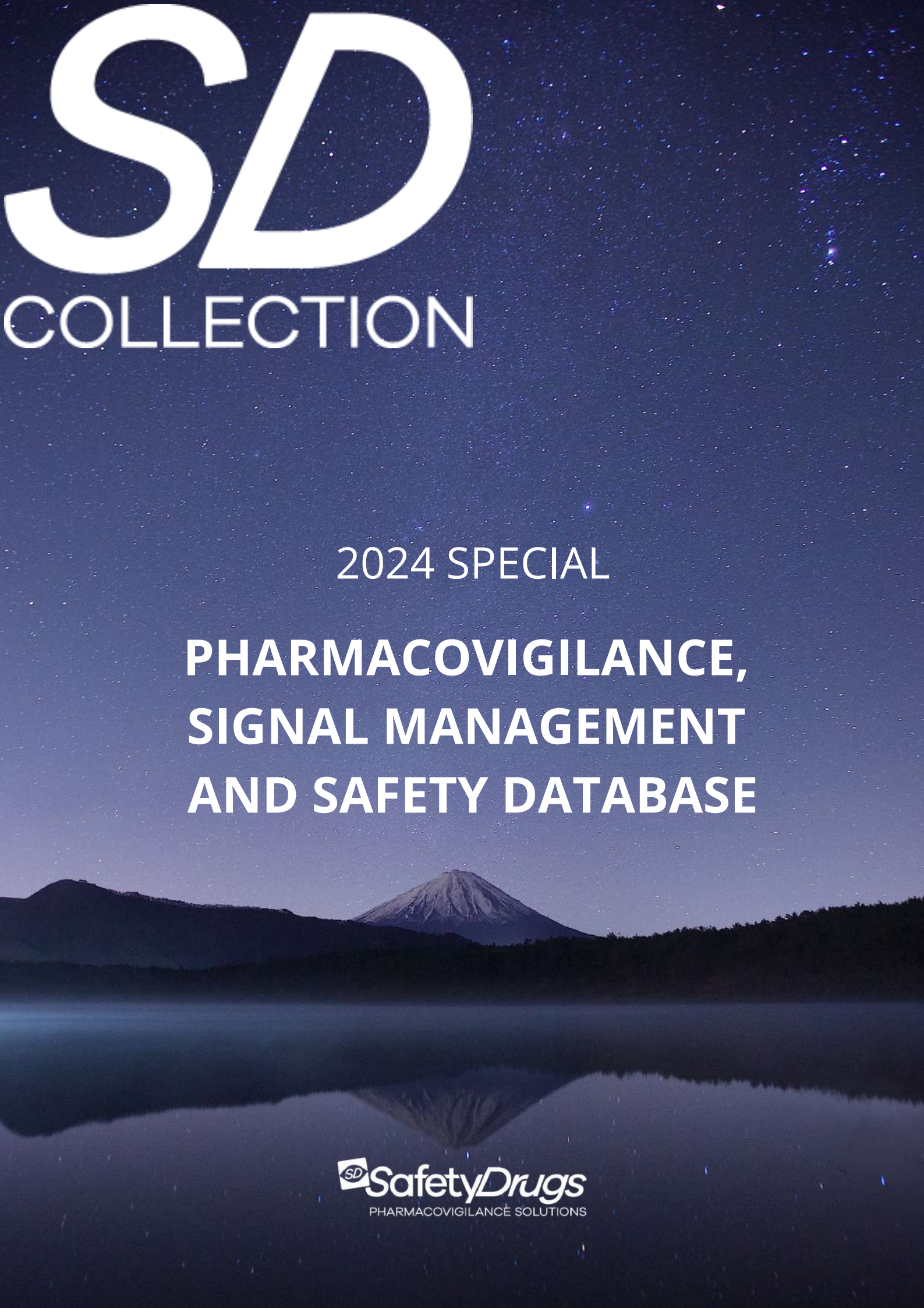
SD
COLLECTION

2024 SPECIAL

PHARMACOVIGILANCE, SIGNAL MANAGEMENT AND SAFETY DATABASE



SafetyDrugs
PHARMACOVIGILANCE SOLUTIONS

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DRUG SHORTAGES: THE APP FOR NOTIFYING PATIENTS IS NOW AVAILABLE

ITALIAN CITIZENS CAN NOW ALWAYS BE UPDATED ON ANY SHORTAGES OF MEDICINES THANKS TO "AIFA MEDICINALI".

DRUG SHORTAGES APP: WHAT AIFA MEDICINALI IS

In December 2022, AIFA, the Italian medicines agency, released an app to make information on drugs and their availability accessible to patients or caregivers. It is called AIFA Medicinali and is available free of charge for mobile devices from Google Play and the App Store.

AIFA Medicinali is an application developed by AIFA, the Italian medicine agency, born from the need of patients with chronic diseases to have information about the availability of medicines. The app allows you to always be updated on any shortcomings of the medicines of interest and to know the marketing status of the medicines authorized in Italy.

Through the app, citizens can also carry out research on medicines and individual packages by directly accessing the AIFA database. They can consult the Package Leaflet of the medicines and the Summary of Product Characteristics.

The app also allows patients or caregivers to manage their medications on a daily basis. A problem encountered is the lack of adherence to therapy, for this purpose, in the AIFA Medicinali, the patient or caregiver can create one or more virtual "lockers" in which to insert the drugs used. Here it is possibile to set alerts to remind you of taking them, entering details such as doses, times, methods of taking and expiry of the drug.
An area is also available where the user can import their health card to always have it available on their device.

The app is available free of charge on Google Play store and on App store.

CLINICAL TRIALS: ITALIAN NATIONAL ETHICS COMMITTEES ARE OPERATIVE

THE TWO ITALIAN NATIONAL ETHICS COMMITTEES FOR CLINICAL TRIALS WILL EVALUATE THE STUDY PROTOCOLS OF THEIR RESPECTIVE COMPETENCIES ON A MONTHLY BASIS.

On 1 February 2022, the Minister of Health established the National Ethics Committee for clinical trials relating to advanced therapies and the National Ethics Committee for clinical trials in the pediatric field.

The two CENs established at AIFA, the Italian competent authority, became fully operational with the registration in the Clinical Trial Information System (CTIS) on January 2023.

The task of the two Committees is to evaluate the study protocols failing within their respective competencies. To this end, ordinary sessions are scheduled monthly.

They will be chaired by Prof. Andrea Biondi and Dr. Alessandro Nanni Costa respectively. The presidents are assisted in their activities by the members appointed with the ministerial decrees of 2 March 2022.

Two specific technical-scientific Secretariats and a Coordination Group have also been set up to support the CENs.

MDR EXTENSION: OFFICIAL THE POSTPONEMENT OF THE TRANSITION PERIOD

REGULATION (EU) 2023/607 EXTENDS THE VALIDITY OF THE CERTIFICATE OF MEDICAL DEVICES UNTIL 2027 OR 2028 BASED ON THE RISK CLASS.

MEDICAL DEVICE REGULATION

In May 2017, the Medical Device Regulation (MDR – EU Regulation 2017/745) was published with the aim of redefining the rules on the marketing of medical devices. The MDR repealed Directive 93/42/EEC.

Among the innovations introduced by the Regulation we mention the adoption of the UDI system, the introduction of the declaration of conformity, the optimization of post-marketing surveillance, the recertification of Notified Bodies, the reclassification of some medical devices and the introduction of EUDAMED, the European database for medical devices.

With the Covid-19 pandemic, the date of applicability had been postponed by one year, to 26 May 2021, but the end date of the transitional period had remained unchanged, 26 May 2024, the day by which medical devices can be placed on the market.

MDR EXTENSION: THE REASONS

The times established with the MDR were not sufficient to get stakeholders to make all the required changes. In fact, the designated notified bodies, which are currently 38, are not sufficient to evaluate and certify the more than 21,000 medical devices by 26 May 2024. Furthermore, many manufacturers, especially small and medium-sized enterprises, are unable to demonstrate compliance to the requirements of the MDR. As a result, many devices will not be ready to be legitimately brought to market in time.

To remedy a shortage of medical devices and to ensure the placing on the market of products that have already started the evaluation process by a Notified Body, the European Commission published an amendment proposal to the Regulation on 6 January 2023. This aims to extend the validity period of certificates and the transition period during which devices can be placed on the market.

The proposal was approved by the European Parliament on 16 February 2023 and was consequently adopted by the European Council. On 20 March 2023, Regulation (EU) 2023/607 was therefore published in the Official Gazette, with immediate entry into force, which modifies the transitional period of the MDR (EU Regulation 2017/745) and the IVMDR (EU Regulation 2017/746).

MDR EXTENSION: WHAT CHANGES

The extension, sanctioned with Regulation 2023/607, intends to allow more time to fulfill the requests of the MDR for all those devices that require the intervention of a Notified Body. Therefore, the transitional period is extended by amending Article 120, as well as Articles 122 and 123.

EXTENSION OF VALIDITY OF MEDICAL DEVICES

According to the MDR, the date by which the recertification of medical devices had to take place was May 26, 2024. With the new Regulation, the certificates of devices that were compliant according to the Directive on May 26, 2021, will continue to be valid and therefore the products will be able to continue to be placed on the market until:

- December 31, 2027 for high-risk devices. That is, all class III devices and class IIb implantable devices (except suture materials, staples, dental filling materials, braces, dental crowns, screws, wedges, plates and prostheses, wires, nails, clips, and connectors) ;
- 31 December 2028 for medium and low risk devices. That is, class IIb devices other than those above, class IIa devices and class I devices sterile or with a measuring function.

These extensions are applicable provided that:

- those devices continue to comply with Directive 90/385/EEC or Directive 93/42/EEC, as applicable;
- there are no significant changes in the design and intended purpose;
- the devices do not present an unacceptable risk to the health or safety of patients, users or other persons, or to other aspects of the protection of public health;
- no later than 26 May 2024, the manufacturer has put in place a quality management system following Article 10(9);
- no later than 26 May 2024, the manufacturer or the authorized representative has lodged a formal application with a notified body with a signed written agreement.

Furthermore, in the case of a medical device with a certificate compliant with the MDD valid on 26 May 2021, but expired on 20 March 2023, the date of application of Regulation 2023/607, the extension of the transition period is applicable on condition that:

- before the expiry of the certificate, the manufacturer has requested the conformity assessment from a Notified Body and has signed a contract,

or alternatively:

- a competent authority has granted a derogation from the conformity assessment procedure or has requested the manufacturer to carry out the conformity assessment.

EXTENSION OF VALIDITY OF CUSTOMIZED IMPLANTABLE MEDICAL DEVICES

A further extension has been granted for class III implantable custom-made medical devices. These may be placed on the market or put into service without a certificate issued by a notified body following the conformity assessment procedure, up to:

- 26 May 2026.
-

This extension is applicable if:

- by 26 May 2024, the manufacturer has submitted a formal application to a notified body for conformity assessment with an agreement signed by 26 September 2024.

EXTENSION OF VALIDITY OF IN VITRO MEDICAL DEVICES

As regards in vitro medical devices, an extension had already been introduced with Regulation (EU) 2022/112. Therefore, there is no news. In vitro medical devices for which the conformity assessment procedure pursuant to the Regulation requires the intervention of a notified body, can be placed on the market or put into service until:

- 26 May 2025 for class D devices;
- 26 May 2026 for class C devices;
- 26 May 2027 for class B devices;
- 26 May 2027 for class A devices placed on the market in sterile conditions.

MEDICAL DEVICE POST-MARKETING SURVEILLANCE

The post-market surveillance activity of medical devices remains the responsibility of the notified body that issued the certificate of conformity.

However, the manufacturer may designate a new ON responsible for this activity through an agreement between the two parties and possibly also with the certifying ON. In this case, the new body will not be responsible for the certification issued by the previous one.

MEDICAL DEVICE SELL-OFF DATE

The sell-off date, i.e. the date beyond which legacy devices placed on the market can no longer be marketed, has been removed. Devices, including in vitro devices, placed on the market before or during transition periods and which are still in the supply chain will be able to continue to be made available without time limits.

EUDAMED

EUDAMED, the European database for reporting adverse events from medical devices, is not yet active. Therefore, no changes to the regulation were reported.

CONCLUSIONS

Medical devices will be able to continue to circulate on the basis of active certificates until a new date. Manufacturers will therefore have more time to have medical devices certified by notified bodies. No changes or extensions for all devices that do not require the intervention of a notified body.

MDR EXTENSION: CLARIFICATIONS ON REGULATION (EU) 2023/607

FOLLOWING THE INTRODUCTION OF THE MDR EXTENSION (EU REGULATION 2023/607), MANY DOUBTS HAVE ARISEN FOR MANUFACTURERS. THE EUROPEAN COMMISSION HAS THEREFORE PUBLISHED A DOSSIER OF CLARIFICATIONS. HERE ARE THE MAIN POINTS.

On 03 March 2023, the Regulation (EU) 2023/607 was published which modifies the MDR and the IVDR as regards the transitional period of some medical devices. Following its introduction, several doubts emerged from the manufacturers. The European Commission has therefore published a dossier of 18 questions and answers (Q&A on practical aspects related to the implementation of Regulation (EU) 2023/607 – Extension of the MDR transitional period and removal of the "sell off" periods) to clarify the various issues.

The areas subject to greater clarification are:

- extension of the MDR transitional period;
- evidence of the requirements satisfaction for benefit from the extended MDR transition period;
- conditions to be fulfilled to benefit from the extended MDR transition period;
- surveillance performed by notified bodies;
- deletion of the "sell-off" date.

MEDICAL DEVICES THAT CAN BENEFIT FROM THE EXTENDED TRANSITIONAL PERIOD

They can benefit from the extension of the transitional period, the medical devices placed on the market after 26 May 2021 (date of application of the MDR):

- belonging to class I whose declaration of conformity has been issued with the MDD and whose conformity assessment according to the MDR requires the involvement of a notified body;
- with valid CE MDD/AIMDD certification.

In addition, they can benefit from:

- devices that have already been recertified: the legacy device and the corresponding MDR-compliant device can be placed on the market in parallel until the end of the related transitional period, provided that the MDD certification has not been withdrawn;
- legacy devices that the manufacturer does not intend to recertify under the MDR: their certification will be valid until 26 May 2024.

CLASS III CUSTOM-MADE IMPLANTABLE DEVICES

Class III custom-made implantable devices can be placed on the market without the relevant certificate until 26 May 2026, provided that the manufacturer has lodged an application with a notified body for conformity assessment no later than 26 May 2024 and signed a written agreement with that notified body no later than 26 September 2024.

EXTENSION OF THE TRANSITIONAL PERIOD FOR EXPIRED CERTIFICATES

If a certificate expired before 20 March 2023 (entry into force of the amending Regulation 2023/607) as long as it is not withdrawn, it will be considered valid until 31 December 2027 or 31 December 2028, depending on the case, only if:

- before the expiry date of the certificate, the manufacturer and a notified body have signed a written agreement for the conformity assessment of the device covered by the expired certificate or of a new device intended to replace it;

or

- a competent national authority has granted a derogation or has required the manufacturer to carry out the applicable conformity assessment procedure within a certain period.

EVIDENCE OF THE SATISFACTION OF THE REQUIREMENTS FOR BENEFIT FROM THE EXTENDED MDR TRANSITION PERIOD

The extension of the transitional period and the concomitant extension of the certificate's validity take place automatically by law. Whenever a manufacturer needs to demonstrate the validity of the certificate, for example in the case of procurement procedures, he has to provide:

- a self-declaration certifying the satisfaction of the requirements and indicating the expiry date of the transitional period;
- a confirmation letter issued by the notified body certifying receipt of the manufacturer's application for conformity assessment and the conclusion of a written agreement.

In addition, the competent authorities should issue certificates of free sale for the duration of the extended validity of the certificate.

The European Commission will update its factsheets for competent authorities in non-EU/EEA countries, for healthcare professionals and healthcare institutions and the procurement ecosystem, explaining how the extended transition period.

ELEMENTS NECESSARY FOR THE FORMAL APPLICATION FOR CONFORMITY ASSESSMENT

The application for a conformity assessment request to a notified body must include:

- information useful for identifying the manufacturer and the devices to be evaluated, possibly also those that will replace a legacy device;
- the information necessary for the notified body to finalize the agreement;
- the elements listed in the conformity assessment referred to in Annexes IX to XI of the MDR;
- information enabling the notified body to verify the qualification of the products as devices, their respective classification and the chosen conformity assessment procedure;
- a schedule of the times, in agreement with the notified body, for the eventual supply of the technical documentation and any other pertinent information;
- documentation on the manufacturer's QMS (Quality Management System).

To benefit from the extension of the transitional period, applications must be submitted by 26 May 2024 and an agreement signed between the manufacturer and the notified body by 26 September 2024. The conformity assessment activities must be completed by 2028.

ELEMENTS NECESSARY FOR THE FINALIZATION OF THE AGREEMENT BETWEEN THE MANUFACTURER AND THE NB

To take advantage of the extension of the transitional period, manufacturers will have to sign a contract with the notified body by 26 September 2024. The agreement, which is based on the formal request for certification presented by the manufacturer to the body, must include an indication of the timing for the submission of the documentation not provided at the time of submission of the application. An example of this is the complete technical documentation for all the devices covered by the formal application.
Further clarifications in this regard could be provided by NBCG-Med (Notified Bodies Coordination Group), in agreement with the MDCG NBO (Notified Bodies Oversight) working group.

"DEVICE INTENDED TO SUBSTITUTE THAT DEVICE"

An insight was dedicated to the term "device intended to substitute that device" used in the MDR. With the indication of device intended to replace the previous device, the device is identified which, usually, differs from the previous one due to significant changes made to the design or purpose.

In this case, the transitional period is only applicable to the pre-existing device. The new device must undergo a full conformity assessment according to MDR before being placed on the market. After MDR certification of the replacement device, the legacy device and the replacement device can be placed on the market in parallel until the end of the relevant transitional period.

SURVEILLANCE PERFORMED BY NOTIFIED BODIES

Some points of uncertainty regarding the surveillance activity performed by notified bodies have been clarified:

- the agreement for the transfer of surveillance from the notified body that issued the MDD/AIMDD certificate to the notified body that certifies according to the MDR must be signed by 26 September 2024. As long as there is no agreement or in any case until 26 September 2024 at the latest, the former body continues to be responsible for adequate oversight in relation to the applicable requirements relating to the devices it has certified;
- in the surveillance transfer agreement from the notified body that issued the certificate according to MDD/AIMDD to the notified body certifying according to MDR, the relevant documentation from the outgoing notified body to the incoming notified body should be included and should also contemplate the possibility for the MDR notified body to suspend or withdraw a certificate issued by the notified body under MDD/AIMDD where duly justified;
- the incoming notified body is not responsible for the conformity assessment activities carried out by the issuing notified body. Its surveillance is limited to surveillance under the MDR;
- on the labeling, including the CE marking, the number of the notified body which issued the certificate following the directive and which is still valid, may continue to be indicated. However, the manufacturer can modify the labeling of pre-existing devices by indicating the number of the notified body to which a formal application has been submitted under the MDR.

MDR EXTENSION, CLARIFICATION ON THE DELETION OF THE SELL-OFF DATE

The sell-off date, that is the deadline for the further making available on the market of devices placed on he market in accordance with the previously applicable Directives, has been deleted.

Therefore:

- medical devices that have been placed on the market prior to 26 May 2021 in accordance with the MDD/AIMDD or after 26 May 2021 during the transitional period provided for in Article 120 MDR (i.e. until 31 December 2027 or 31 December 2028, as applicable) may continue to be made available on the market or put into service without any limitation in time without prejudice to the device's possible shelf-life or expiry date.
- in vitro diagnostic medical devices that have been placed on the market prior to 26 May 2022 in accordance with the IVDD or after 26 May 2022 during the transitional period provided for in Article 110 IVDR (i.e. until 26 May 2025, 26 May 2026 or 26 May 2027, as applicable). Those IVD may continue to be made available on the market or put into service without any limitation in time without prejudice to the device's possible shelf-life or expiry date.

WHY A SAFETY DATABASE IS CONVENIENT FOR PHARMACEUTICAL COMPANIES?

A SAFETY DATABASE IS A FUNDAMENTAL TOOL TO SAVE TIME AND RESOURCES. HERE IT IS THE REASONS WHY A SAFETY DATABASE IS CONVENIENT FOR PHARMACEUTICAL COMPANIES.

WHAT IS A PHARMACOVIGILANCE SAFETY DATABASE AND WHAT IS IT FOR?

International regulations require every pharmaceutical company to monitor the risk/benefit ratio of its drugs. This is an activity called pharmacovigilance. In order to carry out it, pharmaceutical companies must collect reports of adverse events, analyze them, evaluate them and submit periodic reports to the authority. A pharmacovigilance safety database is a tool that helps the company carry out all these tasks.

Data collection. A database allows you to collect and store pharmacovigilance cases regardless of source and format. In fact, reports received directly from the pharmaceutical company can be entered manually, or cases received from the authority can be imported in electronic format (ICSRs).
The safety database also makes it possible to distinguish the typology, therefore for example spontaneous reporting, reporting by the authority or cases from the literature.

Case processing. According to the Good PharmacoVigilance Practices (GVP) guidelines, the process of each case must go through the following phases: data entry (manual or electronic import), Quality Check, Medical Review and, if necessary, submission to the authority or distribution to partners. A computerized safety database is already designed to follow this workflow. Furthermore, it helps the operator by verifying the correctness and completeness of the data through special checks when switching status.

Case submission. With a computerized database it is possible to submit cases to the authorities through automatic tools. An example of this is the gateway which even allows massive sending in the electronic format required by the standards. You can also distribute them directly to partners to comply with Safety Data Exchange Agreements (SDEA).

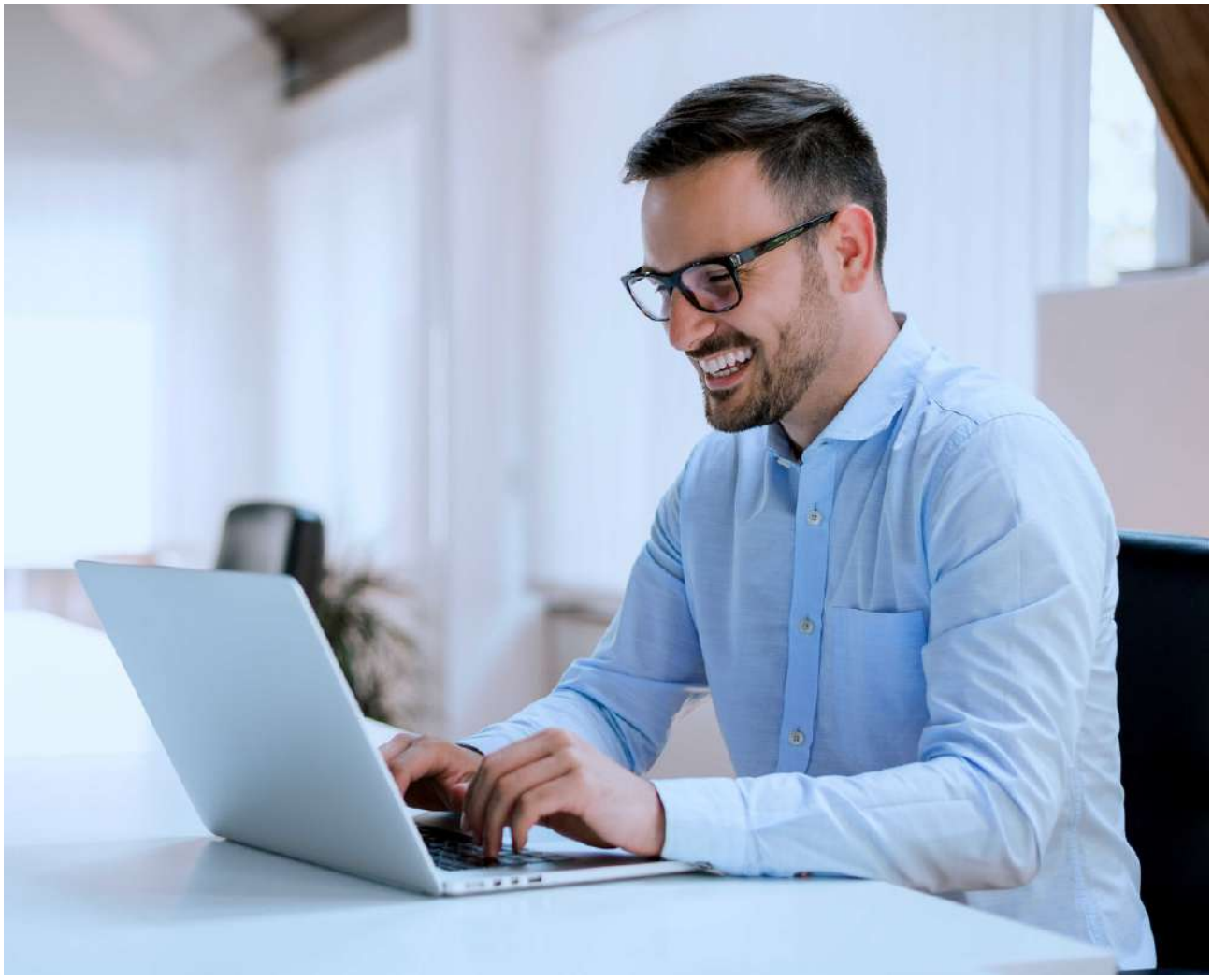
Analysis of collected data. The pharmaceutical company will have to analyze the data collected in order to evaluate the risk/benefit ratio of its products. With a computerized database, the team is facilitated in extracting the pertinent cases through specific search filters. Furthermore, a computerized database makes it possible to integrate a Business Intelligence module for even more detailed analyzes of aggregated data.

Extraction and submission of pharmacovigilance reports. Obligation of the company that holds the Marketing Authorization Holder (MAH), is to send Periodic Safety Update Reports (PSUR). With a computerized safety database, it is possible to quickly extract the lists necessary to complete the PSUR and submit it to the authority.

Signal detection. Another obligation of pharmaceutical companies is to carry out signal detection, i.e., the search for a result that is out of parameters concerning that expected from the risk/benefit ratio and which can therefore modify the safety profile of the drug. Also, in this case it is essential to have a computerized tool capable of helping the operator to detect a potential signal.

HOW A SAFETY DATABASE ALLOWS A PHARMACEUTICAL COMPANY TO SAVE

The pharmacovigilance activity, although aimed at protecting the health of the patient, leads to a great expenditure of resources for pharmaceutical companies. However, the entire process can be optimized with the use of a computerized safety database which allows the pharmacovigilance team to have more precise data, save precious time and meet quality and safety requirements. Consequently, having a database allows you to avoid errors, perform analyzes faster and above all prevent the findings during the inspection phase.



THE ADVANTAGES OF SAFETYDRUGS, THE SAFETY DATABASE

In addition to managing the entire case process, SafetyDrugs further simplifies the daily work of the pharmacovigilance team thanks to tools such as:

- Pre-import triage. It allows you to preview the case to evaluate its actual applicability;
- Duplicate search function. It allows you to detect any duplicate cases compared to those already present in the database;
- Integrated messaging system. It allows you to send emails with attachments or alerts to remember regulatory deadlines and notify you of workflow status changes;
- Tracking notes. It is the case processing diary in which to record follow-up requests, comments and notes of various kinds. It can be printed in a report and linked to notifications;
- Additional reports. In addition to the regulatory reports, there are another dozen to monitor the daily activity of the user for quality assurance and reconciliation purposes.

SafetyDrugs is also recognized as one of the best European products on the market for value for money. Its modular structure makes it possible to adapt to the business model of each company by offering a tailor-made solution.

HOW TO CHOOSE A SAFETY DATABASE: THE GUIDE

CHOOSING A SAFETY DATABASE IS A DELICATE OPERATION THAT TAKES TIME. EVERY PHARMACEUTICAL COMPANY HAS ITS OWN SPECIFIC NEEDS. WE HAVE COMPILED FOR YOU A LIST OF THE MAIN FACTORS TO CONSIDER WHEN CHOOSING A PHARMACOVIGILANCE DATABASE.

HOW TO CHOOSE A SAFETY DATABASE: REQUIREMENTS

Regulatory compliance. It may seem trivial, but the first thing to check in a safety database is compliance with pharmacovigilance regulations, compliance with the reference authority and compliance with the electronic format in force, currently XML ICH E2B (R3).

Implementation mode. A safety database can be available for purchase or in SaaS mode, a cloud database lease formula. Not all software houses offer the dual solution, therefore it is good to adopt the one most in line with the needs of the company.

How to submit ICSRs to the authorities. Cases can be submitted to the authorities by sending the ICSRs via email, but the most effective and immediate way is to use the Gateway. It is a program of massive transmission of data to the database of the authority, for example that of EMA, FDA and MHRA. This is the optimal solution for those with a large volume of cases to submit.

Parameterizable workflow. Every company has its processes, which is why a good database needs to fit perfectly with internal procedures. Therefore, it should have a workflow that allows you to follow a flow in compliance with company pharmacovigilance procedures.

Security requirements. To comply with security requirements, the database must allow users to be parameterized with regulated access and permissions, to track all activities and to preserve data in line with data integrity and privacy requirements (GDPR).

Implementation time. A pharmacovigilance database can take some time to implement, especially if data migration from a previous database is required. Therefore, it is important to evaluate the compatibility of the timing proposed by the supplier with the needs of your company.

Validation. The Computer System Validation of a safety database is an essential activity to comply with current regulations on pharmacovigilance. Make sure that the software house has already provided for the supply of all pre-validation documentation in line with GAMP5 and is available to support the entire validation process.

Assistance. The assistance service provided directly by the developer software house is certainly more efficient, due to the greater knowledge of the product, the attentive care dedicated to its customers and the sensitivity in the timeliness of the response compared to an external management.

Maintenance. Being an IT tool that must comply with requirements and regulations, it needs constant maintenance to be kept up to date and compliant. Make sure the service is included in the fee.

Datacentre. A fundamental requirement of the data center where the database is installed is to have ISO 27001 certification relating to information security management. Furthermore, with the entry into force of the GDPR, the data must be stored within the borders of the European Union.

MedDRA dictionary. It is very useful for a database to have the MedDRA dictionary integrated and provided with a browser to speed up the search for the right term. As it is released updated twice a year by the authority, it is advantageous for the database to be able to bring updates online quickly.

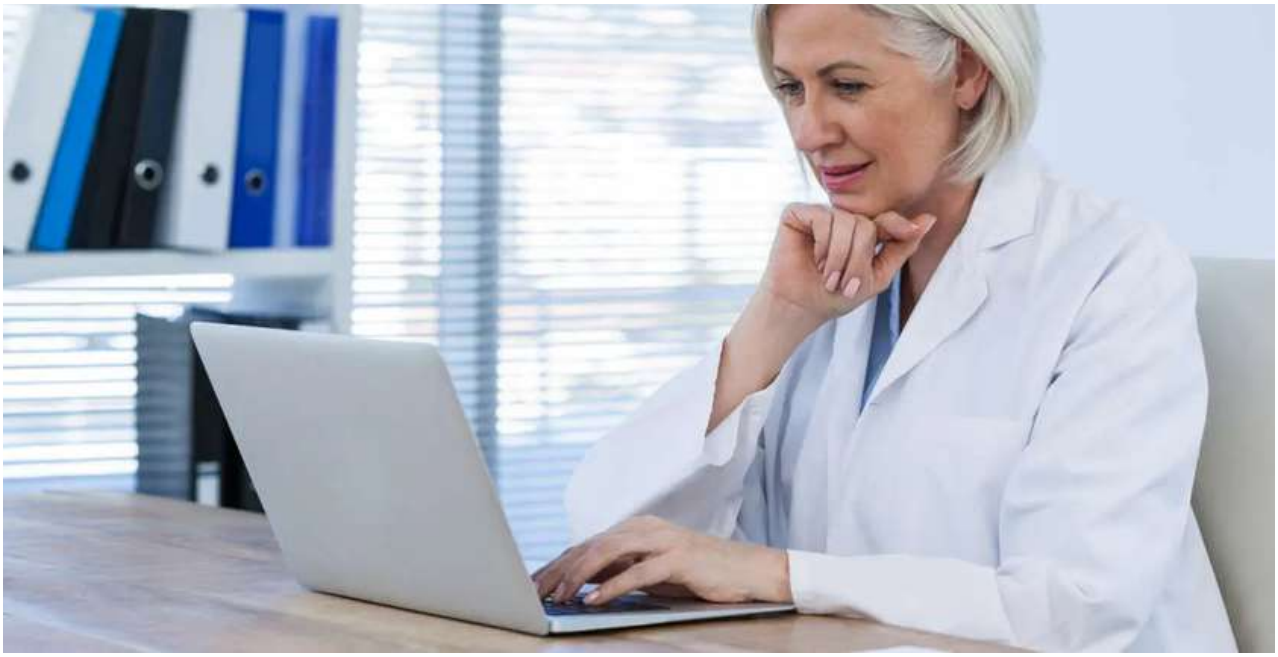
HOW TO CHOOSE A SAFETY DATABASE: USEFUL FUNCTIONS

Advantages. A database by nature must store, manage and extrapolate data. Therefore, evaluate that it has features to facilitate and speed up the activity of the pharmacovigilance team. Among the most useful features are:

- Preview the case first in order to confirm its import
- Automatic detection of duplicate cases
- Copy function to replicate the same contents in a new case
- Messaging and alert system for sending emails and notifications related to regulatory or process deadlines
- Case Agenda to record actions to be done and comments on the case, with the possibility of activating notifications
- Report for monitoring the activities performed in order to evaluate their performance
- Business Intelligence to carry out in-depth and immediate analyzes of aggregated data.

PHARMACOVIGILANCE ICSR MANAGEMENT: 10 BENEFITS OF THE SAFETY DATABASE

THE SAFETY DATABASE IS A FUNDAMENTAL TOOL FOR EFFICIENT PHARMACOVIGILANCE ICSR MANAGEMENT. HERE ARE THE MAIN ADVANTAGES OF USING IT.



Effective pharmacovigilance ICSR management is essential to ensure patient safety and comply with regulations. Pharmaceutical companies have not yet equipped themselves with pharmacovigilance software, they could miss out on numerous advantages that a safety database can offer. We have identified ten of them.

1. EFFICIENT PHARMACOVIGILANCE ICSR MANAGEMENT

A pharmaceutical professional knows that pharmacovigilance ICSR management is crucial to ensuring patient safety and complying with regulations.

A safety database is a specific tool for processing and analyzing data more efficiently and safely than an Excel spreadsheet or other non-computerized systems. Its use allows for greater precision and timeliness in pharmacovigilance operations.

2. REGULATORY COMPLIANCE

Regulations in the pharmacovigilance sector are constantly evolving and becoming increasingly stringent. A safety database is specifically designed to ensure full regulatory compliance.

3. DATA SECURITY
Pharmacovigilance data is extremely sensitive and requires careful protection. A safety database can make use of a technological infrastructure to have environments protected by the highest security requirements. Furthermore, it allows you to back up data and implement a Disaster Recovery plan to ensure operational continuity and compliance with regulatory deadlines.

4. MINIMIZE ERRORS
With a safety database the ICSRs are directly imported and exported in electronic format, therefore no manual intervention is required. The system also warns the user in case of process errors, or missing or inconsistent information, or imminent regulatory deadlines.

5. IN-DEPTH ANALYSIS
The ability to conduct complex analyzes and detect signals (Signal Detection) via the software is a significant advantage. This helps you identify potential problems and make informed decisions promptly. Furthermore, the best databases are equipped with a Business Intelligence module to perform in-depth analyzes of the drugs safety profile.

6. OPERATIONAL EFFICIENCY
The pharmacovigilance database simplifies processes, reducing work time and increasing team efficiency. The speed with which the software can manage data and generate reports saves valuable time and resources for pharmacovigilance ICSR management.

7. USER-FRIENDLINESS
An intuitive interface, specifically designed for the management of adverse cases, simplifies and optimizes the workflow, making it accessible even to those who are not IT experts.

8. CUSTOMIZATION OF DATABASES TO OPTIMIZE THE PHARMACOVIGILANCE ICSR MANAGEMENT
Each pharmaceutical company is unique and pharmacovigilance needs may vary. A database offers solutions designed to adapt to company operating procedures and not vice versa.

9. TECHNICAL SUPPORT
The safety database has a team of experts behind it ready to help the user in case of need. Targeted training, timely assistance and accurate support are services that make a safety database a reliable resource.

10. CONTINUOUS UPDATING
A safety database is under constant analysis to ensure regulatory compliance and to keep up with new technologies. This means that not only will the company have a cutting-edge system when it goes live, but it will also receive regular updates to adapt it to the ever-changing needs of the sector.

In conclusion, a safety database, such as SafetyDrugs, is a fundamental investment for any pharmaceutical company that wants to comply with pharmacovigilance regulations, guarantee data security and save time and resources.

ICSR TRANSFER OUTSIDE OF EU: HOW TO COMPLY WITH THE GDPR WITH SAFETYDRUGS

THE ICSR TRANSFER OUTSIDE OF THE EU ENTAILS RISKS IN TERMS OF COMPATIBILITY BETWEEN PHARMACOVIGILANCE AGREEMENTS AND GDPR. HERE'S HOW YOU CAN BE COMPLIANT WITH SAFETYDRUGS.

In a constantly evolving world, the protection of personal data has become a key priority. For pharmaceutical companies, pharmacovigilance activities involve the management of sensitive patient data, making compliance with the General Data Protection Regulation (GDPR) essential. In this article, we will explore the European Medicines Agency's (EMA) warnings to QPPVs about the risk of non-compliance with the GDPR and how SafetyDrugs offers a solution to ensure compliance.

WHAT IS GDPR?

The GDPR, an acronym for General Data Protection Regulation, is a European legislation that came into force on 25 May 2018. Its mission is to harmonize and strengthen personal data privacy laws in all member countries of the European Union (EU). Among the main changes introduced, we remember:

- the need for explicit consent for the collection and processing of personal data;
- the right to erasure, known as the "right to be forgotten";
- the introduction of rigorous data security measures to protect personal data from the risks of loss, theft or unauthorized access;
- timely notification of data breaches within 72 hours of their discovery;
- the introduction of the DPIA (Data Protection Impact Assessment) for the conduct of data protection impact assessments to identify and mitigate the privacy risks associated with data processing activities.

ICSR TRANSFER OUTSIDE OF EU: THE EMA WARNINGS

The GDPR imposes rigorous requirements on the processing of personal data, which include, to a greater extent, the data present in pharmacovigilance reports as sensitive data. In this regard, the EMA (European Medicines Agency) intervened and, with a letter addressed to the QPPVs and related clarification letter, made it clear to all MAHs (Marketing Authorisation Holder) that for the distribution of ICSRs to partners and various stakeholders outside the EU, it is necessary to comply with the standards dictated by the GDPR.

In particular, EMA has reported that some companies holding marketing authorizations have transferred the case narratives downloaded from EudraVigilance to third countries in full, without the protection of personal data. EMA has therefore drawn attention to the fact that MAHs are responsible for personal data processing activities in the context of pharmacovigilance, including access and subsequent processing of data contained in ICSRs from EudraVigilance. This involves the obligation to comply with the rules established in the GDPR and national data protection laws, when applicable.

EMA also underlines that the use of SCCs (Standard Contractual Clauses) or SDPCs (Standard Data Protection Clauses) by MAHs are not sufficient to ensure compliance with data protection regulations, in particular those provided for by Chapter V of the GDPR. The impact assessment of the data transfer should be conducted before concluding the SCCs, taking into account the laws and practices of the destination third country.

EMA has also published a list of countries, which although non-EU, provide adequate data protection as assessed by the European Commission.

ICSR TRANSFER OUTSIDE OF EU: HOW TO COMPLY WITH THE SAFETYDRUGS GDPR MODULE

Based on the guidance provided by EMA, the SafetyDrugs team has created a new module that can help pharmaceutical companies comply with the rigorous requirements of the GDPR by ensuring privacy compliance in the distribution of pharmacovigilance reports to non-EU countries.

Pharmacovigilants will no longer have to worry about mistakenly sending data subject to privacy, as the GDPR Module adds the "Under data protection" modality to the safety database, which allows:

Creation of a list of data subject to privacy and setting of automatic rules for protection. The module allows you to create a list of non-transferable data outside the EU and set related protection rules:

- sensitive data such as age, gender, medical history, relevant clinical data and other personal data, such as the health history of family members, are replaceable with the "Masked" nullflavor, where permitted by the ICH R3 rules;
- data relating to the location such as, for example, the country code from the Safety Report ID, the WWN code and the Other case identifier, can be replaced with the wording "EU" or "NONEU" based on the origin;
- name of the medicine, which could reveal information about the location, can be replaced with the name of the active substance. Alternatively, a blank space can be used;
- sections of the narrative, such as comments or additional information, can be replaced with parametric text or blank spaces.

GDPR compliant XML export and CIOMS generation. It is possible to export ICSR, in XML R2 and R3 file format, and generate CIOMS with automatic redaction of the data subject to protection. You can also choose whether or not to extract attachments, since they may contain sensitive information.

Receiver management. For each recipient defined as "Under data protection", it is possible to set the elements that must be masked.

Custom parameterization. In SafetyDrugs you can define the GDPR module settings described above.

HOW TO GET THE GDPR MODULE

We are excited to introduce this important enhancement to SafetyDrugs to help companies ensure responsible, GDPR-compliant pharmacovigilance. If your company is interested in learning more about the SafetyDrugs GDPR Module, please do not hesitate to contact us. We'll answer all your questions and walk you through the setup process.

PHARMACOVIGILANCE DATA PROTECTION: HOW WE GUARANTEE MAXIMUM SECURITY

PHARMACOVIGILANCE DATA PROTECTION IS A FUNDAMENTAL ELEMENT FOR PHARMACEUTICAL COMPANIES. TO GUARANTEE SECURITY FOR USERS OF SAFETYDRUGS, THE SAFETY DATABASE, WE HAVE RELIED ON ORACLE DATA CENTRES FOR YEARS.

PHARMACOVIGILANCE DATA PROTECTION: AN ASSIDUOUS COMMITMENT

Where is the data hosted? This is one of the questions we are most often asked by our interlocutors during the product presentation phase. We understand that pharmacovigilance data protection is a crucial element for pharmaceutical companies and this is why we are committed to ensuring data security for our clients. To do this, we relied on the technological partner Oracle: all the data entered into SafetyDrugs is hosted inside a data center whose security standards are among the highest in the world. Here are some of its features.

HIGH QUALITY STANDARDS

Oracle data centre requirements comply with Tier III standards, data security certifications such as PCI DSS, HIPAA, SOC 1/SOC 2, with general security guidelines ISO/IEC 27002, with international standard ISO/IEC 27001 and with Information Security Management Systems standards ISO/IEC 27701, 27017 and 27018.

ADVANCED DATA PROTECTION SYSTEM

During transmission, data is protected by an advanced encryption system* that protects against violations. It is a procedure that is added to various implementations made to the database with the new release: by accessing the database without the necessary decryption keys, it will be impossible for anyone to read the data. The database automatically handles encryption and decryption through the Transparent Data Encryption (TDE) function.

**TLS 1.2 enabled connection negotiated for encryption of at least 128 bits or higher and private key used for encrypted key generation of at least 2048 bits.*

TIMELY ACTIVATION OF DISASTER RECOVERY

In the event of a catastrophic event or cyber-attack, the Oracle Recovery Manager system procedures offer rapid recovery times and certainty about the integrity of the database. Unlike what happens in synchronous copy processes, Oracle limits the risk of data compromise by performing deferred copying on a secondary site with stand-by machines.

ORACLE RELIABILITY

The Oracle brand represents a firm point in the panorama of technology operators. It is a reality whose 430 thousand customers, present in 175 countries around the world, every day safely ride the business opportunities offered by IT tools.

EFFICIENCY OF THE TECHNOLOGICAL STRUCTURE

The choice of the Oracle data center is the pinnacle of the partnership between Max Application, the developer of SafetyDrugs, and the American group, which began in the 1990s with the adoption of their database. Today the technology of our IT services is based on Oracle Cloud: the infrastructure (IaaS), the platform (PaaS) and the software (SaaS), including SafetyDrugs. The complete integration of the three levels of the entire technological structure in a single environment increases the performance of the system and the operational efficiency of the user.

Our decision to choose the Oracle data center to host SafetyDrugs data reflects our ongoing commitment to protecting pharmacovigilance data. High protection, compliance with quality standards and rapid response to extraordinary events confirm the solidity of our decision. With SafetyDrugs, we guarantee pharmacovigilance managers a high-performance and safe product.

SIGNAL MANAGEMENT: THE PROCESS PHASES

SIGNAL MANAGEMENT IS THE PROCESS OF MANAGING SAFETY SIGNALS IN PHARMACOVIGILANCE. HERE'S WHAT PHASES IT CONSISTS OF AND HOW IT IS PERFORMED.

WHAT IS A SAFETY SIGNAL IN PHARMACOVIGILANCE

First of all, it is good to know the definition of a safety signal. A safety signal is an information suggesting a new possible association between a drug and an adverse event, or a known adverse event that occurs with greater impact or in a different way than previously recognized. It is an unexpected result, given by the analysis of various relevant sources, which must be investigated and possibly confirmed.

SIGNAL MANAGEMENT: WHAT IT IS

Signal Management is a fundamental process in pharmacovigilance that aims to detect, evaluate and manage information related to drug safety signals. The goal is to ensure that medicines are used safely and effectively, by promptly identifying and managing potential risks to patient health.

SIGNAL MANAGEMENT REGULATIONS

Signal Management at European level is regulated by Directive 2001/83/EC art. 107h, by Regulation (EC) 726/2004 art. 28 and by the Commission Implementing Regulation (EU) 520/2012. It is also detailed in Good Pharmacovigilance Practices (GVP) Module IX and its Addendum I.

SIGNAL MANAGEMENT PROCESS

According to the GVP, Signal Management consists of the following phases.

1. Signal Detection: investigation and individuation of the signal by analyzing any inherent source.
2. Signal Validation: evaluation of the data supporting the identified signal to verify if the documentation is sufficient to confirm the existence of a cause-effect relationship.
3. Signal Analysis and Prioritisation: identification of signals that require immediate management. These include signals that present significant risks to public health or that influence the benefit-risk balance of a drug.
4. Signal Assessment: evaluation of the signal to detect any new risks, or changes thereof, with a causal association related to the drug and to determine any necessary regulatory actions.
5. Recommendation for Actions: evaluation of the need to take further action.
6. Exchange of information: exchange of information between all interested parties involved.

SIGNAL DETECTION

Signal Detection is the process of looking for signals. It involves constantly monitoring information from various sources, such as, for example, spontaneous case reports, clinical studies, and scientific literature. The aim is to identify potential safety signals and take corrective measures promptly to safeguard public health.

SIGNAL VALIDATION

Signal Validation consists in verifying the reliability and completeness of the information supporting a potential signal. This stage involves the critical analysis of the available information, the robustness of the evidence and the clinical relevance, as well as any additional supporting data. Thanks to the Signal Validation it is possible to confirm or not the existence of a new or changed cause/effect relationship.

SIGNAL ANALYSIS AND PRIORITISATION

During the signal analysis and prioritization phase, various variables are evaluated based on which a priority is assigned or not to the signal. In particular, the impact of the adverse event on the patient is evaluated, taking into account the seriousness, the severity of the clinical manifestation, the reversibility of the event and the ability to prevent its occurrence. In addition, the consequences of treatment interruption on the management or progression of the disease, the presence of therapeutic alternatives and the impact on public health are considered. This last aspect requires a broad evaluation that also takes into account the use of the drug in the general population and in special populations such as pregnant women, children and the elderly.

When analyzing the importance of the signal, it is also essential to consider situations where the drug is used off-label or improperly, i.e. not in compliance with the authorizations.

In prioritizing the signal, the method used by the MHRA (Medicines & Healthcare products Regulatory Agency) can be used. It is based on a score derived from assessing the strength of the causal association between the drug and the adverse event, as well as the public health implications of marketing the drug.

SIGNAL ASSESMENT

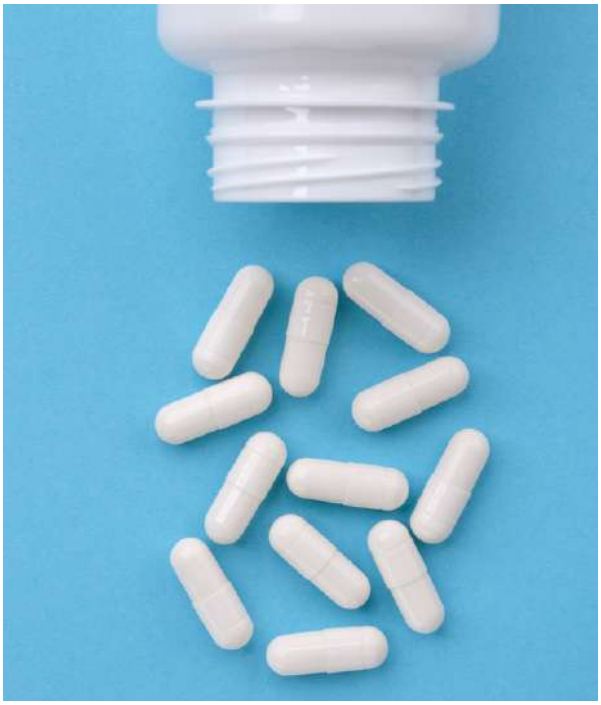
The Signal Assessment consists in the evaluation of the previously identified signal. At this stage, it becomes necessary to conduct further evaluations to determine whether the information gathered is sufficient to obtain a complete picture. The necessary regulatory action is then identified.

In this phase, the Qualified Person for PharmacoVigilance (QPPV) usually consults the dossiers derived from the preclinical and clinical development to look for data that confirm or deny the possible cause/effect relationship between the drug and the adverse reaction. The cases reported in the literature are also examined and experts of both the adverse pathology and the pathology under treatment are consulted to obtain further support.

RECOMMENDATION FOR ACTION

After the evaluation of the signal, the decision phase of the actions to be taken follows. It is a delicate phase as it is necessary to balance the obligation to protect the patient with the risk of adopting excessive actions, such as withdrawing the product from the market. Several times less drastic measures could adequately contain the risk, such as excluding a particular group of patients from administration.

Evaluating the actions to be taken requires the involvement of various company departments, including the regulatory, medical, manufacturing/distribution and commercial sectors. It is essential to trace and record the decisions made and establish the times within which the various company functions must complete the assigned activities.



EXCHANGE OF INFORMATION

The last phase is that of exchanging information with the competent authorities. The Marketing Authorization Holder (MAH) has the responsibility to communicate the validated signals and everything that falls under the definition of Emerging Safety Issue to the health authorities. The MAH may be required to provide periodic signal reviews, risk minimization activities, updates to healthcare professional and patient education materials, and to conduct Post Authorization Safety Studies (PASS).

CONCLUSIONS

In conclusion, Signal Management plays a crucial role in pharmacovigilance to ensure drug safety and protect patient health. The different stages of the process, from signal research and identification to evaluation, prioritization and recommendations for actions to be taken, require in-depth analysis and accurate evaluation of the data.

In this regard, it is important to underline that some tools and resources can simplify and optimize the Signal Management process. A safety database, such as SafetyDrugs, offers an effective solution for data collection and analysis, allowing, thanks to its Business Intelligence module, to identify and highlight potential safety signals in a timely and efficient manner. This tool can provide invaluable support in the early stage of signal identification, facilitating access to pertinent data and contributing to faster and more accurate evaluation.

SIGNAL DETECTION IN PHARMACOVIGILANCE: WHAT IT IS AND HOW IT WORKS

SIGNAL DETECTION PLAYS A FUNDAMENTAL ROLE IN PROMPTLY IDENTIFYING POSSIBLE SIGNALS OF ADVERSE EFFECTS ASSOCIATED WITH THE USE OF A DRUG. HERE'S WHAT SIGNAL DETECTION IS AND HOW IT'S PERFORMED.

WHAT IS SIGNAL DETECTION?

Signal Detection is an analysis activity performed in pharmacovigilance for the identification of an unexpected result concerning the safety profile of a drug. This is a continuous monitoring activity, which is performed throughout the life cycle of the drug, from the clinical development phase to marketing.

Signal Detection is the first of the Signal Management activities, a process of determining new risks or changes to known risks.

According to module IX of GVP (Good Pharmacovigilance Practices), signal management consists of:

- Signal Detection: search and identification of the signal coming from the analysis of any inherent source;
- Signal Validation: Evaluation of the data supporting the detected signal to verify that the documentation is sufficient to confirm the existence of a cause-effect relationship;
- Signal Analysis and Prioritisation: Identify signals that need urgent handling. These include signals with important risks to public health or that influence the risk-benefit ratio of a drug;

- Signal Assessment: evaluation of the validated signal to determine any new risks, or changes thereof, with a causal association related to the drug and any consequent regulatory action;
- Recommendation for Action: Check if further actions need to be taken;
- Exchange of Information: exchange of information between all stakeholders.

ORIGINS OF SIGNAL DETECTION

Signal Detection has its origins during the Second World War when the use of the first radars began to take hold. These instruments were not yet perfected and therefore signaled not only the arrival of enemy bombers but also simply flocks of birds. Operators therefore had to learn to interpret and weigh the signals deriving from the instruments to avoid elevating aircraft unnecessarily. They then began to evaluate the data based on other information such as data from the airports from which the bombers took off or sightings along the route.
The application of Signal Detection in pharmacovigilance maintains the same principle: avoid irrelevant signals, promptly identify useful signals and above all use multiple sources to validate the data.

SIGNAL DETECTION REGULATIONS

Signal Detection in pharmacovigilance is regulated at international and national levels.

Internationally, Signal Detection is regulated by the WHO (World Health Organization), which provides guidelines for the surveillance and management of medicines. The WHO provides VigiBase, a database for international drug monitoring.

ICH (International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use) has developed guidelines for the safety of medicines, including Signal Detection.
In 2010, the CIOMS (Council for International Organizations of Medical Sciences) issued the Report of CIOMS Working Group 165 VIII in Practical Aspects of Signal Detection in Pharmacovigilance.
In the United States, Signal Detection is regulated by the FDA (Food and Drug Administration) through the post-marketing drug surveillance system.

At European level, EMA (European Medicines Agency) has established guidelines for Signal Detection in pharmacovigilance, including Module IX of the GVP (Good Pharmacovigilance Practice).

Furthermore, EMA has set up EudraVigilance, an IT system for collecting reports of adverse reactions in Europe and EVDAS (EudraVigilance Data Analysis System), the system for analyzing the data collected in EudraVigilance.

In Italy, AIFA (Italian Medicines Agency) has published the guidelines for the surveillance of medicinal products, including Signal Detection, as part of the National Pharmacovigilance Plan. Directive 2010/84/EU – Section 3, Article 107 nonies and EU Implementing Regulation n.520/2012.

WHY IS SIGNAL DETECTION PERFORMED IN PHARMACOVIGILANCE?

The drugs marketed come from at least seven/ten years of studies, necessary to obtain marketing authorisation. However, these studies are not sufficient to reproduce the wide variability of situations that can occur once the drug is used by the population, as they are carried out in a limited period of time and in well-controlled experimental conditions. Therefore, through pharmacovigilance, it is essential to continue monitoring adverse reactions even after marketing, looking for potential signals to promptly identify possible risks and implement the necessary corrective actions.

WHAT IS A PHARMACOVIGILANCE SIGNAL?

A pharmacovigilance signal is a more or less strong hypothesis of a possible correlation between a drug and an adverse event that emerged from the analysis of one or more sources. A signal is not sufficient to establish a causal relationship between the drug and the event, but indicates the need for further investigations to clarify the observed association. Evidence of signal may be a previously unknown risk, an increase in the frequency or severity of risk, or the identification of a new risk group.

HOW MANY SIGNALS DOES IT TAKE TO GENERATE A SIGNAL?

The number of reports necessary to generate a signal varies according to the seriousness of the case, the quality of the information and possible evidence from other sources. In some exceptional cases, however, a single notification may be sufficient, as in the case of a positive rechallenge.

THE SOURCES OF PHARMACOVIGILANCE SIGNALS

Pharmacovigilance signals can come from different sources such as:

- Clinical studies. The data is characterized by low number and high reliability.
- Scientific literature (case-reports and systematic reviews). Like clinical studies, they are characterized by low numbers and high reliability. Also, often only new and egregious cases are published, so they are limited.
- Spontaneous reports. They have a high number and a fairly good reliability. However, they may be subject to under reporting or duplication.
- Cases from healthcare databases. Common databases are large and highly reliable. In particular, it is mandatory for MAHs to continuously monitor in EudraVigilance the reports relating to their drugs for Signal Detection purposes.
- Other sources (market research, analysis of drug consumption and social media). Reliability is low, but the number is high. Medical analysis and follow-up implementation are difficult.

SIGNAL DETECTION: HOW TO PERFORM IT

Signal Detection is performed by analyzing the data deriving from the aforementioned sources and can take place through:

- Qualitative analysis. It is usually carried out on small samples of cases or on single cases if the event is serious, unexpected or of particular clinical relevance, for example for rare diseases. This type of analysis, also called “Case by case” could also take place manually without the use of specific software.
- Quantitative analysis. It is carried out on large samples of data mainly through computerized tools such as safety databases and business intelligence. It mainly uses analyzes based on statistical methods, in particular those of disproportionality. Among the most common, the Proportional Reporting Ratio (PRR) or the Reporting Odds Ratio (ROR).

SIGNALS OF DISPROPORTIONATE REPORTING (SDR)

The signals that emerge from the use of statistical methods are called Signals of Disproportionate Reporting (SDR). These, being results of purely statistical analyzes and devoid of any medical evaluation, simply reflect a reporting trend. Therefore, they can only be treated as potential signals that require critical evaluation taking into account other factors such as the biological plausibility of the association and the consistency of the available safety data.

WHAT TO DO AFTER A POTENTIAL SIGNAL HAS BEEN IDENTIFIED?

Upon identification of a potential signal, the Mah must proceed with the Signal Validation in order to confirm or not the existence of a cause-effect relationship.

HOW A SAFETY DATABASE CAN HELP YOU PERFORM SIGNAL DETECTION

Assuming that the collection of data from adverse events within a safety database protects the pharmacovigilant from the risk of errors or omissions of information, a well-designed safety database, such as SafetyDrugs, must provide for the possibility of entering the indication of a possible signal. In this way the doctor, during the phase of evaluating the causal link between drug and reaction, will be facilitated in noting down a suspected signal. Consequently, this information must be able to be extracted in the reports necessary for an analysis for Signal Detection purposes, to speed up the subsequent Signal Validation process.

The Business Intelligence option, available in the most advanced database packages, allows data to be analysed for Signal Detection purposes using quantitative analyses based on indicators of statistical disproportionality such as the Reporting Odds Ratio (ROR), the Proportional Reporting Ratio (PRR) and the Risk Ratio (RR).

SIGNAL VALIDATION: WHAT IS IT AND HOW TO PERFORM IT

SIGNAL VALIDATION IS THE ACTIVITY OF VERIFYING THE RELIABILITY AND COMPLETENESS OF THE INFORMATION SUPPORTING A POTENTIAL SIGNAL. HERE'S HOW IT'S DONE ACCORDING TO GVP.

WHAT IS SIGNAL VALIDATION

Signal Validation is the activity of confirming or not the existence of a new or changed cause/effect relationship on the basis of the documentation collected during the Signal Detection. Signal Validation aims to verify that the information collected in the previous phase is complete and sufficient for signal validation. It is the second phase of Signal Management: it follows the Signal Detection, i.e. the signal research activity that the companies holding the MA are required to carry out to comply with the pharmacovigilance regulations.

HOW TO PERFORM THE SIGNAL VALIDATION

According to the Good Pharmacovigilance Practices – GVP, to carry out the validation of the signal, it is necessary to take into consideration the previous data such as the information reported in the Summary of Product Characteristics (SPC), in the Package Leaflet (FI), in the Risk Management Plan (RMP), in the report security update periodical (PSUR) or in any other source prior to the detection of the signal.

In addition, the straightness of the evidence should be analyzed taking into

account elements such as the number of cases, data quality and consistency, possible mechanism based on biological and pharmacological plausibility, and any supporting data.
The context and clinical relevance must also be analyzed, for which elements such as the severity of the reaction, outcome, possible interactions, or reaction on special populations are investigated.
In addition to these data, other sources may provide additional evidence, including clinical data, findings on similar cases in the scientific literature, information on the epidemiology of the adverse reaction or underlying disease, experimental and/or non-clinical results, or data from health databases.
However, in addition to the indications given in the GVP, there is no common standard that indicates how to analyze the data or how to make a report, though, for example, tables or evaluation grids. It will therefore be the responsibility of the MAH to establish the values within which to validate or not a signal. If there are uncertainties, it is possible to reserve the right to validate a signal later in light of new evidence.

HOW A SAFETY DATABASE CAN HELP YOU PERFORM SIGNAL VALIDATION

The safety database allows reliable collection of data related to adverse events, protecting the pharmacovigilant from the risk of errors or omissions of information. In the case it is possible to insert the indication of a possible signal, through a specific flag, the reference of which can be extracted in useful reports during the validation phase of the signal itself.
The Business Intelligence module, thanks to the quantitative analyses based on indicators of statistical disproportionality, such as ROR, PRR and RR, allows for rapid feedback on drug/reaction correlations that present a statistically disproportional result.

AFI SYMPOSIUM 2023: HERE'S WHAT AROSE

THE 62ND EDITION OF THE AFI SYMPOSIUM TRANSFORMED THE RIMINI PALACONGRESSI INTO A CENTER OF PHARMACEUTICAL EXCELLENCE. HERE'S WHAT WE TALKED ABOUT.

The AFI Symposium 2023 is aimed at its 62nd edition. The Italian event dedicated to the meeting of the protagonists of the pharmaceutical sector was this year entitled The Health Supply Chain: development engine for the Country. The Symposium took place as usual at the Palacongressi in Rimini, over three days. From 7 to 9 June 2023, the most diverse pharmaceutical topics were discussed: from biotechnology to supplements, from clinical research to production, and from medical devices to biocides. There will also be a session dedicated to pharmacovigilance. The agenda of the AFI Symposium 2023 was as follows.

DAY 1 – WEDNESDAY 7 JUNE
10:00 – 13:00 Workshops
14:00 – 15:00 Lectio Magistralis
15:00 – 19:00 Scientific Sessions

- Session I – Biotech: the evolution of advanced therapies for more effective, safe and more accessible drugs to patients
- Session II – Supply Chain and Innovation: innovative processes and technologies to support the patient

DAY 2 – THURSDAY 8 JUNE

09:00 – 19:00 Scientific Sessions

- Session III – Production and Quality: contamination control and containment in pharmaceutical production
- Session IV – Clinical Research: privacy, cybersecurity, new regulations: what impact for research?
- Session V – HTA/Regulatory/Pharmacovigilance: Marketing of a medicinal product: what and how many pre- and post-marketing aspects? Regulatory aspects, HTA, pharmacovigilance
- Session VI – API: API manufacturers and the new European pharmaceutical legislation
- Session VII – Pharmaceutical Sciences: the impact of Pharmaceutical Technology in the treatment of respiratory tract diseases
- Session VIII – AFI/CRS/ADRITELF: new production technologies (electrospinning, microfluidics, 3Dprinting)
- Session IX – YOUNG PEOPLE: A job for the future

The Pharma Women's Square

The Startup Square

Poster Session

DAY 3 – FRIDAY 9 JUNE

09:00 – 13:00 The Scientific Sessions

- Session X – Medical Devices: Medical Devices: a world of innovation – the new rules for building the future
- Session XI – Supplements: Pharmaceutical Production 2022: New challenges and new answers
- Session XII – Biocides: PMC vs. Biocides: from national legislation to European regulation. Where are we at?
- Session XIII – European Regulation: How the European Medicines Regulation will change

New this year is the layout of the stands within the exhibition area which has been renovated to make it more modern and dynamic.

As can be seen from the program, during these three days, the Symposium offered a wide range of scientific sessions that addressed crucial pharmaceutical topics. We have reported the highlights of the various sessions.

SESSION I – BIOTECH: THE EVOLUTION OF ADVANCED THERAPIES FOR MORE EFFECTIVE, SAFE AND MORE ACCESSIBLE DRUGS TO PATIENTS

Session I of the AFI Symposium 2023 explored the evolution of advanced therapies in the field of biotechnology. These represent an increasingly relevant part of the portfolio of biotech companies, as they are demonstrating significant potential in the treatment of a wide range of pathologies including solid tumors, as well as rare or ultra-rare diseases.

The session offered a focused look at the development of these innovative medicines, focusing on discoveries and advances in research, manufacturing and clinical trials. The experts present analyzed the challenges related to the accessibility and sustainability of these therapies.

SESSION II – SUPPLY CHAIN AND INNOVATION: INNOVATIVE PROCESSES AND TECHNOLOGIES TO SUPPORT THE PATIENT

During session II, some very important aspects related to the supply chain and innovation in the healthcare sector were analysed. In particular, three relevant topics were addressed: the supply chain, the management of reference data and the related regulations.

Regarding the supply chain, the challenges and solutions to guarantee the safety and reliability of products during transport, storage and distribution were analysed.

Issues regarding data protection from the point of view of privacy, security and integrity were then brought to light. Reference data management is in fact a crucial aspect for the pharmaceutical industry.

SESSION III – PRODUCTION/QUALITY: CONTAMINATION CONTROL AND CONTAINMENT IN PHARMACEUTICAL PRODUCTION

The third session of the AFI Symposium 2023 jointly addressed the issues of production and quality. In particular, the problems and opportunities related to pharmaceutical production were highlighted, focusing on the prevention of contamination and cross-contamination.

The discussion on contamination control focused on the requirements of the Contamination Control Strategy, recently formalized in the new version of Annex 1 of the EU GMP (Good Manufacturing Practice). The strategies and measures adopted to prevent contamination during pharmaceutical production were explored, with particular attention to the implementation of automated systems that allow higher levels of contamination prevention to be achieved compared to traditional systems.

Another aspect covered was the viral contamination of organic products. We analyzed the methods and measures taken to prevent viral contamination during pharmaceutical manufacturing, taking into account the unique challenges associated with this type of contamination.

The session also addressed the topic of containing cross-contamination, both for processes involving highly active active substances and by presenting new concepts of cleanability and the possibility of remediation of production plants. The new approaches and technologies available to ensure adequate containment and prevention of cross-contamination in the pharmaceutical production process were examined.

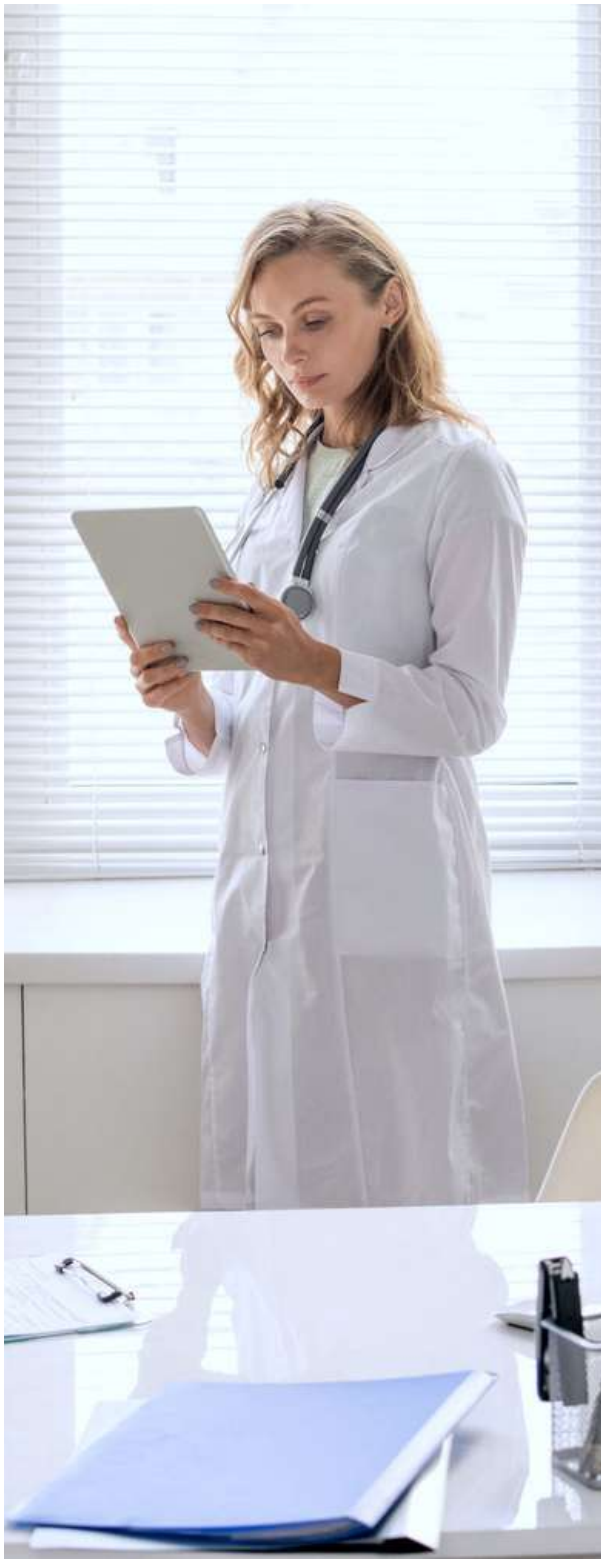
The session concluded with a speech from AIFA (Italian Medicines Agency) regarding the two important quality aspects described above. This intervention provided an important regulatory perspective on contamination control and containment in pharmaceutical production.

SESSION IV – CLINICAL TRIALS: PRIVACY, CYBERSECURITY, NEW REGULATIONS: WHAT IMPACT FOR RESEARCH?

Session IV of the AFI Symposium 2023 addressed issues related to the growing use of digital tools in research and the implications in terms of privacy, cybersecurity and regulations. The use of such tools offers a wide availability of data and a range of means, including artificial intelligence, for their analysis, resulting in opportunities for research progress. However, it is necessary to guarantee the safety of users and the robustness of the data collected.

The session therefore stimulated a discussion on the challenges and opportunities that arise from the use of digital tools, paying particular attention to the patient's point of view as owner of the data and subject to be protected. There was a debate on how to find the right balance to ensure data security without hindering research and without compromising the possibility of improving the patient care pathway.

The second part of the session was dedicated to the discussion between institutions, researchers and companies regarding the evolution of the regulatory and legislative context. The discussion provided insight into the regulatory and regulatory issues related to clinical trials and assessed how stakeholders can address these challenges and capitalize on the opportunities offered by clinical research in the current context.



SESSION V – HTA/REGULATORY/ PHARMACOVIGILANCE: MARKETING OF A MEDICINAL PRODUCT, WHAT AND HOW MANY PRE- AND POST-MARKETING ASPECTS? REGULATORY ASPECTS, HTA, PHARMACOVIGILANCE

Session V addressed various aspects related to the marketing of a medicinal product, both before and after its marketing, focusing on regulatory aspects, Health Technology Assessment (HTA) and pharmacovigilance.

During the session, the process of transforming regulatory activity in the digital era was discussed, highlighting the importance of dematerialisation and the expansion of specialization on non-medicinal health products and patient services.

The HTA Regulation and the new perspectives in the evaluation of health technologies were examined. The role of pharmacovigilance for a Marketing Authorization (AIC) holder was explored in depth, highlighting the critical issues, obligations and potential strategic and commercial advantages for companies associated with this regulatory activity.

At the end of the session, a Round Table dedicated to special productions, which include traditional herbal medicines, homeopathic and allergens, addressed specific themes and issues relating to these product categories, allowing an exchange of knowledge and points of view between experts of the sector.

SESSION VI – API: API PRODUCERS AND THE NEW EUROPEAN PHARMACEUTICAL LEGISLATION

Session VI of the AFI Symposium 2023 focused on the analysis of contents regarding Active Pharmaceutical Ingredients (APIs) within the new European pharmaceutical legislation. We focused on the current political situation and particular emphasis was given to Italy's point of view to these issues.

The session was organized in collaboration with Aschimfarma, the association representing Italian companies producing active ingredients.

SESSION VII – PHARMACEUTICAL SCIENCES: THE IMPACT OF PHARMACEUTICAL TECHNOLOGY IN THE TREATMENT OF RESPIRATORY TRACT DISEASES

Session VII of the 2023 AFI Symposium focused on the importance of the pulmonary inhalation route of administration in the treatment of respiratory diseases, such as COPD (chronic obstructive pulmonary disease) and asthma. This route of administration represents a significant technological and biopharmaceutical challenge. In particular, for drugs in the form of inhalation powders, both single-dose and multi-dose, pharmaceutical development requires the study of numerous critical parameters linked to the micrometric properties of both the active ingredient and the excipients. These parameters include size, specific surface area, and surface characteristics. Furthermore, since these products are combinations of drugs and devices, the performance of the drug is closely linked to the functionality of the device itself.

From a biopharmaceutical point of view, given that the concept of bioequivalence is not applicable for the local target, alternative approaches such as in vitro pharmaceutical equivalence tests are necessary to justify the correlation with efficacy in the clinical context. This represents an additional challenge in the development and evaluation of such medicines.

SESSION VIII – NEW PRODUCTION TECHNOLOGIES (ELECTROSPINNING, MICROFLUIDICS, 3D PRINTING)

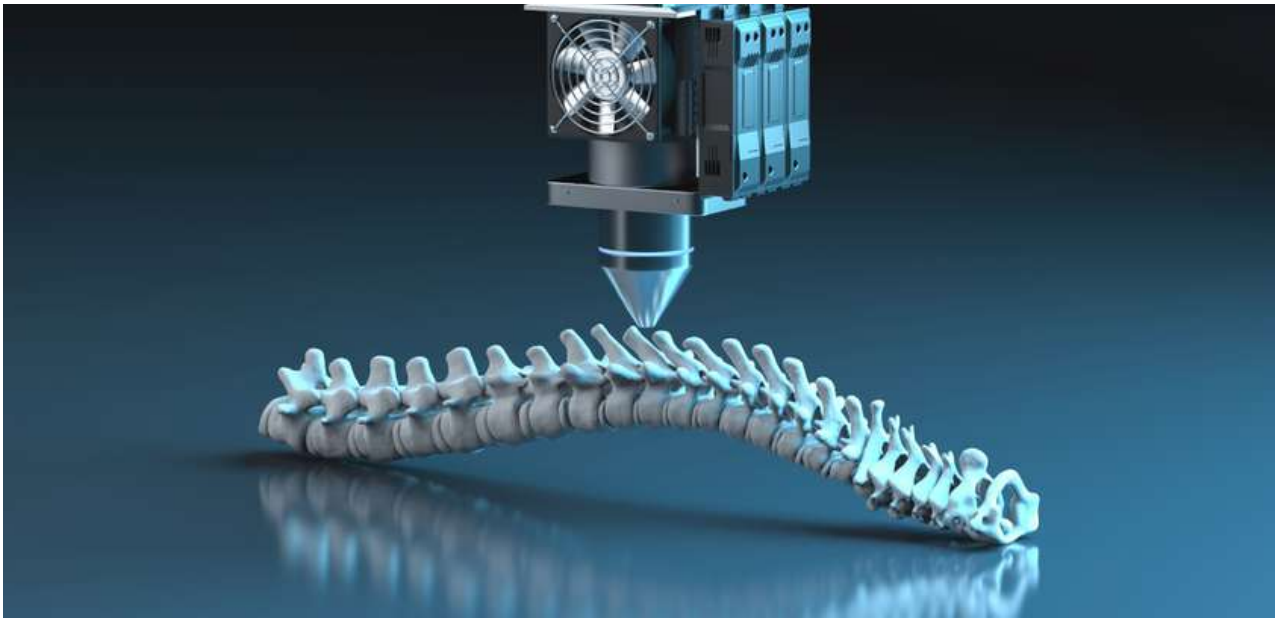
Session VIII of the 2023 AFI Symposium analyzed innovative manufacturing techniques in the pharmaceutical and biomedical fields, including the production of nanosystems via microfluidics, electrospinning and 3D printing. These technologies offer solutions to address the challenges related to the delivery of new chemical entities (NCEs) and molecules of biological origin.

Microfluidics technology is based on the controlled flow of microamounts of fluids in microchannels. The miniaturization of mixing spaces allows precise control of flows, molecular concentrations and separation rates, ensuring the reproducibility of production processes of nanoparticle therapeutic systems based on solvent diffusion. Microfluidic technology offers the advantage of being easily scalable to an industrial level, allowing for rapid production. During the session, a report was presented in which the production approach based on microfluidic technology was illustrated, highlighting its technical characteristics and advantages in the production of new types of lipid nanoparticles.

Electrospinning (electrospinning) is a widely used technology for the production of nanofibrous matrices due to its simplicity. This process is based on the injection of a polymer solution or melted polymer into a high-voltage electric field, which produces polymer fibers on a metal collector. This technology in the pharmaceutical field is relatively recent.

Electrospun matrices find numerous applications, such as the creation of medical devices for healing and the development of supports (scaffolds) for tissue engineering. The advantages and critical issues of electrospinning were presented, showing its applications.

Finally, 3D printing is a technology on which several studies have focused in recent years thanks to its potential in the pharmaceutical sector. 3D printing processes based on the direct extrusion of powders for the production of solid pharmaceutical forms were examined and the formulation and industrial production aspects linked to 3D printing were illustrated, with particular attention to the selection of materials.



SESSIONE IX – SESSIONE GIOVANI, UN IMPEGNO PER IL FUTURO

The IX session of the AFI Symposium 2023 entitled "Youth Session, a commitment to the future" was organized in collaboration with Farmaceutica Younger, an association of young people dealing with their first work experiences in the pharmaceutical sector. This session aimed to increase awareness of the numerous opportunities offered by the healthcare sector to undergraduates and doctoral students in scientific disciplines, as well as underline the importance of a solid network of contacts in the development of one's personal and professional profile.

During the session, speeches were presented by various professional figures working in the pharmaceutical sector, offering a broad overview of the different career opportunities present in the sector and therefore providing participants with a clearer idea of the possible directions to take in their professional path.

Furthermore, a human resources (HR) session was held which addressed issues related to recruitment and job placement. This segment provided useful information on how to navigate the job search process and how to best leverage your skills and experience to obtain job opportunities in the healthcare sector.

As part of the session, an interactive game developed by Farmaceutica Younger specifically for the AFI symposium was proposed. The game allowed participants to test themselves, testing their knowledge of the sector and expanding their network of contacts.

SESSION X – MEDICAL DEVICES: A WORLD OF INNOVATION – THE NEW RULES FOR BUILDING THE FUTURE

Session X of the AFI Symposium 2023 focused on the transition from the old Directive to the new Regulation (MDR 2017/745) currently in place. While some obligations, such as supervision, have already come into force, others, such as certification activities, are encountering some difficulties that have caused delays in actual applicability. The implementation of the new Regulation requires high specialization and close collaboration between professionals from different disciplines, as well as a deep knowledge of the new regulatory requirements.

The Italian Pharmaceutical Association (AFI) presents itself as a meeting and discussion point between sector professionals, competent authorities and notified bodies. This session provided an opportunity to share specific expertise in the fields of substance-based medical devices and software, which are bringing new paradigms of care to patients.

SESSION XI – THE ROLE OF FOOD SUPPLEMENTS IN THE HEALTH SUPPLY CHAIN

Session XI of the AFI Symposium 2023 was dedicated to food supplements. Over the years they have undergone a change in their formulation, going from being mainly composed of vitamins and minerals to being formulated from substances capable of maintaining the normal physiological functions of the human organism. This development is mainly given by the evolution of the concept of health, initially understood as the absence of disease, to arrive at the current concept of general well-being. This progress has led to a constant development of the food supplements market, which is taking on an increasingly important role within the health supply chain.

The session highlighted how these products can contribute to the maintenance of health and well-being, offering specific benefits for certain conditions or physiological needs. The latest research and scientific studies on the role of dietary supplements in promoting health and supporting physiological functions were examined. Scientific evidence has therefore been presented that supports the effectiveness and usefulness of certain food supplements in various areas of interest for human health.

SESSION XII – PMC VS BIOCIDES: FROM NATIONAL LEGISLATION TO EUROPEAN REGULATIONS. WHERE ARE WE AT?

The XII session of the AFI Symposium 2023 was dedicated to Medical Surgical Devices (PMC) and biocides. The old EC Directive n. 98 of 2008 was replaced some time ago by EU Regulation no. 528 of 12 May 2012, the principles of which are still being implemented. This regulation concerns the placing on the market and use of biocides, as well as treated materials or articles used for the protection of humans and animals against harmful organisms such as bacteria or insects, through the action of active ingredients contained in the biocidal product. The regulation provides for the definition of 22 types of biocidal products called Product Types.

The objective of the Regulation is to improve the functioning of the internal market by harmonizing the rules relating to the marketing and use of biocidal products while ensuring a high level of protection of human, animal and environmental health. The provisions of the Regulation are based on the precautionary principle, to protect human and animal health and the environment. The enforcement mechanism of the regulation provides for a gradual replacement of national regulations based on the authorization of related active ingredients, as they are authorized at European level. Therefore, the process of replacing national regulations with Regulation 528/2012 is still ongoing.

During the session, short speeches from the authorities and technical indications were provided to illustrate the current state of the transition from the regulation national to European regulations in the biocidal sector.

Topics such as challenges and practical implications for companies operating in the biocides sector were addressed. The session offered an opportunity for dialogue between the competent authorities, sector experts and interested companies, to promote the correct application of the rules and ensure a high level of protection of human, animal and environmental health in the supply chain of biocides.

SESSION XIII – HOW COMMUNITY LEGISLATION ON MEDICINES WILL CHANGE

During the XIII session of the AFI Symposium 2023, the possible proposals for amendments to Directive 2001/83/EC, i.e. the Community legislation on medicinal products, were illustrated. The planned changes in the Pediatric Regulation and the Orphan Medicines Regulation and their implications on medicines manufacturers, regulatory authorities and other players in the pharmaceutical sector were discussed in detail.

At the end of the in-depth analysis, there was a round table which saw the participation of experts from AIFA (Italian Medicines Agency), Egualia, Farmindustria, Aschimfarma and the University of Insubria. During this round table, experts shared their perspectives, experiences and knowledge on the proposed changes to EU medicines legislation.

The main objective of the session was to provide an overview of possible changes to EU medicines legislation and to promote a constructive discussion on the implications and opportunities offered by these changes.

AFI SYMPOSIUM 2023: CONCLUSIONS

The AFI Symposium 2023 had almost 2000 participants, confirming itself once again as an event of great importance in the Italian pharmaceutical sector. The numerous scientific sessions, workshops and roundtables provided a unique opportunity to share knowledge, explore the latest trends and create meaningful connections in the industry.

The AFI Symposium demonstrated that collaboration and knowledge exchange are fundamental to the progress of the Italian pharmaceutical sector and the well-being of patients. We can't wait to see what the next edition of this successful event holds.

PAJAMA RUN 2023: LET'S RUN TOGETHER FOR CANCER CHILDREN

PIGIAMA RUN IS AN EVENT ORGANIZED BY LILT TO SUPPORT CHILDREN AFFECTED BY CANCER. HERE'S WHAT IT IS AND HOW WE DECIDED TO SUPPORT THE CAUSE.

WHAT IS THE PAJAMA RUN?

Every year, in Italy, over 1400 children and over 800 adolescents fall ill with cancer or leukemia. It is estimated that today in Italy there are more than 44,000 people who have had childhood cancer[1]. The Pajama Run is an event to support the fight against pediatric cancers. Organized by LILT (Italian League for the Fight against Cancer), it consists of a race in which participants wear their own pajamas in support of those who, unfortunately, are forced to wear them all day. This event has reached its fifth edition this year and represents an incredible demonstration of affection and closeness towards young cancer patients.

The month of September is dedicated to raising awareness of pediatric cancers, symbolized by the Gold Ribbon, the golden ribbon that represents the courage and strength of children with cancer. The 15th is the day on which, in various Italian cities, everyone is invited to wear their pajamas and take part in this special race. Participants are asked to make a small donation with the aim of raising funds to be donated to the families of children affected by cancer.

[1] Source Ministry of Health, data updated to 2022.

HOW MAX APPLICATION SUPPORTS THE CAUSE

We at Max Application, the developer of the SafetyDrugs safety database for pharmacovigilance, care about the cause and believe that the Pajama Run is an extraordinary initiative that unites communities in a tangible gesture of solidarity. We have therefore decided to make our contribution to supporting the event in two significant ways.

Firstly, we decided to sponsor the event in the city of Biella, the company's headquarters, thus supporting the organization and implementation of the event at a local level.

Secondly, we encourage the Max Application team to actively participate in the run by supporting the cause with a participation donation. In this way we can contribute in a concrete way to supporting the families of children with cancer and spreading the message of hope and solidarity that this event represents. The invitation was warmly welcomed: 75% of employees will participate to support this noble cause.

PAJAMA RUN 2023: NUMBERS AND IMPACT OF THE EVENT IN BIELLA

We thank everyone who participated and supported the Pigiama Run 2023 with us. It was a special day when we joined forces for such an important cause. Every step we took represented more hope for those brave children and their families. Thank you for being part of this amazing race for life.

We are proud to announce that the nationwide event saw the participation of 11,486 people and raised a total of €190,310. Locally, in the city of Biella, home of Max Application, there were 1,097 participants who helped raise €17,377, exceeding the target of €11,250. These funds will be allocated directly to the families of cancer children living in the Biella area, offering precious support.

For our part, we are thrilled with the great success of the event and with having contributed. Here are some photos of our march.

RALLY LANA 2023

THE RALLY LANA 2023, THE MOST AWAITED AUTOMOTIVE EVENT IN THE BIELLA AREA, TOOK PLACE IN BIELLA FROM 21 TO 22 JULY 2023. HERE'S HOW IT WENT.

WHAT IS RALLY LANA

The Rally Lana is an automotive event held annually in the city of Biella. Born in 1973 as a “Regularità Sprint” and promoted to “International Rally” in 1978, it has become one of the most demanding tests of the Italian Rally Championship. After a 17-year hiatus, the event was given new life in 2018 thanks to “Rally Lana Alive” and “New Turbomark”. This year the 36th edition was held, which took place on 21 and 22 July 2023.

The 2023 Rally della Lana was valid for the Italian flag as part of the Italian Asphalt Rally Championship (CIRA), as well as for the Zone 1 ACI Sport Cup, the Piedmont Val d’Aosta Championship, the Michelin Trofeo Italia, the Pirelli Academy, the Suzuki Rally Cup and the R-Italian Trophy series. Not surprisingly, the event attracted pilots and enthusiasts from different parts of Italy, guaranteeing a high-level competition.

RALLY LANA 2023 ROUTE

The race began on Friday 21st July at 9pm in Piazza del Duomo in Biella and ended on Saturday 22nd July at 5pm in the same location. The route of the Rally Lana 2023 boasted a total competitive distance of 94.150 km on seven "piesse" and offering adrenaline-pumping moments right from the early stages. On the first day, in fact, the famous night climb to the Sanctuary of Oropa was held, added to the pitfalls of the Tracciolino for an opening challenge of almost 24 km. The second day was the turn of a triptych of daytime tests which were repeated twice: Bielmonte, Ailoche and Curino, for a total of around 70km.

RALLY LANA 2023: SPECIAL STAGES

The special stages of the rally presented unique characteristics and technical challenges.

- PS 1 Città di Biella (KM 23.550): with its abundant 23 km it was the longest stage of the 2023 Wool Rally and also one of the longest ever of the Italian Asphalt Rally Championship. It combined the ascent to the Sanctuary of Oropa with the Tracciolino.
- PS 2 – 5 Bielmonte (KM 10.650): this is a route that takes place at high altitude. The climatic conditions were fortunately favorable otherwise they could have made the route difficult.
- PS 3 – 6 Ailoche (KM 11.500): the stretch was characterized by a long series of switchbacks and a long final descent. Particularly difficult is the Ailoche-Caprile crossroads which, being on the counter slope, increases the risk of falling off the route.
- PS 4 – 7 Curino (KM 13.350): it is the typical section of the Rally Lana. This year, just like last year, it was traveled in reverse, having an uphill start, followed by a flat stretch and final descent.

Each test required driving skills, precise trajectories and a good balance between courage and control.

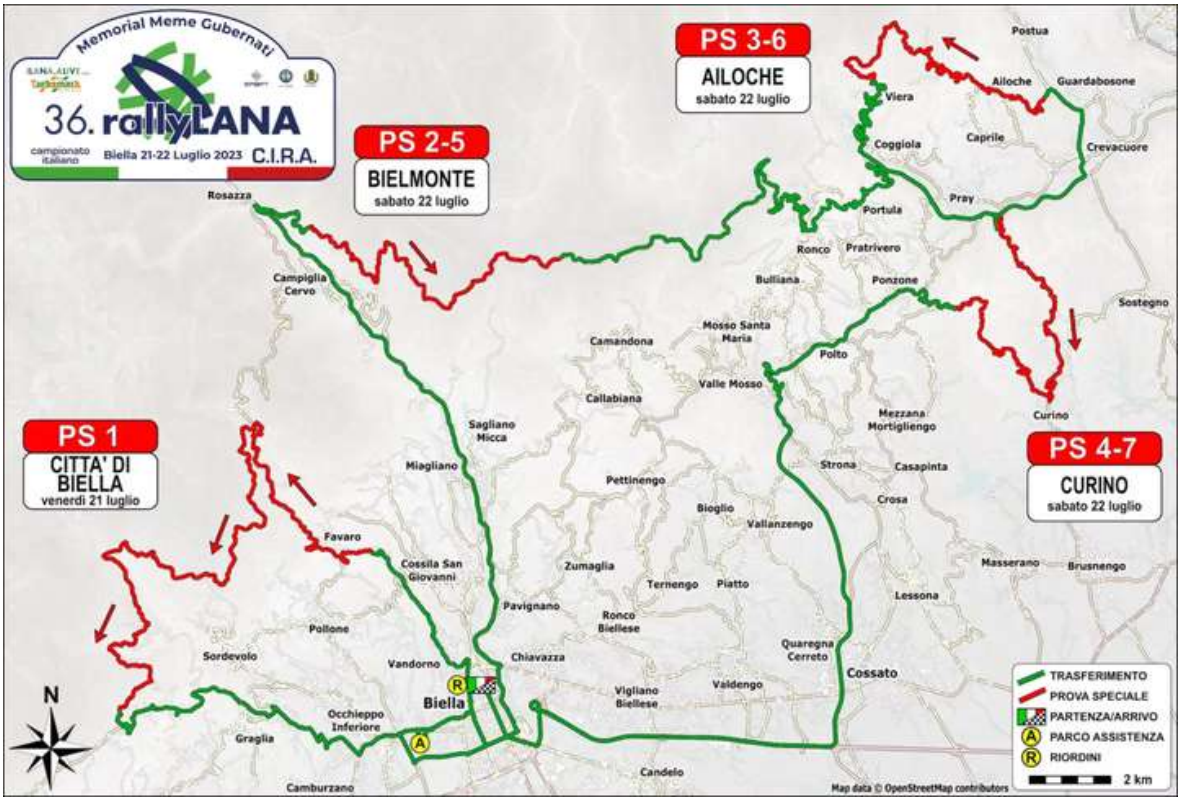


Image source: www.rallly-lana.it

WHO WON THE 2023 WOOL RALLY?

The 2023 wool rally was won by the duo made up of Stefano Albertini and Danilo Fappani aboard a Skoda Fabia Rally2/R5. The two excelled in 3 of the 7 special stages.

In second place on the podium went Simone Campedelli and Tania Canton who competed with a Skoda Fabia.

Bronze medal for the local driver of the wool rally, Corrado Pinzano, winner of the last edition, who, accompanied by Marco Turati, encountered a puncture in the VolksWagen Polo Rally2/R5 suffering a loss of about 30 seconds.

The Rally della Lana in Biella has become an automotive event of great importance in the Italian sports scene. Its history, technical challenges and the participation of high-level riders contribute to making it an eagerly awaited appointment every year. With its 36th edition, the wool rally has confirmed emotions and entertainment for enthusiasts and lovers of road racing.

SafetyDrugs was pleased to have participated again this year as main sponsor in the traditional car race in Biella, the company's mother city. The commitment to support the Rally della Lana reflects its commitment to supporting local initiatives and promoting sport in the area.

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