



Project full title: Up-scaling the global univocal identification of medicines

Call identifier: H2020-SC1-DTH-2019

Deliverable D10.1:

Assessment Framework Socio-Economic Impact

Version: 1.0
Status: Final
Dissemination Level¹: PU
Due date of deliverable: 31.05.2021
Actual submission date: 01.06.2021
Work Package: WP10: Socio-economic impact, legal and governance aspects
Lead partner for this deliverable: EMP
Partner(s) contributing: na
Deliverable type²: R

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Resource consumption estimate:	Person months
EMP	1,0

¹ Dissemination level: PU: Public; CO: Confidential, only for members of the consortium (including the Commission Services); EU-RES: Classified Information: RESTREINT UE (Commission Decision 2005/444/EC); EU-CON: Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC); EU-SEC Classified Information: SECRET UE (Commission Decision 2005/444/EC)

² Type of the deliverable: R: Document, report; DEM: Demonstrator, pilot, prototype; DEC: Websites, patent filings, videos, etc.; OTHER; ETHICS: Ethics requirement; ORDP: Open Research Data Pilot

Revision history

Version	Date	Changes made	Author(s)
0.1	02.02.2021	Structure, content, and key messages	ST, FD
0.2	04.03.2021	Initial draft of Chapters 2-5	ST
0.3	20.03.2021	Initial draft of Chapters 6 and 7	ST
0.4	31.03.2021	Completed initial draft for discussion and review	ST
0.5	06.04.2021	Formatting changes, and increased content for Chapters 3 and 4	ST
0.6	20.04.2020	Increased content for Chapters 5 and 6	ST
0.7	20.11.2020	Revised content and structural changes to Chapter 3	ST, FD
0.8	23.05.2021	Completion of outlook, executive summary, and abstract sections	ST
0.9	24.05.2021	Ready for internal QR	ST, FD, KAS
1.0	31.05.2021	Final after internal QR	ST, KAS

Statement of originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

Deliverable abstract

This deliverable develops an initial socioeconomic impact assessment and cost-benefit analysis framework for UNICOM. The overall framework is use-case driven and incorporates multiple stakeholder perspectives in an effort to provide a comprehensive analysis of UNICOM's impacts. The deliverable presents the necessary background to establish a frame of reference for evaluating the project's socioeconomic impact including selected stakeholders and key use cases for IDMP implementation. It expands on the selected methodological paradigm for evaluating impact, based on a socioeconomic impact assessment tool called ASSIST, including its theoretical foundations and approach to data collection. The deliverable also reports preliminary findings on expected benefits and derived impact indicators for selected stakeholders and briefly details planned UNICOM pilots, all of which will inform the final evaluation of the project's impact.

Keywords: UNICOM, IDMP, socioeconomic impact, cost-benefit analysis, stakeholders, use cases

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List of abbreviations

Abbreviation	Complete form
ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
AE	Adverse Event
ARIA	Azienda Regionale Per L'innovazione e Gli Acquisti
ASSIST	Assessment and Evaluation Tools for Telemedicine
ATC	Anatomical Therapeutic Chemical Classification System
BAID	Batch Identifier
CBA	Cost-Benefit Analysis
CEF	Connecting Europe Facility
CMC	Chemistry, Manufacturing, and Control
CT	Clinical Terminology
DF	Dosage Form
DG	Directorate-General
DW	Datawizard
EDQM	European Directorate for the Quality of Medicines & HealthCare
EHR	Electronic Health Record
EMA	European Medicines Agency
EU	European Union
FDA	United States Food and Drug Administration
FHIR	Fast Healthcare Interoperability Resources
FOUND	Federico II University Hospital
GDP	Gross Domestic Product
GP	General Physician
GTIN	Global Trade Item Number
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICT	Information and Communications Technology
ID	Identification

IDMP	Identification of Medicinal Products
INN	International Nonproprietary Name
ISO	International Organization for Standardisation
IT	Information Technology
IU	International Unit
MAH	Marketing Authorisation Holder
MDM	Master Data Management
ME	Medical Event
MP	Medicinal Product
MPD	Medicinal Product Development
MPI	Medicinal Product Information
MPID	Medicinal Product Identification
MS	Member State
NCA	National Competent Authority
PCID	Packaged Medicinal Product Identifier
PDF	Portable Document Format
PPL	Pilot Product List
SMS	Substance Management System
SPOR	Substances, Products, Organisations And Referentials
SRS	Substance Registration System
UCUM	Unified Code for Units of Measure
UK	United Kingdom
US	United States
WHO	World Health Organisation

1 Executive summary

Medicinal product identification is a worldwide patient safety issue that necessitates a cohesive collaborative solution. Despite efforts by the global medicinal product standardisation community, there is persistent need for a standardised medicinal product information data exchange infrastructure for the reliable identification of medicinal products and their ingredients. The International Organization for Standardization's (ISO) suite of IDMP (IDentification of Medicinal Products) standards for accurate identification along the full life cycle of drugs was conceived to meet this challenge.

The UNICOM project's main goal is to enhance and implement the ISO IDMP suite of standards for the univocal identification of medicinal products across participating Member States and all stakeholders engaged in the life-cycle data management of medicinal products. As a four-and-a-half year trans-Atlantic semantic interoperability project with a wide consortium of over forty European and American partners, UNICOM is well situated to provide the collaborative platform needed for such an ambitious goal. UNICOM integrates diverse perspectives and coordinates their activities by bringing together multiple stakeholders such as standard development organizations, national medicines authorities, pharmaceutical industry, national eHealth authorities, medicinal products database providers, cross-border healthcare services, healthcare professionals, patient advocacy groups, and others, into one European Innovation Action focused on IDMP implementation.

The present deliverable develops an initial Socioeconomic Impact Assessment and Cost-Benefit-Analysis (CBA) framework for UNICOM which will be further detailed and implemented over the course of the project. The overall framework is use-case driven and incorporates multiple stakeholder perspectives in an effort to provide a comprehensive analysis of UNICOM's impacts.

Chapter 2 presents a brief introduction to the project including its context and the goals and objectives for the current deliverable. Chapter 3 expands upon the necessary background and theoretical underpinnings in order to provide a frame of reference for the socioeconomic impact assessment framework. Chapter 4 reports on key use cases for UNICOM and IDMP implementation (including pharmacovigilance and clinical care, regulatory data management, medicinal product development, and cross-border and eHealth services) which guide the stakeholder mapping and classification in Chapter 5. Chapter 6 operationalises the socioeconomic impact assessment framework into the ASSIST methodology, which is a socioeconomic impact assessment tool developed by *empirica*. Chapter 7 then concludes the report by presenting an outlook which includes preliminary findings on the expected benefits of UNICOM from the point of view of the selected stakeholders, i.e., National Competent Authorities (NCAs), pharmaceutical companies, healthcare professionals, and patients, as well as a few details on the planned pilots in UNICOM.

2 Introduction

This introductory chapter briefly explores the context of the UNICOM project within the IDMP domain. It reports on the overarching goal of the current deliverable, D10.1, concrete objectives of the tasks to be performed, and consequent work on socioeconomic impact to be further developed on in WP10.

2.1 Context

The UNICOM project is about improved patient safety and better healthcare for all. Reliably identifying medicinal products for pharmacovigilance reporting and related regulatory processes has been a globally acknowledged challenge for more than half a century. Today, other domains in need of univocal, safe and semantically interoperable data on drugs have been acknowledged, including public health, big data/research applications, healthcare processes involving diverse actors, and measures against falsified medicines. Implementing the International Organization for Standardization's (ISO) suite of IDMP (IDentification of Medicinal Products) standards along the full life cycle of drugs is to finally meet this challenge.

IDMP standards are used to define and classify medicinal products in a coherent manner such that product information can be recorded, coded, and exchanged between global regulators, producers, retailers, and distributors, among others. Following IDMP guidelines helps the regulatory bodies by facilitating prescription production and certification, medical product life cycle management, pharmacovigilance, and risk management. For the clinical domain, IDMP specifications are also applicable to improving processes related to prescription, dispensation, and medicinal product comparisons, amongst others.

UNICOM is a four-year trans-Atlantic project supported by the European Commission. Partners include national Medicines Authorities across Europe, national Digital Health Agencies, healthcare organisations, standardisation bodies, health ICT companies, SMEs, research institutes and other actors involved in the life-cycle management of data on medicinal products. The UNICOM teams closely work with the European Medicines Agency (EMA), the USA Food and Drug Agency (FDA), the World Health Organisation (WHO) and its Collaborating Centres, the pharma industry, and multiple stakeholder associations.

Partners work together to enable existing databases and products that include medicinal information to be adapted towards IDMP-formatted data fields and attributes. This will allow them to physically exchange semantically interoperable information so that they can be accurately cross-referenced with each other, understood and integrated across national borders, and analysed at national, European, and global levels.

2.2 Deliverable Goal

This deliverable D10.1 *Assessment Framework Socio-Economic Impact* is one of the outputs of Task 10.1 *Development assessment framework socio-economic impact*.

The overall goal of this task in WP10 *Socio-economic impact, legal and governance aspects* is to develop a socioeconomic impact assessment and cost-benefit analysis framework that also includes a use case based dual perspective regulatory and clinical impact analysis approach, forecasting potential impact on the project's outcomes. This approach will be realized through the following steps:

1. Establish the directions of impact which the framework will incorporate including better health data access for patients and healthcare providers; improved quality of care, improved patient safety; and the sustainability of European health care systems.
2. Determine general and specific use cases for UNICOM and IDMP implementation in terms of public health and healthcare provisions both domestically and cross-border, including pharmacovigilance and regulatory domains.
3. Develop a data collection and cost-benefit assessment method that analyses UNICOM's impact on selected stakeholder's in terms of the medical and pharma regulatory data space, clinical data quality and interoperability, medicinal product data standardisation practices, pharmacovigilance, and cross-border applications.

4. Define UNICOM-specific indicators for anticipated benefits and costs from a user, stakeholder, and market perspective to inform data collection (T10.2) and feed into the overall socio-economic and cost-benefit analysis in T10.3.

2.3 Objectives

The present deliverable develops a UNICOM socioeconomic impact assessment conceptual framework, i.e. a first outline of an assessment method. Further it analyses the expected benefits of UNICOM from the point of view of National Competent Authorities (NCAs), pharmaceutical companies, healthcare professionals, and patients in a preliminary forecast.

A final and comprehensively detailed method to be applied in the socioeconomic assessment of the project will only be available once the piloting strategy of the project will have been specified in more detail and once the use case scenarios, both clinical and regulatory, will have been fully fleshed out. This assessment framework and its empirical results towards the end of the project will inform D10.3 *Cost-benefit analysis including spill-over effects* and the final report incorporate results from planned pilots in WPs 5-9.

In general, and in an iterative cycle between data collection, evaluation, and impact modelling, this socioeconomic impact assessment strategy should be informing the direction of the project's final cost-benefit analysis; hence the methodological framework as developed in this deliverable needs to be adaptive enough to tailor the measuring process. It will be closely aligned with D12.4, D12.5 and with the WP12 tasks.

For this Task 10.1 in WP10 and this deliverable, these specific objectives need to be pursued:

- ▶ Gather data and literature on:
 - ▷ the medicinal product data value chain
 - ▷ the development and structure of ISO-IDMP standards
 - ▷ pharmacovigilance in European healthcare and incidents of adverse drug events.
 - ▷ the effects of standardisation on the economy and on healthcare
 - ▷ value propositions of different actors in healthcare
 - ▷ EU cross-border ePrescription and eDispensation contexts
- ▶ Review literature on common socioeconomic impact assessment methods and address methodological aspects related to modelling the impact of new standards in healthcare;
- ▶ Develop a cost-benefit analysis framework and establish a meaningful set of impact indicators and processes that are robust to demonstrate socioeconomic impact from multiple perspectives.

3 Background

The implementation of UNICOM, the outputs expected, as well as the tight time frame in which project milestones must be achieved, all require challenging assembly and integration of interdisciplinary expertise across scientific, clinical, health, pharmaceutical, regulatory, and business domains. A socio-economic impact assessment needs to reflect on all these diverse perspectives. In order to develop the evaluation framework for the socioeconomic impact of UNICOM, and indeed of IDMP standardisation, Chapter 3 expands upon the necessary background and theoretical underpinnings. It reports on the economic relevance of the European health sector and examines the burden of adverse drug reactions to exemplify the need for ISO-IDMP standards. It then discusses the importance of standardisation as a concept and its delineated effects in the health sector to provide context for WP10's subsequent efforts to model the specific benefits of IDMP standardisation. The chapter ends with an overview of the differences in value propositions for diverse actors in the health sector which informs WP10's aim of developing use case-based impact scenarios for various stakeholders.

3.1 Burden of Severe Adverse Drug Reactions

The need for IDMP standards first arose in the context of pharmacovigilance, and it is exemplified by the health and socio-economic burden of adverse drug reactions (ADRs). The European Medicines Agency estimated that around 200,000 deaths per year are caused by ADRs across the European Union (EU), and that their "societal economic burden" amounts to around €80 billion for all EU Member States.³

Across medical communities, the urgent need for pharmacovigilance has been acknowledged for decades, but without much impact. However, the last 50 years have seen a growing and significantly greater emphasis placed on pharmacovigilance – not only for national health systems, but also at the global scale. Even after medicinal product approval by regulatory authorities, severe adverse reactions can and do occur, leading to long lists of warnings, and even to product recalls and market withdrawal. Figure 1 shows a brief history of drugs being removed from the market, some of which have ended in lawsuits against the pharmaceutical companies and triggering patient compensations in the order of billions of U.S. dollars.

Drugs	Severe adverse reactions	Year of withdrawal
Thalidomide	Teratogenicity	1961
Practolol	Oculo-mucocutaneous syndrome	1976
Phenacetin	Nephropathy	1980
Benoxaprofen	Jaundice	1982
Tolcapone	Hepatotoxicity	1998
Trovafloxacin	Hepatotoxicity	1999
Cisapride	Cardiac arrhythmias; QT prolongation	2000
Cerivastatin	Rhabdomyolysis	2001
Rofecoxib and valdecoxib	Myocardial infarction	2004–2005
Rosiglitazone	Myocardial infarction	2010
Sibutramine	Cardiovascular diseases	2010

Figure 1. A brief history of severe drug adverse reactions and subsequent product withdrawals⁴

³ European Commission, Staff Working Document, Impact Assessment, SEC(2008) 2670 Volume I, Accompanying Document to the Proposal for a Regulation amending, as regards pharmacovigilance of medicinal products for human use; Regulation (EC) No 726/2004 and the Proposal for a Directive amending, as regards pharmacovigilance,

⁴ Scurti, V., Romero, M., & Tognoni, G. (2012). A plea for a more epidemiological and patient-oriented pharmacovigilance. *European journal of clinical pharmacology*, 68(1), 11-19.

Thalidomide, manufactured by Chemie Grünenthal in the 1950s, was a medicinal product originally intended as a sedative or tranquiliser, but was soon used for treating a wide range of other conditions, including colds, flu, nausea. Later on, it was also prescribed to pregnant women for treating morning sickness. At the time, however, its risks to the unborn child were unknown, globally resulting in more than 10,000 children born with a range of severe deformities, such as phocomelia, as well as thousands of miscarriages. The total number of people affected by the use of thalidomide during the mother's pregnancy is estimated at more than 10,000, of whom approximately 40 percent died at or shortly after the time of birth⁵. Those who survived had limb, eye, urinary tract, and heart defects. Once discovered, the Thalidomide scandal led to global changes in regulations related to pharmacovigilance and medicinal product testing. The primary reason behind the delay in Thalidomide recall was the 51 different trade names it was known by and marketed in different countries; within Italy alone, it was sold under 10 different trade names⁶. Since then, several international lawsuits against the manufacturer and distributors have taken place, and nearly a billion euros have been paid out to victims and their families as compensation⁷.

Similarly, other cases of adverse drug events have also had severe consequences. Vioxx, by Merck, was approved by the FDA in May 1999 for the relief of acute pain osteoarthritis and dysmenorrhoea. In 2001, a meta-analysis in the Journal of the American Medical Association demonstrated that Vioxx damages the heart leading to its recall in September 2004 but not before an estimated 88,000 to 160,000 people had suffered heart attacks with at least 38,000 being fatal. Several federal multidistrict litigations in the U.S were established against Merck & Co. and they agreed to a settlement to pay 950 million dollars and pled guilty to misdemeanor charges of illegal marketing⁸.

Benoxaprofen was originally launched in 1980 as a medicinal product for rheumatoid arthritis. It was suspended by the UK Committee on Safety in 1982 and shortly thereafter recalled globally⁹. Benoxaprofen was associated with a high incidence of adverse effects, including prominent effects on the skin and nails, as well as adverse liver reactions which sometimes proved fatal¹⁰. In the US, the company was charged with false advertising as the drug was previously marketed as having no harmful side effects. The Company pleaded guilty to criminal charges of failing to inform the government about the deaths and illnesses related to and was fined \$25,000. Additionally, the manufacturer was sued in the UK by victims. In 1988 a settlement was reached where the manufacturer agreed to pay £2,275,000 divided among 1200 plaintiffs as well as their legal costs of £4 million¹¹.

3.2 ISO-IDMP and Barriers to the Free Flow of Safe Medicinal Product Information

Often the inability to reliably identify and reconcile medicines prescribed by diverse professionals across health systems, or to integrate pharmacovigilance reports on drugs with different names, but identical active substances contributes substantially to this burden. Presently, various barriers can be identified to a safe, seamless flow of univocal medicinal product data across European and global borders:

- Existence of only national markets for authorised medicinal products;

⁵ Miller MT (1991). "Thalidomide Embryopathy: A Model for the Study of Congenital Incomitant Horizontal Strabismus". *Transactions of the American Ophthalmological Society*. **81**: 623–674;

"Thalidomide Monograph for Professionals". *Drugs.com*. Retrieved 14 November 2019

⁶ Ridings, J. E. (2013). The thalidomide disaster, lessons from the past. *Methods in Molecular Biology*, 947, 575–586.

⁷ Mark, R. (2014). Thalidomide victims receive \$89m compensation. *The Age National*, 6–8.

Newbronner, E., Glendinning, C., Atkin, K., & Wadman, R. (2019). The health and quality of life of Thalidomide survivors as they age – Evidence from a UK survey. *PLoS ONE*, 14(1), 1–18.

Laurence, J. (2012). "Government 's £ 80m for victims of thalidomide – but still no apology." *Independent UK*, pp. 1–4.

EFE (2016) "European Parliament calls on Germany to compensate victims of thalidomide," From <https://www.euractiv.com/en/european-parliament-calls-on-germany-to-compensate-victims-of-thalidomide/50000267-3125731>

⁸ Frieden (2016). "Merck to pay \$950 million for illegal marketing of Vioxx", *CNN Health*, From <https://edition.cnn.com/2011/11/22/health/merck-vioxx-fine/index.html>

⁹ La Rochelle, P., Lexchin, J., & Simonyan, D. (2016). Analysis of the drugs withdrawn from the US market from 1976 to 2010 for safety reasons. *Pharmaceutical Medicine*, 30(5), 277–289.

¹⁰ Onakpoya IJ, Heneghan CJ, Aronson JK. Post-marketing withdrawal of 462 medicinal products because of adverse drug reactions: a systematic review of the world literature. *BMC Med*. 2016;14:10.

¹¹ Hodges, C. (2001). Multi-party actions: A European approach. *Duke J. Comp. & Int'l L.*, 11, 321.

- ▶ Complex marketing strategies of pharmaceutical companies across countries;
- ▶ Insufficient data quality/legacy data for (older) medicines;
- ▶ Absence of ‘fit-for purpose’, globally agreed standards (concepts, data models, resources), coding systems, and implementation guidelines to ensure the ‘physical’ access to and exchange of high-quality data at all levels of use.

These problems persist despite international agreements and requirements on the global exchange of pharmaceutical product safety data. International exchange of pharmaceutical safety data is an established process that helps stakeholders enrich their databases and increase their ability to monitor the safety of pharmaceutical products. However, lack of homogeneity is a major limiting factor in the usability of product safety data from different countries and regions. In order to overcome this, in 1997, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) developed an international standard for the structure of safety data relating to individual patients. This standard, which is coded as ICH E2B, has been updated twice, with the last update, ICH E2B (R3), being published in 2011¹². The updates addressed certain issues that came up during ICH’s subsequent experience with worldwide safety information exchange. In particular, exchange of information between organisations in different geographical areas revealed the inconsistency of data elements in various regions of the world. Striking examples were differences in active substance naming, measuring units or description of dosing¹³.

The enhancements achieved by ICH E2B (R3) would be limited without a common standard for medicinal product identification. Following several consultations, the stakeholders agreed on a solution that could overcome existing variations and national boundaries. This solution necessitated the use of a common standard that would internationally regulate all conceivable characteristics of medicinal products. The International Organization for Standardisation (ISO), the most prominent international standardization organisation was chosen to issue this standard. The technical specifications for such a complex and demanding project considered existing knowledge, know-how and other standards in order to identify a starting point.

Standards developed by Health Level Seven International (HL7), so-called HL7 standards, which support the exchange, integration, sharing, and retrieval of electronic health information, were identified as the best starting platform¹⁴. These standards, already widely applied by various healthcare provision organisations, define how information is packaged and communicated from one party to another, setting the language, structure and data types required for seamless integration between systems¹⁵. Through ISO, IDMP has built upon the original HL7 platform to develop standards appropriate to the characteristics of medicinal products in an effort to overcome the challenges associated with univocal medicinal product identification¹⁶.

The UNICOM project aims to ensure close cooperation among all actors involved in further development, piloting, and broad implementation of IDMP standards. Fully fit-for-purpose, application of the IDMP international “terminology” will be mandatory for EU National and Regional Medicines Authorities; and the use of IDMP “formats and standards” is recommended by EU legislation (Commission Implementing Regulation on the performance of pharmacovigilance activities (EU) No 520/2012 [articles 25 and 26])¹⁷.

By accelerating the further development and diffusion of ISO IDMP standards, UNICOM supports:

- ▶ Regulatory processes of National Medicines Authorities (NMAs) & the European Medicines Agency (EMA) through partial funding of the creation of a single European “Substance Registration System” as a fundamental base for all further IDMP implementation work;

¹² https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-4.pdf

¹³ https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-4.pdf

¹⁴ Dolin, R. H., & Alschuler, L. (2011). Approaching semantic interoperability in health level seven. *Journal of the American Medical Informatics Association*, 18(1), 99-103.

¹⁵ Wood, G. M. (2013). HL7 Basic Overview.

¹⁶ Koshechkin, K., Lebedev, G., & Eduard, F. (2020). Implementation of IDMP Standards as a Means of Creating a Unified Information Space in the Field of Drug Circulation. *Procedia Computer Science*, 176, 1745-1753.

¹⁷ <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:159:0005:0025:EN:PDF>

- ▶ a common IDMP-compatible electronic submission platform for marketing authorisation applications (including variation reporting and renewals) by pharma companies;
- ▶ through focused IDMP implementation efforts at national levels the identification of identical or equivalent medicinal products in the context of EU-wide cross-border digital health services (ePrescription/eDispensation reporting, Patient Summary) including smart substitution where allowed;
- ▶ better healthcare, public health, and medical research (e.g., big data analytics, artificial intelligence applications, etc.);
- ▶ global pharmacovigilance.

Semantic interoperability along the medicine data value chain will enable the seamless exchange and sharing of health data related to medicines across all actors involved in handling or consuming such data and across the full life cycle of a medicine¹⁸. It will facilitate faster and better pharmacovigilance reporting, create economic efficiency gains for industry and service providers, and facilitate the use case of ePrescription/eDispensation in cross-border settings. It will improve safe, reliable recording of medicinal product information in clinical documents (e.g., Patient Summaries, health records) and enable safer communication with and empowerment of patients. Finally, it will improve reuse of medication related data for public health and medical research as well as create new synergies across regulatory, healthcare, public health, and scientific domains.

3.3 European Health Space

UNICOM has to be seen in the context of health systems of the European Union which are a fundamental part of Europe's social infrastructure. The final goal of all health system activities is to promote, maintain, improve, re-establish or at least stabilise the health status of people, independent of their personal situation. This includes care for patients with chronic conditions and illness prevention in healthy populations. The key challenge of today's health systems is to improve the quality, quantity and equal access to these services.

The pharmaceutical sector, as the developer of medicinal products, is an essential component of meeting the challenges of healthcare. In the Official Sector Inquiry published in 2009 by the European Commission (DG Competition)¹⁹, the pharmaceutical sector was shown to be vital to the health of Europe's citizens and medicines to be a major expense, nearing 2% of the EU GDP. The same could be said of the medical devices sector, where the European medical technology industry generates annual sales of roughly € 100 billion, invests some € 4 billion per year in R&D and employs around 575,000 highly skilled workers. Both sectors occupy therefore important positions in the EU economy. In 2019 pharma on its own accounts for 795,000 jobs²⁰ and for some 4% of total manufacturing value added²¹. This share is much higher in some Member States, such as Belgium, Denmark, Sweden and Slovenia, reaching between 8.5 and 10% of manufacturing value added.

As the population of Europe ages, as expectations rise, and as medicine advances, demand for health services rises with it. The scope for increase in the resource base to meet this demand is limited. The task is complicated by the limited availability of mainly financial resources, but quite often also of qualified staff. For quite some time, the health and social services sector is a dominant economic sector of the European Union. In 2002, the sector employed more than 15.5 million people, more than 9% of European employment²², and by 2019 this number grew to nearly 26 million people, nearly 11.4% of European employment²³. Healthcare expenditure already accounts for some 8.5 of European GDP²⁴, with projections of the share rising to 12% by 2030²⁵.

¹⁸ <https://www.ema.europa.eu/en/human-regulatory/overview/data-medicines-iso-idmp-standards-overview>

¹⁹ <https://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>

²⁰ <https://www.statista.com/statistics/316070/european-pharmaceutical-industry-employment/>

²¹ <https://www.statista.com/statistics/1195197/employment-by-sector-in-europe/>

²² Rechel, B., Dubois, C. A., McKee, M., & World Health Organization. (2006). The health care workforce in Europe: learning from experience. World Health Organization. Regional Office for Europe.

²³ <https://www.statista.com/statistics/1195197/employment-by-sector-in-europe/>

²⁴ https://efpia.eu/media/554521/efpia_pharmafigures_2020_web.pdf

²⁵ O.E.C.D. (2019). *Health at a glance 2019: OECD indicators*. OECD Publishing, Paris.

The "Council Conclusions on Common Values and Principles in European Union Health Systems"²⁶ summarise the goals and priorities of Member States in the field of healthcare. Universality, access to good quality care, equity, and solidarity constitute a set of overarching values that are shared across Europe. Universality refers to the universal, i.e. for everyone, access to healthcare; solidarity relates to the financial dimension of ensuring accessibility to all; equity emphasises that access should be according to needs, regardless of ethnicity, gender, age, social status or ability to pay. Member States are also concerned by differences in the quality of health services across the Union, as well as issues of prevention through promotion of healthy lifestyles.

Despite following different approaches, all EU health systems aim at ensuring healthcare provision, which is patient-centred and responsive to individual need. Member States also aim at making the systems financially sustainable, while safeguarding the values listed above. An integral part of the strategy towards sustainability is a shift in focus towards preventive measures, which is expected to reduce the cost burden by avoiding the occurrence of disease and associated treatment costs²⁷.

These efforts are ultimately aiming at optimising the use of resources in order to meet the increasing demand, given the budget constraints²⁸. An associated challenge is to utilise existing and emerging technologies to best effect, even when this means changing established and valued working and clinical practices. Already, we can observe that even organisations in the largely public health sector in Europe increasingly adopt private business practices in their management and other activities²⁹. Organisations providing health services today have to change the way they deliver them. This may require the adoption of new and innovative business models for healthcare provision. Some of these new models are supported, or even driven by the implementation of modern information and communication technologies.

The promise of ICT based health solutions, of which IDMP infrastructure development is a part, is that it facilitates networking, citizen-centred information sharing and exchange, transparency, and collaboration between different healthcare stakeholders. Healthcare professionals are empowered in their role of providing healthcare. Electronic health records, in particular, are expected to facilitate seamless healthcare provision involving various specialists at different locations as needed. Some types of eHealth also allow the individual citizen to become an independent, active, and responsible partner in the system. By being able to access information easily about their condition, different treatment options, health choices and their implications, citizens and patients can be empowered and become involved in the processes of maximising health and optimising provision of healthcare. Evidence shows that ICT-supported healthcare, or more generally eHealth, indeed has the potential to help achieve these improvements and contain cost explosions by enabling healthcare providers to use their resources to better effect, thus expand their capacity and performance to meet increasing demand³⁰.

3.4 Standardisation and its Effects on the Economy

IDMP implementation is at its core implementation of an infrastructure for standardised information. As a component of modern economic infrastructure, standardisation has been cited as a major contributor to the exceptional growth of the economy. In the First Industrial Revolution, interchangeable parts appeared as the first instance of interface standards. In the Second Industrial Revolution (approximately the 1880s to the 1950s), standardisation spread to important industrial infrastructures such as product standards in chemicals and interoperability standards in communication networks. Beyond the scope of standardisation in the previous two industrial revolutions, and the ongoing Third Industrial Revolution is

²⁶ [https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52006XG0622\(01\)&from=EN](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52006XG0622(01)&from=EN)

²⁷ Seychell, M., & Hackbart, B. (2013). The EU Health Strategy—Investing in Health. *Public Health Reviews*, 35(1), 4.

²⁸ Földes, M. E. (2016). Health policy and health systems: a growing relevance for the EU in the context of the economic crisis. *Journal of European Integration*, 38(3), 295-309.

²⁹ Trifonova, S., & Pramatarov, A. (2018). Health Systems Financing in the EU Member States. In 5th International Multidisciplinary Scientific Conference on social sciences and arts SGEM 2018 (pp. 965-976).

³⁰ Tavares, A. I. (2018). eHealth, ICT and its relationship with self-reported health outcomes in the EU countries. *International journal of medical informatics*, 112, 104-113.

being driven by a new generation of products that comprise the integration of an amazing portfolio of complex digital technologies³¹.

The role of standards in the diffusion of technical knowledge and their resulting contribution to economic growth has been demonstrated in various empirical studies. Several detailed econometric studies have established a clear connection at a macroeconomic level between standardisation in the economy, productivity growth and overall economic growth. These studies have been carried out for the UK, Germany, France, Canada and Australia. Estimates vary somewhat from study to study, but overall, the growth of the standards catalogue over recent years may account for between one eighth and one quarter of productivity growth over the period³². The contribution of standards to the growth rate in each country is equivalent to 0.9 % in Germany, 0.8 % in France and Australia, 0.3 % in the UK and 0.2 % in Canada³³. It can be assumed that, mutatis mutandis, these results also reflect on the health sector.

3.5 Specific Impacts of Standardisation in the Health Sector

Mapping the IDMP standards to functional classifications of standards³⁴ further develops the theoretical underpinnings about the impact of IDMP standards.

3.5.1 Codified Information and Variety Reduction

Standardisation is part of the knowledge infrastructure, and as such provides codified information for all. Investments in this infrastructure make such information is available to all, as cheaply as possible, and the beneficial effects of this flow from the use of this information by experts in each market³⁵. Econometric papers suggest that standards can play an important role as the carrier of codified knowledge. When standards are not consistent and implementation is incomplete, knowledge about products and production does not travel easily³⁶. This applies, in particular, also to a sector as knowledge-intensive and knowledge-driven as health.

Standards also serve to reduce variety in the accessibility of diverse data structures³⁷. Variety reduction is usually done with reference to a trade-off between the desire for variety and the potential advantages in terms of scale economies. Any standard that reduces variety is likely to lead to benefits in the form of scale economies. Variety reduction can also have implications for barriers to entry and for transaction costs. Variety reduction standards limit strategies of variety proliferation, which are sometimes used by large organisations in an attempt to limit competition from small scale entrants who cannot match the same degree of variety, thus reducing some barriers to entry. Variety reduction standards can also reduce transaction costs if choice becomes easier in the absence of what seems to the buyer an unmanageable variety of choice³⁸. Applying these considerations to health, it is reasonable to assume that it is much more difficult for these aspects to be realised in medical contexts; contexts with enormous diversity, different cultural settings, steadily rising knowledge and treatment options, the preponderance of diverse national, and even regional health systems etc.

3.5.2 Compatibility and Network Effects

Compatibility and interface functions of standards generate network effects; they play an important role in increasing economic efficiency through network externalities³⁹. In markets with network effects the

³¹ Tassey, G., (2017). The roles and impacts of technical standards on economic growth and implications for innovation policy. *Ann. Sci. Technol. Policy* 1.

³² Swann, G.M.P., (2010). The Economics of Standardization: An Update.

³³ Blind, K. (2013). The Impact of Standardization and Standards on Innovation. *Nesta Working Paper*, p.13/15.

³⁴ Egyedi, T.M., Ortt, J.R., (2017). Towards a functional classification of standards for innovation research. *Handb. Innov. Stand.* 105–131

³⁵ Swann, G.M.P., (2010). The Economics of Standardization: An Update.

³⁶ Xie, Z., Hall, J., McCarthy, I. P., Skitmore, M., & Shen, L. (2016). Standardization efforts: The relationship between knowledge dimensions, search processes and innovation outcomes. *Technovation*, 48, 69-78.

³⁷ Egyedi, T.M., Ortt, J.R., (2017). Towards a functional classification of standards for innovation research. *Handb. Innov. Stand.* 105–131

³⁸ Swann, G.M.P., (2010). The Economics of Standardization: An Update.

³⁹ Egyedi, T.M., Ortt, J.R., (2017). Towards a functional classification of standards for innovation research. *Handb. Innov. Stand.* 105–131

benefit to consumers from joining a network depends on the number of other consumers who join the network. There are circumstances where the value of a product for a consumer does not depend only on the quantity or the quality of the product itself, but also on the availability and variety of complementary goods and/or the number of people using the same product. A mobile phone, for example, is more valuable for a consumer the higher the total number of people using the same or a compatible mobile phone network⁴⁰. A computer is more valuable the more compatible software is available in the market. By facilitating the interchange of information, enabling comparison and evaluation of products, and reducing uncertainty about the product, standards on product information can increase the number of users, create network effects and enable the diffusion of innovations⁴¹. Standards are necessary for the diffusion of a new technology in network industries. Setting a standard has, for instance, proven to be essential for successful innovation in the wireless networking industry, i.e., Wi-Fi. Initially, vendors of wireless equipment developed their own standards. In this way, users of the Wi-Fi technology were locked into a particular vendor's products. It was not until 1999, when the six major companies of wireless technology – Intersil, 3Com, Nokia, Aironet, Symbol and Lucent – agreed on a common standard, that the Wi-Fi market took off⁴².

Similarly, the health sector, with its increasing digitalisation, faces a growing necessity for professionals and health care organisations (family doctors, specialists, secondary and tertiary hospitals, laboratories, physiotherapists, occupational therapists, health insurances, rehabilitation, public health, etc...) to work together to integrate their services for a given patient. This results in the formation of a network, which benefits from the associated network effects described above, and IDMP is well situated as a path-setting example of what this may imply for both improved healthcare services as well as growth of innovation in the health sector industry.

3.5.3 Innovation

Standards play a catalytic role also for innovation. Firstly, the standardisation process reduces the time to market of inventions, research results and innovative technologies⁴³. Secondly, standards themselves promote the diffusion of innovative products, which is most important for the economic impact of innovation. A third important function of standards is that they level the playing field and therefore promote competition and consequently further innovation. Fourth, compatibility standards are the basis for innovation in network industries where they also facilitate the substitution of old technologies by new ones, e.g., by forward and backward compatibility, and also to allow the coexistence of old and new technologies⁴⁴. New platform standards are often the basis for innovation in downstream markets, e.g., the android mobile operating system as platform for numerous mobile services, but also in upstream markets, i.e., the types of available operating systems. Besides these network related functions, a generic characteristic of standards is that they reflect user needs and therefore promote the purchase and diffusion of new products by early adopters. Finally, standards set the minimum requirements for environmental, health and safety aspects and consequently promote trust, a key aspect in adoption of innovative products⁴⁵.

The above-mentioned innovation related aspects are directly applicable to the health sector as well. Innovation in healthcare is expected to continue to increase, keeping pace with the steady growth of the sector, its digitalisation, and evolving trends in both medical devices and medicinal products.

⁴⁰ Weitzel, T., Beimborn, D., & König, W. (2006). A unified economic model of standard diffusion: The impact of standardization cost, network effects, and network topology. *Mis Quarterly*, 489-514.

⁴¹ World trade organization. (2005). *World trade report 2005: Exploring the links between trade, standards and the WTO*.

⁴² World trade organization. (2005). *World trade report 2005: Exploring the links between trade, standards and the WTO*.

⁴³ Tasse, G., (2017). The roles and impacts of technical standards on economic growth and implications for innovation policy. *Ann. Sci. Technol*

⁴⁴ Tasse, G. (2014). The economic nature of knowledge embodied in standards for technology-based industries. In *Routledge handbook of the economics of knowledge* (pp. 199-218). Routledge.

⁴⁵ Swann, G.M.P., (2010). *The Economics of Standardization: An Update*.

3.6 Value Chain Analysis

To help bridge the gap between the generalised effects of standardisation to the impacts of IDMP implementation across regulatory, pharmaceutical, and clinical domains it is helpful to incorporate Michael Porter's concept of value chain analysis.

The value chain analysis concept is well defined by Michael Porter in his book "Competitive advantage: creating and sustaining superior performance:"

"Starting with the generic chain, individual value activities are identified in the particular firm. Each generic category can be divided into discrete activities [...]"⁴⁶

According to Porter, the value chain is a systematic approach to examining the development of competitive advantage.

Competitive advantage is produced from the way firms organise and perform discrete activities. The operations of any firm can be divided into a number of activities. Value for firms' buyers is created through performing the different activities⁴⁷. The ultimate value a firm creates is measured by the amount buyers are willing to pay for the product or service. If the value exceeds the cumulative cost of performing all the required activities, then the firm is considered to be profitable. A firm aims to have competitive advantage over its rivals, this means that the firm can either provide comparable buyer value but perform activities more efficiently than its competitors (lower cost and so the firm has a cost advantage) or perform activities in a unique way that creates greater buyer value and commands a high price (differentiation)⁴⁸.

In order to analyse the specific activities through which firms can create a competitive advantage it is useful to model the firm as a chain of value-creating activities. Porter identified a set of interrelated generic activities common to a wide range of firms. It identifies activities, functions and business processes that have to be performed in designing, producing, marketing, delivering and supporting a product or a service⁴⁹. All the activities in the chain contribute to buyer value.

⁴⁶ Porter, M. E., & Advantage, C. (1985). Creating and sustaining superior performance. *Competitive advantage*, 167, 167-206.

⁴⁷ Ensign, P. C. (2001). Value chain analysis and competitive advantage. *Journal of General Management*, 27(1), 18-42.

⁴⁸ Porter, M. E. (2001). The value chain and competitive advantage. *Understanding business processes*, 2, 50-66.

⁴⁹ Porter, M. E. (2001). The value chain and competitive advantage. *Understanding business processes*, 2, 50-66.

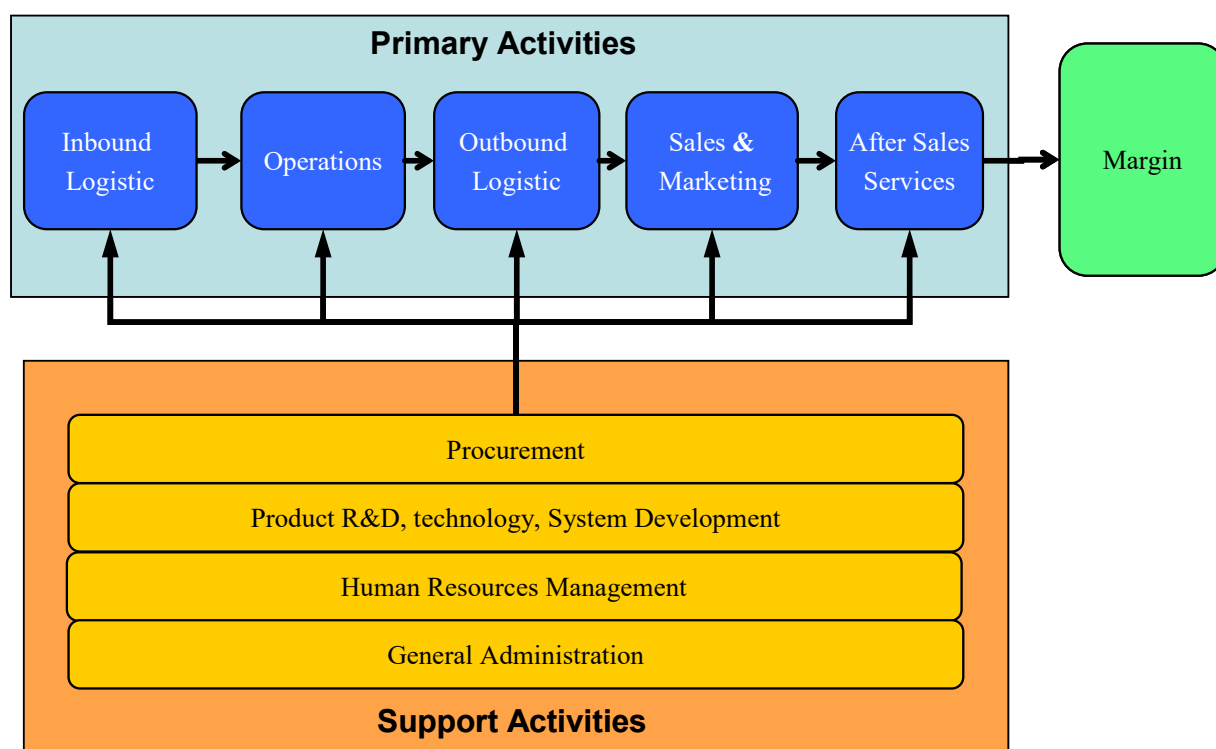


Figure 2. Porter's Value Chain Concept

3.7 Diversity of Value Propositions in Healthcare

When attempting to transfer Porter's value chain model to the health sector, one must account for the complexities and constraints of this sector including the value propositions of various actors. A value proposition is a clear statement of how a proposed implementation relates to some improvement for the user, what specific benefits it brings, and how it differentiates from others.

Modern healthcare is focused on making the best use of finite resources to balance the medical outcomes produced with the needs of all stakeholders in the healthcare arena. Responsibilities and interests of different participants in healthcare are diverse⁵⁰. A physician has interests that differ from those of a patient who receives treatment. A hospital differs from a doctor's office. Health insurance companies negotiate on the payment of medical services with doctors and their associations. Regulatory agencies are focused on ensuring the safety of available medicinal products and the pharmaceutical industry must consider maximising sales and optimising their return on investment. Furthermore, the whole medicinal product value chain, from product development to medical care, is dependent on the transfer of trusted data, across the product's life cycle.

Differences in value chains of the different actors in health systems also leads to competition across various contexts⁵¹. Forms of competition are between health insurers for the decision of the population regarding health insurance; between health care providers to be chosen by the population for delivering health care and between health care providers for contracts with health insurers. Those who supply non-clinical services, e.g., cleaning or catering, compete for contracts with other organisations. There is also competition amongst producers of medicines and medical devices, i.e., the pharmaceutical industry, in

⁵⁰ Rouse, W. B. (2008). Health care as a complex adaptive system: implications for design and management. *Bridge-Washington-National Academy of Engineering-*, 38(1), 17.

⁵¹ Rouse, W. B. (2008). Health care as a complex adaptive system: implications for design and management. *Bridge-Washington-National Academy of Engineering-*, 38(1), 17.

terms of sales, innovation, and product development. Therefore, even if not explicitly promoted or acknowledged, competitive forces are likely to be at play in one way or another.

Competition between providers can take various forms, according to whom (or what) they compete for and what the variables used in that process of competition are. Competition may take place based on price, but also on the basis of quality, timely access, innovation and other factors relevant to patients and to organisations acting on behalf of patients⁵². Health care providers may compete for patients based on price, or based on quality, or both. Quality may refer to an intrinsic quality of the product or service, or may, for example, be waiting time or priority in treatment. Health care providers may compete for budgets within health systems, as in the case of auctions for partnership contracts to provide a health care service⁵³. Competition through choice of geographic location is also an important instrument used by providers to compete for patients in health care markets⁵⁴.

Patients traditionally delegate their health decisions to health professionals. Competition may exist on this choice by the patient⁵⁵. The most obvious example is the choice of GP that will then navigate the patient through the health system. While GPs may compete to be selected by patients, specialized healthcare that requires referral by a GP will compete for a GP's attention. Patients may also select a protection system that has unrestricted access to specialists, in which case specialists compete for patients. Depending on the particular health system, the choice of the patient can be about the treatment or about the doctor, about a particular provider or about an integrated care pathway.

Regulatory authorities in healthcare such as National Competent Authorities (NCAs) typically have value propositions related to pharmacovigilance, public relations, and the development and maintenance of national infrastructure⁵⁶. Pharmacovigilance, including the reporting of ADEs and maintenance of national databases, is a key priority for NCAs as healthcare is primarily under the purview of Member States. NCAs are also interested in garnering public support and in promoting the public's confidence in both their policies as well as in their role ensurers of public safety. They also aim to regulate the workflow by which healthcare data is managed at the national-level and improve the exchange of information among MS, improving the workflow efficiency of their own systems. Regulatory authorities as such, are interested in regulating the system, and increasing the systems reputation and competitive advantage on a macro level.

As demonstrated, the difference in value chains for different actors in the health system as well as competition between organisations of the same type, i.e. different hospitals or different pharmaceutical companies, means that individual stakeholders do not have a value proposition to establish a regional or national infrastructure for standardisation. Such an infrastructure which includes aspects of governance, coordination between competent authorities, standardisation, ID management, security, semantics, etc., then falls under the value proposition of national regulatory bodies. Upon implementation however, the expansion of a national infrastructure for standardisation will have cascading benefits due to network effects, since the more actors participate in the network, the greater will be the value for all.

⁵² Porter, M. E., & Teisberg, E. O. (2004). Redefining competition in health care. *Harvard business review*, 64-77.

⁵³ Goddard, M. (2015). Competition in healthcare: good, bad or ugly?. *International journal of health policy and management*, 4(9), 567.

⁵⁴ Westra, D., Angeli, F., Carree, M., & Ruwaard, D. (2017). Understanding competition between healthcare providers: Introducing an intermediary inter-organizational perspective. *Health Policy*, 121(2), 149-157.

⁵⁵ Katz, M. L. (2013). Provider competition and healthcare quality: More bang for the buck?. *International Journal of Industrial Organization*, 31(5), 612-625.

⁵⁶ Lehoux, P., Miller, F. A., Daudelin, G., & Denis, J. L. (2017). Providing value to new health technology: the early contribution of entrepreneurs, investors, and regulatory agencies. *International journal of health policy and management*, 6(9), 509.

4 Use Cases

The IDMP suite of standards is not simply an IT development project nor is it only about data exchange. Rather, the IDMP family of standards, coding systems, implementation guidance etc. provides an overarching sustainable context for representing life science and regulatory content; which in today's evolving landscape must keep pace with medical breakthroughs and discoveries, emerging biopharmaceutical technologies, new public health threats, increasing demands from consumers, patients and health professionals, diverse local/national/international health systems, changes in regulatory policies, and shifts in geopolitical relationships and agreements.

To better understand this domain and to prepare for assessing the expected impact of the availability of IDMP conformant data it will be helpful to explore some use cases illustrating the discussion, as presented in this chapter.

4.1 Characterisation of Use Case

In software and systems engineering, the phrase use case is used for both a "usage scenario for a piece of software", and a "potential scenario in which a system receives an external request (such as user input) and responds to it"⁵⁷. In the latter case, a use case may consist of a list of actions or event steps typically defining the interactions between a role (actor) and a system to achieve a goal. At a higher level it may be concerned in a more generic mode with illustrating how stakeholder goals may be supported⁵⁸. Applying this concept to the health system field, a use case may describe specific situations where medically relevant information is exchanged between actors/organisations and systems to support health system processes⁵⁹.

In the context of impact assessment, use cases support and facilitate the identification of relevant actors and systems involved, as well as the process(es) ongoing or to be changed to better achieve given or new goals. They can also help in selecting what might be appropriate methods, tools and measurements to identify the expected or realised changes in achieving a project's goals.

IDMP use cases will constitute an initial, high level exploration towards concretely estimating expected improvements in core actor communities. They will help identifying scenarios of both internal and external standardised data use. In terms of internal regulatory uses IDMP integrates with the medicinal product lifecycle as well as product data submissions management. External healthcare uses include clinical treatment protocols, pharmacy-related systems, and adverse event reporting. Consumer and patient uses include medication management in terms of safety alerts and reminders, patient empowerment, and increased provision of cross-border and eHealth services.

Implementation of ISO-IDMP and related infrastructures is expected to:

- ▶ Improve health data access for patients and healthcare providers;
- ▶ Lead to the easier delivery and exchange of medicinal products data;
- ▶ Allow easier exchange of information for regulatory processes by pharmaceutical industry as well as national medicines authorities;
- ▶ Enhance quality of care and patient safety;
- ▶ Support the sustainability of European health care systems.

Use cases can also help clarifying details associated with IDMP implementation in information management and data exchange systems. These details include support and alignment with regulatory policies, guidelines, and manufacturing specifications; requirements for minimum and maximum datasets including conformance and validation requirements; identification of requirements to support emerging pharmaceutical science and technology; engagement with tool and service providers, e.g., integration with EHRs and Clinical Decision Support Systems; and facilitation of data migration planning along the data flow chain.

⁵⁷ Jacobson, I., Ericsson, M., & Jacobson, A. (1994). *The object advantage: business process reengineering with object technology*. ACM Press/Addison-Wesley Publishing Co.

⁵⁸ Jacobson, I. (2004). Use cases—Yesterday, today, and tomorrow. *Software & Systems Modeling*, 3(3), 210-220.

⁵⁹ Cf. ANTILOPE – Advancing eHealth Interoperability. D1.1: Refinement Definition document. 17 April, 2015. It provides for a template for the uniform description of use cases and their accompanying realisation scenarios.

The following subsections expand on key uses cases for IDMP.

4.2 Pharmacovigilance and Clinical Care

Across the health data space, electronic health records (EHRs), patient registries, patient organisations, and research networks, all provide useful insights about patient experiences related to product safety and efficacy and inform pharmacovigilance-related activities; however, data quality, transparency and consistency remain a problem for integrated analysis. Pharmacovigilance and clinical care therefore present key use cases for IDMP implementation.

IDMP implementation supports both active and passive pharmacovigilance surveillance programs. Passive programs such as those using individual case safety reports (ICSRs) for adverse event and product problem reporting are dependent upon human assessment and intervention to confirm the event/problem and report⁶⁰. Interoperability between systems enhances such assessments including enabling better signal detection. Active surveillance programs on the other hand provide an alternative for data mining and sharing using structured queries into a health problem or drug-related question, and often serve as the foundation for pharmacoepidemiologic studies⁶¹. Here IDMP enables improvements in source data which is important for developing standardised queries for drug information and reactions. Furthermore, IDMP infrastructure development also better reconciles clinical terminologies from disparate sources into mapped interoperable models, i.e., terminologies dealing with target populations, clinical indications, contraindications, side effects and adverse event reporting.

More specifically, IDMP provides the reference information to populate drug formularies and electronic medicinal product information databases. Clinical decision support triggers can be set up for monitoring of adverse events including medicinal product side effects and reporting simultaneously to manufacturers, patient registries, and health authorities. IDMP infrastructure supports automation, improves efficiency of reporting, and enhances interoperability between EUDRAVIGILANCE, national Pharmacovigilance Registries, and MAH pharmacovigilance databases.

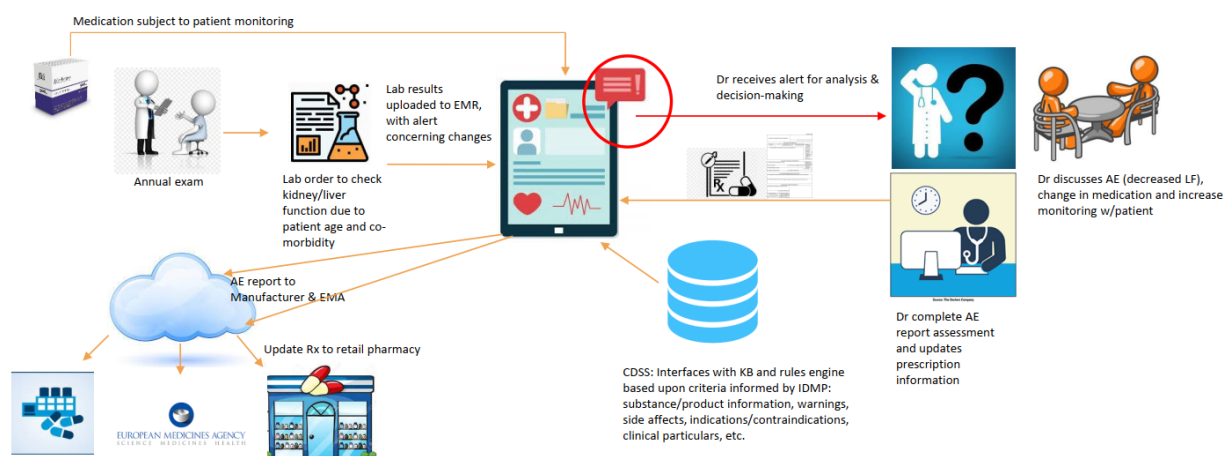


Figure 3. Overview of IDMP applications for pharmacovigilance and clinical care

In terms of clinical care, IDMP supports more efficient updates and validation of medication information to help reduce or eliminate medication errors which may be caused by prescribing the wrong medication (different drugs may sound similar or look similar leading to errors), using the wrong doses (unclear indications for formulations or body weight), contraindications, drug-drug interactions, or patient

⁶⁰ Moses, C., Celi, L. A., & Marshall, J. (2013). Pharmacovigilance: an active surveillance system to proactively identify risks for adverse events. *Population health management*, 16(3), 147-149.

⁶¹ Moses, C., Celi, L. A., & Marshall, J. (2013). Pharmacovigilance: an active surveillance system to proactively identify risks for adverse events. *Population health management*, 16(3), 147-149.

allergies; augmenting the development of electronic clinical care support tools which may automatically check for all of the above-mentioned issues.

IDMP also supports supply chain management (i.e., end-to-end product traceability) and more efficient data exchange for managing drug shortages (due to increased demand e.g., pandemic, flu, or limited manufacturing supply) and reducing incidence of falsified medicines. Falsified medicines may contain ingredients of low quality or in the wrong doses; be deliberately and fraudulently mis-labelled with respect to their identity or source; have fake packaging, the wrong ingredients, or low levels of the active ingredients. IDMP supports investigations because it provides a reference source for testing and validation of ingredients, appearance, dosage form, strength and packaging. Contaminated or suspected falsified medicines may first appear as an AE or product problem report: showing up as a lack of drug effect or overdose; differences in severity or specificity of labeled side effects and adverse events; incongruent appearance, smell or taste; as well as inconsistent packaging, labeling or reconstitution results. Furthermore, IDMP identifiers could be used to validate a case series and trigger inspections based upon inconsistent identifiers, e.g., PhPID, MPID, PCID, BAID, GTIN; manufacturer, distributor, repackaging information and sites; inconsistent substance or product details (AIs, Excipients, DF, RoA, Units of Measurement).

4.3 Regulatory Data Management

Regulatory data management for MPI presents an important use case for IDMP because regulatory bodies such as NCAs and EMA are key actors governing the use of medicinal products across the health sector. In the EU health system regulatory outputs (product approvals, package inserts, and marketing materials) become inputs into the healthcare process, and as such should be as timely, accurate and accessible as possible.

The use of structurally coded IDMP data for MPI exchange between regulatory bodies would lead to direct improvements in tasks related to regulatory intelligence. Regulatory intelligence is the act of gathering and analysing publicly available information (e.g., regulatory decisions, real world evidence, biotechnology, medicinal product information databases, clinical trial data etc.) and incorporating the implications of that information to support opportunities to shape future legislation, regulation, guidance, and policy decisions. It involves continuous monitoring, synthesis, communication, and training across multi-disciplinary teams within the organisation, all enhanced by the semantic interoperability offered by IDMP.

Building on regulatory intelligence, IDMP infrastructure would provide for significant improvements in Master Data Management (MDM) at the regulatory level. MDM is used to define and manage the critical data of an organisation in order to provide, with data integration, a single point of reference. MDM supports quality assurance by streamlining processes for collecting, aggregating, matching, consolidating, persisting, and distributing data throughout an organisation. IDMP structured data, through semantic interoperability, will ensure a common understanding, consistency, accuracy and control in the ongoing maintenance and application use of critical MPI data, via the migration of NCA and EMA databases to IDMP-compatible formats.

IDMP provides a structured format for MPI exchange applicable to both quality assurance tasks and marketing authorisation applications as they relate to new medicinal products, variations, and renewals. IDMP enables faster identification, reconciliation, quality assessment and reuse of information. In terms of marketing authorisation applications IDMP implementation would play a role in improving electronic application forms and assessment reports, summary of product characteristics, package leaflet and labelling. Standardised information can then also be reused across jurisdictions and shared across member states with semantic interoperability according to the specifications of both the centralised and decentralised procedures for European medicinal product marketing authorisation applications⁶². The reuse and automation of data for these applications is expected to have significant efficiency gains as current data technical standards for the Electronic Common Technical Document (eCTD), the mandatory format for new drug applications, are often based on the PDF format⁶³ which is susceptible both to human error and personnel costs when manually retyping information across different systems.

⁶² <https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation>

⁶³ <http://esubmission.ema.europa.eu/ectd/>

The following table shows the relationship of IDMP encoded information and how it will affect various industry/business functions and IT systems currently used to manage different regulatory submissions.

Table 1. Relevance of IDMP for various IT systems used for regulatory submissions in the EU

Business Area	IT System	IDMP Relevance
Regulatory affairs (RA)	Regulatory information management system (RIMS)	Medicinal product
Enterprise resource planning (ERP)		Market authorization information
Clinical development	Clinical trial management system (CTMS) Clinical data repository/warehouse (CDR/CDW)	Pharmaceutical particulars Clinical particulars
Manufacturing & product supply	Enterprise Resource Planning (ERP)	Manufacturing
Research/CMC	Substance database	Substances
Packaging	Labelling system	Packaging information
Quality & support	Enterprise document management system (EDMS)	i.e., SmPC for pharmaceutical particulars and clinical particulars information

4.4 Medicinal Product Development

Currently, a variety of data standards are used to support the capture, management and submission of information to regulatory authorities to support the drug development lifecycle. One of the key issues is the transparency and consistency of data used by all market players in the industry, including regulators, manufacturers, suppliers, and distributors. Under current regulations, individual pharmaceutical companies use different nomenclatures and various ways of recording medicinal products, doses, administration routes or measurement units. As such, there is a demand for standardisation to ensure that information on the ingredients of a medicine, for example, is understood and provided in the same way, regardless of manufacturers, distributors, their locations, languages, or brands, presenting a crucial use case for IDMP.

The development of a new medicinal product can be a lengthy, complex and expensive process and includes key stages where IDMP related information is created, repurposed and continuously updated. Implementation of IDMP can enhance the medicinal product development process as follows:

- ▶ IDMP substance data including integration with EMA SMS/EU-SRS can support medicinal product discovery and research which involves identification of substances for targeted therapy or the diagnosis, cure, mitigation, treatment or prevention of a disease or condition.
- ▶ IDMP MPID's and PhPID's can support automation in the product development pipeline which includes the necessary non-clinical research, clinical studies as well as chemistry, manufacturing, and control (CMC) development to support clinical trials and licensing applications.
- ▶ IDMP encoded data can greatly enhance regulatory review and approval including the submission of data for regulatory review to demonstrate product safety, efficacy and quality for proposed indications.
- ▶ IDMP supports automation and efficiency gains in commercialisation and marketing for ongoing regulatory compliance through safety surveillance and other post market submissions/reports.

In addition, IDMP helps to create and inform reference sources and datasets for observational studies, drug utilisation statistics, knowledge bases, formularies, registries, etc. Access to these datasets can increase the pharmaceutical industry's signal detection capabilities to quickly identify product risks and issues, including coordinating product recalls, by connecting critical product information across disparate health care systems, which in turn informs subsequent product development.

4.5 Cross-Border and eHealth Services

To improve patient safety and healthcare, UNICOM, through supporting the implementation of ISO IDMP standards, promotes the sharing of accurate clinical information and prescriptions between European member states in a cross-border context. Service provision by cross-border programs relies on provision of electronic prescriptions, electronic patient summaries, and electronic product information, all involving MPI data and therefore presenting a key use case for IDMP.

When a pharmacist in one country is given a prescription for a medicinal product from a different country, they typically must first identify the prescribed medicinal product and if the product is not available, find an equivalent product to dispense taking the following information into consideration: substance, dose form and strength, substitution allowances by prescriber, and dispensable amount (package size, number of packages). They must then also report the dispensation to country of affiliation and receive an acknowledgement.

The process is simplified by cross-border ePrescriptions. An ePrescription involves the process of electronically generating and sending a prescription order, so that physicians and other medical practitioners can transmit an electronic prescription to a pharmacy directly from the point of care⁶⁴. In a cross-border context this results in the electronic exchange of patient prescription and dispensing information across one or more geographical borders and locations (e.g., intercontinental, cross-country). It follows then that eDispensation is the process of electronic access authorisation and validation that medication has been provided to the patient⁶⁵. 18 of the 27 EU member states officially plan to exchange ePrescriptions across borders in 2025⁶⁶. The figure below provides a visualisation of the ePrescription/eDispensation process.

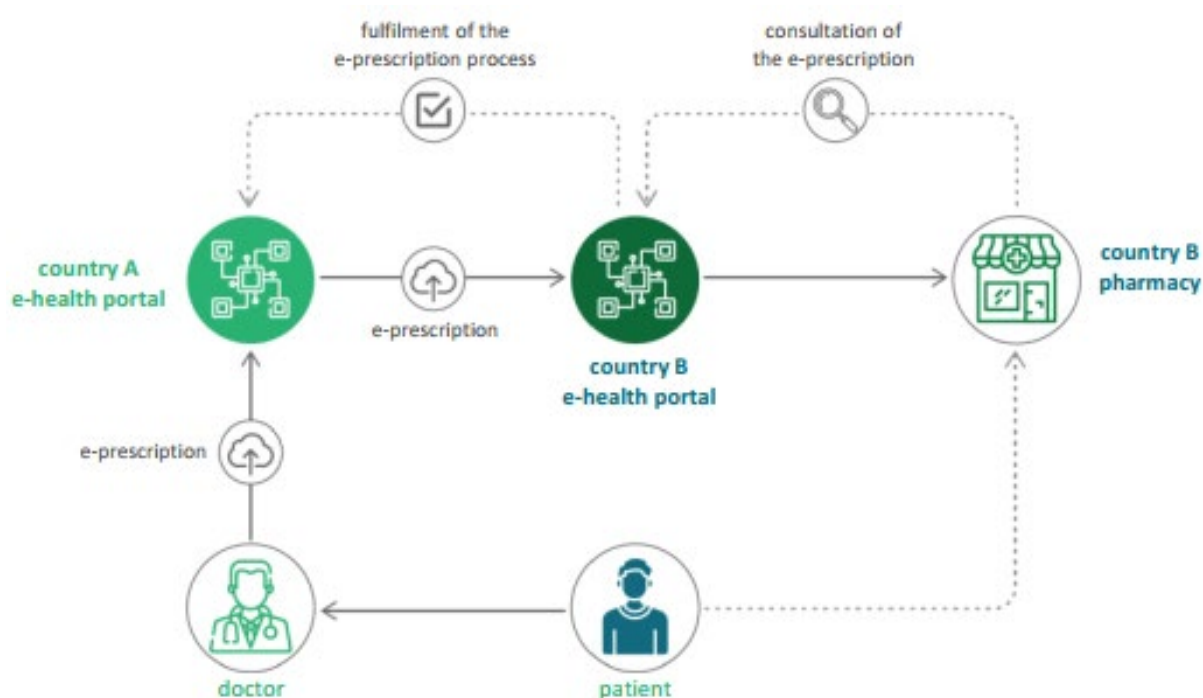


Figure 4. Overview of cross-border ePrescription process.

⁶⁴ Kierkegaard, P. (2013). E-prescription across Europe. *Health and Technology*, 3(3), 205-219.

⁶⁵ Kierkegaard, P. (2013). E-prescription across Europe. *Health and Technology*, 3(3), 205-219.

⁶⁶ https://ec.europa.eu/health/ehealth/home_en

Taken together, ePrescription and eDispensation allows citizens in Europe to retrieve their medication in a pharmacy located in another European country without having to bring the printed prescription and without being concerned about the language barrier. They empower citizens by giving secure access to their health data abroad as well as strengthening cooperation & synergies between Member States and Member States and the Commission. IDMP supports this use case by providing standardized reference information to create the ePrescription dataset.

Presently, prerequisites defined by participating countries govern the outcomes for ePrescriptions. A common data structure is typically used for the exchanged documents including values from a common catalogue and value sets from international controlled vocabularies which support translation (ATC, EDQM, UCUM etc.).

However, during initial testing conducted by WP5, the following challenges and limitations were identified in the current ePrescription data space:

- ▶ Same product is marketed under different names in different countries;
- ▶ The dose form has different "granularity" for the same product, e.g "tablet" vs "film coated tablet" or dose forms are assigned with different conventions, for example in cases where powders are to be used as solutions.
- ▶ There is no standardised international value set for active substances. ATC is currently "stretched" to code INN.
- ▶ Strength is calculated differently for same product e.g. Enoxaparin 100 mg/ml, 2000 Anti-xa IU/0,2ml.
- ▶ The link between substance and strength can be broken as both are allowed to be indicated as "free text" and can end up in different order.
- ▶ It is often difficult to know if a substitution has taken place as representation of a generic prescription is often difficult in current ePrescription formats.
- ▶ The units for package size and strength are not always from controlled vocabularies.
- ▶ It is difficult to represent packages of containers e.g "20 vials of 1 ml each" (granularity of package and amount).
- ▶ Support for combination packages is missing (multiple medicinal products in the same package).
- ▶ Marketing authorisation holder or manufacturer differs or is unknown in ePrescriptions.

ISO IDMP provides necessary framework to address some of these challenges. In situations related to the quality and updating issues of performing mappings and translations, IDMP enables overall more coded data in source systems. This also address issues related to free text as IDMP-coded information is designed to be semantically interoperable. The IDMP-enabled EMA SPOR value sets are aimed to be interoperable with both cross-border and nationally sourced systems, once IDMP is fully implemented across member states. In issues with dose form, ISO IDMP aims to provide the manufactured dose form as well as administrable dose form in a standardised format. Similarly for problems with representing complicated package sizes and their overall amount, IDMP covers combination packages as well as included administration devices. In issues related with representations of generics IDMP offers a pharmaceutical product level description for generic prescribing and substitution decisions.

Electronic Patient Summaries are also essential to proper cross-border healthcare as they can be used while traveling abroad and in situations requiring medical consultations while travelling. Electronic Patient Summaries provide information on important health related aspects such as a patients' allergies, current medication, previous illness, surgeries⁶⁷. They help doctors to formulate an adequate treatment plan, avoiding possible risks (for instance in case of allergies) and in the case of standardised information content, overcome linguistic barriers.

Current limitations of an electronic Patient Summaries and IDMP-implementation's contribution towards overcoming them are listed below:

- ▶ The data model for medication summaries is similar to ePrescriptions and is affected by the same issues to describe complex medications.
 - ▷ With IDMP: increased precision and flexibility in describing medications.
- ▶ Allergies to drugs are expressed with just ATC which results in a lack of precision.

⁶⁷ Remen, V. M., & Grimsno, A. (2011). Closing information gaps with shared electronic patient summaries—How much will it matter?. *International journal of medical informatics*, 80(11), 775-781.

- ▷ With IDMP: allows the possibility to express allergies as linked to specific branded medicinal products and their excipients, or to generic pharmaceutical products, or to specific substances included in the EMA substances database.
- ▶ Vaccines are identified by SNOMED CT concepts or ATC.
 - ▷ With IDMP: substitutes ATC allowing the possibility to indicate either the generic the specific vaccine from a pharmaceutical company, allowing better traceability of possible adverse drug events, or providing indications for subsequent boosters.

In summary electronic medicinal product information can be generated from electronic patient summaries or as an associated pharmacy/dispensation record, based upon IDMP class attributes: e.g., ingredient/product names and identifiers, dose information, packaging information, etc. Many challenges experienced in the communication of medicinal product information can be systematically overcome through different phases of implementation of the ISO IDMP standards. Having an adequate system for substances will facilitate the exchange of information, not only in ePrescription and eDispensation documents, but also in the medication summary, immunization, and allergies related sections of Patient Summaries.

5 Stakeholder Classification and Mapping

The use cases presented in the previous section highlight the various levels where IDMP implementation may have an impact, as it affects actors in various sectors of the health system – not only the regulatory domain, but also the clinical and public health areas. Against the background of the selected use cases, in order to develop an analytical framework for estimating these potential socioeconomic impacts it is firstly suggested to narrow our scope to those actors, users, and stakeholders most affected.

5.1 Design Considerations

Mechanism design theory⁶⁸ and participatory usability evaluations take as their basic premise the view that technology developments should be driven from user requirements rather than from technological capabilities. Thus, the starting point for usability evaluation and systems design is to understand the user population, but also the general stakeholders, in some detail.

An important design step for any impact assessment model is to identify and specify the stakeholders involved. This requires an account of the actual people and organisations affected, which can initially be classified into generic, high level stakeholder groups and, eventually, smaller-size sub-groups. This is important for two reasons. Firstly, a more detailed stakeholder analysis ensures that the full impact of IDMP implementation outcomes is reflected in more detail in the evaluation, which in turn is usually more helpful for better targeting policy interventions to optimise impacts. Secondly, analysing individual stakeholders' perspectives also provides valuable insights on the "who-pays-who-benefits-how-much-and-what" debate.

5.2 Classification of Actors and Stakeholders

Typically speaking, in marketing or commercialisation terms, a user is conventionally defined as a customer or an organisation that acts as a consumer of a good or service⁶⁹. This definition is insufficient for our purposes, however, owing to the interconnected nature of various 'actors' in the healthcare system.

An actor can be defined as an individual entity interacting with a system⁷⁰. Actors are on one hand the provider of a consumption-good or service, and on the other hand a user of a particular good or service. 'Actor' defined more broadly may refer to:

- ▶ a representative person in the statistical or pragmatic sense;
- ▶ an individual person in a unique context;
- ▶ a person working in a collaborative setting;
- ▶ a component of a work system;
- ▶ an organisation;
- ▶ a stakeholder;
- ▶ an end-user, i.e. for whom the product (or service) is developed;
- ▶ an organisation representing users;
- ▶ a customer.

Stakeholders are referred to as being actors within the system who may be affected by the product but who may or may not be direct users of the product. A stakeholder is anyone who is significantly impacted by the product. This includes not only customers and end-users, but development team members as well, and even people with no awareness of the product but who may nonetheless be affected by it. Stakeholders can include developers, researchers, corporations, securities, architects, managers, regulators etc.

Extending the concept to UNICOM and IDMP implementation, for the purpose of this deliverable and the assessment approach, users are understood as actors who consume IDMP-enhanced products or services (e.g- patient empowerment apps, clinical decision support tools, ePrescriptions etc.).

⁶⁸ Myerson, R. B. (2008). Perspectives on mechanism design in economic theory. *American Economic Review*, 98(3), 586-603.

⁶⁹ <https://www.mbaskool.com/business-concepts/marketing-and-strategy-terms/11038-user.html>

⁷⁰ Wegmann, A., & Genilloud, G. (2000, October). The role of "Roles" in use case diagrams. In International Conference on the Unified Modeling Language (pp. 210-224). Springer, Berlin, Heidelberg.

Stakeholders then refers to the broader group of actors that have a vested interest in the outputs and developments of the IDMP implementation infrastructure, like health policy makers, public health, health insurances and others. In addition, these include pharmaceutical companies, national medicines authorities, eHealth service organisations, hospitals, and patient support organisations etc. Assessment perspectives based on stakeholders are most important as they guide the overall assessment process: the results must be useful for them, and, as required, also helpful for those who influence or take health system decisions. From this it follows that the respective perspective should (1) govern the methodology of the assessment framework such that (2) indeed it allows one to measure the effect a technology can have on a range of actors.

Stakeholder mapping then, ultimately, identifies key actors, i.e. both users and stakeholders, already or potentially impacted by the usage and outputs of the proposed development. Stakeholder motivations, activities and longer-term expectations need to be explored in detail at subsequent stages of the impact assessment and evaluation process and operationalised into concrete questionnaires for either interviews or the structuring of the user programme during workshops.

Table 2 below provides an overview of the key stakeholders UNICOM as they relate to ISO-IDMP infrastructure implementation and their involvement in the use cases mentioned in the previous section.

Table 2. UNICOM Stakeholder Mapping and Applicable Use Cases

Stakeholders	Use Cases			
	Pharmacovigilance and Clinical Care	Regulatory Data Management	MP Development	Cross border and eHealth Services
National Competent Authorities for MPs	X	X	X	X
Health Authorities	X	X		(X)
Statutory Insurances	X	X		X
National eHealth Competence Centers				X
EMA and EMA Task Forces	X	X		(X)
eHDSI Organisations				X
Standard Developing Organisations (SDOs)		X	X	X
Medicinal Product Dictionary (MPD) providers	X			X
Pharmaceutical companies: Marketing Authorisation Holders (MAHs)	X	X	X	X
Global and transatlantic medicinal organisations	X			X

Public and private research organisations on medicinal product data	X			
IT/eHealth solutions vendors and representative organisations				X
Healthcare professional representative organisation	X			X
National and international patient umbrella organisations	X			X
Healthcare service providers including hospitals and clinics	X			X
Healthcare professionals such as doctors, nurses, and other clinicians	X			X
Pharmacists including prescribers and dispensers	X			X
Patients	X			X

5.3 Selected Stakeholders

In order to provide a comprehensive overview of the medicinal product lifecycle across its data value chain, the following four stakeholders were selected:

- ▶ National Competent Authorities (NCAs)
- ▶ Pharmaceutical Companies
- ▶ Healthcare Professionals
- ▶ Patients

Taken together, these stakeholders offer the impact assessment framework a representative sample from which to gather data to support the use cases described above.

6 ASSIST as Impact Assessment Evaluation Framework

With respect to the various stakeholders as identified above, it will be necessary to identify and measure the expected, and later the real “impact”, of IDMP infrastructure development. Impact is here defined as any perceived benefit or cost these actors may be confronted with. These terms must be understood in a very broad meaning encompassing not only benefits and costs expressed directly in monetary terms, but also any immaterial impacts which will influence decisions to develop and sustain, to use, or to finance such an infrastructure.

Assessment of qualitative and quantitative impacts of IDMP implementation, including the use of ICT, and the provision of health services supported by that ICT, is a complex issue. It requires an in-depth understanding of each individual case as well as of the framework conditions of the service imposed by the health system it operates in. Only with these factors in mind can benefits of IDMP application be realistically assessed. The sustainability of an innovative interoperable IDMP based eHealth solution for example, strongly depends on the health system’s openness to innovation and available funding.

These considerations and more are all incorporated into ASSIST (Assessment and Evaluation Tools for Telemedicine), a socioeconomic impact assessment tool developed by empirica which has been used in more than 20 EU digital health projects.

6.1 Foundations and Evaluation Model

The theoretical foundations of the proposed impact assessment methodology are grounded in Michael Porter’s Value Chain Concept⁷¹ and the aforementioned economics of standardisation, well as value theory, and in particular, the concept of value added⁷². Value added in economics is the additional value resulting from transformations of factors of production into a ready product. At its simplest, it is the difference between the value of a product and the aggregate value of its individual components. Over the last decades, value added has been a widely used approach supporting decision making on investments and resource usage.

In the UNICOM context, socioeconomic impact can be defined as both the value added as perceived by various actors individually, and as the overall value, including external effects, added to society as a whole from the implementation and use of the IDMP-infrastructure being built up. In other words, the effects and outcomes of a standards implementation such as IDMP can be defined as value-added to society, either in part or as a whole, by implementing and using IDMP-infrastructure. This standpoint, called the social planner’s perspective, encompasses the impacts to all affected actors⁷³. The value added equals the total value of a service provided with the support of IDMP less the total value of a service provided without this kind of support.

$$\text{value added from UNICOM and IDMP} = \text{value of services with UNICOM and IDMP} - \text{value of services without UNICOM and IDMP}$$

This societal perspective includes all stakeholders and aggregates their respective gains and losses, or benefits and costs. Positive effects, or benefits, create value, negative effects, or costs, occur when value is reduced. The total value added is the sum of positive and negative ‘value added’, which is also referred to as net benefit.

This societal perspective can be disaggregated into the benefits and costs of each stakeholder group. Furthermore, what may be a benefit to one group may be a cost to another group, and in the aggregate some of them may cancel out. The analysis must expose these shifts in value in order to provide a reasonable account of the impact of IDMP implementation to individual stakeholders as well as society as a whole. Beyond this, an integrated IDMP related services system may have emergent characteristics, which lead to benefits in the aggregate. For example, shared access to comprehensive

⁷¹ Porter, M. E., & Advantage, C. (1985). Creating and sustaining superior performance. *Competitive advantage*, 167, 167-206.

⁷² Jakub, S., Viera, B., & Eva, K. (2015). Economic Value Added as a measurement tool of financial performance. *Procedia Economics and Finance*, 26, 484-489.

⁷³ von der Schulenburg, J. M. G., Greiner, W., Jost, F., Klusen, N., Kubin, M., Leidl, R., ... & Weber, C. (2007). Deutsche Empfehlungen zur gesundheitsökonomischen Evaluation-dritte und aktualisierte Fassung des Hannoveraner Konsens. *Gesundheitsökonomie & Qualitätsmanagement*, 12(05), 285-290.

patient data facilitated by an integrated healthcare information system cannot be reaped by individual stakeholders alone.

As discussed earlier, IDMP implementation is characterised by a multitude of diverse dimensions which need to be taken into account when aiming for a holistic assessment. This multi-dimensional character of requires an assessment framework which is able to put together several sub-methods into a consistent whole. This whole must be able to deliver a limited set of outcome indicators across its different dimensions to allow for a comprehensive and “final” evaluative judgement of the decision maker(s).

Based on such considerations, Cost benefit analysis (CBA) is proposed as the working paradigm with which to assess the socioeconomic impact of IDMP implementation.

For a comprehensive socio-economic analysis, data to measure the benefits and costs for each specific stakeholder are needed. Monetary values have to be assigned for the economic performance to be evaluated. This enables, in the aggregate, potential common patterns, trends and relationships to be identified. CBA supports the linking of these data. CBA allows different outcomes to be evaluated through common measures, and it can reflect a different allocation of resources before and after an investment in a service⁷⁴. A key merit of CBA is that it allows for comparative, as well as single option evaluation over time.

CBA is often described as an economic tool. It should, however, be seen as aiming to assign monetary values to seek to estimate the net benefit over time arising from the costs and benefits of an investment of resources. In this context, the costs and benefits identified reveal all the stakeholders and actors who can be affected by the investment of resources. These stakeholders range from individual people to the organisations and institutions of a particular society, which, in turn, enables the impact on all stakeholders to be included in a socio-economic evaluation over the selected timescales.

Monetary values assigned to costs and benefits should be based on market prices whenever they are available because prices tend to reflect the best alternative use of the resources available. However, some costs and benefits are social, environmental, organisational or cultural, and have no obvious market price to reflect their values. When dealing with these types of impact, ‘benefits’ should be understood as changes towards a more desired situation, and ‘costs’ should include items like reduced comfort or extra effort associated with the introduction of a service.

CBA is usually considered as the approach of choice for turning theoretical requirements into a pragmatic evaluation tool⁷⁵. Among others the UK Treasury’s Green Book⁷⁶, Germany’s WiBe⁷⁷ and the White House Office of Management and Budget⁷⁸ specify the CBA methodology as an appropriate tool for analysing the impact of investments and activities in domains of public interest, including healthcare.

The result of a CBA assessment, the net impact typically presented in monetary units, complies with two highly desirable conditions of absolute assessment outcome and comparability between options. The latter is given by a direct comparison of net impact values. In this way, CBA leads to a clear information base for final decision making, which can be retraced and, if deemed necessary, modified by the decision maker with own estimates⁷⁹.

Building on a CBA, the overall assessment framework must also be able to identify and account for a change of “utility” or benefits for the stakeholders in a positive as well as a negative direction. Several methods only account for positive, beneficial changes which neglect that newly introduced systems and processes come at a cost. Neglecting costs is especially problematic if the stakeholder receiving the benefit is not the same who has to bear the costs. These benefit shifts are an important reason for

⁷⁴ Boardman, A. E., Greenberg, D. H., Vining, A. R., & Weimer, D. L. (2017). *Cost-benefit analysis: concepts and practice*. Cambridge University Press.

⁷⁵ EHR IMPACT (2008). Methodology for evaluating the socio-economic impact of interoperable EHR and ePrescribing systems.

⁷⁶ UK HM Treasury (2003), *The Green Book - Appraisal and Evaluation in Central Government*.

⁷⁷ Röthig, P. (2009), ICT Investitionen begründen - Wirtschaftlichkeitsberechnungen mit dem WiBe-Konzept.

⁷⁸ White House Office for Management and Budget, (1992) Circular No. A-94 - Guidelines and Discount Rates for Benefit-Cost Analysis of Federal Programs

⁷⁹ Boardman, A. E., Greenberg, D. H., Vining, A. R., & Weimer, D. L. (2017). *Cost-benefit analysis: concepts and practice*. Cambridge University Press.

system failure. In essence it is the sum of costs and benefits, i.e. the net-benefit, that an assessment method needs to determine.

In addition, several assessment frameworks, especially financial ones, do not account for intangible benefits, because they are difficult to measure. In our opinion this is not a good reason for excluding them. As some studies prove there are a number of methods that help to estimate intangible benefits like the willingness to pay approach⁸⁰. Furthermore, tangible costs and benefits are not as easy to measure as their quantitative, monetary metric might suggest. Often costs labelled with the same name can include highly varying concepts. A good example is staff costs. Does the calculation account for part-time employees? Does it include or exclude organisational overheads and social security contributions?

In social sciences there are four commonly applied quality tests a method should pass⁸¹:

- ▶ Construct validity: establishing correct operational measures for the concepts being studied
- ▶ Internal validity: establishing a causal relationship, whereby certain conditions are shown to lead to other conditions, as distinguished from spurious relationships
- ▶ External validity: establishing the domain to which a study's findings can be generalized
- ▶ Reliability: demonstrating that the operations of a study – such as the data collection procedure – can be repeated, with the same results.

Sustainability is a major concern for eHealth projects and their funders. Sustainability can be described as referring to “the ability to continue any given activity into the future within the likely existing resources of an organisation, as part of its ongoing budgetary and management processes”⁸². In the context of assessment, a service model is sustainable when it provides organisations with this above-described ability to continue activities. Therefore, sustainability cannot be regarded as something static. It requires an ongoing process that adapts the service to changing environmental conditions like new technological trends, behaviour of competitors in the market and changes to regulations or customer requirements.

In the overall policy context of the eHealth market, sustainability of a service would also imply the ability of providing the service over the long run and without the active support of research funds or subsidies restricted in their duration.

From this definition we draw the following requirements for a socioeconomic assessment:

- ▶ The method must be able to assess the history of a service and to project its future.
- ▶ A projection requires a service model on which assumptions can be based which also implies the need for a corporate strategy and the development of a business plan.
- ▶ An appraisal must assess the affordability of an undertaking, which means that the needed amount of cash, and cash flow is available and net returns also take into account the cost of financing (e.g. the interest rate of a bank loan).
- ▶ The method should provide a means to assess risks, e.g. those of market development assumptions, competitor behaviour etc.

These basic principles are important and should be applied. Despite this, however, there will remain a degree of uncertainty and failure, if a method is built upon several input variables and these input variables are taken from a number of sources using various methods. Therefore, an assessment framework needs to provide provision to test the rigour of its results and account for the uncertainty necessarily included, e.g., by carrying out sensitivity analysis.

Evaluations have a known tendency to understate costs and overstate benefits. This tendency increases where the basis of estimation relies more on judgement than facts and where the person delivering the estimate has an incentive to overstate performance. The UK Green Book⁸³ calls this optimism bias and proposes to adjust it by decreasing benefits and increasing costs. An assessment framework should provide means to counter optimism bias.

⁸⁰ Olsen, J.A. and Smith, R. (1999) “Who Have Been Asked to Value What? A Review of 54 ‘Willingness-to-Pay’” *Surveys in Health Care*.

⁸¹ Yin, R. K. (2003). Designing case studies. *Qualitative Research Methods*, 359-386.

⁸² Gordon, C. (2009). *Lab for Culture Glossary*. From: <http://www.labforculture.org/en/funding/contents/glossary#50>.

⁸³ UK HM Treasury (2003), *The Green Book - Appraisal and Evaluation in Central Government*.

Most products or services undergo a specific life cycle from the first idea to routine use, and finally they are supplanted by another more appropriate or new service⁸⁴. Important stages in the early phase of development are pilots which are often funded by research agencies or industry. This market validation phase is ideally followed by a scale up to a routine service. This life cycle has two implications: firstly, it means that values such as the number of users are not fixed but vary over time. Secondly for the assessment to be meaningful, it needs a forward looking, formative evaluation to allow for course correcting actions to be taken.

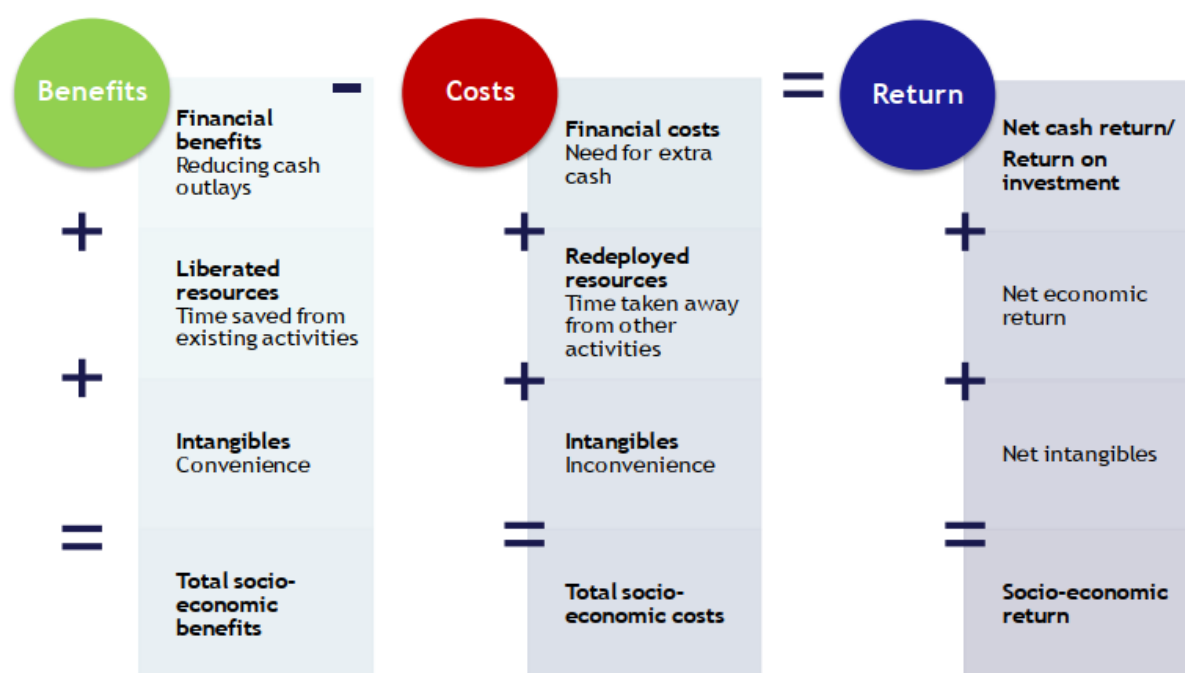


Figure 5. Overview of ASSIST as a CBA Evaluation Model

6.2 Data collection

In principle, all data can be used in a socioeconomic analysis ranging from best guess to data from clinical trials. The better the validity of the data, the more valid the results of the analysis. Within the ASSIST framework data from multiple sources is collected and parsed for a cohesive picture.

Some appropriate metrics can be found in organisations' archives and information systems. These include clinical data and statistics, service utilisation statistics, workload statistics, changes in capital and operational expenditure, and prices. Some costs and most benefits have to rely on estimates and assumptions. Ideally, assessments should perform detailed observational studies to establish precise changes, however, given temporal and budgetary constraints, semi-structured interviews can provide both, qualitative conclusions and some of the information needed to make estimates and assumptions needed for quantifying the impact⁸⁵.

Interviews are proposed as the primary information gathering technique, complemented by distributing detailed questionnaires. The latter alone can be too rigid, leaving little room for elaboration to gain knowledge on the background, context, motivations, drivers, and the eventual impact of individual initiatives⁸⁶. Fully structured questionnaires offer limited scope to capture spontaneous reactions or

⁸⁴ Bashshur, R., Shannon, G., & Sapci, H. (2005). Telemedicine evaluation. *Telemedicine Journal & e-Health*, 11(3), 296-316.

⁸⁵ Westbrook, J. I., Braithwaite, J., Georgiou, A., Ampt, A., Creswick, N., Coiera, E., & Iedema, R. (2007). Multimethod evaluation of information and communication technologies in health in the context of wicked problems and sociotechnical theory. *Journal of the American Medical Informatics Association*, 14(6), 746-755.

⁸⁶ Yin, R. K. (2003). Designing case studies. *Qualitative Research Methods*, 359-386.

subtle affinities, or reluctance by stakeholders, and are resource intensive. Qualitative methods using semi-structured group interviews offer scope to seek consistent information and to reflect specific healthcare settings, such as changes to clinical and working practices. They are also fruitful and open enough to elucidate stakeholders' perspectives, to cover a wide range of opinions and the strength of opinions held⁸⁷. Thus, the process of evaluation is often as insightful as the eventual results.

Data gathered from the planned UNICOM pilots will be integrated with the results of the interviews and questionnaires to provide a comprehensive socioeconomic impact assessment framework.

⁸⁷ Morse, J. M. (Ed.). (1994). *Critical issues in qualitative research methods*. sage.

7 Outlook

For the development of the impact assessment framework, we outlined the general key elements and dimensions which are relevant when assessing and estimating the potential and experienced impact of IDMP infrastructure implementation. We identified the major actors and beneficiaries as those who will have to make decisions whether and under what circumstances to use or invest in such an infrastructure, and also developed initial thoughts on the value propositions behind the support for and realisation of such an infrastructure. Furthermore, we undertook an initial classification of IDMP related resources and services which will be provided as elements or as functionalities to which beneficiaries may attach an added value. Our methodological considerations in the previous chapter allowed us to translate these theoretical and conceptual issues into an empirical measurement framework, based on the conceptual framework underlying the ASSIST tool and its measurement approach and benefit-cost measures. We identified basic assumptions underlying the general methodology, briefly reviewed measurement theory, reflected on how to categorise and measure benefits and costs, and how measurement and indicator development can be conceptualised.

In order to assess benefits and costs of IDMP in practice, the assessment plan includes evaluation of both ex-ante quantitative impact indicators and an empirical survey of impact indicators deemed most important by stakeholders. This evaluation will then add explanatory power to extract the value-added from IDMP implementation. The overall evaluation framework as developed in this deliverable serves as a theoretical guidance in operationalising the indicators.

7.1 Planned Pilots

An IDMP compliant pilot product list (PPL), based on about 35 active substances (based on WP 2 work) leading to more than 1,000 individual medicinal products and even more packages in participating countries will be used as HL7/FHIR formatted testing demonstrator and deliver input data for four pilot subprojects, pilots A-D, which are currently planned for UNICOM. Details about the pilots, including their requirements and their implementation are currently under development, and therefore subject to change.

The pilot product list, led by WP8 and WP9 and developed in close cooperation with WPs 1 to 7, proposes to be a central tool in UNICOM to demonstrate and test IDMP structured data preparation and exchange, with a small subset of substances and medicinal products. Its implementation will allow project partners, such as NCAs and eHealth organisations, to experiment with their data processes and move towards exchanging IDMP-structured medicinal product data with a prototyped UNICOM IDMP FHIR server or with other organisations.

Pilot A, led by ARIA in WP7, is a study which aims to incorporate 10.000 ePrescriptions with IDMP structured data in a testing environment in collaboration with CEF eHDSI. The pilot will test anonymous data routinely used by the European Commission's CEF teams to validate IDMP enhanced ePrescription IT systems. Pilot B, led by ARIA and DW in WP7, intends to prototype patient summary applications with 500 people. Pilot C will position itself as a clinical pilot with 25 patients, implemented at a hospital in Naples, and led by FOUND in WP8. Pilot D, led by DW in WP8, plans to validate IDMP-based citizen empowerment tools implemented in existing mobile health applications with 25 people. Both Pilots B & D will prototype novel digital App features via a web browser or mobile device and survey participants on both their experience using the App and on their value perception.

7.2 Expected Impacts and Preliminary Findings

A key initial step in the ASSIST framework is to model impact indicators of increasing specificity to be able to eventually attach monetary values to benefits and costs. Through the present framework development process, these preliminary indicators were based upon desk research, as well as work done for related deliverables including D1.1, D12.2, D4.14, and D4.16. Discussions between participants of workshops related to these deliverables as well those on stakeholder engagement within the wider UNICOM space informed our initial findings.

As mentioned previously, we selected NCAs, pharmaceutical companies, healthcare professionals, and patients, as key stakeholders in an effort to provide a representative sample across the medicinal product lifecycle.

Based on these, Table 3 below shows preliminary impact indicators for the selected stakeholders, classified according to their use cases. Impact indicators here refer to operationalised benefits and costs for IDMP implementation, and upon which further data will be collected over the course of the project. At the same time, these indicators will be reviewed in close exchange with the stakeholders involved and adapted as may be needed and as the empirical work develops. As discussed previously, data collection for implementation of the ASSIST framework will incorporate data from primary sources, which in our case refers predominantly to the direct involvement of users and actors, through stakeholder workshops, expert interviews, semi-structured questionnaires and eventually the UNICOM pilot projects.

Table 3. Preliminary Impact Indicators

	NCA's	Pharmaceutical Companies	Healthcare professionals	Patients
Pharmacovigilance and Clinical Care	<ul style="list-style-type: none"> ▶ AE reports use consistent product IDs, and so can be easily shared across jurisdictions. ▶ Signal management can draw on a more accurate set of AE reports, that can be integrated globally to increase the scope of analysis. ▶ Supporting other strategic business cases like drug shortage management and supply challenges ▶ Facilitates the retrieval of medicine information for the rapid and efficient handling of urgent situation (e.g. recalls) involving medicinal product defect. ▶ Better tracking to support efforts for anti-falsified medicines 	<ul style="list-style-type: none"> ▶ Increase the industry's signal detection capabilities to quickly identify product risks and issues including coordinating product recalls. ▶ Reduction in counterfeit products ▶ Better predictions of drug shortages and increased sales from meeting those shortages 	<ul style="list-style-type: none"> ▶ Reduce prescription drug errors, track patient fulfilment of prescriptions, reduces the number of lost prescriptions, better monitoring of controlled substance prescriptions. ▶ Reduced time needed for patient prescription refill requests and for answering questions related to prescription clarifications ▶ Improved automated clinical decision support tools, e.g- for dosage checking and duplicate substances in prescriptions. ▶ Instant notification of allergies, drug interactions, duplicate therapies and other clinical alerts. ▶ Improved submission process and reduction in errors for Adverse Drug Event (ADE) and Medical Event (ME) reports. ▶ Allows for a better integrated single workflow from patient intake to prescription to follow-up monitoring. 	<ul style="list-style-type: none"> ▶ Enables better monitoring of controlled substance prescriptions reducing the chance of wrong prescription that lead to ADR, e.g- by double checking of prescriptions and reducing lost prescriptions ▶ Highlights important drug information for easy identification of side-effects or for improved diagnostic support ▶ Reduced time needed for patient prescription refill requests and for answering questions related to prescription clarifications

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	NCA's	Pharmaceutical Companies	Healthcare professionals	Patients
Regulatory Data Management	<ul style="list-style-type: none"> ► Better communication and faster response times regarding product licensing, lifecycle management, decisions notices, data import, business and statistical reporting. ► Data submitted once can be re-used: e.g.- information provided as part of authorisation procedures can be used as the pharmacovigilance submission. ► Different regulatory aspects can be processed in parallel: e.g- substance data can be approved before conclusion of complete medicinal product regulatory process. Applicants and NCAs will be able to process IDMP/FHIR compatible data right from the beginning of regulatory activities in order to improve decision making ► Automate and feed regulatory processes and regulatory documents with IDMP/FHIR compatible data ► Reduce operational risks associated with current legacy systems. ► Efficiency gains on transferal of data and quality of data 	<ul style="list-style-type: none"> ► Reduced time and cost for multiple marketing authorization applications ► Reduces time to market for products and diffusion of products across markets ► Reduced cost of reporting information to NCAs and EMA etc. 	---	---
Medicinal Product Development	<ul style="list-style-type: none"> ► Assessment and scientific evaluation of a medicine is improved by providing access to data in a standard format. ► Allows proactive and reactive access to CT data thereby improving communication and transparency. ► Stakeholders will access clinical trial data using agreed and well-supported standards. ► Inspections of manufacturing sites will be based on more accessible information which streamlines inspections. 	<ul style="list-style-type: none"> ► IDMP can help with better drug discovery, shorten development time, reduce development costs, and reduce risk of failure and risk of safety issues. ► New products can be better compared with existing therapies (including via ADR reporting) which stimulates innovation. 	---	---

	NCA's	Pharmaceutical Companies	Healthcare professionals	Patients
Cross Border and eHealth Services	<ul style="list-style-type: none"> ►Facilitating the identification and exchange of product and substance information globally. ►Promote x-border and e-prescription programs. Supporting patient and eHealth focused initiatives like the ePI initiative with good quality data 	<ul style="list-style-type: none"> ►Increase patient engagement and support allowing digital tools geared towards medication adherence, education, advice, coaching. ►IDMP could allow linking of a digital solution/service to particular substances or medicinal products across different countries and life cycle products ►Master data management enabled solutions can lead towards greater integration across multiple systems, e.g- access to better data can better help determine which substances are preferred in which countries and which medical products are prescribed. ►Increased sales of medicinal products due to increased x-border and e-prescription implementation 	<ul style="list-style-type: none"> ►Help meet meaningful use requirements for ePrescriptions. ►Enhanced interoperability between ePrescriptions, EHR's, electronic patient summaries and related tools. 	<ul style="list-style-type: none"> ►Supports e-Patient Summary, e.g- use the barcode of any medicinal product you are considering buying in a pharmacy to check it is safe to take alongside your current health condition ►Supports e-Prescription and medication substitutions, e.g- check that a replacement prescription that you have been issued accurately corresponds to the usual medicine you take in your normal country ►Supports medication list e-transfers, e.g- transmit your medicines list electronically to a health professional ►Reduces language barriers, e.g- show a list of medicines to a health professional from whom you need healthcare, displayed in your usual language.
Costs	<ul style="list-style-type: none"> ►Technical implementation ►Legislative changes ►New training Required 	<ul style="list-style-type: none"> ►Transition Costs ►Continued Compliance Costs 	<ul style="list-style-type: none"> ►Transition Costs ►Potential retraining needed ►Continued Compliance Costs 	<ul style="list-style-type: none"> ►Potential fees paid for use of cross border services depending on the member state.