# MELCAYA

NOVEL HEALTH CARE STRATEGIES FOR MELANOMA IN CHILDREN, ADOLESCENETS AND YOUNG ADULTS

**Grant Agreement: 101096667**

# D2.6 NevustoMel initiation package

Funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the Health and Digital Executive Agency. Neither the European Union nor the granting authority can be held responsible for them.

# Document Information

| | |
|---|---|
| **Deliverable number:** | D2.6 |
| **Deliverable title:** | NevustoMel initiation package |
| **Deliverable version:** | v2.0 |
| **Work package number:** | WP2 |
| **Work package title:** | Understanding triggers and transitions from normal melanocytes to nevus to melanoma |
| **Due date of delivery:** | 31.10.2023 |
| **Actual date of delivery:** | 28.11.2023 |
| **Dissemination level:** | Public (PU) |
| **Type:** | R – Document, report |
| **Author(s):** | Susana Puig (HCB)<br>Adrián López (FCRB) |
| **Contributor(s):** | Cristina Carrera (HCB)<br>Joan Antón Puig (HCB)<br>Teresa Torres (FCRB) |
| **Reviewer(s):** | Heather Etchevers (AMU) |
| **Project name:** | Novel health care strategies for melanoma in children, adolescents and young adults |
| **Project Acronym:** | MELCAYA |
| **Project starting date:** | 01.12.2022 |
| **Project duration:** | 48 months |
| **Rights:** | MELCAYA consortium |

## Document history

| Version | Date | Beneficiary | Description |
|---|---|---|---|
| 0.1 | 12.04.2023 | HCB | First draft version |
| 0.2 | 15.05.2023 | AMU | Revised draft |
| 0.3 | 28.06.2023 | HCB | Revised draft |
| 0.4 | 20.09.2023 | HCB | Revised draft<br>(after Ethical Committee review) |
| 1.0 | 20.11.2023 | FCRB | Final draft |
| 2.0 | 26.09.2024 | FCRB | Revised final draft |

## Executive Summary

The purpose of this deliverable is to present all the documentation necessary for the initiation of the MELCAYA work package 2 clinical study NevustoMel. It contains the final version of the study protocol and corresponding regulatory/ethics approval by the ethical committee of the study sponsor (Hospital Clínic de Barcelona). The protocol includes an introduction in which a review on relevant literature, the objectives of the study, the design and study procedures are presented. Details on data collection and management are also discussed, as well as ethical considerations such as how incidental or secondary findings will be communicated or how personal data will be processed. The documents presented in this deliverable will be subsequently used by the other clinical sites for approval in their respective ethical committees.

 

# 1. General information

## 1.1. Identification of the study

Title: Understanding the transition from normal melanocytes to nevus to melanoma (NevustoMel)

Code or protocol identification number: NCT06605417 (*https://clinicaltrials.gov/*)

Version and date: v2 (03/06/2024)

## 1.2. Identification of the sponsor/principal investigator

Name: Susana Puig

Institute and department: Hospital Clínic de Barcelona, Dermatology service

Adress: Carrer de Villaroel 170, 08036 Barcelona (Spain)

## 1.3. Identification of site investigators

**Researcher 1**

Name: Cristina Carrera Alvarez

Institute and department: Dermatology Department, ICMiD Hospital Clínic Barcelona

Adress: Villarroel 170, 08036 Barcelona

**Researcher 2**

Name: Joan Anton Puig Butille

Institute and department: Hospital Clinic de Barcelona, Molecular Biology CORE laboratory

Adress: Carrer de Villaroel 170, 08036 Barcelona (Spain)

**Researcher 3**

Name: Teresa Torres Moral

Institute and department: Melanoma Unit (IDIBAPS), Hospital Clínic de Barcelona

Adress: Carrer de Villaroel 170, 08036 Barcelona (Spain)

## 1.4. Identification of the principal investigators from participant centers

**Researcher 1**

Name: Heather Etchevers

Institute and department: French National Institute of Health and Medical Research, Medical Genetics

Address: Boulevard Charles Livon 58 Le Pharo, Marseille 13284, France

**Researcher 2**

Name: Ines Brecht

Institute and department: Eberhard Karls Universitaet Tuebingen (UT), Pediatric Oncology and Hematology

Address: Hoppe-Seyler-Straße 1, 72076, Tübingen, Germany

**Researcher 3**

Name: Daniela Massi

Institute and department: University of Florence, Department of Health Sciences

Address: Viale Pieraccini 6, 50139, Florence, Italy

**Researcher 4**

Name: Andrea Ferrari

Institute and department: Fondazione Irccs Istituto Nazionale Dei Tumori, Pediatric Oncology Unit

Address: Giacomo Venezian 1, 20113, Milan, Italy

**Researcher 5**

Name: Mario Mandalà

Institute and department: University of Perugia (Medicine and Surgery department)

Address: Via Gambuli, 1, 06132 (Perugia, Italy)

**Researcher 6**

Name: Titus J. Brinker

Institute and department: Deutsches Krebsforschungszentrum Heidelberg (Clinical Biomarkers for Oncology group)

Address: Im Neuenheimer Feld, 223, 69120 (Heidelberg, Germany)

**Researcher 7**

Name: Alexander Eggermont

Institute and department: Prinses Maxima Centrum Voor Kinderoncologie (Clinical and Translational Immunotherapy department)

Address: Heidelberglaan 25, 3584 CS (Utrecht, Netherlands)

**Researcher 8**

Name: Hildur Helgadottir

Institute and department: Karolinska Institutet (Oncology and Pathology department)

Address: Karolinska vägen, A2:07, 17177 (Stockholm, Sweden)

**Researcher 9**

Name: Piotr Rutkowski

Institute and department: Maria Sklodowska-Curie National Research Institute of Oncology (Soft Tissue/Bone Sarcoma and Melanoma department)

Address: ul. W K Roentgena 5, 02781 (Warsaw, Poland)

**Researcher 10**

Name: Daniel Orbach (Pediatrics department)

Institute and department*:* Institut Curie

Address: Rue d'Ulm 26, 75231 (Paris, France)

**Researcher 11**

Name: Josep Maria Borràs Andrés

Institute and department: Catalan Institute of Oncology

Address: Av Gran Via De L'Hospitalet 199-203, 08908 (Barcelona, Spain)

**Researcher 12**

Name: Ewa Bien

Institute and department: Medical University of Gdansk (Pediatrics, Haematology and Oncology

department)

Address: Ulica M Sklodowskiej Curie 3a, 80210 (Gdansk, Poland)

**Researcher 13**

Name: Thomas Eigentler

Institute and department: Charité Universitätsmedizin Berlin (Dermato-oncology department)

Address: Chariteplatz 1, 10117 (Berlin, Germany)

## 2. Justification

Large/giant congenital melanocytic nevi (L/GCMN) are a rare condition, with an estimated incidence of less than 1 in 20.000. However, these patients have a significantly higher risk of developing melanomas or other malignancies relative to people with common small congenital melanocytic nevi: approximately 1 in 20 of these children will develop either cutaneous or extracutaneous melanoma before adulthood [1,2]. Postzygotic *NRAS* mutations are detected in approximately 80 % of patients with L/GCMN with many other MAPK pathway-activating mutations making up a large proportion of the remainder [3]. The reasons why they progress to proliferative nodules and/or melanoma is still unknown, although it is likely that epigenetic and non-coding genetic factors are playing a key role [4]. To develop more adapted therapies and advance beyond the current state of the art, it is vital to identify all endogenous and non-cell-autonomous influences on the predisposition of L/GCMN to malignant transformation and how they may converge or diverge from that of Spitz-type or conventional melanomas in CAYA patients.

## 3. Study hypothesis

A series of 21 L/GCMN (53 fresh frozen biopsy samples corresponding to 40 phenotypically characterized areas of L/GCMN and 13 satellite lesions) was analyzed with a multigene panel and RNA sequencing by the partner Hospital Clínic de Barcelona (HCB), identifying mutations in 76.2 % (16/21) of the L/GCMN. A *NRAS* mutation was detected in 57.1 % (12/21) and mutations in other genes (*BRAF*, *KRAS*, *APC* and *MET*) in 14.3 % (3/21) of patients. RNA sequencing showed novel fusion transcript ZEB2-ALK and SOX5-RAF1 in L/GCMN from two patients [1]. Preliminary work has established the feasibility of conducting a longitudinal study in stable versus clinically changing L/GCMN or CAYA melanoma volunteers through simple, periodic blood draws [5]. Clinical partners involved in the study routinely conduct whole-exome sequencing (WES) of

L/GCMN samples, but the cost/benefit ratio of the additional information provided by whole genome sequencing (WGS) needs assessment in the context of the discovery of potential epigenomic states that influence clinical outcome. A preliminary survey of retrospectively excised CAYA melanomas, L/GCMN and proliferative nodules samples between participant institutions shows that many are compatible with the spatial transcriptomic approaches needed in this study.

## 4. Objectives of the clinical study

The primary objective of this study is to identify the molecular identity profiles of all cellular states that characterize the progression from benign nevi to malignant melanoma in CAYA patients with L/GCMN. The secondary objectives are:

- To longitudinally characterize the cell-free DNA (cfDNA) from CAYA patients.
- To improve the early diagnosis and treatments for intermediate conditions such as L/GCMN through evidence-based interpretation of personal risk from endogenous or exogenous sources.
- To test pre-clinical strategies to best model and improve patient response.

## 5. Study design

NevustoMel is an international multicentric retrospective cohort study with molecular and experimental design. It will involve the genomic characterization of cell-free DNA and affected tissues from patients. Methylomics and single-cell multi-omics will be used to identify co-existing molecular (transcriptional and epigenomic) states at single-cell level and will be generated from affected tissues. These results will be exploited using machine learning-assisted integration of multi-modal transcriptomics, epigenomics and spatial information. Integrated analyses of single-nucleus RNA sequencing from a selection of frozen tissues and spatial transcriptomics on formalin-fixed paraffin-embedded samples will allow the comparison of the findings to ground-state Human Developmental Cell Atlas data. Distinctions will be validated either with *in situ* hybridization (such as RNA sequencing) or immunostaining on test cohort tissues. These results will be complemented with *in vitro* functional analyses, high throughput sequencing and bioinformatic analyses.

## 6. Participant selection

### 6.1. Subject inclusion criteria

To be eligible for participation in the study, an individual must meet the following criteria: congenital nevus with estimated size of 20 cm or more in adulthood (> 18 years old). The justification for this targeted age range is based on the idea that L/GCMN are present from birth in all patients and all of them will be included in the study.

### 6.2. Subject exclusion criteria

An individual will be excluded for the molecular studies if there is no available biological material or there is no signed informed consent.

## 7. Treatment and study calendar

Due to the retrospective nature of the study, no interventions are planned within the study population. Instead, a review and/or analysis of pre-existing medical records, biological samples and data from previous studies will be performed. Study procedures will be limited to the date range from which retrospective data, samples and/or records will be reviewed, which go from January 2005 to December 2021. The study will run for 26 months after ethics approval obtention, including data extraction, curation and analysis. Over the course of the study, various reports will be prepared such as interim analysis and review of the collected data. As this study is part of a European project, several reporting obligations are due to the European Comission such a study initiation package (including study protocol and ethics approval), midterm recruitment report and report on the status of posting the results in a public repository.

## 8. Statistics

### 8.1. Sample size

Data will be obtained from a series of 21 L/GCMN frozen formalin-fixed paraffin-embedded (FFPE) blocks and slides, fresh tumor samples and plasma obtained from blood draws gathered by Hospital Clinic de Barcelona combined with additional samples identified by other participating clinical partners and patient associations. The goal would be to achieve a total N = 100.

### 8.2. Statistical analysis

Descriptive statistics will be used to assess demographic and clinical characteristics. Baseline data will be summarised and presented in tabular form. Normally distributed data will be

presented as a mean with standard deviation (SD). Dichotomous and categorical data will be presented in proportions. Normality of the data will be assessed using histograms PP and linearity will be assessed using scatter plots. Differences between continuous variables will be assessed using Student's t-tests or Mann-Whitney-U test and categorical variables will be assessed using Chi squared test. Paired t-tests will be used for normally distributed continuous repeated measures, while the Wilcoxon signed-rank test and the McNemar test will be used for dichotomous data. Pearson r correlation and Spearman correlation coefficient rho (r) will be used to evaluate the degree of relationship between variables. Crude and adjusted odds ratios and corresponding 95 % confidence intervals (95 % CI) will be calculated using linear regression for continuous outcomes and logistic regression for dichotomous outcomes.

## 9. Ethical and legal aspects

### 9.1. Legal and ethical basis

The partners have a lawful basis for the re-use of health data for scientific purposes under specified conditions and with adequate safeguards i.e., legitimate interests (article 6.1 (f) GDPR), combined with 'scientific research' article 9.2 (j) GDPR. In the cases that the subjects could be re-identified, the guidelines on registry-based studies (EMA/426390) will be followed to ensure that access and use of the proposed data poses minimum to no risk to the study subjects or their fundamental rights and freedoms. In the cases where pre-existing ethics approvals are currently not in place, an authorization (or an amendment in the case of existing approval) to access and use this data will be requested from each partner's respective local ethics committee or national competent body prior to study start-up.

All study materials, including clinical and laboratory protocols, will be submitted to pertinent Institutional Review Boards (IRBs) for review and approval. Approval of the study protocol will be obtained prior to participant/case selection. Any changes to the study protocol, materials, etc. will be subjected to ethics review and approval before the changes are implemented into the study. All participating institutions will comply with international ethical standards regarding principles for medical research involving human subjects and data (Declaration of Helsinki, 2013). In the particular case of Hospital Clínic de Barcelona, compliance at the Spanish level with the Ley 14/2007 de 3 de julio, de Investigación biomédica will be ensured. On top of that, the guidelines set out in the International Conference on Harmonisation of Good Clinical Practice (ICH GCP) and the EMA/426390/2021 (Guideline on registry-based studies) will be followed.

### 9.2. Communication of incidental/secondary findings

In the event that incidental/secondary finding occur during the study, the researcher is expected to inform an officer from his or her local Ethics Committee and coordinate a consultation with the medical professionals involved in the study from their participating institution to review and evaluate if the finding is relevant and how it should be communicated to the participant. In case of doubt, consultation can be made with other medical experts within the consortium. Contact with the patient would be done through the practitioner that generally attends the patient, using the available data recorded in the clinical history (if any). For minors, the general practitioner would contact with the parents or legal representatives (signatory of the informed consent). Ideally, a medical appointment would be scheduled when sharing this information to reassure the patient and avoid unnecessary stress.

The general conditions that must be always met to communicate an incidental/secondary finding are the following:

- It may affect a participant's health and welfare.
- It is scientifically and clinically valid.
- Ethical approvals have been obtained and the participant or their legal representative has opted in to receiving such results through their clinician(s) in the informed consent form.

Incidental and secondary findings will not be communicated:

- When the clinical information is anonymized, as it will be justifiably impractical or impossible to contact the research participant.
- When the participant has indicated that he/she does not want to be informed about such findings.

### 9.3. Supervision of legal-ethical issues

The institutions involved in this study will establish an Ethical Monitoring Board (EMB) that will act as liaison between them and local competent IRBs. This will be done to ensure that data collection methods and clinical aspects of the study protocol are efficacious and in agreement with competent IRBs policies and procedures, as well as to oversee the process of obtaining scientific advice and regulatory guidance from the appropriate regulatory agencies. In addition, access to regulatory expertise will be ensured through each institution ethics committee. Communication between the partners and competent IRBs will be continuous in order to verify

that the study is in compliance with European and national regulatory guidelines.

## 10. Data management

### 10.1. Data storage

All data will be stored in a secured electronic database known as Xarxa Melanoma approved by the Ethical Committee of the Hospital Clínic de Barcelona on the 14/04/2015 (Reg. HCB/2015/0298). This database is routinely used by dermatology medical professionals of our hospital and complies with international standards on data protection and offers a consistent, auditable and integrated electronic database environment. Each institution involved in the clinical studies will count with a local data protection officer (DPO) to advice on highly complex, sensitive or large-scale data processing. Upon completion of the study, data will be preserved for a minimum of 10 years to guarantee continued accessibility and data discovery. Personal data information will only be kept for updating follow-up by the local center investigator. The sponsors will only use the data collected for other scientific purposes if participants have given prior consent and if the legal basis for processing is still in place (see section 9.1). After that, paper and electronic records will be destroyed or erased per institutional/University policy.

### 10.2. Data codification

Before uploading the collected patient data to the database, a codification procedure will be implemented at each local data source center. The procedure will be carried out in the following way: a researcher from our center will assign a code to the clinical information of each patient, which will be kept in a separated database to which only the Principal Investigator or authorized personnel in his research team will have access to. In that way, without knowledge of the respective assignment of code and patient, no re-identification of individual persons is possible. Data processing will be carried out exclusively by persons who had no direct patient contact during data collection.

### 10.3. FAIR data

All published data will be identified by a digital object identifier (DOI) to ensure that it is findable and made available through scientific publications and publicly accessible data repositories such as Zenodo. Priority will be given to open access high impact journals. The Directory of Open Access Journals or a similar index will be used to determine the most appropriate one for submission of the study data and results to ensure immediate and unrestricted access to new knowledge. Open data formats (such as XML, PNG, HTML) will be used to increase data

interoperability. The data will be released under an open access license, for instance, Creative Commons Attribution International Public Licence (CC BY) or similar. This will facilitate the reuse of data and ultimately maximize the overall impact.

## 11. Treatment of data, record keeping and data confidentiality

The processing, communication and transfer of personal data of all participants shall comply with Regulation EU 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of data and the Organic Law 3/2018 of December 5 on the Protection of Personal Data and guarantee of digital rights. The legal basis that justifies the processing of your data is the consent you give in this act, in accordance with the provisions of article 9 of EU Regulation 2016/679. The data collected for these studies will be only identified by a code, so no information will be included that would allow to identify the participants. Only the study physician and his collaborators with the right to access the source data (medical history) could relate the collected data with the patient's medical history. The identity of the participants will not be available to any other person except for a medical emergency or legal requirement. Health authorities, Research Ethics Committee and personnel authorized by the study sponsor may have access to the identified personal information when necessary to verify data and procedures of the study, but always maintaining confidentiality in accordance with current legislation.

Only the encrypted data will be transferred to third parties and other countries, which in no case will contain information that can directly identify the participant (such as name and surname, initials, address, social security number, etc.). In the event that this transfer was to occur, it would be for the same purpose of the study described and guaranteeing confidentiality. If encrypted data is transferred outside the EU, whether to entities related to the hospital where the patient participates, to service providers or collaborating researchers, the data of the participants will be protected by safeguards such as contracts or other mechanisms established by the data protection authorities.

Data processing will be done in accordance with EU Regulation 2016/679. As a result, a record of all the processing activities will be kept and a risk assessment of those activities will be performed to know what measures will be needed and how to implement them. In addition to the rights already provided for in the previous legislation (access, modification, opposition and

cancellation of data, deletion in the new Regulation), participants can now also limit the processing of data collected for the project that is incorrect, request a copy or transfer them to a third party (portability). To exercise these rights, they should contact the principal investigator of the study or the Data Protection Officer of the Hospital Clínic de Barcelona through protecciodades@clinic.cat. Likewise, they have the right to contact the Data Protection Agency if they are not satisfied. Data cannot be deleted, even if a patient leaves the study, to ensure the validity of the research and comply with legal duties and drug authorization requirements. The Investigator and the Sponsor are obliged to keep the data collected for the study for at least 25 years after its completion. Subsequently, personal information will only be retained by the health care facility and by the sponsor for other scientific research purposes if the patient has consented to do so, and if permitted by applicable law and ethical requirements.

## 12. Management of biological samples

FFPE blocks and slides and fresh tumor samples and plasma obtained from blood draws will be prepared, processed, and shipped between research centers correctly whenever required to achieve the study objectives (detailed in section 4). The sample exchange will be carried out within the framework of an established scientific collaboration through the MELCAYA research project funded by Horizon Europe programme (HORIZON-MISS-2021-CANCER-02-03). Where necessary, the Parties shall cooperate in order to enable one another to fulfil legal obligations arising under applicable data protection laws (the Regulation EU 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data and relevant national data protection law applicable to said Partner). When a Partner (the “Provider”) sends biological material to another Partner (the “Recipient”) in respect of the study, a bilateral material transfer agreement (MTA), shall be concluded between such Parties to specify the conditions applying to such transfer of material. The material shall only be used for the purpose of the study and only for as long as is necessary for that purpose. The Recipient will be entirely responsible for the use of the biological material and the Provider shall have no obligation or liability for the material, except for gross negligence or willful misconduct. Material provided in the performance of the study shall remain the property of the Provider. The Recipient shall not be entitled to transfer the material to any third partner (including another consortium partner) without the Provider’s prior written consent. Finally, in the event that there are leftover biological samples after the completion of the relevant analyses, they will be returned to their

original center.

## 13. Financing

NevustoMel study was conceived independently of any commercial organization and will be coordinated, managed and analyzed in independent form. The costs related to the analyses envisaged on the samples, for research purposes only, will be supported by the research funding of MELCAYA project (HORIZON-MISS-2021-CANCER-02-03, proposal number: 101096667).

## 14. Publication policy

The transmission or dissemination of the data, through scientific publications and/or presentation in congresses, conventions, and seminars, may be carried out only after each of the researcher's written authorization. The Principal Investigator (sponsor) of the study undertakes the responsibility to produce a report on the study, publish all data collected as described in the protocol and ensure that the data are reported responsibly and coherently. In particular, the publication of the data deriving from this study will be independent of the results obtained. The transmission or dissemination of data, through scientific publications and/or presentation in congresses, conventions and seminars, participation in multicentric studies, will take place only following a purely statistical elaboration of the same, or otherwise in an anonymized form.

## 15. References

[1] Castilla E, Dutra M, Oriol Parreiras I, Epidemiology of congenital pigmented naevi. Incidence rates and relative frequencies, *British Journal of Epidemiology* **104** 307-315 (1981).

[2] Price H, Schaffer J, Congenital melanocytic nevi-when to worry and how to treat: Facts and controversies, *Clin Dermatolog* **28(3)** 293-302 (2010).

[3] Martins da Silva V, Puig S, Puig Butillé J Malvehy J, Genetic abnormalities in Large to Giant Congenital Nevi: Beyond NRAS mutations, *J Invest Dermatol.* **139(4)** 900-908 (2019).

[4] Fouchardiere A, Boivin F, Etchevers H, Macagno N, Cutaneous melanomas arising during childhood: An overview of the main entities, *Dermatopathology* **8(3)** 301-314 (2021).

[5] Calbet Llopart N, Puig S, Malvehy J, Puig Butille J, Detection of cell-free circulating BRAF V 600 E by droplet digital polymerase chain reaction in patients with and without melanoma under dermatological surveillance, *Br J Dermatol.* **182(2)** 382-389.

Villarroel 170
08036 Barcelona (Spain)
T. +34 93 227 54 00
www.clinicbarcelona.org



DICTAMEN DEL COMITÉ DE ÉTICA DE LA INVESTIGACIÓN CON MEDICAMENTOS

ANA LUCIA ARELLANO ANDRINO, Secretario del **Comité de Ética de la Investigación con medicamentos del Hospital Clínic de Barcelona**

Certifica:

Que este Comité ha evaluado la propuesta del promotor, para que se realice el estudio:

CÓDIGO:
DOCUMENTOS CON VERSIONES:

| Tipo | Subtipo | Versión |
|---|---|---|
| Protocolo | | v1.0 (20/07/2023) |

TÍTULO: Understanding the transition from normal melanocytes to nevus to melanoma (NevustoMel)
PROMOTOR:
INVESTIGADOR PRINCIPAL: SUSANA PUIG SARDÁ

y considera que, teniendo en cuenta la respuesta a las aclaraciones solicitadas (si las hubiera), y que:

- Se cumplen los requisitos necesarios de idoneidad del protocolo en relación con los objetivos del estudio y están justificados los riesgos y molestias previsibles.
- La capacidad del investigador y los medios disponibles son apropiados para llevar a cabo el estudio.
- Que se han evaluado la compensaciones económicas previstas (cuando las haya) y su posible interferencia con el respeto a los postulados éticos y se consideran adecuadas.
- Que dicho estudio se ajusta a las normas éticas esenciales y criterios deontológicos que rigen en este centro.
- Que dicho estudio cumple con las obligaciones establecidas por la normativa de investigación y confidencialidad que le son aplicables.
- Que dicho estudio se incluye en una de las líneas de investigación biomédica acreditadas en este centro, cumpliendo los requisitos necesarios, y que es viable en todos sus términos.

Este CEIm acepta que dicho estudio sea realizado, debiendo ser comunicado a dicho Comité Ético todo cambio en el protocolo o acontecimiento adverso grave.

y hace constar que:
1º En la reunión celebrada el día 14/09/2023, acta 17/2023 se decidió emitir el informe correspondiente al estudio de referencia.
2º El CEIm del Hospital Clínic i Provincial, tanto en su composición como en sus PNTs, cumple con las normas de EMA/CHMP/ICH/135/1995

3º Listado de miembros:

**Reg.** HCB/2023/0843



HOSPITAL CLÍNIC DE BARCELONA
Villarroel, 170 - 08036 Barcelona (España)
Tel. 93 227 54 00 Fax 93 227 54 54
www.clinicbarcelona.org

**Presidente:**

- JOSEP MARÍA MIRÓ MEDA (Médico Enfermedades Infecciosas, HCB)

**Vicepresidente:**

- JULIO DELGADO GONZÁLEZ (Médico Hematólogo, HCB)

**Secretario:**

- ANA LUCIA ARELLANO ANDRINO (Médico Farmacólogo Clínico, HCB)

**Vocales:**

- JOSE RIOS GUILLERMO (Estadístico. Plataforma Estadística Médica. HCB)
- OCTAVI SANCHEZ LOPEZ (Representante de los pacientes)
- MARIA JESÚS BERTRAN LUENGO (Médico Epidemiólogo, HCB)
- JOAQUÍN SÁEZ PEÑATARO (Médico Farmacólogo Clínico, HCB)
- SERGI AMARO DELGADO (Médico Neurólogo, HCB)
- EDUARD GUASCH CASANY (Médico Cardiólogo, HCB)
- MARINA ROVIRA ILLAMOLA (Farmacéutico Atención Primaria, CAP Eixample)
- PAU ALCUBILLA PRATS (Médico Farmacólogo Clínico, HCB)
- JOSE TOMAS ORTIZ PEREZ (Médico Cardiólogo, HCB)
- ELENA CALVO CIDONCHA (Farmacéutica Hospitalaria, HCB)
- CECILIA CUZCO CABELLOS (Enfermera, HCB)
- PAULA MARTÍN FARGAS (Abogada, HCB)
- SALVATORE BRUGALETTA (Médico Cardiólogo, HCB. Miembro del CEA, HCB)
- XAVIER CANALS-RIERA (Ingeniero Telecomunicaciones)
- JOSEP DÍAZ CORT (Licenciado en Ciencias Físicas. Catedrático en Informática)
- GASPAR MESTRES ALOMAR (Médico, Angiología, Cirugía Vascular, HCB)
- MARTA FRANCH SAGUER (Abogada)
- ANNA MARÍA GUIJARRO PÉREZ (Servicio de Atención a la Ciudadanía, HCB)
- BEGOÑA ROMAN MAESTRES (Doctor en Filosofía)
- LINA LEGUIZAMO MARTÍNEZ (Médico Farmacólogo Clínico, HCB)

En el caso de que se evalúe algún proyecto del que un miembro sea investigador/colaborador, este se ausentará de la reunión durante la discusión del proyecto.

Para que conste donde proceda, y a petición del promotor,

Motivo: Certifico la precisión e integridad de este documento
Fecha: 2023.11.08 15:54:21 +01'00'

Barcelona, a 8 de noviembre de 2023

**Reg.** HCB/2023/0843



HOSPITAL CLÍNIC DE BARCELONA
Villarroel, 170 - 08036 Barcelona (España)
Tel. 93 227 54 00 Fax 93 227 54 54
www.clinicbarcelona.org