

Data Protection Impact Assessment

Submitting controller details

Name of controller	MSD Italia Srl., a subsidiary of Merck & Co., Inc. Rahway, New Jersey, USA ("MSD")
Subject	Name of Study: CMV PED Study - A Retrospective Observational Study To Understand The Clinical And Economic Burden Associated With Cytomegalovirus Reactivation and Related Health Outcomes In Paediatric Patients Receiving Allogeneic Hematopoietic Stem Cell Transplantation In Italy: RevOps ID NO: NIS103043
Name of Global Privacy Office point of contact Data Protection Officer for Italy	

Step 1: Identify the need for a DPIA

Explain broadly what project aims to achieve and what type of processing it involves. You may find it helpful to refer or link to other documents, such as a project proposal. Summarise why you identified the need for a DPIA.

The aim of this retrospective observational study is to evaluate demographic and the clinical characteristics of the Italian paediatric population undergoing allogeneic HSCT, in terms of CMV seroprevalence, underlying disease, usage of immunosuppression.

It is a Retrospective, Multicenter Observational study (the "Study") and it will be held in Italy as required under the applicable legislation on Observational Studies such as:

- AIFA guideline March 2008, as applicable;
- DM 30/11/2021, as applicable;
- Good Clinical practices, as applicable;
- Good Pharmacoepidemiology Practices (GPP)
- European Regulation 679/2016 (GDPR);
- Legislative Decree 196/2003 as modified by Legislative Decree 10 August 2018, n. 101 (the Italian Privacy Code);
- General provisions and relevant prescriptions issued by the Italian Data Protection Authority including the Provision containing the requirements relating to the processing of particular categories of data, pursuant to art. 21, paragraph 1 of Legislative Decree 10 August 2018, n. 101" issued on June 5, 2019 (Provision n.146/2019);Deontological rules for the processing for statistical or scientific research purposes issued by the Italian Data Protection Authority pursuant to art. 20, paragraph 4, of Legislative Decree 10 August 2018, n. 101 - 19 December 2018;
- Deontological rules for the processing for statistical or scientific research purposes issued by the Italian Data Protection Authority pursuant to art. 2-quarter and 106 of Legislative Decree 196/2003 (Provision n. 298 of May 9th , 2024)



Objective of the Study as further described in the attached protocol:**Primary objective**

The aim of this study is primarily to evaluate demographic and the clinical characteristics of the Italian paediatric population undergoing allogeneic Hematopoietic Stem Cells Transplantation (HSCT), in terms of CMV seroprevalence, underlying disease, usage of immunosuppression.

In the study there will not be collected any information regarding an MSD product or class or products in this setting.

Secondary Objective & Hypothesis

- To analyse CMV outcomes in terms of:
 - rates of clinically significant CMV infection (CS-CMVi) by day +100, day +200 and during the first year post allogeneic HSCT.
 - number of per population and per patient cs-CMVi recurrency
- To assess opportunistic infections in terms of rates of other viral, bacterial, fungal infections during the first-year post-transplant.
- To assess allogeneic HSCT and CMV related complications during the first year after transplantation and risk factors (underlying condition, donor type, stem cell source, conditioning intensity, immunosuppressive therapies used, acute GvHD).
- To assess the current standard of care in CMV management during the first-year post-transplant.
- To assess the economic burden (expressed in terms of re-hospitalization and length of stay (LOS) resource utilization (exams, diagnostic tests, visits, concomitant drugs) during the first-year post-transplant.
- To assess the all-cause mortality during the first-year post-transplant.

Data collecting of Study participant healthcare data will be conducted by the study team at each hospital site retrospectively from clinical charts (paper or electronic). Medical Records (MR) will be used to describe the risk factors, patient characteristics, treatment patterns, and healthcare resource utilization of subjects who had a CMV infection.

The retrospective data will be captured in consecutive patients undergoing allogeneic HSCT from January 2018 to June 2020 with maximum 12 months of follow-up period for each patient.

The data of the patients undergoing allogeneic HSCT after June 2020 will not be captured in order to avoid any possible bias due off label access to Letermovir (MSD product).

Monitoring of subject data and processing of patients pseudonymised data will be managed by the Clinical Research Organization (CRO) by onsite Source Data Verification (SDV). Remote Source Data Verification (SDV) could be performed according to the technical availability of the study site, in compliance with Health Authority requirements on remote SDV and upon acceptance of the DPO study site. Pseudonymised data will be shared, remotely, with few MSD (Sponsor) authorized personnel. Healthcare data may be shared with the Regulatory Authority (for inspection purposes as per legislation). Pseudonymisation of healthcare data is performed by the Investigator and will occur prior to transfer patient data to the Sponsor. Storing and archiving of data are required as per Good Pharmacoeconomics Practice (GPP) and all applicable local laws, rules and regulations relating to the conduct of the observational studies.

Step 2: Data Collection

What Personal Data will be Collected?	
With regard to patients data	Select as applicable:
Information that identifies the individual and their personal characteristics	Date of birth <input type="checkbox"/>
	Age (at the moment of the allogeneic HSCT) <input checked="" type="checkbox"/>
	Sex <input checked="" type="checkbox"/>
	Gender <input checked="" type="checkbox"/>
	Racial/ethnic origin <input type="checkbox"/>
	Physical description <input type="checkbox"/>
	Health information (Underlying condition and Conditioning regimen) <input checked="" type="checkbox"/>
	Healthcare cost and resources utilization <input checked="" type="checkbox"/>
	Education level <input type="checkbox"/>
	Marital status <input type="checkbox"/>
	Date and cause of death <input checked="" type="checkbox"/>
	Date of transplant; Type of transplant; Donor type <input checked="" type="checkbox"/>

What Sensitive Personal Data will be collected?

Select as applicable:

Information relating to the individual's physical or mental health or condition and information relating to genetic information (biological samples such as chromosomal or DNA samples) and biometric information (such as fingerprints or facial recognition)	<input checked="" type="checkbox"/> Note, no genetic nor biometric data will be collected.
Is the Research Study/Clinical Trial being conducted on a rare condition?	<input type="checkbox"/>
Does the research involve a recorded interview or photographs that could identify the participant?	<input type="checkbox"/>
Information relating to the individual's sex life.	<input type="checkbox"/>
Information relating to the individual's sexual orientation	<input type="checkbox"/>
Information relating to the individual's lifestyle (only smoking habits and alcohol consumption)	<input type="checkbox"/>
Information relating to any offences committed or alleged to be committed by the individual	<input type="checkbox"/>
Information relating to criminal proceedings, outcomes, and sentences regarding the individual	<input type="checkbox"/>
Information which relates to the education and any professional training of the individual	<input type="checkbox"/>
Employment and career history	<input type="checkbox"/>
Information relating to the financial affairs of the individual	<input type="checkbox"/>
Information relating to the individual's religion or other beliefs	<input type="checkbox"/>
Information relating to the individual's membership of a trade union.	<input type="checkbox"/>

What is the lawful Basis for Collecting this Information?

<p>Explicit Consent</p> <p>Art. 6, (1) (a) of the GDPR in conjunction with art. 9 (2) (a) for the purpose to process the data of living patients for the Study purposes.</p>	<input checked="" type="checkbox"/>
Legitimate interests of the Hospital (Controller of Medical Records)	<input type="checkbox"/>
Legitimate interests of the Study Sponsor (Controller of Study Data)	<input type="checkbox"/>
Vital Interests of the data subject or another person	<input type="checkbox"/>
Carried out (internally) by a not-for-profit organisation	<input type="checkbox"/>
Information that has been already made public by data subject	<input type="checkbox"/>
Necessary for substantial public interest	<input type="checkbox"/>
<p>Necessary for reasons of public interest in the area of public health</p> <p>Article 6(1)(c) legal obligation in conjunction with Article 9(2)(i) of the GDPR processing is necessary for reasons of public interest in the area of public health, such as pharmacovigilance</p> <p>This lawful basis will apply in relation to the processing of data of all patients involved in the Study for pharmacovigilance purposes.</p>	<input checked="" type="checkbox"/>
<p>Archiving purposes in the public interest/ Scientific or Historical Research purposes/ Statistical purposes</p> <p>Article 9(2) (j) for scientific research purposes in accordance with applicable law including art. 110 of the Italian Privacy Code and provision n. 298 of May 9th, 2024.</p> <p>This lawful basis in conjunction with the favourable opinion of the Italian Supervisory Authority will apply in relation to the processing of the data of all deceased or untraceable patients for the study purposes.</p>	<input checked="" type="checkbox"/>
<p>Other</p> <p>For deceased and untraceable patients where consent cannot be collected the legal basis is the provision n. 298 of May 9th, 2024 of the Italian Supervisory Authority issued in accordance with art. 110 of Legislative Decree 196/2003 as amended together with the favourable opinion of the competent EC.</p>	<input checked="" type="checkbox"/>

Step 3: Describe the processing

Describe the nature of the processing:

How will you collect, use, store and delete data?

In consideration of the fact that the disease evaluated in the study affects subjects suffering from severe comorbidities presenting a significant mortality rate and given the retrospective nature of the study and the large sample size needed for the study, also patients deceased and untraceable will be included. This approach will allow to avoid bias resulting from the exclusion of such subjects (patients selected for the outcomes) that could compromise the scientific quality of the study and the purpose of the research.

In such cases, Italian Privacy Law (Art. 110 of Legislative Decree 196/2003 as modified by Decree 19/2024 (the "Privacy Code")), with regard to the processing of personal data, for medical, biomedical and epidemiological research, states that "consent is also not necessary when, due to particular reasons, informing the data subjects is impossible or involves a disproportionate effort, or risks making it impossible or seriously compromise the achievement of the research objectives. In such cases, the data controller shall a) adopt appropriate measures to protect the rights, freedoms and legitimate interests of the data subject; b) obtain, the favourable opinion from the competent ethics committee at local level; c) adopt and comply with the safety measures identified by the Italian Privacy Authority pursuant to article 106, par. 2, d) of the Privacy Code. Therefore, before starting the Study, the Protocol shall have obtained the favourable opinion of both the local Ethics committee and the Sponsor shall comply with the Italian privacy Authority provision 298 of May, 9th /2024 that provides among other things the obligation to publish this DPIA and notify the Privacy Authority accordingly.

For patients enrolled into the observational study only data needed for the purposes of the study will be collected.

For living patients, the data will be collected by the Principal Investigator (or delegated clinical staff) from the Hospital medical records after explicit consent is given by the patient or by his legally designated representative if he is minor.

For deceased patients and untraceable patients the data controller shall obtain the prior favourable opinion from the competent ethics committee at local level and shall adopt and comply with the safety measures identified by the Italian Privacy Authority pursuant to article 110 of Legislative Decree 196/2003 as modified by Law Decree 19/2024, including the publication of this DPIA.

Furthermore, the data will be collected by the Principal Investigator (or delegated clinical staff) from the Hospital medical records only after he adopted and documented all necessary measures to contact the patients such as browsing through their clinical records, contacting such telephone numbers as may be available at site, or obtaining contact information from population and/or health care registers in order to ensure compliance with the applicable Privacy Law and he gave evidence of the practical impossibility to collect the patient consent.

Clinical patient data will be pseudonymized by the Investigator prior to sharing them with the Sponsor. The key for the pseudonymisation will be maintained by the Study site. The Sponsor cannot access the key to identify the patients.

The study data will be entered in the CRO's proprietary eCRF [REDACTED] with Remote Data Entry mode by the Investigators of the sites, who will be authorized by the Principal Investigators and suitably trained by Sponsor's representatives (CRO). The study data in the eCRF software [REDACTED] will be verified with the source by the CRO authorized representative (CRA), during on site or remote source data verification. Remote SDV will be performed in agreement with local DPO requirements and using the validated platform provided by the investigational site.

For the Health Care Professional (HCP)'s data, names and work contact details will be uploaded into validated, secure Sponsor systems used for the purposes of managing clinical trials [REDACTED]

At the end of the Study the CRO will transfer to Sponsor the pseudonymised Study data through [REDACTED] with the appropriate protections to the manager designated by MSD. The Sponsor may retain the pseudonymized Study data for 5 years as per GPP; the Sponsor representatives (CRO) and its vendor will delete all data at the end of the Study.

The Sponsor will not transfer pseudonymised Study data outside EU. Pseudonymised Study data will be stored at Sponsor facilities in accordance with its internal procedure. Only the final report drawn up with a level of aggregation such as not to allow in any way the identification of the interested parties to whom they refer will be stored into the [REDACTED]. The information will remain in our corporate network where we applied the appropriate security controls. Our Cyberfusion centre continuously monitor the network for unauthorised access.

Data at the Study sites will be stored as per the hospital policy and regulatory requirements for observational studies.

Information on how the Sponsor collects, uses, stores, and deletes data is provided to the Study participant in the privacy notice and Informed Consent Form.

What is the source of the data?

Patient data will be collected directly from the patient medical records by the Principal Investigator (or delegated clinical Staff)

Will you be sharing data with anyone? You might find it useful to refer to a flow diagram or other way of describing data flows.

Data collected at the study sites by the investigators (clinical staff) will be entered into the eCRF (electronic Case Report Form) [REDACTED]

The data will be managed by the CRO (Clinical Research Organization which is the qualified Sponsor representatives which will act on behalf of the Sponsor) through the system [REDACTED]

[REDACTED] instance with segregated access on application level.

This system complies with the requirements of art. 32 GDPR, the requirements of ICH E6 GCP(R2) and FDA 21 CFR Part 11.

[REDACTED]

The data report will be also shared with research ethics committees and competent authorities when completing safety reporting as required per the legislation and when reporting the aggregate data results of the Study.

The final report drawn up with a level of aggregation such as not to allow in any way the identification of the interested parties to whom they refer will be stored at [REDACTED]

What types of processing identified as likely high risk are involved?

The Study involves the collection of Study participants data including deceased or untraceable subjects not providing explicit consent prior to their personal data being processed.

The processing done by MSD will only take place after approval of the competent EC and after the publication of the DPIA and of the Information notice pursuant to art. 14 of GDPR. MSD will only collect the pseudonymised data and will not be able to re-identify the individual. There is a risk related to monitoring activities where monitors may be able to access, at site, the subject identifiable data. However, Monitors are designated by the CRO as subject authorised to process the data in compliance with GDPR and shall act in accordance with the instruction of the controller. Monitors are trained by the CRO on the functioning of the e-CRF [REDACTED]. They are required not to share identifiable data nor copy or record or bring outside sites data records. They have entered into confidentiality agreements with CRO. They also have to follow sites policy and local DPO requirements when accessing data records for monitoring purposes.

Describe the scope of the processing:

What is the nature of the data?

Having regard to patients' data the data to be collected will be information relating to **eligible paediatric patients** who have been treated by the hospital as described paragraph STEP 2 "What data will be collected". The scope of the processing patient data is to evaluate the demographic and the clinical characteristics of the Italian paediatric population undergoing allogeneic Hematopoietic Stem Cells Transplantation (HSCT), in terms of CMV seroprevalence, underlying disease, usage of immunosuppression.

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Does the data include special category or criminal offence data?
Data relating to criminal offences will not be collected.
How much data will you be collecting and using? How often?
This is a multicenter, observational, retrospective study on paediatric patients undergoing allogeneic HSCT. The selected sites will be the most representative of Italy because they will be the ones performing about 2/3 of the allogeneic HSCT in paediatric population per year in Italy. Data associated with patients medical history including information on diagnosis, treatment, intercurrent illnesses, and healthcare will be collected and used throughout the duration of the observational study. The retrospective data will be captured in consecutive patients undergoing allogeneic HSCT from January 2018 to June 2020 with maximum 12 months of follow-up period for each patient.
How long will you keep it?
The Sponsor may retain the pseudonymised study data for 5 years as per GPP.
How many individuals are affected?
<div></div>
What geographical area does it cover?
<p>Data will be collected from participants in Italy and from HCPs (health care professional) at the associated Italy sites. Data processing will take place within Italy and the EU. Standardised safeguards will be put in place for data transfers from the CRO to the Sponsor. No Study patients data will be transferred outside the EU and between subsidiaries. Only the final report drawn up with a level of aggregation such as not to allow in any way the identification of the interested parties to whom they refer will be stored into the <div></div></p> <p><div></div> The information will remain in our corporate network where we applied the appropriate security controls. Our Cyberfusion centre continuously monitor the network for unauthorised access.</p> <p>Exclusively for Pharmacovigilance purposes, the Patients personal data may also be shared with Sponsor's parent company (Merck & Co., Inc.) and/or its Group companies in accordance with the Binding Corporate Rules, Furthermore Merck & Co., Inc self-certified to, and participate to, EU-US Data Privacy Framework. Vendor contracts include contractual clauses and data processing agreements to define the terms for data processing.</p> <p>HCPs personal data will be shared with Sponsor's parent company (Merck & Co., Inc.) and/or its Group companies in accordance with the Binding Corporate Rules, Furthermore Merck & Co., Inc self-certified to, and participate to, EU-US Data Privacy Framework.</p>
Describe the context of the processing:
What is the nature of your relationship with the individuals?
<p>The individuals whose information will be collected and processed are patients at the Study sites. Living patient will consent to be part of the observational Study directly or, if they are still minor, through their legally designated representative. For deceased and untraceable patients the Sponsor shall have obtained the favourable opinion of the local Ethics Committee and shall publish the Data Protection Impact Assessment (DPIA) or an extract in advance on the MSD website, notifying the Italian Data Protection Authority accordingly, before commencing the Study in order to collect their data. This is in accordance with article 110 of the Privacy Code, as amended, as well as with the Italian Data Protection Authority decision of May 9th, 2024 n. 298.</p>

Please note that the processing of deceased and untraceable patients is necessary since it allows to avoid bias resulting from the exclusion of such subjects (patients selected for the outcomes) that could compromise the scientific quality of the study and the purpose of the research.

How much control will they have? Would they expect you to use their data in this way?

With regard to Living subjects:

Before agreeing to take part in the Study, the study doctor or one of his delegated staff members, explains the study information to each participant and to their legally designated representatives, if participants are still minor as outlined in the participant information sheet, so they understand how their information will be shared for the purposes of the Study. Participants or their legally designated representatives if they are still minors provide explicit consent prior to participating in the Study. Participants can withdraw from the Study at any time without giving a reason. The patient data will be deleted if patient withdraws consent.

With regard to Deceased patients / Untraceable patients:

The Investigator before collecting the data shall adopt all measures necessary to contact the patients and if they are still minor their legally designated representative such as browsing through their clinical records, contacting such telephone numbers as may be available at site, or obtaining contact information from population and/or health care registers in order to ensure compliance with the applicable Privacy Law and shall give evidence of the practical impossibility to collect the patient consent.

For patients who, as a result of the research carried out, should be untraceable or deceased, the information referred to in art. 14 of the GDPR will be made public through suitable methods, such as their publication on the Sponsor's and Investigator's site website and through specific information panels at Investigators' sites. In any case, if during the course of the study, as soon as the untraceable patients will contact the relevant site for any reason, including for check-ups, the Investigator will collect the informed consent signature for eligible patient and written privacy consent in order to allow him/her or the legally designated representative to exercise his rights under Privacy law. This DPIA will also be published on the Sponsor's website.

HCPs (health care professional) are provided with a privacy notice related to the processing of their personal data for the purposes of conducting the Study. Their data cannot be withdrawn as it will be needed to support the results of the Study according to the regulations.

Do they include children or other vulnerable groups?

Yes

Are there prior concerns over this type of processing or security flaws? Is it novel in any way? What is the current state of technology in this area? Are there any current issues of public concern that you should factor in? Are you signed up to any approved code of conduct or certification scheme (once any have been approved)?**With regard to Living subjects:**

There are no prior concerns over this type of processing, sharing or security flaws. Novel methods are not being used. The technology is appropriate for the data processing. There are no current issues of public concern.

With regard to **Deceased patients / Untraceable patients** the concern lay on the fact that the data will be collected without the consent of the subjects. There are no security flaws, novel methods are not being used. The technology is appropriate for the data processing. There are no current issues of public concern.

Data will be collected and processed in accordance with art. 110 of the Italian Privacy Code. The Sponsor will obtain the prior local Ethic Committee approval and will adopt the security measures identified by the Italian Data Protection Authority in its decision of May 9th, 2024, and will publish this Data Protection Impact Assessment (DPIA) in advance on the MSD website, notifying the Italian Data Protection Authority accordingly.

Describe the purposes of the processing:**What do you want to achieve?**

Data will be used for analysis and reporting to regulatory authorities. Participant data will be in an aggregated and anonymised form.

What is the intended effect on individuals?

There is no direct intended effect related to the data processing on the individuals.

What are the benefits of the processing – for you, and more broadly?

The Study may be of benefit of the Sponsor during the procedures with Regulatory Authorities in relation to its products. The Study may also be of benefit to the public since Allogeneic Hematopoietic Stem Cells Transplantation (HSCT) offers life-saving treatments for children suffering from oncological, haematological, and immunological diseases. However, the procedure renders the child severely immunocompromised and with that at risk of infections. Human CMV infection is a frequent complication after allogeneic HSCT in children with remarkable morbidity and mortality. Importantly, although CMV infection in allogeneic HSCT has been extensively investigated in adults, considerably less data exists within the paediatric population. The currently available antiviral drugs for paediatric patients are used as prophylactic, pre-emptive or therapeutic medicines, but the major challenge is drug toxicity (bone marrow- and renal toxicity). There is a big unmet medical need for efficacious and well-tolerated drugs to prevent CMV. Consequently, the management of CMV varies widely between centers as clinicians have many choices to make, but with limited data available to aid decision making. An important data gap in Italy is data related to the local clinical disease and economic burden of CMV in paediatric allogeneic HSCT recipients. Even if data is available on the number of allogeneic HSCT procedures performed every year in paediatric patients, we miss consolidated data on CMV-seroprevalence in the under 18 population (more specifically the recipient (R) and donor (D) positivity, and the combination frequency), the usage of immunosuppression, the underlying condition, the CMV reactivation

rate and recurrency (CMV infection/disease), the Graft vs Host Disease (GvHD) prevalence, and the re-hospitalization rate post-transplant.

This observational retrospective analysis will provide useful information for clinicians and payers, and local guidelines committee members, to improve the understanding of CMV clinical and economic burden and clinical management of paediatric patients undergoing allogeneic HSCT in Italy.

Step 4: Consultation process

Consider how to consult with relevant stakeholders:

Describe when and how you will seek individuals' views – or justify why it is not appropriate to do so.

With regards to **living subject**:

Explicit consent will be sought from the Study participants or their legally designated representative if the participant is a minor to process their healthcare data. The management of their data is extensively outlined in the patient privacy notice and informed consent form (ICF) for the Study, which has to be approved by the ethics committee. No Study data will be collected or processed until the ICF is reviewed, understood and signed by the patient to be enrolled into the observational study.

Minors will receive information on the Study in a way adapted to their age and mental maturity and from investigators or members of the investigating team who are trained or experienced in working with children. The explicit wish of a minor who is capable of forming an opinion to refuse participation in, or to withdraw from, the Study at any time will be respected by the investigator.

In order to do so minors will receive a written document which includes simplified information on the study and a simplified notice on the processing of their data.

With regards to **untraceable patients**:

The investigators shall adopt all necessary effort to contact participants or their legally designated representative if the patient is still a minor before collecting their data.

For untraceable and deceased patients, the privacy notice referred to in art. 14 of the GDPR will be made public. The management of their data is extensively outlined in the patient privacy notice and informed consent form (ICF) for the Study, which will be approved by the ethics committee.

Moreover, if during the course of the Study, as soon as the untraceable patients or a legally designated representative if the participant is still a minor, will contact the relevant site for any reason, including for check-ups, the Investigator will collect the informed consent signature for eligible patient and written privacy consent in order to allow him to exercise his rights under GDPR.

Finally for untraceable and the deceased patients the processing of their data will be subject to the prior favourable opinion of the sites' Ethic Committees and this DPIA will be rendered public and notified to the Italian Privacy Authority as provided by Provision 298/2024 of the Privacy Authority.

With regards to **HCPs (health Care professional)**:

Data will only be collected in accordance with applicable law and Sponsor requirements. A privacy notice will be provided to all applicable personnel.

Who else do you need to involve within your organisation?

Data processing arrangements have been discussed as appropriate by the Medical Affairs observational study team, Sponsor representative, Data Protection Officer, and the Global Privacy Office.

Do you need to ask your processors to assist?

An IT Risk assessment has been conducted with regard to the CRO. A Data Management Plan is in place between the CRO and the Sponsor. The CRO assisted the Sponsor in relation to this document. In addition to their routine data privacy training per the sites internal processes, the Study sites will be trained by the CRO acting on behalf of the Sponsor on appropriate data processing methods and data privacy at their site during initiation visit and/or subsequent training sessions.

Do you plan to consult information security experts, or any other experts?

Information and technologies Risk Assessment team has been involved. No additional consultations are deemed necessary at this time.

Step 5: Assess necessity and proportionality

Describe compliance and proportionality measures, in particular:

What is your lawful basis for processing?

The sharing of information is the minimum necessary to achieve the goals of the Study. Processing will be minimised in conformance with the GDPR.

With regard to **Living subjects**: The processing is carried out under the GDPR lawful basis of 6(1)(a) (consent) in conjunction with 9(2)(a) (explicit consent).

With regard to **Deceased patients/Untraceable patients**: In case of Deceased patients or Untraceable patients, where there is impossibility to inform the patient, the processing will be carried out under art. 110 of the Italian Privacy Code in conjunction with GDPR lawful basis 9(2)(j) (for scientific research purposes) and the Italian Privacy Authority Provision n. 298/2024 provided that the Study protocol has obtained the prior favourable opinion of the local Ethics Committees.

Does the processing actually achieve your purpose?
The processing and sharing of the data will achieve the objectives of the observational study described above (please refer to STEP 1 entitled: Identify the need for a DPIA).
Is there another way to achieve the same outcome?
No.
How will you prevent function creep?



Study staff at sites, Sponsor representatives (CRO) and third parties will ensure that everyone is aware of the regulations, privacy requirements and contractual obligations. This is achieved through training and other organisational controls.

In collecting, processing, transmit and store the data, the necessary measures will be adopted by the CRO and its suppliers to increase the level of data security as shown in the attached PIA as document 2 which are summarized hereto.

The data of the patients will be pseudonymized by assigning a unique identification code so as not to be able to trace the interested party in any way. The investigators will be the only ones to keep the identification key (subject identification list).

The eCRF [REDACTED] platform where the patient's data will be managed and stored during the Study has been tested to ensure that data is recorded and attributed to the correct patient. The use of a dedicated database is envisaged with a user who can access only that database, further guaranteeing data protection and segregation and the inability to mix data even within the same project. The system resides on CRO's server located in Europe. CRO and its suppliers will adopt suitable [REDACTED] with access via username and password to ensure high levels of security and confidentiality of information, ensuring data transmission via a secure and encrypted connection channel. The system provides a backup system [REDACTED] that allows a complete recovery of the data. Backup files are encrypted and copied to different locations via encrypted connections to preserve data privacy and confidentiality. There is a disaster recovery system. The computer system keeps track of any unauthorized access that has in any case been blocked.

Data transmission will always take place in protected mode. Any transmission by means of portable storage media can only be made to the person in charge of receiving indicated by the Company. Any portable computing device or any portable storage medium including all backup data is kept in encrypted form, using a commercially supported encryption solution. The encryption solutions will be implemented [REDACTED]

[REDACTED] which will be transmitted only to the specifically indicated subjects MSD Italia using a transmission channel other than that used for Personal Data.

With specific reference to the processing operations of the data stored in the database, logical access to the e-CRF [REDACTED] takes place by entering a personal username and password. Users are not allowed to write down the password on the terminal or in any other place accessible to others. The password must consist of a combination of numbers and letters with a minimum of 8 characters. The password has a configurable validity period [REDACTED]. After a predetermined number [REDACTED] of consecutive login attempts with incorrect username and/or password, the system automatically disables the user. Procedures are also provided for periodically checking the quality and consistency of the authentication credentials and the authorization profiles assigned to the persons designated for processing [REDACTED]

The pseudonymised data will be stored, in Italy, in a place protected by MSD for the time provided for in the Protocol at the end of which they will be destroyed. Access to the data will be allowed only to personnel authorized for this purpose and exclusively for the purposes related to the Study.

[REDACTED]

The final report will contain anonymized and aggregated data with a level that will not allow reidentification of subjects upon the occurrence of the 1% singularity. The information will remain in our corporate network where we applied the appropriate security controls. Our Cyberfusion centre continuously monitor the network for unauthorised access. Access to the final report will be allowed only to personnel authorized for this purpose and exclusively for the purposes related to the Study.

How will you ensure data quality and data minimisation?

Data quality is ensured through Good Clinical Practice (GCP), Good Pharmacoepidemiology Practice (GPP), training, design, and maintenance of system functionality, monitoring processes, audit, and inspection. Data minimisation is undertaken by specifying data requirements in the observational study protocol and within the submission executed to Regulatory Authorities (including the Italian Privacy Authority) and Ethics Committees. The data capture system (eCRF: electronic case report form) used for observational study is programmed to only collect the necessary data required for the purpose of the Study.

What information will you give individuals?

Participants in the Study will be given information about the Study and the associated data processing in the patient privacy notice and information sheet and consent form prior to agreeing to participate in the Study. HCPs (health care professional) will be given information about the data usage in the data privacy form.

Minors will receive a simplified document which includes information on the Study in a way adapted to their age and mental maturity from investigators or members of the investigating team who are trained or experienced in working with children. The explicit wish of a minor who is capable of forming an opinion to refuse participation in, or to withdraw from, the Study at any time will be respected by the investigator. The document the minors will receive will also include simplified information on the processing of their data.

For patients who, as a result of the research carried out, should be untraceable, the information referred to in art. 14 of the GDPR will be made public through their publication on the Sponsor's website and of the investigator's site as well as through specific information panels at Investigators' sites or through the MSD Italia website as the last option. In any case, if during the course of the study, as soon as the untraceable patients or their legally designated representative if the patient is still a minor will contact the relevant site for any reason, including for check-ups, the Investigator will collect the informed consent signature for eligible patient and written privacy consent in order to allow him to exercise his rights under Privacy law. The DPIA will also be published on the Sponsor's website.

How will you help to support their rights?

The Study participants will be given details of the site's data protection officer in the privacy notice and patient information sheet and consent form, should they wish to discuss the use of their information. Sponsor contact details are also listed.

Minors who come of age during the study execution will be given the privacy notice and his/her consent will be collected before that subject can continue to participate in the Study.

The CRO (which will act on behalf of the Sponsor) will monitor activity at the Study site to ensure data is processed according to the regulations, policies, processes, and contractual obligations.

What measures do you take to ensure processors comply?

Site activities are routinely monitored by the CRO to ensure compliance.

CRO and Sponsor have drafted a Data Management Plan and entered into a Data Processing Agreement which provides auditing activities by Sponsor on CRO in order to ensure CRO compliance to its obligations. An IT Risk assessment has been conducted on CRO in order to assess the confidentiality, integrity, and availability of the data by measuring both technical and organisational controls. CRO is allowed to partially sub-contract Study related activities or services to its Vendor appointed as sub-processors who has entered into a written agreement with CRO with terms that are at least as protective of Personal Information as the obligations set out in the DPA between Sponsor and the CRO. Consultants (i.e. health care professionals involved in the study) entrusted by MSD or by the CRO for drafting the final reports or scientific articles will be appointed as processor or sub-processor through a Data Processing Agreement with MSD or the CRO. The DPA will be an attachment to the project specific contract.

How do you safeguard any international transfers?

Exclusively for Pharmacovigilance purposes, the patient's personal data may also be shared with Sponsor's parent company (Merck & Co., Inc.) and/or its Group companies and as such the Sponsor may transfer the patient personal data to a location outside of the EU.

Furthermore, the final report drawn up with a level of aggregation such as not to allow in any way the identification of the interested parties to whom they refer will be stored into [REDACTED]

[REDACTED] Our Cyberfusion centre continuously monitor the network for unauthorised access. Access to the final report will be allowed only to personnel authorized for this purpose and exclusively for the purposes related to the Study.

In relation to such transfers Sponsor has in place appropriate measures under GDPR in particular the Binding Corporate Rules as well as SCC. Furthermore Merck & Co. Inc has certified to the US Department of Commerce that it adheres to the EU-US Data Privacy Framework.

Finally, the signature and the name of the HCP (health care professional) can be stored into the [REDACTED]

[REDACTED] The information will remain in our corporate network where we applied the appropriate security controls. Our Cyberfusion centre continuously monitor the network for unauthorised access.

Step 6: Identify and assess risks

INHERENT RISKS			
Risk description	Initial Severity	Initial Likelihood	Overall risk
1. Study subjects not providing explicit consent prior to their personal data being processed.	• High	High	High
2. Data collection and storage; Data records compromised at the Study site.	• High	• Low	Medium
3. Data collection; additional data collected over what is required for the research objective.	• low	• Low	low
4. Data sharing and storage; Sponsor or sponsor representatives' (including Study vendors) systems compromised/accessed/miss-used by unapproved persons. Personal data disclosed outside of those that need to know.	• medium	• Low	Low
5. Data not securely deleted or destroyed when the retention period expires (from sponsor or sponsor representatives' [including study vendors] systems)	• medium	• Low	Medium
6. Malicious attack on IT infrastructure that may result in a loss of the Confidentiality, Integrity, or Availability e.g. Hacking, Ransomware, or any type of Cyber incident	• High	• Low	Medium
7. Data security incidents are not reported or reacted to, meaning that incidents are not addressed or appropriately processed.	• High	• Low	Medium
8. Potential identifiability of the pseudonymized data in particular when the information is shared by mistake via email or uploading subjects specific documents in the eTMF	• High	• Low	Low

9. Potential Identifiability of the data in particular when the data are shared for the purpose of drafting final reports or scientific articles or during the retention period.	• High	• Low	Low
RATIONAL FOR RATING			
Risk	Severity	Likelihood	
1. Data subjects (i.e. Study participants) not providing explicit consent prior to their personal data being processed.	High: If patients are not aware that the controller is processing their information and they would not be able to exercise their rights.	High (Study participants) Limited (site researchers) As mentioned, the Study protocol includes deceased and untraceable patients.	
2. Data collection and storage; Data records compromised at the Study site	High: Risk is considered to have a maximal severity, given data records at Study sites are fully identifiable and contain sensitive healthcare data on Study participants.	Low: Data records stored at Study sites have restricted access as per the institutional robust policies and SOPs. Access is only permissible to appropriate HCPs (health care professional), other limited staff members where necessary, and to Sponsor representatives (monitors) as outlined in the participant information sheet.	
3. Data collection; additional data collected over what is required for the research objective.	low: Under GDPR and associated local regulations, data must only be collected where required for the research objective (data minimisation). Thus, any deviation from this requirement would be considered an important non-compliance.	Low: The Sponsor, also through CRO, ensures (and routinely oversight and control) that the databases have been carefully designed to only collect information required by the approved protocol, and in line with ICH-GCP, GPP and applicable legislation. Data of site researchers will only be collected as per applicable legislative obligations and Sponsor requirements, and a privacy notice will be issued to all applicable personnel.	

RATIONAL FOR RATING		
Risk	Severity	Likelihood
4. Data sharing and storage; Sponsor or sponsor representatives' (including study vendor) systems, compromised/accessed/miss-used by unapproved persons. Personal data disclosed outside of those that need to know.	medium: Whilst the data may contain sensitive healthcare information, all participant data transferred out of the study site would be pseudonymised per GCP, which would limit any potential harm.	Low: The 'coded' data which is provided to the Sponsor is maintained electronically (web hosted) and linked to a secure database located in the EU (Germany) managed by the CRO and its vendor. Written agreements are in place over any sub-contracted activities, including database management and archiving. The database is fully validated in accordance with Good Clinical Practice guidelines and clinical trial legislation, This includes security, access permissions, change control, audit trail, data integrity and archiving. Furthermore, all third-party vendors used by MSD are assessed for data protection requirements which extends to their systems used for the Study. This process provides confirmation that the systems meet acceptable standards.
5. Data not securely deleted or destroyed when the retention period expires (from sponsor or sponsor representatives' [including study vendors] systems)	medium: The confidentiality of personal data could be breached where the data is improperly deleted or retained for longer than necessary. This could have an impact on the individuals and cause them distress.	Low: The Sponsor has data retention policies in place which align with regulatory requirements for the maintenance of clinical trial data. The Sponsor also conducts assessments on any vendors utilised to ensure their policies are acceptable prior to vendor employment.
6. Malicious attack on IT infrastructure that may result in a loss of the Confidentiality, Integrity, or Availability e.g. Hacking, Ransomware, or any type of Cyber incident	High: Individuals may be caused distress if their medical information is made public.	Low: The technical maintenance of the information systems of the Sponsor, the CRO and site are governed by policies and process to ensure up-to-date data security is always in place.
7. Data security incidents are not reported or reacted to, in meaning that incidents are not addressed or appropriately processed.	High: Our contracts require our vendors to report incidents as soon as they become aware.	Low: Data security incidents are identified through Sponsor and its vendors monitoring and assigned to responsible persons. Processes exist for reporting and managing incidents.

RATIONAL FOR RATING		
Risk	Severity	Likelihood
8. Potential identifiability of the pseudonymized data in particular when the information is shared by mistake via email or uploading subjects specific documents in the eTMF	High: CRO employees are required to report incidents or potential incidents as soon as they become aware. They are trained on the procedure to follow in order to reduce the impact of the incident	Low: Processes exist for reporting and managing incidents and data breaches. Sponsor and CRO ensures that the CRO EDC is designed to allow the entry of only requested pseudonymized data (privacy by design). During the study, the data entered in the EDC system will be identified by a code agreed with MSD that will include the code of the trial centre and the number of the enrolled subject CRO representative will perform the SDV activity to ensure verification of existence and consistency of the data with the sources maintained at the sites. The interpretation key for the subjects' codes will be kept at the investigational site only. The CRO and its vendors as well as the other consultants are provided with instruction and training on the how to manage an incident and a serious breach.

RATIONAL FOR RATING		
Risk	Severity	Likelihood
<p>9. Potential Identifiability of the data in particular when the data are shared for the purpose of drafting final reports or scientific articles or during the retention period.</p>	<p>High: Some study related factors such as small population [REDACTED] the patients' location throughout the country, their pathology (in particular if rare), may increase the risk of patient re-identification.</p>	<p>Low: Once all study sites will be closed, further sharing of study specific information will be done using data aggregation methods or a specific data masking tool in order to minimize the potential identifiability of the data. The data masking process will be conducted in compliance with GDPR, Policy EMA 070 and other applicable guidelines focused on the publication of observational study results. Re-identification risks will be evaluated before data sharing upon reaching 1% of singularities identified out of the total number of records included in the dataset. The pseudonymised or aggregated data will be shared by the CRO and or MSD with the HCPs involved in the Study who will be entrusted with the drafting of scientific publications and will act as processor or sub-processor of the Sponsor or of the CRO through a specific data privacy agreement. The Sponsors will adopt anonymization techniques that considers all factors related to the study including the size of study population, in order to ensure adequate personal data protection and compliance with the applicable EU legislation in this area (including 05/2014 opinion of the Article 29 working party).</p>

Step 7: Identify measures to reduce risk

Measures to mitigate the identified risks above	Residual Severity	Residual Likelihood	Overall residual risk
<p>1. For living and traceable patients the explicit consent is collected by site personnel before collecting data. Informed consent of Study participants will be routinely checked by CRO representatives acting on behalf of the Sponsor during site monitoring visits. The Sponsor before starting the Study conducts regular data privacy training internally and to CRO, to allow Sponsor and</p>	<ul style="list-style-type: none"> Medium 	<ul style="list-style-type: none"> Low 	<p>Medium</p>

<p>CRO personnel to have appropriate oversight of site activities, and to ensure Sponsor and CRO personnel maintains compliance with regards to the collection of study participants data.</p> <p>In case of Deceased patients or Untraceable patients, the HCP (health care professional) will collect patient data from medical chart and data entry into the database of the study, provided that the protocol has obtained both the prior favourable opinion of the local Ethics Committee and of the Italian Data Protection Authority in accordance with the provisions set forth in the relevant Italian Privacy Law.</p> <p>The privacy notice pursuant to art.14 of the GDPR will be published on the MSD Italia website or clinical site or physically published at the clinical site. As soon as the patients will go to the clinical site for any reason, the clinical staff will submit the privacy notice and the consent to the subjects. Furthermore, as prescribed by the Italian Privacy Authority the following measures are in place:</p> <p>■ All patient data will be pseudonymized: ■</p> <p>■</p> <ul style="list-style-type: none"> - The eCRF ■ has been tested to ensure that data is recorded and attributed to the correct patient. The use of a dedicated database is envisaged with a user who can access only that database, further guaranteeing data protection and segregation and the inability to mix data even within the same project. The system resides on servers located in EU, Italy, with encrypted hard drives. All the processes for the development, management, administration, and maintenance of the system are defined having as input the requirements of the European Data Protection Regulation, the ISO 27001 standard and all the most stringent best practices in terms of information security. - The connection to the application and the transmission of data take place via the certified line (HTTPS). The data are stored on encrypted hard drives and are destroyed at the end of the study in order to limit data processing to what is really necessary and indispensable (minimization process - privacy by default). - The CRO and its suppliers will adopt suitable ■ ■ with access via username and password to ensure high levels of security and confidentiality of information, ensuring data transmission via a secure and encrypted connection channel. The system provides a backup system 			
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that allows a complete recovery of the data. Backup files are encrypted and copied to different locations via encrypted connections to preserve data privacy and confidentiality. There is a disaster recovery system. The computer system keeps track of any unauthorized access that has in any case been blocked.

Data transmission will always take place in protected mode.

The data may be sent

- The pseudonymised data will also be delivered to the Sponsor on [REDACTED]

<p>with the appropriate protections to the manager designated by MSD Italia. The files</p> <p>The receipt and correct readability of the files will be documented.</p> <ul style="list-style-type: none"> - The pseudonymised data will be stored in a place protected by MSD Italia for the time provided for in the Protocol at the end of which they will be destroyed. Access to the data will be allowed only to personnel authorized for this purpose and exclusively for the purposes related to the Study. Only the final report drawn up with a level of aggregation such as not to allow in any way the identification of the interested parties to whom they refer will be stored into <p>The final report will contain anonymized and aggregated data with a level that will not allow reidentification of subjects. Access to the final report will be allowed only to personnel authorized for this purpose and exclusively for the purposes related to the Study.</p>			
<p>2. All data at the Study sites will be maintained in accordance with the applicable institutions policies and SOPs. Access will be restricted to authorised personnel only.</p> <p>The Study staff are trained as required per the institutions policies on data privacy. Where trial data is to be viewed by the Sponsor representatives (CRO and its monitors), the Sponsor representatives has thorough processes in place to determine that this activity can be done whilst maintaining compliance with the relevant legislation. Monitors are designated by the CRO as subject authorised to process the data in compliance with GDPR and shall act in accordance with the instruction of the controller. Monitors are trained by the CRO on the functioning of the e-CRF and related IT system. They are required not to share identifiable data nor copy or record or bring outside sites data records. They also have to follow sites policy when accessing data records for monitoring purposes.</p> <p>If remote review of medical records is completed (if agreed by the Sponsor and Study site DPO), the Sponsor will follow the Study site policies and procedures for remote access to participant's medical records. The method used to remotely view the medical records will vary between the sites, for example by using video calls, screen sharing, or by directly accessing electronic medical records systems.</p> <p>In all cases the site will use secure systems and maintain access control so that viewing is restricted to records of site Study participants only in a confidential</p>	<ul style="list-style-type: none"> • medium 	<ul style="list-style-type: none"> • Low 	<p>Medium</p>

environment. The same data sharing restrictions in existing agreements will apply while remotely viewing the medical records. The Sponsor will not record or print screen from the remote monitoring session. All privacy requirements (e.g., GDPR,) to protect participant's medical records and other personal health information will be complied with.			
3. The Sponsor and Sponsor representatives (including trial vendors) have designed their databases to only collect information required to fulfil regulatory requirements and meet the research objectives. The Sponsor and Sponsor representatives have processes in place to ensure that site researchers data will only be collected as per applicable legislative obligations and Sponsor requirements. Sponsor and CRO personnel receive regular data privacy training which would include the requirement to ensure data minimisation, that is, to only collect data where necessary and appropriate.	• Low	• Low	Low
4. Data stored in Sponsor or Sponsor representatives' system have safeguards in place to prevent any unauthorised access (please refer to answer 1 of STEP 7). Access to physical premises are controlled via appropriate security measures. Only pseudonymized Study subject data is maintained, thus minimising the risks associated with any breaches.	• Low	• Low	Low
5. The Sponsor has detailed data retention policies in place which are compliant with regulatory requirements for observational studies data retention and GDPR.	• Low	• Low	Low
6. Sponsor and CRO have technical support services to maintain the confidentiality, integrity, and availability of their IT systems according to their policies and procedures. They have appropriate intrusion detection and firewalls rules in place.	• Low	• Low	Low
7. Site staff are trained at the start of the study on data privacy requirements. Monitoring of the Study conduct by site is performed on a regular basis by CRO representatives to assess quality, compliance, and issues. Any incidents will be handled as per site and Sponsor processes.	• Low	• Low	Low
8. CRO has measures in place to manage incident and data breaches (refer to SOP DPR001 Personal Data Breach and Incident Response Plan and ISM004 ISMS - Managing Negative Events and Incidents). CRO personnel is regularly trained on security awareness and on the correct procedure for detecting and managing potential data breach. Account to the eTMF is granted only to authorized staff. Periodic quality controls of the systems /EDC and eTMF are performed to ensure correct data entry and correct document management.	• High	• Low	Low
9. In order to analyse the data, the CRO will apply the aggregation techniques by using a validated statistical software and will compute the following summary measures according to the type of data: for quantitative data: mean, standard deviation, minimum and maximum. If the data is available for less than 10 patients, the result will not be presented.; for qualitative data:	• High	• Low	Low

absolute frequencies and percentages. If the aggregation is not feasible, the data will not be presented. Processing exists for identifying and managing re identifications risks. Furthermore, MSD and CRO provides for the carrying out of periodic checks aimed at assessing the persistence of the effectiveness of the data anonymisation measures with respect to technological evolution and will remove any singularity should it become aware of it at a later stage after the application of the anonymisation measures and will keep track of these events in order to repeat the re-identification risk assessment upon reaching 1% of singularities identified out of the total number of records included in the dataset, as required by the provisions of the Italian Supervisory Authority.			
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Step 8: Sign off and record outcomes

Item	Name/position/date	Notes
<div style="background-color: black; width: 100px; height: 15px; margin-bottom: 5px;"></div> Global Privacy Officer/DPO/DPO	Signature/Date: <div style="background-color: black; width: 200px; height: 30px; margin-top: 5px;"></div>	
Summary of DPO advice: study includes both untraceable and deceased patients and the MSD relies on a position paper from the Garante to authorize this processing. In accordance with Italian Applicable law, the processing of the personal data relating to untraceable and deceased patients can take place only after obtaining the prior favorable opinion of the local Ethical committee and in accordance with applicable law including the Italian Privacy Authority provisions and prescriptions. Compliance with the data protection authority prescriptions shall be in place for all the duration of the processing. This DPIA and the information notice pursuant to article 14 of the GDPR must be published. When publishing the results of the study the data must be sufficiently anonymized by aggregating the results and eliminating low numbers that can lead to the re-identification of patients. An example of this would be to replace the exact number where there are less than 5 patients with the words "Less than 5".		
DPO advice accepted by <div style="background-color: black; width: 100px; height: 15px; margin-bottom: 5px;"></div> Medical Operations Director	Signature and date <div style="background-color: black; width: 150px; height: 30px; margin-top: 5px;"></div>	
This DPIA will keep under review by: <div style="background-color: black; width: 100px; height: 15px; margin-bottom: 5px;"></div> Medical Operations Director	<div style="background-color: black; width: 150px; height: 30px; margin-top: 5px;"></div>	