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sanofi

PV and PTC Requirements for Digital Properties

Patient Safety & Pharmacovigilance (PSPV)

Version 6.0

Objectives

After completing this training, you should be able to:

- **Identify the content of the Digital Properties Pharmacovigilance (PV) packet**

- **Explain the importance of Pharmacovigilance (PV) Data reporting**
  (also referred to as Safety Vigilance Data or safety information)

- **Recognize and report Pharmacovigilance Data**
  - Types and definitions of Pharmacovigilance Data, including Adverse Events (AEs)
  - The what, how and where of Pharmacovigilance Data reporting
  - Appropriately apply the reporting process applicable to the project:
    - **The PV Portal or**
    - **The Unsolicited Individual Safety Information (ISI) Collection & Documentation Form (Unsolicited ISI form)**

- **Identify and report Product Complaints (PC)** (also known as Product Technical Complaints (PTCs))
  - Definition, Requirements, Examples, What to report

- **Comply with the regulatory and company requirements for the monitoring of Digital Properties**
  - Report PV Data to the relevant local PV department using the Decision Tree Algorithm
  - Maintain the acknowledgements of receipt of submitted PV Data
  - Conduct reconciliation of PV Data collected from Digital Properties

Training Requirements

- All Services Providers employees and sub-contractors/agents involved in the conduct of a project on behalf of Sanofi must complete pharmacovigilance and PTC training **prior** to the start of the project

- Services Providers must ensure that any new staff assigned to the Sanofi project complete pharmacovigilance training prior to involvement

- Training must be repeated annually, and at the time of the release of an updated version of this training upon Sanofi's request

- All training completion must be tracked

- Certificates of training completion must be made available to Sanofi upon request, e.g., at time of inspection or audit

Digital Property PV Packet, General Information and Important Communications

• The DP PV Packet is made available to Internal staff and Services Providers monitoring Digital Properties via the **Sanofi PV Resources Toolbox** and it contains the following:

1. Instructions for Self-Registration and Training Access iLearn
2. Unsolicited Individual Safety Information (ISI) Collection & Documentation Form (Unsolicited ISI form)
3. Decision Tree Algorithm "Determining the relevant PV contact to send Pharmacovigilance Data to"
4. PV Data Reconciliation Form
5. PV contact list
6. PTC contact list

•Significant changes to the DP PV Packet will be communicated by the Project Owner or Sanofi Patient Safety & Pharmacovigilance (PSPV) and all updates will be visible on the **Sanofi PV Resources Toolbox**

•General Information and Important Communications related to the PV requirements applicable to Digital Properties can also be found on the Sanofi PV Resources Toolbox

Guidance for PV Data Reporting

- This training provides explanations on various types of PV Data for your information and awareness
- It is your responsibility to report Pharmacovigilance data that you become aware of throughout the duration of the activity you are conducting on behalf of Sanofi
- It is important to collect as much information as possible at the time of the initial contact to allow for an accurate and complete medical assessment of the reported safety information by Sanofi PV
- Internal Staff and Services Providers are not required to apply any medical judgement or interpretation of safety information that they are made aware of
- Always report data exactly as it is reported to you
- If PV Data are reported via email, the report must be reported to the most relevant local PV department. Instructions on what country PV Data need to be reported to are provided in the Decision Tree Algorithm added to the contract, to the PV Packet and described in this training material

What is Pharmacovigilance?

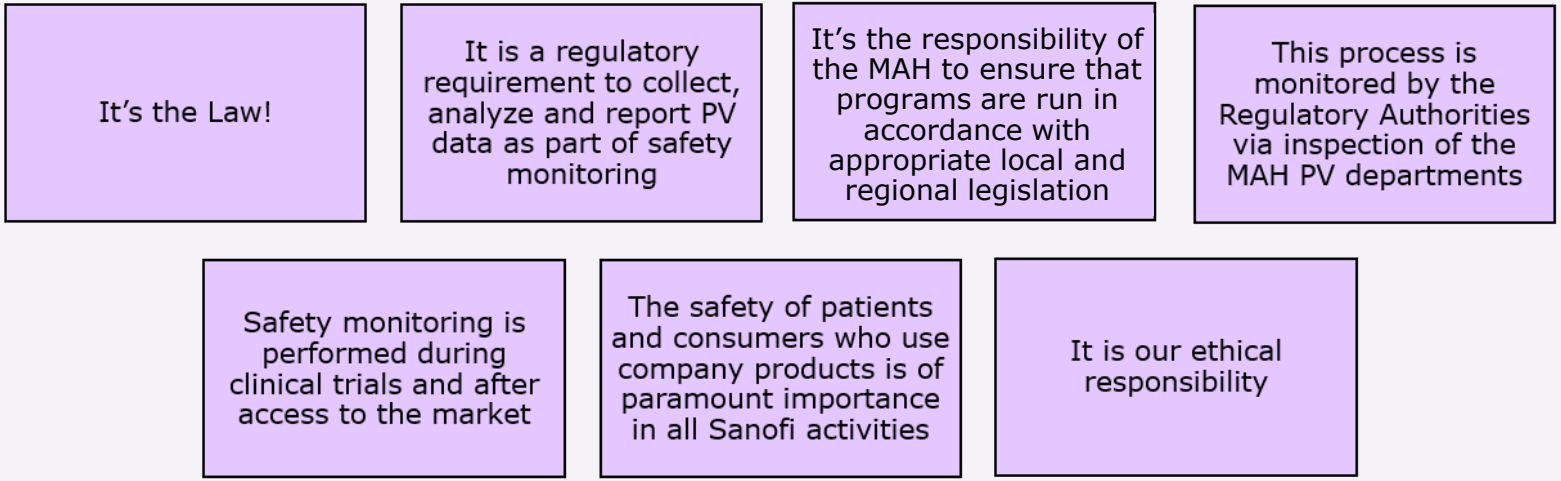
The etymological roots are:
- *Pharmakon (Greek) = Drug*
- *Vigilare (Latin) = To keep awake or alert, to keep watch*

WHO definition:

Pharmacovigilance is the "Science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems"

Why is Pharmacovigilance required?

This is how we protect patients!



MAH= Marketing Authorization Holder

Consequences of non-compliance for Sanofi

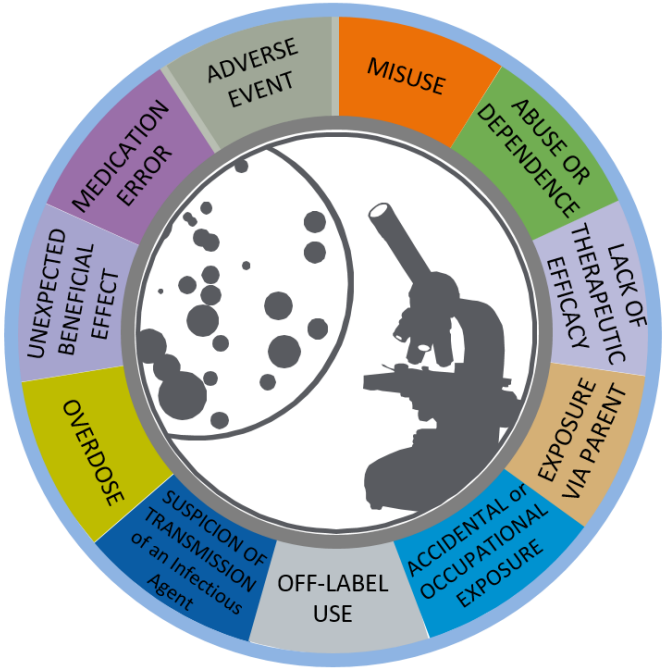
- Harm to patients
- Legal and Regulatory actions
- Fines
- Withdrawal of marketing application for the product
- Loss of consumer confidence
- Risk of sanctions from Regulatory Authorities
- Financial Consequences
- Jeopardizing company image, reputation, credibility
- Criminal Charges

Types of Pharmacovigilance Data

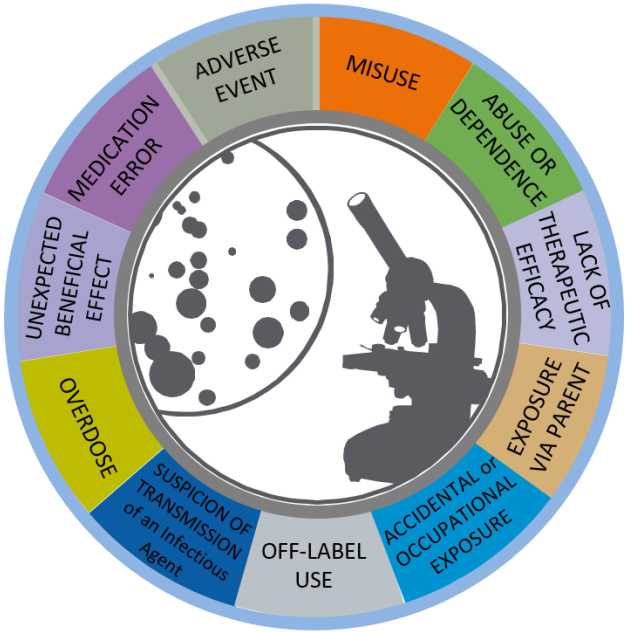
Services Providers can receive PV Data via different channels such as fax, phone calls, emails, text messages, directly from interactions with patients or Health Care Professionals, etc.

All such Pharmacovigilance Data should be reported to the Sanofi PV department within one (1) business day of receipt of information

In the next slides, you will learn more about types of Pharmacovigilance data that you must be able to identify as PV data.



Types of Pharmacovigilance Data



Adverse Event

Any untoward medical occurrence in a patient administered a medicinal product and that does not necessarily have to have a causal relationship with this treatment.

An adverse event can therefore be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product

Example: A patient experienced nausea after taking a Sanofi sleeping pill.
Example: "Patient who suffers from minor migraine headaches noticed an increase in severity and frequency after starting treatment with a Sanofi product.

Pharmacovigilance Data

Definition of a Serious Adverse Event

An Adverse Event is considered as serious if one or more of the following criteria are met:

- Death- the event resulted in the death of the patient
- Life-threatening event- At the time of the event the patient was in a life-threatening condition or immediate risk of death
- Hospitalization (initial or prolonged)-The adverse event required inpatient hospitalization or resulted in prolongation of the hospitalization
- Disability or permanent damage- the event resulted in the patient suffering from persistent or significant disability or incapacity
- Congenital anomaly/birth defect- A patient receiving a Sanofi product gave birth to a baby with congenital anomaly/birth defect
- The Event is Medically Important- If the adverse event does not satisfy any of the above criteria, but has important medical significance

Pharmacovigilance Data

Death

DEATH

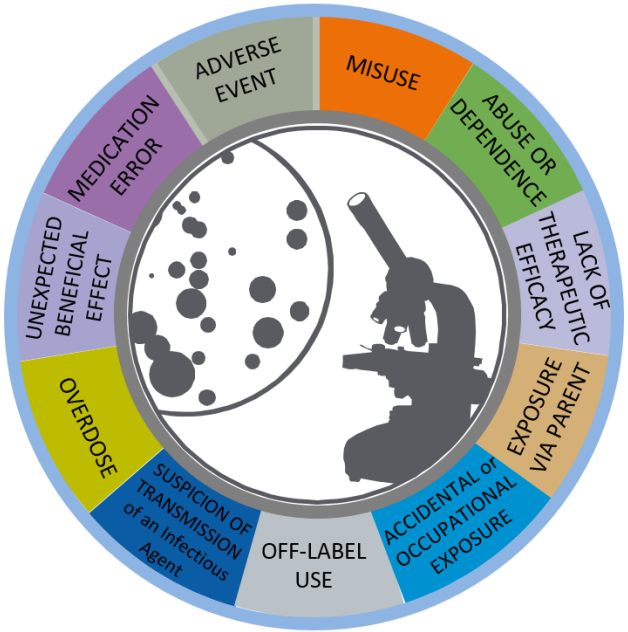
Death of a patient or consumer using a Sanofi product must be reported:

- whether the death is related or not to the use of the product

- whether the cause of the death is known or unknown

Death must be reported to the PV department as soon as possible but at the latest within one (1) business day

Types of Pharmacovigilance Data



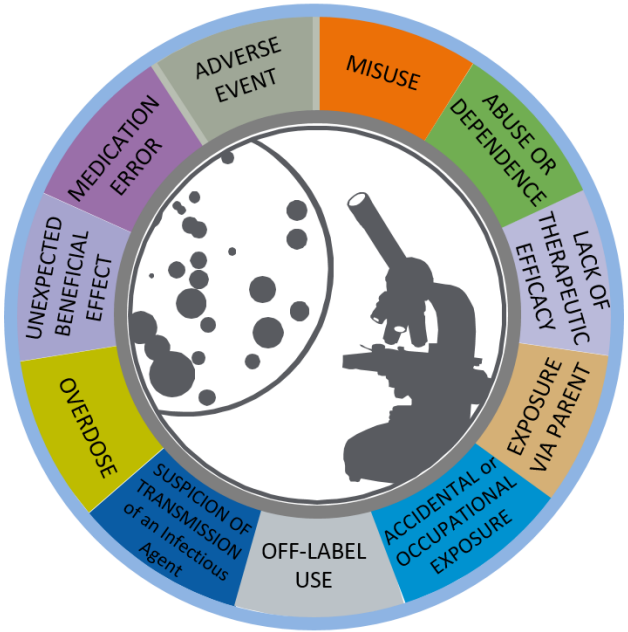
Misuse

Definition: The intentional and inappropriate use of a medicinal product by a patient not in accordance with the authorized product information

Example: A patient continued her cough medicine after her cough resolved because she thought it was helping her to sleep better.

These situations need to be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



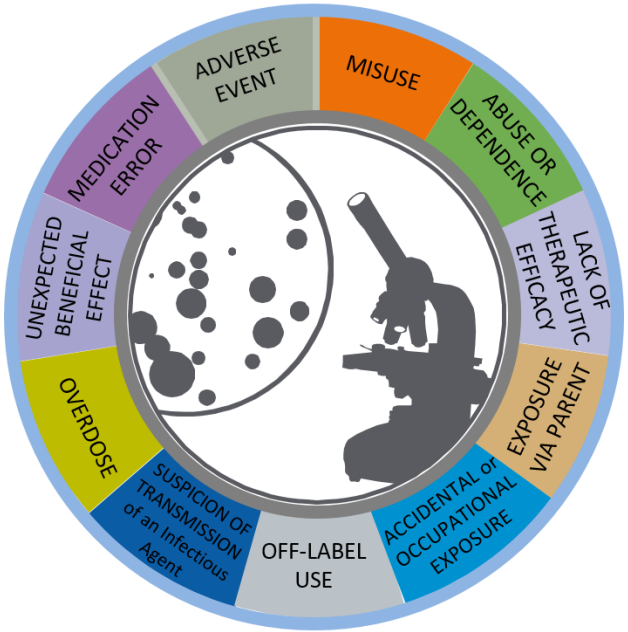
Abuse or Dependence

Persistent or sporadic, intentional excessive and non-therapeutic use of medicinal products which is accompanied by harmful physical or psychological effects

Example: A young man recovered from back surgery but continued to take a Sanofi product containing opioids due to an addiction.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



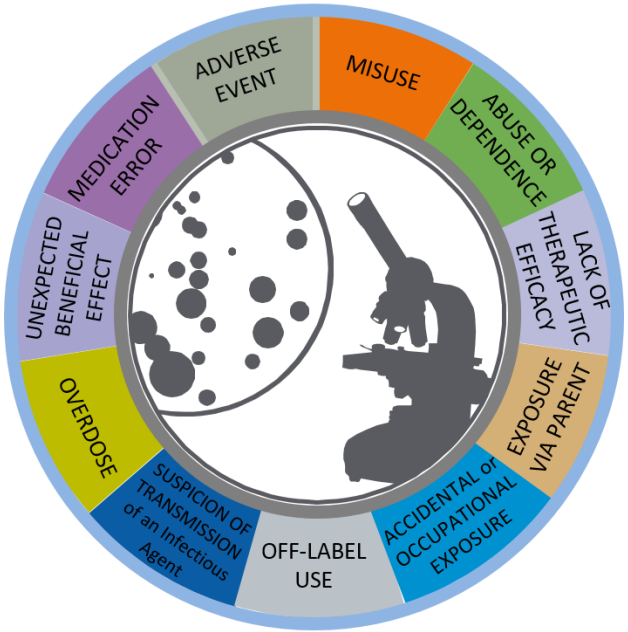
Lack of Therapeutic Efficacy

Failure to produce the expected pharmacological action for an approved indication

Example: Frederick was taking a Sanofi product for gastro-esophageal reflux. After five days as prescribed by the doctor, his condition did not improve.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



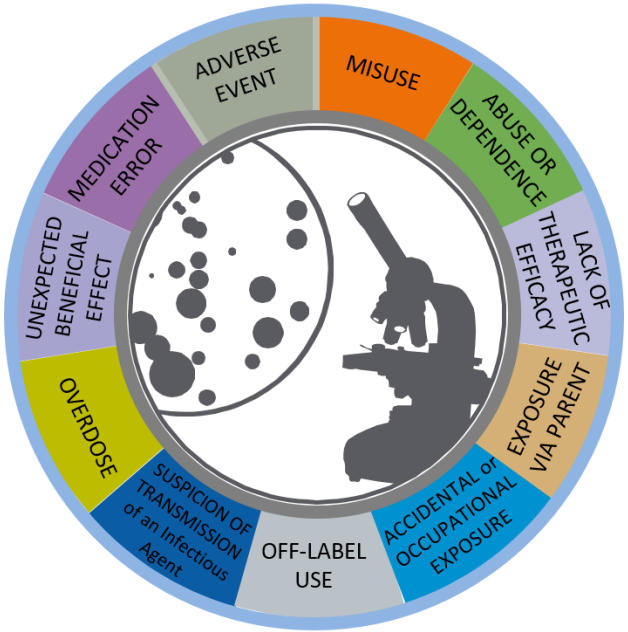
Exposure via Parent

Exposure to a Sanofi product during pregnancy, child exposure during breastfeeding, or conception (via mother or father), or possible exposure of a fetus or child via parent

Example: Sue continued to use her Sanofi allergy medicine while pregnant.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



Accidental or Occupational Exposure

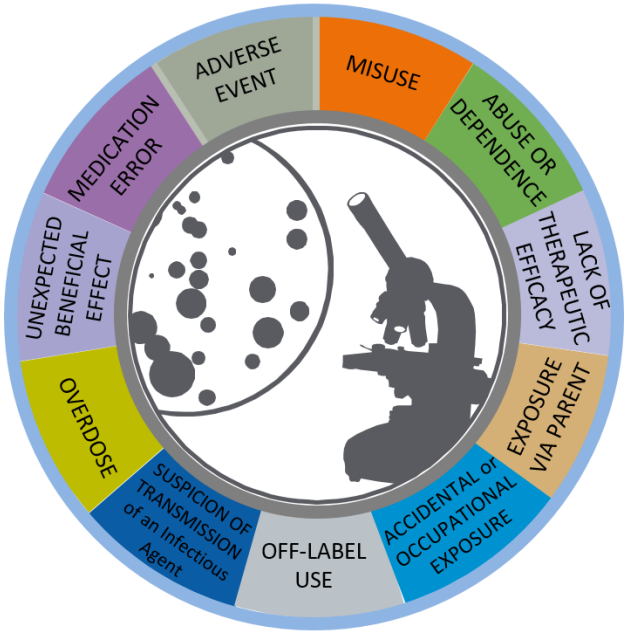
An exposure to a medicinal product as the result of one's professional or non-professional occupation

Example: A nurse reported a rash on her arm after being accidently splashed with a Sanofi product when preparing to administer the product.

Example: A mother who was administering a Sanofi ointment to their child accidentally got some in her eyes.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



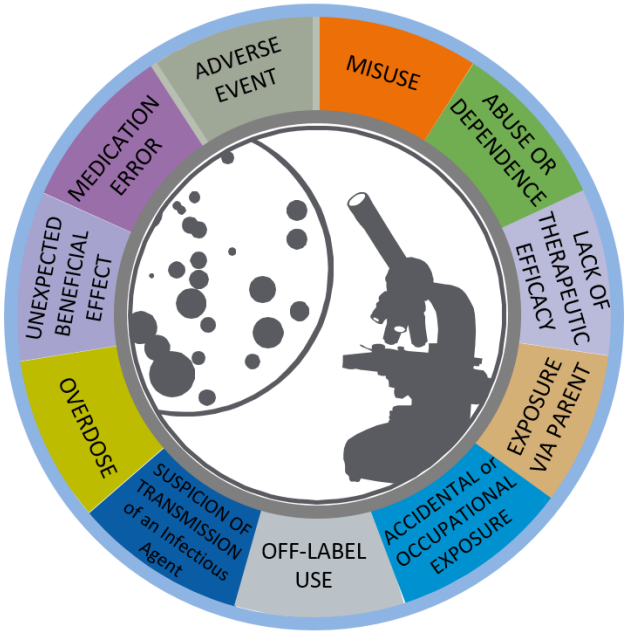
Off-label Use

A medicinal product is intentionally prescribed by a healthcare professional for a medical purpose not in accordance with the local authorized product information

Example: A patient was prescribed a Sanofi product to treat her migraine although this product is not approved for the treatment of migraines.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



Suspected transmission of an infectious agent

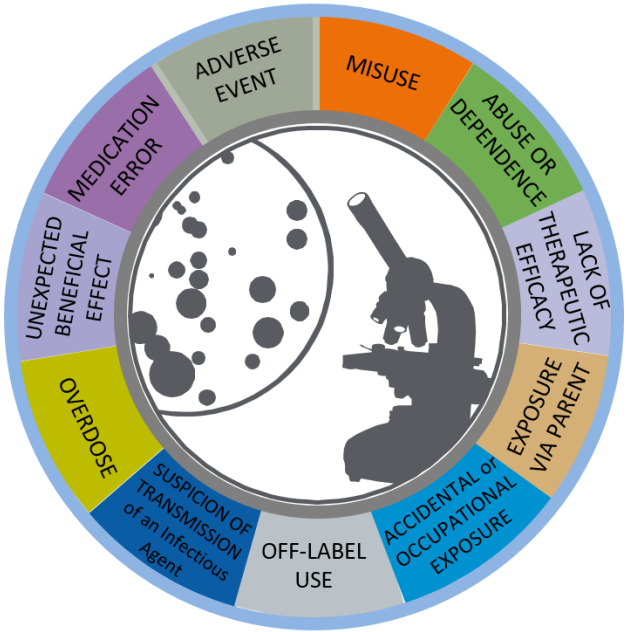
Transmission of an infectious agent via a medicinal product associated or non-associated to an Adverse Event

Example:

Robert was administered an injectable Sanofi product and two days later developed a blood infection The doctor thinks the product may have been contaminated.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



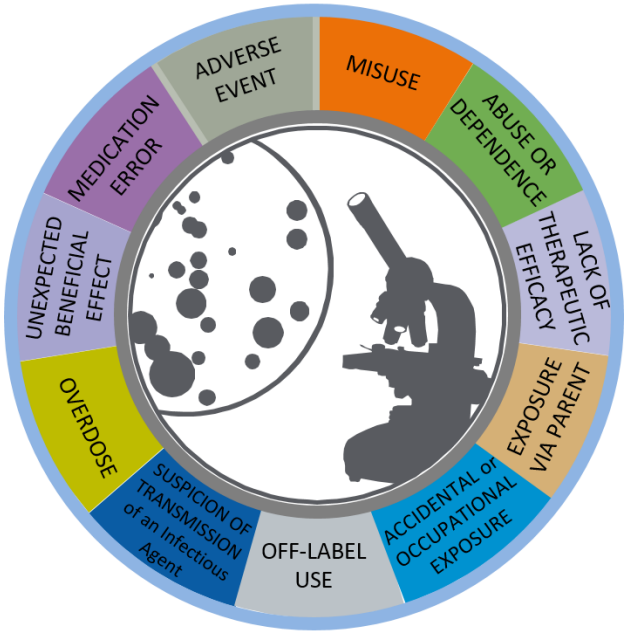
Overdose

The intentional or non-intentional administration of a drug dosage, which means quantity of a drug given per administration or per day above the maximum recommended dosage according to the authorized product information.

Example: A patient took 5 puffs corresponding to 5 mg of his Sanofi medicine. He feels perfectly well.
The maximum recommended dose is 3 puffs corresponding to 3 mg.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



Unexpected Beneficial Effect

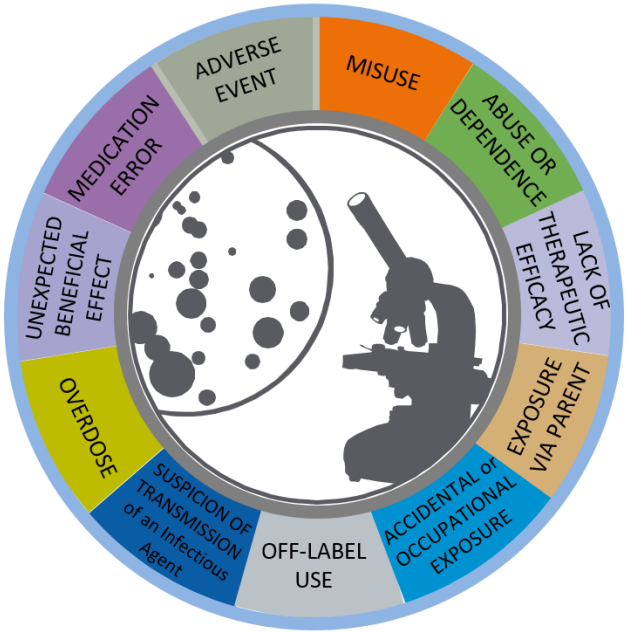
Any unanticipated beneficial effect occurring after the administration of a medicinal product that brings an improvement or cure of a disease or a symptom for which the product is not authorized.

Example:

A patient's wife noticed that her husband has more hair on his head since starting his new Sanofi migraine medication.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Types of Pharmacovigilance Data



Medication Error

Any unintentional error by the health care professional, patient, consumer or third party involving a drug or a health product which can cause a risk or an adverse event

Medication error may occur during the prescribing, dispensing or administration of medicinal product. Medication error may be proven or potential (intercepted before administration to the patient).

Example: A patient realized that her doctor prescribed the wrong dosage. Even though the patient did not take the medicine, this is considered a medication error.

These situations must be reported to Pharmacovigilance even if not associated with an adverse event.

Other Types of Pharmacovigilance Data
DRUG INTERACTION

Drug Interactions can cause safety events

A drug interaction is the alteration of the intensity of the pharmacological effects of one product by concurrent administration of another medical product, alcohol, food supplement etc. These interactions can induce an increase or a decrease of the expected product effect.

Examples of effects on patients and consumers are mainly clinical symptoms or biological changes that must be reported as Adverse Events.

Example: A patient experienced serious bleeding after being prescribed a certain antibiotic while taking a blood thinner.

Other Important Data to Report

INCIDENTS

Pharmacovigilance Data is not limited to Medicinal Products.
Incidents involving Medical Devices also need to be reported

An incident (in the context of **medical device)** is any malfunction or deterioration in the characteristics or performance of a medical device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect.

A serious incident can, therefore, be any inadequacy in the design labeling or the instruction for use which directly or indirectly, might lead to the death or a patient, user, or other persons or to a temporary or permanent serious deterioration in their state of health or to a serious public health thread.

Incidents are identified following Sanofi's assessment of Product Complaints; therefore, any product complaint should be reported to the **local Quality group** within one (1) business day

Record Retention

All PV records should be retained according to provisions agreed upon in the contract or specified in Sanofi document retention policies

At the end of the project or upon request by any patient or user for deletion of their personal data in accordance with applicable laws on personal data protection, such data shall be retained only in anonymized or pseudonymized form

During the retention period, all source data and information will be made available to Sanofi Patient Safety & Pharmacovigilance (PSPV) upon request, including, but without limitation, in case of a regulatory inspection

Sanofi PSPV department must be notified prior to destruction of any PV Data

If Sanofi PSPV wishes to keep the source data or any other form of PV Data or information, this information should be transferred to Sanofi PSPV

PRODUCT COMPLAINTS (PC / PTC) REPORTING REQUIREMENTS

Product Complaints Reporting Requirements

Product Complaint (PC) is also referred to as Product Technical Complaint (PTC)

A complaint is defined as any written, electronic, or oral communication that alleges **deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a drug product or a medical device** after it is released for distribution.

Suspected counterfeit cases of Sanofi products should also be reported.

All PTCs with or without an AE should be reported to the **local Quality group within one (1) business day** from receipt* using the local PTC contact list

**Date of receipt of PTC case by any employee or any person acting on behalf of Sanofi, such as services providers.*

Product Complaints Scenarios

Product aspects variation (color, smell, taste)	Leakage	Mix-up of products/dosages	Missing/damaged label
Broken product	Damaged packaging (primary or secondary)	Bent needle	Jammed/blocked pen
Missing product/component (pills, blisters, leaflet, dropper, syringe, etc.)	Missing batch number, manufacturing/expiration date	Spray defect, Dissolution issues	Lack of efficacy related to specific unit
Foreign body	Suspect Counterfeiting	Cannot refresh the data of a digital medical devices	

What to collect for a Product Complaint

All Product Complaints should be transmitted to the local Sanofi Quality department and should include the following:

Reporter (source) of the PTC with contact information (e.g., name, address, telephone, e-mail, etc.)	Number of units involved in the complaint and their availability for retrieval or evidence of defect (e.g., photo)	Detailed description of the potential PTC and AE description, if linked with PTC case* **In a case of PTC with PV event, remember to report the case to Sanofi Pharmacovigilance and Quality departments.*
Product information • Drug/Device involved • Dosage • Package Size • Lot # and Expiration Date • Unique Device Identifier (UDI), if available	Date of Receipt	

DO NOT DELAY REPORTING AN EVENT
if you are not sure if it is a PTC or if you do not have all the information – report whatever information you have as soon as possible but **no later than within <u>one (1) business day of receipt</u>.**

MANAGEMENT OF PV DATA IN DIGITAL PROPERTIES

Where might you come in contact with PV Data when monitoring Digital Properties?

PV Data can be found in many parts of a Digital Property.
Some examples include the following:

- ✓ **Blogs**
- ✓ **Comment Field**
- ✓ **Open Text Field**
- ✓ **"Contact us" Field**

All digital channels through which PV Data can be reported must be reviewed to determine if PV Data are mentioned, and if they are, the PV Data must be transmitted to Sanofi PSPV as soon as possible but no later than **one (1) business day**.

What to Report

Report all information about the PV Data as reported or identified

Patient/User: To whom the event or safety situation happened

Sanofi Suspect Product (drug/device/vaccine*) the trade name or INN of the Sanofi product which was suspected to be associated with the safety information.
*For vaccines, usually no trade name is reported and instead of INN a disease against which the vaccine was applied for protection is mentioned (e.g. Influenza-Vaccine, Hepatitis vaccine etc.).

Event(s) verbatim: the event or safety information description

Reporter: the person who reported the safety information to the person who is reporting the safety information to Sanofi (ex. Patient, Caregiver, Health Care Professional)

Also report:
Digital Property information: Digital Property ID or Digital Property Name
The Digital Property ID (or URL, or Channel Name) will be provided by the Sanofi Digital Property Owner and should be included
in the Project Name or Number field in the Unsolicited ISI form
or
in the event description field if the PV Portal is used

Do not delay reporting even if you are not sure it is PV Data or if you do not have all the information – report whatever information you have as soon as possible !

When to Report

Pharmacovigilance Data must be reported as soon as possible but no later than within one (1) business day of Internal Staff or Services Providers becoming aware of the PV Data.

Date of becoming aware of PV Data is for example the day of monitoring of the Digital Property as per required frequency.

Information should be submitted within timelines even if you are unsure that the information qualifies as Pharmacovigilance Data or if all information is not yet available.

Sanofi PSPV will review and decide how to handle the information

The clock starts ticking as soon as any representative of Sanofi or of the Services Provider working on behalf of Sanofi is made aware of Pharmacovigilance Data

How to report when using PV Portal

With the "PV Portal", Services Providers can report AEs/PV Data through an easy-to-use web portal.
Service Providers must register (sign-up option) at the time of the first report, and then access the PV Portal with the "sign-in" option.

As contact information is provided at time of sign up, this contact information (including e-mail address used for sending the acknowledgement of receipt purpose) will be auto-populated in the portal for every new reported safety information.

The portal utilizes a smart web form which contains various support features to guide the user at time of reporting.

- Some of the features are:
  - Mandatory fields are marked with the "*Required" tag.
  - Some fields include information buttons next to the question or answer to provide additional details or instructions for entering or selecting information correctly in the field.
  - Additional documents can be attached to the form, if necessary, using the document upload feature.
  - Once the report is submitted the user will immediately be provided with a portal reference ID.
  - After submission, a report can be downloaded if the user wishes to maintain a local pdf copy.

- Registered users have access to a dashboard where they can see and retrieve the reports they previously submitted via the portal.

- For corrections to a previously submitted report, registered users can retrieve the report in the dashboard, correct the data as needed, add "Correction to a Previously Submitted report" in "patient details" tab and submit the report.

NOTE: For additional information, refer to the "help with reporting" hyperlink available at the bottom of the PV portal.

How to report using the Unsolicited Individual Safety Information Collection & Documentation (Unsolicited ISI) Form

- For new reports:
  - Complete the PDF form electronically utilizing all dropdown lists and date formatted fields
  - Each Unsolicited ISI form is sent in a separate email to Sanofi PV as per instructions provided
  - Email Subject Line Naming Convention: Digital Property ID or Name - Sanofi Product

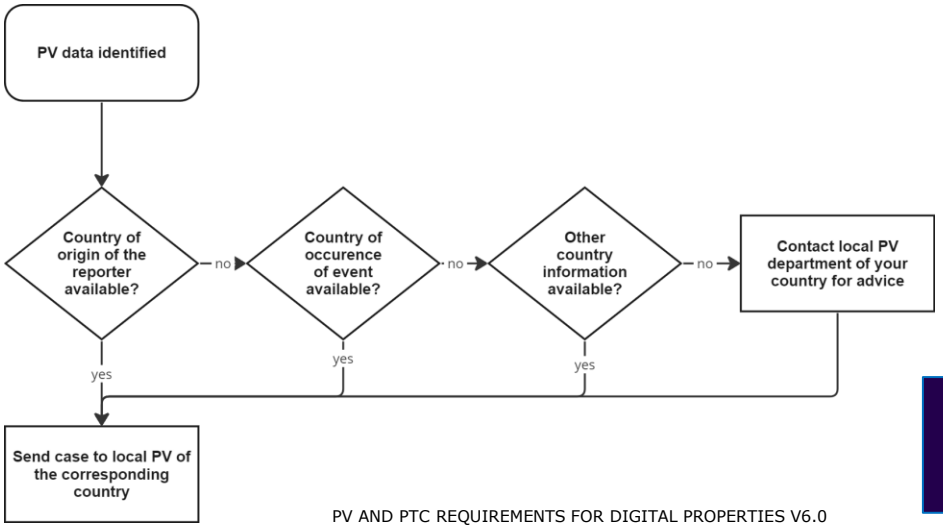
Email size less than 15 MB

- For corrections to a previously submitted report:
  - A corrected version of the Unsolicited ISI form must be sent in a separate email
  - The "Additional information" field of the form must state "Correction to Previously Submitted report" and must include details of the changes
  - Email Subject Line Naming Convention:
    - **Correction to Previously Submitted Report -** Digital Property ID or Name - Sanofi Product**–INBOX ID***
    - ***If you received an INBOX ID for the original report, the INBOX ID corresponding to the original report must be included in the subject line of the corrections email.

- Send completed form to the relevant PV contact as per information in the Sanofi PV Resources Toolbox and according to the Decision Tree Algorithm

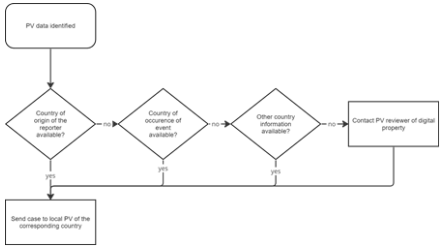
Decision Tree Algorithm

- For multi-country Digital Properties using the ISI form, the algorithm below must be used to determine the correct PV contact where PV Data must be reported.
- The route for single country projects is to be advised by the local PV contact
- If the post contains information related to a Product Complaint, the Quality group of the same country receiving PV Data must be contacted too.



See a printable version of the Decision Tree Algorithm in the PV packet

Decision Tree Algorithm-Instructions



Step by step to identify the relevant country to report PV Data to :

Country of origin of the reporter available?

In most cases the country of origin of the reporter is represented by the location of the reporter. This can be identified using the post content or Social Media Program settings, e.g.

- Location mentioned in the post
- Location mark in social media portal (usually indicated by a location icon)
- Domain extension in the email address e.g., ".fr" = France

Country of occurrence of event available?

If the location of the reporter can't be determined, the country of event should be used to determine the corresponding country. The information could be found in the post.

Other country information available?

Other information from the post can help identifying the country. e.g., a note in the post about the country where the post has been actually submitted or the language used to write the post.

If the post has no information about a country, the domain extension or URL of the social media program can be another indication. e.g., twitter.com/SanofiUS = US

If there are still doubts, the Service Provider can contact the Sanofi local PV department of the country in which the activity is being conducted i.e., the country where the information was received, or where the review took place

Acknowledgement of Receipt (ACK) of submitted PV Data

- Services Providers must ensure the successful transmission of the PV Data to Sanofi PV by confirming the acknowledgement of receipt.

When using the PV Portal

- Once the report is submitted the user will immediately be provided with a portal reference ID to be noted on the reconciliation form
- A confirmation email will be sent to the email address provided at registration and which will be auto-populated for registered users in the applicable section
- The acknowledgement of receipt emails must be kept on file by Internal staff and Services Providers

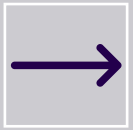
When using the Unsolicited ISI form

- An acknowledgement of receipt email will be provided to the sender. These emails should be kept on file.

If Services Providers do not receive an acknowledgment of receipt, the spam/junk folder must be checked. If the acknowledgment is still not found, the report should be resent as soon as possible and no later than one (1) business day.
If after resending the report, you still don't receive an acknowledgment of receipt, please contact your local PV.

Reconciliation – What is it?

A periodic reconciliation process must in place for all Digital Properties



Ensures that any PV Data collected has been transmitted to the Sanofi PSPV department and tracked

A reconciliation form with instructions is provided in the PV Packet

This reconciliation will take place on a regular basis, depending on the project type

Reconciliation process

Internal staff and Services Providers monitoring Digital Properties will generate a listing of all PV Data identified in each property using the reconciliation template provided by Sanofi and will send it to:

→ Sanofi Local PV (for single-country digital properties)

→ Email addresses specified in the reconciliation template (for multi-country digital properties)

Sanofi PV will inform the sender of the reconciliation form if there are missing reports

Missed reports must be forwarded by Internal staff or Services Provider to the local PV contact immediately and no later than one (1) working day

In case of any discrepancies, appropriate corrective and preventive measures must be implemented and communicated to the local PV contact for review and agreement

- A separate reconciliation template must be completed for each Digital Property
- The reconciliation form should be sent during the first 10 working days of every month from project launch to project closure
- Reconciliation must be documented, and records retained
- The reconciliation form in the PV Packet contains further information on how to complete the reconciliation form

SUMMARY of the Key Points

- Services Providers must monitor the Digital Property at the frequency agreed upon for the project.
- Services Providers/Internal staff must communicate any PV Data to Sanofi PSPV as soon as possible, but at the latest within one (1) business day of awareness of PV Data
- When communicating PV Data, Services Providers/Internal staff must provide information about the Patient/User, the product, the event(s) including Digital Property ID/Name, and the reporter. However, if information is not complete, the available PV Data must be submitted within timelines
- All available PV Data must be either submitted through the PV Portal or recorded on the Sanofi Individual Safety Information Collection & Documentation Form and the form must be sent to local PV (list of contacts is included with the PV Packet)
- For single country properties the reconciliation occurs as specified by Sanofi at the end of the outsourced activity period or once a month if the activity is longer than 30 days