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sanofi

- PV and PTC Requirements for Patient Programs (PP)

Patient Safety & Pharmacovigilance

Version 9.0

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Objectives

After completing this training, you should be able to:

- **Identify the content of the Patient Programs (PP) 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 program:**
 - **The PV Portal or**
 - **The Solicited Individual Safety Information (ISI) Collection & Documentation Form (Solicited 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 in the conduct of Patient Programs**
 - **Report appropriately Pharmacovigilance and Product Complaint Data from Patient Programs**
 - **Maintain the acknowledgements of receipt of submitted PV Data**
 - **Complete the additional activities required for Patient Programs:**
 - **Reconciliation**
 - **Quality Control (QC) Checks**
 - **Forward relevant information to personnel delivering products**

TRAINING REQUIREMENTS

- All Services Providers employees, sub-contractors/agents and Internal Staff involved in the conduct of a Sanofi Patient Program must complete pharmacovigilance and Product Complaint (PC or PTC) training prior to the start of the program
- Services Providers/Internal Staff must ensure that any new staff assigned to the Sanofi Patient Program complete PV and PTC 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 available upon request, e.g., at time of inspection or audit

Patient Program (PP) PV Packet, General Information and Important Communications

- The PP PV Packet is made available to Internal staff and Services Providers working on Patient Programs via the **Sanofi PV Resources Toolbox** and it contains the following:

1. Instructions for Self-Registration and Training Access iLearn
2. Solicited Individual Safety Information (ISI) Collection & Documentation Form (Solicited ISI form)
3. PV contact list
4. PTC contact list
5. PV Data Reconciliation Form / PV Data Quality Control Check Form

- Significant changes to the PP PV Packet will be communicated by the PP Leader or local PV and all updates will be visible on the **Sanofi PV Resources Toolbox**
- General Information and Important Communications related to the PV requirements applicable to Patient Programs can also be found on the Sanofi PV Resources Toolbox

Pharmacovigilance Requirements 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

What is Pharmacovigilance?

The etymological roots are:

- *Pharmakon (Greek) = Drug*
- *Vigilare (Latin) = To keep awake or alert, to keep watch*

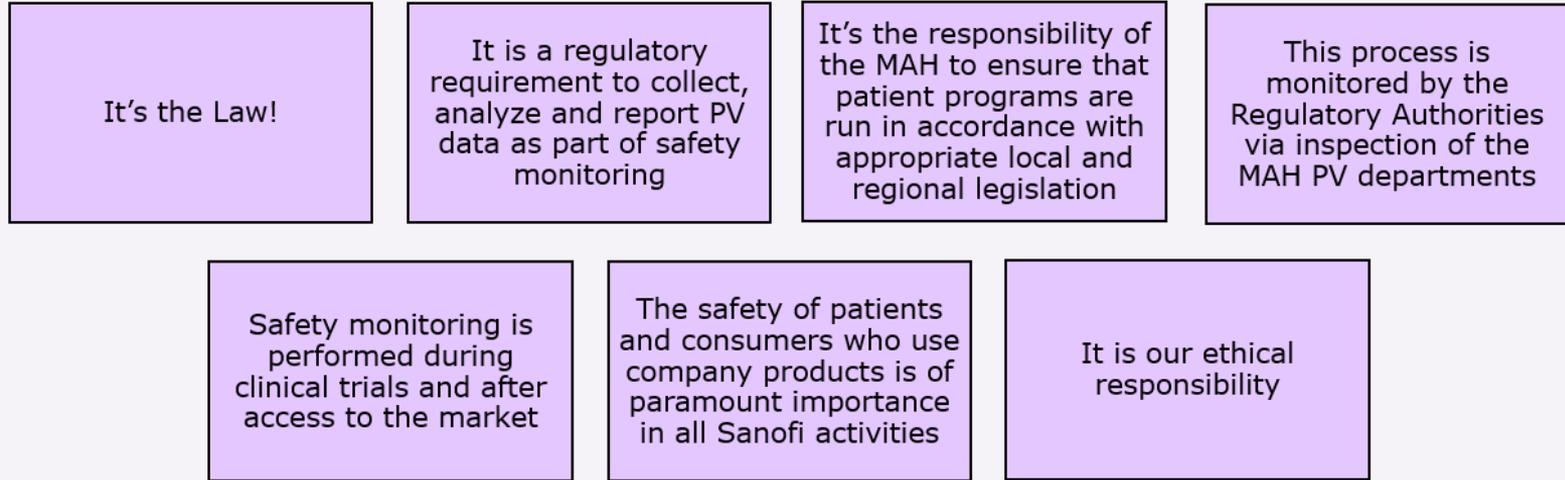


WHO definition:

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

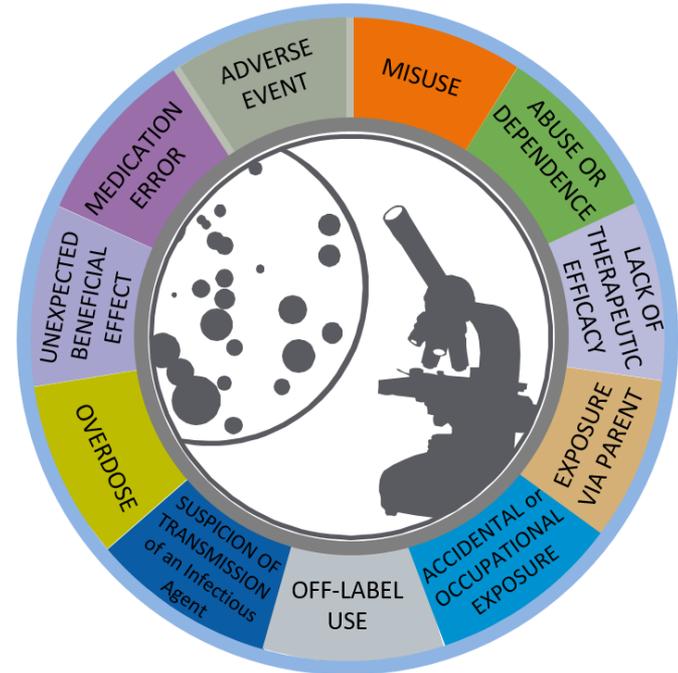
Criminal Charges

Types of Pharmacovigilance Data

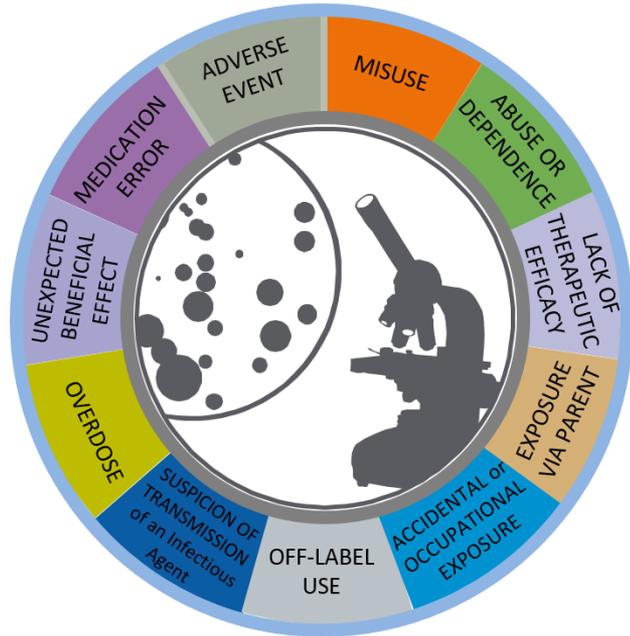
Services Providers can receive PV Data via different channels such as fax, phone calls, emails, text messages, directly from interactions with patients or Health Care Professionals, etc.

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

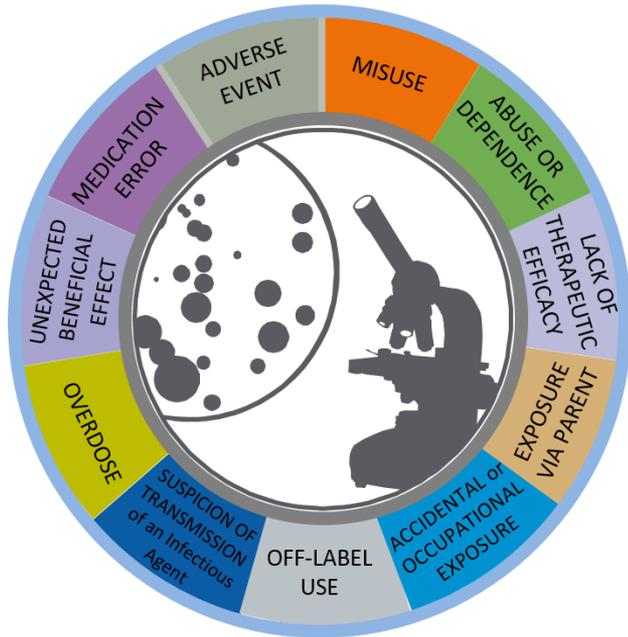
Death of a patient or consumer using a Sanofi product must be reported:

- 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



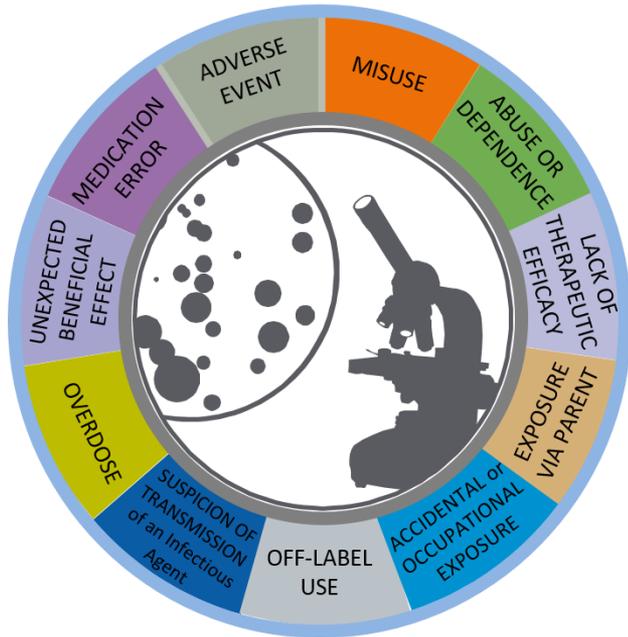
Misuse

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



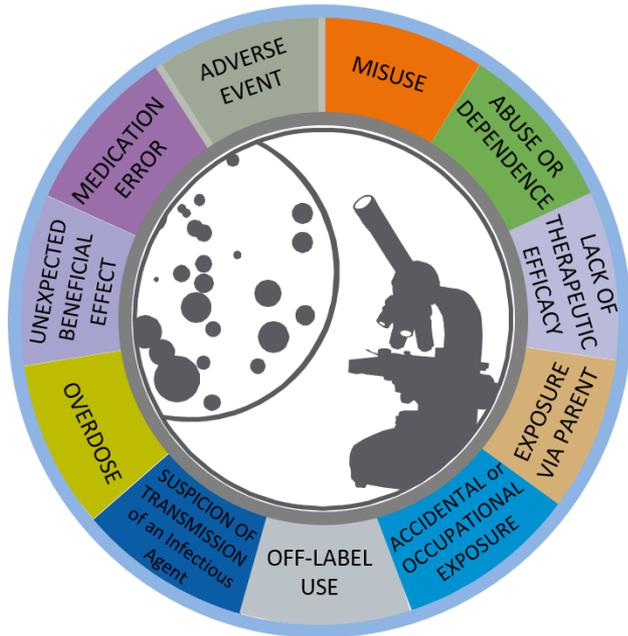
Abuse or Dependence

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



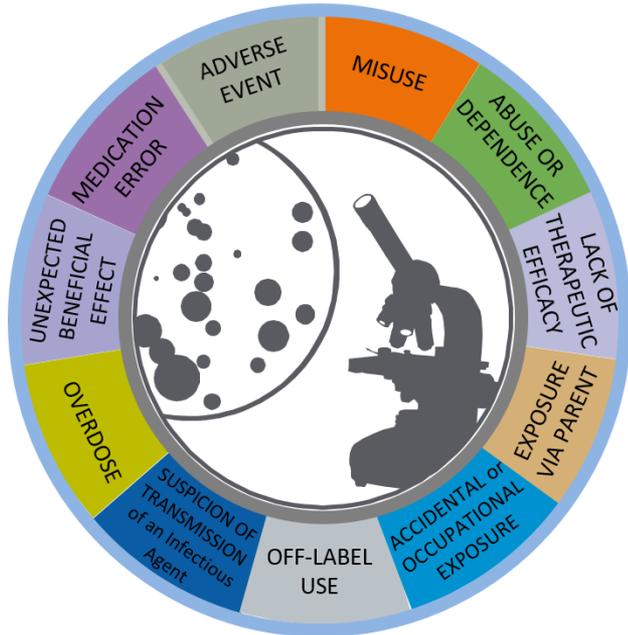
Lack of Therapeutic Efficacy

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



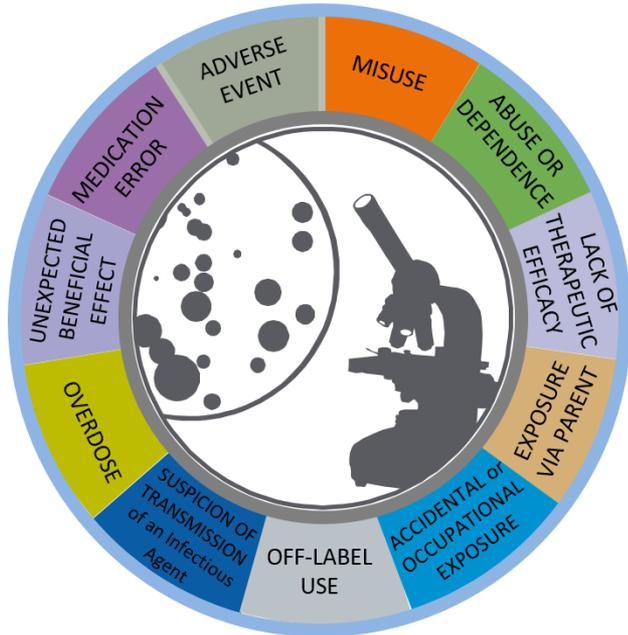
Exposure via Parent

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

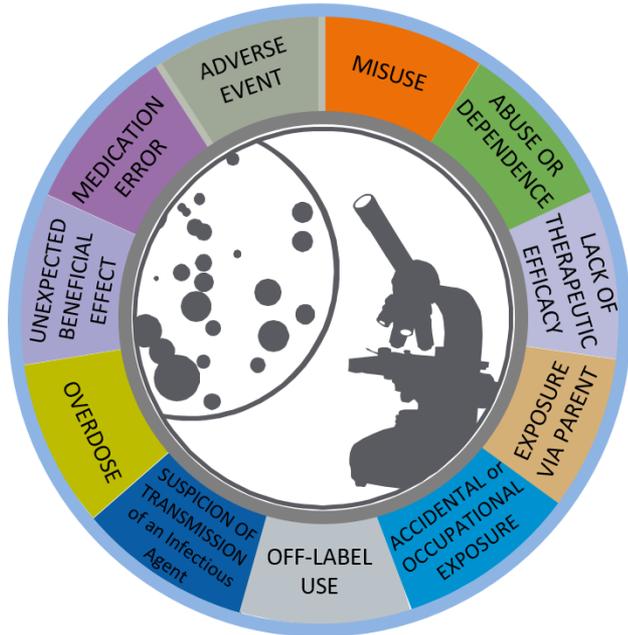
An exposure to a medicinal product as the result of one's professional or non-professional occupation

Example: A nurse reported a rash on her arm after being accidentally 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



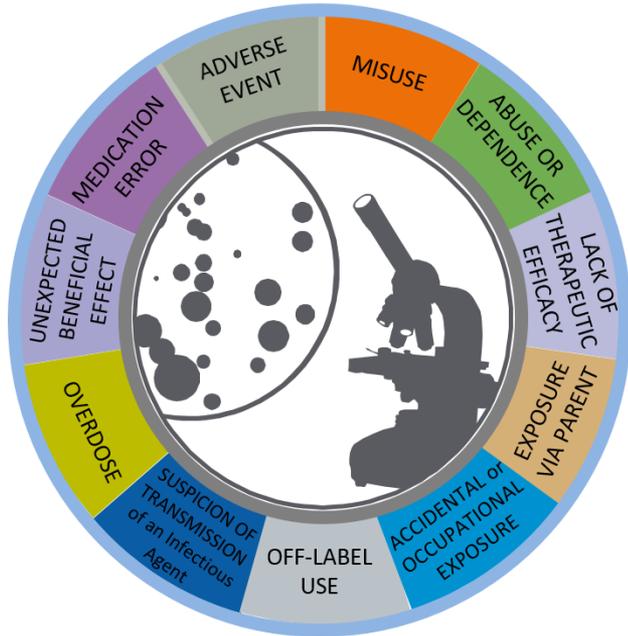
Off-label Use

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

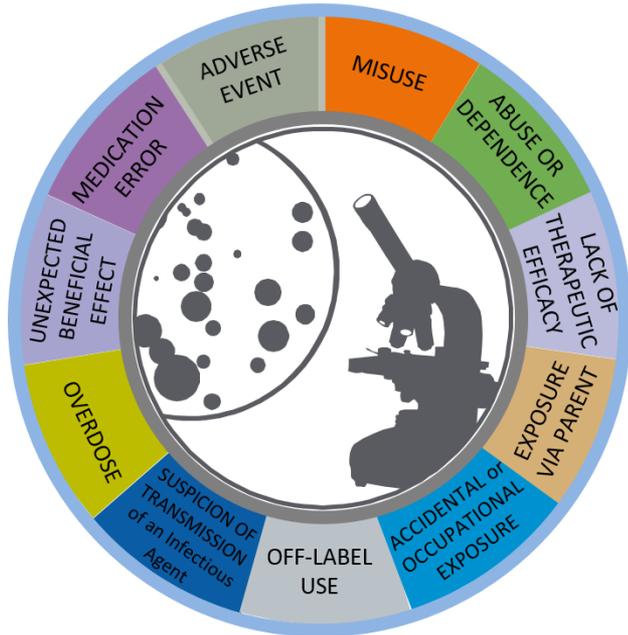
Transmission of an infectious agent via a medicinal product associated or non-associated to an Adverse Event.

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



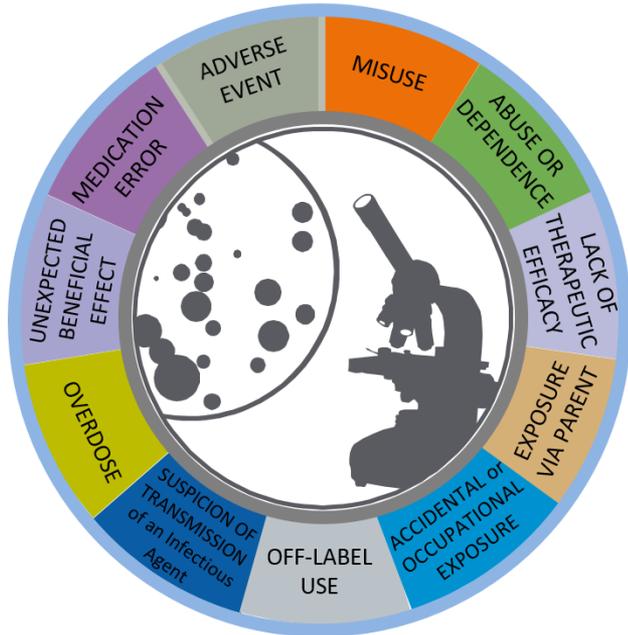
Overdose

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

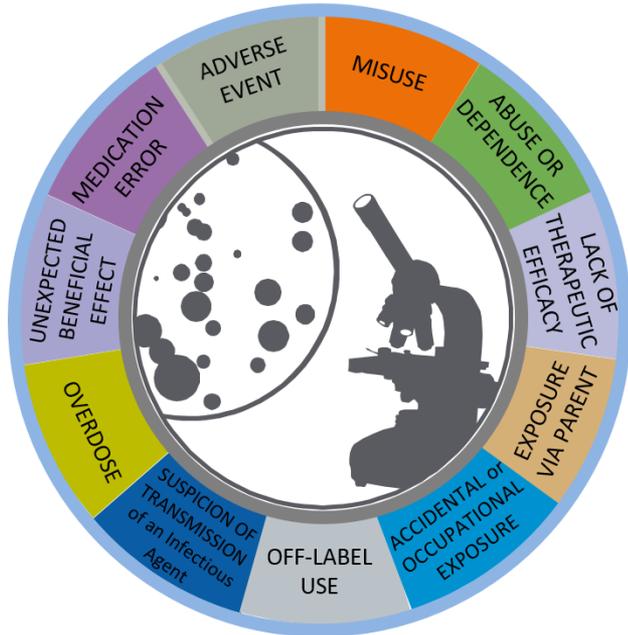
Any unanticipated beneficial effect occurring after the administration of a medicinal product that brings an improvement or cure of a disease or a symptom for which the product is not authorized.

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.

An incident can, therefore, be any inadequacy in the 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 serious deterioration in their state of health.

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 of receipt**.

Record Retention

All PV records should be archived according to provisions agreed upon in the contract

At the end of the activity or upon request by any patient 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 this period, all source data and information will be made available to the Sanofi PSPV department 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 Definition

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 PTC department and should include the following:

<p>Reporter (source) of the PTC with contact information (e.g., name, address, telephone, e-mail, etc.)</p>	<p>Number of units involved in the complaint and their availability for retrieval or evidence of defect (e.g., photo)</p>	<p>Detailed description of the potential PTC and AE description, if linked with PTC case*</p> <p><i>*In a case of PTC with PV event, remember to report the case to Sanofi Pharmacovigilance and Quality departments.</i></p>
<p>Product information</p> <ul style="list-style-type: none">• Drug/Device involved• Dosage• Package Size• Lot # and Expiration Date• Unique Device Identifier (UDI), if available	<p>Date of Receipt</p>	

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 one (1) business day of receipt.**

MANAGEMENT OF PV DATA IN PATIENT PROGRAMS

What? When? How? Where?

General Principles for reporting safety information

WHAT TO REPORT?

Report all available information and at least:

Patient
Product
Event(s)
Reporter

HOW and WHEN TO REPORT?

- Use the reporting process applicable to the program:
 - The PV Portal or
 - The Solicited Individual Safety Information (ISI) Collection & Documentation Form (Solicited ISI form)
- Report as soon as possible and no later than within one (1) business day of receipt or identification of PV Data

WHERE TO REPORT?

Follow the instructions that apply to the reporting process you are using in the Patient Program you are working on.

The Local PV contact details are in the PV contact list included in the PV Packet

Explanation and details in the next slides

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**

WHAT? WHEN? HOW? WHERE?

Key elements

WHAT:

Patient: 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:

Patient Program information: Program Number and Program Name

Patient unique ID: Must be less than 20 characters without any special characters

WHEN:

Pharmacovigilance data must be reported as soon as possible but no later than **one (1) business day of receipt** even if you are unsure that the information qualifies as Pharmacovigilance data or even if all information is not yet available (ex. Patient information). Sanofi PSPV will review and decide how to handle the information.

For Sanofi PV, the clock starts ticking as soon as safety information is reported to Internal Staff or to any representative of Services Providers or any of their subcontractors working on the patient program.

HOW and WHERE :

See instructions in the slides dedicated to the PV Data reporting process used in the Patient Program you are working on.

How to complete relationship of the AE/PV Data to a Sanofi product

Related = at least reasonable possibility that the suspect product caused the adverse event

Not Related = no obvious reasonable possibility that the suspect product caused the adverse event

Not Reported = The question on whether or not the adverse event or other PV data was caused by the suspect product was not asked to the reporter or causality was not provided by the reporter

Unknown = The reporter was asked whether or not the adverse event was caused by the suspect product and the reporter did not know

How to report PV Data when using the Solicited ISI Collection & Documentation Form

Solicited Individual Safety Information Collection & Documentation Form (Solicited ISI Form) is included in the PV Packet

- For new reports:
 - Complete the PDF form electronically utilizing all dropdown lists and date formatted fields
 - Patient ID should not exceed 20 characters and must not contain any special characters
 - Each Solicited Individual Safety Information Collection & Documentation form is sent in a separate email to Sanofi PV as per instructions provided
 - Email Subject Line Naming Convention:

Patient Program (or PP) - Sanofi product - Program name - Patient Unique ID

**e-Mail
size less
than 15
MB**

- For corrections to a previously submitted report:
 - A corrected version of the Solicited 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 – Patient Program (or PP) - Sanofi product- Program Name – Patient Unique ID -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 the completed form to the PV contact as per information provided in the Sanofi PV Resources Toolbox

How to report PV Data 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 data (including e-mail address used for ACK 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 PV 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.

Acknowledgement of Receipt 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 Solicited ISI form

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

If Internal staff or 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.

The sources of data during a Patient Program (1 of 2)

Typical Sources

- During a face-to-face visit
- During an organized call with the patient or the HCP
- From an email, text message, or other written communication
- Notification by family members/ caregivers/ HCPs ad-hoc interaction
- Any audio or video records

PV Data must be transmitted to Sanofi PV as soon as possible but no later than **one (1) business day**

The sources of data during a Patient Program (2 of 2)

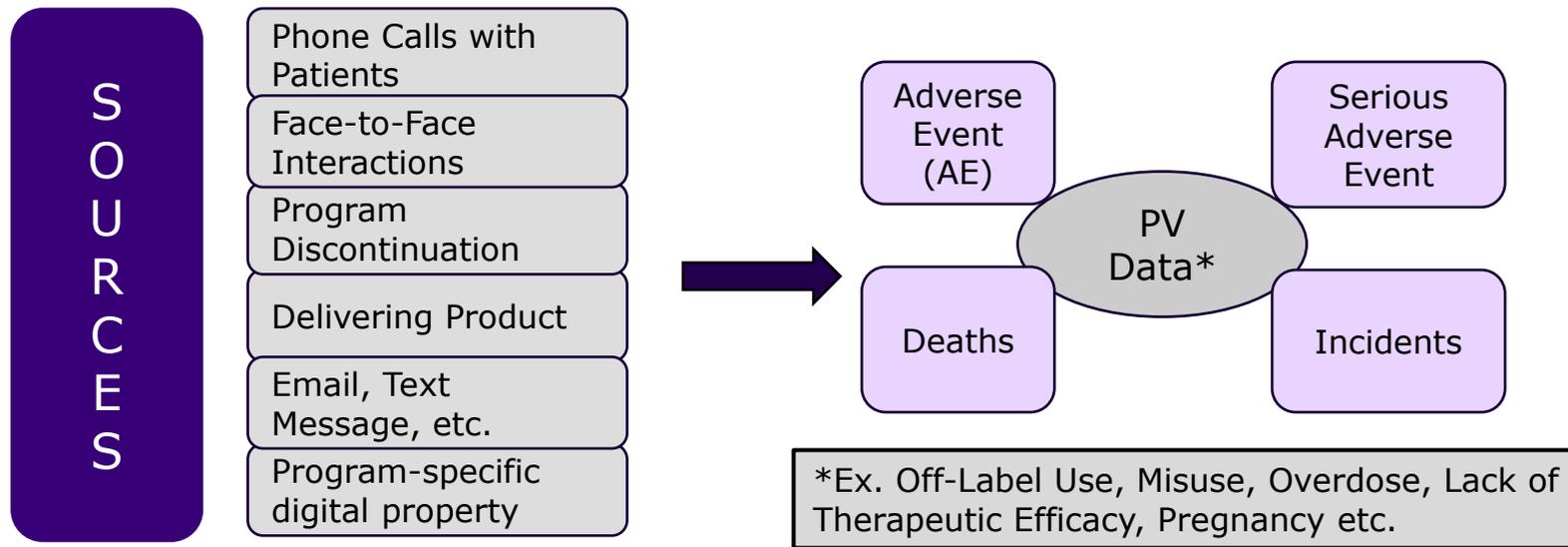
Non-Typical Sources

- During a delivery of product to the patient's home, which involves a planned interaction between the delivery personnel and the patient, e.g., the patient mentions to the delivery driver that a rash occurred following the last administration of a Sanofi product
- If non-renewal of the prescription, discontinuation from the program is related to adverse events or other PV data, e.g., death, lack of efficacy, etc.
- If abnormal lab values are tracked as per PP specification
- Through Patient Program-specific digital property

PV Data must be transmitted to Sanofi PV as soon as possible but no later than **one (1) business day**

Checkpoint

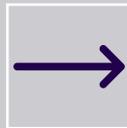
At this point you should be clear on the different types of PV Data that can be identified during a Patient Program



Reconciliation – What is it?



A periodic reconciliation process between the Services Provider/Internal staff and the Sanofi PSPV department is required



Ensures that any PV data collected by the PP personnel has been transmitted to the local PV and tracked



Occurs on a pre-defined periodic basis to be communicated by Sanofi



Frequency:
Minimum monthly or a more frequent period which is determined by the local PV contact

Reconciliation – How is this done?

The Services Provider/Internal Staff will generate a listing of all PV Data reports identified during the reconciliation period and send the listing to Sanofi PV using the Sanofi reconciliation form*

*Form is available in the PV Packet

Sanofi PV will inform the Services Provider/Internal Staff if there are missing reports

Detail of those reports should be forwarded by the Services Provider/Internal Staff to Sanofi PV** immediately and no later than **one (1) business day**

**Local PV contact information is included in the PV Packet

In case of any discrepancies, appropriate corrective and preventive measures must be implemented by the Services Provider/Internal Staff and communicated to Sanofi PV for review and agreement

Reconciliation must be documented, and records retained

Quality Control (QC) Check - What is it?



To ensure PV Data are appropriately identified and handled, the Services Provider/Internal Staff is required to implement QC checks for all sources through which AEs and other PV Data can be reported e.g., phone calls, emails, text messages, audio and video, etc.

The sources are not limited to the typical source of two-way interactions between the patient and Services Provider/Internal Staff and must be extended to the non-typical sources like the study drop-out reasons, pregnancy, hospitalization, death, etc.

Guidance on how to determine appropriate sample size, depending on PP design will be provided by Sanofi PSPV. QC check results will be documented on the PV Data Quality Control Check Form provided by Sanofi

Frequency:

Minimum once a month, for the duration of the PP, or more frequently if required by the Sanofi local PV contact

Quality Control (QC) Check – How is this done?



The methodology of the QC check will be determined by Services Provider/Internal Staffs and local PV contact based on the design of the PP, volume of PV data, etc.

QC checks must be performed by Services Provider/Internal Staff members not directly involved with the PP

Results of the QC Checks must be documented on the PV Data Quality Control Check Form*

The Services Provider/Internal Staff must send the PV Data Quality Control Check form to local PV

* Form is available in PP PV packet

If unreported PV Data are identified through the QC checks, details of those events must be forwarded by the Services Provider/Internal Staff to Sanofi PV immediately and no later than **one (1) business day**

In case of any discrepancies, appropriate corrective and preventive measures must be implemented by the Services Provider/Internal Staff and communicated to Local PV for review and agreement

Quality Checks must be documented, and records retained

Quality Check –Example

I took Dream® to sleep but now I have a headache and cannot sleep.



Service Provider reports 'Headache'



QC reviewer identifies two Adverse Events; "Headache" and "Cannot sleep"



QC Reviewer must submit the event of 'Cannot sleep' and implement corrective action.

Recording of Interactions

If interactions consist of a telephone conversation or a face-to-face interaction, then a recording of that interaction should occur or alternatively a summary of that interaction must be tracked as this becomes the source data of the PP.



Requirements for Contracted Delivery Services

For Services Providers/Internal Staff who contract a delivery service to deliver PP products, the following applies:

Any information received by the delivery driver from or about the patient during the delivery should be transmitted to the PP Services Provider/Internal Staff immediately for further investigation and need for reporting to Sanofi PV.

Summary of the Key Points (1 of 2)



- Services Providers/Internal PP staff must communicate any PV Data to Sanofi PV as soon as possible, and no later than one (1) business day of receipt of PV Data
- When communicating PV Data, Services Providers/Internal staff must provide information about the patient, the product, the event(s), the reporter and the PP Name/Number as well as any additional data that will allow Sanofi PV to conduct an accurate and complete medical assessment of the reported safety information
- 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
- All available PV Data must be entered in the electronic form on the PV Portal or recorded on the Sanofi Individual Safety Information Collection Form and the form must be sent to the relevant Sanofi PV department (list of contacts is included with the PV Packet), as agreed for the program

Summary of the Key Points (2 of 2)



- Reconciliation occurs monthly at a minimum, or at a period determined by the local PV contact
- Service Providers and Internal Staff are required to conduct Quality Control checks for all PPs to ensure that all PV Data are appropriately identified and sent to Sanofi PV