945406 – HARMONY PLUS

Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms in Hematology - PLUS

WP4 Involvement of Patients, HTA and Regulators

D4.02 SOP for engaging participation of consulting and informing the POs and patients in research projects of WP2 and HARMONY PLUS

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Document History

Version	Date	Description
V1.0	16/06/2021	First draft
V1.1	01/07/2021	Second draft
V1.2	26/07/2021	Third draft
V1.3	5/08/2021	Final draft for IMI submission

List of Acronyms

Acronym	Description
AEMPS	Spanish Agency of Medicines and Medical Devices /*Agencia Española de Medicamentos y Productos Sanitarios*
AIFA	Italian Medicines Agency / *Agenzia Italiana Del Farmaco*
AIM	International Association of Mutual Benefit Societies
ALL	Acute Lymphoblastic Leukemia
AML	Acute Myeloid Leukemia
BfArM	Federal Institute for Drugs and Medical devices / *Bundesinstitut für Arzneimittel und Medizinprodukte*
CatSalut	Catalan Health Service / *Servei Català de la Salut*
CLL	Chronic Lymphocytic Leukemia
COS	Core outcome sets
DoA	Description of Action
EEA	European Economic Area
EHA	European Hematology Association
EMA	European Medicines Agency
EU	European Union
F2F	Face-to-Face meeting
FDA	Food and Drug Administration
HM	Hematologic Malignancy
KOL	Key Opinion Leader
MDS	Myelodysplastic Syndrome
MM	Multiple Myeloma
MOH	Ministry of Health
NHL	Hon-Hodgkin Lymphoma
OS	Overall survival
PO	Patient organisation
PRO	Patient-reported outcome
PROM	Patient-reported outcome measure
QoL	Quality of life
RCT	Randomised controlled trial
RWD	Real-world data
RWE	Real-world evidence
SOP	Standard Operating Procedure
WP	Work Package
WG	Working group

D4.02 SOP FOR ENGANGING PARTICIPATION OF CONSULTING AND INFORMING THE POS AND PATIENTS IN RESEARCH PROJECTS OF WP2 AND HARMONY PLUS

1. PUBLISHABLE SUMMARY

The importance and benefits of patient involvement across the entire health related research and development spectrum are well documented. HARMONY and HARMONY PLUS are based and built on a structure that involves patients consistently in both the project consortium and the work done by it.

It is therefore logical and essentially important that patients and their organisations participating in HARMONY and HARMONY PLUS through the Patient Cluster are granted the possibility to participate in the design, submission, evaluation, interpretation, and dissemination of research projects run on the HARMONY Big Data Platform.

The Standard Operating Procedures (SOP) and Recommendations on Patient Involvement in HARMONY PLUS is a short compendium of rules and procedures to be used in relation to research projects run on the HARMONY Big Data Platform to make sure that the patient perspective is adequately and consistently represented.

The HARMONY PLUS project will follow the same procedure than the one established for the submission of research project proposals in the HARMONY project (116026) regulated in the SOP for the Submission of HARMONY Research Project Proposals (see Annex I). This document concerns the inclusion of patients in the development and submission of research project proposals, and the dissemination of their results.

This Standard Operating Procedure and Recommendations contains a description of the benefits and recommended processes for engaging patients and patient organisations (PO) in biomedical R&D (research and development) projects and processes within the HARMONY and HARMONY PLUS projects.

2. INTRODUCTION:

2.1. HARMONY and HARMONY PLUS

The overarching aim of HARMONY PLUS is to generate, operate and use a pan-European big data platform that integrates disease information and improves understanding on the most effective and efficient means to treat hematologic malignancies (HM). In addition, the project aims to enhance market access to innovative therapies. HARMONY and HARMONY PLUS aim to unite and align stakeholders from clinical, academic, patient, HTA, regulatory, payers, and pharmaceutical fields with regards to the use and relevance of clinical endpoints and standard core outcomes.

2.2. Background

The rise of genotype-based therapies, increasing demand for earlier access to innovative therapies, as well as the focus on **outcome-based** research means that early trial designs need to address not only the regulatory hurdles of safety and efficacy but satisfy the demands of healthcare payers and patients' preferences. Hence, to increase market access to innovative treatments, a greater level of forward thinking that anticipates the criteria against which drugs will be evaluated by regulators/HTA/and payer organisations is needed. Links need to be established with HTA and reimbursement agencies at the earliest possible time points in the research and development programmes for these requirements to be met.

To mitigate this issue a common understanding from all stakeholders (clinical, pharmaceutical, academic, regulator, HTA, reimbursement, and patients) as to what is required to enhance the probability of meeting market access requirements in a timely manner is required. The objective of common metrics and core outcomes are to generate harmonised data that could enhance the acceptability of outcomes presented to regulators, HTAs, and payers.

Real world evidence (RWE) can be used to complement randomized controlled trial (RCT) evidence and to confirm the generalisability of RCTs to real life populations. It can also be used for designing more efficient clinical trials, understanding a drug's benefit/risk profile and aid market access by providing information for health economic models, indirect comparative effectiveness data and value demonstration. Whilst regulatory authorities often require the collection of RWD post-authorisation to monitor safety and effectiveness, payers and HTA across Europe have different views on the use of RWE.

The use of real-world data (RWD) faces a number of challenges including data accessibility, timely collection, the investment required to collect the data, dealing with missing data, and any bias within the data including the potential confounding[1] and firm causal conclusions. Generating RWE can be carried out throughout the entire process of clinical development and help to fill in any knowledge gaps for stakeholders. The ideal approach is to keep all the stakeholders in mind from the beginning in order to create evidence that can serve more than one purpose.

[1] A Confounder is an extraneous variable whose presence affects the variables being studied so that the results do not reflect the actual relationship between the variables under study.

HARMONY is a big data project. RWD and clinical trial data, amongst others, forms a proportion of the information within a Big Data platform. To better utilise big data and establish the development of health-based outcomes-focused healthcare systems, the data type, source, and quality are critical to enable outcomes to be pooled effectively. This includes defining, prioritising, and selecting what outcomes and data (biological, clinical, demographic) should be considered and collected. The entire spectrum of research and subsequent care delivery should be considered, starting from the development of innovative medicines and treatments, to market access and adoption, diffusion, and use in healthcare systems by providers and patients.

As a general principle, HARMONY and HARMONY PLUS are implemented with the active and formal inclusion and involvement of patient constituencies through their representative organisations. Nine patient umbrella organisations for the different haematological malignancies participate through a contractual scheme.

2.3. Work Package 4 (WP4) of HARMONY PLUS

The work of WP4 of HARMONY PLUS focuses on the following core objectives:

1. To engage key stakeholders, and in particular the patient organizations, by collecting their inputs and supporting long-term implementation of the research projects.
2. To support the decision-making process for access (regulatory and reimbursement) of innovative medicines for HMs by identifying regulatory and HTA consultation mechanisms useful for HARMONY and HARMONY PLUS visibility and recognition and by developing a Proof of Principle project using one of these consultation mechanisms.

WP4 aims to achieve the following specific objectives:

1. The Stakeholders and Patients' Organizations Forum (SPOF) will offer support to WPs, in particular to WP2 for developing a Core Outcomes Set for each new indication of HARMONY PLUS. The support takes the form of consultation of the stakeholders of the HARMONY PHSFF[2], and in particular of the patients' organizations.
2. Streamline the patient organizations (POs) involvement into the research projects developed in WP2 and keep the POs informed about their progress, as well as disseminate results of research projects to POs, in collaboration with WP2 research leads.
3. Development of guidance and decision tools to identify appropriate procedures and resources for regulatory, HTA, payer engagement in Europe with respect to the activities that are being undertaken by the individual projects and studies within HARMONY PLUS.
4. Proof of principle project: Subject to the identification of an appropriate topic in collaboration with WP2 and WP3, deliver an early regulatory/HTA scientific advice procedure on the appropriateness of evidence to be used in regulatory and/or reimbursement submission.

This SOP and Recommendations was created as part of Task 4.2 and aims at making sure that the interaction of patient organisations and other stakeholders involved in HARMONY PLUS is

[2] The HARMONY PHSFF stands for the HARMONY Public Health Stakeholder Feedback Forum. The consultation mechanism is described in detail in the Annex to this SOP.

standardised, meaningful and easy to organise.

2.4. Patient involvement in biomedical research and development

2.4.1 General

Even though patient involvement in medicines research and development is a relatively new concept, a substantial body of evidence on its workings and benefits, and on the different methodologies of public and patient involvement has been generated from approximately 2010 onwards. The methodology described here and developed for HARMONY PLUS is based on these existing and documented experiences.

A key document in this regard is the 'EUPATI Guidance for Patient Involvement in Medicines Research and Development (R&D); Guidance for Pharmaceutical Industry-Led Medicines R&D published by the European Patients' Academy for Therapeutic Innovation[3]'. It contains general guidance and recommendations for the organisation and conduct of patient involvement in R&D projects conducted in commercial and other settings.

However, this document does not describe the general benefits, advantages, and potential drawbacks of patient involvement in R&D. Instead, it focuses on the processes and best practices that have proven to be effective when it comes to involving patients in R&D for meaningful results and an equitable distribution of priorities in the design and implementation of research projects under HARMONY and HARMONY PLUS.

Geissler, Ryll et al. give a detailed description (Figure 1) of the different tasks where patients can be involved easily and meaningfully[4]. As HARMONY and HARMONY PLUS focus primarily on early stage research, longitudinal studies and the exploration of novel diagnostic and treatment options, the recommendations contained in this document also focus on the earlier stages of research and development. However, patient involvement is (and should be) present across the entire lifecycle of medicines.

[3] Warner K, See W, Haerry D, Klingmann I, Hunter A and May M (2018) EUPATI Guidance for Patient Involvement in Medicines Research and Development (R&D); Guidance for Pharmaceutical Industry-Led Medicines R&D. Front. Med. 5:270. doi: 10.3389/fmed.2018.00270

[4] Geissler J, Ryll B, di Priolo SL, Uhlenhopp M. Improving Patient Involvement in Medicines Research and Development: A Practical Roadmap. Therapeutic Innovation & Regulatory Science. 2017;51(5):612-619. doi:10.1177/2168479017706405

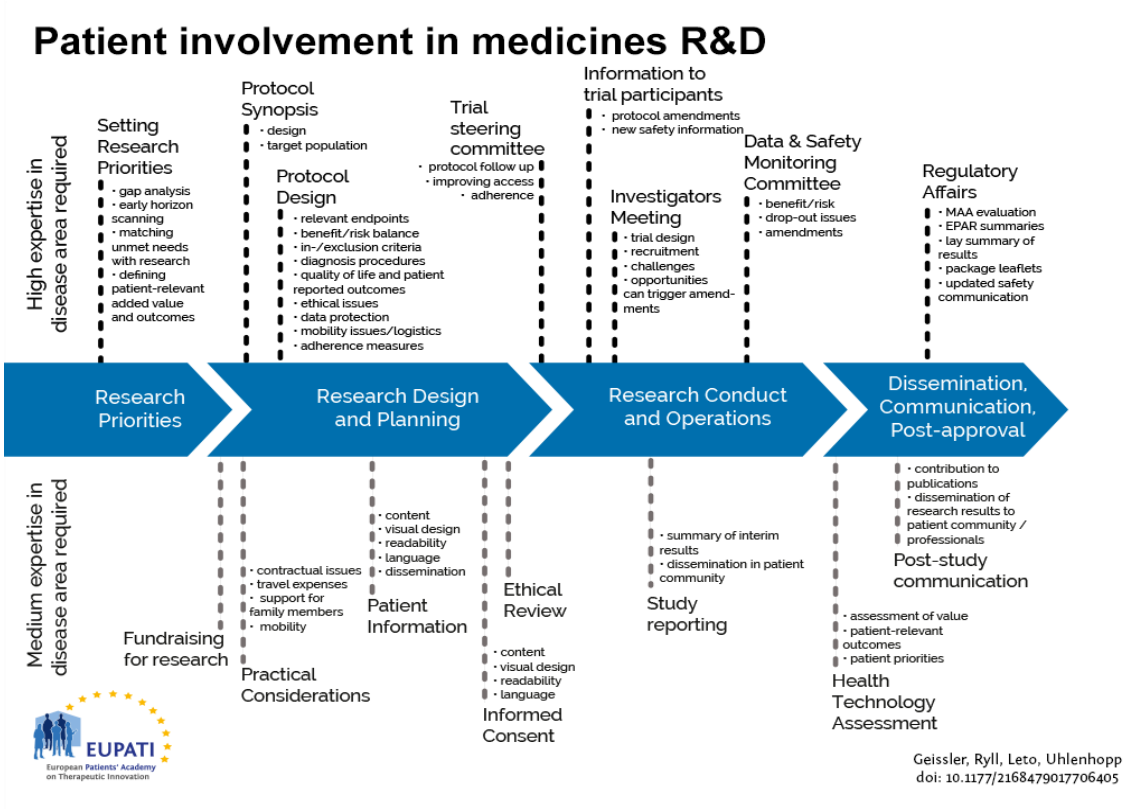

Figure 1. *Patient involvement in medicines R&D*

For the definition of the term "patient", the definition of EUPATI[1] is adopted:

"[…] we use the term "patient" which covers the following definitions:

- *"Individual Patients" are persons with personal experience of living with a disease. They may or may not have technical knowledge in R&D or regulatory processes, but their main role is to contribute with their subjective disease and treatment experience.*
- *"Carers" are persons supporting individual patients such as family members as well as paid or volunteer helpers.*
- *"Patient Advocates" are persons who have the insight and experience in supporting a larger population of patients living with a specific disease. They may or may not be affiliated with an organization.*
- *"Patient Organization Representatives" are persons who are mandated to represent and express the collective views of a patient organization on a specific issue or disease area.*
- *"Patient Experts", in addition to disease-specific expertise, have the technical knowledge in R&D and/or regulatory affairs through training or experience, for example EUPATI Fellows who have been trained by EUPATI on the full spectrum of medicines R&D."*

In HARMONY and HARMONY PLUS, patients are represented through their respective disease-specific umbrella organisations with one of them acting as a hub for their work in the project.

2.4.2 The importance of patient involvement

In addition to the moral and ethical benefits of involving the end users and their representatives (e.g., in case of paediatric HM) in the R&D process, there are also substantial scientific and even financial benefits that can be gained from consistent and meaningful patient involvement.

The importance and merits of patient involvement in research and development are commonly acknowledged and offer benefits for all involved parties. Patient involvement also makes sure that clinical and medical research work more effectively together and deliver what patients really need. The discovery, development, and evaluation of new treatments is also improved if patients provide input throughout the design, conduct, and evaluation of studies and projects.

These improvements are based on the collaborative identification and understanding of patients' unmet needs, their research priorities, patient-centric clinical study design, and meaningful outcome measures and study endpoints. We encourage engagement with patients, caregivers, patient advocates, patient experts and patient organizations, and we also encourage and actively support the upskilling of patient organizations and patients to be able to be involved in such work. Contribution to and collaboration with "patient academies" and masterclasses for patients are linked to meetings organised under HARMONY Plus.

This engagement should be promoted throughout the entire funding framework, partnering concept, research and development process (including clinical trials), regulatory and market access processes, and the post-approval stages including pharmacovigilance. Involvement also extends to other work such as the sharing of evidence and outcomes with patients and patient groups. It is important for patients to be included in the review process, and during the conduct of clinical and other research and studies.

Involvement also enables increased credibility of knowledge and data, prevention of potential challenges that patients may face during the conduct of a study, and more effective dissemination (notification to other parties) and use of research outcomes in clinical practice. This SOP and recommendations focus on early involvement in the design and conduct of research on the HARMONY Big Data Platform.

2.4.3 Benefits of working with patients in R+D

The benefits of working with patients in R+D include:

- Better representation and understanding of the patients' unmet medical needs
- Better understanding and inclusion of RWE
- Improved buy-in from patient communities for relevant research projects
- Consistent and targeted dissemination of results
- Empowerment of the patient communities
- Flatter and more efficient research teams and organisations

3. SCOPE

This SOP and Recommendations apply to all research project proposals submitted to the HARMONY Alliance and HARMONY PLUS Big Data Platform for processing. They apply to research project proposals submitted by any stakeholder in the HARMONY Alliance, including patient organisations and/or the Patient Cluster.

The SOP and the Recommendations also apply to research projects submitted by patient organisations that participate in the HARMONY and HARMONY PLUS consortium through the Patient Cluster.

4. RESPONSIBILITIES

The Patient Cluster coordinates the work of the associated patient organisations that participate in the HARMONY Alliance. The Patient Cluster is led and coordinated by LeNET.

Role/job function	Responsibilities
Consortium partner	Participation in the general steering and conceptual development of the project, and contract signatory and beneficiary
WP Co-lead	Co-leading WP6 with CELGENE
Patient Cluster coordinator	Coordinating the work and contributions of patient organisations as members of the Patient Cluster

5. SPECIFIC PROCEDURE

The following procedure (figure 2) should be used to make sure patient involvement happens in research projects submitted and processed under HARMONY and HARMONY PLUS.

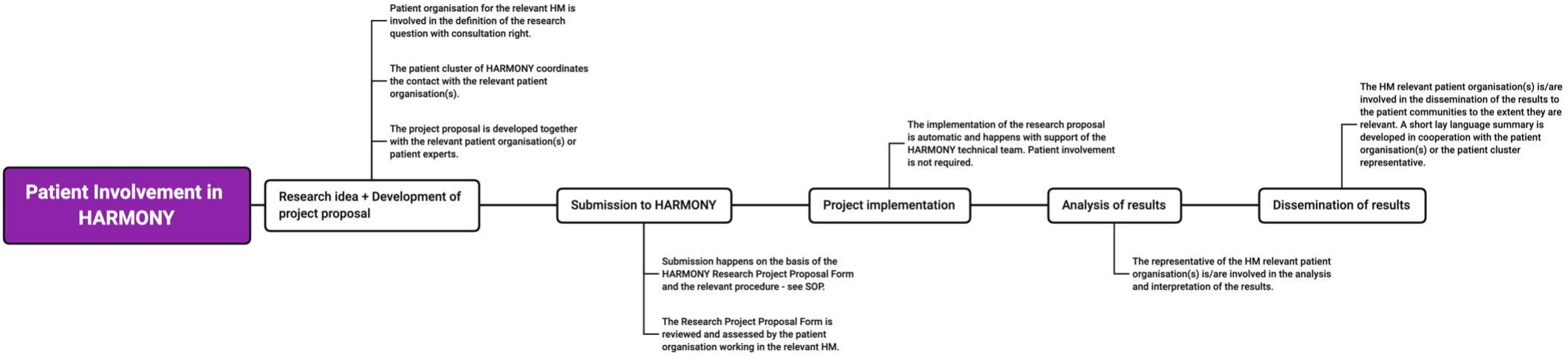

Figure 2. *Patient involvement procedure in HARMONY and HARMONY PLUS*

5.1. Research idea and the development of the research proposal

The patient cluster of HARMONY coordinates the contact with the relevant patient organisation(s). LeukaNET coordinates the Patient Cluster by way of emails and telephone conferences. Regular reports and assessments are developed and submitted to the HARMONY Office by LeukaNET upon consultation with the Associate Members.

These include:

- LeukaNET Leukemia Advocates Network, Consortium Member and Patient Cluster Coordinator
- ALAN Acute Leukemia Advocates Network, Associated Member
- CCI Childhood Cancer International Network, Associated Member
- CLLAN CLL Advocates Network, Associated Member
- CML Advocates Network, Associated Member
- Lymphoma Coalition, Associated Member
- The MDS Alliance, Associated Member
- MPE Myeloma Patients Network, Associated Member
- MPNAN MPN Advocates Network, Associated Member

The project proposal should be developed together with the relevant patient organisation(s) or patient experts to the extent possible. The patient organisation for the relevant HM should be involved in the definition of the research question with consultation right to the extent possible. For best results, the representative(s) of the patient organisation concerned or of the Patient Cluster should be part of the research team from its establishment, and its involvement should be consistent throughout the implementation of the research project.

Research ideas can originate from all stakeholder groups individually, but the proposal should be developed together.

Research project proposals submitted by the Patient Cluster or its members

1. The Patient Cluster makes sure that the research project team includes representatives of other stakeholder groups, especially clinicians and KOLs.
2. Submission of the project proposal to the HARMONY Office happens by using the standard procedure and the Research Project Proposal Form.
3. All other tasks like analysis and interpretation, and dissemination are to be implemented by the Patient Cluster or its member patient organisation with the involvement of the multi-stakeholder research team for the given project.

5.2. Submission of the project proposal to the HARMONY Platform

Submission happens based on the HARMONY Research Project Proposal Form and the relevant procedure – see SOP on Research Proposal Forms (Annex 1).

The Research Project Proposal Form is reviewed and assessed by the patient organisation working in the relevant HM.

The SOP for the Submission of HARMONY Research Project Proposals located (see Annex 1)

5.3. Project implementation

Research projects are implemented automatically and with support from the HARMONY PLUS technical team. Patients do not always have sufficient technical knowledge to influence all stages of this procedure, e.g., interventions of patients in the operation of the HARMONY Big Data Platform are unlikely. In each case, the possible contribution of patients should be considered and explored.

5.4. Analysis of results

As with all research projects, the analysis of results and findings is a process that requires consensus and can be contextual. Therefore, the participation of the representative(s) of the patient communities involved is recommended and necessary. The research team should include the representative of the patient organisation of the HM concerned or of the Patient Cluster. The patient representative should be involved in:

- the design of the implementation of the research project;
- the implementation of the project;
- the analysis and interpretation of the research results;
- the dissemination of the results and findings.

5.5. Dissemination of results

The visibility and understandability of the research results and their possible impact on the patient's health and quality of life are key requirements. Therefore, the representative of the patient organisation working in the relevant HM or of the Patient Cluster should be involved in the dissemination of results in the form of different communication vehicles such as communiques, scientific papers, conference contributions, etc. The official inclusion of a patient author is recommended, and the patient author should also be an active contributor to the implementation of the project as per good scientific practice. Patient organisations and the Patient Cluster have sufficient knowledge and skills to develop lay language summaries of the research findings for the dissemination of results, and several of them command sufficient scientific knowledge and preparedness to make meaningful contributions to research projects.

Proposals to conduct a Research Project using the HARMONY Platform may be submitted by: [5]

1. Any HARMONY Beneficiary(ies):

see overview: *https://www.harmony-alliance.eu/en/partners*

a. HARMONY Third Parties under articles 11 and 12 of the Grant Agreement,
b. Linked Third Parties, and
c. Affiliate Entities

must submit their research project proposals through the Beneficiary that controls (in the case of affiliated entities) or has a legal link with them.

2. Any Associated Member(s), with relevant data contribution judged on a case-by-case basis. See overview: https://www.harmony-alliance.eu/associated-members.

3. Any other organization or institution with interest in the project (Third Party), via the payment of a fee in cash or making an in-kind contribution to support the objects of the Action.

The diagram in Annex IV of the SOP for the Submission of HARMONY Research Project Proposals outlines the processes by which the HARMONY Project reviews and evaluates any submitted Research Project Proposal. The HARMONY Coordination Office will coordinate the Admission and Evaluation processes: harmonyoffice@ibsal.es.

5. FORMS, TEMPLATES AND PROCEDURES

The Standard Operating Procedure (SOP) for the submission of HARMONY Research Project Proposals can be found as Annex 1 to this document.

6. REFERENCES

The Research Project Proposal Form can be found as Annex 2 to this document.

[5] Standard Operating Procedure (SOP) for the submission of HARMONY Research Project Proposals

List of Figures

STANDARD OPERATING PROCEDURE (SOP) FOR THE SUBMISSION OF HARMONY RESEARCH PROJECT PROPOSALS

OBJECTIVES AND SCOPE

This Standard Operating Procedure (SOP) describes the procedures and steps for the submission and approval of research projects to the HARMONY Platform. It outlines the responsibilities of the HARMONY Bodies/Beneficiaries involved and details the interactions required to ensure the application of a standard procedure in a timely manner.

WHO MAY SUBMIT A RESEARCH PROJECT PROPOSAL?

Proposals to conduct a Research Project using the HARMONY Platform may be submitted by:

1. **Any HARMONY Beneficiary(ies):**
   see overview: https://www.harmony-alliance.eu/en/partners
   a. HARMONY Third Parties under article 11 and 12 of the Grant Agreement,
   b. Linked Third Parties, and
   c. Affiliates Entities
   must submit their research project proposals through the Beneficiary that controls (in the case of affiliated entities) or has a legal link with them;

2. **Any Associated Member(s),** with relevant data contribution judged on a case-by-case basis.
   See overview: https://www.harmony-alliance.eu/associated-members

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LEGENDA

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Version Number: v 07	Review date: 08/03/2017

Revision Chronology			
SOP ID Number:	Effective date:	Reason for Change:	Author:
HARMONY/SOP/01/01	04/02/2017	New SOP	Santiago Moralejo
HARMONY/SOP/01/02	05/02/2017	Coordinator Review	Jesús M. Hernández
HARMONY/SOP/01/03	06/02/2017	WP2 Review	Lars Bullinger
HARMONY/SOP/01/04	15/03/2017	EC Approval	
HARMONY/SOP/01/05	27/03/2017	SC Approval	

A. HOW TO SUBMIT A RESEARCH PROJECT PROPOSAL?

1. Complete the HARMONY Research Project Submission Form (Annex V). The following is the minimum information that is required for the research project proposal to be considered:
    a. An **abstract** or summary of the research project, describing:
        i. the significance/unmet need of the project;
        ii. the hypothesis and/or anticipated major outcome of the research project;
    b. An overview of the analysis including in particular:
        i. The **key variables** which need to be available in the data to address the research project;
        ii. an estimation of the minimum number of patient **datasets needed** to conduct the research project;
        iii. A list of recommended **data sources** or data custodians and the estimated number of available datasets from the recommended data sources;
        iv. and the suggested **statistical analysis plan** to address the research project
    c. The potential impact of the research outcome.
    d. A description of any anticipated ethical difficulties and the procedures adopted to prevent or address them.

2. Submit the Form electronically on the HARMONY website or by email to the HARMONY Coordination Office at Harmonyoffice@ibsal.es with the subject: RP – IS "title of the research project".
3. The HARMONY Coordination Office (HCO) will acknowledge the receipt of the research project proposal.
4. **ADMISSION:** All submitted Research Project Proposals will undergo a review for admission. The proposal will be admitted and eligible for evaluation if it is complete and all the required documentation is enclosed. The Coordinator together with the WP2 Leadership will have a period of **15 days** to review it for admission (Annex VI).
5. The HCO must contact the submitter when a decision is made regarding the admission and eligibility for evaluation of the research project proposal, and if missing documentation, additional information, or clarification of the project research proposal arises during the review.

B. ASSESMENT AND EVALUATION PROCEDURE

All admitted Research Project Proposals will be anonymised by the HCO before submission to peer expert members of the HARMONY Project to minimise evaluation biases. In addition, all the reviewers will reveal any potential conflict of interest.

1. The Research Project Proposal will be sent to the KOL (public and private) of the appropriate disease pillar(s) within **WP2** for evaluation. The HM disease pillar will issue a structured **approval / rejection assessment**, (Annex VII) evaluating the scientific, socioeconomic and other merits and viability of the proposal. In case of approval, the assessment might expand the scope and data sources of the initial proposal.
2. The assessment will be sent to the HCO, who will inform the Executive Committee.
3. The HCO must contact the submitter if the research project is rejected.
4. The HCO will then send the approval assessment to **WP4, WP5** and **WP6** Leaders for intra-work package analysis. Both WPs will issue an **evaluation report** (Annex VIII) that might expand the initial proposal with recommendations about (but not limited to) additional data sources; outcomes; applicable analytic tools; and end- points.
5. These reports will be sent to the HCO for compilation, and will be added to the approval assessment issued by WP2.
6. The HCO will send all previous documents to **WP8** Leaders for their **report on the compliance with legal and ethical requirements** (Annex IX). WP8 Leaders might request the advice of the External Ethics Advisory Board and their non-binding recommendations will be considered in the WP8 compliance report.
7. The HCO must be contacted immediately should a reviewer identify a major flaw that makes the project not approvable in any of the previous stages and the review can stop until this issue is resolved.
8. The HCO must contact the submitter if the proposal does not receive a favourable legal/ethical opinion by WP8 Leadership. The research project may be resubmitted as a new application upon revision to comply with the legal recommendations.
9. If the proposal receives a favourable opinion from WP8, the Coordinator must confirm the economic viability of the research project against the resources needed and inform the **Executive Committee** for final approval and estimation for execution, pending the recommendation for assigned budget of the **DQSC**.

C. TIMELINE FOR ASSESSMENT AND EVALUATION

The HARMONY Project estimates that a decision to conduct the Research Project will be made within 60 days once the Research Project Proposal Submission has been admitted. The overall number of proposals received and/or the need for additional information or clarifications during the evaluation process may affect this time period. The submitter will be notified if this timeline is longer than anticipated.

This period is composed of the following steps:

1. The HM disease pillar will have a period of **15 days** from the reception of the research project application to issue a structured **approval or rejection assessment** of the research project Proposal.
2. WP4, WP5 and WP6 will have a period of **15 days** to issue an **evaluation report** about the research proposal.
3. WP8 will have a period of **15 days** from the reception of the report to issue their reasoned clearance with regard to the **legal and ethical elements** of the research proposal.
4. The HARMONY **Executive Committee** will have a period of **15 days** to inform the submitter and start negotiations towards execution.

D. EVALUATION CRITERIA

The following elements will be considered during the evaluation:

1. The relevance of the HM-specific research project or unmet need submitted to study, its specific aims and objectives;
2. The hypothesis and/or anticipated major outcomes of the research project;
3. The suitability of the recommended data sources and data custodians;
4. The existing datasets available in the platform and the estimation of the additional number of patient datasets needed to conduct the research project;
5. The appropriateness of the proposed statistical analysis plan and sample size and;
6. The availability of the key variables required to address the research project on the existing and suggested data sources.
7. The potential impact of the research project.
8. The anticipated ethical difficulties and the procedures adopted to prevent them.

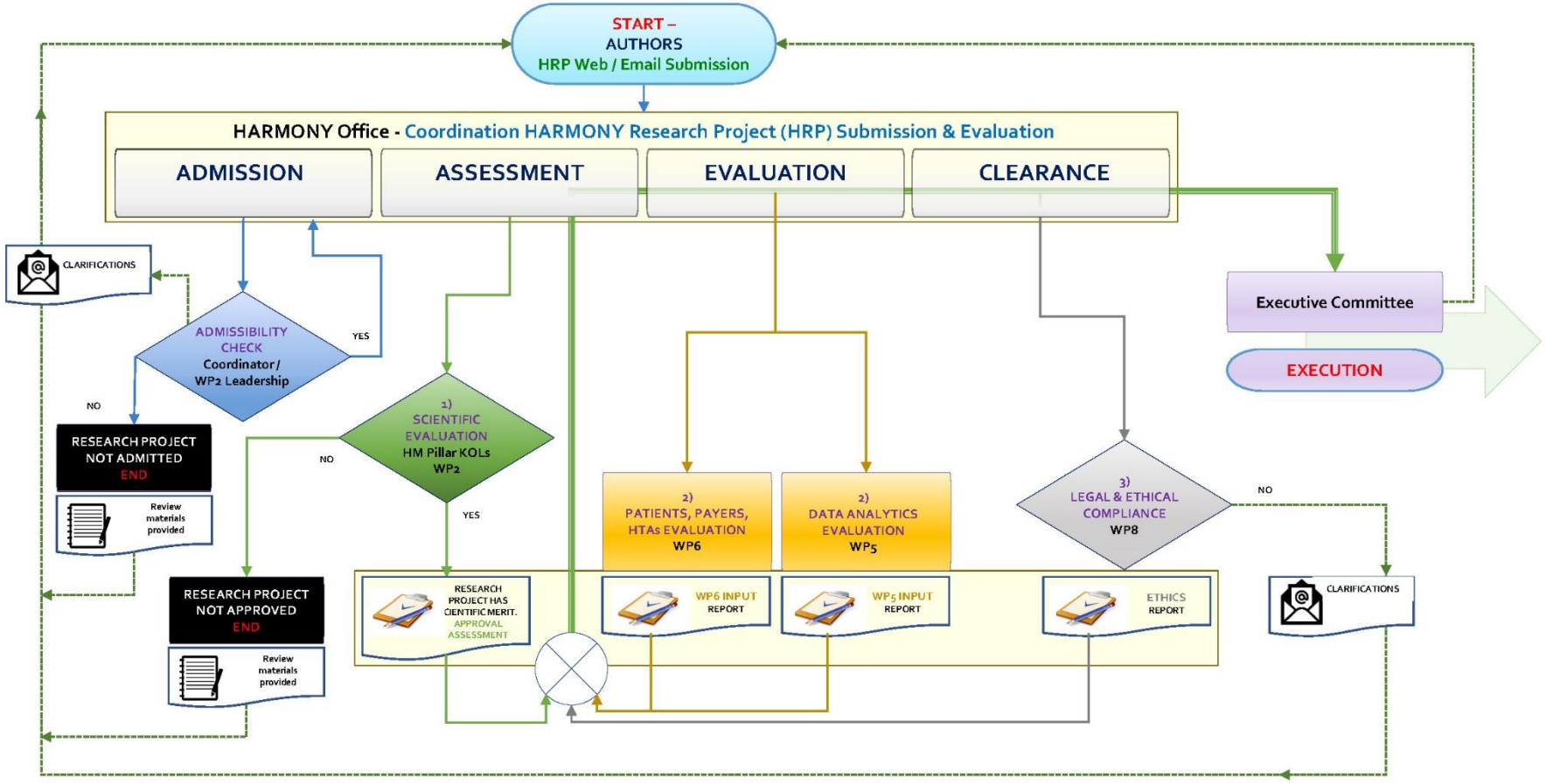
WP2 Special attention should be placed on points 1 to 4 and 7 of the evaluation criteria.
WP4 and WP5 should give special consideration to points 4, 5 and 6 of the evaluation criteria.
WP6 should give special consideration to on points 1, 2, 6 and 7 of the evaluation criteria.
WP8 should focus in the compliance of the Research Project proposal with the legal and ethical aspects of the HARMONY project.

ANNEX I - DEFINITIONS

1. "**Beneficiary**" or "**Participant**" means a legal entity who has signed the Grant Agreement number 116026 with the IMI2 JU or the Form of Accession. There can be two types of Beneficiaries in an IMI2 Action, i.e.:
    a) Beneficiaries receiving IMI2 JU funding; and
    b) Beneficiaries not receiving IMI2 JU funding, such as in particular those EFPIA Beneficiaries not eligible to IMI2 JU funding or not requesting it.

    For the list of Beneficiaries, please refer to Annex II.
2. "**Affiliated Entity**" means any legal entity that is under the direct or indirect control of a Beneficiary, or under the same direct or indirect control as the Beneficiary, or that is directly or indirectly controlling a Beneficiary. Control may, in particular, take either of the following forms:
    a) the direct or indirect holding of more than 50 % of the nominal value of the issued share capital in the legal entity concerned, or of a majority of the voting rights of the shareholders or associates of that entity;
    b) the direct or indirect holding, in fact or in law, of decision-making powers in the legal entity concerned.
3. "**Associated Member**" means a legal entity not signing the Grant Agreement 116026 with the IMI2 JU or the Form of Accession (it is not a "Beneficiary") with not assigned budget. As such they participate in the provision of patient datasets and can receive supportive funding (variable budget).
    Associated Members will join the project by signature of an "Associated Member Engagement Framework" and an "Associated Member Agreement".
    For the list of Associated Members, please refer to Annex III.
4. "**Third Party**" shall mean a legal entity which is not a party to the Grant Agreement number 116026, neither falls in the "Associated Member" category.
5. "**Linked Third Parties**" shall mean any legal entity which has a legal link to a Beneficiary implying collaboration that is not limited to the Action.
6. "**Data Quality Supervision Committee**" means the governance body responsible for the management of quality patient data sets as further defined in Clause 11.7 of the Consortium Agreement.
7. "**Coordinator**" means the Beneficiary in charge of the grant administration. In this case, Prof Dr Jesús María Hernández Rivas.
8. "**Executive Committee**" means the governance body responsible for the provision of overall leadership of the Action and coordination of the different consortium bodies.
9. "**Work Package**" or "**WP**" means a sub-division of the Action as described in Annex 1 of the Grant Agreement number 116026. "**Work Package Leader(s)**" means the leader(s) of a Work Package.
10. "**Research Project**" means the HM-specific research question, study, outcome to be analysed.

ANNEX II – SUBMISSION AND EVALUATION OF A RESEARCH PROJECT PROPOSAL



ANNEX III – ADMISSION REVIEW FORM

ADMISSION Review - Research Project Proposal			
Title:			
Author(s):		*E-mail:*	
Organisation:		*Date:*	

ADMISSIBILITY CRITERIA		
1	**RESEARCH PROJECT PROPOSAL:** The HM-specific research project is clearly stated, describing the significance and/or unmet need and the major outcome with well-defined aims.	☐ Yes ☐ No
	Comments / Clarification request:	
2	**ANALYSIS PROPOSAL:**	
	• Suitable data sources are identified	☐ Yes ☐ No
	• Number of available datasets is stated	☐ Yes ☐ No
	• Statistic Approach is present	☐ Yes ☐ No
	• Suggested sample size is stated	☐ Yes ☐ No
	• Key variables are identified	☐ Yes ☐ No
	Comments / Clarification request:	
3	**IMPACT:** The anticipated major outcome and potential impact of work is well described.	☐ Yes ☐ No
	Comments / Clarification request:	

ADMISSIBILITY RECOMMENDATION: *Check one (type letter X in the appropriate box).*	
Admitted	☐
Admitted with minor revisions/ additions (state in "Comments / Clarifications")	☐
Invite re-submission for a new review after major revisions/additions	☐
Reject	☐
HM-PILLAR: *Please indicate the HM pillar(s) that should evaluate the proposal*	

Research Project Proposal Assessment			
Project title:			
Reviewer:		*Email:*	
Organization		***WP #:***	**2**
Role/Function in HARMONY			

ASSESSMENT	
1	**RESEARCH PROJECT PROPOSAL:** *The HM-specific research project is clearly stated, describing the significance and/or unmet need and the major outcome with well-defined aims. Please consider whether implementing the research project would enhance the scientific and/or medical knowledge, result in improved outcomes for the patients, and/or empower policy makers and clinicians to optimize care for patients.*
	General Comment:
	Additional Comments: *(i.e. recommendations)*
2	**ANALYSIS PROPOSAL:** *Please review the feasibility, reliability, and appropriateness of the following topics of the research project* • Suitable data sources are identified • Number of available datasets is stated • Statistic Approach is present • Suggested sample size is stated • Key variables are identified
	General Comment:
	Additional Comments: *(i.e. recommendations)*
3	**IMPACT:** *Please provide your comments and recommendations to whether the anticipated major outcome and potential impact of work is well described and the HARMONY stakeholders would care or benefit from the hypothesis and/or outcome of the research project*
	General Comment:
	Additional Comments: *(i.e. recommendations)*

ASSESSMENT: *Check one (type letter X in the appropriate box).*	
Accept	☐
Reject	☐

Research Project Proposal Evaluation			
Title:			
Reviewer:		*WP #:*	

EVALUATION (WPs 4, 5 & 6)	
1	**RESEARCH PROJECT PROPOSAL:** *The HM-specific research project is clearly stated, describing the significance and/or unmet need and the major outcome with well-defined aims. Please consider whether implementing the research project would enhance the scientific and/or medical knowledge, result in improved outcomes for the patients, and/or empower policy makers and clinicians to optimize care for patients.* **General Comment:** **Additional Comments:** *(i.e. recommendations)*
2	**ANALYSIS PROPOSAL:** *Please review the feasibility, reliability, and appropriateness of the following topics of the research project* • Suitable data sources are identified • Number of available datasets is stated • Statistic Approach is present • Suggested sample size is stated • Key variables are identified **General Comment:** **Additional Comments:** *(i.e. recommendations)*
3	**IMPACT:** *Please provide your comments and recommendations to whether the anticipated major outcome and potential impact of work is well described and the HARMONY stakeholders would care or benefit from the hypothesis and/or outcome of the research project* **General Comment:** **Additional Comments:** *(i.e. recommendations)*

Research Project Proposal Ethics Clearance			
Title:			
Reviewer:		*WP #:*	**8**

1	**ETHICAL REVIEW (WP8 ONLY):**	
	General Considerations:	
	Ethics clearance *(The proposal is "ethics ready")*	☐
	Conditional Ethics Clearance *(The proposal raises ethical issues that must be addressed before the research project is executed)*	☐
	Reasons: *Please provide your comments and recommendations on the ethics requirement(s) that need to be considered for ethical clearance. Please specify any additional documents or information that needs to be submitted*	
	No Ethics clearance *(If this option is selected the proposal will not be estimated for execution)*	☐
	Reasons: *Please provide a clear explanation of the ethical issues that preclude the research project from execution*	

Completing all parts of this form is mandatory, even if there is no financial relationships to disclose.

Kindly complete this section to identify any situation in which you might have an actual, perceived, or potential conflict of interest you may have as HARMONY Reviewer for this Research Project Proposal.

Even when financial relationship does not result in bias, the integrity of HARMONY may be considered at risk because of the potential perception that bias may occur. Transparency regarding the financial interest of the HARMONY Reviewers is critical.

You are responsible for the accuracy and completeness of the submitted information.

Your disclosure is part of the Research Project Assessment and will be published with it.

Financial Support for the Research Project Proposal:

*(**Financial Support** consists of anything of monetary value received by you (**direct financial support**) or the institution of which you are an employee (**indirect financial support**) during the two preceding calendar year, including but not limited to, salary, royalty, intellectual property rights, consulting fees, honoraria, ownership interest, research support or any other financial benefit from any commercial entity which has (potentially or perceived) interests that may conflict with those of HARMONY.)*

1. Did you or your institution at any time receive financial support or services from a third party (Government entity, commercial entity, private foundation, academic institution, or other) for any aspect of the submitted Research Project Proposal? ☐ Yes ☐ No

Please declare any financial relationship(s) to disclose, namely:
(Use the table below to disclose your financial relationships with entities in the biomedical arena that could be perceived to influence your decision about the submitted Research Project Proposal. Report all sources of revenue paid to you or your institution on your behalf during the two preceding calendar years. If there is a question, it is better to disclose a relationship than not to do so.)

Name of the company or institution	*Direct*	*Indirect*
	☐ *Yes* ☐ *No*	☐ *Yes* ☐ *No*
	☐ *Yes* ☐ *No*	☐ *Yes* ☐ *No*
	☐ *Yes* ☐ *No*	☐ *Yes* ☐ *No*
	☐ *Yes* ☐ *No*	☐ *Yes* ☐ *No*
	☐ *Yes* ☐ *No*	☐ *Yes* ☐ *No*
(Add rows as needed)		

2. Would anyone associated with you benefit from or be detrimentally affected by your proposed decision about the submitted Research Project Proposal?
   ☐ No
   ☐ Yes Explain:

Intellectual Property:

3. Do you have patents, whether planned, pending or issued, broadly relevant to the submitted Research Project Proposal?
   ☐ No
   ☐ Yes Explain:

Relationships not covered above:

4. Are there other relationships or activities or do you hold any personal or professional views or biases that may lead others to reasonably conclude that you are not an appropriate person to deal with the submitted Research Project Proposal?
   ☐ No
   ☐ Yes Explain:

By signing below, you attest that the information provided is correct, that you have disclosed any financial relationship, and that none of the information provided disqualify or limit your professional skills to participate as an expert in the evaluation of the submitted Research Project Proposal under review, even if some of the answers above are affirmative.

Signature: Date:

Print name:

Or

☐ ***Decline your participation as HARMONY Reviewer for this Research Project Proposal.***

HARMONY

RESEARCH PROJECT **SUBMISSION FORM**

Research Project Proposal

Project Title: (Max. 150 characters)			
Disease Pillar(s)			
Date of document:			
Author (1):		Email:	
Organisation:		Phone:	
Author (2):		Email:	
Organisation:		Phone:	
Author (3):		Email:	
Organisation:		Phone:	

RESEARCH PROJECT PROPOSAL:

(Please use this section to provide a summary of the research project's background and to introduce the HM-specific research project to be addressed, describing the significance / unmet need of the project; and to provide the specific aims of the project, including the study objectives, the hypothesis to be evaluated and / or the anticipated major outcome of the research project. Finally, please provide an estimation of the anticipated project timeline and the key milestones dates for the research project. Sub-sections can be used for clarity. Please ensure that the scientific purpose is clearly described and clarify how it will contribute to enhance the scientific and/or medical knowledge or will be used to empower policy makers and clinicians to optimize care for patients. This information will be used to determine the scientific merit of the proposed work.)

ANALYSIS PROPOSAL:

(With regards to scientific integrity of the research ***it is recommended that the research project proposals should provide sufficiently pre-defined details on the methodology of the analysis to be applied. Pre-specification, whenever possible, is an important feature of the scientific quality of the research****. Thus, this section should provide a clear description of the research methods to be used to address each of the specific aims posed. Please specify the tools, modelling, and methods to conduct an outcome-driven analysis of the research project. Subheading can be used to differentiate the following sub-sections: identification of suitable datasets, where the author(s) should list suggested data sources to the research project and the number of datasets available in those databases; sample size: an estimation of the number of patient datasets needed to conduct the research project; key variables which need to be present in the data; and the analytical and statistical methods and proposed approach to answer the research project.)*

IMPACT

(This section should be used to describe the potential impact of work: risk factors, surrogate parameters, classical and additional end-points, outcome definitions and measures, etc. Figures, graphs, and tables can be used in this section.)

ETHICS

(This section should describe how the proposal intends to address any anticipated ethical concerns or difficulties in relation to the aims and objectives, the research and analysis methodology, and the potential of the Research Project.)

REFERENCES AND SUPPLEMENTARY MATERIAL

(Please use this section to include any additional information you want to include to supplement your Research Proposal.)

ADDITIONAL INFO FOR WP7 | COMMUNICATION & DISSEMINATION PURPOSES

HARMONY Research Projects will be presented in the HARMONY communication channels (website, presentations etc.). For this purpose, we need additional information such as:

PARTNERSHIP

(If available at this stage, please list the collaborating organizations by: Full name, country – on alphabetic order of name organization)

HARMONY
Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms in Hematology

innovative medicines initiative

D6.01 HARMONY Stakeholder Forum

116026 – HARMONY

Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms in Hematology

WP6: Stakeholder Forum, Patients, Payer/Provider, HTA, EMA alignment and optimization

Lead contributor	Jan Geissler, LeukaNET
	Hélène Chevrou-Séverac, Celgene
Other contributors	All WP6 members, in particular
	Katy Harrison, NICE
	Julia Stingl, BfArM
	Christina Donatti, Janssen
	Piero Fantacci, Menarini
	Tamas Bereczky, LeukaNET

Due date	M06/M07
Delivery date	4 July 2017
Deliverable type	Word document (V1.7)
Dissemination level	Public

Description of Action	Version	Date
	7	11/1/2018

Table of Contents

Document History

Version	Date	Description
V1.0	13/04/2017	First proposal on the Stakeholder Forum document
V1.1	07/05/2017	Integration of comments from the WP6 consultation – version 2
V1.2	05/06/2017	Integration of supplementary comments from WP6 leaders and tasks leaders – version 3
V1.3	15/06/2017	Version 4 presented here; after final check with WP6 leaders
V1.4	3/7/2017	Revision Christine Donatti
V1.5	4/7/2017	Revision Jan Geissler, response to comments, submission to HARMONY office
V1.6		Revision Jan Geissler: Stakeholder Cluster Leads
V1.7	11/1/2017	Revision Jan Geissler: Patient organisations cluster update

List of Acronyms

Acronym	Description
HTA	Health Technology Assessment
PHSFF	Policy Health Stakeholder Feedback Forum ("Stakeholder Forum")
WP	Work Package
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicine Agency
IMI	Innovative Medicines Initiative
SF	Same as PHSFF ("Stakeholder Forum")
LT	Leadership Team
TC	Teleconference
F2F	Face-to-Face

HARMONY STAKEHOLDERS FORUM

1. PUBLISHABLE SUMMARY:

The Policy Health Stakeholder Feedback Forum (PHSFF, "Stakeholder Forum") acts as a key platform of interaction and consultation between all stakeholder groups from HARMONY and outside of HARMONY. Collecting input and discussing viewpoints from patient organisations, haematologists/clinicians, regulators and HTA bodies will be crucial to shape the work of HARMONY, especially in WP2, WP5, WP6 and WP7, alongside the implementation of the HARMONY project.

2. SCOPE:

This document presents the objectives of the The Policy Health Stakeholder Feedback Forum (PHSFF, "Stakeholder Forum"), the implementation of the PHSFF and the way to consult the PHSFF for the different HARMONY WPs.

3. PURPOSE AND OBJECTIVES (as described in the DoA):

The Policy Health Stakeholder Feedback Forum (PHSFF, "Stakeholder Forum") acts as a key platform of interaction and consultation between all stakeholder groups. Collecting input and discussing viewpoints from patient organisations, haematologists/clinicians, regulators and HTA bodies will be crucial to shape the work of HARMONY, especially in WP2, WP5, WP6 and WP7.

The PHSFF will discuss barriers, gaps, and needs potentially leading to a consensus on innovative solutions in the area of Big Data. There will be three face2face meetings, after which a report will be written. The report will document enablers and barriers, opportunities and constraints. Depending on the topics in consultation, the reports can provide the basis of white papers which will be developed and disseminated in collaboration with WP7.

The PHSFF will be structured by the following stakeholder clusters:

1. Patient organisations
2. Haematologists / clinicians
3. Medicines authorities (EU/EMA and national level)
4. HTA bodies
5. Payers[1]
6. Pharmaceutical industry

The PHSFF will liaise with these stakeholder clusters to understand viewpoints, concerns and requirements which support the work in HARMONY.

The PHSFF's discussion and consultations with stakeholders will consider the outcomes definitions and validation (coordinated by WP2), the evidence frameworks for innovative technologies (developed in Task 6.2), and the Clinical Value framework to quantify therapeutic value of innovative technologies for HMs (task 6.3). It will also consider the research question developed by WP2, whenever accurate,

[1] to the extent that payers will agree to participate in HARMONY meetings

including the pilot research questions, as well as the discussions of novel methodologies and proof-of-principle study discussed in task 6.4. Finally, SF will also be a place to collect research questions from all these stakeholders.

The clusters will meet in virtual meetings plus three face2face meetings over the whole 5-year project period.

The key to successful and effective stakeholder integration is the generation of relevant evidence to address uncertainties and support decision-making in relation to regulatory approval, HTA recommendations, reimbursement approval and patient access. Evidence from randomized controlled trials (RCTs) has traditionally been the gold standard for decision-making regarding market access of cancer drugs. In recent years, considerable amounts of data have been generated from increasingly diverse sources (e.g. electronic health records, real-world data), and these offer new opportunities for evidence collection. HMs are characterised by remarkable heterogeneity, and patient sub-populations are often not adequately characterized in RCTs. Despite the great potential of aggregating individual-level data sets, there are still many practical difficulties, including constraints to data sharing between different healthcare systems.

Different initiatives have been proposed to identify and address these problems (EUnetHTA projects; INNO-HTA, INTEGRATE-HTA; Advance_HTA; IMI GetReal; IMI ADAPT-SMART, European Medical Information Framework/EMIF), but none has specifically considered the particular challenges of HMs.

HARMONY is in a privileged position to provide a discussions forum between all relevant stakeholders developing or using high-quality data sets; discussions that will address uncertainties in decision-making regarding access to new drugs for HMs, brainstorm around and set the path for development of treatment guidelines and new clinical treatment pathways, and likely provide a solid evidence base to inform increasingly personalised therapeutic approaches.

WP6 will develop a new model for multi-stakeholder dialogue by creating a Policy Health Stakeholder Feedback Forum (PHSFF) involving the HARMONY partners and associated members, and external experts at the EU and Member State level. This will enable broad representation of the diverse models of healthcare systems in the EU, and include patients and clinicians, regulators, HTA bodies and payers, as well as stakeholders involved in evidence generation. This Forum will be essential to provide input and advice into the WP tasks to ensure the generalisability and applicability to the agencies within EU member states of the frameworks for evidence and clinical value. The following issues will also be discussed in the PHSFF: e.g. behavioural, ethical, legal, social implications as well as gender and age dimensions).

Regarding the EMA/IMI-funded initiatives, some of their topics or approaches might overlap the ones of the HARMONY project, in particular regarding the consultation of decision-makers. So in order to stay aware of the potential collaboration and get some learnings from these initiatives, a meeting can be set with relevant participants of these initiatives in order to inform the WP6 members about them.

Regarding relationship with Policy Makers, given that their responsibilities are linked to legislations which are difficult to influence, this stakeholders cluster will be created later on and in collaboration with WP7, with the idea to bring them information on the HARMONY project, in particular about the objective of bringing the right therapy to the right patient at the right time.

4. IMPLEMENTATION:

4.1. Stakeholder Clusters

The Stakeholder Forum consists of 6 different clusters. Each cluster is chaired by a cluster lead taken from the WP6 members. The Cluster Lead will propose a list of experts or organisations within that stakeholder cluster, get in touch with them to obtain their approval for participating into the SF consultations, maintain the list of stakeholders and stakeholders' participation active (or replace them whenever necessary), check their availability prior to schedule any F2F or teleconference meeting, formally invite them to consultations, send them feedback about results of the consultation, and communicate them about the progress of the HARMONY project. The coordination of the consultation of cluster members will done by the task 6.1 lead and its subteam; it means organisation of the consultation (by email, phone or F2F meeting), setting a date for the consultation, providing briefing book to experts, keeping track of feedback received, producing the summaries.

To avoid asynchronous point-to-point communication and a disconnect clusters, the coordination between cluster leads will be done by the Task 6.1 Lead, the subteam and cluster leaders, keeping the WP6 Leads informed.

4.1.1. Patient organizations

The patient organisations cluster is organised by the seven disease areas of the HARMONY project. LeukaNET (Jan Geissler and Tamas Bereczky) will act as the cluster lead and budget holder to coordinate overall patient input into the project and provides the interface to all WPs through the HARMONY Steering Committee.

Each disease area will have a named person as a disease area lead. Each disease lead in this cluster is liaising with e.g. WP2 and WP5 on disease-specific questions, but also makes sure that it provides a report on that interaction to the WP6 coordinators, to keep discussions on the HARMONY Steering Committee level in sync.

The disease-specific umbrella organisations identified so far are:

- Multiple Myeloma: Myeloma Patients Europe
- AML: Acute Leukemia Advocates Network / Leukemia Patient Advocates Foundation and International MDS Alliance
- ALL: Acute Leukemia Advocates Network / Leukemia Patient Advocates Foundation
- CLL: CLL Advocates Network
- NHL: Lymphoma Coalition Europe (tbc)
- MDS: International MDS Alliance
- Pediatric Hematological Malignancies: Childhood Cancer International

The above umbrella organisations encompass about 200 disease-specific patient organisations (mostly organisations operating on a country level) in their membership.

Additional patient organisations (e.g. national organisations or umbrellas in hematology or

cancer) can be included in the patient organisations cluster's consultations whenever necessary.

In addition, an interface to cross-disease patient initiatives is being established, to allow consultation of the wider patient community on disease-unrelated issues, e.g. on Big Data and value. More specifically:

- EUPATI (especially its Alumni Network and National Platform Network)
- ePAG of the EuroBloodNet ERN (for the link to EuroBloodNet)
- European Patients' Forum (for EU policy)
- EURORDIS (for rare diseases)

4.1.2. Hematologists / clinicians

The hematologists/clinicians cluster consists of two subgroups:

1. The clinicians through HARMONY consortium members and associate members
2. Medical associations

The leads of this cluster will be Celgene (Yann Guillevic) and EHA (Carin Smand).

Members of the clinicians include the clinical leads of the seven disease areas in HARMONY:

- Multiple Myeloma: Sonneveld, San Miguel, Boccadoro
- AML: Ossekoppele, Huntly, Lo Coco
- ALL: Gökbuget, Dombret, Ribera
- CLL: Ghia, Pospisilova, Bosch
- NHL: Salles, Dreyling, Montoto
- MDS: Fenaux, Kuendgen, Santini
- Pediatric Hematological Malignancies: Moorman, Reinhardt, Locatelli

The medical associations will be consulted on transversal fields. They include:

- EHA (for hematology and value framework)
- ESMO (for medical oncology)
- ECCO (for multidisciplinarity and EU policy)

4.1.3. Medicines authorities (EU/EMA and national level)

The medicines authority cluster will be coordinated by Janssen and will collect input from regulatory authorities into HARMONY's activities both in terms of methodology and experience. Members of the medicines authorities cluster may be:

- EMA
- BfArM
- AEMPS
- European Medicines Agency
- Swedish Medical Products Agency
- MHRA

- AIFA
- SwissMedic

4.1.4. HTA bodies and projects

The cluster lead of HTA experts will be the NICE (Katy Harrison).

The HTA cluster of the Stakeholder Forum will aim to involve a representation of HTA bodies from across Europe, up to 7 HTA agencies in Europe. The agencies will be chosen according to their willingness to participate in these consultations. The aim is to ensure that there is an understanding of processes and policies that affect the selection and definition of health outcomes and explore big data offers potentials to reduce decision uncertainty in HTA assessment of innovative technologies. The cluster already has a good connection with EUnetHTA through NICE and will connect with relevant European projects as appropriate.

4.1.5. Payers

The cluster lead will by Celgene (Hélène Chevrou-Séverac).

Payers have a very different profile across European healthcare systems and into countries as well.

Payers are defined as any decision-makers who are involved in setting therapies price and/or reimbursed price or in deciding about regional or hospital healthcare budget allocation.

When taking the example of the French healthcare system, the reimbursed price of therapies is negotiated by the CEPS (Comité Economique des Produits de Santé) sitting in the Ministries of Health and Finance; while the hospital budget allocation for drugs is decided by the hospital pharmacist in collaboration with physicians. In Germany, the reimbursed price of drugs is negotiated between the drug manufacturer and the Sickness Funds association (GKV-Spitzenverband). Prices can also be re-negotiated by hospital whenever the drug is used into hospitals settings. In England, the price negotiation can happen with the National Health System (NHS) under the PPRS (Pharmaceutical Price Regulation Scheme) or with each Clinical Commissioning Groups (CCGs). Therefore, a list of stakeholders will be made according to this complexity, and involving 'Payers' of the different levels.

However, it is important to pay attention to the fact that collaboration of these stakeholders can be difficult to set for projects done in a Private-Public partnership. Indeed, both at the national and local levels, it can be challenging sometimes to find 'Payers' willing to collaborate with the pharmaceutical industry. Additionally, for national 'Payers' the price negotiation is 1/ based on the HTA appraisal of the comparative clinical benefit of new therapies; 2/ highly driven by national law and regulations, and very little by research; therefore, it might not be a highly relevant stakeholders group for the HARMONY project. The cluster lead will therefore assess first the willingness of these stakeholders to participate to the SF.

4.1.6. Pharmaceutical industry

This cluster will be led by Celgene (Hélène Chevrou-Séverac).

The following companies, members of the HARMONY consortium, as well as member of the EFPIA, will be the key stakeholders of this cluster:

- Novartis
- Celgene
- Amgen
- Janssen
- Bayer AG
- Menarini Ricerche S.p.A
- Takeda

5. CONSULTATIVE MECHANISM:

5.1. Type of consultations

The Stakeholder Forum has identified three mechanisms for eliciting stakeholder feedback through consultation and discussion within the clusters, or across multiple clusters at a time.

5.1.1. Face2Face Meetings / Feedback in person

Three face2face meetings of the Stakeholder Forum are foreseen within the duration of the HARMONY project. Three F2F meetings will occur during the five years of the project. The budget planned for these meetings is €30'000 (within Leukanet). This budget is expected to cover the flights of participants from the patients' association clusters, potentially from the HTA agencies, Medicine Agencies and Payers clusters whenever necessary and aligned with the countries' law and codes covering the relationship of the industry with public agencies members. The budget should also cover the catering services. The venue of the F2F meeting will be organized into the offices of the Pharmaceuticals Companies participating to HARMONY.

A written Stakeholder Forum Feedback Report will be produced, providing summaries of the discussions, describing the consensus and disagreement on the topics discussed. The report will be done by the task 6.1 lead and subteam.

5.1.2. Feedback by electronic surveys and E-Mail

An electronic system owned or located on the HARMONY internet platform will be used to elicit feedback from the clusters on a specific topic, either through mechanisms established by WP7 or WP6. The survey will be distributed to stakeholders of each cluster by the cluster lead. A Stakeholder Forum Feedback Report will be produced by task 6.1 lead and subteam providing summaries of the qualitative and quantitative feedback received.

E-Mail may also be used for consultations, however is not seen as very efficient to collect and document feedback in a structured way.

5.1.3. Feedback and discussion by teleconference

A teleconference system will be used for group discussions. The system to be used for such consultation will be clarified later. A Stakeholder Forum Feedback Report will be produced in the form of minutes by the task 6.1 and subteam.

5. PROCESS TO SET UP A CONSULTATION:

5.1. Requesting a consultation

Channel 1:

When a WP member (thereafter called **the applicant)** would like to activate a consultation of the SF, an email request should be sent to WP 6 leadership team (thereafter called **WP6 LT**) with the following information (with copy to the WP leads to which the applicant belongs to):

- Objectives of the consultation
- Clusters the applicant would like to consult and eventually number of stakeholders per cluster
- Involved partners in HARMONY (other WP members, etc…)
- Type of consultation: individual TC or group TC with length of the TC, or electronic consultation or F2F meeting (please note that some restrictions apply to the F2F meetings)
- Expected date to consult them

Channel 2:

Through the HARMONY Steering Committee, the WP6 LT will map out when, how and where the stakeholders' feedback from the clusters across the different WPs is required, so WP6 LT can plan ahead accordingly.

Remarks: the SF consultation doesn't intend to replace the Early Scientific Advice or Parallel Scientific Advice consultation of the EMA and HTA agencies on drugs in development or in pre-launch or post-launch phase.

5.2. Validation of the objectives of the consultation

For both channels, the WP6 LT will communicate the topic of the consultation to the Steerco to obtain their approval to go to the next step of the consultation process. Feedback is expected in a timeframe of a working week (5 days).

Once the SteerCo has given a positive feedback on the topic of the consultation, the Task 6.1 Lead and subteam will distribute the objective of the consultation to the cluster leads. The Task 6.1 and cluster leads will:

- assess and validate which clusters are relevant to be consulted on the topic of the consultation,
- give recommendation regarding the type of the consultation
- assess feasibility of the timeline for consultation

The output of this step will be a written answer on these three points to the applicant, with copy to his/her WP leads.

Once the principle of making a consultation for the topic submitted by the applicant has been agreed by Task 6.1, then the next steps are implemented to organize the consultation.

5.3. Preparing the consultation

The Task 6.1 Leadership Team (thereafter, **Task6.1 LT**) will set a TC with the APPLICANT and his/her team to get the supplementary details of the consultation: more detailed objective of the consultation, targeted stakeholders, type of consultation, length of consultation, and possible dates for the consultation; as well as information to send stakeholders ahead to maximize the consultation, type of feedback expected, format of feedback; any logistical resources needed.

The following steps are required to be done by the APPLICANT and his/her team to prepare the consultation

- Provide to the Task 6.1 Leadership Team (thereafter, Task6.1 LT) an invitation letter which will be provided to the stakeholders. The letter should follow the HARMONY format with related logo, present the objectives of the consultation, the type of consultation and include expected dates / timelines (depending on the type of consultation) of the consultation and output required to the stakeholders
- Set themselves the TC consultations with stakeholders, in case of TC with only one stakeholder at a time
- Prepare a presentation or a briefing book and/or questionnaire to submit to the stakeholders
- Take minutes of the TC or F2F meeting with the stakeholders

The following steps will be set by the Task6.1 LT for organizing the consultation:

- Submit the stakeholders lists to the APPLICANT and pick up with him/her the names of the ones to be consulted
- Set up the venue of the consultation for F2F meeting and support for organizing the trips of the Stakeholders invited to the meeting; and manage the budget for the event
- Support for group TC (consultation of multiple stakeholders in one TC), to the extend it's no more than one TC per cluster
- Ask the Cluster Leads to:
    - Contact the chosen stakeholders and send them the invitation letter
    - Secure the consultation with a minimum of stakeholders from their clusters. Or find replacement whenever necessary
    - Attend the meetings when appropriate from APPLICANT standpoint or wished by the Lead

5.4. Dissemination and Tracking of feedback by each cluster

The following steps are required to be done by the APPLICANT and his/her team to finalize the consultation:

- Prepare a summary report of the output of the consultation (following the HARMONY internal review process)
- Send the summary report to each stakeholder consulted in a joint email with the Cluster Lead, plus the HARMONY SC
- Collaborate with Task6.1 LT and WP6 LT and WP7 LT for developing and implementing a dissemination plan of the findings of the consultation to other HARMONY participants and externally whenever appropriate.

The following steps will be set by the Task6.1 LT for ending the consultation:

- Ask the Cluster Leads to:
    - Send the summary report to each stakeholder consulted in a joint email with the applicant
    - Thank the stakeholders for their participation by an email or a letter with official template of HARMONY project
- Collaborate with the applicant, WP6 LT and WP7 LT for developing and implementing a dissemination plan of the findings of the consultation to other HARMONY participants and externally whenever appropriate

The aforementioned reports about the feedback received will be provided to all cluster members as well as to the HARMONY Steering Committee, consisting of the Work Package leads and to the WP6 members.

The WP leads are responsible to disseminate the feedback to the WP members concerned. They are also responsible to feed back to the Stakeholder Forum and the HARMONY Steering Committee where the feedback has been incorporated in the work and implementation of the WP.