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ORIGINAL RESEARCH ARTICLE

Quality of MedDRA® Coding in a Sample of COVID-19 Vaccine Medication Error Data

Katarina Kralova[1] · Carol-Ann Wilson[2] · Nicolas Richebourg[1] · Joan D'souza[3]

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Abstract

Introduction In recent years, there has been increasing interest from regulatory agencies and scientific organisations into the recording, coding and reporting of medication errors. Accuracy and consistency in the handling of medication error reports ensure the safety and effectiveness of medicines and provide reliable information to both healthcare professionals and patients.

Objective The authors have examined a sample of *Medical Dictionary for Regulatory Activities* (MedDRA®) coded reports that describe medication errors to assess the accuracy and consistency of MedDRA® coding, and to identify the main types of coding errors for the newly introduced COVID-19 vaccines.

Methods The sample of coded terms was assessed by two MedDRA® experts applying the Four Eyes Principle. It included 1500 reported terms drawn from the Uppsala Monitoring Centre database reported up to 25 August, 2021, describing medication errors for COVID-19 vaccines with their assigned MedDRA® terms.

Results One third of the records could not be assessed because of incomplete or unclear verbatims. In one third, MedDRA® term assignments were correct, but another third of the sample was not adequately coded. The most frequent coding errors corresponded to vague MedDRA® Preferred Term assignments despite more detailed information being available in the verbatim for a more precise coding. This observation is similar to findings in the EudraVigilance database, where some of the most frequently assigned MedDRA® terms for medication errors also represent vague concepts.

Conclusions The findings indicate that understanding of medication error documentation and of the importance of accurate extraction of information from case narratives, as well as knowledge of MedDRA® content and coding guidelines need to be reinforced. The authors provide useful references to training opportunities and to the applicable International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use-Endorsed Guides for MedDRA® users.

1 Introduction

The concept of an adverse reaction encompasses "a response to medicinal product which is noxious and unintended", resulting not only from the authorised use of a medicinal product, but also from medication errors and uses outside the terms of the marketing authorisation [1]. Medication errors may occur when storing, prescribing, transcribing, preparing, dispensing, administering or monitoring medicinal products in clinical practice. They may lead to or have the potential to lead to harm to the patient and can be due to human or process-related factors. It is estimated that medication errors account for 18.7–56% of all hospital adverse events [2]. In a recent report, the World Health Organization (WHO) has identified medication errors as a leading cause for injury and preventable harm in patients [3].

Recording and reporting requirements of such cases differ between regions, depending on local regulations and healthcare advice. As an example, the European Medicines Agency developed a Good Practice Guide to support the recording, coding, reporting and assessment of medication errors associated with suspected serious and non-serious adverse reactions to national pharmacovigilance databases

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Katarina Kralova, Carol-Ann Wilson and Joan D'Souza are members of the ISoP Special Interest Group for Medication Errors.

✉ Katarina Kralova
katarina.kralova@sanofi.com

[1] Sanofi Global Pharmacovigilance, Paris, France

[2] Berlin, Germany

[3] Zürich, Switzerland

Key Points

Precise, accurate and consistent MedDRA® coding in pharmacovigilance databases is a crucial prerequisite for a reliable and reproducible safety data analysis to identify medication errors as one of the main causes of preventable harm to patients' health, with the aim of preventing such incidents.

A quality review of coding within cases submitted to the Uppsala Monitoring Centre database for reporting medication errors with COVID-19 vaccines revealed substantial quality deficiencies in the extraction of medication error data from the Individual Case Safety Reports and their code assignments for a large proportion of the reported incidents.

Raising awareness of the deficiencies in documentation and coding of medication errors will help to establish a reliable basis for the assessment of such errors, to ensure adequate drug and vaccine use in line with valid labelling requirements.

and/or EudraVigilance [2, 4] and a Good Practice Guide on risk minimisation and prevention of medication errors [5]. EudraVigilance is a centralised European database for reporting and evaluating suspected adverse reactions of medicines, maintained by the European Medicines Agency on behalf of the regulatory network in the European Union. The increased awareness of the topic of medication errors since 2005 is reflected by an increase of case reports of medication errors in EudraVigilance [6]. Medication error safety concerns were listed in the risk management plan for almost a quarter of centrally authorised products approved in the European Union in the years 2010–17 [7].

In addition, the owner of the *Medical Dictionary for Regulatory Activities* (MedDRA®), i.e. the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, provides detailed guidance for MedDRA® coding purposes, including medication errors and other product use errors and issues [8, 9]. MedDRA® is a rich and highly specific standardised medical terminology to structure medical information for data analysis purposes. It facilitates the international exchange of regulatory information for medical products used by humans in both the pre- and postmarketing phases [10, 11].

Since 2020 and the worldwide COVID-19 pandemic, a global focus was placed on the evaluation of the safety and effectiveness of the approved COVID-19 vaccines and the provision of reliable information to healthcare professionals and patients [12, 13]. In this context, precise recording of the reported adverse events and their adequate translation into coded terms is required for efficient, effective and reproducible identification and retrieval of the relevant safety data and an accurate subsequent risk-benefit analysis. Coding quality is also highly relevant for the safety monitoring of the proper use of COVID-19 vaccines and for the identification of vaccination errors. Inaccurate coding could lead to misinterpretation of the reported data, and an under- or overestimation of the frequency of certain medication errors, resulting in erroneous understanding and communication of this safety topic.

Currently, no available publication addresses medication errors with COVID-19 vaccines focusing specifically on the quality of the reported data including coding aspects. The authors have examined a sample of MedDRA®-coded reported terms for the newly introduced COVID-19 vaccines to assess the accuracy and consistency of MedDRA® coding in the medication error area and to identify the main types of coding errors.

2 Methods

The chosen sample for this investigation corresponded to a data extract of coded data for adverse events representing medication errors reported for COVID-19 vaccines drawn from the Uppsala Monitoring Centre (UMC) VigiBase®. VigiBase® is the WHO's global database of Individual Case Safety Reports (ICSRs) from national pharmacovigilance centres in the countries participating in the WHO Program for International Drug Monitoring. Thereby, it provides a comprehensive overview of global reporting and coding practices. According to the WHO and UMC policy and guidelines, reports sent from the Program for International Drug Monitoring member countries to VigiBase® are anonymised and do not allow patient identification. To further ensure anonymisation of the data, the dataset did not contain information on the countries of origin of the reported incidents nor case narratives.

All ICSRs for COVID-19 vaccines received into VigiBase® reported up to 25 August, 2021 were included in this investigation. The terminology used for adverse event coding in VigiBase® is MedDRA®, a hierarchical terminology with five levels: Lowest Level Terms (LLTs), PTs, High Level Terms, High Level Group Terms (HLGTs) and System Organ Classes. Lowest Level Terms represent synonyms, quasi-synonyms and lexical variants of the Preferred Term (PT), the medical concept level term. The LLT level is the data entry level and based on the ICH guidance for MedDRA® term selection, selected LLTs should reflect the reported information as specifically and completely as possible [8, 9]. The PT level represents unique single medical

concepts and is used for data retrieval, presentation and analysis purposes [14].

Only MedDRA® HLGT *Medication errors and other product use errors and issues* and the PTs and LLTs within it were considered for this investigation because all relevant MedDRA® terms for medication errors and issues are grouped under this HLGT. The extraction included:

- Identification of the vaccine class (COVID-19 vaccines without specification of the specific product based on data protection considerations).
- Data elements <primarysourcereaction> and <reportedterm> describing the reported incident.
- MedDRA® HLGT name, MedDRA® PT name and MedDRA® LLT name.

Of note, the UMC does not perform any manual coding for these terms as this has been performed by the reporting competent authority. Therefore, the MedDRA® term selection lies with the national pharmacovigilance centres.

The sample of coded terms for medication errors and issues reported for COVID-19 vaccines consisted of 1500 reported terms (verbatims) with their assigned MedDRA® codes extracted in a spreadsheet format. Two independent MedDRA® expert reviewers applied the following grid to each line of the table during the manual review (Table 1).

During a reconciliation step, the two reviewers and the remaining two authors discussed and were aligned on the final assessment.

Table 1 Categorisation applied for the assessment of accuracy of documentation and coding

No entry = correct coding
1 = Insufficient verbatim information, foreign language, verbatim does not relate to vaccines, verbatim not meaningful, verbatim does not match the assigned code (additional narrative information was obviously used for coding purposes), MedDRA® term was directly copied into verbatim field, not codable
2 = Wrong Preferred Term
3 = Wrong Lowest Level Term
4 = Inappropriate split-coding (selection of more than one MedDRA® term where there is no single Lowest Level Term that captures all information contained in each verbatim)

MedDRA® Medical Dictionary for Regulatory Activities

3 Results

The results of the review of the 1500 data sets for medication errors with COVID-19 vaccines extracted from UMC database are summarised below. A total of 518 verbatims (34.5%) could not be further evaluated because of category 1 errors described in the table above. Clarifications of these errors were not possible in the absence of access to the ICSRs and narratives. Among the category 1 errors, in 219 cases, the free text zone describing the medication error was not available. When available, the text was mostly limited to a brief description that in the remaining 299 cases would have required further clarification from the reporter.

The remaining 982 verbatims (65%) were evaluated for coding accuracy.

Of these 982 verbatims, 499 (50.8%) have not been adequately coded:

- In 270 cases (27.5%), an incorrect PT was assigned.
- In 168 cases (17.1%), an incorrect LLT was assigned.
- In 61 cases (6.2%), the necessary split-coding was not performed or was done incorrectly.

It must be noted that incorrect LLT selection does not lead to incorrect PT assignments in all instances. As an example, a report of an intracutaneous administration of the vaccine was coded to LLT *Incorrect route of product administration* instead of LLT *Intramuscular formulation administered by other route* without affecting the assigned PT because both LLTs are linked to PT *Incorrect route of product administration*.

The most frequently incorrect, often vague, PT assignments were:

- PT *Medication error*, in 63 cases (23.3%).
  Example: The verbatim "The vaccination with the second dose, even though the patient had anaphylactic reaction to the previous dose of the same COVID-19 vaccine (actual med error)" was coded to LLT *Medication error* (PT *Medication error*) instead of LLT *Documented hypersensitivity to administered product* (PT *Documented hypersensitivity to administered product* under High Level Term *Product monitoring errors and issues*).
- PT *Vaccination error*, in 59 cases (21.9%).
  Example: The verbatim "Expired vaccine used" was coded to LLT *Vaccination error* (same PT) instead of LLT *Expired vaccine used* (PT *Expired product administered*).
- PT *Product dose omission issue*, in 27 cases (10.0%).
  Example: The verbatim "Possible missed second dose (incomplete vaccination schedule)" was coded to LLT *Missed dose* (PT *Product dose omission issue*) instead of LLT *Incomplete course of vaccination* (PT *Incomplete course of vaccination*).
- PT *Expired product administered*, in 19 cases (7.0%).
  Example: The verbatim "A patient was vaccinated yesterday with the first dose of the XXXX vaccine after 6 h of the first vial puncture, vaccinated 40 min after timeframe window" was coded to LLT *Expired vaccine used* (PT *Expired product administered*) instead of LLT *Poor*

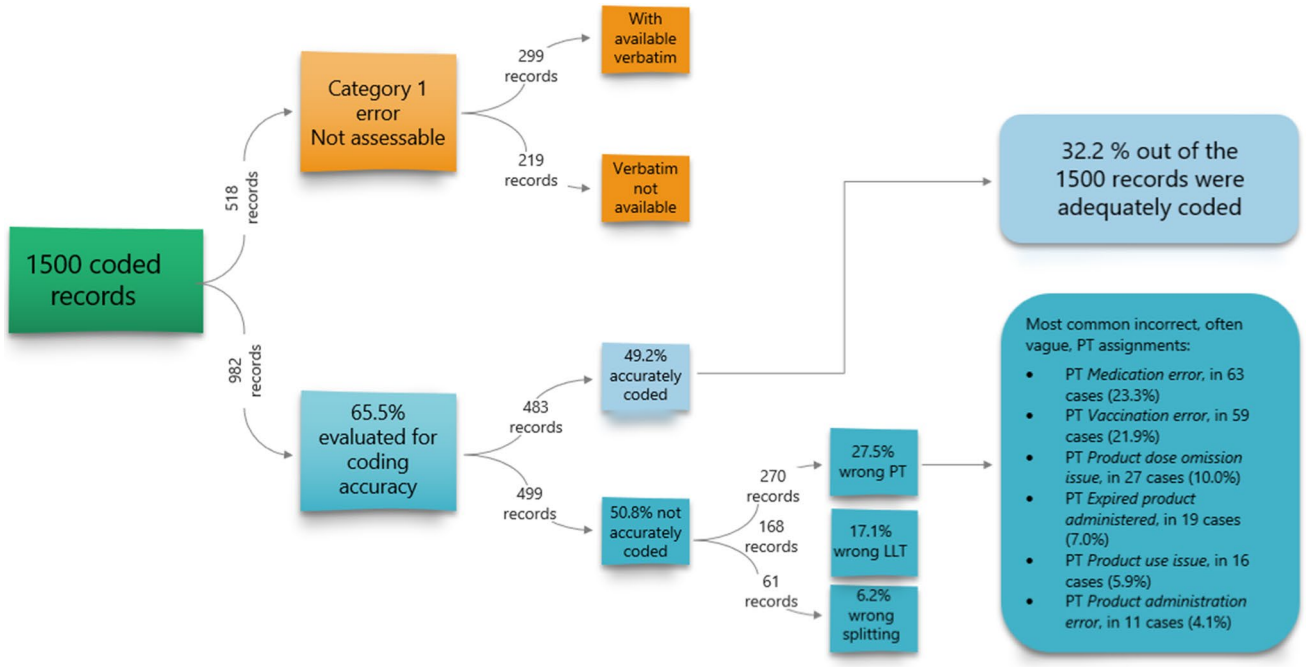

Fig. 1 Breakdown of coding accuracy assessment in the sample of records. *LLT* Lower Level Term, *PT* Preferred Term

quality vaccine administered (PT *Poor quality product administered*) for capturing the beyond-use date.

- PT *Product use issue*, in 16 cases (5.9%).

  Example: The verbatim "Bung contamination" was coded to LLT Product use issue (PT Product use issue) instead of LLT Inadequate aseptic technique in use of product (PT Inadequate aseptic technique in use of product).
- PT *Product administration error*, in 11 cases (4.1%).

  Example: The verbatim "Doses from vials with product quality issues injected into patients (actual medication error)" was coded to LLT *Product administration error* (PT *Product administration error*) instead of LLT *Poor quality vaccine administered* (PT *Poor quality product administered*).

Overall, only 483 verbatims (32.2%) out of the 1500 were adequately coded. This finding reveals substantial quality deficiencies of both the medication error data extraction from ICSRs and their code assignments for many reported incidents (Fig. 1).

4 Discussion

Many regulatory agencies and scientific organisations have a high interest in medication and vaccination error reporting and analysis, in order to take preventive measures to minimise the risk of such errors to patients [15–18]. In this context, precise and consistent coding of reported medication errors using the MedDRA® terminology enables the identification of trends in specific types of errors.

In their analysis, the authors focused exclusively on coding quality, as the anonymised data set did not allow for any further investigations, such as geographical comparisons or a root cause analysis, without access to the corresponding narratives. The large number of available MedDRA® LLTs provides a high degree of granularity. However, this granularity cannot compensate for vague and ambiguous original reports and inadequate term extraction from case narratives. The appropriate coding with MedDRA® requires correct term extraction from available case narratives to capture the nature of the error [8, 9, 17]. The authors' experience revealed that one third of the records could not be assessed for adequate coding because of missing, incomplete or unclear term extraction from the case information.

Another third of the records were not adequately coded. The most frequent errors of coding identified corresponded to incorrect, often vague PT assignments, despite more detailed information being available in the extracted reported terms, allowing for a more precise coding. There is no shortage of more specific LLTs in MedDRA® to account for the assignment of vague codes since COVID-19 vaccines were approved at the beginning of 2021 (MedDRA® version 23.1). Up to this version, many additions have already been made to the terminology to reflect clinical practice. MedDRA® users need to be familiar with the granularity of MedDRA® terms that can be used for the coding of

medication errors and issues to avoid resorting to simpler solutions such as assigning non-specific terms. The remaining third of records were coded correctly.

The selection of vague terminology terms can result in a misleading data output that compromises signal detection, understanding of trends and data analysis [8, 18]. Such errors may ultimately prevent the frequency of different types of medication errors from being understood as a basis for remedial action.

A similar analysis on COVID-19 vaccine medication error data has not been retrieved from bibliographic searches. However, as the UMC database draws data from multiple sources, the high percentage of inadequately coded terms can be considered a reflection of overall coding practices. This assertion is supported by the fact that the authors' observations are comparable to findings in the EudraVigilance database. Looking at the ten most frequently assigned PTs from HLGT *Medication errors and other product use errors and issues* for reported medication errors and issues (the same HLGT on which the study presented here is based), these incidents are frequently coded to very general and vague MedDRA® PTs such as: PT *Medication error*, PT *Product use issue*, PT *Product administration error*. The PT *Product use in unapproved indication* and PT *Product dose omission issue* are also vague and do not allow differentiation between medication error/issue, medicinal product misuse and off-label use (Table 2).

The consistent findings in the two datasets indicate that there is a need to improve the understanding of the documentation and assessment of medication errors as well as of MedDRA® content and related coding guidelines. Dedicated training is a key prerequisite for data entry and coding [9]:

- to improve the level of precision and extent of case documentation; and
- to improve the quality of coding.

Appropriate efforts can contribute to achieving the WHO's ambitious goal of reducing the frequency of medication errors by 50% within 5 years, at least to some extent [3].

Limiting factors of this study include missing or unclear reported terms for a part of the data set, unavailability of narratives to fully understand the events reported and an impossibility to request additional information. Because of these limitations, the root cause of medication errors with COVID-19 vaccines cannot be demonstrated through the present analysis. However, the authors' conclusions are valid because most of the available reported terms could be verified for accuracy of their match to the assigned MedDRA® term. The method of the quality-control review was in line with the common practice [19]. To mitigate a potential subjective component of this approach, a quality review according to the Four Eyes Principle with subsequent reconciliation among the authors has increased the validity and reliability of the results.

Table 2 Most frequent Preferred Terms under High Level Group Term *Medication errors and other product use errors and issues* assigned to corresponding reported incidents in the EudraVigilance database (all cases and medicinal products, data up to March 2021)

	MedDRA® Preferred Term	Count
1.	Product use in unapproved indication	61,727
2.	Product dose omission issue	39,649
3.	Inappropriate schedule of product administration	38,596
4.	Product use issue	26,866
5.	Incorrect dose administered	24,238
6.	Wrong technique in product usage process	23,236
7.	Medication error	20,494
8.	Product administration error	16,037
9.	Accidental overdose	14,513
10.	Incorrect route of product administration	11,941

MedDRA® Medical Dictionary for Regulatory Activities

It would be relevant to complete and further refine this work by examining full narratives of medication errors from the original reporting sources, with an emphasis on relevant term extraction and coding.

Despite these methodological limitations, this work highlights that coding skills around medication errors need to be reinforced. The MedDRA® Maintenance and Support Services Organization offers several MedDRA® coding training courses including coding of medication errors [20]. In addition, both the MedDRA® Term Selection: Points to Consider and the MedDRA® Points to Consider Companion Document, the ICH-Endorsed Guides for MedDRA® Users, provide detailed guidance for medication error and other product use issue coding, with numerous helpful practical examples [8, 9].

5 Conclusions

The full use of available coding options in the MedDRA® terminology requires a clear understanding of MedDRA® terms and correct application of related coding guidelines. The content of original reported information must be retained in term extraction. Accurate and consistent MedDRA® term selection is essential to provide a basis for possible corrective and preventive actions, to minimise the risk of medication errors, and to support adequate drug and vaccine use according to the authorised product information.

Raising awareness of the deficiencies in documentation and coding of medication errors is a first step in the effort to improve these processes. The provision of suitable training for the relevant parties involved in these processes represents

a further step forward. The aim of the authors' contribution is precisely to help to establish a connection between the two.

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Declarations

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Conflicts of interest Katarina Kralova, Nicolas Richebourg and Joan D'Souza have no conflicts of interest that are directly relevant to the content of this article. Carol-Ann Wilson is serving as a consultant for the MedDRA® Maintenance and Support Services Organization, contributing to training activities and terminology maintenance tasks.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication The authors acknowledge the Uppsala Monitoring Centre, which provided and gave permission to use the data analysed in the present study.

Availability of data and material Requests to access the datasets should be directed to the first author and will be granted on reasonable request.

Code availability Not applicable.

Author contributions The coding quality review was performed by C-AW, KK and NR. All authors contributed to the final data reconciliation and to manuscript drafting and revision. All authors approved the final version to be published and agree to be accountable for all aspects of the work.

References

1. European Union. Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use. OJ 53(L348), 74–99 (2010). https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:348:0074:0099:EN:PDF. Accessed 9 May 2022.
2. Pharmacovigilance Risk Assessment Committee. Good practice guide on recording, coding, reporting and assessment of medication errors (EMA/762563/2014) (2015). https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/good-practice-guide-recording-coding-reporting-assessment-medication-errors_en.pdf. Accessed 11 Jan 2023.
3. World Health Organization. Medication without harm: global patient safety challenge on medication safety. Geneva (2017) License: CC BY-NC-SA 3.0 IGO. https://www.who.int/publications/i/item/WHO-HIS-SDS-2017.6. Accessed 30 Nov 2022.
4. Goedecke T, Ord K, Newbould V, et al. Medication errors: new EU good practice guide on risk minimisation and error prevention. Drug Saf. 2016;39:491–500. https://doi.org/10.1007/s40264-016-0410-4.
5. Pharmacovigilance Risk Assessment Committee. Good practice guide on risk minimisation and prevention of medication errors (EMA/606103/2014) (2015). https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/good-practice-guide-risk-minimisation-prevention-medication-errors_en.pdf. Accessed 11 Jan 2023.
6. Newbould V, Le Meur S, Goedecke T, et al. Medication errors: a characterisation of spontaneously reported cases in EudraVigilance. Drug Saf. 2017;40:1241–8. https://doi.org/10.1007/s40264-017-0569-3.
7. Hoeve CE, Francisca RDC, Zomerdijk I, et al. Description of the risk management of medication errors for centrally authorised products in the European Union. Drug Saf. 2020;43:45–55. https://doi.org/10.1007/s40264-019-00874-7.
8. International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). MedDRA® term selection: points to consider: ICH-endorsed guide for MedDRA® Users, Release 4.22 based on MedDRA® Version 25.0 (March 2022). https://admin.meddra.org/sites/default/files/guidance/file/000714_termselptc_r4_22_mar2022.pdf. Accessed 3 Mar 2022.
9. International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). MedDRA® points to consider companion document: ICH-endorsed guide for MedDRA Users, Release 2.0 (2020). https://admin.meddra.org/sites/default/files/guidance/file/000515_companionptc_r2_0_Oct2020_1.pdf. Accessed 3 Mar 2022.
10. International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Introductory guide MedDRA Version 25.1 (September 2022). https://admin.meddra.org/sites/default/files/guidance/file/intguide_25_1_English.pdf. Accessed 2 Sep 2022.
11. Brown EG, Wood L, Wood S. The medical dictionary for regulatory activities (MedDRA). Drug Saf. 1999;20:109–17. https://doi.org/10.2165/00002018-199920020-00002.
12. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 11 March 2020. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Accessed 25 Nov 2022.
13. Kalinke U, Barouch DH, Rizzi R, et al. Clinical development and approval of COVID-19 vaccines. Expert Rev Vaccines. 2022;21(5):609–19. https://doi.org/10.1080/14760584.2022.2042257.
14. International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). MedDRA® data retrieval and presentation: points to consider: ICH-endorsed guide for MedDRA users on data output. Release 3.22 based on MedDRA® Version 25.0 (March 2022). https://admin.meddra.org/sites/default/files/guidance/file/SMQ_intguide_25_1_English.pdf. Accessed 4 Aug 2022.
15. US Food and Drug Administration Center for Drug Evaluation and Research (CDER). Safety considerations for product design to minimize medication errors. Guidance for Industry (2016). https://www.fda.gov/files/drugs/published/Safety-Considerations-for-Product-Design-to-Minimize-Medication-Errors-Guidance-for-Industry.pdf. Accessed 24 Nov 2022.
16. European Medicines Agency. Recommendations on medication errors (2016). https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/medication-errors/recommendations-medication-errors. Accessed 11 Nov 2022.
17. Cousins D, Gerrett D, Richards N, et al. Initiatives to identify and mitigate medication errors in England. Drug Saf. 2015;38:349–57.
18. Elhawary MA, Rostom H, Edwards B, et al. Medication Errors Special Interest Group of the International Society of

Pharmacovigilance and the trends in international collaboration for patient safety. Drug Saf. 2022;45:97–9. https://doi.org/10.1007/s40264-021-01145-0.

19. Nair GJ. Ensuring quality in the coding process: a key differentiator for the accurate interpretation of safety data. Perspect Clin Res. 2013;4:181–5. https://doi.org/10.4103/2229-3485.115383.
20. MedDRA course descriptions. https://www.meddra.org/course-descriptions. Accessed 24 Nov 2022. MedDRA training schedule. https://www.meddra.org/training/schedule. Accessed 24 Nov 2022. Recorded training sessions. https://www.youtube.com/c/MedDRAMSSO/playlists. Accessed 24 Nov 2022.

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