ERA4Health Partnership

# DELIVERABLE 16.1

# Report on eligibility and selection criteria

# WP16

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| #1 | Marta del Álamo | ECRIN | 16 October 2024 |
| | Sabrina Lémeret | ECRIN | |
| | Elena Toshi | ISS | |
| | Maria Jose Ruiz | ISS | |
| | Martine Bateaux | ANR | |
| | Cristina Nieto | ISCIII | |

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*1 PU = Public*
*SEN = Sensitive*

D16.1. REPORT ON ELIGIBILITY AND SELECTION CRITERIA

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## GLOSSARY / LIST OF ACRONYMS

| Abbreviation | Full description |
|---|---|
| **AICIB** | Agency for Clinical Research and Biomedical Innovation |
| CTU | Clinical Trials Unit |
| CRO | Clinical Research Organisation |
| **CSO-MoH** | Israel Ministry of Health |
| **DLR** | Deutsches Zentrum Fur Luft-Und Raumfahrt |
| **ECRIN** | European Clinical Research Infrastructure Network (https://ecrin.org/) |
| **ERAB** | Ethics and Responsible Research and Innovation Advisory Board |
| **FWF** | Fonds Zur Förderung der wissenschaftlichen forschung |
| **FWO** | Fonds Voor wetenschappelijk onderzoek-vlaanderen |
| **GMP** | Good Manufacturing Practice |
| **IICS** | Investigator-initiated Clinical Studies |
| **ISCIII** | Instituto de Salud Carlos III |
| **IT-MoH** | Ministero della Salute |
| **LCS** | Latvijas Zinatnes Padome |
| **LMT** | Lietuvos mokslo taryba |
| **RCN** | Research Council of Norway |
| SRIA | Strategic Research and Innovation Agenda |
| **STAB** | Strategic Advisory Board |
| **TWiCs** | Trials within cohorts |
| **ZonMw** | Zongonderzoek Neterland Zon |

## EXECUTIVE SUMMARY

This deliverable aims to describe, evaluate, and propose eligibility/selection criteria for the calls on Investigator Initiated Clinical Studies (IICS) that will be launched by the ERA4Health partnership. The intended audience of this deliverable are ERA4Health partners.

The above-mentioned objective was achieved by implementing the following tasks:

- Collecting feedback from the survey developed by Task 15.1. Among others, this survey interrogated ERA4Health current funders about the specificities of the IICS funded and fundable at national level.
- Collecting feedback from targeted interviews to ERA4Health partners that expressed willingness to participate in the ERA4Health call for IICS through the 15.1 survey.
- Collecting feedback from the Workshop "Funding mechanisms for investigator-initiated clinical studies" organized in Brussels (MS8) on 7-8th February 2024. Main discussions about eligibility criteria were based on a "Scoping paper" previously circulated among ERA4Health partners.
- Collecting feedback from the Virtual Workshop "Supplementation of ERA4Health´s SRIA with investigator-initiated clinical studies".

At the time of drafting this deliverable, the following eligibility criteria for the Pilot Call had been defined:

- Pragmatic/comparative-effectiveness interventional studies involving recruitment in at least 3 countries and lasting max 4 years (that could add a potential cost-neutral extension)
- Studies on diagnosis, prevention and treatment
- Treatment studies including medicinal products and procedures. Medical devices should be excluded
- Communicable diseases (infectious diseases), vaccines, rare diseases, neurological diseases and cancer are excluded as fundable topics

Eligibility criteria linked to the scientific scope of future calls for IICS (ERA4Health Phase 2) will consider:

- Treatment and prevention studies, including TWiCs, on the field of nutrition and healthy life-style
- Prevention interventional studies, targeting outpatients on the field of cardiovascular diseases
- Treatment and diagnosis through academic innovation and drug repurposing studies, specially- but not restricted-to the field of nanomedicine

The selection procedure (evaluation) will be based, for both IICS pilot call and Phase 2 calls, on a 2-step call. The specific approach, that will include special assessment of the study´s feasibility, it is described in

the call text documents (Deliverable D. 16.2). As an specific selective measure for IICS the proposed evaluation procedure includes an interview to the study´s sponsor. This evaluation procedure for the ERA4Health IICS Phase 2 calls can be modified/updated based on the experience of the IICS Pilot Call.

## 1. PURPOSE AND OBJECTIVES

The way in which research funding is allocated is a critical part of the scientific system. It determines what research is conducted, by whom, and in which locations. Getting those decisions right can have a significant impact on the progress of science, and in the case of health research, the development of new life-saving interventions.

***Purpose***

This deliverable aims to describe, evaluate and recommend possible eligibility/selection criteria to ensure the quality of the study implementation plans in forthcoming applications for the Investigator Initiated Clinical Studies (IICS) call(s) that will be launched by the ERA4Health partnership. The intended audience of this deliverable are ERA4Health partners, in particular those that will participate in the upcoming call(s) for IICS.

***Objective***

To recommend eligibility criteria and selection/evaluation procedures for supported multi-country IICS

# 2. METHODOLOGY

We first developed an analysis of the specificities of national calls for clinical studies, as aligning the ERA4Health Investigator-Initiated Clinical Studies (IICS) calls with national preferences should increase the chances of setting up a successful call on IICS within the ERA4Health partnership.

## 2.1. ANALISIS OF NATIONAL IICS CALLS

The survey developed by WP15 (see Deliverable D15.1) interrogated ERA4Health partners and new potential funding organizations about the specificities of the funded and fundable IICS through national funding schemes.

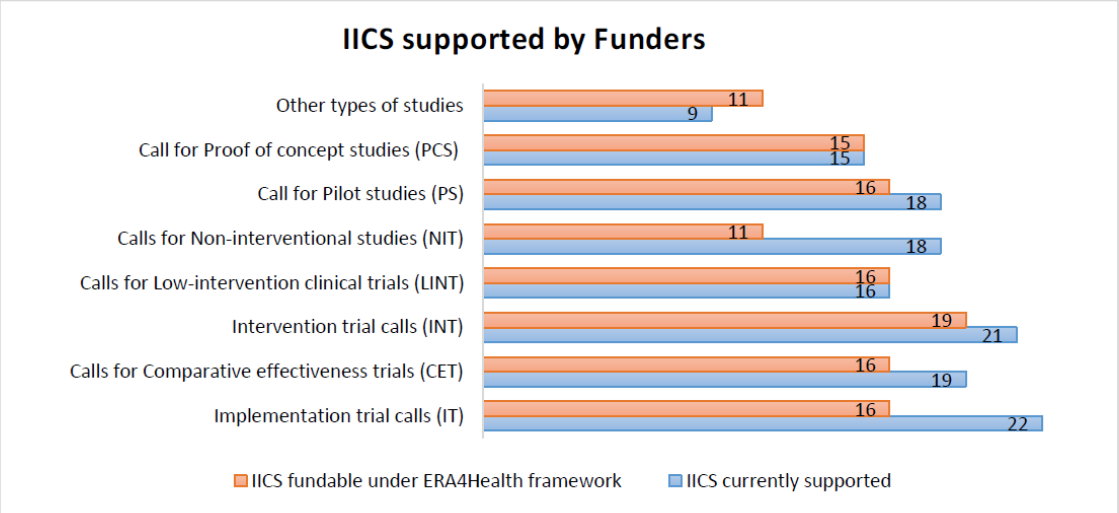


**Figure 1. IICS currently supported and fundable under the ERA4Health framework**

Figure 1, describes current and planned (ERA4Health) funding strategies for supporting academic trials. Calls for intervention trials, implementation trials and comparative effectiveness trials and low-intervention trials are those considered more favorable to be implemented through ERA4Health.

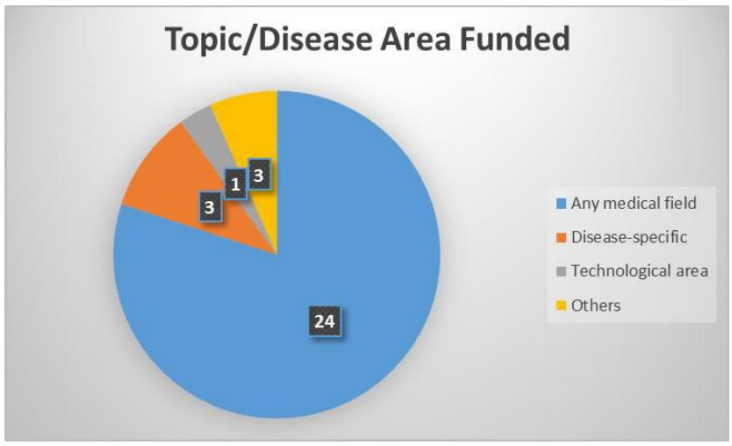


**Figure 2. Fundable topics or Disease area**

Specific topics/diseases area are usually linked to the institution's priorities and national research policies. However, most funders indicated as priority “any medical field”.

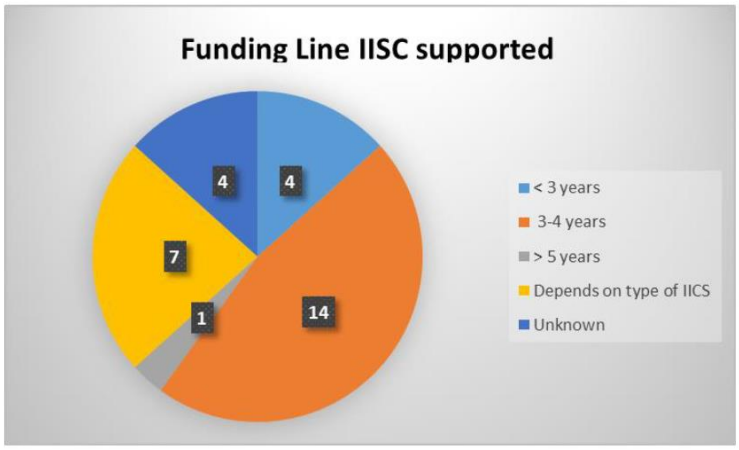


**Figure 3. Funding line duration for IICS**

The funding line information indicated that most funders (14) support IICS with grants of 3-4 years of duration that is in line with the initial ERA-Net structure of this partnership.


**Figure 4. Funding available at national level dedicated to IICS**

Regarding the availability of funding dedicated to IICS at national level: 58,6% of participants described having an established targeted budget line for IICS. Moreover, 5 participants indicated the availability of more than 1000K EUR, 5 are willing to commit less than 250k EUR, 2 can commit an amount in the range of 500-700 and 750-1000K EUR

These results reveal that:

a) funders show notable preference for supporting interventional trials, including comparative effectiveness trials and low-intervention trials and pilot studies (figure 1)
b) Most funders do not fund exclusively a specific research topic and are open to fund any medical disease/topic area (figure 2)
c) Most funders launch calls for funding IICS with an average duration of 3-4 years (figure 3)
d) Most funders do not have a defined funding line for IICS (figure 4)

To refine the information gathered through this survey, targeted personal interviews (*Annex 1*) were performed to funders having expressed willingness to participate in the ERA4Health Call on IICs.

11 interviews were conducted involving the funders listed in Table 2.

*Table 1 and 2* summarize the results of targeted interviews for questions related to eligibility criteria.

**Table 1. Fundable studies (different specificities)**

| FUNDABLE STUDIES | Number of positive responses |
|---|---|
| **Health products** | 10 |
| **Procedural interventions** | 10 |
| **Biotherapy and regenerative medicine** | 11 |

| | |
|---|---|
| **Academic sponsored involving industry** | 7 |
| **Registration trials** | 6 |
| **Repurposing** | 11 |
| **Personalized medicine** | 11 |
| **Primary care** | 9 |
| **Nurse initiated** | 9 |
| **Digitalisation in healthcare** | 11 |

**Table 2. Funding and funding extensions (Question number 16, targeted interviews)**

| Partner | Most funders support IICS with grants of 3-4 years duration. Would your organization extend this funding without additional costs? If the answer is yes, for how long would you do so? |
|---|---|
| **FWF (Austria)** | *Yes, up to 4 years with possibility of 12 month cost-neutral extension* |
| **AICIB (Portugal)** | *Not applicable, as not currently funding IICS. Agrees that 4 years is too short for IICS* |
| **ZonMW (Netherlands)** | *Large projects can last up to approximately 7 year. Because of state aid regulations, there is a maximum of during 10 years duration of a project. It is known that trial duration is an issue, but some applicants apply for 4-5 years thinking that they might have more chances to get funding* |
| **BMBR/DLR (Germany)** | *Yes, as long as inevitably needed: no-cost extensions are possible if the trial successful completion can be assumed. This is a case-by-case decision.* |
| **FWO (Belgium)** | *Yes, FWO currently allows no cost extension of the initial 4 years grant for up to two years (so for up to 6 years in total). However, in the current partnership projects (which are shorter), it is not allowed, but this is also the rule for all the partners.* |
| **LMT (Lithuania)** | *Yes, for now LMT funds projects for max 3 years, but if it is a no cost extension it is feasible. It would* |

| | |
|---|---|
| | *be done through no cost extensions, the initial grant would be 3 years.* |
| **ISCIII (Spain)** | *Yes, under our Law of Grants: 1,5 years more of cost-neutral. Extension can be provided to grants of 3 years under justified request.* |
| **IT-MoH (Italy)** | *Yes. No further information provided, not discussed in detail.* |
| **LCS (Latvia)** | *Yes, not more than 4 years* |
| **RCN (Norway)** | *Yes, not discussed in detail, but 6 years duration might be possible* |
| **CSO-MOH (Israel)** | *Yes. We agree to extend it. Our projects usually last 3 years, but in 95 % of cases we extend the projects. We could extend the funding*. |

## 2.2. SCOPING PAPER

Considering the results presented above, we developed a scoping paper to provide relevant contextual information to help ERA4Health partners defining eligibility criteria for supported multi-country IICS, scoping the **first** planned call for funding (First/Pilot Call) in terms of:

- Objectives of the clinical study
- Topics
- Other criteria

The document (*Scoping paper "Eligibility criteria for supported Investigator-initiated Clinical Studies (IICS) through the ERA4Health Partnership (Pilot Call)"- Annex 2*) suggests possible specifications for the Pilot call and discusses other possibilities.

The document recommends focusing the ERA4Health IICS pilot call on comparative-effectiveness / combination / optimization, pragmatic, interventional studies, excluding topics that are already funded or planned to be funded through other partnership initiatives (infectious diseases, rare diseases, personalized medicine). This document was meant as a basis for discussion during a workshop (see 2.1.3) and Management Board meetings. The final decisions to refine specifications/eligibility/evaluation criteria are to be taken by ERA4Health consortium for each call.

## 2.3. WORKSHOP: FUNDING MECHANISMS FOR INVESTIGATOR-INITIATED CLINICAL STUDIES

This workshop (*Agenda Annex 3*) pursued three objectives:

a) Discussing funding mechanisms to adapt the current Joint Transnational Call funding model to IICS
b) Discussing the eligibility (scoping paper- *Annex 2*) criteria for the first IICS call with funders
c) Discussing the evaluation/selection procedure

Objective a) was tackled during the first day of the workshop, dedicated to presenting different initiatives that are currently funding, or planning to fund, multinational clinical studies in Europe using a transnational model. Part of the second day was dedicated to discussing how some elements presented by these initiatives can be integrated in the ERA4Health funding model by IICS and to present different alternatives.
Objective b) and c) were addressed by break-out sessions (*Annex 3*) and a plenary session discussion during the second day of the workshop.

The results of this workshop are summarized in a specific report that has been published in the ERA4Health website.

## 2.4. WORKSHOP: SUPPLEMENTATION OF ERA4HEALTH SRIA WITH INVESTIGATOR-INITIATED CLINICAL STUDIES

This workshop pursued the following objective:

- Discussing eligibility criteria of IICS calls with experts in the scientific fields of interest of ERA4Health to update the current version of the SRIA including specificities of IICS

The workshop (*Agenda-Annex 4*) was organized as an on-line plenary session followed by three break-out sessions, covering the main areas of interest of ERA4Health:

- Nutrition and healthy lifestyles
- Cardiovascular diseases
- Nanomedicines

Experts were suggested by members of the Management Board, especially those funding and/or willing to fund IICS within ERA4Health. The profile of the selected experts included:

- Clinical trials experts (pharmacologists and academic clinical trial units´ personnel)
- Scientists with expertise in the areas of interest of ERA4Health

ERAB (Ethics and Responsible Research and Innovation Advisory Board) and STAB (Strategic Advisory Board) members also participated in the Workshop.

Selected participants received the supporting material before the Workshop: current SRIA, adapted scoping paper (see section 2.2), and scoping questions (*Annex 6*). Full methodology and Outputs of this workshop are part of Deliverable D. 9.1. (First update of the SRIA) (due date M24).

# 3. RESULTS

## 3.1. PILOT CALL ON IICS

Eligibility criteria for the Pilot call on IICS proposed by the scoping paper:

- Comparative effectiveness studies (combination/optimization), pragmatic interventional studies on diagnosis, prevention and treatment
- Exclude topics already funded through other partnerships/initiatives

were generally accepted by the break-out sessions´ working groups of the workshop described in section 2.3. Further eligibility specifications agreed by the Management Board:

- Prioritize ERA4Health areas of interest
- Duration: 4 years
- Minimum number of participating countries: 3
- Maximum number of participating countries: 5

The evaluation procedure will be structured as a 2-steps call, with a deep evaluation of both sponsor and coordinating investigator´s capacities, for projects invited to submit full proposals. The document "Governance and Evaluation" – which is part of Deliverable D.16.2. Template documents supporting the calls for multicountry IICS"- describes the procedure. In summary, the main features of this procedure are:

- Pre-proposals will be assessed by three reviewers with a scientific/clinician background for evaluation.
- Full proposals will be allocated to three Peer Review Panel (PRP) members (a subset of the reviewers who participated in the pre-proposals evaluation) who fit the profile

of the application and as far as possible, including at least one PRP member who had reviewed the corresponding pre-proposal. One of the three reviewers will have specific expertise in clinical trial methodology and biostatistics

- The reviewers will perform the assessment of the full proposals and complete a written evaluation form with scores and comments for each criterion. In addition, the full proposals will be reviewed by a patient advocacy representative.
- An online interview with the investigating coordinator and a representative of the sponsor, will take place. The representative of the sponsor needs to be specified in the full proposal by the applicants depending on the legal structure of the respective organisation. Two additional representatives of the research consortium (a maximum of 4 total attendees) could be invited to attend this online interview, if they can provide specific expertise important for the assessment of the capacity of the consortium to perform the clinical study (e.g. representative of a CRO/CTU, in case that the sponsor has delegated a responsibility in that entity, or the biostatistician expert of the research consortium). During the interview a qualitative assessment of the feasibility of the trial will be performed, considering especially:

    - The previous experience of the coordinating investigator and the sponsor in conducting multicentre and/or multinational clinical trials
    - Daily management and operational aspects of the study
    - Planned risk mitigation measures
    - The governance and communication among committees that they will put in place to ensure the feasibility of the trial

Deliverable D 16. (Template documents supporting the calls for multicountry IICS) describes the selection procedure in detail.

## 3.2. FUTURE CALLS FOR IICS

A broad scope of target morbidities is foreseen, however some medical areas will be excluded from funding if IICS funding is already covered by other European programmes or collaborative funding activities could be pursued (including but not limited to personalized medicine, rare diseases, infectious diseases, antimicrobial resistance or neurodegenerative diseases).

For instance, observational stratification cohorts could be as part of the aim for future calls under the personalized medicine research programs.

The main expectation facing IICS funded within this partnership is to generate the highest level of clinical evidence in response to specific scientific questions. The aforementioned should contribute to support public healthcare systems.

The IICS calls in ERA4Health will align with the areas of interest of ERA4Health, yet with other features:

*Nutrition- and lifestyle-related diseases, prevention and public health strategies*

Poor diet quality is implicated in almost every disease and health issue. The evidence is clear that diet quality, including diet composition is critical to health. Diet quality is pertinent across virtually all health conditions; including cancers, cardiovascular disease, diabetes, neurological mental health, maternal and child health, and gastrointestinal disorders.

Treatment and prevention studies are considered main areas of interest. Prevention studies, especially on younger population are of great interest and are usually not covered by pharmaceutical industry. Prevention studies have, nevertheless, two main caveats: a) these studies require long follow ups, many times not aligned with funding timelines and b) they are more suitable to be run in the primary care setting, for which multinational studies are considered specially challenging.

Exploration of research findings into practice, e.g. translation of dietary recommendations/menu plans for evaluating their impact for this field should be considered as of main interest in the field of nutrition.

New trial methodologies, specially TWiCs (Trials within cohorts) are considered a great opportunity for research in this area, taking into account the number of already stablished cohorts.

*Cardiovascular diseases*

In this area of interest, the main focus would be prevention studies, and to do so multinational clinical studies on high-risk patients or on treatments that are not covered by the pharmaceutical industry or on very specific types of cardiovascular diseases are reported as the most relevant, while also considering TWiCs if the cohort already exists. They should be carried out in an interventional set-up, on outpatients and primary care patients (acknowledging that this group will include healthy volunteers), taking into account the different care systems in the various countries. More specifically, underserved target groups that should be included are the elderly (80+), female, patients suffering from obesity or familial hypercholesterolemia, pregnant women, patients with comorbidities due to inflammation, stressing the fact that a real representation of the population that is served is key. All natures of health product could be relevant for these calls, but attention should be paid to the capacity to execute the study given the type of intervention chosen. Finally, the participation of industry is relevant since the projects funded in ERA4Health could lead to later results where the input from industry, also in the context of drug repurposing, or start-ups for devices, would be essential. Collaboration among specialties (e.g. neurology) is essential.

*Nano and advanced technologies for disease prevention, diagnostic and therapy*

In this area of interest, treatment and diagnosis were selected as the top priorities for IICS calls on nanomedicine, prevention (which can include vaccination) was also rated as important. In terms of study objectives, academic innovation and repurposing studies should be the main focus areas. The preferred study settings for carrying out these studies are primarily hospitalized patients and outpatients, followed by healthy volunteers. Concerning the populations, the strong need to address underserved populations was stressed, including those with chronic or rare diseases. Regarding the nature of health products, the group emphasized that a broad inclusion of health products is necessary, especially biopharmaceuticals and advanced therapies. Finally, industry participation should have a supporting role favoring technological application and exploitation, providing therapeutic agents, GMP manufacturing of the nanomaterials and excipients, and providing financial support.

## 4. CONCLUSIONS

The first call for IICS (**Pilot Call**) will be based in the following eligibility criteria:

- Pragmatic/comparative-effectiveness interventional studies involving recruitment in at least 3 countries and lasting max 4 years
- Studies on diagnosis, prevention and treatment
- Interventional studies including medicinal products and procedures. Medical devices excluded
- Topics exclude communicable diseases (infectious diseases), vaccines, rare diseases, neurological diseases and cancer

Eligibility criteria linked to the scientific scope of future calls for IICS (ERA4Health Phase 2) will consider:

- Treatment and prevention studies, including TWiCs, on the field of nutrition and healthy life-style
- Prevention interventional studies, targeting outpatients on the field of cardiovascular diseases
- Treatment and diagnosis through academic innovation and drug repurposing studies, especially on the field of nanomedicine

The selection procedure (evaluation) will be based, as for the pilot call, on a 2-step call. The specific approach, that will include special assessment of the study´s feasibility through targeted interviews with the coordinator and sponsor, it is described in the call text documents (Deliverable D. 16.2). The selection procedure for the ERA4Health IICS Phase 2 calls can be modified/updated based on the experience of the IICS Pilot Call.

# 5. REFERENCES

# 6. ANNEXES

## 6.1. ANNEX 1. QUESTIONNAIRE TARGETED INTERVIEWS FUNDERS

**ERA4Health - WP 16, tasks 16.1 and 16.2**

**Questionnaire for funders**

Name of ERA4Health partner/funder:

Name of interviewee:

1. In the interventional study context, which kind of intervention does your organization support or would your organization be willing to support?

☐ Diagnostic trial

☐ Prevention trial

☐ Therapeutic trial

☐ All of them

☐ None of them

2. Does your organization fund or would your organisation be willing to fund interventional phase I studies?

☐ Yes

☐ No, only phase II studies (please specify why)

☐ Both interventional phase I and II studies

3. If you are able to fund across borders, is there a national roadmap in your country focusing on specific health priorities or does your organisation have preferred topics?

☐ Yes (please specify)

☐ No

4. Does your organization fund or would your organization be willing to fund IICS on health products (medicine, medical devices/MedTech)?

☐ Yes (please specify)

☐ No

5. Does your organization fund or would your organization be willing to fund IICS on procedural interventions?

☐ Yes

☐ No

6. Does your organization fund or would your organization be willing to fund IICS on biotherapy and regenerative medicine?

☐ Yes

☐ No

7. Does your organization fund or would your organization be willing to fund IICS industry/SME sponsored trials?

☐ Yes

☐ No

8. Does your organization fund or would your organization be willing to fund academic sponsored trials involving industry/SME?

☐ Yes

☐ No

9. Does your organization fund or would your organization be willing to fund registration trials?

☐ Yes

☐ No

10. Does your organization fund or would your organization be willing to fund drug repurposing trials?

☐ Yes

☐ No

11. Does your organization fund or would your organization be willing to fund personalized medicine studies - only interventional studies?

☐ Yes

☐ No

12. Does your organization fund or would you organization be willing to fund trials in the primary care?

☐ Yes

☐ No

13. Does your organization fund or would your organization be willing to fund nurse-initiated trials?

☐ Yes

☐ No

13. The area of digitalisation in healthcare has increased in the last years. Would your organization be interested in funding this area?

☐ Yes

☐ Yes, it already does

☐ No (please, explain why)

14. What do you think about the Public Patient Involvement (PPI) in the clinical research projects? Is this a strength or a weakness of an IICS?

☐ It is a strenght (please, specify why)

☐ It is a weakness (please, specify why)

15. Most funders support IICS with grants of 3-4 years duration. Would your organization extend this funding without additional costs? If the answer is yes, for how long would you do so?

☐ Yes (please, indicate the duration)

☐ No (please, explain why)

16. For (E4H) responders to D15.1 who declared that their funding for IICS depends on the type of IICS, enquire about the amount they would allocate to a IICS according to the type they fund.

(please specify)

## 6.2. ANNEX 2. SCOPING PAPER



**SCOPING PAPER**

**Eligibility criteria for supported Investigator-Initiated Clinical Studies (IICS) through the ERA4Health Partnership**

**(PILOT CALL)**

Marta del Álamo[1], Sabrina Lemeret[1], Sabine Klager[1], Martine Batoux[2], Richard Imrich[3], Jacques Demotes[1]

[1] *ECRIN (European Clinical Research Infrastructure Network)*

[2] *ANR (French National Research Agency)*

[3] *BCM-SAS (Biomedical Research Center Slovak Academy of Sciences)*

### 1. OBJECTIVES OF THIS SCOPING PAPER

This document aims to provide relevant contextual information to help ERA4Health funders define eligibility criteria for supported multi-country IICS (Investigator Initiated Clinical Studies), scoping the first planned call for funding (Pilot call) in terms of:

- Objectives of the clinical study
- Topics
- Other criteria

The document suggests possible specifications for the Pilot Call and discusses other possibilities.

### 2. INVESTIGATOR INITIATED CLINICAL STUDIES (IICS)

Clinical research involves testing new discoveries by carrying out carefully controlled investigations on patients – known as clinical studies. This includes testing not only new or repurposed medicines, but also comparing various treatment regimens (combination of drugs, different treatment dosage or schedules), medical devices, therapies without medicinal products (e.g. radiation or procedural interventions - surgical procedures, psychotherapy), diagnostic procedures, prevention measures, as well as optimizing the use of existing medicinal products and procedures to promote better health and welfare and/or cost saving to the society. Many of these studies and trials are non-commercial, initiated by investigators, usually driven by pressing public health needs and scientific opportunities, which do not offer a strong business case to private companies. This is referred to as investigator-initiated clinical studies (IICS) where the investigator conceives the research and develops the protocol.

1

## 6.3. ANNEX 3. AGENDA WORKSHOP- FUNDING MECHANISMS FOR INVESTIGATOR-INITIATED CLINICAL STUDIES


## 6.4. ANNEX 4. BREAK OUT SESSIONS OUTLINE

**ERA4Health Workshop**

**Funding mechanisms for Investigator-Initiated Clinical Studies**

**BREAK-OUT SESSIONS (February 9th 10.10-11.30 am)**

**SCOPING PAPER**

## Eligibility criteria for supported Investigator-Initiated Clinical Studies (IICS) through the ERA4Health Partnership

## (PILOT CALL)

3 BREAK OUT SESSIONS Break-out sessions 1-3 (on-site). Moderators: Sabrina Lemeret, Martine Batoux, Jacques Demotes

Break-out session 4 (on-line). Moderator: Marta del Álamo

The following questions, already tackled in the Scoping Document, will be discussed in small groups

1. **What should be the objective of the ERA4Health Pilot Call?**

- Funding innovation
- Funding drug repurposing
- Funding comparative-effectiveness

2. **What should be the topics for the Pilot Call?**

- ERA4Health areas of interest: Cardiovascular diseases, nutrition, nanomedicine
- Other topics (as suggested in the scoping paper)
- Other topics

**3. What intervention areas should be covered?**

- Prevention
- Diagnosis
- Treatment

4. **Should this pilot call be aligned with research projects and already identified areas?**

5. **Are unmet needs covered**?**

**WHO: The WHO often identifies priority areas for clinical research based on global health challenges and needs. While the WHO doesn´t specially outline uncovered needs for clinical research in Europe alone, its priorities often resonate with regions worldwide, including Europe. Some overarching areas where the WHO emphasizes the need for clinical research include:

- Infectious diseases
- Non-communicable diseases, including cardiovascular diseases, cancer, diabetes and chronic respiratory diseases, including preventive strategies, early detection and innovative treatments

- Maternal and child health
- Health systems strengthening
- Global Health Security, including pandemic preparedness
- Health Equity and Social Determinants of Health
- Digital Health and Innovation
- Environmental Health
- Health Policy and Governance
- Ethics and Equity in research

*** Source:*

*Several WHO documents and initiatives touch upon the priorities and needs for clinical research, including:*

1. ***Global Strategy on Digital Health 2020-2025**: This document outlines WHO's strategic priorities for leveraging digital technologies to improve health outcomes, including areas such as telemedicine, mobile health, health data management, and digital health interventions.*
2. ***WHO Global Strategy for Women's, Children's and Adolescents' Health (2016-2030)**: This strategy highlights key priorities for improving maternal, newborn, child, and adolescent health globally, including the importance of research to address health inequities and improve access to essential healthcare services.*
3. ***WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020**: This action plan outlines WHO's strategic objectives for addressing non-communicable diseases (NCDs), including cancer, cardiovascular diseases, diabetes, and chronic respiratory diseases, and emphasizes the importance of clinical research to develop effective prevention and treatment strategies.*
4. ***WHO Research for Universal Health Coverage**: WHO promotes research to inform policies and practices aimed at achieving universal health coverage (UHC). Research priorities include health systems strengthening, health financing, service delivery models, and strategies to address health inequities.*
5. ***WHO Global Health Observatory (GHO)**: The GHO provides access to a wide range of health data, indicators, and research publications, which can inform clinical research priorities and interventions at the global, regional, and national levels.*
6. ***WHO Research Priorities for the Environment, Climate Change, and Health**: This initiative identifies research priorities and knowledge gaps related to the health impacts of environmental factors and climate change, including areas such as air pollution, water quality, vector-borne diseases, and occupational health risks.*

(B) HTAs. Health Technology Assessments (HTAs) play a critical role in evaluating the clinical and cost-effectiveness of healthcare interventions, technologies, and services. While HTAs primarily focus on assessing the value of healthcare interventions rather than identifying specific uncovered needs for clinical research, they can indirectly highlight areas where additional research is warranted based on gaps in evidence or unmet healthcare needs.

In Europe, HTAs conducted by various national and regional agencies, as well as collaborative networks such as the European Network for Health Technology Assessment (EUnetHTA), may identify uncovered needs for clinical research through their assessment processes. Some of the areas where HTAs may indicate the need for further clinical research in Europe include:

1. **Comparative Effectiveness**: HTAs often evaluate the comparative effectiveness of different healthcare interventions, including pharmaceuticals, medical devices, surgical procedures, and healthcare delivery models. Identified gaps in evidence or uncertainty regarding the relative effectiveness of interventions may signal the need for additional comparative clinical research.
2. **Long-term Outcomes**: HTAs typically assess the short-term and, to some extent, medium-term outcomes of healthcare interventions. However, there is often limited evidence on long-term outcomes, particularly for chronic conditions or interventions intended for use over extended periods. Research focusing on long-term safety, efficacy, and patient outcomes may be needed to inform HTAs adequately.
3. **Subpopulations and Subgroup Analyses**: HTAs may identify subpopulations or patient groups for which there is limited evidence regarding the effectiveness or safety of interventions. Additional clinical research focusing on specific patient subgroups, such as pediatric patients, older adults, individuals with comorbidities, or minority populations, may be necessary to address these gaps in evidence.
4. **Real-world Evidence**: HTAs typically rely on data from randomized controlled trials (RCTs) and systematic reviews conducted in controlled settings. However, there is increasing recognition of the importance of real-world evidence (RWE) derived from observational studies, registries, electronic health records, and other sources. Clinical research that generates high-quality RWE to supplement traditional trial data may help address uncertainties identified in HTAs.
5. **Health Economics and Cost-Effectiveness**: HTAs assess the cost-effectiveness of healthcare interventions by comparing the incremental costs and health outcomes associated with different options. Additional health economic research may be needed to better understand the long-term cost-effectiveness implications of interventions, particularly in areas where evidence is limited or conflicting.
6. **Patient-Centered Outcomes**: HTAs often consider clinical endpoints and surrogate markers when evaluating healthcare interventions. However, there is growing recognition of the importance of patient-centered outcomes, including quality of life, patient satisfaction, functional status, and

symptom relief. Clinical research that incorporates patient-reported outcomes and addresses patient preferences may help fill gaps in evidence identified by HTAs.

7. **Emerging Technologies and Innovations**: HTAs may encounter challenges in assessing the value of emerging technologies, novel therapies, or innovative healthcare delivery models due to limited data or uncertainties regarding their effectiveness, safety, or cost-effectiveness. Research focusing on the evaluation of emerging technologies and innovations may be necessary to inform HTAs and support evidence-based decision-making.

Overall, while HTAs themselves do not identify uncovered needs for clinical research in Europe explicitly, the findings and recommendations arising from HTA processes can highlight areas where additional research is needed to address knowledge gaps, improve the quality of evidence, and support informed decision-making in healthcare. Collaboration between HTA agencies, researchers, policymakers, and stakeholders is essential to identify and prioritize research priorities that align with the needs of healthcare systems and populations in Europe.

## 6.5. ANNEX 5. AGENDA WORKSHOP- SUPPLEMENTATION OF ERA4HEALTH SRIA WITH INVESTIGATOR-INITIATED CLINICAL STUDIES


## 6.6. ANNEX 6. SCOPING QUESTIONS WORKSHOP- SUPPLEMENTION OF ERA4HEALTH SRIA WITH INVESTIGATOR INITIATED CLINICAL STUDIES

**Questionnaire for discussion with the experts during the expert workshop for the SRIA supplementation with IICS, break-out sessions**

Context

The ERA4Health partnership focuses on funding research, through Joint Transnational Calls (joining national funding)

ERA4Health was initiated in November 2022 and has already launched 4 Joint Transnational Calls for pre-clinical studies in the areas of interest of the partnership, which are i) Prevention and Public Health strategies, ii) Nutrition- and lifestyle-related-diseases, iii) Cardiovascular diseases, iv) Nano and advanced technologies for disease prevention, diagnostic and therapy.

As part of its mission, ERA4health will also launch calls for Investigator-Initiated Clinical Studies (IICS). A first pilot call will be launched by the end of 2024. In this context, the current version of the Strategic Research and Innovation Agenda (SRIA) needs to be completed to include more information about the objectives of the IICS to be funded.

Please find below the questions that we would like to address during the online workshop that we organize on 07 June 2024 in the context of the update of the SRIA.

*Please keep in mind that:*

- *Calls objectives should consider the added value of the multinational component*
- *The term "investigator-initiated" can be interpreted differently in different countries, especially where the term is considered equivalent to "non-commercial" in reference to industry´s involvement.*

1. What should be the focus of multinational IICS calls in the areas of interest of ERA4Health?
    i. Prevention
    ii. Diagnosis
    iii. Treatment

2. In the frame of ERA4Health areas of interest, what would be the most relevant objectives of the multinational IICS to be funded, among:
    i. Non-interventional studies
    ii. Interventional studies
        1. Academic-driven repurposing studies
        2. Comparative effectiveness
        3. Academic innovation
    iii. Trials within cohorts (TWiCs)
    iv. Other

3. What is the most relevant set up?

- Hospitalized patients
- Outpatients
- Primary care patients

- Healthy volunteers

4. What are the most relevant populations to be included in the multinational IICS calls in the areas of interest of ERA4Health ?

5. Are there any specific underserved population that should be included in the calls for multinational IICS within the areas of interest of ERA4Health?

6. What should be the nature of the health product:

    a. chemical drug,
    b. biopharmaceuticals,
    c. advanced therapy medicinal product,
    d. medical device,
    e. or studies without health product (procedural intervention)

7. What could be the role of industry, if any?