude from the scope of this Directive medicinal products supplied in response to a bona fide unsolicited order, *including those* prepared in accordance with the specifications of an authorised healthcare professional and for use by an individual patient under their direct personal responsibility *or prepared in accordance with the specifications of a competent authority.* However, in such case Member States shall encourage healthcare professionals and patients to report data on the safety of the use of such products to the competent authority of the Member State in accordance with Article 97. For allergen medicinal products supplied in accordance with this paragraph, the competent authorities of the Member State may request the submission of relevant information in accordance with Annex II.

Observation:
During the pandemic, hospitals' pharmaceutical departments were authorised to compound medicines in short supply and most urgently needed, eg. ICU medicines. Such needs are not unique to the pandemic and countries may have already taken steps to make this practice possible in duly justified cases, or may find useful to do so. In view of the immense difficulties brought by shortages, it is necessary to allow such a practice, in a well-regulated framework. A definition should be included for the term "bona fide unsolicited order".

Chapter 1

Article 4 (59)

ORIGINAL	ADMENDED
'adverse reaction' means a response to a medicinal product that is noxious and unintended	*'adverse reaction' means a response to a medicinal product that is noxious and unintended and includes medication errors and uses outside of the terms of the marketing authorisation, including the misuse and abuse of the medication product*

Justification:
3 different definitions of 'adverse reaction' are defined in the revised Directive, which uses the definitions from Directive 2001/83/EC. None of these definitions include adverse reactions from medication errors which is contained in the amended definition from Directive 2010/84/EU. Standardised terms of 'adverse reaction' are required in both pieces of the reformed pharmaceutical legislation to ensure consistency in the reporting and recording of adverse reactions with National Competent Authorities and for the EudraVigilance database.

Section 7: Chapter VI Product information and labelling

Article 66

ORIGINAL	ADMENDED
1. The particulars laid down in Annex IV shall appear on immediate packagings other than those referred to in the paragraphs 2 and 3. 1. The particulars laid down in Annex IV shall appear on immediate packagings other than those referred to in the paragraphs 2 and 3. 2. The following particulars at least shall appear on immediate packagings that take the form of blister packs and are placed in an outer packaging that complies with the requirements laid down in Articles 65 and 73.	1. The particulars laid down in Annex IV shall appear on immediate packagings other than those referred to in the paragraphs 2 and 3. 2. The following particulars at least shall appear on immediate packagings that take the form of blister packs and are placed in an outer packaging that complies with the requirements laid down in Articles 65 and 73. (a) the name of the medicinal product; *(b) the strength of the medicinal product;* (c) the name of the marketing authorisation holder placing the product on the market;

(a) the name of the medicinal product; (b) the name of the marketing authorisation holder placing the product on the market; (c) the expiry date; (d) the batch number. 3. The following particulars at least shall appear on small immediate packaging units on which the particulars laid down in Articles 65 and 73 cannot be displayed, shall include at least the following labelling particulars: (a) the name of the medicinal product and, if necessary, the route of administration; (b) the method of administration; (c) the expiry date; (d) the batch number; (e) the contents by weight, by volume or by unit.	(d) the expiry date; (e) the batch number. *Each single dose of the blister pack shall include the following labelling particulars:* *(a) the name of the medicinal product;* *(b) the strength of the medicinal product;* *(c) a data matrix barcode in which the following information is encoded:* *(i) the Global Trading Index Number (GTIN)* *(ii) the expiry date;* *(iii) the batch number.* 3. The following particulars at least shall appear on small immediate packaging units on which the particulars laid down in Articles 65 and 73 cannot be displayed, shall include at least the following labelling particulars: (a) the name of the medicinal product and, if necessary, the route of administration; (b) the method of administration; (c) the expiry date; (d) the batch number; (e) the contents by weight, by volume or by unit.

Justification:

To decrease the risk of medication errors blister packs must also bear information about the strength of the medicinal product. Moreover, manufacturers should be obliged to include single unit dose barcodes on each cell of the blister. Barcoding medicinal products to the single unit dose and bedside scanning of medications have for example proven to be an efficient way to diminish medication errors and adverse drug events. In Dutch hospitals alone the use of single unit dose barcoding would save 47 patient lives each year. While in Denmark, a 57% decrease in medication administration errors on a haematological ward was observed after the introduction of single unit dose barcoding. This measure resulted in a cost-effectiveness ratio of 2.01 euro per avoided administration error. Similar financial findings were reported by a study for Dutch hospitals which concluded that the country-wide usage of single unit dose barcoding could lower healthcare spending by 21 million euros per year. EAHP recommends a wider application of single unit dose barcodes to lower medication errors for the benefits of patients.

Chapter XI Pharmacovigilance, Section 1

Article 97 (1) - addition

ORIGINAL	ADMENDED
Member State responsibilities for pharmacovigilance activities	Member State responsibilities for pharmacovigilance activities

1. The Member States shall: (a) take all appropriate measures to encourage patients, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the competent authority of the Member State and may involve organisations representing consumers, patients and healthcare professionals for those tasks where appropriate; (b) facilitate patient reporting through the provision of alternative reporting formats in addition to web-based formats; (c) take all appropriate measures to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports; (d) ensure that the public is given important information on pharmacovigilance concerns relating to the use of a medicinal product in a timely manner through publication on the web-portal and through other means of publicly available information as necessary; (e) ensure, through the methods for collecting information and where necessary through the follow-up of suspected adverse reaction reports, that all appropriate measures are taken to identify clearly any biological medicinal product prescribed, dispensed, or sold in their territory that is the subject of a suspected adverse reaction report, with due regard to the name of the medicinal product, and the batch number.	1. The Member States shall: (a) take all appropriate measures to encourage patients, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the competent authority of the Member State and may involve organisations representing consumers, patients and healthcare professionals for those tasks where appropriate; (b) facilitate patient reporting through the provision of alternative reporting formats in addition to web-based formats; (c) take all appropriate measures to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports; (d) ensure that the public is given important information on pharmacovigilance concerns relating to the use of a medicinal product in a timely manner through publication on the web-portal and through other means of publicly available information as necessary; (e) ensure, through the methods for collecting information and where necessary through the follow-up of suspected adverse reaction reports, that all appropriate measures are taken to identify clearly any biological medicinal product prescribed, dispensed, or sold in their territory that is the subject of a suspected adverse reaction report, with due regard to the name of the medicinal product, and the batch number; *(f) facilitate harm reduction from adverse events through developing and implementing corrective patient safety plans for safe medicinal product administration and handling which can include the deployment of digital medication safety systems in hospitals and ambulatory care settings.*

Justification:

80 million people in Europe have reported experiencing serious medication errors during hospitalisation. To close gaps in the current EU pharmacovigilance policy and legislation tackling the downstream determinants of harm to better protect the health of European citizens from medication hazards in healthcare settings is required. Currently, the Netherlands is the sole European Member State with the only national programme for medication traceability (OECD, 2022) which has been proven to reduce harm from medication errors associated with prescription, wrong time and administration.

A study by Jessrun, Hunfeld et al (2022) in Erasmus MC, University Medical Center Rotterdam, The Netherlands has shown that based on 2,260,870 administered medications in the entire hospital annually, a total of 102,210 MAEs and 59,830 potentially harmful MAEs were estimated to be avoided. The intervention was associated with an increased incremental cost of €1,808,600 annually. The cost-effectiveness ratio was €17.69 per avoided MAE and €30.23 per avoided potentially harmful MAE. https://doi.org/10.1016/j.sapharm.2022.07.006

Article 106 (5)

Recording and reporting of suspected adverse reactions by Member States

ORIGINAL	ADMENDED
Member States shall ensure that reports of suspected adverse reactions arising from an error associated with the use of a medicinal product that are brought to their attention are made available to the EudraVigilance database and to any authorities, bodies, organisations or institutions, responsible for patient safety within that Member State concerned. They shall also ensure that the authorities responsible for medicinal products within that Member State are informed of any suspected adverse reactions brought to the attention of any other authority within that Member State. These reports shall be appropriately identified in the forms referred to in Article 102 of [revised Regulation (EC) No 726/2004]	Member States shall ensure that reports of suspected adverse reactions arising from an error, *including those* associated with the use, *administration, and dispensation* of a medicinal product, *by professionals,* that are brought to their attention are made available to the EudraVigilance database and to any authorities, bodies, organisations or institutions, responsible for patient safety within that Member State concerned. They shall also ensure that the authorities responsible for medicinal products within that Member State are informed of any suspected adverse reactions brought to the attention of any other authority within that Member State. These reports shall be appropriately identified in the forms referred to in Article 102 of [revised Regulation (EC) No 726/2004]

Observation:

Medication errors equate to 3% of national healthcare budgets. In OECD member countries, 3 million avoidable hospital days, costing an annual total of $51 billion are associated with hospital-acquired medication harm. Over 180,000 bed days are consumed due to the 237 million medication errors that occur at some point in the medication process in England.

The EMA's (2015) 'good practice guidance on recording, coding, reporting and assessment of medication errors ' states that it is good practice that competent authorities in EU Member States are also aware of adverse reactions associated with medication errors. However, research by the OECD (2023) shows that one-quarter of responding countries advised that political leaders are not informed on patient safety in their health system.

Therefore, for high-performing health systems, unintended medication errors should be recorded in the EudraVigilance database to support European policy-making to prevent and manage medication errors in healthcare settings.

Chapter XI Pharmacovigilance, Section 4 periodic safety update reports

Article 107 (5)

ORIGINAL	ADMENDED
/	*Competent Authorities of the Member States, members of the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use and the coordination group by means of a repository referred to in Article 104 of [revised Regulation (EC) No726/2004) shall ensure that reports of adverse reactions arising from medication errors associated with the incorrect administration and dispensation of a medicinal product available in the EudraVigilance database are included in periodic safety update reports, and cooperate with healthcare professionals to define, if needed, corrective action to achieve high standards of medication safety in healthcare settings, such as the implementation of digital medication safety systems.*

Justification:
To adequately tackle the problem of medication errors downstream in the pharmaceutical supply chain, an article is required to incorporate action in the Directive to submit medication error reports to the EudraVigilance database.

Currently, the directive is built under the premise of adverse events that are related directly to the side effects of a medicinal product but not those that are related to unintended medication errors.

Medication errors arise from mistakes in the everyday manual medicinal product administration and handling processes in healthcare settings rather than coming from HCPs not from the medicine itself. Therefore, for high-performing health systems, unintended medication errors should be recorded in the EudraVigilance database to support European policy-making to prevent and manage medication errors in healthcare settings.

(2) EMA (2013) Good practice guidance on recording, coding, reporting and assessment of medication errors.
(3) OECD (2023) Health Working Papers No. 150 "Advancing Patient Safety Governance in the COVID-19 Response"

Article 107 (6)

ORIGINAL	ADMENDED
/	*The Agency and Member States shall cooperate to achieve high standards of safety in public health delivery, including in the prescribing, administration and monitoring of medicinal products, by supporting the digital transition of health systems in cooperation with healthcare professionals and service providers.*

Observation:
Despite the ongoing digital revolution, healthcare professionals, including hospital pharmacists, continue to perform these critical tasks of prescribing and dispensing medication to patients manually. Taking barcode medication administration (BCMA) as one example, a survey by ECAMET (2022) found that only 30% of 317 hospitals used BCMA. The introduction of barcode scanning during medication dispensing can reduce medication error rates by up to 76% reduction (Courtney, 2020). In another study of closed-loop medication management systems over 80% of nurses considered the system helpful in preventing medication errors and ensuring patient safety (Shi, et al., 2018). Widespread evidence now exists demonstrating the value of BCMA for patient safety. Therefore investments in hardware and software for digital tools for patient safety are needed to ensure Europe's health systems can guarantee high, performing, safety, quality care.

Article 112 (8)

ORIGINAL	ADMENDED
Procedure for regulatory action on periodic safety update reports	Procedure for regulatory action on periodic safety update reports
1. In the case of a single assessment of periodic safety update reports in accordance with Article 110(1) which recommends action concerning more than one marketing authorisation that does not include any centralised marketing authorisation, the coordination group shall, within 30 days of receipt of the assessment report of the Pharmacovigilance Risk Assessment Committee, consider the assessment report and reach a position on the maintenance, variation, suspension or revocation of the marketing authorisations concerned, including a timetable for the implementation of the agreed position.	1. In the case of a single assessment of periodic safety update reports in accordance with Article 110(1) which recommends action concerning more than one marketing authorisation that does not include any centralised marketing authorisation, the coordination group shall, within 30 days of receipt of the assessment report of the Pharmacovigilance Risk Assessment Committee, consider the assessment report and reach a position on the maintenance, variation, suspension or revocation of the marketing authorisations concerned, including a timetable for the implementation of the agreed position.
2. If, within the coordination group, the Member States represented reach an agreement on the action to be taken by consensus, the chairperson shall record the agreement and send it to the marketing authorisation holder and the Member States. The Member States shall adopt necessary measures to maintain, vary, suspend or revoke the marketing authorisations concerned in accordance with the timetable for implementation determined in the agreement. In the event of a variation, the marketing authorisation holder shall submit to the competent authorities of the Member States an appropriate application for a modification, including an updated summary of product characteristics and an updated package leaflet within the determined timetable for implementation.	*2. Upon receipt of a periodic assessment report that records adverse reactions arising from a medication error decide whether any corrective action is required to achieve high standards of medication safety in hospitals and ambulatory care settings.* 3. If, within the coordination group, the Member States represented reach an agreement on the action to be taken by consensus, the chairperson shall record the agreement and send it to the marketing authorisation holder and the Member States. The Member States shall adopt necessary measures to maintain, vary, suspend or revoke the marketing authorisations concerned in accordance with the timetable for implementation determined in the agreement.

If an agreement by consensus cannot be reached, the position of the majority of the Member States represented within the coordination group shall be forwarded to the Commission which shall apply the procedure laid down in Article 42. Where the agreement reached by the Member States represented within the coordination group or the position of the majority of Member States differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the coordination group shall attach to the agreement or the majority position a detailed explanation of the scientific grounds for the differences together with the recommendation.

3. In the case of a single assessment of periodic safety update reports in accordance with Article 110(1) that recommends action concerning more than one marketing authorisation that includes at least one centralised marketing authorisation, the Committee for Medicinal Products for Human Use shall, within 30 days of receipt of the report of the Pharmacovigilance Risk Assessment Committee, consider the report and adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisations concerned, including a timetable for the implementation of the opinion.

4. Where the opinion of the Committee for Medicinal Products for Human Use referred to in paragraph 3 differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use shall attach to its opinion a detailed explanation of the scientific grounds for the differences together with the recommendation.

5. On the basis of the opinion of the Committee for Medicinal Products for Human Use referred to in paragraph 3, the Commission shall, by means of implementing acts: (a) adopt a decision addressed to the Member States concerning the measures to be taken in respect of marketing authorisations granted by the Member States and concerned by the procedure provided for in this section; and (b) where the opinion states that regulatory action concerning the marketing authorisation is necessary, adopt a decision to vary, suspend or revoke the centralised marketing

In the event of a variation, the marketing authorisation holder shall submit to the competent authorities of the Member States an appropriate application for a modification, including an updated summary of product characteristics and an updated package leaflet within the determined timetable for implementation. If an agreement by consensus cannot be reached, the position of the majority of the Member States represented within the coordination group shall be forwarded to the Commission which shall apply the procedure laid down in Article 42. Where the agreement reached by the Member States represented within the coordination group or the position of the majority of Member States differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the coordination group shall attach to the agreement or the majority position a detailed explanation of the scientific grounds for the differences together with the recommendation.

4. In the case of a single assessment of periodic safety update reports in accordance with Article 110(1) that recommends action concerning more than one marketing authorisation that includes at least one centralised marketing authorisation, the Committee for Medicinal Products for Human Use shall, within 30 days of receipt of the report of the Pharmacovigilance Risk Assessment Committee, consider the report and adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisations concerned, including a timetable for the implementation of the opinion.

5. Where the opinion of the Committee for Medicinal Products for Human Use referred to in paragraph 3 differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use shall attach to its opinion a detailed explanation of the scientific grounds for the differences together with the recommendation.

6. On the basis of the opinion of the Committee for Medicinal Products for Human Use referred to in paragraph 3, the Commission shall, by means of implementing acts: (a) adopt a decision addressed to the Member States concerning the measures to be taken

authorisations and concerned by the procedure provided for in this section. 6. Article 42 shall apply to the adoption of the decision referred to in paragraph 5, point (a), and to its implementation by the Member States. 7. Article 13 of [revised Regulation (EC) No 726/2004] shall apply to the decision referred to in paragraph 5, point (b). Where the Commission adopts such decision, it may also adopt a decision addressed to the Member States pursuant to Article 55 of [revised Regulation (EC) No 726/2004].	in respect of marketing authorisations granted by the Member States and concerned by the procedure provided for in this section; and (b) where the opinion states that regulatory action concerning the marketing authorisation is necessary, adopt a decision to vary, suspend or revoke the centralised marketing authorisations and concerned by the procedure provided for in this section. 7. Article 42 shall apply to the adoption of the decision referred to in paragraph 5, point (a), and to its implementation by the Member States. 8. Article 13 of [revised Regulation (EC) No 726/2004] shall apply to the decision referred to in paragraph 5, point (b). Where the Commission adopts such decision, it may also adopt a decision addressed to the Member States pursuant to Article 55 of [revised Regulation (EC) No 726/2004].

Justification:

To adequately tackle the problem of medication errors downstream in the pharmaceutical supply chain, an article is required to incorporate action in the Directive to submit medication error reports to the EudraVigilance database.

Currently, the directive is built under the premise of adverse events that are related directly to the side effects of a medicinal product but not those that are related to unintended medication errors.

Medication errors arise from mistakes in the everyday manual medicinal product administration and handling processes in healthcare settings rather than coming from HCPs not from the medicine itself. Therefore, for high-performing health systems, unintended medication errors should be recorded in the EudraVigilance database to support European policy-making to prevent and manage medication errors in healthcare settings.

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This position paper was supported by an educational grant by Becton, Dickinson and Company, based on independent research by EHMA and their Alliance partners. BD has had no influence or editorial control over the content of this report, and the views and opinions of the authors are not necessarily those of BD.