Brussels, 19 May 2025

COST 074/25

DECISION

Subject: Memorandum of Understanding for the implementation of the COST Action "Network for Cardiovascular Pharmacogenomics and Precision Medicine" (CardioPharmaGENET) CA24165

The COST Member Countries will find attached the Memorandum of Understanding for the COST Action Network for Cardiovascular Pharmacogenomics and Precision Medicine approved by the Committee of Senior Officials through written procedure on 19 May 2025.

MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA24165
NETWORK FOR CARDIOVASCULAR PHARMACOGENOMICS AND PRECISION MEDICINE
(CardioPharmaGENET)

The COST Members through the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action, referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any document amending or replacing them.

The main aim and objective of the Action is to establish a multidisciplinary, pan-European network of researchers, stakeholders, and policymakers to harmonize the reporting, analysis, storage, and protection of cardiovascular pharmacogenomic data, creating a centralized knowledge hub and delivering clear recommendations to ensure the equitable and consistent integration of PGx insights into clinical practice. This will be achieved through the specific objectives detailed in the Technical Annex.

The present MoU enters into force on the date of the approval of the COST Action by the CSO.

OVERVIEW

Summary
CardioPharmaGENET aims to advance personalized medicine in cardiovascular care by leveraging pharmacogenomics (PGx) to optimize drug therapies. In cardiovascular medicine, this approach is especially critical, given the significant patient variability in drug responses to therapies. The main goal is to establish a pan-European network that addresses several key challenges that hinder the widespread adoption of PGx in cardiovascular care. These challenges include the lack of a centralized knowledge hub for clinicians and policymakers, insufficient integration of pharmacogenomics into clinical practice, and inconsistent policy frameworks across Europe. The project also seeks to utilize AI and machine learning to streamline the analysis of large-scale genomic data and enhance clinical decision-making.
The initiative will form five working groups to tackle these issues: WG1 will evaluate the current landscape of cardiovascular PGx, identifying key gaps in research, clinical integration, and available resources; WG2 will develop optimized guidelines for applying PGx in cardiovascular therapies, focusing on patient stratification based on genetic and demographic profiles; WG3 will focus on advancing digital and AI tools to improve PGx data analysis and implementation in clinical settings; WG4 will analyze regulatory frameworks across Europe, proposing policy changes to facilitate seamless integration of PGx into healthcare systems; WG5 will handle communication, dissemination, and stakeholder engagement, ensuring that findings and guidelines are accessible to all stakeholders, including clinicians, researchers, and policymakers. By addressing these challenges, the project will help bridge the gap between PGx research and clinical practice, improving cardiovascular patient outcomes and promoting equitable healthcare access across Europe.

Areas of Expertise Relevant for the Action	**Keywords**
● Clinical medicine: Cardiac and Cardiovascular systems ● Health Sciences: Health services, health care research ● Medical biotechnology: Genomics, comparative genomics, functional genomics ● Biological sciences: Molecular biology and interactions ● Biological sciences: Ethics of biological sciences	● pharmacogenomics ● cardiovascular diseases ● personalized medicine ● clinical practice

Specific Objectives
To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination
● To standardize research methodologies across Europe to improve the comparability of pharmacogenomic studies, ensuring that variant interpretation and clinical guidelines are consistent across countries
● To establish a comprehensive, centralized European pharmacogenomics database, accessible to clinicians, researchers, and policymakers, to consolidate fragmented data and improve decision-making
● To revise and implement AI-based tools to streamline the analysis of large-scale pharmacogenomic data, improving the precision and speed of clinical decision- making while ensuring compliance with the EU AI Act
● To collaborate with European policymakers to propose uniform pharmacogenomic regulations and standards, to facilitate broader clinical implementation

Capacity Building
● To promote cooperation among European and international researchers, focusing on knowledge

exchange and best practices in pharmacogenomics
● To provide training, mentorship, and research opportunities for YRIs, particularly from underrepresented regions (ITC countries), through programs such as STSMs and training schools
● To equip healthcare providers and researchers with the necessary tools and knowledge through targeted webinars and roundtable discussions to facilitate the integration of pharmacogenomics into cardiovascular care

TECHNICAL ANNEX

1. S&T EXCELLENCE

1.1. SOUNDNESS OF THE CHALLENGE

1.1.1. DESCRIPTION OF THE STATE OF THE ART

The Global Burden of Cardiovascular Diseases Collaboration reported global cardiovascular disease (CVD) mortality at 19.8 million deaths in 2022, reflecting an ongoing rise due to aging populations and preventable risk factors like high blood pressure, poor diet, and air pollution. Eastern Europe remains a hotspot for cardiovascular mortality, with some of the highest rates, while Western Europe fares better [1]. Pharmacogenomics (PGx) can play a significant role in managing CVDs by tailoring treatments to a patient's genetic profile, improving drug efficacy, reducing adverse effects, and optimizing therapeutic outcomes.

Personalized medicine offers numerous advantages to both the patient and the clinician, including enhanced diagnostic accuracy and the ability to identify the most effective treatment options based on a patient's unique characteristics. It also enables targeted therapies that improve the chances of successful outcomes while minimizing side effects. Additionally, personalized medicine facilitates better disease prevention, boosts patient engagement, lowers healthcare costs, and fosters research and innovation. At the core of a personalized approach to the patient lies **pharmacogenomics (PGx)**. Abandoning the “one-size-fits-all” model of therapy prescription that was employed before, this field holds a great promise of **decreasing the frequency, consequences, and costs associated with the adverse drug reactions (ADRs), optimizing the selection of the most suitable therapy regimen for each patient, and achieving the best possible results [2].** PGx-guided treatments have been shown to reduce ADRs by up to 30%. In a European study using a 12-gene panel, PGx-guided prescriptions lowered ADR rates to 21%, compared to 28% in the control group. Additionally, PGx interventions decreased hospital stays by 15% and emergency room visits by 7%, yielding significant cost savings. For Medicare populations, these savings amounted to $315 per member per month, while corporate programs reduced healthcare costs by $128 per member monthly, proving PGx's wide benefits [3].

Furthermore, successful incorporation of PGx into clinical practice is associated with a number of **health-related and economic benefits.** In a very recent study from the USA, it was shown that incorporating PGx testing in overall health care of the self-insured employee population resulted in 39% fewer inpatient and 39% less emergency department visits, while outpatient visits increased by 21%, indicating a move away from costly acute care towards preventive care. Pharmacy costs increased slightly by $26.30 per member per month, but there were reductions in total medical costs, particularly in inpatient settings [4].

In cardiovascular medicine, PGx is especially important, considering **the number of drugs and conditions** that would benefit from regular implementation of genetic testing. Despite development of direct oral anticoagulants (DOACs), **warfarin** remains indicated for a range of patients due to its availability and low cost. However, the dosage, therapeutic effect, and initiation of warfarin therapy depend on *CYP2C9* and *VKORC1* genotyping, whereby interindividual patient variability can be as high as 20-fold [5]. **Clopidogrel** therapy is severely influenced by *CYP2C19* genotype. *SLCO1B1* analysis and therapy guided by it optimize treatment in terms of dosage and minimize the risk of **statin**- associated myopathy [6]. **Beta-blockers,** such as carvedilol, metoprolol, nebivolol, and propranolol, are all metabolized by *CYP2D6*, and their dosing depends on this enzyme [7].

The Clinical Pharmacogenetic Implementation Consortium (CPIC) produces its guidelines, based on rigorously reviewed evidence, that are published in the *Clinical Pharmacology and Therapeutics,* the journal of the American Society for Clinical Pharmacology and Therapeutics, and are accessible on CPIC's website (https://cpicpgx.org). These guidelines aim to guide clinicians on translating an individual patient's genotype into specific phenotypic drug responses, thereby advancing personalized medicine significantly. In the USA, all drugs with PGx guidelines are regulated by **the Food and Drug Administration (FDA)** and guidelines are curated and presented through the **PharmGKB** project (https://www.pharmgkb.org/), the most authoritative and inclusive PGx platform worldwide. In Europe, **the European Medicines Agency (EMA)** supports the integration of PGx into drug development and post-market safety by issuing guidelines and regulatory advice. It ensures that PGx data is considered in clinical trials and medicinal product evaluations, with a focus on optimizing treatment efficacy and minimizing adverse reactions. The EMA also plays a role in post-marketing surveillance to monitor genetic variability in drug responses. However, the extent of guideline harmonization and variant

annotation is still lagging behind the work performed in the USA. While EMA issues **guidelines and scientific recommendations** for the inclusion of pharmacogenetic data in drug development and labeling, it has no legislative power in this regard. In its Guideline on Good Pharmacogenomic Practice published in 2018 [8], EMA gives an overview of the testing process, without variant classification and annotation or recommendations for implementation in practice.

Apart from this, several other obstacles towards successful implementation of PGx in clinical practice have been observed, such as lack of clinical utility perception, since many healthcare providers are concerned that PGx disrupts traditional care pathways, insufficient national regulations and poor integration into healthcare systems, infrastructure limitations, including inadequate electronic health record (EHR) systems that fail to support PGx data, a lack of resources and expertise, with many clinicians needing more training to effectively interpret and apply genetic data, and the absence of robust national databases for PGx information, which results in inconsistent application and understanding across different regions [9].

Based on those identified benefits and issues associated with PGx implementation in clinical practice, it is timely to create an interdisciplinary pan-European network that will address specific challenges and collectively work towards fulfilling the objectives related to easier incorporation of PGx in cardiovascular medicine in Europe.

1.1.2. DESCRIPTION OF THE CHALLENGE (MAIN AIM)

The Action addresses several pressing challenges that currently limit the effective use of PGx in cardiovascular care across Europe. While PGx offers the potential to personalize treatments and significantly improve patient outcomes, especially in cardiovascular diseases, the integration of these innovations into clinical practice remains fragmented and slow. The challenges we seek to address are rooted in gaps related to clinical implementation, policy alignment, and technological advancements. European Society of Cardiology Working Group on Cardiovascular Pharmacotherapy points out variations in population demographics, resource availability, expertise, and legal frameworks between countries, as the main factors which contribute towards delayed adoption of PGx in clinical practice, in addition to the advanced education of the clinical workers and building digital infrastructure [10]. Similar conclusions were generated in the UK, whereby the UK National Health Service (NHS) faced challenges in implementing genomic medicine in clinical practice [11].

Based on this, we have defined the following challenges that need to be addressed:

Challenge 1: Lack of comprehensive pharmacogenomic research specific to cardiovascular drug response. Current PGx data often stem from broader studies, limiting our understanding of how genetic variations uniquely impact cardiovascular medications. This gap hinders the ability to fully personalize treatments, as many cardiovascular drugs still lack validated PGx guidelines, reducing the potential benefits of tailored therapy in managing cardiovascular diseases.

Challenge 2: Lack of a centralized knowledge hub for clinicians and policymakers. The absence of a centralized, accessible knowledge repository for pharmacogenomic guidelines and clinical best practices hampers the widespread adoption of PGx. Clinicians, researchers, and policymakers often rely on fragmented and disparate resources, leading to inconsistency in how PGx is understood and applied in clinical settings.

Challenge 3: Insufficient integration of pharmacogenomics into clinical practice. Despite numerous research initiatives exploring the potential of PGx, its translation into clinical settings has been limited. Many clinicians still lack the necessary tools and training to apply PGx insights in patient care, causing a gap between scientific advancements and practical applications. This limits the ability of healthcare providers to deliver personalized treatments based on genetic profiles.

Challenge 4: Need for more efficient use of AI in pharmacogenomics. AI has the potential to revolutionize how PGx data is analyzed and applied in clinical settings. However, there is currently an underutilization of AI technologies in this field. More efficient use of AI tools is needed to analyze large-scale genomic data, streamline clinical decision-making, and support the harmonization of guidelines across Europe. Ensuring that AI applications adhere to the regulatory standards outlined in the EU AI Act will also be critical to maintaining trust and ethical standards in this evolving landscape.

Challenge 5: Inconsistent policy frameworks across Europe. While individual European countries are making strides in pharmacogenomics, the regulatory frameworks remain fragmented. The lack of a unified, Europe-wide approach to policy and regulation around PGx limits its implementation. This inconsistency creates disparities in patient access to personalized medicine and hinders the scale of PGx integration in cardiovascular care.

Challenge 6: Gaps in collaboration and knowledge exchange. Numerous initiatives and consortia focus on research or PGx implementation in specific areas of medicine, but few efforts are coordinated across Europe. International collaboration, particularly between the USA and Europe, is underutilized,

slowing progress toward harmonized guidelines and policy reforms.
Based on these facts, **the primary aim of CardioPharmaGENET is to provide a multidisciplinary, international, and inclusive pan-European network of researchers, stakeholders, and policymakers in order to harmonize how pharmacogenomic guidelines are reported, analyzed, stored, and protected, in order to produce a centralized knowledge hub of cardiovascular PGx data across Europe and offer recommendations for policymakers, ensuring that PGx insights are consistently and equitably integrated into clinical practice.**

1.2. PROGRESS BEYOND THE STATE OF THE ART

1.2.1. APPROACH TO THE CHALLENGE AND PROGRESS BEYOND THE STATE OF THE ART

To address the key challenges of PGx implementation in cardiovascular care across Europe, the Action takes a **multi-faceted approach that tackles the barriers of resource variation, expertise gaps, digital infrastructure needs, and disparities in health equality, while promoting collaboration and upskilling of healthcare professionals.**
The lack of sufficient expertise in PGx within the current clinical workforce is a significant challenge (challenges 2 and 6). To address this, CardioPharmaGENET focuses on **extensive training programs**, including **Training Schools, webinars, and Short-term Scientific Missions (STSMs).** These will provide practical, hands-on learning opportunities for healthcare professionals across Europe. The training will focus on equipping researchers, clinicians, and industry representatives with the knowledge to integrate PGx into cardiovascular treatment plans, helping to close the expertise gap and enable more widespread use of personalized medicine. This way, we will foster a **cross-border exchange of knowledge** to allow healthcare providers to gain insights from leading institutions and apply those lessons in their local contexts, further standardizing the clinical application of PGx.
A critical enabler of PGx in clinical settings is the **digital infrastructure required to handle large-scale genomic data** and integrate it into clinical decision-making (challenge 4). To address this, CardioPharmaGENET focuses on **advancing digital support tools** that can streamline PGx data analysis and application in real time. This includes collaborating with **artificial intelligence (AI), machine learning (ML) and database development experts** to produce an user-friendly platform for, at the first place, clinicians and industry representatives, helping them make data-driven decisions at the point of care. These tools will comply with the **EU AI Act** to ensure the ethical, transparent, and responsible use of AI in healthcare. The diversity in healthcare systems, resources, and legal frameworks across European countries presents one of the primary barriers to a unified approach for PGx in cardiovascular care (challenge 5). To overcome this, the Action will focus on **activities towards harmonizing PGx guidelines at the EU level**, ensuring consistency in clinical applications across the EU and beyond. CardioPharmaGENET will establish a central hub of knowledge that provides clear, evidence-based recommendations, so that clinicians in resource- limited settings can access the same tools as those in more advanced healthcare systems. By working closely with policymakers, the Action aim is to propose **policy changes that align regulatory frameworks**, making PGx integration more seamless across borders. This harmonization effort will address existing differences in how pharmacogenomics is applied, helping reduce disparities in patient outcomes based on geography or resources and advocating for more equitable healthcare across Europe.
One of the central goals of CardioPharmaGENET is to ensure that PGx implementation does not widen the existing gaps in healthcare across different populations (challenges 1 and 5). By setting up the groundwork towards harmonizing guidelines, increasing awareness, and improving access to PGx resources, the network will work to ensure equitable access to personalized treatments. Our policy recommendations will focus on reducing disparities and ensuring that even underserved or resource-limited areas can benefit from the advances in pharmacogenomics. Finally, the Action will foster collaboration between key European and U.S. PGx initiatives, including partnerships with the **Ubiquitous Pharmacogenomics (U-PGx)** project, the **Clinical Pharmacogenetics Implementation Consortium (CPIC)**, and other international consortia (challenge 6). This will promote the exchange of best practices and innovative approaches, ensuring that Europe remains at the forefront of PGx integration.
Through these strategies, CardioPharmaGENET will address the pragmatic barriers to PGx implementation and accelerate its adoption across Europe, ultimately improving cardiovascular care outcomes.

1.2.2. OBJECTIVES

1.2.2.1. Research Coordination Objectives

Objective no.	Objective name	Challenge addressed	Target group	KPIs
1	To standardize research methodologies across Europe to improve the comparability of pharmacogenomic studies, ensuring that variant interpretation and clinical guidelines are consistent across countries	C1, C2, C3	Researchers and academia Industry representatives	Number of peer-reviewed OA publications Number of produced reports and documents Number of organized events by WG1 and WG2
2	To establish a comprehensive, centralized European pharmacogenomics database, accessible to clinicians, researchers, and policymakers, to consolidate fragmented data and improve decision-making	C1, C2	Researchers and academia Industry representatives Policymakers	Established platform on the Action website Number of entries in the portal in different categories (publications, infrastructure, methods, research teams, genetic markers, etc.) Number of publication outputs
3	To revise and implement AI-based tools to streamline the analysis of large-scale pharmacogenomic data, improving the precision and speed of clinical decision-making while ensuring compliance with the EU AI Act	C4	Researchers and academia	Number of reviewed algorithms in use Number of publication outputs and events by WG3
4	To collaborate with European policymakers to propose uniform pharmacogenomic regulations and standards, to facilitate broader clinical implementation	C5	Policymakers Industry representatives	Produced Policy Brief as an Action output Number of meetings with policymakers Number of participants in the roundtable discussion

1.2.2.2. Capacity-building Objectives

Objective no.	Objective name	Challenge addressed	Target group	KPIs
5	To promote cooperation among European and international researchers, focusing on knowledge exchange and best practices in pharmacogenomics	C6	Researchers and academia	Number of meetings between the representatives Number of joint publications Number of joint projects Number of Consortium members from countries

				other that COST Full Members
6	To provide training, mentorship, and research opportunities for YRIs, particularly from underrepresented regions (ITC countries), through programs such as STSMs and training schools	C6	YRIs and scientists from ITCs	Number of YRIs attending the Training Schools Number of YRIs attending the STSMs Number of participants from ITCs in Training Schools and STSMs Number of leadership positions occupied by YRIs, ITC representatives and women
7	To equip healthcare providers and researchers with the necessary tools and knowledge through targeted webinars and roundtable discussions to facilitate the integration of pharmacogenomics into cardiovascular care	C3, C6	Clinicians Pharmaceutical industry Patients	Number of attendees at targeted webinars Number of clinics/hospitals reporting easier integration of PGx into their daily practice Number of clinicians and industry representatives participating in research activities related to our Action

2. NETWORKING EXCELLENCE

2.1. ADDED VALUE OF NETWORKING IN S&T EXCELLENCE

2.1.1. ADDED VALUE IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

The primary aim of the Action is to enhance the implementation of cardiovascular PGx through a comprehensive review of existing guidelines, evidence-based recommendations, and policy proposals designed to facilitate the integration of personalized medicine into clinical practice. The **COST Action framework** is particularly well-suited for this initiative, as it promotes interdisciplinary collaboration and knowledge sharing among diverse stakeholders across Europe. The focus of the Action is novel and consists of synthesizing existing evidence and best practices while engaging a wide range of participants, including researchers, clinicians, genetic counselors, and industry representatives, to create a cohesive strategy for implementing PGx. This collaborative approach will not only address current gaps in the application of pharmacogenomics in clinical practice, but also foster innovation and adaptability within healthcare systems, ultimately improving patient outcomes in cardiovascular care.
The Action aligns with several **Sustainable Development Goals (SDGs).** Namely, it supports **SDG 3: Good Health and Well-being** by improving cardiovascular health outcomes through personalized treatment strategies. By fostering innovation in PGx, it contributes to **SDG 9: Industry, Innovation, and Infrastructure**, advancing healthcare solutions. Additionally, by engaging diverse stakeholders and fostering international collaboration, the Action promotes **SDG 17: Partnerships for the Goals**. Lastly, by advocating equitable access to these innovations, it supports **SDG 10: Reduced Inequalities**, ensuring the benefits of precision medicine are accessible to all.
CardioPharmaGENET also aligns with several key **Horizon Europe Health 2025-2027** and **EU4Health** priorities by focusing on improving healthcare systems and fostering overall collaboration. Specifically, we address the Horizon priority of **reducing the burden of non-communicable diseases (NCDs)** through the overall general aim of the Action. By working on **equal access to healthcare** and facilitating the adoption of PGx into clinical practice, the network also supports **health system resilience** and contributes to reducing healthcare inequalities, in line with **EU4Health** objectives. Furthermore, through collaboration and the creation of policy frameworks, the Action contributes to both programmes' aims of strengthening **digital health**, fostering the safe deployment of **AI**, and ensuring evidence-based, patient-centered care that improves cardiovascular outcomes across Europe and beyond. Furthermore, in line with the **AI Act**, we will ensure the responsible integration of AI technologies by reviewing existing AI-driven tools in cardiovascular

pharmacogenomics, focusing on compliance with safety and ethical standards, as well as protection of patient data protection. This includes supporting AI's safe use in clinical settings for personalized treatment recommendations, while adhering to the AI Act's requirements for transparency, risk management, and bias mitigation, ensuring patient trust and system reliability. The Action efforts align well with several previously funded COST Actions, too. CardioPharmaGENET builds upon the progress made by previous collaborations, such as **CA17129 CardioRNA,** which explored means of translating transcriptomics research in clinical practice in cardiovascular medicine to improve personalized approach to each patient, **CA18216 VascAgeNet**, which focused on use of vascular aging measures to reduce the burden of CVDs, and **CA21153 AtheroNET**, which employed multiomics approach in prevention, diagnosis, and treatment of atherosclerotic cardiovascular disease. Finally, CIG application **IG16225 IMproving Preclinical Assessment of Cardioprotective Therapies** was working towards improved cardioprotection using innovative preclinical approaches. However, while these initiatives contributed significantly to cardiovascular research and care, they did not directly address the need for harmonizing pharmacogenomic guidelines and means of reporting the research across Europe, nor did they provide a centralized knowledge repository. CardioPharmaGENET seeks to fill this gap by integrating pharmacogenomics into clinical practice and promoting a unified policy approach at the EU level.

The Action will foster and strongly promote collaboration with already existing successful European and international initiatives in pharmacogenomics by engaging with key consortia and initiatives. Significant partners will include the **Ubiquitous Pharmacogenomics (U-PGx)** project, which focuses on implementing PGx testing across multiple European countries to optimize treatment strategies. The **EU-PIC (European Pharmacogenomics Implementation Consortium)** is another essential partner, promoting the integration of pharmacogenomics into routine clinical practice across Europe. Additionally, we will connect with the **Clinical Pharmacogenetics Implementation Consortium (CPIC)**, which plays a pivotal role in establishing guidelines and standards for the clinical application of PGx. By leveraging these established networks, the Action aims to share insights, harmonize approaches, and enhance the implementation of PGx in clinical settings across both continents, ultimately improving patient outcomes and fostering innovation in personalized medicine.

There are numerous projects and initiatives which are dedicated to researching and implementing PGx in clinical practice across various medical fields. **However, a significant gap remains in efforts aimed at providing a centralized knowledge hub and harmonizing guidelines across Europe.** While these initiatives successfully advance PGx, they often operate in silos, focusing on localized implementations without a unified framework. This lack of coordination results in inconsistent practices and hinders the development of a centralized knowledge repository. Our initiative seeks to address this gap by advocating for the establishment of centralized PGx knowledge in cardiovascular medicine across Europe, to make it easier and more feasible to ensure continuous communication, information flow, more informed decision making, and the dialogue between the researchers, industry and policymakers, setting up the groundwork for the harmonization of PGx guidelines and policies at European level, ensuring a cohesive approach to integrating pharmacogenomics into clinical care.

2.2. ADDED VALUE OF NETWORKING IN IMPACT

2.2.1. SECURING THE CRITICAL MASS, EXPERTISE AND GEOGRAPHICAL BALANCE WITHIN THE COST MEMBERS AND BEYOND

This initiative draws on a diverse range of experts from different fields and geographic regions, which is vital to ensure that the created guidelines can be effectively implemented across Europe. The Action includes specialists from **pharmacology, genetics, cardiology, molecular biology, clinical medicine, bioinformatics, biomedical engineering, psychology, health economics, public health policy, and patient advocacy,** providing the necessary multi-disciplinary perspective to tackle the complexity of PGx in clinical practice. Pharmacologists and geneticists will lead the way in understanding the molecular basis of drug responses, while cardiologists and clinical researchers focus on the practical integration of PGx into clinical workflows. Bioinformaticians and biomedical engineers will manage the complex genetic data analysis required for personalized therapies, while health economists will evaluate the financial implications of PGx implementation. Additionally, public health experts will ensure the Action's recommendations fit the broader healthcare policy landscape, and patient representatives will help shape patient-centered approaches.

To ensure geographical balance, the Action prioritizes the involvement of participants from the **Inclusiveness Target Countries (ITCs)**. This will ensure that less-represented regions gain access to cutting-edge PGx knowledge, reducing healthcare inequalities, but also to extend the EU-based recommendations to non-EU member countries.

In support of this **geographical and disciplinary diversity,** the Action will be promoted in major European conferences in cardiovascular medicine and genetics, through the **ITC Grants and Dissemination Conference Grants,** including the following meetings that were already mapped: European Society of Cardiology (ESC) Congress, European Society of Human Genetics (ESHG) Conference, European Association of Preventive Cardiology (EAPC) EuroPrevent Congress, European Society of Pharmacogenomics and Personalized Therapy (ESPT) Annual Congress, HUGO International Human Genome Meeting (HGM), and International Society of Applied Biological Sciences (ISABS) Conference, whereby many of these conferences and meetings are occasionally or regularly held in ITCs.

To ensure the work produced by the network aligns with international standards, the Action plans to collaborate with key global pharmacogenomics organizations, particularly the **Pharmacogenomics Knowledgebase (PharmGKB) and the Clinical Pharmacogenetics Implementation Consortium (CPIC),** both based in the USA, through their representatives' participating in the Action events, trainings schools and webinars as speakers. These organizations provide crucial resources for PGx, including curated genetic data and clinical guidelines that we can incorporate into our European recommendations. By collaborating with PharmGKB and CPIC, the Action will benefit from the latest global advancements in PGx, while also contributing to CardioPharmaGENET network findings and insights from the European healthcare context. This is particularly important considering rapid development of the field in the USA, evident in increased adoption across healthcare systems, a streamlined approach towards the PGx studies through the U.S. Food and Drug Administration (FDA), and the efforts of the American Medical Association (AMA) in education of practitioners with the purpose of easier incorporation of PGx data into the clinical practice [12]. In Australia, extensive collaborations with PharmGKB and CPIC have already been established with the purpose of standardization of guidelines and more effective education of professionals in the field [13].

The Action will maintain close communication with European bodies, including the **European Commission**, to ensure that the recommendations created by the network align with broader EU policies on personalized medicine and healthcare innovation. This will be enabled by dedicated work of the network members, as well as through activities such as **COST Connect meetings.** Such dialogue will help us influence policy decisions and promote the integration of PGx in healthcare systems across Europe. By presenting our work at high-level conferences and engaging with policymakers through the **Policy Brief** and **roundtable discussions**, we aim to promote PGx as a potential cornerstone of future healthcare strategies in cardiovascular medicine.

2.2.2. INVOLVEMENT OF STAKEHOLDERS

The Action engages a broad range of stakeholders to enhance the impact of PGx in cardiovascular medicine. **Researchers and academia representatives** will benefit from access to novel information and collaborative opportunities, advancing the field of precision medicine. **Clinicians** will use our findings to get more thorough education and potentially develop personalized treatment strategies, improving patient outcomes. **Genetic counselors** will play a crucial role by providing expertise in interpreting genetic data and guiding personalized treatment decisions, ensuring that patients and clinicians can fully leverage the benefits of PGx advancements in cardiovascular care. **Pharmacy representatives** will help develop our recommendations and prepare the deliverables, in order to structure the PGx guidelines to optimize medication use, and they represent the core of our network. **Patient organizations** will ensure our research remains patient-centered and addresses real-world needs. **Policymakers and NGOs** will support translating research into policy recommendations, promoting equitable access to PGx innovations and equal opportunities for all. **Industry representatives, including relevant SMEs** will benefit from the analysis of biomarkers and drug targets, while **international collaborations** will enable global knowledge sharing.

To ensure **continuous stakeholder engagement,** the Action will implement various activities. **Multi-disciplinary working groups** will be established at the beginning of the Action to encourage continuous collaboration among researchers, clinicians, and industry partners. STSMs will facilitate hands-on one-on-one collaboration, while Training Schools will be open to equip stakeholders with essential PGx knowledge. **Regular targeted webinars** will provide updates on the latest research, while being specifically designed for different stakeholder groups, and a **dedicated stakeholder conference** will foster dialogue between key groups. **Roundtable discussions** will ensure that feedback is integrated, keeping the Action aligned with stakeholder needs and maximizing its impact. In order to specifically address the **needs of patients and caregivers,** separate focus group meetings will be organized to integrate patient-centered approaches and ensure research addresses real-world clinical needs.

Apart from this, the Action plans additional, specialized activities aimed exclusively at engaging and

keeping the stakeholders associated with the Action will implement regular feedback loops through surveys or open forums, ensuring stakeholders can share their concerns and suggestions throughout the Action. Among the educational activities of the Action, we will organize stakeholder-specific training programs and demonstrations to provide tailored education based on the needs of industry, academia, and healthcare professionals. Public-private partnerships will be promoted to encourage industry engagement in research and development phases. Co-authorship opportunities on research publications and reports will be offered to the stakeholder representatives who contribute significantly to the Action.
CardioPharmaGENET will also collaborate with the **Enterprise Europe Network (EEN)** to engage small and medium-sized enterprises (SMEs), fostering their involvement in the development and application of innovative pharmacogenomics solutions. Finally, social media and professional networks like LinkedIn and ResearchGate will be widely used to keep stakeholders informed and engaged through ongoing updates.

3. IMPACT

3.1. IMPACT TO SCIENCE, SOCIETY AND COMPETITIVENESS, AND POTENTIAL FOR INNOVATION/BREAKTHROUGHS

3.1.1. SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS (INCLUDING POTENTIAL INNOVATIONS AND/OR BREAKTHROUGHS)

Overall, the Action aim is to enhance patient care through personalized medicine by facilitating networking, conducting reviews, making recommendations, developing innovative solutions, and understanding the economic implications of PGx. This initiative promises significant impacts across scientific, technological, and socioeconomic domains, targeting various stakeholders including clinicians, researchers, policymakers, and patients.
Scientific impacts: **(1) Advancement of knowledge in pharmacogenomics:** The comprehensive literature review and analysis of current practices will clarify the research landscape in PGx. **Target groups:** Researchers and healthcare providers will benefit from evidence-based recommendations that can be shared across the European scientific community. **(2) Development of clinical practice guidelines:** By summarizing existing guidelines and formulating new recommendations, this COST Action will enhance the integration of PGx into clinical settings. **Target groups:** Healthcare professionals will have access to standardized guidelines that ensure effective utilization of PGx information for patient stratification and treatment optimization. **(3) Facilitation of multidisciplinary collaboration:** Emphasizing networking among diverse stakeholders will foster interdisciplinary research efforts. **Target groups:** Geneticists, pharmacologists, genetic counselors, and health economists will stimulate innovative methodologies and approaches to complex clinical questions in pharmacogenetics.
Technological impacts: **(1) Innovation in computational tools and data management:** Identifying technological constraints and developing a centralized data-sharing platform will represent a significant technological advancement. **Target groups:** Researchers and clinicians will access a wealth of pharmacogenomic data, leading to innovations in ML and AI that improve drug response predictions. **(2) Enhancement of clinical decision support systems (CDSS):** Better integration of PGx data into clinical workflows will facilitate the development of sophisticated CDSS. **Target groups:** Clinicians will benefit from tailored recommendations based on patient-specific genetic data, enhancing patient care by reducing adverse drug reactions and optimizing therapeutic efficacy. **(3) Promotion of Open Access (OA) data sharing:** Advocating for OA to research outputs will encourage transparency and collaboration. **Target groups:** The scientific community will benefit from a centralized repository for pharmacogenetic data that facilitates knowledge transfer and validation of findings.
Socioeconomic impact: **(1) Reduction in healthcare costs:** Implementing pharmacogenomic testing can reduce adverse drug reactions and ineffective therapies, leading to decreased hospitalizations. **Target groups:** Policymakers and healthcare providers will be informed about the financial benefits of personalized medicine strategies. **(2) Improved patient outcomes and quality of life:** Optimizing treatments based on genetic profiles will enhance patient outcomes and satisfaction, while improving the patient privacy protection standards. **Target groups:** Patients will experience better adherence and improved health status due to personalized care. **(3) Support for health policy development:** Insights generated from this COST Action will inform policymakers about integrating pharmacogenetics into clinical practice. **Target groups:** Health policymakers will be better equipped to

promote personalized medicine and enhance patient care.

3.2. MEASURES TO MAXIMIZE IMPACT

3.2.1. KNOWLEDGE CREATION, TRANSFER OF KNOWLEDGE AND CAREER DEVELOPMENT

The focus of the Action is on the knowledge evaluation and presentation to the stakeholders, transfer of skills and expertise, and career development for Young Researchers and Innovators (YRIs). This structured approach promotes interdisciplinary collaboration, encourages YRIs, and ensures wide dissemination of findings.

Knowledge creation will be enabled by focusing on how PGx can optimize cardiovascular therapies by conducting reviews and gathering data on existing practices, genetic markers, and clinical guidelines across Europe. WG1 will focus on mapping the current R&D landscape and clinics employing PGx, while WG2 will develop and assess pharmacogenomic guidelines, genetic markers, and study design. WG3 will focus on technological advancements like AI/ML integration in clinical practice, while WG4 will examine policy and regulatory frameworks. This structure ensures that the knowledge created is comprehensive and relevant to clinical applications, technological innovation, and regulatory improvement. The collaborative environment, driven by researchers from across Europe, **ensures that the most recent findings in PGx are consolidated and made available to clinical and research institutions.** This knowledge will be disseminated in the form of reports, summary tables, scientific publications, position papers, and policy recommendations, all aimed at improving cardiovascular care across Europe.

Transfer of knowledge will be facilitated through various channels, ensuring broad engagement with stakeholders. A central component of this will be the Action website, which will serve as a hub for sharing updates, publications, and data, through a specialized platform. Additionally, Management Committee (MC) and Working Group (WG) meetings, webinars, Training Schools, and Short-term Scientific Missions (STSMs) will provide direct knowledge transfer opportunities to researchers and clinicians. The structure of the Action ensures that communication flows between all WGs and stakeholders. For example, WG5 and the Science Communication Coordinator (SCC) will oversee communication and dissemination efforts, including updates on social media, newsletters, Action flyers and organizing an Action stakeholder conference and a round table event within the WG4 framework. These events will serve as a key strategy for engaging not only researchers but also policymakers, industry representatives, and patient advocacy groups, ensuring that the knowledge generated is effectively transferred to those who can implement it. Finally, knowledge transfer will be enabled by Action presentations at numerous conferences organized by the third parties or even entire parallel sessions, which will promote the Action. In all these efforts, special attention will be dedicated to participants from the Inclusiveness Target Countries (ITCs).

Career development is another significant priority of the Action, aimed at YRIs, particularly those affiliated to institutions from ITCs. The Action structure promotes their involvement through leadership opportunities in the WGs and science communication team, and provides support through mentorship and training initiatives. Furthermore, the network is planning to establish **the Young Researcher and Innovators (YRI) Committee** at the beginning of the Action implementation, to ensure that the needs of YRIs will be promoted throughout the Action. The specific opportunities for YRIs will include three Training Schools (more detail given in Section 4), providing hands-on experience in applying PGx in clinical practice, data analysis, and bioinformatics, as well as STSMs, which will be available through at least three out of four years of the Action timeframe, will allow YRIs to collaborate with leading European institutions, enhancing their skills and expanding their professional networks. The Action will also facilitate advanced knowledge absorption through YRI participation in webinars and preparation of high-quality publications. Each annual MC meeting will feature a dedicated YRI session, whereby they will be given an opportunity to present their recent research to the network and promote their success. MC meetings will regularly contain briefs from the YRI Committee, voicing the needs of YRIs in the network. Finally, the Action is planning to reserve at least 50% of leadership positions for women and YRIs, to catalyze faster and more efficient career development in these target groups.

3.2.2. PLAN FOR DISSEMINATION AND/OR EXPLOITATION AND DIALOGUE WITH THE GENERAL PUBLIC OR POLICY

The **scientific and clinical communities** are central to the uptake of PGx applications in clinical practice and will be targeted through high-quality OA publications, produced through systematic reviews and evidence-based reports. These papers will document the state-of-the-art in PGx and its

application in cardiovascular treatment optimization. Moreover, the Action will feature scientific conferences, webinars, and roundtable discussion to foster knowledge exchange and enable direct engagement among researchers and clinicians.
Engagement with **policymakers and regulatory bodies** will be a focus of the Action, to ensure that the scientific conclusions will be communicated to this group of stakeholders. The Action will produce the Policy Brief and organize specialized round table discussion aimed at presenting recommendations on integrating PGx into cardiovascular treatment guidelines. These efforts will emphasize the potential cost savings and improved patient outcomes that PGx-guided therapies can offer, but also present current legislation in EU and non-EU countries. The aim is to start a dialogue related to the importance of harmonization of PGx implementation guidelines across Europe and future efforts which will be required to address the regulatory aspect.
Engaging with the **general public** is critical for raising awareness and ensuring widespread acceptance of PGx. The Action will maintain an active online presence through its website, which will be designed to present simplified, easy-to-understand content about the benefits of PGx in cardiovascular treatment. Regular updates, success stories, and educational materials will be shared through social media channels and newsletters targeted at non-expert audiences, **including patients and, especially, patient advocacy groups** as the bridge between the Action and patients, as the end-users. Educational online flyers will be produced for patients, caregivers and patient groups, in order to ensure knowledge transfer and exploitation of the Action efforts in the broader community.
The Action will also collaborate with the **pharmaceutical and healthcare industries,** using dissemination tools to promote the economic and clinical benefits of PGx-guided therapies. Webinars, case-study demonstration activities, roundtable discussion, and the stakeholder conference with industry representatives will ensure that the insights generated are shared with those involved in drug development and healthcare delivery.
The **long-term sustainability of the Action's outputs** will be ensured through the website and its embedded PGx platform, which will remain active for at least five years after the Action ends. This platform will serve as a hub for knowledge dissemination and a resource for healthcare professionals, researchers, and policymakers. In addition, the social media channels will continue to provide updates on the ongoing developments in PGx and cardiovascular medicine, ensuring that stakeholders remain engaged with the Action outputs. The exploitation of Action outcomes will focus on transforming the knowledge generated into practical applications that can be integrated into clinical practice. By maintaining its dissemination activities, the Action will ensure the long-term use and exploitation of its findings, promoting PGx as a standard tool in cardiovascular treatment.
In order to achieve this, the Action will apply for the CIG (the COST Innovators Grant) and will engage in relevant COST Connect events, in order to ensure the funding and the human resources for ensuring the long-term sustainability of the Action outputs. Outside this, the Action will generate new joint research projects between the network members on topics of this COST Action to continue with our efforts.

4. IMPLEMENTATION

4.1. COHERENCE AND EFFECTIVENESS OF THE WORK PLAN

4.1.1. DESCRIPTION OF WORKING GROUPS, TASKS AND ACTIVITIES

WG1 - Current landscape and status of PGx in cardiovascular medicine
The aims of this WG are to: **(1) Evaluate the existing R&D landscape in Europe,** focusing on the capabilities, resources, and gaps related to pharmacogenomics in cardiovascular medicine, based on the identification of the key institutions and collaborations that drive PGx innovation and recommendations for future progress in the field; **(2) Conduct a comprehensive review of European clinics and hospitals** that have integrated PGx-guided decisions into their clinical practice for cardiovascular conditions; **(3) Perform a literature review of previous studies on pharmacogenomics in cardiovascular medicine,** with a focus on genetic markers that influence drug response and efficacy; and **(4) Pinpoint the current technological constraints** and areas where knowledge is lacking in applying PGx to cardiovascular medicine, such as limitations in genotyping, bioinformatics tools, and clinical decision support systems.
In order to meet these aims, the following tasks will be completed: **T1.1 - Conducting a review of current R&D infrastructure in Europe** by recording and listing the collaborations, research teams, laboratories, and clinical groups undertaking studies on genetic markers and evaluation of their clinical significance. **T1.2 - Reviewing the European clinics/hospitals using PGx-guided decisions** in their

practice will result in a non-exhaustive list of institutions that have successfully integrated the use of actionable pharmacomarkers in their practice and experiences resulting from such approach. **T1.3 - A position paper dealing with PGx technological limitations and knowledge gaps** in cardiovascular medicine will result from consultations with research and implementation teams from previous tasks, to pinpoint the areas for future improvement. **T1.4 - Knowledge transfer.** STSMs will be organized for researchers and innovators to conduct their research in PGx of actionable variants. Training School will revolve around data collection and analysis methods towards functional classification of PGx markers. Additionally, at least two webinars will be held each year of Action implementation.
Deliverables: D1.1 - A table of R&D infrastructure and research efforts addressing PGx of cardiovascular diseases. D1.2 - A table of institutions that have successfully implemented PGx in their routine practice with the list of successes and challenges. D1.3 - A position paper on current research and infrastructural gaps and challenges with expert recommendations towards the future development of the field.
Milestone 1: Producing relevant conclusions on success and challenges of PGx research and implementation in Europe.

WG2 - Pharmacogenetic guideline development and optimization

This WG aims to: **(1) Explore and identify cardiovascular therapies** where the application of PGx can optimize treatment outcomes, including the evaluation of drugs where genetic factors influence efficacy, safety, and dosing, leading to personalized treatment approaches; **(2) Provide a comprehensive review of existing PGx guidelines and recommendations** for actionable genetic variants in CVDs, in order to highlight current clinical practices and the genetic markers that guide therapeutic decisions, ensuring they are based on the latest evidence; **(3) Develop strategies for patient stratification** based on diagnosis, genetic profile, and demographic characteristics such as age, gender, ethnicity, or comorbidities to support more tailored decision-making in clinical practice by identifying subgroups that benefit most from PGx-guided therapies.
The tasks for this WG are defined as follows: **T2.1 - Systematically summarizing the conditions in cardiovascular medicine** in which application of PGx is possible, including the therapies with variants of known or predicted information content. **T2.2 - PGx guidelines and actionable variants in current use** will be ordered from the highest towards lower in terms of the evidence level. **T2.3 - Patient stratification** based on diagnosis, genetic profile, and demographic characteristics which all influence optimal dosage of the therapy, will be analyzed in order to offer it as an additional tool in decision-making process. **T2.4 - Knowledge transfer.** STSMs will be organized for researchers and innovators to conduct their research in terms of experience in real-life applications of PGx in clinical practice. If the actual patient interaction is deemed impossible, the trainees will be performing data curation and analysis. Training School will revolve around gathering knowledge in preparing and designing PGx research in cardiovascular medicine, starting from variant selection and patient stratification, all the way to delivering optimized therapy to the bedside. Additionally, at least two webinars will be held each year of Action implementation, starting in year 2.
Deliverables: D2.1 - The list of cardiovascular conditions for which PGx can be applied in therapy optimization, along with actionable or recommended variants and literature evidence. D2.2 - The list of PGx variants, from the highest towards lower evidence levels, matched with therapies and conditions to which they are relevant in cardiovascular medicine. D2.3 - A document/report describing the patient stratification workflow for the application in this field. D2.4 - A position paper on current research and infrastructural gaps and challenges with expert recommendations towards the future development of the field.
Milestone 2: Comprising information about PGx variants in CVD with real-life applications. Milestone 3: Produced practical guidelines on successful design of research and discovery studies.

WG3 - AI/ML use in PGx of cardiovascular medicine

Aims of this WG are to: **(1) Develop and refine personalized medicine approaches** in cardiovascular pharmacotherapy by analyzing the development and creation of advanced dosing algorithms through ML and AI techniques to provide groundwork for improving the accuracy of dosage recommendations based on patient-specific genetic data; **(2) Give recommendation on the optimal computational resources** necessary for processing large-scale PGx data while identifying current technological and methodological limitations that hinder pharmacogenomic research; **(3) Create a standardized, secure, and scalable platform** on the Action website that allows for the storage, management, and updating of pharmacogenomic data across Europe, to facilitate data sharing among researchers, clinicians, and institutions; **(4) Assess required IT systems in clinics and hospitals** for the seamless integration of PGx data into clinical workflows.
The aims will be met through the following activities: **T3.1 - Analyzing the role of ML and AI** in development of pharmacogenomic dosing algorithms, by providing an overview of techniques, methods, platforms, and models used for previous work in PGx algorithm development, making it

easier to pinpoint future improvement and gap closure areas. **T3.2 - Computational infrastructure analysis across Europe** and identification of research bottlenecks will be performed to detect computational biocenters of PGx data processing in Europe, their success stories and challenges and provide matchmaking for faster and more efficient exchange of resources, infrastructure and expertise in the future. This will also cover the assessment of expertise in biostatistical approaches to genetic data analysis in the field. **T3.3 - Platform development for storage and update of PGx data** across Europe will be done within the Action website, to provide the most extensive repository of cardiovascular PGx data in Europe, including the findings from WG 1-3 (genetic markers with evidence and application levels, R&D efforts and infrastructure, computational capabilities, and similar). **T3.4 - Overview of needed IT systems in clinics and hospitals** to provide an expert recommendation on how to produce, maintain and secure IT systems that will allow for successful integration of PGx in daily use with patient applications. **T3.5 - Knowledge transfer.** STSMs will be organized for researchers and innovators to conduct investigations in computational needs in PGx of cardiovascular medicine. Training School of WG3 will revolve around PGx algorithm development and biostatistical models in genetic data analysis and translation to clinical practice. Additionally, at least two webinars will be held each year of Action implementation, starting in year 2.
Deliverables: D3.1 - Overview of previous publications which announced the use of ML/AI techniques for PGx algorithm development. D3.2 - Development of a platform that will serve as a central repository of collected PGx data in Europe. D3.3 - A report with expert opinion on the needs of IT systems in hospitals and clinics for implementation of PGx in practice. D3.4 - A position paper on current research and infrastructural gaps and challenges with expert recommendations towards the future development of the field.
Milestone 4: Systematic knowledgebase on computational and infrastructural state of cardiovascular PGx in Europe. Milestone 5: Functional cardiovascular PGx platform is available online.

WG4 - Policy regulation of PGx guidelines and impact analysis across Europe

WG4 aims to: **(1) Conduct a thorough socioeconomic analysis** of the current costs associated with ADRs and suboptimal therapy in cardiovascular care and potential cost savings by implementing targeted therapies and personalized treatments based on PGx testing, aiming to achieve an annual reduction in treatment costs across the EU; **(2) Perform a country-specific review of existing guidelines** on the use of PGx in cardiovascular care, including testing practices, data analysis, patient privacy protections, and the practical limits of PGx application in daily clinical practice, to provide a comprehensive understanding of current regulatory frameworks across the EU; **(3) Evaluate the authority and guidelines under the EMA** related to the use of PGx in cardiovascular medicine, highlighting regulatory issues and areas for policy development; **(4) Analyze the challenges of data sharing between EU and non-EU countries** concerning PGx integration, to identify barriers to collaboration and propose solutions for more seamless PGx implementation across borders.
The following tasks will be completed through this WG: **T4.1 - Impact analysis of economics of PGx,** including current expenses related to ADRs and therapy optimization, as well as potential savings in case of applying targeted therapies and personalized treatments for each patient. This task will aim to approximate annual decrease of treatment costs for patients in cardiovascular medicine across the EU by applying PGx and associated testing expenses. **T4.2 - Country-wise review of present guidelines** related to the application of PGx in cardiovascular medicine, including testing practices, data analysis and sharing, patient privacy protection, and limits of PGx application in the daily practice. **T4.3 - Authority and guidelines under the EMA competence** will be analyzed and reported to the European Commission as an output of this Action. **T4.4 - Data sharing across the EU countries and non-EU member countries** will be analyzed in a separate task to understand the obstacles of incorporating PGx in regimens of patients requiring cross-border medical care and telemedical support. **T4.5 - Stakeholder engagement.** Round table will be organized to bring together the stakeholders to discuss the limits of PGx policy regulation and economic impact. Beforehand, two major webinars will be held to discuss the topics of (a) economic impact, both positive and negative, of regular PGx testing in cardiovascular medicine in the EU and other European countries, and (b) policy regulations, including regulatory bodies and valid guidelines, on the extent of PGx application to the bedside.
Deliverables: D4.1 - A publication on economic impact of PGx across the EU, with a dedicated section to non-EU member countries and their specifics. D4.2 - A report on country-based overview of relevant guidelines detailing the use of PGx in daily practice. D4.3 - Policy Brief on the position of EMA in the context of PGx in cardiovascular medicine and issues related to patient privacy, data sharing and cross- border cooperation.
Milestone 6: Successfully performed economic and regulatory analysis of the current state of PGx in Europe.

WG5 - Communication, dissemination and exploitation

The aims of this WG are to: **(1) Establish a comprehensive website** as the central hub for communication, dissemination, and data sharing, supported by regular updates through social media, newsletters, and visual materials; **(2) Facilitate the exchange of knowledge and foster collaboration by organizing a mid-Action stakeholder conference,** as well as disseminating scientific publications, reports, and visual content; **(3) Ensure that Action outcomes, including open access (OA) publications, reports, and visual materials, are widely accessible** to both scientific and public audiences to maximize the impact of the Action through effective communication and the dissemination of key findings.
The tasks of WG5 are as follows: **T5.1 - Website development** will be completed in the first Action semester for use as the main communication and dissemination channel, including the news, events, open call announcements, visual material repository, scientific section on Action publication, medium for publication the deliverables, and data sharing platform developed in synergy with WG3. Further communication will be organized through social media profiles, including LinkedIn and Instagram, among others. **T5.2 - Dissemination activities,** through regular updates of the social media channels, dissemination conferences and ITC grants for attending the conferences organized by the third parties, and publication of visual materials (Action infographics, biannual newsletter, leaflets). **T5.3 - Communication activities,** including OA publications of review articles and dedicated journal sections, as well as deliverables in form of reports. **T5.4 - Stakeholder conference** will be held mid-way the Action lifetime in a central European location, aiming to bring together all interested parties (researchers, clinicians, genetic counselors, patient organizations, industry representatives, policymakers and regulatory bodies, representatives from economics and social scientists, etc.) to discuss the outputs and recommendations for the field.
Deliverables: D5.1 - Action website. D5.2 - Development of a platform that will serve as a central repository of collected PGx data in Europe. D5.3 - Biannual newsletter (min. 7 newsletters throughout the Action lifetime). D5.4 - OA journal publications covering deliverables from other WGs. D5.5 - A position paper on current research and infrastructural gaps and challenges with expert recommendations towards the future development of the field.
Milestone 7: Functional website serving as a central information hub for the Action visibility. Milestone 8: Successful engagement of all identified target groups and stakeholders through stakeholder conference and other activities.

4.1.2. DESCRIPTION OF DELIVERABLES AND TIMEFRAME

WG	Deliverable no.	Deliverable name	Delivery time
WG1	D1.1	A table of R&D infrastructure and research efforts addressing PGx of cardiovascular diseases	Year 1, Q4
WG1	D1.2	A table of institutions that have successfully implemented PGx in their routine practice with the list of successes and challenges	Year 1, Q4
WG2	D2.1	The list of cardiovascular conditions for which PGx can be applied in therapy optimization	Year 2, Q2
WG2	D2.2	The list of PGx variants, from the highest towards lower evidence levels, matched with therapies and conditions to which they are relevant in cardiovascular medicine	Year 2, Q4
WG2	D2.3	A document/report describing the patient stratification workflow for the application in this field	Year 3, Q1
WG3	D3.1	Overview of previous publications which announced the use of ML/AI techniques for PGx algorithm development	Year 2, Q2
WG3	D3.3	A report with expert opinion on the needs of IT systems in hospitals and clinics for implementation of PGx in practice	Year 3, Q2
WG4	D4.1	A publication on economic impact of PGx across the EU	Year 3, Q3
WG4	D4.2	A report on country-based overview of relevant guidelines detailing the use of PGx in daily practice	Year 4, Q2

WG4	D4.3	Policy Brief on the position of EMA in the context of PGx in cardiovascular medicine and issues related to patient privacy, data sharing and cross-border cooperation	Year 4, Q3
WG5	D5.1	Action website	Year 1, Q2
WG3, 5	D3.2, D5.2	Development of a platform that will serve as a central repository of collected PGx data in Europe	Year 3, Q2
WG5	D5.3	Biannual newsletter	Year 1, Q4, continued twice a year
WG5 (1, 2, 3, 4)	D5.4 (D1.1, D1.2, D2.1, D2.2, D2.3, D3.1, D3.3, D4.1)	OA journal publications covering deliverables from other WGs	Starting from year 2, Q1
WG5 (1, 2, 3)	D5.5 (D1.3, D2.4, D3.4)	A position paper on current research and infrastructural gaps and challenges with expert recommendations towards the future development of the field	Year 4, Q1

4.1.3. RISK ANALYSIS AND CONTINGENCY PLANS

Risk	**Contingency measures**
Low participation from key stakeholders (clinicians, policymakers, industry representatives) Likelihood: M, Effect: H	Actively identify and engage stakeholders at the beginning of the Action through targeted outreach and personalized invitations Use incentives, such as travel grants for participation, to increase engagement
Disagreement among stakeholders regarding pharmacogenetic guidelines may lead to conflicting recommendations, undermining consensus-building efforts Likelihood: L, Effect: M	Facilitate structured discussions and consensus-building webinars to align perspectives Use anonymous surveys to gauge opinions before discussions to identify common ground
Issues with the website or data-sharing platform could impede the accessibility and usability of shared pharmacogenetic data Likelihood: L, Effect: H	Conduct thorough testing of the website and data-sharing platform before launch Provide training and support for users to ensure they can navigate the system effectively
Varying regulations across countries may complicate data sharing and collaboration efforts Likelihood: M, Effect: L	Consult with legal and economy experts to understand regulatory frameworks in different countries Develop clear guidelines for compliance and ensure all stakeholders are informed
Low uptake of review articles and recommendations by the intended audience may limit the Action's impact on clinical practice Likelihood: M, Effect: M	Engage with key opinion leaders to promote the findings and recommendations Utilize multiple channels for publication and presentation to reach diverse audiences
Conflicts arising among the Action partners Likelihood: L, Effect: H	Management of conflicts will be done through the actions of the MC to find consensual solutions MC voting will be transparent through the eCOST system for any decisions requiring such approval, to ensure that the majority of Action members agree with activities. The MC and CG will deal with the case, if any, to operate in line with Code of Conduct in the COST Annotated Rules for COST Actions. Careful election of Action members to the leadership positions

4.1.4. GANTT DIAGRAM

Task	Year 1				Year 2				Year 3				Year 4			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Annual MC meetings																
CG meetings																
WG meetings																
T1.1																
T1.2																
T1.3																
T1.4																
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T5.4																
Final meeting																

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