

PART 1 (COUNCIL DECISION 2002/813/EC)

SUMMARY NOTIFICATION INFORMATION FORMAT FOR THE RELEASE OF
GENETICALLY MODIFIED ORGANISMS OTHER THAN HIGHER PLANTS IN
ACCORDANCE WITH ARTICLE 11 OF DIRECTIVE 2001/18/EC

In order to tick one or several possibilities, please use crosses (meaning x or X) into the space provided as (.)

A. General information

1. Details of notification

- | | | |
|-----|--|----------------------------------|
| (a) | Member State of notification | Germany |
| (b) | Notification number | B/DE/17/PEI3131 |
| (c) | Date of acknowledgement of notification | 05/07/2017 |
| (d) | Title of the project | |
| | A Phase I study of MAGE-A1-specific TCR-transduced T cells in patients with relapsed/refractory multiple myeloma | |
| (e) | Proposed period of release | From 01/09/2016 until 31/01/2020 |

2. Notifier

Name of institution or company:

MAGE-A1 Consortium

Max-Delbrück-Center for Molecular Medicine (MDC), Robert-Rössle-Str. 10, 13125 and
Institute of Immunology, Charité Campus Buch, Lindenberger Weg 80, 13125 Berlin
Germany

3. GMO characterisation

Autologous T cells, transduced *ex vivo* with the γ -retroviral vector MP71 expressing the T cell receptor (TCR) T1367 against the cancer-testis antigen MAGE-A1

(a) Indicate whether the GMO is a:

viroid	(.)
RNA virus	(.)
DNA virus	(.)
bacterium	(.)
fungus	(.)
animal	

-	mammals	(X) Genetically modified autologous T lymphocytes
-	insect	(.)
-	fish	(.)
-	other animal	(.)

specify phylum, class

(b) Identity of the GMO (genus and species)

Genus: Human
Species: Homo Sapiens

Autologous human CD8⁺ T cells transduced *ex vivo* with GMP-grade replication-deficient Myeloproliferative Sarcoma Virus (MPSV)-derived vector (pMP71) containing the gene for a human MAGE-A1-specific T cell receptor (TCR). Expression of the HLA-A*02:01-restricted TCR should enable transduced T cells to recognize and lyse MAGE-A1-expressing (cancer) cells. TCR α - and β -chain genes are linked by a P2A site to facilitate equimolar expression of both genes. The human constant regions of the TCR α - and β -chains have each been modified to contain corresponding murine amino acids (4 or 5, respectively) and an additional cysteine residue. The final TCR α - and TCR β -chain sequences were codon-optimized.

(c) Genetic stability – according to Annex IIIa, II, A (10)

Due to genomic integration of the MAGE-A1-specific TCR construct, guided by the retroviral vector, the resulting GMO is genetically stable. The retroviral vector itself is replication incompetent, since all components that would allow for further transfer are not incorporated in the vector. Gag/pol and env genes are genomically integrated only in the packaging cell line and not part of the viral vector genome. Thus, further spread is not possible. Identity and integrity of the vector as well as absence of replication-competent retrovirus in the vector and the master cell bank have been confirmed by the manufacturer of the retroviral vector (EUFETS GmbH). In addition even upon accidental release of the GMO into the environment it would rapidly lose viability and therefore the genetic sequences would be lost.

4. Is the same GMO release planned elsewhere in the Community (in conformity with Article 6(1)), by the same notifier?

Yes (.) No (X)
If yes, insert the country code(s) ...

5. Has the same GMO been notified for release elsewhere in the Community by the same notifier?

Yes (.) No (X)
If yes:
- Member State of notification ...
- Notification number B/././...

Please use the following country codes:

Austria AT; Belgium BE; Germany DE; Denmark DK; Spain ES; Finland FI; France FR; United Kingdom GB; Greece GR; Ireland IE; Iceland IS; Italy IT; Luxembourg LU; Netherlands NL; Norway NO; Portugal PT; Sweden SE

6. Has the same GMO been notified for release or placing on the market outside the Community by the same or other notifier?

Yes (.) No (X)
If yes:
- Member State of notification ...
- Notification number B/././...

7. Summary of the potential environmental impact of the release of the GMOs.

As the release of the GMO, transduced autologous T cells, is limited to patient administration in a hospital setting (Phase I trial) an environmental impact is not expected.

- Due to intense washing and dilution steps the GMO does not contain residual vector (as tested and calculated) and is produced using vector without replication-competent retrovirus (RCR). Thus, no replication of the vector with resulting impact on health in the T cell product and the patient is expected.
- There are no known diseases in humans caused by natural infection of gamma-retroviruses, thus, no impact on patient's health is expected due to the retroviral vector.
- Neither T cells nor gamma-retroviral vectors are transmittable by aerosols or urine/feces from a patient to another person.
T cells are not viable outside the patient from which the cells were derived unless sophisticated culture conditions (presence of antigen and/or growth factors) are applied *ex vivo*. Thus, even in the unlikely event of a release outside of the patient the GMO inactivates rapidly.
Transmission of modified T cells can only happen by accidental injection. However, the GMO is not viable in an immune-competent allogenic person due to Host-versus-Graft effect. Thus, no impact on other humans is expected.
- The GMO is manufactured at the Experimental and Clinical Research Centre (ECRC), MDC and Charité, Campus Buch, Berlin, where it is safely stored in the vapour phase of liquid nitrogen. Transport to the patient treated at Charité, Campus Benjamin Franklin, Berlin, is performed in a temperature-controlled GMO-transport box, which will also serve for short-term storage for few hours. Thus, the GMO is tightly secured. However, even when GMO is released outside a patient by accident, it inactivates quickly at room temperature and transgenic sequences will be lost.

B. Information relating to the recipient or parental organism from which the GMO is derived

1. Recipient or parental organism characterisation: human T cells

(a) Indicate whether the recipient or parental organism is a:

(select one only)

- | | |
|-------------------------|-----|
| viroid | (.) |
| RNA virus | (.) |
| DNA virus | (.) |
| bacterium | (.) |
| fungus | (.) |
| animal | |
| - mammals | (X) |
| - insect | (.) |
| - fish | (.) |
| - other animal | (.) |
| (specify phylum, class) | |

other, specify

2. Name

- | | | |
|-------|---|--------------|
| (i) | order and/or higher taxon (for animals) | - |
| (ii) | genus | Homo |
| (iii) | species | Homo sapiens |
| (iv) | subspecies | - |
| (v) | strain | - |
| (vi) | pathovar (biotype, ecotype, race, etc.) | - |
| (vii) | common name | human |

3. Geographical distribution of the organism

(a) Indigenous to, or otherwise established in, the country where the notification is made:

Yes (X) No (.) Not known (.)

(b) Indigenous to, or otherwise established in, other EC countries:

(i) Yes (X), following questions not applicable to humans

If yes, indicate the type of ecosystem in which it is found:

Atlantic	..
Mediterranean	..
Boreal	..
Alpine	..
Continental	..
Macaronesian	..

(ii) No (.)

(iii) Not known (.)

(c) Is it frequently used in the country where the notification is made?

Yes (.) No (.)

(d) Is it frequently kept in the country where the notification is made?

Yes (.) No (.)

4. Natural habitat of the organism

(a) If the organism is a microorganism

water	(.)
soil, free-living	(.)
soil in association with plant-root systems	(.)
in association with plant leaf/stem systems	(.)
other, specify ...	

- (b) If the organism is an animal: natural habitat or usual agroecosystem:
5. (a) Detection techniques Not applicable for Homo sapiens
- (b) Identification techniques
6. Is the recipient organism classified under existing Community rules relating to the protection of human health and/or the environment?
Yes (.) No **(X)**
If yes, specify
...
7. Is the recipient organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?
Yes (.) No **(X)** Not known (.)
- If yes:
- (a) to which of the following organisms:
- humans (.)
animals (.)
plants (.)
other (.)
- (b) give the relevant information specified under Annex III A, point II. (A)(11)(d) of Directive 2001/18/EC
8. Information concerning reproduction: Not applicable for Homo sapiens
- (a) Generation time in natural ecosystems:
- (b) Generation time in the ecosystem where the release will take place:
- (c) Way of reproduction: Sexual .. Asexual ..
- (c) Factors affecting reproduction:
9. Survivability: Not applicable for Homo sapiens
1. ability to form structures enhancing survival or dormancy:
- (i) endospores (.)
(ii) cysts (.)
(iii) sclerotia (.)
(iv) asexual spores (fungi) (.)
(v) sexual spores (funghi) (.)

- | | | |
|--------|----------------|-----|
| (vi) | eggs | (.) |
| (vii) | pupae | (.) |
| (viii) | larvae | (.) |
| (ix) | other, specify | ... |

2. relevant factors affecting survivability:

10. Dissemination: Not applicable for Homo sapiens

(a) Ways of dissemination

(b) Factors affecting dissemination

11. Previous genetic modifications of the recipient or parental organism already notified for release in the country where the notification is made (give notification numbers)
..., B/././...

not applicable

C. Information relating to the genetic modification

1. Type of the genetic modification

- | | | |
|-------|-------------------------------|------------|
| (i) | insertion of genetic material | (X) |
| (ii) | deletion of genetic material | (.) |
| (iii) | base substitution | (.) |
| (iv) | cell fusion | (.) |
| (v) | others, specify | ... |

2. Intended outcome of the genetic modification

Grafting MAGE-A1 specificity onto patient's T cells for adoptive T cell therapy of cancer. MAGE-A1-specific TCR-transduced T cells are provided as a personalized T cell immunotherapy to patients with relapsed/refractory multiple myeloma (RR-MM) whose tumors express the MAGE-A1 antigen.

3. (a) Has a vector been used in the process of modification?

Yes **(X)** No (.)

If no, go straight to question 5.

(b) If yes, is the vector wholly or partially present in the modified organism?

Yes **(X)** No (.)

If no, go straight to question 5.

4. If the answer to 3(b) is yes, supply the following information

(a) Type of vector

plasmid (.)
 bacteriophage (.)
 virus (X)
 cosmid (.)
 transposable element (.)
 other, specify

(b) Identity of the vector

The vector used is a replication-deficient MP71-derived retroviral vector

(c) Host range of the vector

The vector is murine leukemia virus (MLV)-based and pseudotyped by gibbon ape leukemia virus (GALV)-env. Therefore, dividing human and several animal cells can be infected, e.g. patient autologous T cells stimulated with anti-CD3/28.

(d) Presence in the vector of sequences giving a selectable or identifiable phenotype

Yes (X) No (.)

antibiotic resistance (.)

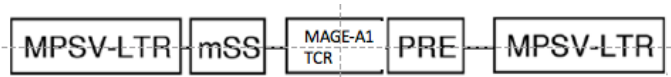
other, specify

- MAGE-A1 TCR (transgene): identifiable/selectable by antigen/MHC multimer staining or antibodies specific for the TCR β -chain
- PRE element: detectable by polymerase chain reaction

(e) Constituent fragments of the vector

The retroviral vector particle is composed of MLV structural proteins, pseudotyped with GaLV glycoproteins.

The vector genome construct is the MP71 construct which contains myeloproliferative sarcoma virus (MPSV) long terminal repeats (LTRs), a modified leader sequence containing a mRNA splice side (mSS) derived of murine embryonic stem cell virus (MESC), the posttranscriptional regulatory element (PRE) of woodchuck hepatitis virus and the MAGE-A1 TCR. The MAGE-A1 TCR is encoded by two genes (α - and β -chain), linked by a P2A site derived of porcine Teschovirus. The constant region of the TCR chains is human-derived with insertion of 4 murine amino acids in the α -chain and 5 murine amino acids in the β -chain. The variable region is completely derived from human sequences, which were, however, selected using a humanized mouse model (Li et al., 2010). Only the transfer vector is inserted into the recipient organism.



Constituent fragment	Donor organism/source	Intended function	Literature
LTR	Myeloproliferative sarcoma virus (MPSV)	Guiding integration, transcription, and translation	Engels et al., 2003
mSS	Modified leader	Regulatory element	Hildinger et

	sequence of murine embryonic stem cell virus containing splice donor and acceptor	enhancing expression	al., 1999
MAGE-A1 TCR variable regions	Homo sapiens	Providing MAGE-A1 specificity	Obenaus et al., 2015
MAGE-A1 TCR constant regions	Mus musculus, Homo sapiens	Enhance expression, decrease mispairing	Sommermeier et al., 2010
P2A-site	Porcine Teschovirus	Linking TCR α - and β -chain to ensure equal expression of both chains	Leisegang et al., 2008
PRE-element	Woodchuck hepatitis virus	Regulatory element enhancing expression	Schambach et al., 2000

(f) Method for introducing the vector into the recipient organism

- (i) transformation (.)
- (ii) electroporation (.)
- (iii) macroinjection (.)
- (iv) microinjection (.)
- (v) infection (.)
- (vi) other, specify ...
Ex vivo transduction of autologous T cells.
- (vii)

5. If the answer to question B.3(a) and (b) is no, what was the method used in the process of modification?

- (i) transformation (.)
- (ii) microinjection (.)
- (iii) microencapsulation (.)
- (iv) macroinjection (.)
- (v) other, specify (.)

6. Composition of the insert

- (a) Composition of the insert
See C4 (e)
- (b) Source of each constituent part of the insert
See C4 (e)
- (c) Intended function of each constituent part of the insert in the GMO
See C4 (e)
- (d) Location of the insert in the host organism

- on a free plasmid (.)
- integrated in the chromosome (X)
- other, specify ...

(e) Does the insert contain parts whose product or function are not known?
 Yes (.) No (X)
 If yes, specify ...

D. Information on the organism(s) from which the insert is derived

1. Indicate whether it is a:

- viroid (.)
- RNA virus (X)
- DNA virus (X)
- bacterium (.)
- fungus (.)
- animal
 - mammals (X)
 - insect (.)
 - fish (.)
 - other animal (.)
 (specify phylum, class) ...
- other, specify ...

The retroviral vector LTRs of MPSV and the mSS sequence of MSCV are RNA virus-derived, the PRE-element of woodchuck hepatitis virus is DNA virus (Hepadnavirus)-derived. The human MAGE-A1 specific TCR is obtained from human TCR loci transgenic mice (Li et al., 2010), the constant region is human and mouse derived. See also C4 (e).

2. Complete name

MPSV-LTR/MESV-mSS: Group: Group VI (ssRNA-RT)
 Order: Unassigned
 Family: Retroviridae
 Subfamily: Orthoretrovirus
 Genus: Gammaretrovirus
 Species: Myeloproliferative sarcoma virus (LTR)/
 Murine embryonic stem cell virus (mSS)

PRE-element: Group: Group VII (dsDNA-RT)
 Order: Unassigned
 Family: Hepadnaviridae
 Genus: Orthohepadnavirus
 Species: Woodchuck hepatitis virus

MAGE-A1 TCR: Homo sapiens

3. Is the organism significantly pathogenic or harmful in any other way (including its extracellular products), either living or dead?

MPSV/MESV: Yes
Woodchuck hepatitis virus: Yes
Homo sapiens: Not applicable

If yes, specify the following:

- (b) to which of the following organisms:

humans (.)
animals (X)
plants (.)
other ..

- (b) are the donated sequences involved in any way to the pathogenic or harmful properties of the organism

Yes (.) No (X) Not known (.)

If yes, give the relevant information under Annex III A, point II(A)(11)(d):
...

4. Is the donor organism classified under existing Community rules relating to the protection of human health and the environment, such as Directive 90/679/EEC on the protection of workers from risks to exposure to biological agents at work?

Yes (.) No (X)

If yes, specify

5. Do the donor and recipient organism exchange genetic material naturally?

Yes (.) No (X) Not known (.)

E. Information relating to the genetically modified organism

1. Genetic traits and phenotypic characteristics of the recipient or parental organism which have been changed as a result of the genetic modification.
The gene-modified T cells express an additional TCR of known specificity (MAGE-A1).

- (a) is the GMO different from the recipient as far as survivability is concerned?

Yes (.) No (X) Not known (.)

Specify ...

- (b) is the GMO in any way different from the recipient as far as mode and/or rate of reproduction is concerned?

Yes (.) No (X) Unknown (.)

Specify ...

- (c) is the GMO in any way different from the recipient as far as dissemination is concerned?

Yes (.) No (X) Not known (.)

Specify ...

- (d) is the GMO in any way different from the recipient as far as pathogenicity is concerned?

Yes (.) No (X) Not known (.)

Specify ...

2. Genetic stability of the genetically modified organism

The MAGE-A1 TCR is introduced in the T cells by retroviral gene transfer. After chromosomal integration of the MP71 vector the gene modified autologous T cells are genetically stable and the vector is an integral part of the host DNA.

3. Is the GMO significantly pathogenic or harmful in any way (including its extracellular products), either living or dead?

Yes (.) No (X) Unknown (.)

- (a) to which of the following organisms?

humans (.)

animals (.)

plants (.)

other ...

- (b) give the relevant information specified under Annex III A, point II(A)(11)(d) and II(C)(2)(i)

The replication-deficient retroviral vector genome is integrated in the T cell genome. No new viral particles can be generated in the final host cell since the gag, pol and env genes are absent from this viral vector. The transgene inserted in the retroviral vector encodes a human TCR. No pathogenic factors, cytokine-coding sequences, oncogenes, antibiotic resistance genes or otherwise hazardous inserts are present in the integrated vector.

4. Description of identification and detection methods

- (a) Techniques used to detect the GMO in the environment

- Detection of MAGE-A1 TCR (transgene) positive T cells by antigen/MHC multimer staining or antibodies specific for the TCR β -chain
- Detection of PRE element by polymerase chain reaction

- (b) Techniques used to identify the GMO

- Detection of MAGE-A1 TCR (transgene) positive T cells by antigen/MHC multimer staining or antibodies specific for the TCR β -chain
- Detection of PRE element by polymerase chain reaction
- TCR1367mmc vector to the original DNA plasmid can be verified by sequencing.

F. Information relating to the release

1. Purpose of the release (including any significant potential environmental benefits that may be expected)

Investigational Medicinal Product (IMP) for a Phase I Clinical trial. Eudract No.: 2017-001208-30 as Gene Therapy Medicinal Product.

Contact of IMP with the environment is not expected to have any effects on the environment, neither negative nor positive.

2. Is the site of the release different from the natural habitat or from the ecosystem in which the recipient or parental organism is regularly used, kept or found?

Yes (.) No (X)

If yes, specify ...

3. Information concerning the release and the surrounding area

- (a) Geographical location (administrative region and where appropriate grid reference):

The GMO is not released in the environment but transduced cells are infused into a patient in a restricted, controlled area (clinical site).

- (b) Size of the site (m²): Not applicable

- (i) actual release site (m²): ... m²
(ii) wider release site (m²): ... m²

- (c) Proximity to internationally recognised biotopes or protected areas (including drinking water reservoirs), which could be affected:

The GMO is to be administered into the patient, and thus, no environmental sites outside the hospital room will be affected. During transport of the GMO from manufacturing and storage site to the patient, the GMO will be contained in a GMO transport box. In the very unlikely event of release of the GMO into the environment, the GMO will inactivate fast at room temperature. Containment measures during administration of MAGE-A1 TCR T cells to the patients will also exclude accidental release of MAGE-A1 TCR T cells into the environment. According to Biosafety level 2 personal protective equipment will be used to avoid exposure to MAGE-A1 TCR T cells of the medical personnel involved in the administration of the product.

- (d) Flora and fauna including crops, livestock and migratory species which may potentially interact with the GMO

Not applicable

4. Method and amount of release

- (a) Quantities of GMOs to be released:

MAGE-A1 TCR T cells will be infused in a single treatment. The maximum target dose a patient might receive is approximately 5×10^{10} MAGE-A1 TCR viable T cells per dose.

- (b) Duration of the operation:
The administration will be completed within 30 minutes.
- (c) Methods and procedures to avoid and/or minimise the spread of the GMOs beyond the site of the release
The GMO will be transported and short-term stored in an GMO transport box. In the case of accidental release, the GMO will inactivate rapidly at room temperature.

5. Short description of average environmental conditions (weather, temperature, etc.)
Hospital rooms have to fulfill hygiene conditions required for the treatment of immune-compromised patients.
6. Relevant data regarding previous releases carried out with the same GMO, if any, specially related to the potential environmental and human health impacts from the release.
None

G. Interactions of the GMO with the environment and potential impact on the environment, if significantly different from the recipient or parent organism

Target organism is humans. Therefore, not applicable.

1. Name of target organism (if applicable)
 - (i) order and/or higher taxon (for animals) ...
 - (ii) family name for plants ...
 - (iii) genus ...
 - (iv) species ...
 - (v) subspecies ...
 - (vi) strain ...
 - (vii) cultivar/breeding line ...
 - (viii) pathovar ...
 - (ix) common name ...
1. Anticipated mechanism and result of interaction between the released GMOs and the target organism (if applicable)
3. Any other potentially significant interactions with other organisms in the environment
None expected.
4. Is post-release selection such as increased competitiveness, increased invasiveness for the GMO likely to occur?
 Yes (.) No (X) Not known (.)
 Give details
 ...
5. Types of ecosystems to which the GMO could be disseminated from the site of release and in which it could become established

Not applicable.

6. Complete name of non-target organisms which (taking into account the nature of the receiving environment) may be unintentionally significantly harmed by the release of the GMO

None. The gene-modified T cells only survive in the autologous patient form which they were derived.

- | | | |
|--------|---|-----|
| (i) | order and/or higher taxon (for animals) | ... |
| (ii) | family name for plants | ... |
| (iii) | genus | ... |
| (iv) | species | ... |
| (v) | subspecies | ... |
| (vi) | strain | ... |
| (vii) | cultivar/breeding line | ... |
| (viii) | pathovar | ... |
| (ix) | common name | ... |

7. Likelihood of genetic exchange in vivo

- (a) from the GMO to other organisms in the release ecosystem:
None

- (b) from other organisms to the GMO:
None

- (c) likely consequences of gene transfer:
None

8. Give references to relevant results (if available) from studies of the behaviour and characteristics of the GMO and its ecological impact carried out in stimulated natural environments (e.g. microcosms, etc.):

No simulations clinical trials have been carried out with this GMO. Similar clinical trials have successfully been done with CD19-CAR transduced T cells to treat B cell malignancies.

9. Possible environmentally significant interactions with biogeochemical processes (if different from the recipient or parental organism)
Not applicable.

H. Information relating to monitoring

1. Methods for monitoring the GMOs

Monitoring of patients will include

- Multiparameter immunological cell monitoring by flow cytometry. The GMO MAGE-A1 TCR-positive T cells will be identified by multimer staining.
- quantitative PCR of the PRE element for detection of transfused T cells in the blood and bone marrow of patients.

Patients will continue to be followed at regular intervals post-infusion per health authority guidance as defined in the treatment protocol.

2. Methods for monitoring ecosystem effects
Not applicable
3. Methods for detecting transfer of the donated genetic material from the GMO to other organisms
Not applicable
4. Size of the monitoring area (m²)
Not applicable
5. Duration of the monitoring
See Study Protocol
6. Frequency of the monitoring
See Study Protocol

I. Information on post-release and waste treatment

1. Post-release treatment of the site
Instruction for transport, handling and disposal are defined for the clinical trial material in a separate document (IMPD). People involved in the clinical trial will be trained about the procedures and measures to be taken in case of unexpected spread/accidental release, accordingly.
2. Post-release treatment of the GMOs
All IMP waste, as well as any material that came into contact with the IMP will be inactivated according to the hospital bio-hazard disposal procedures.
 - (a) Type and amount of waste generated
Contaminated material used for the administration of MAGE-A1 TCR T cells including cryobags and infusion lines that have been in contact with MAGE-A1 TCR T cells.
 - (b) Treatment of waste
Inactivation as potentially infectious medical waste.

J. Information on emergency response plans

- 1.) Methods and procedures for controlling the dissemination of the GMO(s) in case of unexpected spread

Risk of dissemination after unexpected spread is regarded very low, as the GMO (gene modified T cells) is not able to survive outside of the human body and does not release replication competent viruses. Application of the GMO to patients will be done in suitable and confined areas within the clinical site. Accidental injury with GMO-contaminated needles will induce a strong alloresponse in the affected person which prevents further spread of the GMO. Instruction for transport, handling and disposal are defined for the

clinical trial material in a separate document. People involved in the clinical trial will be trained about the procedures and measures to be taken in case of unexpected spread/accidental release, accordingly.

2.) Methods for removal of the GMO(s) of the areas potentially affected

Decontamination procedures according standard for hospital clean rooms are regarded save methods.

3.) Methods for disposal or sanitation of plants, animals, soils, etc. that could be exposed during or after the spread

Not applicable.

4.) Plans for protecting human health and the environment in the event of an undesirable effect

Patients treated with the GMO in the authorized clinical trial setting will be monitored regularly. Emergency response is defined in the clinical protocol and is under the responsibility of Investigator and Sponsor responsible of the trial.

Staff handling the IMP have to follow handling instructions and protecting measurements laid down in the written instructions for the Clinical Trial and to follow hospital standards (e.g. need to wear specific clothing, gloves or surgical mask, follow standard disinfection procedures).

Literature

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