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A Comprehensive Overview of Council for International Organizations of Medical Sciences (CIOMS)

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ABSTRACT:

The Council for International Organizations of Medical Sciences (CIOMS) is a pivotal non-governmental organization established in 1949 through a joint initiative by the World Health Organization (WHO) and UNESCO. This review delves into the multifaceted contributions of CIOMS to the field of medical sciences, particularly in the realm of ethical guidelines and drug safety. CIOMS plays a crucial role in harmonizing ethical standards for biomedical research, especially in diverse cultural and socio-economic contexts, ensuring that research practices uphold respect for individuals and communities globally. CIOMS has significantly influenced the formulation of international guidelines, such as the International Ethical Guidelines for Health-Related Research Involving Humans. These guidelines provide comprehensive frameworks for ethical research conduct, addressing issues such as informed consent, confidentiality, and the protection of vulnerable populations. Moreover, CIOMS has been instrumental in promoting pharmacovigilance through its guidelines on drug safety and adverse drug reaction reporting, which have been adopted widely to enhance global health safety standards. The organization's collaborative approach, involving various stakeholders including government agencies, academia, and industry, has fostered a platform for dialogue and consensus-building. This review highlights key milestones in CIOMS's history, its evolving role in the dynamic landscape of medical research ethics, and its ongoing efforts to address emerging challenges such as digital health, personalized medicine, and global health emergencies. By synthesizing its historical impact and current initiatives, this review underscores CIOMS's enduring commitment to advancing ethical standards and promoting global health through its leadership in medical sciences.

Keywords: Council for International Organizations of Medical Sciences (CIOMS), Ethical guidelines, Drug safety, Biomedical research, Informed consent, Pharmacovigilance, Global health, Medical research ethics

CIOMS I (1990):International Reporting of Adverse Drug Reactions[1,10,11]

The goal of this working group was "to develop an internationally acceptable reporting method whereby manufacturers could report post-marketing adverse drug reactions rapidly, efficiently and effectively to regulators." It noted the fact that post marketing surveillance is necessary because premarketing studies in animals and humans have "inherent limitations." It noted the need for standardization internationally
The report established several conventions that have largely been adopted, including the following:

- The concept and format of a report ("a CIOMS I report") from the manufacturer receiving the event to the regulators.
- "Reactions" are different from "events." "Reactions" are reports of clinical occurrences that have been judged by a physician or healthcare worker as having a "reasonable possibility" that the report has been caused by a drug. "Events" have not had a causality evaluation made, and thus may or may not be related to or associated with the drug.
- Causality is discussed. No particular method of assessing causality is recommended. The report recommends that manufacturers not separate out those spontaneous reports that they receive into those that seem to be drug-related and those not seemingly drug-related. The physician, by making the report to the manufacturer, indicates that there is some level of causality possible in the report. This is a "suspected reaction." This has become a fundamental concept in most spontaneous reporting systems around the world, wherein all spontaneous reports from physicians (now extended to all healthcare providers, and in some countries, such as the United States and Canada, to consumers) are to be considered possibly related to the drug; that is, they are "reactions," not "events."
- Because labels for marketed drugs differ from country to country, it is recommended that all reactions be collected at one point and then submitted to local authorities on a country-by-country basis based on whether the reactions are labelled locally.
- The report discusses the four minimum requirements for a valid report:

1. An identifiable source (reporter),
2. A patient (even if not precisely identified by name),
3. A suspect drug, and
4. A suspect reaction.

- The report recommends that all reports be sent in as soon as received and no later than 15 working days after receipt, to create a common worldwide deadline. This concept has been adopted, but the 15 working days has been changed to 15 calendar days because of differences in the designation of "working days" and nonworking days (holidays) around the world. The reporting clock starts the date the report is first received by anyone anywhere in the company.
- The CIOMS I form was created. It is essentially the same form still used now. This form is to be used for reporting to regulatory authorities.
- Reactions are to be reported in English

CIOMSII (1992): International Reporting of Periodic Drug-Safety[2,12,13]

Update Summaries

This working group proposed a standard for Periodic Safety Update Reports (PSURs) of reactions received by manufacturers on marketed drugs. This standard, with modifications from the ICH and other organizations, has been widely adopted. The document defined several key terms:

- CIOMS Reportable Cases or Reports: "serious, medically substantiated, unlabelled ADRs with the 4 elements (reporter, patient, reaction, suspect drug)."
- Core Data Sheet (CDS): A document prepared by the manufacturer containing all relevant safety information, including adverse drug reactions (ADRs). This is the reference for "labelled" and "unlabeled." This concept, which has been widely accepted, has since gotten more complex, and one must distinguish labeling from listing (e.g., unlabeled and unlisted).
- International Birth Date (IBD): The date that the first regulatory authority anywhere in the world has approved a drug for marketing.
- Data Lock-Point (Cut-Off Date): The closing date for information to be included in a particular safety update.
- Serious: Fatal, life-threatening, involves or prolongs inpatient hospitalization.
- The sections of the PSUR include the following:

Scope

1. Subject drugs for review
2. Frequency of review and reporting

Content

1. Introduction
2. CDS
3. Drug's licensing (i.e., marketing approval) status
4. Review of regulatory actions taken for safety, if any
5. Patient exposure
6. Individual case histories (including a "CIOMS line listing")
7. Studies
8. Overall safety evaluation
9. Important data received after the data lock-point

Other fundamental concepts were established:

- Reports should be semi-annual and not cumulative (unless cumulative information is needed to put a safety issue into context).
- The same report goes to all regulatory authorities on the same date irrespective of the local (national) approval date of the drug.
- Reactions reported should be from studies (published and unpublished), spontaneous reports, published case reports, cases received from regulatory authorities, and other manufacturers. Duplicate reports should be eliminated.
- The manufacturer should do a "concise critical analysis and opinion in English by a person responsible for monitoring and assessing drug safety."

CIOMS III (1995and1998/1999):Guidelines for Preparing Core Clinical Safety Information on Drugs (1995), Including New Proposals For Investigator's Brochures(1998/1999)[3,14,15,16]

The CIOMS III guideline is now out of print but established and extended several fundamental concepts now in use in much of the world. The idea of the CDS introduced in CIOMS II was extended to the Core Safety Information (CSI). The CDS contains all of the key core data (not just safety data) on a drug. The CSI contains (only) core safety information and is a subset of the CDS.

Several fundamental concepts were introduced:

- The CSI is the core safety information that should appear in all countries' labeling for that drug. Additional information could be added at the national level, but the core information should be included in all countries' labels. The CSI (and national labels) are guides for healthcare professionals and contain the most relevant information needed for the drug's use.
- Marketing considerations should not play a role in preparing the CSI.
- The CSI was proposed primarily as a medical document and not as a legal or regulatory document.
- Every drug should have a CSI prepared and updated by the manufacturer.
- Adverse events (AEs) due to excipients should be included.
- AEs that have no well-established relationship to therapy should not be included.
- The CSI should include important information that physicians are not generally expected to know.
- As soon as relevant safety information becomes sufficiently well established, it should be included. The specific time when it is included occurs when the safety information crosses the "threshold for inclusion," which is defined as the time when "it is judged that it will influence physicians' decisions on therapy."
- Thirty-nine factors were proposed that can be ranked and weighed for an AE for a particular drug to see whether the information has crossed the threshold. An extensive discussion on the threshold is given:
    a. The threshold should be lower if the condition being treated is relatively trivial, if the drug is used to prevent rather than to treat disease, if the drug is widely used, or if the ADR is irreversible.
    b. Hypersensitivity reactions should be noted early.
    c. Substantial evidence is required to remove or downgrade safety information.
- Ten general principles were proposed:
    1) In general, statements that an adverse reaction does not occur or has not yet been reported should not be made.
    2) As a general rule, clinical descriptions of specific cases should not be part of the CSI.
    3) If the mechanism is known, it should be stated, but speculation about the mechanism should be avoided.
    4) As a general rule, secondary effects or sequelae should not be listed.
    5) In general, a description of events expected as a result of progression of the underlying treated disease should not be included in the CSI.
    6) Unlicensed or "off-label" use should be mentioned only in the context of a medically important safety problem.
    7) The wording used in the CSI to describe adverse reactions should be chosen carefully and responsibly to maximize the prescriber's understanding. For example, if the ADR is part of a syndrome, this should be made clear.
    8) The terms used should be specific and medically informative.
    9) The use of modifiers or adjectives should be avoided unless they add useful important information.
    10) A special attribute (e.g., sex, race) known to be associated with an increased risk should be specified.
- Where possible, frequencies should be provided, although it is admitted that this is very difficult with spontaneous safety data. A proposed classification is:
    a. Very common: ≥1/10 (≥10%)
    b. Common (frequent): ≥1/100 and <1/10 (≥1% and <10%)
    c. Uncommon (infrequent): ≥1/1000 and <1/100 (≥0.1% and <1%)
    d. Rare: ≥1/10,000 and <1/1000 (≥0.01% and <0.1%)
    e. Very rare: <1/10,000 (<0.01%)

Many of these recommendations have been adopted in one form or another around the world, though not in their totality. The revised edition (1998/1999) of this document appeared as CIOMS V.

CIOMS IV (1998): Benefit–Risk Balance for Marketed Drugs[4,17,18,19]

Evaluating Safety Signals

From the preface of the report: "CIOMS IV is to some extent an extension of CIOMS II and III. It examines the theoretical and practical aspects of how to determine whether a potentially major, new safety signal signifies a shift, calling for significant action in the established relationship between benefits and risks; it also provides guidance for deciding what options for action should be considered and on the process of decision-making should such action be required. The report looks at the general concepts of benefit risk analysis and discusses the factors influencing assessment, including stakeholders and constituencies, the nature of the problem (risk), the indication for drug use and the population under treatment, constraints of time, data and resources, and economic issues. It recommends a standard format and content for a benefit risk report:

Introduction

1. Brief specification/description of the drug and where marketed
2. Indications for use, by country, if there are differences
3. Identification of one or more alternative therapies or modalities, including surgery
4. A very brief description of the suspected or established major safety problem

Benefit evaluation

1. Epidemiology and natural history of the target disease(s)
2. Purpose of treatment (cure, prophylaxis, etc.)
3. Summary of efficacy and general toleration data compared with
4. Other medical treatments
5. Surgical treatment or other interventions
6. No treatment

Risk evaluation

1. Background.
2. Weight of evidence for the suspected risk (incidence, etc.).
3. Detailed presentations and analyses of data on the new suspected risk.
4. Probable and possible explanations.
5. Preventability, predictability, and reversibility of the new risk.
6. The issue as it relates to alternative therapies and no therapy.
7. Review of the complete safety of the drug, using diagrammatic representations when possible (risk profiles); when appropriate, focus on selected subsets of serious AEs (e.g., the three most common and three most medically serious adverse reactions).
8. Provide similar profiles for alternate drugs.
9. When possible, estimate the excess incidence of any adverse reactions known to be common to the alternatives.
10. When there are significant adverse reactions that are not common to the drugs compared, highlight important differences between the drugs.

Benefit-risk evaluation

1. Summarize the benefits as related to the seriousness of the target disease and the purpose and effectiveness of treatment.
2. Summarize the dominant risks (seriousness/severity, duration, incidence).
3. Summarize the benefit–risk relationship, quantitatively and diagrammatically if possible, taking into account the alternative therapies or no treatment.
4. Provide a summary assessment and conclusion.

Options analysis

1. List all appropriate options for action.
2. Describe the pros and cons and likely consequences (impact analysis) of each option under consideration, taking alternative therapies into account.
3. If relevant, outline plans or suggestions for a study that could provide timely and important additional information.
4. If feasible, indicate the quality and quantity of any future evidence that would signal the need for a revaluation of the benefit-risk relationship.
5. Suggest how the consequences of the recommended action should be monitored and assessed.

Several examples of benefit-risk analyses are given (quinine and allergic hematologic events, felbamate and blood dyscrasias, dipyrone and agranulocytosis, temafloxacin and renal impairment and hypoglycaemia, remoxipride and blood dyscrasias, clozapine and agranulocytosis, sparfloxacin and phototoxicity).

No example of a real benefit–risk report is given using this format. This type of report seems eminently possible in situations where the risk is small and there is no urgent or immediate action needed to protect the public health. However, in situations in which immediate action is needed, usually in multiple markets around the world, the preparation of such a report is probably not feasible.

CIOMS V (2001): Current Challenges In Pharmacovigilance: Pragmatic Approaches[5,20,21,22]

The CIOMS V report is a 380-page document that covers a wide variety of current issues in drug safety. A summary of some of the proposals follows. Not all these recommendations are universally accepted or required.

The sources of individual case reports are recommended as follows:

Traditionally, the primary source of safety information on marketed drugs was spontaneous reports, with occasional literature reports also appearing. New types of reports are now appearing, including internet reports, solicited reports from patient support programs, surveys, epidemiologic studies, disease registries, regulatory and other databases, and licensor and licensee interactions. Consumer reports were often not analysed unless medical validation was obtained.

The CIOMS V report makes various recommendations, some of which are noted below:

Consumer reports

1. Consumer reports should be scrutinized and should receive appropriate attention.
2. The quality of a report is more important than its source.
3. Spontaneous reports are always considered to have an implied causal relationship to the drug.
4. Respect privacy and the laws and regulations governing it.
5. If a report is received from a third party, that party should be asked to encourage the consumer to report the information to his or her physician or to authorize the sponsor/authority to contact the physician directly.
6. All efforts should be made to obtain medical confirmation of serious unexpected consumer reports. The regulators may be in a better position to get this information if companies have been unsuccessful.

Literature

1. Cases may appear in letters to the editor.
2. There may be a long lag time between the first detection of a signal by a researcher and his or her publication of it.
3. Publications may be a source of false information and signals.
4. Companies should search at least two internationally recognized literature databases using the International Normalized Nomenclature name at least monthly.
5. Broadcast and lay media should not ordinarily be monitored. If such information is made available to the company, it should be followed up.
6. Judgment should be used in regard to followup, with the strongest efforts made for serious unexpected ADRs.

The internet

1. Protection of privacy is particularly important regarding internet cases.
2. A blank ADR form should be provided on a website to facilitate reporting.
3. A procedure should be in place to ensure daily screening of a company's or regulator's website(s) to identify potential case reports.
4. Companies and regulators do not need to routinely surf the net beyond their own sites other than to actively monitor relevant special home pages (e.g., disease groups) if there is a significant safety issue.
5. The message should be consistent around the world because the internet does not respect geographic (or linguistic) boundaries.

Solicited reports

1. Solicited ADR reports arising in the course of interaction with patients should be regarded as distinct from spontaneous unsolicited reports.
2. They should be processed separately and so identified in expedited and periodic reporting.
3. To satisfy post marketing regulations, solicited reports should be handled in the same way as study reports: causality assessments are needed. Serious unexpected ADRs should be reported on an expedited basis.
4. Serious expected and nonserious solicited reports should be kept in the safety database and reported to regulators on request.
5. Signals may arise from solicited reports, so they should be reviewed on an ongoing basis.

Aspects of clinical trial reports

1. In general, safety information reported expeditiously to regulatory authorities should be reported to all phase I, II, and III investigators who are conducting research with any form of the product and for any indication.
2. It is less important to notify phase IV investigators; they will ordinarily use the available up-to-date local official data sheet as part of the investigator's brochure
3. Quality of life studies should be handled like clinical trial data.

CIOMS VI (2005): Management of Safety Information from Clinical Trials[6,23,24]

The CIOMS VI working group focused on clinical trial safety, which represents a departure from the focus of the earlier working groups that concentrated primarily on post marketing safety issues. The report, available from the CIOMS office in Geneva, like the CIOMS V report runs some 300 pages. The most important points are summarized here. The reader is referred to the report for further detail. Keep in mind that these recommendations are quite new and have not been put into regulations in all jurisdictions.

General Principles and Ethical Considerations

- The concepts of pharmacovigilance presented here apply to trials in phases I through IV.
- Any study that is not scientifically sound should be considered unethical.
- Informed consent is the cornerstone of human subject research, but there are situations in which it is either not possible or appropriate (such as in anonymous tissue sample studies, epidemiologic research, or emergency treatment protocols).

Systematic Approach to Managing Safety Data

- The concepts of pharmacovigilance, risk management, assessment, and minimization should be applied to the study phases and the post marketing period. Sponsors must have in place a well-defined process to readily identify, evaluate, and minimize potential safety risks. The process should start before the first phase I study. A formal development risk management plan should be developed.
- A dedicated safety management team should be formed for each development program to review safety information on a regular basis so that decisions can be made in a timely manner. The review should be at least quarterly, and the team should consider changes to the investigator's brochure, informed consent, and protocol as needed.
- When licensing partners are involved, a joint safety committee should be created, with clear roles and responsibilities. This should ideally be defined in the initial contract. A project management function should be set up to ensure scheduling, tracking, and timelines.

Data Collection and Management

- The investigator should report to the sponsor (immediately if judged critical) any information considered to be important in regard to safety even if the protocol does not call for it. The sponsor must carefully train the investigative site in this matter.
- The collection of "excessive" data can have a negative impact on data quality. Case report form fields should collect only those data that can be analysed and presented in tabular form. All other data should be collected as text comments.
- Safety monitoring in phase IV studies may not require the same intensity as for phase I-III trials, but the same principles and practices should apply.
- If a company provides any support for an independent trial it does not sponsor (investigator-initiated studies/trials), the company should still obtain at a minimum all serious suspected adverse reactions.
- The company should do its own causality assessment and, if appropriate, report it to the health authorities, even if the investigator has already done so.

➢ Risk Identification and Evaluation

A. Ongoing safety evaluation

- Sponsors should develop a system to assess, evaluate, and act on safety information on a continuous basis during drug development to ensure the earliest possible identification of safety concerns to allow risk minimization.
- The integrity of the studies should not be compromised by the safety monitoring and analysis.

B. Safety data management

- Safety data should be handled using consistent standards and criteria, with care and precision.
- Safety evaluations must be individualized for each product because there are no standard approaches to evaluating or measuring "an acceptable level of risk."

C. Review of safety information

- Safety data analysis should involve both individual case reports as well as aggregate data. Individual cases should be reviewed within specified time frames and aggregate data on a periodic basis.
- The evaluation should be done in the context of the patient population, the indication studied, the natural history of the disease, and currently available therapies.
- Causality determinations should be done for all reported cases. The investigator causality assessment should be taken into account when the sponsor is reviewing the safety information.
- AEs of special interest should be identified in the protocol and handled as if they are serious even if they do not meet the regulatory definition of serious.

Frequency of Review of Safety Information

- Safety review of all data should be done frequently:
- Ad hoc for serious and special interest AEs
- Routine periodic review of all data whose frequency varies from trial to trial or program to program
- Reviews triggered by specific trial or program milestones
- At the time of study completion and unblinding

Analysis and Evaluation

- Subgroup analysis, though possibly limited by small sample size, should be done for dose, duration, gender, age, concomitant medications, and concurrent diseases.
- Data pooling should include studies that are of similar design. This can include all controlled studies, placebo-controlled studies, studies with any positive control, studies with a particular positive control, and particular indications.
- If the duration of treatment varies widely among participants, data on the effect of treatment duration should be analyzed.

CIOMS VII (2006): Development Safety Update Report (DSUR)[7,25,26,27]

This working group has created the concept of the DSUR, which will be the premarketing equivalent of the Periodic Safety Update Report for marketed products. Its report has been published and it will likely be adopted throughout the world as the PSUR has been. A brief summary of There should be one DSUR for one chemical entity. The goal is to include all new, pertinent, clinical, and nonclinical safety information, that is, the drug's safety profile. It

will include both cumulative and interval summaries of key safety data and will attempt to evaluate safety data to patient exposure. It will describe new safety issues, summarize known and potential risks, and give an update on the status of the clinical development program. It will note any urgent or emerging issues and will note changes to clinical trial protocols, consent forms, and the IB. It is not meant to be a signal detection tool or a means to document or discuss individual cases. The DSUR should be prepared in parallel to the PSUR if the drug is already on the market. The first authorization anywhere in the world to conduct a clinical trial will be the developmental international birth date, in the same way that the first approval anywhere in the world creates an international (marketing) birth date. It will be prepared annually by the sponsor and submitted to the regulatory agencies within 60 days of the data lock point. An executive summary plus line listings of serious ADRs will be sent to IRBs and ethics committees. The reference labeling document will be the investigators' brochure in place at the beginning of the reporting period. It may contain some proprietary information, which may need to be redacted if the document is sent to places other than regulatory agencies.

The contents include:

a) Title Page
b) Table of Contents
c) Executive Summary
d) Introduction
e) Worldwide Marketing Authorization Status
f) Update on Actions Taken for Safety Reasons
g) Changes to Reference Safety Information
h) Inventory and Status of Ongoing and Completed Interventional Clinical Trials
i) Estimated Patient Exposure in Clinical Trials
j) Presentation of Safety Data from Clinical Studies
k) Significant Findings from Interventional Clinical Trials
l) Observational and Epidemiological Studies
m) Other Information
n) Information from Marketing Experience
o) Late-Breaking Information
p) Overall Safety Evaluation
q) Summary of Important Risks
r) New Actions Recommended
s) Conclusions
t) Appendices to DSUR

CIOMS VIII (2010): Signal Detection (Points to Consider in Application of Signal Detection in Pharmacovigilance[8,28,29,30]

This working group has developed and published a consensus document on signalling for consideration by sponsors, health agencies, and others who deal with drug safety. It takes a life cycle view of signaling. This is a well written summary of the state of the art of signaling. It is not prescriptive in the sense of mandating a "one-size-fits-all" policy but rather comes forward with conclusions and recommendations to be tailored to the particular product and situation.

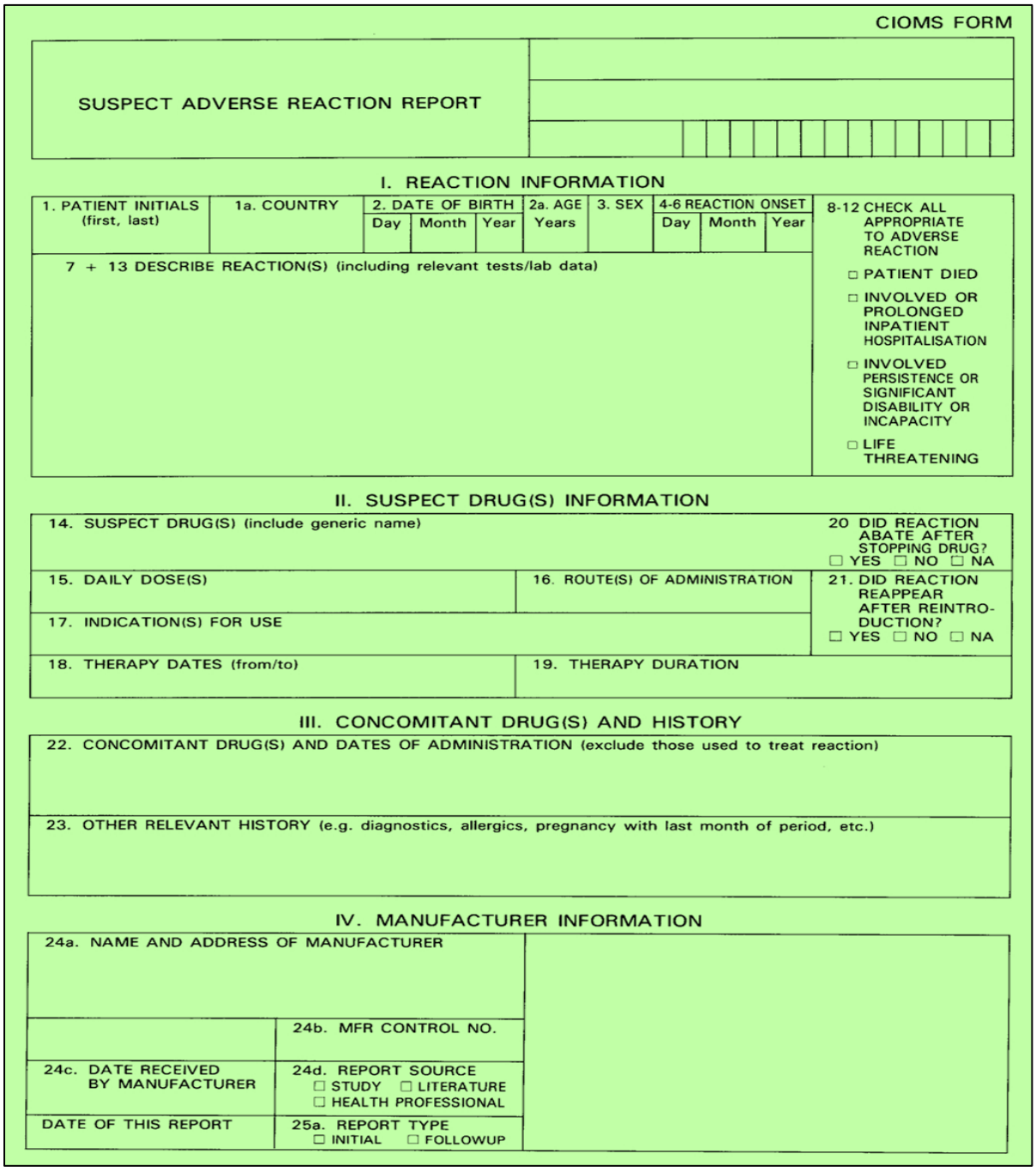
The sections include:

- Background-pharmacovigilance and key definitions.
- Overview of approaches to signal detection including the traditional approaches, and statistical data mining methods including their interpretation within an integrated overall approach to signalling.
- Spontaneously reported drug safety-related information and its use and limitations in signaling
- Databases that support signal
- Traditional methods of signal detection including case and case series review and the analyses of larger databases
- More complex quantitative signal detection methods including disproportionality analysis, Bayesian methodologies, frequentist versus Bayesian approaches, evaluating data-mining performance, and potential conflict of interest
- How to develop a signal detection strategy
- Overview of signal management, including prioritization, evaluation, options analysis of potential and identified risks, reporting and communicating risks
- Future directions in signal detection, evaluation, and communication, including new algorithms and use of non-spontaneous report databases

Other Areas

CIOMS is or has worked on vaccine vigilance, standardized MedDRA queries, drug development and pharmacovigilance in resource-poor countries, and other areas in drug development

CIOMS FORM



CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE Years	3. SEX	4-6 REACTION ONSET Day	Month	Year	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
										☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)	20 DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA
15. DAILY DOSE(S) / 16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA
17. INDICATION(S) FOR USE	
18. THERAPY DATES (from/to) / 19. THERAPY DURATION	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER	
	24b. MFR CONTROL NO.
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE ☐ INITIAL ☐ FOLLOWUP

Standardized document including the minimum required information for the appropriate reporting of adverse drug reactions. The Council for International Organizations of Medical Sciences (CIOMS) create this Form with the purpose of providing an international reference to unify the reporting procedure between different countries. Different national and international regulatory authorities have created their own reports based on the CIOMS Form I, firstly established in 1987.

Conclusion:

The Council for International Organizations of Medical Sciences (CIOMS) has played a pivotal role in shaping the landscape of medical ethics, research, and pharmacovigilance on a global scale. Over the years, CIOMS has been instrumental in developing guidelines that harmonize ethical standards in biomedical research, ensuring the protection of human subjects and fostering international cooperation. These guidelines, such as the CIOMS Ethical Guidelines and the CIOMS/WHO International Ethical Guidelines, have provided a robust framework that researchers and regulatory bodies worldwide rely upon to maintain high ethical standards. Furthermore, CIOMS has significantly contributed to pharmacovigilance and drug safety, addressing the critical need for monitoring adverse drug reactions (ADRs) and enhancing patient safety. By collaborating with the World Health Organization (WHO) and other international bodies, CIOMS has developed comprehensive guidelines and reporting systems that aid in the detection, assessment, and prevention of ADRs, thereby improving public health outcomes. In addition to its foundational work in ethics and safety, CIOMS has continually adapted to the evolving landscape of medical science, addressing contemporary challenges such as emerging infectious diseases, advances in genomics, and the ethical implications of new technologies. The organization's ability to convene experts from diverse fields and foster consensus has been crucial in responding to these dynamic changes effectively. Overall, CIOMS remains a cornerstone institution in the realm of international medical sciences, advocating for ethical integrity, scientific rigor, and patient safety. Its ongoing efforts to update and refine guidelines reflect a commitment to responding to the needs of the global medical community and safeguarding the welfare of patients worldwide. As medical research and practice continue to advance, CIOMS's role in guiding and standardizing ethical and safety practices will undoubtedly remain vital.

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