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Accelerated Development of VAccine beNefit-risk Collaboration in Europe

Grant Agreement nº115557

D2.4 Final report on landscape analysis, synergies, added value of synergies for ADVANCE and future opportunities

WP2 – Creation of synergies for benefit-risk monitoring in Europe

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DEFINITIONS[1]

- Participants of the ADVANCE Consortium are referred to herein according to the following codes:
  - **P95.** P95 (Belgium)-coordinator
  - **UNIBAS**. Universitaet Basel (Switzerland) - Managing entity of the IMI JU funding
  - **EMA.** European Medicines Agency (United Kingdom)
  - **ECDC.** European Centre for Disease Prevention and Control (Sweden)
  - **SURREY.** The University of Surrey (United Kingdom)
  - **SYNAPSE.** Synapse Research Management Partners, S.L. (Spain)
  - **OU.** The Open University (United Kingdom)
  - **LSHTM.** London School of Hygiene and Tropical Medicine (United Kingdom)
  - **PEDIANET.** Società Servizi Telematici SRL (Italy)
  - **KI.** Karolinska Institutet (Sweden)
  - **ASLCR.** Azienda Sanitaria Locale della Provincia di Cremona (Italy)
  - **AEMPS.** Agencia Española de Medicamentos y Productos Sanitarios (Spain)
  - **AUH.** Aarhus Universitetshospital (Denmark)
  - **UTA.** Tampereen Yliopisto (Finland)
  - **WIV-ISP.** Institut Scientifique de Santé Publique (Belgium)
  - **MHRA.** Medicines and Healthcare products Regulatory Agency (United Kingdom)
  - **SSI.** Statens Serum Institut (Denmark)
  - **RCGP.** Royal College of General Practitioners (United Kingdom)
  - **RIVM.** Rijksinstituut voor Volksgezondheid en Milieu * National Institute for Public Health and the Environment (Netherlands)
  - **GSK.** GlaxoSmithKline Biologicals, S.A. (Belgium) – EFPIA Coordinator
  - **SP.** Sanofi Pasteur (France)
  - **NOVARTIS.** Novartis Pharma AG (Switzerland)
  - **Merck.**
  - **CRX**. Crucell Holland BV (Netherlands)
  - **PFIZER**. Pfizer Limited (United Kingdom)
  - **TAKEDA**. Takeda Pharmaceuticals International GmbH (Switzerland)
  - **EMC**. Erasmus Universitair Medisch Centrum Rotterdam (Netherlands)

- **Grant Agreement.** The agreement signed between the beneficiaries and the IMI JU for the undertaking of the ADVANCE project (115557).
- **Project.** The sum of all activities carried out in the framework of the Grant Agreement.
- **Work plan.** Schedule of tasks, deliverables, efforts, dates and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.
- **Consortium.** The ADVANCE Consortium, comprising the above-mentioned legal entities.
- **Project Agreement.** Agreement concluded amongst ADVANCE participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

[1] To be completed with terms and abbreviations related to the actual content of the document

EXECUTIVE SUMMARY[2]

ADVANCE aimed to build synergies to avoid duplication and leverage learnings from other IMI and EC funded projects.

Relative to the list of external initiatives that were initially identified as potentially relevant from the initial landscape analysis, only for a small proportion of the complete list synergies in any form were ultimately established (<15%). About one third of external initiatives that were assessed as relevant by the WP leads led to synergies and approximately half of highly relevant initiatives. The majority of the synergies as established for projects which had overlapping partnership between the external initiative and ADVANCE.

Regarding the type of synergy established, output utilization was the most frequent form of synergy and mainly proved valuable in accelerating the work of ADVANCE by reuse of tools and other previous development work. Strategic alignment provided primarily opportunity for stakeholder engagement and dissemination. Establishing joint work requires the coincidental situation of aligned work plan and deliverable schedules or modification thereof if foreseen sufficiently far in advance. This applied only to very few external initiatives, namely MOCHA, EMIF.

The following key lessons learnt were gained from this experience and are provided as recommendation for future work.

1. The consortium is the primary source for identifying and establishing relevant external initiatives,
2. Prioritise synergies with immediate and apparent external initiatives;
3. Synergies are most effective if involving common partners between projects, where relevant;
4. Public availability of work plan descriptions and deliverables is encouraged to facilitate the identification and assessment of feasibility of potential synergies;
5. Limit formalisation of synergies where required for the exchange of resources and intellectual property

The landscape analysis of those project with possible relevancy for sustainability revealed a number a number of different approaches to sustainability and underlying funding mechanisms. The experiences from these projects can be used to support the development of the post-ADVANCE sustainability.

[2] Maximum 2,000 characters (including spaces)

1. Background

1.1. The ADVANCE project

The ADVANCE project aims to establish a blueprint of an efficient and sustainable pan-European framework that can rapidly deliver robust quantitative data for benefit and risk assessments of vaccines that are currently on the market. Such a framework would allow regulators and public health authorities to make fast, informed decisions regarding vaccination strategies, and help to maintain or restore public confidence in vaccines, particularly when questions are raised in the media about the safety of specific vaccines.

1.2. Project structure

The project revolves around the three needed pillars for the intended framework: data sources (WP3), methods (WP4) and best practice mechanisms (WP1). These form an integrated core "triangle" (see Figure 1) strengthened by leverage of existing results, initiatives and projects, through synergetic collaboration (WP2), refined and validated through selected proof of concept studies (WP5) and leading to blueprint or model for benefit-risk monitoring of vaccines in Europe (WP7). WP6 provides the necessary coordination, management and communication backbone of the project as a whole.

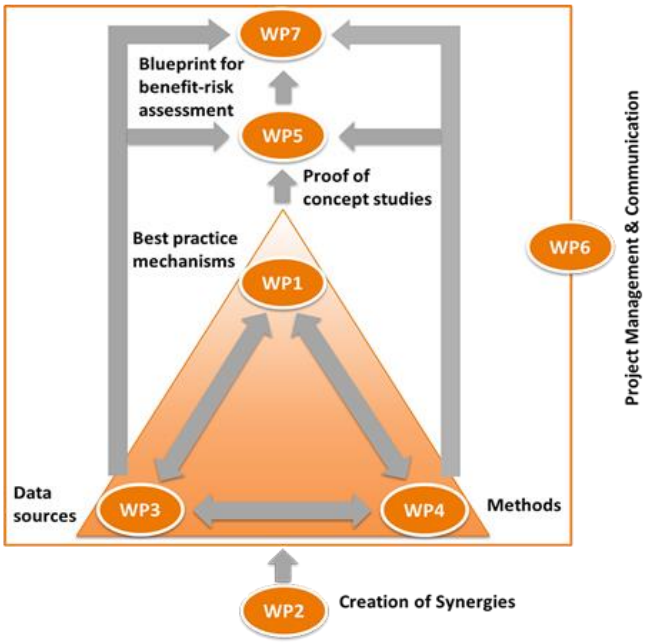

Figure 1. Diagram of the ADVANCE project structure.

1.3. Current deliverable

The current deliverable from WP2 is the final report on the synergies that were utilised in ADVANCE and the value they provided. It provides a summary of the lessons learnt and practical guidance to support future opportunities for leveraging efforts across initiatives. In addition, a final landscape analysis was performed to update the repository. As part of this effort, the external initiatives were additionally mapped to the topic of sustainability, blueprint and training/dissemination. An overview is provided of external initiatives that are specifically relevant to the current focus of ADVANCE.

2. Final landscape analysis

At the beginning of ADVANCE, initiatives relevant to the project's scope were identified and described in a repository, made available to the ADVANCE consortium (see Deliverable 2.1). All initiatives were mapped against a number of mapping terms reflecting the Work Packages' activities. This resulted in synergy maps for the 117 initially identified initiatives (see Deliverables 2.1 and 2.2).

During the course of ADVANCE, the repository was further expanded with newly identified initiatives. These initiatives were suggested by ADVANCE partners - including WP2 members -, identified by repeated screening of funding databases, or based on spontaneous requests for collaboration. The final landscape analysis is the result of this ongoing work. In addition, we added "sustainability" as a mapping term and previously identified initiative underwent a repeated analysis. The feedback from interactions with external initiatives, or follow up and review of such initiatives progress and outputs was used to clean the repository.

An extract of the repository is provided in Annex I, listing key information of the identified projects. The full repository is added to this deliverable as a separate file and available on the ADVANCE website.

As such landscape analyses provide essential input about the gaps and potential synergies in the research field of an initiative, it is important to have such an analysis done prior to or in the initial phase of a project. Therefore, we prepared a tool with a generic template that can be used easily by any initiative to facilitate a landscape analysis. This tool is submitted as a separate file with this deliverable.

3. Established synergies and added value for ADVANCE

3.1. Recent established synergies

Since the last deliverable from WP2, synergies achieved with other initiatives were related to leveraging outputs (e.g. from the Global Research in Paediatrics project (GRIP), from the European Medical Informatics Framework (EMIF) (catalogue), with TESSY (ECDC), and VENICE). The EMIF project is using the ADVANCE Codemapper. We are currently in the process of establishing synergies with the DRIVE consortium. ADVANCE invited DRIVE leaders/coordinators to the governance workshop that was organised by EMA.

3.2. Overview of established synergies

An outline of the established synergies in the ADVANCE project is summarised below. The synergies are presented according to the initial mapping terms for which potential for synergies and leverage were identified (see Deliverable 2.1). The extract of the repository provided in Annex I indicates the type of synergies that were established for each external initiative. The description below is limited to the more tangible outcome utilisations and strategic alignment.

Table 1. Areas of potential synergy and leverage as identified from the synergy mapping (Deliverable 2.1)

WP	WP Title	Identified areas of synergy and leverage
WP1	Best practice and code of conduct for benefit-risk monitoring of vaccines	• Public-private/public-public collaborative models
WP3	Data sources for rapid and integrated benefit-risk monitoring	• Data sources, access, integration, linkage • data collection systems
WP4	Methods for burden of disease, vaccination coverage, vaccine safety & effectiveness, impact and benefit-risk monitoring	• Vaccine Program Monitoring • Benefit/risk assessment
WP5	Proof-of-concept studies of a framework to perform vaccine benefit-risk monitoring	• Infrastructure • Common data model • Distributed networks • Data sharing and pooling

3.2.1. Public-private/public-public collaborative models

Through EMA who was leading the work on the development of the ADVANCE best practice guidance, which includes the governance and a code of conduct, the collective members of the **European Network of Pharmacoepidemiology and Pharmacovigilance (ENCePP)** were asked to participate in an ADVANCE survey in 2014 to identify existing models of partnerships, collect experience and learn from interactions between public and private partners.

As part of the open forum that was established to gather needs and interests for public private partnerships, **I-MOVE**, and the **EMA Patient Representatives** attended several WP1 workshops allowing exchanges and discussions with the WP1 members.

Following IMI recommendations, a Governance workshop was organised in March 2017 at the European Medicines Agencies offices in London to solicit input from a larger group of European stakeholders (public health institutes, health organisations, patient associations and other organisations that are not part of the ADVANCE consortium). About 70 senior experts attended the

workshop. It successfully allowed open discussion by a large panel of European experts in vaccine B/R monitoring on the challenges faced when setting up public and private interactions, using a concrete proposal of a governance framework put forward by the ADVANCE group. In reaction to discussions during the workshop, ADVANCE adapted its governance framework, to provide key principles and a generic model with options to enable adjustments to take into consideration the context and the project specificities. The report of this workshop is available on the ADVANCE website. Also patient organisations (e.g. the European Cancer Patient Coalition) participated to this workshop.

The ADVANCE code of conduct was reviewed through a transparent public review, organized by EMA, to which many parties commented.

Several outputs from external initiatives, e.g. **ENCePP** Code of Conduct, **ISPOR** guidance, have been incorporated in the ADVANCE Code of Conduct. This ADVANCE Code of Conduct in turn is considered by **EMIF** while **EnCEPP** uses ADVANCE reports to build guidelines.

3.2.2. *Data sources, access, integration, linkage*

Several synergies were deployed to support the design and dissemination of the ADVANCE International Research Readiness (AIRR) survey, an instrument developed in WP3 to assess the readiness of data sources for participating in vaccine research studies. For this purpose:

- Existing survey tools from the projects of **PARENT, GRIP** and **TIRRE2** were analysed to support the design stage of the AIRR survey.
- Privacy and ethics considerations of the European projects **VENICE, EHR4CR and PARENT** were identified and analysed to gain a better understanding of current practices and regulations in European countries and to be incorporated in the survey.

For the purpose of building the ADVANCE web catalogue of meta-data profiles of data sources, in addition to the meta-data collected through the AIRR survey, ADVANCE also reused meta-data collected by the International Research Opportunity Instrument (MIROI) through the H2020 Models of Child Health Appraised (**MOCHA**) project.

A Memorandum of Understanding (MoU) was established to formally facilitate the synergy and provide a base for joint work in the context of WP3 including:

- Sharing of database contact information between the projects for the purpose of getting responses for their respective database profiling survey instruments;
- Sharing of collected meta-data of databases with permission from the respective database owners;
- The meta-data exchange was possible since both meta-data collection instruments were semantically annotated using the same Data Source Ontology (DSO). Schemas of both survey instruments had around 60 percent overlap for the meta-data collected and the overlapping meta-data was considered useful to have an initial assessment of appropriateness of databases to participate in vaccine benefit risk studies.

The exchange of meta-data was carried out by researchers of the University of Surrey who were actively participating in the relevant work streams of both projects.

The results from the AIRR survey, containing information on identified and characterised databases, are stored and made available in the **EMIF** catalogue/browser. Careful considerations were made to upload the data on PARENT, however since the project has ended, EMIF was preferred.

3.2.3. *Infrastructure and data collection systems*

The remote research environment (RRE) called OCTOPUS was used in WP5 to upload local output from the fingerprint and the pillars and SAS programs by the local database custodians. The OCTOPUS RRE is a platform created for the EC-funded **ARITMO** project.

The general experience with **VAESCO, VSD, EU-ADR, mini-Sentinel** known within the consortium or obtained through further interactions, contributed to the further enhancement of the remote research infrastructure deployed by ADVANCE.

For the purpose of building the vaccine ontology VaccO, the European Medicines Agency's comprehensive database **Article 57 database** provided detailed information for ADVANCE about the vaccines, such as their authorization status, country-specific brand names, target diseases, administration routes and components.

The JERBOA tool that was developed in the **EU-ADR, SOS, ARITMO, SAFEGUARD, VAESCO, SOMNIA** and **EMIF** project was used in ADVANCE for fingerprinting of events and the population.

The ADVANCE Codemapper was used by **EMIF**.

Surveillance data on pertussis from **TESSY** (ECDC) were used to benchmark rates of vaccine preventable diseases.

3.2.4. *Vaccine Programme Monitoring*

The publicly available **Vaccine Scheduler from ECDC** was used for comparing childhood vaccines schedules between European countries in the proof of concept studies. Questionnaires were sent by WP4 to the **VENICE** group to collect data on past vaccination schedules.

3.2.5. *Benefit/risk assessment*

ADVANCE was used as a test case for the MCDA method which was previously extensively evaluated by the **PROTECT** consortium that was led by EMA. MCDA is a generic, highly structured approach to aid decision-making by decomposing a complex problem into pieces, evaluating and judging the pieces and reassembling the pieces into a coherent whole. Both the European Medicines Agency and **PROTECT** recommended further investigation of MCDA for real-life applications. The comparison of the benefit-risk (BR) of wP and aP pertussis vaccine formulations in children prior to the pre-school-entry booster was used as this test case for the MCDA.

ADVANCE members were invited by EMA at the **PROTECT** final meeting to support knowledge exchange.

For the work in WP4 on the MCDA, ADVANCE has built on the application of the Disability-Adjusted Life Years (DALY) used within the **BCoDE** (Burden of Communicable Diseases in Europe) project to calculate the burden of infectious diseases in the European member states. **BCoDE** has also appraised methods of WP4.

The burden of adverse events work in WP4 was built on the published reference set of **GRIP.**

Various existing systems were reviewed for the appraisal of vaccine benefit-risk methodology. These included, but were not limited to the **VSD, VAESCO, PRISM** and **Mini-sentinel, OMOP, OHDSI** and **GRiP**.

Published data on the **PRISM** characterisation were used in WP5 for benchmarking of the fingerprints.

3.2.6. *Common data model*

Database experts were asked to extract study-specific data into a simple common data model (CDM), partly building on foreground of previous work and experience from projects that had ended and employed these models such as **EU-ADR SOS, ARITMO, and SAFEGUARD.** The data in this CDM were used in the fingerprinting step (the actual running of characteristics on the population, event and vaccines in the database using standardised scripts) and the POC teams on coverage, safety and benefit.

3.2.7. *Other*

Although no areas of synergy were initially identified for WP2 and WP7 in the course of the project two additional synergies arose in the area of synergy creation itself as well as in the area of long-term sustainability.

The limitations posed by the current level of information about (deliverables of) initiatives available in the public domain to identify potential synergies have led to explorations with **eTRIKS** on how identifiability of other initiatives can be improved to facilitate synergy creation. The **CORDIS** database was approached to inquire about the possibilities to include such information. However, the request was declined because currently the Descriptions of Work as used in the Horizon 2020 research funding programme are considered confidential. Further explorations with IMI were not undertaken in this direction as this was not considered part of the scope of ADVANCE.

At time of this report, several discussions are planned with external initiatives on the approach to sustainability after the project's completion to support the discussion within ADVANCE on the post-ADVANCE framework. These include **EU2P**, **PARENT**, **BioVACSAFE** etc. In addition, outreach to the **European Research Infrastructure Consortium (ERIC)**, **Transvac**, **I-Move, GAVI** are also considered.

4. Summary of synergy creation and lessons learnt

From the initially as potentially relevant external initiatives identified in the initial landscape analysis, only with few synergies were established (~ 15%). About one third of external initiatives that were assessed as relevant by the WP leads led to synergies and approximately half of the highly relevant initiatives. The majority of the synergies were established for initiatives that had overlapping partners between the external initiative and ADVANCE. Establishing synergies thus relies on a combination of insight in the work of one's own WP, as well as insight into the work plan of the external initiative. In absence of such mutual understanding of work plans (from both initiatives, more resource intensive explorations are needed to gain insight and understanding, and thus identify possibilities for synergy.

Regarding the type of synergy established, output utilisation was the most frequent form of synergy and mainly proved valuable in accelerating the work of ADVANCE by reusing tools and other previous development work – such as for the CDM. Strategic alignment provided primarily opportunity for stakeholder engagement and dissemination, with the WP1 workshops as key examples. Joint work was achieved in only few occasions. As described in Deliverables 2.3 establishing joint work requires the coincidental situation of aligned work plan and deliverable schedules or modification thereof if foreseen sufficiently far in advance. This applied only to very few external initiatives. The joint work with MOCHA is probably the most optimal example. Output utilisation and strategic alignment occurred throughout the project, whereas join work required time to be established and no new initiative was undertaken in the later phases of the project.

Many synergies have occurred in ADVANCE without formalising the collaboration. Of all the synergies that were established, only the synergy with MOCHA was formalised in the form of a Memorandum of Understanding (MoU). Originally, the purpose of the Memorandum of Understanding (MoU), as viewed by ADVANCE, was to establish the overarching framework for collaboration and to facilitate and develop existing synergies between the parties in relevant activities, in accordance with policies and procedures for each party and of the projects. The MoU had no legally binding status. It served as a documented tangible expression of interest of each of the parties to explore and possibly thereafter establish active collaborations.

In addition to MOCHA, establishing a MoU with an external initiative was proposed in several instances but never accomplished. Early in the project, ADVANCE discussed the possibility of establishing an MOU with ECDC for various relevant ECDC projects (including TESSY, VENICE, BCODE). However, ECDC considered a MoU to be a legally binding document. This experience resulted in an alternative documented expression of interest, namely the Letter of Intent to describe the interaction between the different parties. A MoU was also prepared to be signed between ADVANCE and EMIF. However, this MoU could not be countersigned by EMIF because this would have required an amendment of the EMIF Project Agreement to provide a mandate to the coordinator to proceed with signatures. Eventually, a formal MoU was deemed not necessary to engage in relevant collaborations with EMIF. Due to the shared background and overlap of partners in the ADVANCE and EMIF coordination teams (EMC, Synapse Research Management Partners), there has been a natural exchange of information from the beginning of the ADVANCE project.

These experiences triggered debate around the need of a MoU for the purpose as originally defined when ADVANCE was approached by IMI-DRIVE project to establish a MoU. The MoU for this was built on the template developed by ADVANCE. The decision taken was that for the initial stage of knowledge exchange and considering that most relevant output is in the public domain, a MoU would not be needed at this stage.

Finally, we reviewed the external initiatives that were initially identified as relevant but for which no synergy was ultimately established in order to understand the reasons behind this. We found that a number of initiatives concerned initiatives on basic science and clinical trial research, which appeared to have been selected initially on the basis of their topic of research, but otherwise have not been relevant to the deliverables of ADVANCE to date. These initiatives have been removed from the final repository. Some relevant initiatives identified in the initial landscape analysis were consolidated. For example, EDSN, EU-IBD, EUVAC-net are now under the Vaccine Preventable Disease group (VPD) of ECDC, and EVACO is now considered part of VENICE and falls under this synergy. This has been reflected in the repository as well. In addition, the lack of sufficient information for several projects did not promote to explore further options. The remaining list also contained some initiatives which bear relevance only for the current and future work of ADVANCE on sustainability, establishing the Blueprint and dissemination as described under section 5.

4.1. Lessons learnt

ADVANCE aimed to build synergies to avoid duplication and leverage learnings from other IMI and EC funded projects. The following key lessons were learned from this experience.

1. **The consortium is the primary source for identifying and establishing relevant external initiatives**

As the project consortium brings together experts in the field of the project's scope, these experts have proven to have extensive knowledge on relevant initiatives for creating synergies. Many projects are highly specific and so are tasks. Those appointed to do the work know best what their requirements are and which needs for external knowledge (and thus potential synergies) exist.

2. **Prioritise synergies with immediate and apparent external initiatives**

Synergies proved most successful for external initiatives where relevancy is apparent and immediate to motivate external engagement. Synergies are best established early in the process because they take time to implement, specifically when foreseeing joint work, and might rely on reallocation of resources.

3. **Synergies are most effective when involving common partners between initiatives, where relevant**

Effective collaborative synergies were established primarily when partners owned foreground in the collaborating projects (e.g. EMIF, MOCHA, PROTECT), specifically when pertaining to joint work. This facilitated easy sharing and synergies, because decisions about use of such foreground can be made more easily.

4. **Public availability of work plan descriptions and deliverables is encouraged to facilitate the identification and assessment of feasibility of potential synergies**

The experience from the landscape analysis and synergy creation for ADVANCE has shown that

readily available information on the work plan of external initiatives (i.e. objectives, deliverables and timelines) is needed to facilitate the identification, exploration and implementation of synergies between initiatives.

When such information is not available through common partners, facilitating synergies between initiatives would benefit from publicly accessible information on the work plans so that relevancy in terms of content and timelines can be better assessed. We thus encourage consortia to make such information available on their public websites.

5. Limit formalisation of synergies where required for the exchange of resources and intellectual property

Formalisation of synergies, using a MOU or other document, should be reserved to address situations where sharing of resources and/or intellectual property between two parties would require this.

5. Future Opportunities

As part of the final landscape analysis, all initiatives were re-reviewed and mapped for their possible relevancy regarding the current focus of ADVANCE: on sustainability, Blueprint and dissemination. The mapping is presented in Annex I. We comment here on few specific examples of (models of) sustainability of research initiatives.

Table 2. Example of approaches to sustainability as established by external initiatives.

Approach to sustainability	**Example projects**
Full service/Network model	**OHDSI** The OHDSI provides a forum for researchers to work together on problems of shared interest. OHDSI currently have over 140 researchers from across the globe who are connecting as part of an international network and sharing research ideas. OHDSI serving data holders by building tools and establishing processes to help standardize and analyze data in a higher quality and more efficient way. All of the tools and evidence which is generated should be made open-source and freely available to everyone. Contributions consists of: - in-kind contributions to the collaborative. - variety of funding sources to fund contributions such as public government grants, industry contracts, private foundation grants and other opportunities. - unrestricted grant providing the foundational support for the entire collaborative, and would be used to support personnel and shared infrastructure. - funding the acquisition or licensing of a patient-level databases that can be placed within the OHDSI central coordinating center infrastructure and used for analysis - direct funding of a specific body of work under grant or contract with any of the OHDSI collaborating organizations. The majority of the funding goes to direct cost associated with personnel, but money may also be allocated to technical infrastructure and licenses. In terms of order of magnitude of support, the types of funding opportunities that the teams are actively soliciting usually involve direct costs paid per year with a 3-5 year commitment.
Full service/Network model	**i~HD** The European Institute for Innovation through Health Data (i~HD is arising in part out of the EHR4CR project, to develop and promote best practices in the governance, quality, semantic interoperability and uses of health data, including its reuse for research. It is governed by its member stakeholders, public and private, through an elected Board and oers. It is enhanced by a mixture of membership subscriptions, fees from providing services such as certication and accreditation, specific project grants and other income from education, training and expert advisory roles. The first EHR4CR service provider, Custodix https://www.custodix.com, is now launching its operational platform, InSite (www.insiteplatform.com), for Europe-wide deployment, to be governed by i~HD. An early adopter Champion Programme has been launched as a first step in building a pan-European network connected to the InSite Platform. The objectives are to start building a network and community of hospitals open to data re-use for research, to further validate and improve the technology and to refine the business model, creating a win for all stakeholders. The Champion Programme serves at proving the value of Real World Data for clinical research and the InSite technology on a wide scale.

Approach to sustainability	**Example projects**
	Membership fees range from euro 100 to 25000. **CIRN Network** CIRN functions as a network of networks and serves as a primary source of research capacity to provide date to inform public health decision-making about immunization programs to improve the health of Canadians. CIRN's niche is at the interface of clinical research, surveillance and epidemiological research, and public health program evaluation. CIRN's focus is on late-stage vaccine evaluation of program implementation. The networks within CIRN include but are not limited to clinical trial network, reference laboratory network, immunization clincs networks. CIRN receives funding from governmental organizations (PHAC and CIHR), but also established partnerships with industry stakeholders.
Toolbox	**Euroreach**, The findings from the EuroREACH project feed into a digital compendium of health data initiatives and information systems, the Health Data Navigator (HDN). It was developed as part of the EuroREACH project and serves as a toolbox to researchers, policy makers and other stakeholders. Ultimately it aims to improve the quality of comparative health systems analysis and performance measurement and to encourage cross-country exchange of good practice data use. The HDN lists national and international data bases relevant for performance assessment with a particular focus on patient-level and disease-oriented data. An important added value of the HDN is to inform visitors of the appropriateness and quality of data they may want to use. In particular, data sources reported in the HDN are described in greater detail where information exists in regard to accessibility, coverage, quality, linkage and strenghts and weaknesses. http://www.euroreach.net/compendium **ECOM** The toolbox consists of different products that together form an evidence-based behavioural and communication package for health professionals and agencies throughout Europe in case of major outbreaks of infectious diseases. Each tool can be accessed online.A video gives a quick overview over type and purpose of the tools contained in the "ECOM Toolbox. https://vimeo.com/132125883 **IMI Get Real** Get Real makes 4 different tools available to support real world evidence generation • RWE Navigator http://www.imi-getreal.eu/Tools/RWE-Navigator • PragMagic http://www.imi-getreal.eu/Tools/PragMagic • Addis http://www.imi-getreal.eu/Tools/ADDIS • Sure Real http://www.imi-getreal.eu/Tools/Sure-Real In addition, a course is offered (paid) as well as recorded webinars.
Distributed database model	**Global Burden of Disease** The Global Burden of Disease (GBD) provides a tool to quantify health loss from hundreds of diseases, injuries, and risk factors, so that health systems can be improved and disparities can be eliminated. Collected and analyzed by a consortium of more than 2,300 researchers in more than 130 countries, the data capture premature death and disability from more than 300 diseases and injuries in 195 countries, by age and sex, from 1990 to the present, allowing comparisons over time, across age groups, and among populations. The role of the GBD collaborator is to review and provide timely feedback and suggestions related to interpretation of GBD results, data sources, and/or methodological approaches pertaining to their area of enrolled expertise. GBD data are freely available to the world's researchers and policymakers. Funding is provided through the Bill and Melinda gates foundation.

Approach to sustainability	**Example projects**
Online Service Model (quasi fixed modules)	**EU2P** In 2016, the Eu2P programme in pharmacovigilance and pharmacoepidemiology officially launched online Short Courses in Drug Safety in order to answer to healthcare professionals' and organisations' specific training needs and limited study time availabilities. EU2P received IMI funding until 2016. **EUPATI** he "EUPATI Programme", under the auspices of the European Patients Forum, whilst maintaining the spirit of a Public Private Partnership, based on approximately 25% of the annual budget of the IMI EUPATI project, combined with the full course content released under Creative Commons, was chosen in 2016 as the post-IMI sustainability model for 2017 and beyond. The EUPATI Programme can be described as a "Patient community-driven educational programme to maintain EUPATI throughout 2017-2019, focused on maximum exploitation of the EUPATI Patient Expert Training Course, on conduct of further EUPATI Patient Expert Training Courses, maintenance of the EUPATI Toolbox and the EUPATI brand, the EUPATI National Platforms, the EUPATI Fellow Alumni Network, the IT infrastructure, and on implementing updates of core EUPATI educational material". This approach ensures the continuity of EUPATI as a programme as well as a trusted brand for patient education in R&D, while facing the realities of a post-EU-funded project period and working towards longer term financial sustainability. **PATIENTS LIKE ME** PatientsLikeMe is a health information sharing website for patients. Patients have the opportunity to share both personal stories and health data about your conditions to help uncover great ideas and new knowledge. PatientsLikeMe is a for-profit company which sells the information patients share about their experience with the disease and sell it to our partners (i.e., companies that are developing or selling products to patients). **Safe SciMet.** Online paid training modules.
Association / Foundation / Federation	**ASPHER** ASPHER is a membership organisation of institutions, spread across EU and wider across WHO European Region, which are collectively concerned with the education and training, and professionalism, of those entering and working within the public health workforce. It promotes activities which foster exchange of information and best practices amongst its members in an effort to achieve high standards of public health education and training across Europe. Association with paying members. (Euro 375 to 2500 depending on the service package and country). The strategic planning effort, among other things, has indicated members' enormous dedication to the Association and strong and cohesive vision for the future. Members seek to continually make the Association stronger, assure continuity, sustainability and growth of successful endeavors as well as the involvement of all member institutions in the Association's activities. We are truly proud of the fact that the Association keeps growing and making an ever larger and more noticeable impact within European health policy and higher education and training. The Association's agenda through 2020 will reinforce this impact even more.

Approach to sustainability	**Example projects**
	Implementation of the ASPHER 2020 relies on the following assumptions: (i) Members of ASPHER accept the way forward and take part with their competence, time and other resources; (ii) Qualified groups are formed with well-defined tasks leading towards achievement of the individual objectives; (iii) Key partners are involved and take part in the planned activities. Their results are considered, implemented and recognized by ASPHER members and stakeholders; (iv) Funding and other resources are available. **Open PHACTS** The Open PHACTS Foundation is a registered charity dedicated to developing and sustaining the Open PHACTS Discovery Platform. This is made possible by the contributions and support of the Foundation Industry and Academic Members. Access to the Open PHACTS Discovery Platform and API will always be free, in line with the Foundation's goals as a charity. However like any open system we rely on an engaged community to continue to meet users' needs, and contributors to sustain our information infrastructure. The members themselves ensure the sustainability of the Open PHACTS Discovery Platform, and direct the development and strategy of the Open PHACTS Foundation. **OpenEHR** The openEHR Foundation relies on community membership and Industry Partnership for governance and financial independence. The funds will be used to provide the website and core services, develop the openEHR Technical Specifications, Clinical Archetypes and Templates for use throughout the world. Participation in the openEHR community, and access to the openEHR specifications and other IP is free to all. Formal membership is paid, and allows participation in the formal processes of the Foundation. (Euro 15-13.500 per year) - Industry partner - the openEHR Foundation Industry Partners are the key collaborators taking openEHR forward as a comprehensive, portable and language independent EHR solution forward to support quality health software around the world. - Organisational Partnership is aimed at jurisdictional, academic or other non-profit organisations who wish to support the openEHR mission **PHARMATRAIN** The PharmaTrain Federation is the successor organisation of the IMI project and is managing and further developing these valuable assets.

Two projects were identified where a post-project sustainability is planned: ASSET, DRIVE.

The landscape analysis of those project with possible relevancy for sustainability revealed a number of different approaches to sustainability and underlying funding mechanisms. The experiences from these projects can support the development of the post-ADVANCE framework.

ANNEXES

Annex I. Repository of initiatives

The repository was cleaned based on the following aspects:

- Initiatives that were not or no longer considered relevant
- Initiatives for which no additional information could be found.
- Databases (out of scope of WP2)
- Advisory committees
- Scientific societies
- Dated initiatives (<2000)
- Basis scientific and experimental research
- Projects which have been absorbed or transferred to other initiatives. (i.e. EDSN to Tessy)

An extract of the repository is provided below: providing the type of synergy established and opportunities to support the development of sustainability.

Name / Acronym	**Website**	**Levels of synergy**	**Sustainabilty**
ARITMO	http://www.aritmo-project.org/	Outcome Utilisation	
ASPHER	http://www.aspher.org/		Dissemination, Sustainability
ASSET	http://www.asset-scienceinsociety.eu/	Explored	
BCoDE	https://ecdc.europa.eu/en/publications-data/toolkit-application-calculate-dalys	Strategic Alignment	
BIG	http://www.big-project.eu/	Strategic Alignment	
BIOVACSAFE	http://www.biovacsafe.eu/	Strategic Alignment	
CIRN	http://cirnetwork.ca/		Dissemination, Sustainability
CISA	https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/		Dissemination
CNODES	https://www.cnodes.ca/		Dissemination
DRIVE	http://cordis.europa.eu/project/rcn/211596_en.html		
DSEN	http://www.cihr-irsc.gc.ca/e/40269.html		Sustainability
ECOM	http://ecomeu.info/	Explored	Sustainability
EHR4CR	http://www.ehr4cr.eu/		
EMA art. 57	http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000336.jsp	Outcome Utilisation	
EMIF	http://www.emif.eu/	Outcome Utilisation; Joint Work	Blueprint
EMTRAIN	http://www.emtrain.eu/		
EnCEPP	http://www.encepp.eu	Outcome Utilisation	Sustainability

Name / Acronym	Website	Levels of synergy	Sustainabilty
EpiNorth	http://www.epinorth.org/		Blueprint
EpiSouth	http://www.episouthnetwork.org/		Blueprint
eTRIKS	http://www.etriks.org/	Outcome Utilisation	
EU2P	http://www.eu2p.org	Strategic Alignment	Sustainability
EU-ADR	http://www.euadr-project.org;		
EUPATI	https://www.eupati.eu/	Strategic Alignment	
EUROCAT	http://www.eurocat-network.eu/		
EUROmediCAT	http://www.euromedicat.eu/		
EURO-MOMO	http://www.euromomo.eu/		Blueprint
EuroREACH	http://www.euroreach.net/		Sustainability
EuroREACH: Health data navigator	http://www.healthdatanavigator.eu/		
EuroTravNet	http://www.istm.org/eurotravnet		
EVACO (part of Venice II)	http://venice.cineca.org/evaco.html	Outcome Utilisation	
EXPLORE	http://explore-fp7.eu/		
Flu Activity & Surveillance	http://www.cdc.gov/flu/weekly/fluactivitysurv.htm		
FluID	http://www.who.int/influenza/surveillance_monitoring/fluid/en/		
Framework for interaction between EMA and Patients			Blueprint
GBD	http://www.healthdata.org/gbd	Outcome Utilisation	Sustainability
GeoSentinel	http://www.istm.org/geosentinel		
GETREAL	http://www.imi-getreal.eu/		
Global Collaborative Vaccine Safety Network	http://www.who.int/vaccine_safety/en/		Blueprint
GRiP	http://www.grip-network.org/index.php/cms/en/home	Outcome Utilisation	
GVSI	http://www.who.int/vaccine_safety/initiative/en/		Blueprint
i-HD	http://www.i-hd.eu/		Sustainability

Name / Acronym	Website	Levels of synergy	Sustainabilty
IMEDS	http://reaganudall.org/innovation-medical-evidence-development-and-surveillance	Explored	
I-MOVE/I-MOVE+	https://sites.google.com/site/epiflu/; http://www.i-moveplus.eu/	Strategic Alignment	
iPROVE	http://iprove-roadmap.eu/about/	Explored	
Sentinel	https://www.sentinelinitiative.org/	Strategic Alignment	Blueprint
MOCHA	http://www.childhealthservicemodels.eu/	Outcome Utilisation; Joint Work	
OHDSI	http://www.ohdsi.org/	Explored	Sustainability
Open PHACTS	http://www.openphacts.org		Sustainability
OpenEHR	http://www.openehr.org		Blueprint, Sustainability
Optimunise	http://www.indepth-network.org/optimunise/		
Parent	http://www.patientregistries.eu/	Strategic Alignment	
PatientsLikeMe	http://www.patientslikeme.com/	Strategic Alignment	Dissemination, Sustainability
PERSISCOPE	http://periscope-project.eu/		
PHARMASECURITY	http://www.sussex.ac.uk/globalhealthpolicy/research/pharmaceuticalsandsecurity	Strategic Alignment	
PHARMATRAIN	http://www.pharmatrain.eu/	Strategic Alignment	
PREFER	http://www.imi-prefer.eu		
PREPARE	https://www.prepare-europe.eu/		
PRISM	http://www.populationmedicine.org/research/therapeutics-research-infectious-disease/research/post-licensure-rapid-immunization-safety-monitoring		
PROMOVAX	http://www.promovax.eu/	Strategic Alignment	
PROTECT	http://www.imi-protect.eu/index.shtml	Strategic Alignment; Outcome Utilisation	
SAFEGUARD	http://www.safeguard-diabetes.org	Strategic Alignment	
SafeSciMET	http://www.safescimet.eu		
Salus	http://www.srdc.com.tr/rndprojects/salus/		Sustainability

Name / Acronym	Website	Levels of synergy	Sustainabilty
SOS	http://www.sos-nsaids-project.org/?q=home		
TEDDY	https://www.teddynetwork.net/		
TELL ME	http://www.tellmeproject.eu/	Strategic Alignment	
TESSy	http://www.ecdc.europa.eu/en/activities/surveillance/tessy/Pages/TESSy.aspx	Outcome Utilisation	Blueprint
The benefit-risk methodology project	http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/document_listing/document_listing_000314.jsp&mid=WC0b01ac0580665b63		
TRANSFORM/ TIRRE	http://www.transformproject.eu	Outcome Utilisation	
UNISEC	http://www.uniseccconsortium.eu/		Blueprint
Vaccine scheduler	http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx	Outcome Utilisation	Blueprint
Vaccine Sentimeter	http://healthmap.org/viss/	Strategic Alignment	Blueprint
VAESCO	http://vaesco.net/vaesco.html		
Venice I - III	http://venice.cineca.org		
VDP	https://ecdc.europa.eu/en/about-us/who-we-are/disease-programmes/vaccine-preventable-diseases-programme		
VSD	http://www.cdc.gov/vaccinesafety/activities/vsd.html		Blueprint
WEB-RADR	http://web-radr.eu		