Regulatory Informatics and Labelling Management Systems – Recent Developments and Description of a State-of-the-Art Labelling Management Software in the Pharmaceutical Industry

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List of abbreviations

BPM	Business Process Management
CA	Competent Authority
CAP	Centrally Authorized Product
CP	Centralized Procedure
DADI	Digital Application Dataset Integration
DCP	Decentralised Procedure
DM	Document Management
DMS	Document Management System
eAF	electronic Application Form
ECM	Enterprise Content Management
eCTD	Electronic Common Technical Document
EDMS	Electronic Document Management System
EMA	European Medicines Agency
ePI	electronic Product Information
ERP	Enterprise-Resource-Planning
EU	European Union
FHIR	Fast Healthcare Interoperability Resources
GMP	Good Manufacturing Practice
GUI	Graphical User Interface
GxP	Good ‘x’ Practice
HCP	Healthcare Professional
HL7	Health Level Seven
HMA	Heads of Medicines Agencies
IDMP	Identification of Medicinal Products
ISO	International Organization for Standardisation
MA	Marketing Authorization
MAA	Marketing Authorization Application
MAH	Marketing Authorization Holder
MedDRA	Medical Dictionary for Regulatory Activities

MRP	Mutual Recognition Procedure
OMS	Organization Management Services
PI	Product Information
PL	Package Leaflet
PMS	Product Management Services
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
RA	Regulatory Affairs
RI	Regulatory Informatics
RIMS	Regulatory Information Management System
RMS	Referentials Management Services
RWE	Real-world evidence
SaaS	Software as a Service
SmPC	Summary of Product Characteristics
SMS	Substance Management Services
SPL	Structured Product Labelling
SPOR	Substance, Product, Organization and Referential
WCM	Web Content Management
xEVMPD	eXtended EudraVigilance Medicinal Product Dictionary
xEVPRM	eXtended Eudravigilance Medicinal Product Report Message

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1. Introduction, problem statement and aim of the thesis

1.1 Product Information (PI) texts in the European regulatory framework

PI texts are required by pharmaceutical legislation in Europe for every medicinal product for human use. These texts can be divided between the packaging material and the Summary of Product Characteristics (SmPC). In general, the latter is a virtual document drawn up and maintained by the marketing authorization holder (MAH) and describes all the information and particulars needed for the medicine's safe and intended use. The SmPC is made available to healthcare professionals (HCPs), i.e. doctors, nurses and pharmacists, the targeted reader group for this type of PI. The legal basis of the SmPC is Art. 11 of Directive 2001/83/EC.

The packaging material can be further split into the Package Leaflet (PL) and the Labelling documents. The Labelling contains the particulars that will be displayed on the primary and secondary packaging. The PL accompanies the medicinal product, usually inside the secondary packaging. It contains information in terms of the corresponding SmPC but in a patient-friendly manner. Overall, the PL needs to be clearly written and easily understandable, enabling users to act appropriately. The design must be clearly legible. The detailed requirements of the PL are stated in Art. 59 of Directive 2001/83/EC.

The outer Labelling is a virtual document that displays the information content that will appear on the secondary packaging of the medicinal product, e.g. the outer carton of the medicine. The outer packaging is usually defined as the packaging into which the immediate packaging is placed. The immediate packaging displays the information that will appear on the primary packaging, e.g. blister strips or bottle Labelling, if applicable. The legal requirements are stated in Art. 54, Art. 59 and Art. 62 of Directive 2001/83/EC.

For medicinal products authorized via the centralized procedure in the European Economic Area, the corresponding requirements of the PI texts for such medicinal products are described in Regulation (EC) No 726/2004.

The life cycle of these documents begins with the submission of the Marketing authorization application (MAA), before the actual market launch of the medicinal product. The PI texts must be submitted to the competent authorities (CAs) as part of the marketing authorization (MA) dossier upon submission of the MAA. Changes to these documents may

already be necessary during the MA procedure due to comments from the authorities or as new scientific information emerge.

After the MA has been granted, the approved PI texts are located in the so-called 'maintenance' phase, which is part of the maintenance of the MA. This 'maintenance' field is required because authorities must be notified of any change to the product, and therefore any change to the PI documents. Major changes to the content of these documents need the CA's approval. Such changes are implemented via variation applications following the specified terms and requirements in the so-called 'Variation Regulation', Commission Regulation (EC) No 1234/2008.

PI documents are frequently subject to changes during their lifecycle. The reason for this is Art. 23 (3) of Directive 2001/83/EC, which states that '*The marketing authorization holder shall ensure that the product information is kept up to date with the current scientific knowledge, including the conclusions of the assessment and recommendations made public by means of the European medicines web-portal established in accordance with Article 26 of Regulation (EC) No 726/2004*'.

Following the legal character of PI texts, MAHs are legally obliged to provide the appropriate and scientifically up-to-date SmPCs and packaging materials.

Medicinal products are highly regulated products. They are defined as 'goods of special nature' and may therefore not be marketed without approval from the CA. This is also the reason an MAA has to be submitted to the CA before marketing and why every change to the MA needs the approval of the CA. The maintenance of the PI documents only ends when the MA expires, i.e. when it is withdrawn.

PI texts have a significant influence on patient safety, since the information provided by the PI texts dictates the correct use of the medicine. PI documents have significantly impact on patient well-being and efficacy of treatment. If information provided by the SmPC and packaging materials are defective, misleading or outdated, considerable damage can be caused to a patient's health, up to the death of the patient. Poorly maintained PI texts have a great potential to negatively affect a medicine's safe and effective use.

Critical documents require a special document management (DM) to assure document safety, quality, integrity, reliability and backup. In general, a risk management on every

document type managed should be performed to evaluate the document's criticality. Based on the results, the appropriate actions should be undertaken. (1)

Please refer to **Table 1** for the risk assessment of PI texts, which concludes that PI documents need to be regarded as critical documents.

To sum up, PI documents must be specially controlled in pharmaceutical companies to comply with legal requirements and to ensure patient safety.

Table 1: Risk assessment of PI documents

Criteria	Risk	Probability	Seriousness	Total Score	Risk description
Availability	Latest approved version of PI cannot be found / not sure which is the latest approved version	2	2	4	Common problem in Regulatory departments if there is no proper DM. Especially a problem where PI texts are subject to many changes. Preventive measure: Implementation of proper rules for DM
Availability	Patient/HCP cannot find the corresponding PI for the medicine	1	1	1	Low risk as printed PL inside the medicine pack ensures that there is the relevant information available at point of administration of the medicine
Confidentiality	PI is published too early - violation of competitors' patents or market exclusivity rights	1	2	2	During drug development, the corresponding PI has to be considered as highly confidential. Appropriate security standards/data protection rules are necessary. Post-marketing, confidentiality of PI data is usually not an issue
Confidentiality	Competitors get to know unintentionally what products are developed	1	3	3	
Unalterability	Information in PI documents gets altered unintentionally	2	3	6	Very difficult to detect such changes and publishing/printing of deficient PI data leads to many subsequent risks (see below). MAH is liable for health damage caused by defective PI on the medicine. Therefore, this if of high criticality

Unalterability	Wrong version of PI gets submitted to authorities	2	2	4	May lead to the refusal of a regulatory procedure (e.g. variation), a substantial amount of reworking (document correction, additional submission of regulatory sequences (for validation issues or responses, response to assessors comments and deficiency letters)), or may necessitate resubmission of variation if the wrong PI version has been approved by authority and correction is needed
Unalterability	Wrong PI version is published on websites and other digital platforms	2	2	4	May be replaced quickly after noticing. However, hard to detect, therefore a critical issue
Unalterability	Wrong PI version is used for packaging process	2	3	6	May necessitate re-packaging or disposal of medicines if packaging materials are deficient. Worst case: product recall necessary due to deficient packaging materials of products placed on the market
Unalterability	HCP provides wrong instructions for use to the patient due to deficient SmPC/PL	1	3	3	Low probability because there are many steps between prescription and use of the medicine that are supposed to mitigate wrong use of medicines (doctor, pharmacist, PL). However, altered PI always bears the risk of wrong administration and therefore risks patient safety and treatment efficacy. Therefore, the seriousness is high
Unalterability	Patient uses/takes medicine in a wrong way due to deficient PL	1	3	3	Low probability because there are many steps between prescription/purchase and use of the medicine that are supposed to mitigate wrong administration (doctor, pharmacist, PL). However, altered PI always bears the risk of wrong administration and therefore risks patient safety and treatment efficacy, especially for over-the-counter medicines. Therefore, the seriousness is high
					Score Low: 1, Medium: 2, High: 3

Note: Adapted from (1)

1.2 Problem statement

At first glance, it seems as though it should be easy to draw up, maintain and handle PI documents throughout the whole lifecycle process of a medicinal product. The commonly used formats are Microsoft Word documents (docx) and Portable Document Format (PDF). In general, docx documents are used to draw up the initial PI texts and to amend them. For some activities, it is necessary to convert the Word files into a stable, trustworthy format so the content cannot be altered. Both document types can easily be transferred between stakeholders via email or filesharing solutions. For storing, lifecycling and archiving, electronic folders, e.g. Windows folders, can be used. The folders are either stored in a decentralized location, e.g. personal computers or hard drives, or on a centralized platform, e.g. shared network drives and folder systems.

However, for many pharmaceutical companies, it is not as simple as that. Depending on the size of the company, dozens, hundreds or even thousands of PI documents have to be created, maintained and appropriately managed in a controlled way. A large number of PI-related processes have to be carried out on a daily basis.

Handling important documents manually and without the use of adequate technical solutions leaves a lot room for errors. **Figure 1** summarizes the most common challenges faced when documents and information are managed and stored inefficiently.

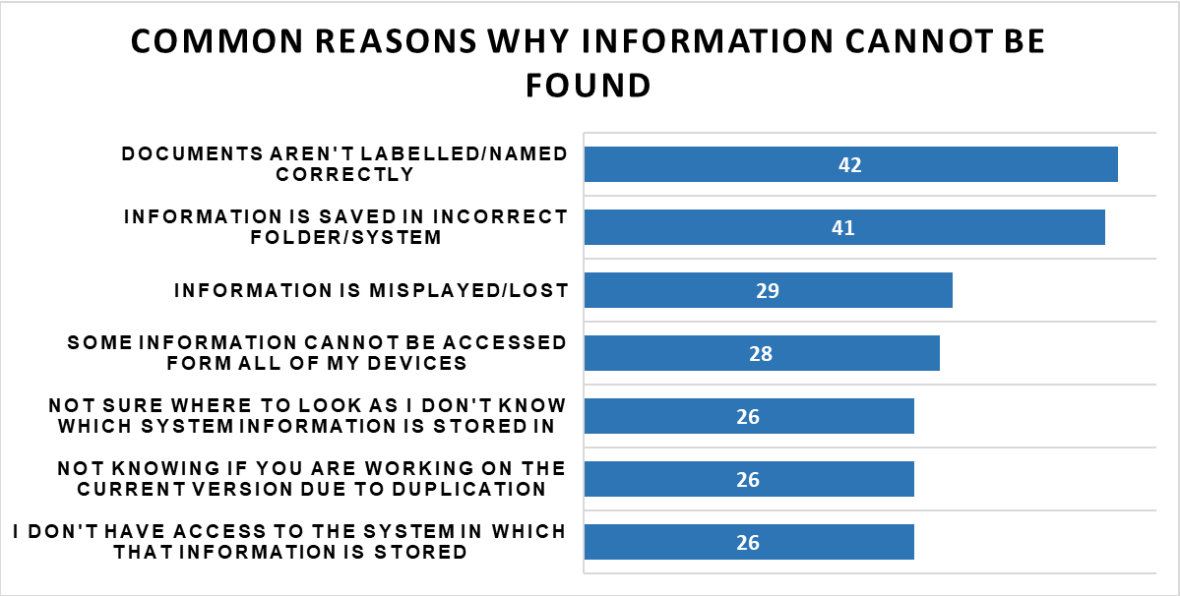

Figure 1: Common challenges faced when searching for information

Source: *(2)*

These challenges mainly emerge when documents are stored inadequately and only in semi-structured databases, e.g. exchange servers, shared network drives or electronic clouds without the use of controlled DM mechanisms.

The insufficient management of PI documents leads to many problems in terms of efficiency and quality losses for concerned departments in the pharmaceutical industry.

Searching for the correct document or checking if the document at hand is the correct, most up-to-date version is time-consuming for the company's employees, significantly reducing process efficacy and reliability, and overall employee productivity.

Submitting a wrong document causes a substantial amount of reworking and longer approval times. Besides, this may also lead to an increase in regulatory fees, for example, if erroneously submitted and approved PI documents need to be corrected via an additional variation.

Another problem is that regulatory documents, including PI texts, are often distributed by email within companies and with external partners. At first glance, this way of processing document-related processes seems logical, as both the necessary information and the documents can be forwarded together to the relevant stakeholders. In reality, however, this type of process control consumes vast amounts of unnecessary time, as the constant

sending of documents back and forth creates an incredibly high administrative burden. This leaves the employees and partners involved with less time for their actual tasks. For example, if no controlled business process management (BPM) tool is used, Regulatory Affairs (RA) managers are constantly busy distributing and sharing documents and related information to different departments and external partners manually. This leaves less time for the actual regulatory tasks such as preparing regulatory documents, compiling dossiers and performing submission activities such as variations and renewals.

This is even more the case when files are handled and stored inconsistently within a company. A classic example is that the involved departments, such as RA, Medical Affairs and Pharmacovigilance (PV), use independent shared network folder systems for their departmental DM with no access rights for other document storages.

As stated above, PI documents need to be regarded as critical. Therefore, it becomes clear that pharmaceutical companies need to take action and rethink their DM of PI. Modern technical solutions are necessary to regain full control of PI documents and related business-processes. A proper IT solution ensuring document quality, integrity, reliability and backup is needed. An adequate solution for improving PI DM in pharmaceutical companies is the introduction of a suitable Document Management System (DMS) or Enterprise Content Management (ECM) solution. In fact, the concepts overlap to a large extent and a clear demarcation is not possible. Both concepts focus on improving DM and document-related processes in order to improve the quality and the access to the documents and to the information stored in them. Therefore, and for simplicity reasons, the term ‘DMS’ is used throughout this thesis as a placeholder for both concepts. Both concepts, their benefits and the reasons for implementing a DMS is further discussed in Section 4.3.

By implementing a specific Labelling management software, pharmaceutical companies are able to increase regulatory efficiency in the related departments. In Section 4.6, the benefits of Labelling Management Systems will be further discussed and the need for their use for every RA department will be justified.

1.3 Aim of this thesis

This Masters thesis aims to provide clear guidance on which technical specifications and functionalities are important for a state-of-the-art Labelling Management solution. Another focus is on non-technical specifications (including vendors' services) that are crucial for a successful implementation. The special legal character of medicinal products as well as the current pharmaceutical legislation and guidance documents in the European Union (EU) are taken into account. The aim is not to recommend a specific software solution that is available on the market. This is not helpful because the DMS software market constantly changes as new developments emerge and existing software solutions are developed further.

The benefits of, as well as the critical issues regarding utilizing an adjusted DMS on PI management are discussed. Furthermore, recent and current developments in the field of Regulatory Informatics (RI) are linked to the topic of PI management and further explored.

2. Materials and Methods

2.1 Literature search

In order to obtain a good overview of the published literature on the topic of DM, various search terms were used, and the suggested literature sources were analysed for their significance. The significant information was then used to prepare the Masters thesis. For the literature search, university library catalogues (Goethe Universität Frankfurt, Rheinische Friedrich-Wilhelms Universität Bonn) as well as the catalogue of the 'Deutsche Nationalbibliothek' were used.

Publishers are obliged to make all published German-language media works (books, journals, video and audio files, electronic publications and web publications) available to the 'Deutsche Nationalbibliothek'. The 'Deutsche Nationalbibliothek' is obliged to collect, inventory, index and bibliographically record all German-language media works, to safeguard them in perpetuity and to make them available to the general public (3). Access to all German-language literature on the topic of DMS/ECM thus enables a very comprehensive literature search. The search terms used for the literature search in the library catalogues are listed in **Annex I**.

A focused search was also performed on the World Wide Web to obtain additional suitable scientific sources, appropriate publications and field reports. The same search terms as for the literature search in the libraries were used.

The literature search was continued until no further relevant information on the topic of DMS/ECM could be found. Due to having access to all German-language literature and the exhaustive research, it can be stated that the literature research is very comprehensive. The literature and resources obtained in this way served as material for the preparation of this Masters thesis.

2.2 Market analysis

The current DMS/ECM market was examined in order to draw up a concrete list of specifications for the selection of a state-of-the-art Labelling Management system. For this purpose, previously published market surveys of the DMS/ECM market in Germany were analysed. The analysis showed that there are many different DMS/ECM solutions on the

market, most of which are offered internationally. In addition, the internet was searched for additional DMS/ECM applications available on the market. Their specifications and characteristics have also been screened. Furthermore, the internet was searched for market surveys, experience reports and other sources that were considered helpful to elaborate the current situation of the DMS/ECM market. All findings were used to perform a comprehensive analysis of the current DMS/ECM market.

The market analysis focused on technical functionalities, technical and non-technical specifications and services offered by DMS/ECM vendors and service providers. The results of the market analysis are presented in **Annexes II-VII**.

The importance of each functionality and specification for a state-of-the-art Labelling Management System was subsequently evaluated. Published field reports of DMS/ECM implementations in companies and 'lessons learned' were also assessed. The essential specifications and functionalities that a state-of-the-art Labelling Management System should offer to users were elaborated, including vendor services that are essential to a successful implementation.

The result is a scientifically based list of specifications that reflects the requirements for a suitable DMS to manage PI documents. The specifications are intended to serve as an aid for pharmaceutical companies that are considering a DMS in the area of Labelling/PI management. This is particularly useful as the DMS/ECM market is very confusing: pharmaceutical companies can be overwhelmed by the vast number of different software vendors and service providers, all of which are offering different packages with different software modules and functionalities. As a consequence, the range of offered specifications, technical functionalities and services is immense and can hardly be surveyed. Assigned project teams are having a hard time identifying which specifications and functionalities are really important for a specific Labelling Management Solution that is fit for purpose, easy to use and leads to efficiency gains.

In combination with a thorough literature search, this Masters thesis elaborates specifications, technical requirements and vendor services needed for a state-of-the-art DMS for the management of PI documents.

3. RI

3.1 How can RI be defined?

RI can be seen as the overlap between RA and IT. Wherever the classic tasks of RA - such as the preparation and maintenance of MA dossiers, regulatory activities (MAA, Submission of Renewals and Variations) and interaction between different stakeholders - come into contact with IT developments, the field of RI emerges. **Figure 2** illustrates this overlap that creates the new field of RI.

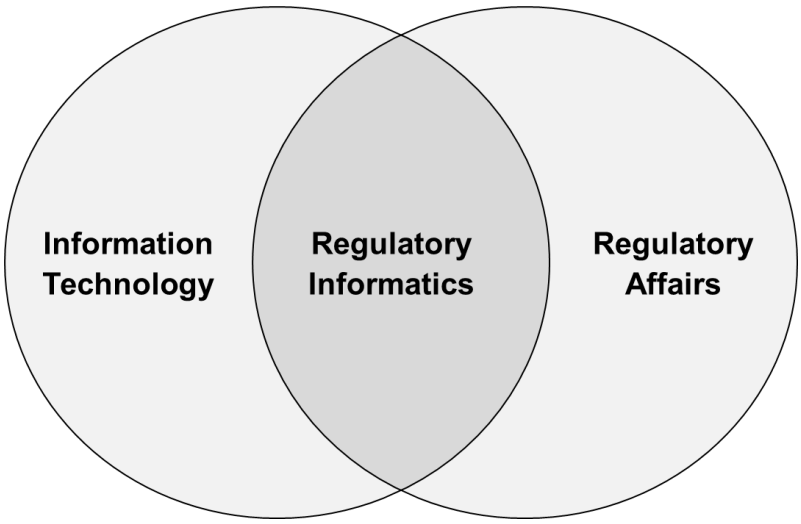

Figure 2: How IT, RA and RI are interconnected

RI projects are usually drawn up to facilitate regulatory activities, promote the sharing and re-use of medicinal product data or lower the administrative burden, thereby empowering regulatory decision-making and ultimately enhancing regulatory efficiency. In general, advantages are sought for both industry and regulators in every RI project.

In the following paragraphs, important RI projects that have been implemented as well as RI projects currently being implemented or under development are outlined. The focus is on RI projects that are related to PI.

3.2 Past developments

3.2.1 electronic Common Technical Document (eCTD)

The is a standardized format for submitting regulatory documents, such as clinical trial applications, marketing authorization applications, and periodic safety update reports (PSURs), to health authorities. It is designed to facilitate the electronic submission of documents and ensure the consistency, completeness, and quality of the information submitted. The eCTD format is organised into a series of modules, each of which contains special types of information. The content of the eCTD modules may vary depending on the requirements of the authority, whereas the overall format ensures a harmonized approach for organising and submitting regulatory documents. It is a structured electronic file format that uses XML as a backbone to organise the incorporated documents in a hierarchical format. The XML metadata allows the automatic electronic processing of the submitted documents. (4,5,6,7)

The use of eCTD has become widespread in the pharmaceutical industry and is now accepted by many CA worldwide as a standard format for electronic submissions. The adoption of eCTD as a common format streamlines the regulatory submission processes, reduces submission processing times, and improves the overall quality of the information submitted.

Key learnings from the eCTD project still influence current RI projects:

- a globally harmonized and consistent format simplifies the preparation of regulatory documents on industry side as well as the review process for the authorities
- Organization of regulatory documents in a clear format facilitates to keep track of submissions and optimise handling of regulatory document
- Saving significantly amounts of resources by simplifying the preparation and submission of regulatory documents and accelerating regulatory decision making and

Overall, the eCTD format provides a standardized and efficient means for submitting regulatory documents, improving the quality and speed of the review process and facilitating the approval of safe and effective medicinal products.

3.2.2 Art. 57 database (data submission on authorized medicines)

The submission and maintenance of data on authorized human medicines has been mandatory since July 2012 (8).

All MAHs of medicinal products in the EU must submit information on authorized medicinal products upon first authorization and any subsequent variation of the MA to the European Medicines Agency (EMA) within 30 days of approval. This legal obligation derives from Art. 57 (2) of Regulation (EC) No 726/2004, which is also the eponym for this database. The database is also sometimes referred to as the eXtended EudraVigilance medicinal Product Dictionary (xEVMPD). Art. 57 has been introduced into the depicted regulation with Regulation (EU) No 1235/2010 on pharmacovigilance. Thus, xEVMPD can be seen as a pharmacovigilance database to facilitate pharmacovigilance activities and the work of regulatory systems in the EU. (9) Moreover, MAHs are obliged to upload SmPCs to the database, as well as new versions when they become available.

MAHs submit the information on authorized medicines with the use of the eXtended EudraVigilance Product Report Message (xEVPRM). This format has been introduced by the EMA and enables the exchange of data on human medicines between systems. (10,11)

xEVMPD uses wide range of controlled vocabulary, coding for indications and MedDRA terminology, among other data standards, to ensure the collection of high-quality information on human medicines in a centralized database. It is the first European database that covers information on all medicinal products authorized in the EU, including medicines authorized via centralized procedure (CP), mutual recognition procedure (MRP) and decentralised procedure (DCP) as well as purely nationally authorised medicines.

3.2.3 Structured Product Labelling (SPL)

SPL is a document markup standard approved by Health Level Seven (HL7) and adopted by the Food and Drug Administration (FDA) as a mechanism for exchanging product and facility information in the USA. (12) It is based on an eXtensible Markup Language (XML) standard, which is used to encode documents in a format that is both human-readable and machine-readable. Therefore, XML allows data to be exchanged between different systems and

software applications. XML is used to encode data in a structured manner, meaning that XML can use structured information from databases. XML is a flexible format that can be used to store a wide range of data types, including text, numbers and dates. (13,14,15)

The use of XML enables SPL to use structured data, e.g. controlled vocabulary, from databases in the PI. This allows the information to be easily understood and processed by both humans and computer systems. SPL is based on the HL7 international standard for exchanging electronic health information, and it is designed to be interoperable with other systems that use HL7 standards. SPL allows the use and presentation of data in a consistent structure using standard terminology aimed at improving the integrity of the PI and keeping patients safe. (16)

SPL documents contain both the labelling content of (all text, tables and figures) for a product and additional machine-readable information (including drug listing data elements and clinical data elements). Drug listing data elements include coded information about the product (including product and generic names, ingredients, ingredient strengths, dosage forms, routes of administration, appearance and administration schedule) and the packaging (package quantity and type). Clinical data elements include coded information about the clinical use of the product (including indications and use, contraindications, drug interactions, warning and precautions and use in special populations). (16)

To conclude, the SPL is an initiative in the USA to allow the use of structured data on human medicines in the PI. It further facilitates the use of data from the International Organization for Standardization (ISO) for the identification of medicinal products (IDMP) and allows the use of machine–machine communication. It is considered one of the first approaches in the pharmaceutical field worldwide to make use of structured information in PI texts. The SPL project is the first approach to implement controlled data into PI of medicinal products, moving away from purely free-text based PI documents as the common standard. The SPL is the role model many similar projects worldwide, including the currently emerging electronic Product Information (ePI) initiative in the EU.

3.3 Current Developments

3.3.1 ISO IDMP

The ISO has developed standards to identify and describe the particulars of medicinal products for human use. The standards are defined as ISO IDMP standards and aim at using standardized definitions for the identification and description of a medicine's particulars. The implementation of these standards is supposed to facilitate the reliable exchange of medicinal product information in a robust and consistent manner (8). Art. 25 and Art. 26 of Commission Implementing Regulation (EU) No 520/2012 obliges EU member states, MAHs and EMA to use the ISO IDMP standards for medicinal products for human use. (17)

ISO IDMP consists of five separate standards to allow the ultimate and clear description and characterization of human medicines. **Table 2** and **Figure 3** depict these five standards.

Table 2: The five ISO IDMP standards *(18)*

ISO identification number	Topic
ISO 11238	Substances
ISO 11239	Pharmaceutical forms, units of presentation, routes of administration and packaging
ISO 11240	Units of measurement
ISO 11616	Regulated pharmaceutical product information
ISO 11615	Regulated medicinal product information

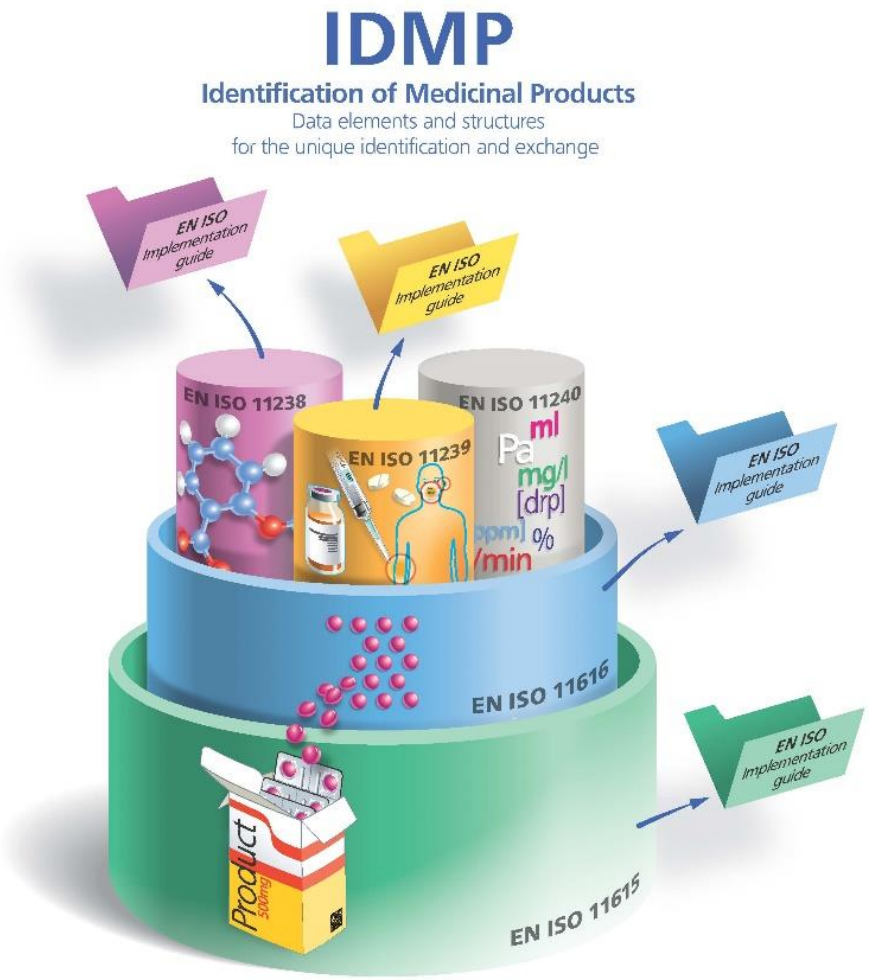

Figure 3: ISO IDMP data elements and structures

Source: *(19)*

The ISO IDMP standards cover the entire medicinal product lifecycle, including products in development, investigational products, products under evaluation and authorized products. (8)

The use of standardized terms to describe the particulars of medicinal products is crucial to enhancing and simplifying the exchange of information on human medicines between stakeholders globally. Through the use of structured, standardized data, the interoperability between formerly independent systems is improved significantly, therefore enabling consistent communication of medicinal product data worldwide.

3.3.2 Substance, product, organization and referential (SPOR) programme

The SPOR programme was set up by the EMA, aimed at implementing the ISO IDMP standards in the EU. It consists of four independent databases to enable the use of IDMP: Information on Substance, Product, Organization and Referential (SPOR). Hence its four dominions are called Substance Management Services (SMS) containing structured information on ingredients and materials; Product Management Services (PMS) containing structured data on authorized medicinal product; Organization Management Services (OMS), providing structured data on organizations; and Referentials Management Services (RMS) containing controlled vocabularies used to describe particulars of medicinal product. (20,21,18,22) **Table 3** presents the four dominions of SPOR and describes the harmonized structured data they contain. **Figure 4** illustrates how the four SPOR dominions and the five ISO IDMP standards are interconnected.

EMA has established the so-called *SPOR (ISO IDMP) Task Force* that is responsible for advising on the planning, development, implementation and maintenance of the ISO IDMP standards in the EU, in-line with requirements defined at international level and based on agreed EU implementation principles (18,20,22). Since January 2023 onwards, the SPOR Task Force is no longer in operation as the EMA is abolishing all governance bodies and introducing a new 'EMA Agile governance model'. The new governance model aims to foster the development implementation of new IT projects. (23,24)

Table 3: SPOR master data services *(18)*

SPOR dominion	Description
SMS	Harmonized data and definitions to uniquely identify the ingredients and materials that constitute a medicinal product.
PMS	Harmonized data and definitions to uniquely identify a medicinal product based on regulated information (e.g. MA, packaging and medicinal information).
OMS	Data that comprises of organization name and location address data for organizations such as MAH, sponsors, regulatory authority and manufacturers.
RMS	List of terms (controlled vocabularies) used to describe attributes of products e.g. lists of dosage forms, units of measurements and routes of administration.

The difference between ISO IDMP and SPOR is that the ISO IDMP standards apply to human medicinal products, whereas SPOR applies to both human and veterinary medicinal products. Moreover, ISO IDMP covers the entire medicinal products lifecycle, including development, while the SPOR PMS covers only the authorized medicinal product part of IDMP. (8,25,26) Interestingly, the OMS module is not covered by an ISO IDMP standard.

The exchange of data between SPOR databases and respective stakeholders will be performed using the ISO IDMP-compatible HL7 Fast Healthcare Interoperability Resources (FHIR) standard. The FHIR standard is a set of guidelines and a framework for representing and exchanging healthcare data in a structured and consistent manner. The standard enables the electronic exchange of healthcare data between different IT systems. The new FHIR format will also replace the Art. 57 data format, as the latter is not ISO IDMP compatible. (11,21,27)

Of note is that the PMS data will consist of a match and merge of xEVMPD data and data from the EMA's in-house database, called SIAMED II. However, SIAMED will only provide data for Centrally Authorized Products (CAPs). (11). As a consequence of this data migration, the Art. 57 database will be replaced when PMS is fully implemented. MAHs need to prepare the use of the new FHIR standard as well as update their existing IT infrastructure in order ensure continuous interoperability.

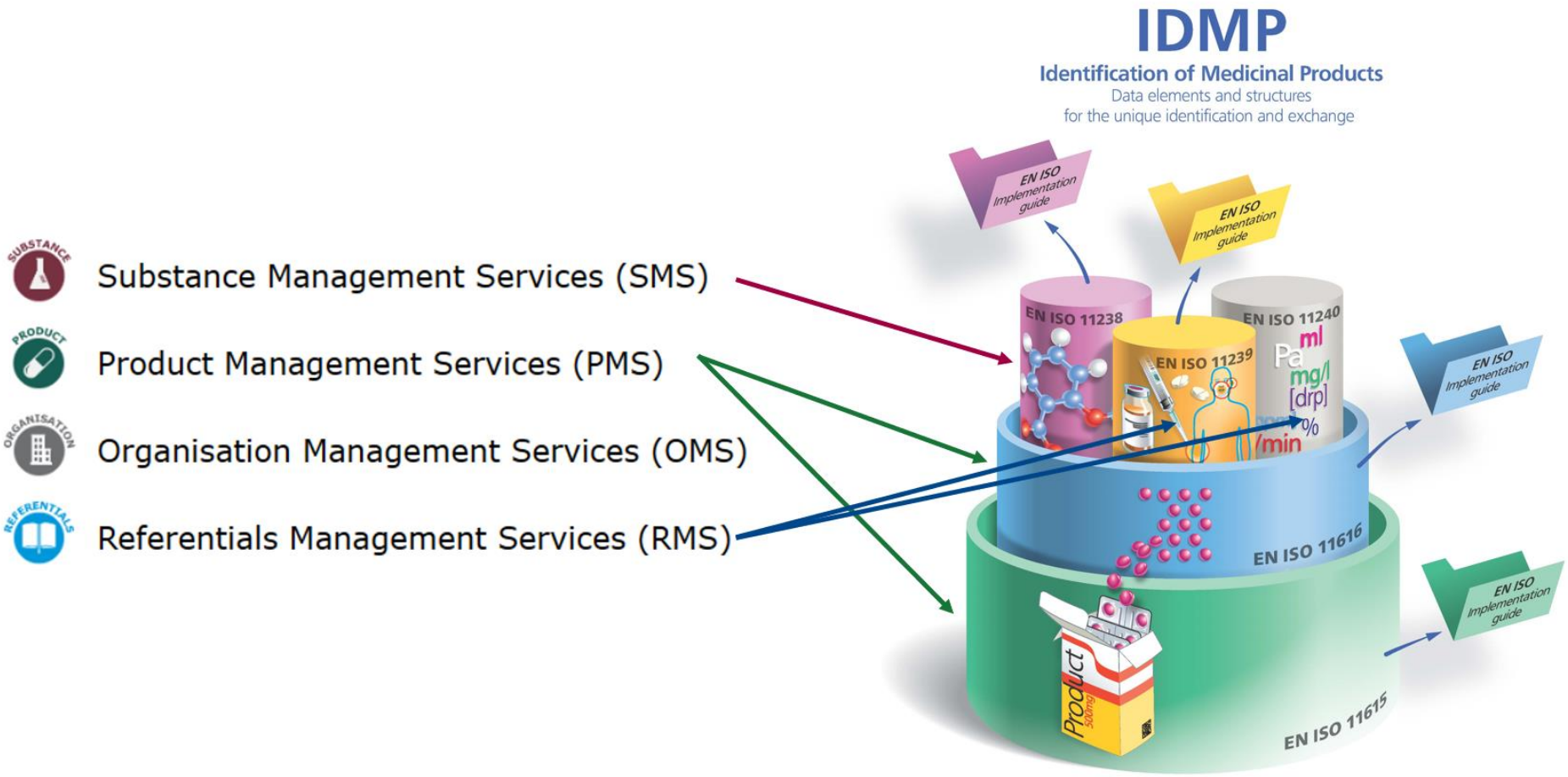

Figure 4: How ISO IDMP and SPOR databases are connected

Source: Adapted from *(23)*

The use of SPOR is supposed to save work and facilitate the use of ISO IDMP standards in the EU while creating a common European database on human medicines and related information that every stakeholder can access. The use of harmonized, structured data promotes the sharing and re-use of data on human medicines. In the future, it is envisaged that the SPOR master data will support regulatory activities for MAHs and authorities. Therefore, the IT systems of MAHs and authorities need to empower the use of SPOR data. The use of harmonized, structured data promotes the sharing and re-use of data on human medicines. The structured data from these databases is supposed to feed other applications in the future, e.g. the web-based electronic Application Forms (eAF) and the ePI (cf. Sections 3.3.3 and 3.3.4).

It is also envisaged that the controlled information from databases such as SPOR will be used in the PI. Therefore, it is essential that future PI management tools enable the use of the ISO IDMP data.

3.3.3 Digital Application Dataset Integration (DADI)/web-based eAF/Product Lifecycle Management (PLM) portal

For each regulatory activity, whether an MAA, a renewal or a variation, the applicant must attach an application form to the submitted documents and explain its submission to the authorities concerned. Currently, PDF- based eAF are used. Applicants have to fill in the specified information fields of each eAF manually, check the information and then electronically sign and lock the PDF.

The currently used PDF-based eAF works interactively, meaning that the PDF is not static but uses an XML backbone to allow limited functionalities such as drop-down menus and pick lists and, to some extent, also automatic data filling from SPOR master data. (25,26,28) However, these functionalities are very limited and PDF performance is poor, which leads to excessive preparation time for the creating application forms. Moreover, data filling is mostly done manually, which leaves room for error and thus reduces data quality. The use of the PDF XML standard does not allow re-use of application forms due to poor system stability and performance. The connection of all SPOR master data systems is not feasible and thus the full implementation of the ISO IDMP standards is not possible. To conclude,

the PDF-based eAF is no longer fit for purpose and needs to be replaced with another, more reliable format.

In 2021, the DADI project was started in order to make the future form-filling and submission handling process more efficient. (29) The project is now more commonly referred to as web-based eAF rather than DADI, although it is still the same. The project aims at replacing the current PDF-based eAF with eAFs created in EMA's PLM portal. The web-based eAFs facilitate the use of the ISO IDMP standards and therefore further accelerate ISO IDMP implementation in Europe. The web-based forms allow form-filling in an interactive web format, using controlled vocabulary and structured information on human medicines from SPOR master data systems. The connection of all four SPOR data management services allows users to pre-populate high-quality data on medicines. Over time, more and more free-text fields in the web-based eAF will be replaced with drop-down and pick lists to increase data consistency and quality. After completion, the PLM portal allows the generation of eAFs in PDF format for human readability, but also the generation of a FHIR message as a new data standard to enable machine readability, machine–machine communication and electronic processing. (25,26,28)

3.3.4 Electronic Product Information (ePI)

In 2020, the joint collaboration of the EMA, Heads of Medicines Agencies and the European Commission set out key principles for the development and use of an electronic version of the PI in the EU after consulting with stakeholders. Many advantages are foreseen in using an electronic version of the PI texts. In particular, the introduction of an electronic PL that will at first complement the printed PL and then perhaps completely replace it, is seen as a major step for the future. Consequently, the ePI project has been established to develop a common European Standard for a harmonized electronic version of PI and to drive forward the use and implementation of ePI in Europe. (30)

The key principles outline the expected benefits from an electronic version of PI. The main purpose of an ePI is to improve access to up-to-date PI on medicines when and where it is needed. (30) Furthermore, an ePI is supposed to use semi-structured information and allow interoperability with IT systems such as SPOR master data. 'Semi-structured' means that

the new format of the PI will use structured data, such as controlled vocabularies and reliable information from IT databases, alongside unstructured information like free-text subsections and graphics. This will enable the use of high-quality information and also facilitate the sharing and re-use of data. The currently used Word (docx) and PDF files are insufficient and cannot meet demand. Hence, a new technical standard had to be developed that meets the desired functionalities and interoperability features.

The EU common standard for ePI was developed until 2021. It outlines the technical aspects of the EU ePI. Just like the web-based eAF (c.f. section3.3.3), it uses the FHIR standard. This standard uses XML-based document formats (such as XML and JSON) which enables the use of semi-structured information in PI texts. Of notice is that the ePI standard is quite similar to the US SPL standard. Consequently, the new ePI standard will no longer allow the use of Microsoft Word to draw up and maintain the PI texts. New software tools are needed to handle the XML-based document formats. (31,32,33)

All in all, the ePI is supposed to benefit public health, create efficiency gains for regulatory systems, support multilingual packaging, interact with other ongoing digital initiatives at EU and global level and counteract and prevent medicines shortages while complementing the paper PL (30).

In the long term, it is envisaged that the paper PL will be removed from the package and only an electronic version will be made available. This process will most likely be stepwise. As of 2023, multiple ePI pilot projects are ongoing or planned for medicinal products that are exclusively administered or dispensed in the hospital setting. The main goal of these studies is to create evidence that paper-based PL and analogue PL can be regarded as equal.

Table 4 presents the current PI-related challenges and describes how the ePI will help mitigate them.

Table 4: Description of common challenges with the current PI situation and how ePI will help solve these issues

Challenges with current PI	Expected advantages of ePI
Patient does not receive latest PL information due to packaging process lag and shelf-life of medicine	Patient has access to most up-to-date PI through use of the electronic version
New safety relevant information not available for distributed/dispensed medicines	Inclusion of new safety-relevant information into ePI possible even after distribution of batch / for dispensed medicines. Therefore, new information available
PI contains only free-text information and is drawn up manually without the help of structured data	ePI has a semi-structured format. And so carries structured data to some extent. This promotes the use of controlled, harmonized data from SPOR and other databases and thereby increases the quality of PI data, reducing the risk for errors
Patients may only access one language of the patient information via the printed PL	ePI offers the possibility of presenting the patient information in all available languages for that product
Medicines are supplied for each national market, re-allocation of packages in case of shortages is difficult and has boundaries	ePI facilitates the re-allocation of packages and helps mitigate shortages
PL hard to read for some patients due to style/format aspects; difficult to find important information	ePI format allows display of PI in various formats and enables the use of technical features (e.g. read-out functionality; search functionality). Thereby, PI handling is facilitated
Patient has a hard time to find information that is important for their special situation	Applications will use the ePI to deliver personalized medicinal product information to HCP and patients based on patient characteristics and their medical condition, highlighting important information

Note: Adapted from (30)

3.3.5 eCTD 4.0

eCTD 4.0 has been in the pipeline for a long time. The CTD structure remains unchanged. However, eCTD 4.0 will use additional technical aspects and functionalities such as document re-use, document ordering, metadata correction, two-way communication and enhanced document lifecycle capabilities. The latter will enable wider replacement

strategies for documents, e.g. one-to-many, many-to-one and many-to-many replacement. (34) This is a huge advance in terms of eCTD handling. However, the release of eCTD 4.0 is currently not being pushed forward by the relevant stakeholders, and eCTD 4.0 implementation has been postponed multiple times in the past. As of December 2022, piloting and implementation of eCTD 4.0 is planned for 2024 the earliest. (35)

With the ePI project in mind, some more changes to the upcoming new major eCTD version are still necessary to fully accommodate the current developments in RI. The 'working documents' folder submitted with the eCTD sequences needs to incorporate the new ePI standard to become part of the authority's assessment. Therefore, the handling of modern document formats needs to be accepted by industry and regulators. This will allow the use of machine–machine communication that will facilitate the assessments of PI changes on regulator side. However, until then, many more steps are necessary to streamline the processes.

3.3.6 Data Analysis and Real World Interrogation Network (DARWIN) EU

DARWIN EU (Data Analysis and Real World Interrogation Network) is a network of healthcare databases that has been established to support real-world evidence (RWE) research in the European Union. The network aims to bring together healthcare databases from different countries and different types of healthcare organizations, including hospitals, primary care providers, and health insurance companies. (36,37,38)

Selected data partners will provide the DARWIN EU Coordination Centre with results of analyses of the data, which then can be further processed and used. This data can be used to support a wide range of research questions, including the effectiveness of treatments, the safety of treatments, and the cost-effectiveness of treatments. The aim is to make better use of RWE when assessing medicines, which is generated every day in the healthcare system. The real-word data are supposed to support scientific evaluations. Ultimately, high-quality, real-world data should be used for the assessment of MAAs, extensions and variations. It is also envisaged that RWE will be used by scientific committees, e.g. the Pharmacovigilance Risk Assessment Committee, to support scientific decision-making in PSUR assessments and signal assessments. (36,37,38)

4. Document Management Systems and Product information

4.1 Electronic documents

Electronic documents are all types of unstructured information that exist as a closed unit, or file, in a data processing system. Such documents are differentiated in scanned paper documents and in electronically created documents. Electronic documents can consist of every combination of text, graphics, data, audio, pictorial or other information representation in digital form. Data processing systems are usually computer systems that allow users to create, modify, maintain, archive, retrieve or distribute such documents. (13,39,40,41)

4.2 Lifecycle of electronic documents

In general, documents have a basic lifecycle. The lifecycle of an electronic document begins with its creation or initial capture (e.g. through scanning of paper documents), continues with using and processing the document, and ends with its legally compliant archiving and/or destruction (see **Figure 5**).

Figure 5: Lifecycle of an electronic document

Source: Adapted from *(13,42)*

However, when taking a closer look at the subdivision using/processing of documents, it becomes clear that DM becomes more complex.

At the beginning, documents either exist in electronic form or on paper. The latter must be converted into digital data by imaging, i.e. scanning, before storage in the document archive is possible. The capturing/creation of documents also includes the indexing and first storage of that document in a computerized system. (43).

Electronic documents can then be processed in many ways. The lifecycle of each document is different and depends on the document type. For example, some documents are subject to many changes throughout their lifecycle, while others are more static and never changed

after their initial creation or capture. Some documents remain in a valid state for a long time, while other documents are regularly superseded. (39,44)

A detailed description of a document lifecycle, including possible processes a document might be subject to, is presented in **Figure 6**.

It becomes clear that the handling of a document at each stage of its lifecycle should follow established fixed rules and requirements to ensure that the document is fit for its intended purpose and available in high quality. (45)

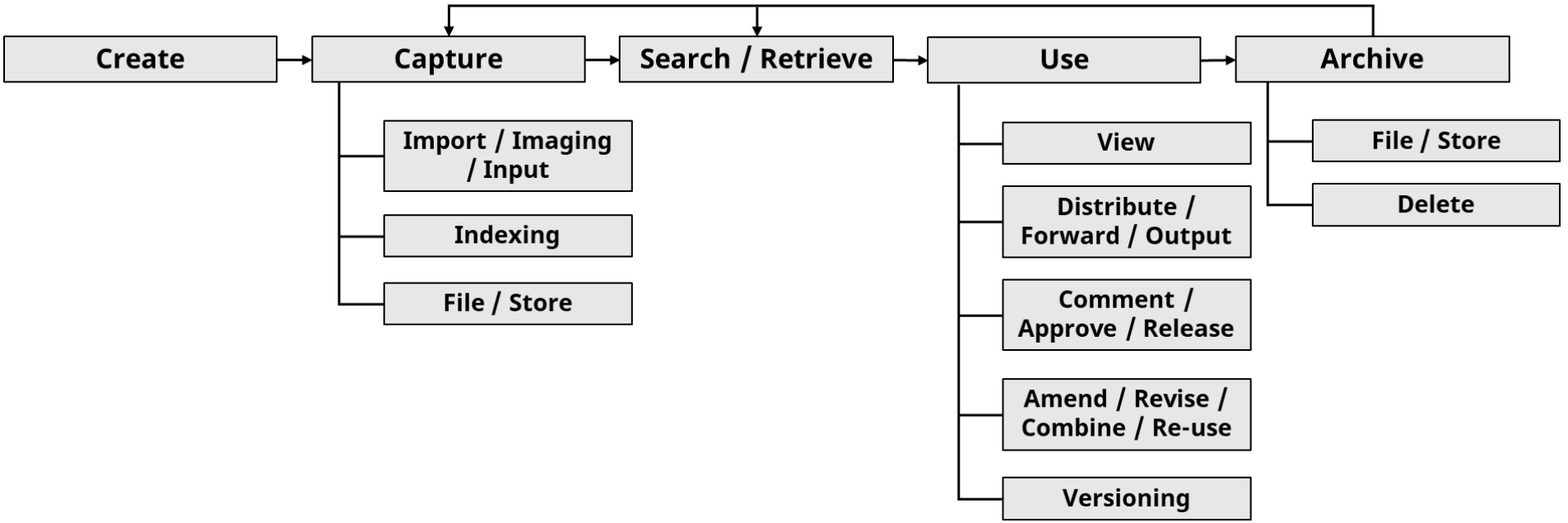

Figure 6: Detailed document lifecycle

Source: Adapted from *(13,42)*

4.2.1 PI lifecycle

As stated in the introduction, the PI documents accompany the whole product lifecycle of a medicinal product from development to the expiration of the MA. Within this lifecycle, the PI documents are frequently subject to change, mainly due to the legal obligation stated in Art. 23 of Directive 2001/83/EC (as previously discussed). In the following, a simplified PI document lifecycle is introduced in order to illustrate how PI documents are handled within pharmaceutical companies. **Figure 7** displays the simplified lifecycle of PI documents for medicinal products.

The PI lifecycle starts with the creation and subsequent internal review/approval of the PI document, where the document status is 'draft'. After review and internal approval, the PI document receives the status 'reviewed/ready for submission'. It is then submitted to the CA and assessed for the first time during the MAA. During this phase, the document has the status 'submitted' and is locked for any further adaptions. After the PI document has been approved by the CA, it officially comes into force. It therefore receives the status 'approved', indicating that it can be used for subsequent activities, such as packaging or publishing. If any other change is necessary to the PI after first approval, the PI document needs to be revised and the process starts again, beginning with the revision of the PI document instead of the initial creation. PI documents are frequently subject to changes after first authorization. Any change of the PI is considered to be a change to the MA and consequently has to be submitted to the CA. The revision cycle is run through many times during the PI lifecycle.

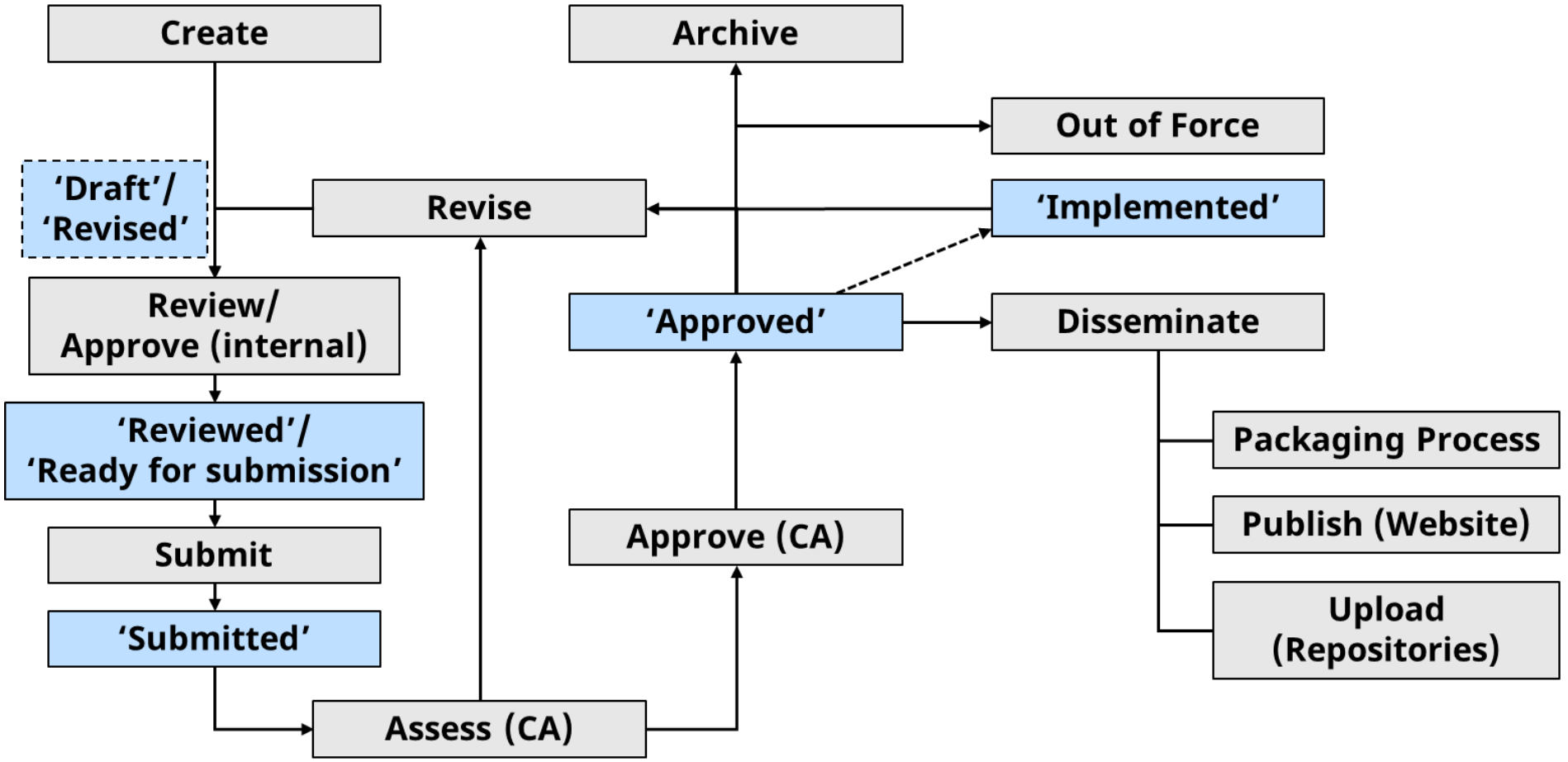

Figure 7: PI lifecycle

The assessment of the authorities can result in additional revisions that need to be carried out by the applicant or by the MAH. This can necessitate one or multiple re-submissions of the amended PI to the authority within one submission cycle. When a medicinal product is no longer marketed and the MA expires, the currently active PI documents for that medicine will go out of force.

At least every approved version of the PI document should be archived. This enables the traceability of all changes during the PI lifecycle. In fact, it is advisable to archive intermediate versions and tracked versions of PI documents as well. Such documentation can be helpful to comprehend why certain changes have been performed, and it also allows preservation of editors' and assessors' comments.

Sometimes, implemented versions are created from approved versions and used for the dissemination process. From a legal perspective, such a condition does not exist, as only PI documents that have been approved by the CA can be used for publishing and printing. However, such versions are sometimes used by pharmaceutical companies to correct small errors like misspellings in approved versions. Such minor changes are then notified to the authorities with the next regulatory opportunity.

To conclude, PI texts are frequently subject to change during their lifecycle. Considering this as well as the need to comply with regulatory requirements creates the necessity for a well-functioning and suitable DM for PI.

In the next section, the concepts of DMS and ECM are briefly introduced. Their aim to increase document quality and facilitate document handling is also explored. Afterwards, it will be elaborated how DMS/ECM can support the PI lifecycle.

4.3 Introduction to DMS and ECM

The main driver for the development of applications that support DM were the challenges that erupted when more and more documents had been transferred from paper format to electronic format. Basic operating systems are not designed to manage large numbers of electronic documents in an efficient way. **Table 5** depicts time-consuming challenges

associated with inadequate DM and outlines how DM/ECM programs help to solve these problems.

Table 5: Time consuming challenges that may occur with inappropriate DM and how DMS help solve these issues

Time consuming challenges with DM	DMS solution
Document cannot be found due to inconsistent document storage	Safe and reliable storage of documents at a single repository, search functionalities and metadata allow rapid document retrieval at any time
Document has to be searched for in multiple repositories	
The same file is stored in multiple repositories, which leads to problems regarding the actuality of these multiple instances	The DMS serves as a central access point, prevents duplicate storage of documents
Documents must be requested from other departments because they use a different filing system with restricted access (‘data silos’)	Flexible, adaptable access permissions allow individual access solutions for every user; every user has access to all the documents needed to do work
Document version unclear/not sure whether to have the current version	Document versioning guarantees that the current version is displayed
Document history unclear; no access to outdated version statuses to track document evolution and changes made	Versioning and audit trail allows keeping track of changes and auditing
Document-related processes are handled manually, resulting in a high administrative overhead	Workflow component of DMS accelerates document-related processes
Documents are transmitted and disseminated manually via email	Automated dissemination of documents based on predefined rules and settings

DM/ECM applications are specialized solutions designed and optimized for DM. As has already been stated, the terms DMS and ECM are often used synonymously. In fact, the concepts overlap to a large extent and a clear demarcation is not possible. A basic consideration behind the two concepts is that a large part of the information processed in corporate processes is stored in documents. The rapid, simple and reliable provision of these relevant documents with the required information thus represents the central task of both systems. (14,43,46)

Hence information is the only resource that multiplies through division, the capture, management, storage and retrieval of documents is of great importance. The goal of DMS is to ensure fast, efficient and secure access to the resource information that is mostly stored in documents. (43)

Therefore, DMSs support the entire lifecycle of a document. This lifecycle starts with the capture (creation or import) and storage of a document, continues with retrieval, editing, correction, forwarding and long-term archiving, and finally ends with the (verifiable) destruction of the documents. In every lifecycle phase, the DMS offers specific features and specifications to the user to fully support the management of the documents in the lifecycle phase. This allows DM to be as productive and simple as possible. In addition, DMSs can help to significantly improve the management of document-related processes in the company. The ultimate goal is to empower users of a DMS to reduce their administrative burden and enhance the efficient and effective handling of documents and document-related processes. The steadily increasing number of document inventories within companies can thus still be overseen and properly managed. (45,46,47,48)

It should be noted that, in the case of document-dependent processes, documents and processes are always linked. Documents can be the trigger of processing, the object of processing or the result of processing. (49) However, inefficient internal business processes cannot be improved by the use of a DMS alone, as it only serves as a supporting tool. It is therefore important that the business processes are also evaluated during project planning and that any necessary changes are made to the business processes so that the DMS can be used profitably in the company.

4.4 Introduction to Labelling DMSs

As mentioned at the beginning, PI documents need to be classified as critical documents because the information in them is crucial for patient safety. Thus, any system for managing PI must also be considered critical. DMSs for managing PI documents are subject to specific technical requirements regarding accuracy, integrity, reliability, trustworthiness and performance. Furthermore, special requirements towards technical functionalities are necessary to ensure appropriate creation, modification, maintenance, archiving, retrieval

and distribution of PI documents. In addition, many non-technical requirements such as services from service providers are needed to ensure proper DM of PI texts. In the following, I want to further describe and evaluate these requirements and functionalities, with special focus on the technical requirements and functionalities.

The large number of DMS solutions available on the market does not make it easy to select suitable software among those on offer. Due to the highly regulated field of medicinal products and the special obligations that are related to PI documents, considerable risk management is necessary. 'Off-the-shelf' solutions are usually not specialized for the management PI documents. The multitude of technical possibilities and the complexity of the issues involved make it necessary to find an individual solution for PI and Labelling. Another option is to use an 'off-the-shelf' solution after a considerable amount of effort has been put into customization programming and adaptation.

4.5 Points to consider for a Labelling DMS

4.5.1 On-premise or cloud-based solutions?

An on-premise solution is a type of software delivery model where the software is installed and run on the customer's own servers and IT infrastructure. The organization that runs the licensing software is then responsible for maintaining and updating the software, as well as for ensuring its availability and security. Investments in IT resources, hardware and personnel are required to run on-premise software solutions.

In contrast, a cloud-based solution is a mode of software delivery where the customer accesses the software over the internet or intranet via a web browser. It is hosted on internal or external servers.

Web-based applications that are provided in the cloud come with many advantages. As they are accessed via a browser, they are independent of the operating system (e.g. Windows, Linux or IOS) (42,50)

However, on-premise solutions should always be favoured if the software needs to handle sensitive data that is not supposed to be stored in the cloud. Such data should rather be stored on an internal IT infrastructure that is cut off from the internet, reducing the risk

posed by hackers. It should be kept in mind that every new software solution has to be in line with the organization's compliance and data protection requirements. Common disadvantages of on-premise software solutions are their local implementation and limited flexibility regarding durability. On-premise solutions are ageing quickly due to constant development.

4.5.1.1 Private cloud computing, public cloud computing or community cloud computing?

In general, cloud-based software can be provided via two settings. The cloud solution can either be run on a private cloud or on a public cloud. A private cloud is a cloud that is dedicated to a single organization. It is run on the company's own IT infrastructure and provided to the employees via the internet. An advantage is that private clouds offer more control and security over the data and the software. This can be very suitable for companies that have a strict compliance strategy and handle much sensitive and critical data. The key disadvantage is that the customer has to provide and is responsible for the IT infrastructure of that private cloud. (42,51)

A public cloud works differently. It is maintained by a third-party provider, which provides the cloud to customers over the internet. The IT infrastructure, like servers, storage, and the network is owned by the third-party provider. Therefore, the provider is responsible for maintaining and updating the IT infrastructure and ensuring the availability and security of the data. A key benefit is that such solutions are very cost-effective and convenient for customers, especially small and medium-sized companies, as they do not need to invest in and manage the public cloud. In this setting, however, the customer is highly dependent on the cloud-service provider. All the data is stored externally on the provider's cloud. Therefore, such solutions should preferably not be used by companies that need to store and manage many sensitive and critical data that need a high level of data protection. (42,51)

Another cloud programming option is the use of a community cloud. This kind of cloud is also operated by a third-party provider, but is used by organizations in the same industry, or by organizations with similar compliance and security requirements. Community clouds

are more customized than public clouds. They are drawn up to the specific needs of a certain industry sector, e.g. pharmaceutical companies. They offer greater security standards than public clouds, as the infrastructure is shared only by companies with similar security and compliance requirements. Community clouds provide organizations with cost-effective, secure and cloud computing solution, while also providing the benefits of a shared IT infrastructure.

Annex VII presents the cloud delivery models offered by DMS on the market. The market analysis has shown that there is a wide range of cloud deployment models offered, based on the two principles of private and public clouds and the intermediate variant – community cloud. There are also hybrid cloud models for DMS solutions. This means that only some of the DMS modules are operated in a cloud, while other modules are run in the company's own data centre.

4.5.2 Application service providing/Software as a Service (SaaS)?

In recent years, the use of SaaS to implement new software solutions in companies has increasingly become standard. The SaaS model offers the IT software as a cloud-based solution. Using the SaaS model has many benefits. The internal IT administration effort is significantly reduced because the software is operated externally. Moreover, such solutions are very flexible and scalable, significantly more so than client-based applications. It facilitates the cross-site implementation of software solutions. SaaS models can be easily scaled at any time during operation. For example, additional affiliates or business units can be connected to the software without any problems. Additional storage space can easily be activated by the provider with the push of a button. (42,52,53)

In general, SaaS solutions are up to date in terms of connectivity with, and integration in, third-party IT software systems. This is ensured by open interfaces, for example WebService, SOAP or REST and other connectors. (52,53)

However, there are also limitations to SaaS models. Usually, they come with very few possibilities to develop or customize the application to specified needs. SaaS mostly works as an ‘off-the-shelf’ solution that allows a great amount of flexibility and scalability.

However, it is not intended to be a customized software that is developed only for the needs of one company.

4.5.3 Client selection

When selecting a new DMS, a decision must be made whether to pick a DMS that is accessed and utilized via the operating system client (e.g. Windows, Linux, MAC OS) or a web-based client.

Software applications using web clients have some benefits. Usually, such systems are cloud-based. They can be easily accessed from anywhere in the world via web browsers (e.g. Microsoft Edge) regardless of the used operating system. The only prerequisite is an internet connection. Furthermore, the use of mobile devices is supported. Many web-based systems operate browser-independently by using HTML5 as a programming standard. (43,42)

On the other hand, operating-system-based applications, e.g. applications using Windows as a client, offer more control and customization options, better performance and offline capabilities, since the program is run directly on the user's own computer. Such software can either be a cloud solution or an on-premise solution. (43)

Appendix VI shows the clients supported by the DMSs on the market, including supported mobile clients.

Potential customers should evaluate which option best suits internal IT policies, internal IT infrastructure and the needs of the affected departments. Both options have pros and cons – no general recommendation can be made.

4.5.4 Special requirements for computerized systems managing GxP-relevant documents

For Good 'x' Practice (GxP) relevant processes, specialized DMS solutions are necessary to meet the requirements that are set out in the pharmaceutical legislation. For example, computerized systems that are used as part of Good Manufacturing Practice (GMP) regulated activities need to meet certain criteria according to the Commission Directive

2003/94/EC and subordinate guidance documents. Worth noting is Chapter 4 of the GMP guideline focusing on documentation particulars of GMP activities and Annex 11 laying down special requirements towards computerized systems that operate within GMP-related activities. Of note is also the Aide-Mémoire 07121203 on 'Monitoring of computerized systems' that provides a detailed interpretation of Annex 11 and gives at hand guidance on how to inspect a computerized system. The requirements outlined in these guides should be strictly adhered to in order to ensure GxP-compliant management of documents and data. (1,45,54,55,56,57)

PI documents are not specifically covered by GxP requirements. According to Commission Directive 2003/94/EC, batch-related documentation for a medicinal product has to be retained for a certain period. This also includes information on the packaging material and Labelling. However, there is no legal obligation to draw up, maintain and revise PI documents under GxP-regulated conditions.

Nonetheless, PI documents need to be considered as critical and important documents due to their legal character and due to the impact that defective PI documents can have. Poorly maintained PI texts have great potential to negatively affect the medicines safety and efficacy. PI documents have an indirect effect on the product quality. Therefore, DMSs that manage PI documents need to have special technical and non-technical requirements in order to guarantee that the PI documents are of high quality and can reliably be used when marketing the medicinal product.

4.6 Benefit aspects

Potential savings and benefits that can be achieved through the introduction of a DMS: (13,14,39,41,44,46):

- Reducing document turnaround times
- Degrade search times for document retrieval and information searches
- Ensuring the long-term retrieval of documents
- Increasing quality and reliability of documents
- Avoiding media discontinuity (switching between applications)
- Improving collaboration within the company and with external stakeholders

- Ensuring compliance with legal obligations and internal policies
- Lowering administrative burden on employees
- Use of relieved employees for higher-value activities (‘job enrichment’)
- Reducing office space costs (when paper archives are replaced)

In the following, the benefit aspects are described more detailed.

4.6.1 Time savings and cost benefits

One of the most important reasons for introducing a DMS is the generation of time benefits. The fast and targeted retrieval of documents is made possible through various document-related technologies, such as a comprehensible file system, metadata management and advanced search functionalities. This significantly speeds up search processes for required documents and their information and ensures that documents can be retrieved at any time during their lifecycle. The secure retrieval of documents means that the information stored in them can be accessed in a rapid and reliable way. This is often perceived to be the most common benefit of DMS solutions. (14,39,41,44,42,56,58)

Another aspect of a DMS is the reduction of throughput times of document-based processes. Significant time savings can be achieved through the partial or full automation of recurring processes. So-called workflow components of DMSs enable the automatic distribution of documents based on predefined rules and settings. For example, the distribution of electronic documents can be carried out in a controlled way via a digital workflow managed by DMSs. This saves users from having to write emails to distribute documents. (14,44,56).

Taken together, these aspects lead to an acceleration of daily work, as DMSs support administrative activities or even automate them. This ultimately increases the efficiency of the company's internal processes and thereby enhances the company’s productivity. Employees are thus freed up for new tasks or have more time to perform their actual core tasks. (58,59,60,61)

The time advantages inevitably also result in cost advantages. The greatest cost advantage comes from not having to engage in time-consuming and thus cost-intensive search efforts.

This results from the fact that the easy and long-term retrieval of documents ensures fast and secure access to the required documents via DMS. (14,39,44)

The DMS allows the central administration of documents in a controlled way. This prevents the duplication of work and duplicate storage of the same documents, as well as reducing problems regarding the actuality of such multiple instances ('Is this the latest version of the document?'). (39)

In pharmaceutical companies, DMSs can also mean considerable time benefits for employees handling PI documents. DMS solutions support employees in administrative activities. Searching for a specific PI document or the correct version is simplified, as DMSs facilitate document retrieval through a suitable folder structure and search functions and a reliable archiving system. Employees in RA can therefore be sure to find documents more quickly and reliably than before.

Document-dependent processes in RA can be carried out with the support of a DMS solution. This eliminates manual activities such as preparing and sending documents via email. It also semi-automates asking colleagues for their review or approval. For example, the preparation, review and internal approval of dossier-related documents and PI documents can be performed with the help of the workflow component of a DMS. To sum up, DMS allows employees to devote more time to their actual tasks because they are supported by a suitable DMS solution that lowers their administrative workload.

Table 6: Description of common problems with PI handling and how DMS functionalities help mitigate these problems

Cost and time-consuming PI-related problems	**DMS solution**
Not sure which is the currently approved version of the PI	Document versioning ensures that the current version is displayed to the user.
Wrong document version used for PI revision, reworking necessary	
Wrong PI texts have been submitted to authority	DMS displays which documents are in status ‘ready for submission’
Version history of the PI is not available; not sure which adaptations have been performed in the past	DMS shows version history of every document, allowing full transparency and traceability of changes

Cost and time-consuming PI-related problems	DMS solution
No tracking which PI document version has been/is used for certain batches for packaging process	Metadata assignment allows clearly specifying which PI document version are used for packaging process
Wrong PI documents used for packaging/publishing process	DMS ensures that only certain documents with prior approval can be used for packaging/publishing process
Insufficient permission control allows untrained or unauthorized personnel to alter PI documents	DMS provides suitable access control mechanisms to ensure that only trained and authorized personnel may alter PI texts
Document creation is inefficient when many experts are involved – changes must be implemented gradually	DMS offers useful collaboration tools such as co-authoring. This can significantly speed up the creation and revision of documents.
PI documents need to be distributed to internal stakeholders (e.g. different departments) manually via email	Workflow module of a DMS can partially or fully automate the PI distribution between different stakeholders within the company.
Approved PI documents are disseminated manually, without the use of automation tools	Workflow component automates the dissemination process of approved PI documents. Integration with Enterprise Resource Planning (ERP) and Web content management modules simplifies the distribution process.

4.6.2 Quality benefits

In general, the most essential component of a DMS is to allow the reliable access and retrieval of important documents and thus of important information at any time. This increases the qualitative work results, as documents can be retrieved and processed rapidly and in an audit-proof manner. This enhances transparency and increases the ability to provide documents and information quickly. Comprehensive search options, such as attribute-assisted and full-text search options support users in finding the right document quickly and at any time. In combination with enhanced document security, including the ability to set permissions and control access, the quality of a document rises significantly. Access control mechanisms of a DMS ensure that documents, and thereby the information included in them, cannot be altered or lost unintentionally. Moreover, other functionalities

like versioning, version history, audit trail and archiving assure that the whole lifecycle of a document stays transparent and audit-proof. Therefore, a DMS intends to store important documents (as well as documents with sensitive or critical information) effectively and safely while ensuring the quality of the document's information. Likewise, the quality and security of document-based processes increase when they are carried out with the help of a DMS. DMS programs use workflow components with predefined rules and settings that allow the safe and reliable execution of document-related processes via workflows. Thereby, workflow components increase process and decision-making quality and transparency. (56,58,59,60)

Receiving quality benefits by introducing a DMS for Labelling purposes has similar advantages and is, besides reducing time-consuming administrative tasks, one of the key drivers for implementing a DMS for the management of PI documents. It is important for PI texts that their content is protected and cannot be changed unintentionally. PI texts must display the correct information about the medicine, especially the instructions for use and safety information. When using a DMS, PI documents are stored in a secure place with restricted access. Appropriate handling functionalities allow the creation, revision, distribution and archiving of PI documents in a controlled, audit-proof manner. Altogether, these circumstances improve PI document quality extensively.

4.6.3 Compliance with legal requirements

The fulfilment of compliance obligations is considerably simplified with the use of a DMS. The use of an appropriate DMS program ensures to comply with legally required retention periods for documents. Appropriate long-term archiving tools in combination with sufficient retrieval allow the safe and reliable retrieval of documents any time in the future. Access control and corresponding security measures are of particular importance to guarantee that documents are archived safely and remain so throughout their entire retention period. Many DMSs use audit trail to allow complete traceability and documentation of any document-related changes and tasks. (39,60,62)

The use of a suitable DMS can also increase the compliance of PI management with legal requirements. DMS solutions guarantee that PI documents are safely managed and stored

throughout their entire lifecycle. Access control and security mechanisms ensure that only authorized and trained personnel are able to alter the archived documents. Such precautions reduce the risk that PI documents contain errors or any deficiencies that are related to improper DM.

4.6.4 Improved collaboration

Use of a suitable DMS should be considered to improve collaboration within the company, but also to improve business-to-business (B2B) and business-to-customer (B2C) relations. Collaboration tools enable the flexibilization and acceleration of business processes through facilitated communication between process participants. (14,42) Therefore, appropriate collaboration tools can be a key driver behind higher business productivity.

Helpful collaboration tools are also extremely important for the DM of PI texts. A state-of-the-art Labelling Management System should provide adequate collaboration tools, such as co-authoring capabilities. In Section 5.2.2.11, I will evaluate more detailed what collaboration tools a Labelling DMS should offer and justify their needs.

4.6.5 Conclusion

To conclude, a Labelling DMS can bring many benefits for a pharmaceutical company. However, it is important to carefully evaluate the costs and resources required for implementation and maintenance, as well as to plan for user adoption and compliance with the system. If these factors are carefully considered, a DMS can significantly improve PI quality, PI-related processes and collaboration, leading to increased efficiency and reduced risks.

5. Requirements for a Labelling DMS

In the following Sections, important specifications, functionalities and non-technical requirements that are important for a state-of-the-art Labelling DMS will be presented and discussed. These requirements are based on the results of the market analysis that has been performed to evaluate the available DMS functionalities and specifications.

5.1 Technical requirements for a Labelling DMS

After thorough market research to identify the full range of offered DMS functionalities and technical specifications, the technical requirements needed for a state-of-the-art Labelling DMS have been selected and their necessity carefully assessed. The results are presented in **Table 7**. Selected technical requirements and their relevance are discussed in Section 5.1.2.

For the results of the market analysis concerning technical specifications and functionalities currently offered by DMS vendors, please see **Annex II**.

5.1.1 Feature/criteria development (technical requirements)

Table 7: Technical requirements to be considered for a state-of-the-art Labelling Management System

Criteria (technical requirements and specifications)	Must or want?
Compatibility with existing IT infrastructure	Must
Integration with RIMS and eCTD management software	Must
Data integrity	Must
Data security and data protection	Must
Mobile access	Must
Compatibility with EU ePI project	Must
User personalization	Want
System performance/system reliability	Want
Scalability and extensibility	Want
Developability	Want
Integration with document editors (e.g. MS Office)	Want

Integration of CCDS/CSI management	Want
Integration with Artwork Management System	Want
Integration with ERP system	Want
Integration with Web Content Management (WCM)	Want

5.1.2 Description of selected technical requirements

5.1.2.1 Compatibility with existing IT infrastructure (client, network)

Every new IT system to be implemented must fit into the existing IT infrastructure of the respective company. This includes full compatibility with the client used (e.g. Windows, Linux) and the network used. This is one of the important ‘must’ criteria for selecting a suitable Labelling DMS (cf. Section 4.5.3).

5.1.2.2 User personalisation

In addition to the global view ('all documents that the user is allowed to see'), a DMS should also offer the user a personalized view ('all documents that are binding for me'; ‘my documents’). This and other filter features can help to ensure that the employee is not overwhelmed by the number of documents managed in the DMS. (56).

Moreover, it is advisable that users are able to personalize their Graphical User Interface (GUI). System users can therefore adapt their GUI to their personal needs, which in return increases user satisfaction and business performance. Labelling DMS should have the appropriate specifications to personalize the GUI and other functionalities, such as search functionalities and filter options.

5.1.2.3 Data integrity

Data integrity refers to the accuracy, completeness and consistency of data over its entire lifecycle, from creation to disposal. It ensures that data is not altered, lost or destroyed in an unauthorized manner. In the context of DM, this is important to ensure that the documents are reliable and of high quality. Special storage technologies are necessary to ensure the immutability of managed documents, in terms of both their content and their metadata.

For a Labelling DMS, appropriate data integrity measures are of great importance. DMS software needs to be thoroughly validated so that document data, i.e. the document content and its metadata, are not being altered or lost in an unauthorized manner. Only if this is assured can the managed PI documents remain in a reliable and high-quality state, i.e. carry the correct medicinal product information.

5.1.2.4 Data security and data protection

Besides handling different documents formats, DMS can handle various types of business document. Depending on the types of document and their criticality and confidentiality, appropriate security measures are necessary to ensure that the stored data is reliable, trustworthy and of high quality. The restriction of user access is one of the key principles for reaching a higher level of data quality. However, there is more to data security than this. A DMS should have, besides a well-functioning access-management tool, proper precautions to ensure that data cannot be stolen or compromised by third parties, e.g. hackers. Therefore, the software needs to have a validated set of security standards to protect the documents and prevent any unauthorized access and alteration to the system. A sufficient back-up policy to ensure that documents cannot become ultimately lost or deleted is demanded. If such preparations are executed well, high document and data quality can be assured by the use of DMS.

Another point is the criticality of documents. As mentioned above, PI documents have to be considered critical because a small amendment to the particulars in the PI texts can have a large impact on patient safety (cf. Section 1.2 Problem statement). Implementing a safe and secure place in terms of IT security measures where PI texts are created, maintained, updated and stored is an important reason for implementing a DMS for labelling activities. The DMS for labelling should therefore provide adequate data protection and data security measures to prevent unauthorised access to and modification of the stored documents.

5.1.2.5 Integration with document editors (e.g. MS Office, XML editors)

The integration of document editors into the system can lead to great efficiency gains in terms of PI document creation, adaptation and review (cf. Section 5.2.2.5)

5.1.2.6 Integration with ERP system

Many DMSs are linked to ERP systems, mainly because ERP systems are usually not optimized for DM. The DM modules included in ERP systems usually have less DM functionalities than specialized DMS/ECM modules. (42,46,62)

For a Labelling DMS, an interface with the ERP system used in the pharmaceutical company should be considered. This is because the packaging materials, i.e. PL and labelling texts, must be used for printing and packaging processes. Interoperability between the systems leads to efficiency gains, as the documents with the corresponding metadata (cf. **Table 10**) can be selected in the ERP system and integrated into the electronic packaging process of the ERP.

5.1.2.7 Integration with Web Content Management (WCM)

A WCM enables you to organize, manage, and publish web content to a website or portal. It facilitates the creation, publishing, and management of web content for non-technical users. WCM is often integrated or connected to a DMS to ensure effective management of digital content throughout its lifecycle – from creation to archiving. (43,42,63,64)

For any Labelling DMS, a suitable interface to a WCM module that is currently used within the company should be considered. The interoperability between the two systems creates room for automation and can thereby create efficiency gains. For example, the replacement of PI documents on the company's website can be done automatically as soon as a new 'approved' or 'implemented' version is created.

5.1.2.8 System performance and system reliability

Another important characteristic of a computerized system is the system’s performance and reliability. System performance and overall reliability should be high and consistent. This include that the system is robust and therefore less prone to errors. DMSs should be

designed to allow a sufficient number of users a simultaneous access without loss of performance. (39,40,59,65)

System performance is also important for Labelling DMS. If the system is rolled-out in many countries (i.e. many simultaneous accesses are to be expected), system performance needs to be considered when selecting a new DMS. Otherwise, the use of the DMS can become a burden for employees and reduce targeted efficiency gains.

5.2 Technical functionalities

After thorough market research to identify the full range of offered DMS specifications and capabilities, the technical functionalities and features needed for a state-of-the-art Labelling DMS have been selected and their necessity carefully assessed. The results are presented in **Table 8**. Selected technical functionalities and features and their relevance are discussed in Section 5.2.2.

For the results of the market analysis concerning technical specifications and functionalities currently offered by DMS vendors, please see **Annex II**.

5.2.1 Feature/criteria development (technical functionalities)

Table 8: Technical functionalities and features to be considered for a state-of-the-art Labelling Management system

Criteria (technical functionalities and features)	Must or want?
Storage and retrieval	Must
Export/import	Must
Comprehensive filing structure	Must
Management of various formats (Office, PDF, XML, JSON, HTML)	Must
Versioning and version management	Must
Metadata management	Must
Workflow component	Must
User management and access control	Must
Archiving	Want
Check-in/Check-out	Want

Criteria (technical functionalities and features)	Must or want?
Document editing	Want
Document viewer	Want
Format converter	Want
Collaboration and sharing	Want
Audit trail	Want
Comprehensive search functions	Want
Automated linking of related documents	Want
Automated document classification	Want
Automated metadata assignment	Want

5.2.2 Description of selected technical functionalities

5.2.2.1 Storage and retrieval

The basic principle of a DMS is that documents are stored at a central access point in a controlled manner and that document retrieval can occur at any time. The safe locating and assessing of documents when needed is usually ensured by appropriate folder structuring systems and search functionalities. (13,14,44,42,63)

5.2.2.2 Versioning and version management

Versioning is one of the basic functions of a DMS. It enables users to version a document during its lifecycle, in other words to assign a new version number for every revision of the document. Old versions of the document are archived in an audit-proof manner and thus ensure detailed documentation of the document history. Thereby, versioning increases reliability and traceability and prevents outdated or wrong document versions being distributed. Clear version management helps a user assess whether the displayed document is the most current document version that should be used for further activities. Versioning is mostly done automatically or on the basis of rules, but manual versioning is also feasible. (14,43,44,45,42,46,48,66,67)

Generally, the means of differentiating between minor and major versions has proven suitable in the life-science-industry. For example, the version number can obey the syntax ‘X.Y’, where X and Y are natural numbers (1, 2, 3) and X represents the major version

number, Y the minor version number. If one specifies that all approved versions of a document must have a minor version number '0', then each new approved version results in a new major version (e.g. 1.0, 2.0,). This has the advantage that a minor version number not equal to '0' immediately indicates that this document version has not been released. The minor version merely has the function of marking documents under revision and thus documenting the creation of the next released version (e.g. 1.1, 1.2). In many companies, minor versions are also used as officially released versions. (56)

Before introducing a new Labelling Management System, the aspect of versioning should be carefully examined, as a DMS usually does not support all variants of numbering. The kind of versioning that is needed should be carefully assessed.

It should be determined in advance what version systematic is most appropriate to manage the PI documents in the company. If a systematic with minor/major versions is used, a distinction needs be made between major and minor versioning. For example, a new major version can express that the PI has been revised internally and is set as ‘ready for submission’ for the regulatory activity. However, other types of versioning may also be suitable for dealing with PI. The decision is at the discretion of the pharmaceutical company and its staff.

5.2.2.3 Comprehensive filing structure

A state-of-the-art DMS should have a comprehensive filing structure that consists of folders and subfolders in a hierarchical form. The folder structures should be designed to organize and categorize documents in a logical and meaningful way. The goal of a comprehensive filing structure is to make it easy for users to find the documents they need, while also ensuring that documents are properly classified and stored for easy retrieval. Therefore, organized and hierarchical folder structures are used and visualized via the GUI. The other possibility is to use a filing structure that uses folders arranged in a flat manner. In this case, all documents are stored in one level in folders. In such a case, the retrieval of documents is solely possible via search functionalities. Appropriate metadata management is important to be able to retrieve documents easily via metadata search options. (45,67)

Both systems can be considered adequate for state-of-the-art Labelling DMS solutions. However, many users still prefer to use hierarchical folder structures since this is the more common form for managing files. A decision must be made what folder structure should be used, taking into account the preferences of the employees.

Flexible file creation tools can also be used. The flexible file links different documents managed in the DMS and puts them into a virtual folder based on their metadata. This enables users to see what documents are linked and ensures that all the relevant documents are displayed. This facilitates efficient work and prevents administrative efforts such as searching for individual documents. (42,46,68) Labelling Management Systems should allow the creation of flexible/virtual files. For example, all PI texts of a specific MRP/DCP number can be instantly displayed and put into a virtual folder for further processing. Such functionality can be helpful for increasing the efficacy of PI-related processes.

5.2.2.4 Export/import

Export/import functionality refers to the ability of a DMS to transfer or move a document from one system or platform to another.

The export feature allows users to save a copy of a document from the DMS and transfer it to another system or device for use or backup purposes. The export function is usually combined with a document converter in order to allow the distribution of the document's content in various formats.

For example, a user may convert a PI document stored in Word format into a PDF file, and then export and save that PDF file to their local computer or external storage device to allow the re-use of the document in other systems. Preferably, the converted documents can directly be exported into other IT systems, e.g. into the eCTD manager (c.f. section5.1.2.6 and 5.1.2.7)

The import feature, on the other hand, allows users to bring a document from an external source into the DMS. For example, a user may import a set of files from their local computer into the DMS, or import the document from a shared folder system or cloud.

The export/import functionality is one of the most basic DMS features and allows sharing documents with other departments or external partners, or transferring them to different computerized systems.

5.2.2.5 Document viewer/editor

The display and editing of documents should be done via integrated display programs (viewers) and text editing programs to ensure that the DMS still retains full control over the documents. It is important that the viewer and editor fits the document types managed and that all document formats used are supported by the DMS. (43,56,69)

Preferably, common document editors such as Microsoft Office should be integrated so that any change to a PI text can be made inside the DMS without document check-in/check-out. To fully manage updates/revisions of documents inside the DMS is one of the prerequisites for collaboration tools. Only when the document stays inside the DMS can interoperable collaboration tools such as co-authoring be used. Other sophisticated document viewers and editors may also need to be integrated to support the creation and adaptation of all required document formats.

5.2.2.6 Check-in/Check-out

The check-in/check-out functionality enables users to control access to, and editing of, digital content. The purpose of check-in/check-out is to prevent multiple users from making changes to the same document simultaneously, which can result in version conflicts and data loss. When a user checks out a document, they are given exclusive rights to access and edit it. From the time of check-out, the document is locked and other users are unable to implement changes. This functionality makes it possible to edit the document even when using specialized document editing programs that are not integrated into the DMS, such as advanced XML editors. (14,44,63,67)

However, the classic check-in/check-out functionality comes with disadvantages. For example, when the document is checked out and locked for any other activities,

simultaneous co-authoring is not possible. A possible solution is that for documents in status ‘draft’ (cf. **Figure 7**), co-authoring is activated, but not for any other document status.

Consequently, when defining the required specifications for a new Labelling DMS, it should be carefully considered whether or not to use classic check-in/check-out functionality.

5.2.2.7 Audit trail

An audit trail is a functionality that fully tracks document activities and changes for all documents throughout their entire lifecycle. This includes tracking of information on who created, modified and accessed the document and for what reason. In general, audit trail functionality should be considered for all computerized systems based on risk assessment. (1,44,45,42,54)

For GxP-relevant documents, a DMS should log all GxP-relevant changes and deletions to the document, together with the reason for the change. The audit trail should at least contain the name/function of the person performing the action, as well as the reason for, and time stamp, of the action. It should be readily available when needed and convertible into a generally intelligible form. The audit trail should be printable and must not be capable of being altered or deleted. (1,45,54,56)

The functionality of the audit trail should also be considered for non-GxP systems as only through the use of audit trails do electronic programs remain transparent in their use. An audit trail should also be considered for Labelling-specific DMSs to ensure traceability of all PI-related processes and changes made to PI texts. In this way, the entire labelling process becomes more transparent.

5.2.2.8 Comprehensive search functionality

A core functionality for reliable and fast document retrieval is the search module. Each search module of a DMS can empower the use of different search mechanisms: (13,44,45,46,56,63,67)

- Basic search (name of the document)
- Full-text search (searches the content of documents for keywords)

- Intelligent search (uses machine learning and AI to understand the meaning of the search query, resulting in better search results)
- Metadata search (searches for documents with specific metadata)
- Faceted search (allows filtering search results based on specific categories and metadata)

In general, modern search modules combine these search functionalities into a comprehensive/advance search module that combines multiple search mechanisms. (56)

Labelling DMS should especially empower the search for documents with specific metadata (cf. **Table 10**) in order to allow the safe and reliable access and retrieval of PI documents. Hit lists for search queries should be clearly displayed and individually customizable. A filter list for hit functions makes it possible to further narrow down the search in the event of a high number of search hits and thus maintain an overview.

5.2.2.9 Workflow component

A workflow component in a DMS refers to a set of automated steps or processes that are used to manage the flow of documents and tasks within an organization. It is used to display and optimize document-based processes. It allows users to define and manage the processes and steps involved in document management, and to automate many of the manual tasks that are associated with document processing, e.g. document distribution. The use of workflows aims to facilitate the timely execution of review and approval processes, reduce the risk of errors, and improve the efficiency and productivity of document management activities. Stand-alone workflow programs are also sometimes referred to as BPM applications. (14,43,44,45,42,47,63,67,70)

Workflows are typically used to manage document approvals, document routing, and document processing.

In general, a differentiation between three different workflow types can be made: (43,44,63)

- Production workflow (synonym: Regular workflow)
- Flexible workflow
- Ad-hoc workflow

Production workflows are used to automate frequently reoccurring document-related processes in order to minimize manual document handling and processing and therefore reduce the administrative burden for users. Flexible workflows are more adaptable, meaning they can be adjusted to the special need of a specific workflow, but still using a workflow template as a basis. The latter refers to the ability of a workflow engine to create new workflows from scratch immediately when needed, in order to fit a unique document-based process. (48,63).

Annex IV presents common workflow features that are available on the market. To allow smooth and efficient handling of document-related processes, it is important to evaluate the available workflow features of a DMS and compare them with a previously defined list of specifications that the workflow component should meet.

For Labelling Management Systems, the incorporation of a well-functioning Workflow engine is essential in order to maximise time benefits in PI document handling and therefore improve the efficacy of PI document management processes. As stated before, PI texts are constantly subject to changes during their lifecycle, each of which triggers approval and distribution processes. A workflow engine can help to automate these processes, track progress and ensure timely execution. The workflow engine can greatly reduce the amount of manual work that is necessary for PI document management in companies. **Table 9** indicates PI-related processes that can be streamlined with a DMS workflow engine.

Table 9: Essential workflow features for PI document handling

Workflow	**Description**
Creation/adaptation workflow	Sets a document in status 'draft' and enables multiple users to create or adapt a PI document. Helpful when multiple users from different departments need to be involved into the creation/adaptation of the PI document (cf. **Figure 7**)
Review workflow	After amendment of a PI text, a review workflow can be used to execute 4-eyes principle. A co-worker reviews the proposed changes and can give feedback to the adaptor. **Figure 8Figure 9** illustrates a possible flexible template for a combined review/approval workflow. After positive execution of workflow, the document has the status 'reviewed' (cf. **Figure 7**)
Approval workflow	Allows the use of approval workflows where supervisors are asked to approve the proposed changes. Such a workflow should be flexible, i.e. the involvement of related departments (e.g. Medical Affairs or PV) should be possible, if needed. **Figure 9** illustrates a possible flexible template for a combined review/approval workflow. After positive completion of the workflow, the document is set as 'ready for submission' (cf. **Figure 7**)
Distribution workflow	Workflow that is initiated after a document is set as 'approved', i.e. the document has been approved by the CA. The document is then automatically distributed to the respective addressees, i.e. ERP tool to initiate the electronic packaging process, artwork department for creation of mock-ups, marketing department for publishing and upload in repositories (cf. **Figure 7**)
Overarching CP/MRP/DCP workflow	An overarching workflow that allows national translations to be produced following the amendment of the corresponding common texts of the European procedures (CP/MRP/DCP)

Figure 8 describes a possible template for a flexible creation/adaptation workflow that allows for the creation and revision of PI documents. It is flexible because related departments, such as PV and Medical Affairs, can be included in the workflow as needed.

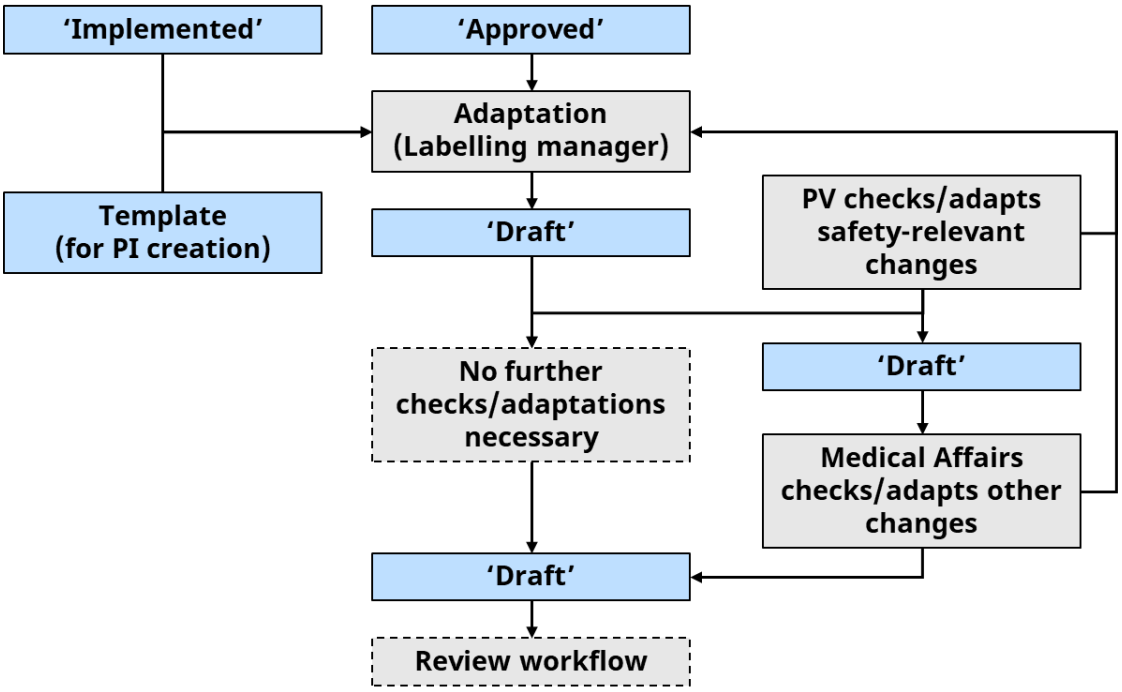

Figure 8: Adaptable creation/adaptation workflow for PI documents

Figure 9 depicts another possible scenario – the combined review/approval workflow. This is an adaptable workflow: related scientific departments can be included in the review process as needed.

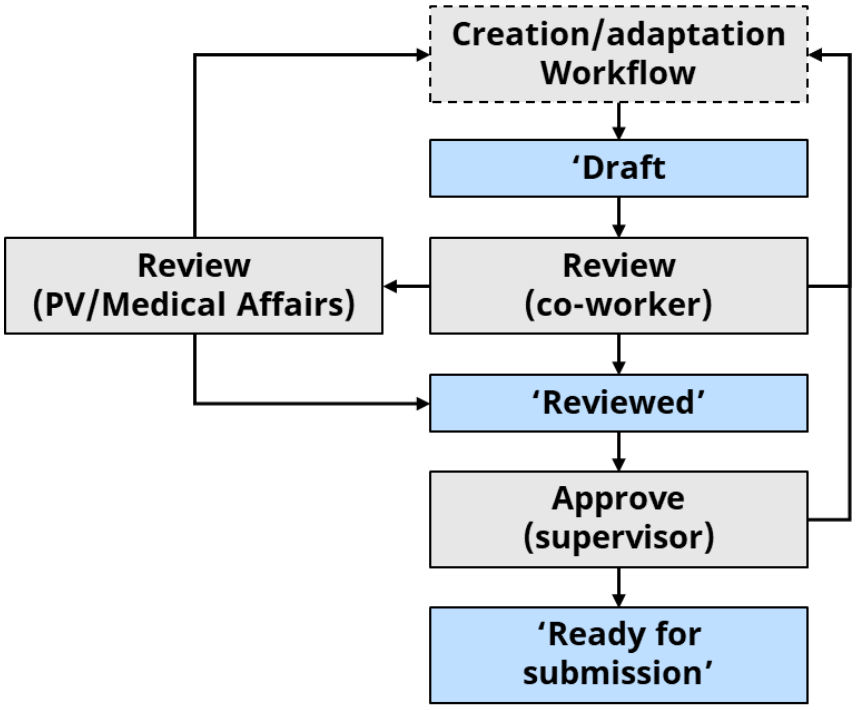

Figure 9: Adaptable review/approval workflow

5.2.2.10 User management and access control

In order to ensure that documents are of reliable and of high quality, appropriate user access control mechanisms are needed to only permit authorized users to access the DMS and perform changes to documents and their content. Therefore, DMS are concepted to be a closed computerized system, requiring user accounts and password-protected access mechanisms to control who uses the system and to prevent unauthorized access. (14,40,44,45,42,67)

DMS usually offer very convenient options for restricting document access to authorized users. For this purpose, the DMS should have a good role- or activity-based authorization concept. Preferably, the authorization concept should allow different types of access (e.g. read-only, user, super-user, administrator) and be multi-level, i.e. allow different access and rights configurations for different groups of employees. Certain document types should only be allowed to be revised by certain users. (56,71)

A Labelling DMS should use a comprehensive user management system that provides appropriate access control mechanisms as well as a profound authorization concept that allows the use of different user types. Editing rights should be limited to users of the concerned departments, e.g. RA, Medical Affairs, PV. This guarantees that only authorized and trained personnel can alter PI documents and distribute them. Thereby, PI document reliability and quality is greatly improved.

However, for pharmaceutical companies, consideration should be given to granting all employees read-only and download rights for PI documents with ‘approved’ or ‘implemented’ status. This ensures that employees in other departments have a secured and trustworthy access to the most current PI documents, e.g. for publishing or information purposes.

5.2.2.11 Collaboration/sharing

The experience of the Covid-19 crisis has shown how important it is to have suitable collaboration tools that enable employees to work together remotely. This was the only way to maintain the productivity of operational processes despite Covid-19 restrictions. (47)

Collaboration tools promote operational collaboration and generate both time and mobility benefits. Such tools are also needed in the pharmaceutical industry. For any pharmaceutical company, developing new products means collaborating in multidisciplinary, transnational teams. Appropriate tools can enable this cross-location collaboration of project teams. (42,46,47,63).

Labelling DMSs should provide a set of suitable collaboration functionalities or offer interfaces that empower such tools. The creation or revision of PI texts often necessitates that many different experts are working on PI documents. Appropriate collaboration tools should allow multiple users to perform activities on a document simultaneously. However, this collaboration should not compromise audit trail and versioning functionality. A functionality that enables collaborative real-time editing is to be strived for. Especially in the development of new PI texts from scratch for medicines under development, collaboration tools that allow simultaneous adaptation of documents should be considered. Other collaboration tools – like instant messaging within the DMS, leaving notes and marks for certain documents and email notifications – may also be useful to speed up PI-related activities between different parties.

5.2.2.12 Attribute/metadata management (database-supported)

Metadata/attributes provide information about other data, in the case of DMS information about the stored documents. Metadata is used to identify and describe documents the content, context, and purpose of the document. Metadata helps organize, categorize, and identify documents so that they can be found and retrieved more easily. It is a basic functionality for every DMS and therefore a ‘must’ criteria for any DMS. (13,14,43,41,45,42,63)

Metadata management is the process of creating, organizing, maintaining, and utilizing metadata to describe and characterise documents in a DMS. It involves defining and capturing information about documents, including attributes like author, date created, and file format, as well as relationships between data elements. It is important for metadata management that, prior to implementation, necessary attributes are predefined and used for each document, if applicable. This means that certain attributes of documents have to

be made mandatory and filling them cannot be omitted. Preferably, pick lists and drop-down menus that use predefined values should be utilized. (45,42,67)

Table 10 lists document attributes/metadata that can be used for the proper management of PI documents in a DMS. However, it is at the discretion of the pharmaceutical company to decide what metadata is needed to process its PI documents. Depending on the company's specific needs, other or additional metadata may be required.

Table 10: Metadata needed for proper DM of PI documents

Attribute/metadata	Description
Document name	Indicates what document this is. The document name should be as comprehensive as possible and should follow a predefined structure. For example: '*SmPC/PL/Labelling_INN_Strenth_Dosage Form_Date of last revision_Country.Document format*'; 'SmPC_Clopidogrel_25mg_caps_20230204_DEdocx'
Document creator	Displays who created the document initially or imported the document into the system for the first time
Last editor/reviser	Shows the last user who edited the document
Date of last revision	Records the last revision of the document that is stated at the end of SmPCs and PLs.
Document language	Indicates language of the PI document
Document format	States the format of the stored document or file (e.g. docx, PDF, XML, JSON)
Version number	Specifies the version of the document (cf. Section 5.2.2.2), suggested format: 'major.minor', e.g. '2.1'
Document type	Indicates the PI document type (Annex I, Annex II, Annex III; SmPC, PL, Labelling)
Document status	Unique description of the document's status, e.g. 'Draft', 'Reviewed'/'Ready for submission', 'Submitted', 'Approved', 'Implemented' (cf. **Figure 7**) crucial function for PI handling
Associated MA procedure numbers (MRP/DCP number)	Links the document with respective EU procedures, enables file creation of related documents
Associated MA number	Connects the document with associated EU (CAP) or national MA number; enables file formation of related documents

Attribute/metadata	Description
MAH	Records the MAH that is noted in the document. Many companies use multiple distribution companies in the same country
Associated countries	States countries this PI document is relevant for. A necessary feature in cases where multilingual packaging is used
Active substance(s)	Notes active substance(s) that are contained in the medicinal product
Packaging process / publishing relevance	States if this PI document version is used for packaging process / publishing
Dosage form	Records the dosage form of the medicinal product described in the PI text.
Strength	Saves the strength(s) of the associated medicinal product(s).
Notes	Free-text field to note important information that is not covered by other metadata

5.2.2.13 Automated metadata assignment and document classification

Automated metadata assignment means the ability of a DMS to automatically assign metadata to documents as they are created or captured and keep them up to date throughout their lifecycle in DMS. (41,43)

The mapping of metadata should preferably be semi-automatic. This means that during import/creation and each time a document is revised, the DMS has the technical possibility to pre-fill some of the metadata based on the document content. (43) Automatic maintenance of PI metadata based on the information stored in the RIMS should also be considered.

Automatic document classification can also be useful in managing PI documents. Based on the content (e.g. headers), the DMS automatically classifies a document as SmPC, PL or Labelling. In the case of a CAP, the DMS should be able to recognise that the entire PI (SmPC, PL and Labelling) is stored in one document.

The use of automation mechanisms for all DMS functions should be considered to minimize the manual work required to manage PI texts in a DMS and thus achieve efficiency and effectiveness gains.

5.2.2.14 Management of various formats (Office, PDF, XML, JSON, HTML) and format converter

The new DMS should be able to handle all necessary file formats. As a minimum, the DMS should permit the use of common Office formats (43). A list of document formats supported by DMS programs is given in **Annex V**.

The Labelling DMS must enable management of common document formats such as Microsoft Office formats and PDF. It should also be able to use modern data formats enabling the use of semi-structured content that supports machine–machine readability of data (e.g. XML, JSON and HTML). In fact, XML, JSON, and HTML are not currently used for PI documents in the EU. However, the handling of such document formats will become more and more important for the life science industry. The European ePI project will make use of XML-based document formats and thus the handling will become mandatory in the future.

At the same time, there should be a sophisticated document converter that can convert document formats. This is important for Labelling DMS because the so-called ‘working documents’, i.e. the docx files, have to be converted into a stable PDF format in order to be included in the eCTD sequence. In view of the ePI project and SPL, the document conversion functions will become even more important in the future. The XML-based files need to be converted into a human-readable format so that they can be used for publishing and printing purposes.

5.2.2.15 Archiving

DMSs play an important role in ensuring audit-proof document management and legally compliant archiving. This component is used for long-term and unchangeable storage of documents and their information. In addition to storing the ordinary document format, the archiving modules also convert the documents into stable formats such as PDF/A to ensure

long-term storage. This module can be used to manage documents that are subject to retention. The retention period of each document can thus be checked and tracked. Archiving should not be limited to storing the most recent version. In combination with version management, outdated versions of documents should also be stored. The appropriate archiving of previous document versions is also one of the prerequisites for having a full audit trail. (14,43,44,45,42,56,63,67,69)

Although PI texts do not have a strictly defined retention period by law, versions of a specific PI document should be stored as long as they are in force. A product's corresponding PI should be available at least as long as it is on the market. The minimum archiving period may therefore be defined as the date of the last batch release plus the maximum shelf-life. For a product that is not marketed, the version that is currently approved by the CA and part of the MA dossier should be archived as a minimum.

5.3 Non-technical requirements for a Labelling DMS

Non-technical requirements are defined as any requirement for a DMS that is not purely linked to technical particulars, i.e. software features and functionalities. These requirements also include requirements that are related to the services the vendor is supposed to provide to the user of the DMS solution.

The results of the market analysis on offered non-technical DMS specifications and vendor services are presented in **Table 11**. Selected non-technical requirements and provider services and their relevance are discussed in Section 5.3.2.

For the results of the market analysis concerning non-technical specifications and vendor services currently offered by DMS vendors, please see **Annex III**.

5.3.1 Feature/criteria development (non-technical requirements)

Table 11: Non-technical requirements and vendor services to be considered for a state-of-the-art Labelling Management system

Criteria (non-technical requirements and vendor services)	Must or want?
User adoption/user acceptance	Must
Software implementation and configuration	Must
Capacity for development and updatability	Must
Adjustment programming/customisation	Must
Alignment with business processes	Must
User training	Must
User support	Must
Technical support	Must
Software vendor/service provider qualification	Must
Compliance with regulatory and industry standards	Must
Compliance with internal policies	Must
Validation of (hardware) and software modules	Want
On-site service/release support	Want
Migration services	Want
Recovery services	Want
Cost-effectiveness	Want
Global implementation	Want
Prompt implementation	Want

5.3.2 Description of selected non-technical requirements

5.3.2.1 User adoption/user acceptance (user-friendly interface and intuitive navigation)

Ensuring a high rate of user acceptance is one of the key challenges of a new computerized system. A high user adoption/user acceptance is important for the successful implementation and operation of a new DMS. The software should be easy to use and allow the user a certain amount of freedom, e.g. by offering possibilities to customize the GUI. In general, the GUI should be appealing for the user, not be overloaded and enable intuitive

navigation inside the DMS. The DMS should allow simple handling despite offering high functional diversity. (62,69,72,73)

5.3.2.2 Compliance with regulatory and industry standards

A DMS must meet certain rules and regulations set by governments, industry organizations, or other bodies. This helps to ensure that data is protected and used in an appropriate and ethical manner, and that information is secure and accessible. Examples of regulatory and industry standards that a DMS may need to comply with include data privacy regulations (such as GDPR), data security standards (such as ISO 27001), and document management standards (such as ISO 15489).

A Labelling management software must be set up in accordance with these requirements and must also support PI document management in such a way that PI documents comply with legal obligations. If GxP-relevant documents are also managed, the concerned legal requirements and guidelines need to be fulfilled in order to be fully compliant with the GxP standards (cf. Section 4.5.4)

5.3.2.3 Compliance with internal policies

A Labelling Management system must adhere to the rules and regulations established by the company itself, such as internal IT policies and guidelines and policies set by management. Some organizations have detailed internal policies related to ensuring that document storage, processing, and sharing are done in accordance with corporate policies on document retention, access control, and security. Any new DMS that is to be implemented must meet these criteria.

5.3.2.4 User training

Adequate user training is a crucial factor in the successful implementation of a DMS. User acceptance is one of the key challenges when planning to implement a new DMS or when switching to a new DMS solution. It is a major reason why companies in the life-science-industry do not implement a proper DMS or fail to implement a new DMS. (56)

Appropriate user training facilitates the introduction of a new DMS and improves users' ability to use the system effectively. Effective training can help users understand the features and capabilities of the DMS. This also increases user adoption and satisfaction, which in turn leads to improved productivity as users are able to manage and access documents more effectively. (39,40,56,73,74,75,76)

Some common elements of DMS user training include:

- Overview of the DMS and its features
- Explanation of the filing structure and how to organize documents
- Demonstration of how to create, edit, and manage documents
- Instructions on how to search and retrieve documents
- Introduction to versioning and collaboration tools
- Explanation of access control and user management
- Specialized trainings for certain user groups
- Reoccurring drop-in sessions as a low-threshold assistance offer

5.3.2.5 User support

For the successful implementation of and maintenance of a DMS, user support should be sufficient and cover various types of assistance and resources that are available to users to help them use the system effectively and efficiently. This helps user to understand and effectively use the various feature sand functionalities of a Labelling DMS.

Useful user support services for a Labelling DMS are:

- Helpdesk/hotline
- Remote online support
- Online blogs/internet forum

Moreover, there should a sufficient on-site service and release support when implementing a new DMS, i.e. throughout the ‘go-life’ phase. Such services are important to ensure a smooth begin of operation and that adjustment programming needs, bug fixes etc. can be performed shortly after ‘go-life’.

5.3.2.6 Software vendor/service provider qualification

The pharmaceutical industry is an industry with complex governance, security, audit and data management requirements. Preferably, the vendor should have a track record of implementing such systems in this sector. This ensures that the vendor has sufficient experience in setting up a DMS that meets the specific requirements of the pharmaceutical industry.

Many pharmaceutical companies also have internal policies regarding third-party services and vendor qualifications. The software provider must meet the requirements set forth in these policies.

5.3.2.7 Adjustment programming/customization

Adjustment programming and customization of a DMS is the process of adapting a DMS to the specific needs and requirements of an organization. This enables a customized DMS that improves the effectiveness and efficiency of document-related processes.

Customization programming is urgently needed when an 'off-the-shelf' DMS is selected to be implemented as a Labelling DMS to meet specific PI document management requirements. Such customization programming may mean programming specific workflow templates, document metadata fields, integration specific applications, and other technical specifications and functionalities required for proper DM of PI texts.

5.3.2.8 Technical support (software updates, system maintenance, bug fixes)

Sufficient technical support must be provided as part of the services rendered by the provider. This refers to support for the users of the DMS for any technical questions or problems that may arise when using the system. Technical support should be reliable and effective, i.e., of high quality and available at least during normal business hours. This will ensure that technical issues are resolved quickly, DMS downtime is reduced, and the DMS is always functioning effectively. Technical support should include system maintenance,

troubleshooting, and software updates during operation to allow the system to run smoothly.

5.3.2.9 Capacity for development and updateability

It is important that when selecting the DMS suitable for the intended purpose, a look into the future is already taken. The selected software solution should be capable of development. It should also be updateable, i.e. new versions with enhanced functions, software improvements and bug fixes should be introduced regularly. This is important to ensure smooth system operation and high system performance throughout its useful life. (62).

When looking at the market of DMS providers, it becomes clear that a constant development is taking place and that the entire field of IT is constantly evolving and changing. A current identification DMS should therefore be updateable and capable of development in order to keep up with the changes. This way, the DMS remains 'state-of-the-art' over a longer period of time.

5.3.2.10 Migration services

Migration service refers to the process of transferring existing documents, metadata and other data from one system to a new one. In terms of DMS, this may mean migrating documents stored in an outdated DMS application to the new DMS, along with all metadata and other data associated with the documents. The vendor should offer an appropriate migration service and be experienced in it. This reduces the time and effort required to migrate to a new DMS for the organization and the internal IT department involved. Data migration is complex and can involve a variety of tasks, such as converting data to a format compatible with the new system, maintaining existing document relationships and metadata, and ensuring that data is properly indexed and organized in the new DMS. (14)

The vendor migration service ensures that documents from the previously used DMS are reliably transferred to the new system. The introduction of Labelling management software should be considered when documents need to be transferred from an outdated DMS.

5.3.2.11 Cost effectiveness

Refers to the balance between the implementation and use of a DMS and the associated costs. A DMS is considered cost-effective if the benefits it provides, such as increased efficiency, improved collaboration, and better document management, outweigh the costs of implementation, maintenance, and ongoing use. (39,63)

Before introducing a new Labelling Management System, the economic efficiency of a new implementation must be carefully evaluated. This means evaluating whether the benefits, i.e., new functions, technical features, and services provided by the vendor, outweigh the costs and effort associated with implementing a new computerized system (e.g. licensing costs, user training, document migration).

To maximize cost-effectiveness, pharmaceutical companies should carefully evaluate their needs and requirements when choosing a Labelling DMS, and select a system that provides the features and functionalities they require at a cost that is within their budget.

5.3.2.12 Global implementation

With any new Labelling DMS, the implementing pharmaceutical company must consider the dimension of the rollout: Local, in core markets, or global. Each case places different requirements on the DMS, especially in terms of scalability and performance. In addition, some DMS vendors offer their DMS only for certain countries and are not able to support a global implementation.

The scope of the new application must be carefully considered before selecting a new DMS solution. Using a common solution for all PI management processes worldwide provides room for harmonization and full interoperability within the organization. A global implementation can also be more cost-effective than using a specific Labelling software in each country. A common DMS solution that enables full interoperability between countries should at least be considered for common markets such as the EU.

5.3.2.13 Alignment with business processes

In general, potential software solutions should be examined to determine whether they can be well integrated into business processes. The integration into existing processes and interoperability with established IT systems is one of the key requirements for enabling smooth implementation of a DMS. (47)

The introduction of electronic systems always offers the opportunity to rethink and redesign processes that are still paper based. A pure 1:1 mapping of existing business processes in a new DMS is rarely desirable. The use of electronic automation tools creates opportunities that manually managed, or paper-based processes do not offer. (56)

When introducing a new Labelling DMS, it is important to evaluate the existing document-based processes before selecting a new system. There is often potential for significant productivity increases. Inefficient document workflows, e.g. review or approval workflows of PI documents with too many stakeholders involved, can only be improved to a limited extend via a new workflow component. An adaptation of the underlying business workflow is necessary to speed up such processes. Since business processes in companies are constantly evolving, the DMS should be adaptable to ensure that it can align to changing document-dependent processes in the future.

6. Labelling DMS – current trends that need to be considered

6.1 Digital transformation

Digital transformation is also becoming increasingly important for pharmaceutical companies. Many pharmaceutical companies have recognized the potential of digitalization and have digitalized the processes in the company. Only a few processes still run with paper-based documents, the paperless office has become everyday life.

Nevertheless, the potential for digitization is far from exhausted in many companies. Often, corresponding digitization strategies have already been implemented, but only for overarching systems such as booking systems and not in all departments. Manual filing structures for documents and information have often not yet been replaced by suitable document and information management software. Specialized tasks and processes are digitalized, but still executed manually without the use of appropriate computerized systems to automate them.

In many RA departments, the use of RIMS is still considered an additional expense. However, a superior, adaptable RIMS with an integrated state-of-the-art Labelling DMS is the future of regulatory maintenance in the pharmaceutical sector. These systems will promote the reuse and sharing of medical data through interoperability between systems as well as reduce the administrative burden through comprehensive tools.

6.2 Artificial intelligence (AI)

AI is currently a hot topic in the IT world. Recently published AI models such as ChatGPT from OpenAI offer new opportunities for many industry sectors. The integration of AI programs into existing IT applications will become more important in the future.

The generation of human-like texts based on input is interesting for the creation and maintenance of PI. For example, AI can help translate the scientific language of a SmPC to produce a corresponding PL written in patient-friendly and clear lay language. The integration of AI models into Labelling DMSs should therefore be considered in the future. However, limiting factors such as data security and compliance factors need to be carefully evaluated.

6.3 Cloud technologies, web-based applications and mobile devices

There is a current trend that documents, data and applications are increasingly being shifted to the cloud. The main driver for this is that cloud solutions have many advantages compared to on-premise and server-based applications. Such solutions are usually more cost-effective but offer greater flexibility and scalability and are easy to implement. Cloud solutions mostly use web-based clients to allow users more flexibility in terms of access possibilities – users can use any mobile device to log into the system using a web browser. Consequently, users only need a mobile device and internet connectivity to access web-based cloud programs from anywhere in the world. Some cloud delivery models include that the vendor provides the entire IT infrastructure and resources. Cloud applications are much better at meeting the principles of a modern workplace than on-premise programs – flexibility, agility and mobility.

As discussed in Section 4.5.1, a decision must be made whether a cloud-based or on-premise DMS should be used for a Labelling DMS. Over the next few years, more and more DMS solutions using cloud technologies will enter the market. Nonetheless, on-premise solutions installed using the customer's IT infrastructure and following established licensing models (e.g. a licence fee for every workplace) will still be offered, due to the advantages concerning data security.

7. Conclusion and outlook

7.1 Importance of a state-of-the-art Labelling management software for pharmaceutical companies

The creation and maintenance of PI documents and the management of the associated processes is a special task in pharmaceutical companies. The operations are mostly executed digitally, but often without the use of appropriate computerized systems specialized in PI document management. Therefore, PI maintenance and PI-related processes are mainly performed manually, relying entirely on user actions.

An appropriate DMS that provides a wide range of technical features, technical specifications and non-technical requirements (e.g. appropriate provider services) can help improve the efficiency and effectiveness of the PI management process. Formerly manual tasks can be automated or semi-automated, significantly reducing the administrative burden on employees in RA and related departments. Thereby, employees are relieved for higher-value tasks (‘job enrichment’). A state-of-the-art Labelling management software helps to ensure that PI documents are of high quality and meet regulatory requirements, increasing patient safety and reducing legal risks.

After analysing the DMS/ECM market and the functionalities, specifications and services offered by software vendors, as well as the requirements placed on modern Labelling management software, it becomes clear that a thorough software selection is necessary. Ultimately, the aim is to find the most suitable software solution that meets all the requirements of a Labelling DMS. However, the selection process and the detailed requirements are always up to the discretion of the pharmaceutical company and its employees. This is because each company has different IT policies, IT infrastructure and additional or different technical or non-technical requirements that a new Labelling Management system must meet. However, the requirements outlined in Section 5 can be used as a helpful guide to identify the company-specific requirements for a modern Labelling Management software.

7.2 RI and PI management

It is not easy to keep track of the large number of RI projects currently running in the EU. However, it is important to keep an eye on the ongoing RI projects so that necessary industry adaptation can be prioritized and pharmaceutical companies do not get into the situation of losing touch with the IT transformation that is currently developing.

This multitude of projects mainly arise from the fact that the so-called 'Digital Transformation' (cf. Section 6.1) is progressing and encompasses more and more sub-areas and departments of pharmaceutical companies.

In general, two key characteristics are needed to combine RI projects and the exchange of healthcare data in the EU: interoperability and harmonization. Both are needed to allow the exchange of healthcare data via machine–machine communication. Data sharing and re-use of data is thus promoted. State-of-the-art Labelling Management systems need to offer both characteristics too. PI texts are subject to great harmonization and interoperability efforts. These efforts are currently emerging and will develop and increase over time. There is an urgent need for the digital transformation of the current PI format and PI handling because the currently used technical specifications are insufficient.

In the following paragraphs, I want to point out the importance of current RI projects and elaborate on which of these projects will have a significant impact on the PI management in future. Furthermore, it will be outlines what aspects of PI documents need to be subject to digital transformation to allow them to fit into the new, emerging RI environment.

7.2.1 Use of the FHIR standard for the exchange of healthcare data

The implementation of the new FHIR standard as a common basis for the exchange of healthcare data is a hot topic. The FHIR data format is going to replace the Art. 57 data format, which has previously been used to submit medicinal product data to xEVMPD under the Art. 57 obligation. This step is necessary because the Art. 57 data format is not ISO IDMP compatible. For a transition period, xEVMPD will be running in parallel with SPOR PMS. For this period, complete interoperability between xEVMPD and SPOR PMS is needed, which can only be achieved via FHIR data transmission. MAHs need to be prepared to comply with the legal obligation set out in Art. 57 of Directive 2001/83/EC as soon as

submission via xEVPRM will be precluded. There are also plans to transition the U.S. SPL, which uses an XML-based data standard from HL7, into an FHIR-compatible standard to streamline the exchange of healthcare data among regulatory agencies worldwide.

It is crucial for MAHs to understand that the FHIR standard is going to be used as the new, common standard to exchange electronic data on human medicines in various RI projects, including

- SPOR master data
- Submission of medicinal product data according to Art. 57 of Directive 2001/83/EC
- Web-based eAF (formerly DADI)
- EU ePI common standard
- US SPL

In summary, FHIR will enable the exchange of medicinal product data between different IT systems in a consistent and reliable manner. Therefore, regulatory authorities and industry need to be proactive and implement tools that enable the transfer of human medicinal product data in FHIR data format with each other and other stakeholders.

7.2.2 ISO IDMP/SPOR master data compatibility

The use of ISO IDMP standards in the EU is currently evolving step by step and will become mandatory for MAHs. The implementation of ISO IDMP standards is a big challenge for MAHs, as all in-house product data will have to be transferred into an ISO IDMP information model. This affects all data storages, including every MA dossier and their content in the EU. With regard to PI documents, the ISO IDMP standards for SmPC, PL and marking must be used from a certain point onwards. MAHs are still completely naïve regarding this issue yet. They are rarely prepared to fully implement the ISO IDMP standards into all regulatory dossiers and related PI documents in the EU. However, the full implementation of the ISO IDMP standards is envisaged in the EU and legally obliged by Art. 25 and Art. 26 of Commission Implementing Regulation (EU) No 520/2012. This harmonization step will be a burden for MAHs.

Therefore, it is crucial that MAHs start preparing for the reliable and correct use of SPOR master data in all RA fields, including PI documents. Technical solutions are necessary to fully link all stored medicinal product data and to allow at least the semi-automatic transformation of non-ISO IDMP compliant data into an ISO IDMP compliant format. The SPOR databases and PI documents can only be meaningfully linked with the help of an overarching RIMS. The following section describes the significance of RIMS in this context.

7.2.3 RIMS connectivity

A RIMS is a specialized software solution for the pharmaceutical industry that allows the management of all information related to the medicinal products of the company. It can be considered as an overarching ECM system aimed at managing all the data the company has on its medicines. Such systems help MAHs and applicants ensure compliance with legal requirements.

In the future, RIMSs will be the link between the SPOR master databases and the MAHs. RIMSs will facilitate the conversion of non-ISO IDMP compliant data on the MAHs side into an ISO IDMP compliant format. This will enable MAHs to meet their legal obligation to use the ISO IDMP standards.

A link between RIMS and DMS is currently not necessary. Nonetheless, many RIMS solutions provide general DMS solutions to allow appropriate handling of various documents that are necessary for eCTD preparation. However, as stated above, an adequate interface between the company's own RIMS and the DMS solution regarding SPOR master data will be indispensable. Only a suitable interface can ensure that the mandatory use of ISO IDMP standards is also guaranteed for PI documents. Therefore, full interoperability between the systems is crucial. Standalone DMS solutions will not meet be able to implement the ISO IDMP standards in PI documents as such systems will not have a connection to SPOR. Another possibility is that a modern DMS component for marking is a module of a RIMS.

7.2.4 eCTD compatibility

One important feature is a technical interface that allows full interoperability between eCTD management software and the DMS. Although not a prerequisite, it is recommended that a suitable interface is being installed. This facilitates business processes; hence, the media disruption between the two systems is bridged. PI documents can be transmitted smoothly between the two systems. Prepared PI documents set as 'ready for submission' in the DMS can easily be transferred to the correct eCTD sequences using the underlying metadata of the respective document. This connectivity also minimizes the risk of operating errors which occur when handling documents manually, such as misplacing of documents or unintentionally altering their content or metadata.

Moreover, the new EU common standard for ePI implies new requirements for submission activities. Authorities need to accept the new document format of the ePI via 'working documents' folder. PI documents are currently submitted as docx files within the working document folder. This folder is handled outside the eCTD dossier and submitted to the authorities together with the respective eCTD sequence.

In the future, the eCTD requirements should be modified to include other, modern document formats such as XML and JSON documents. This would allow document types that are currently submitted to authorities via the 'working documents' folder to also be included in the eCTD, where they would be versioned and archived. This would allow ePIs to be transmitted directly to agencies as part of the eCTD sequence after import from the tagging DMS. However, this would require significant changes to the eCTD specifications.

7.2.5 ePI compatibility

The future of PI handling is ePI handling. The recently released EU common standard for the electronic version of PI clearly describes the use of modern document formats (XML, JSON) that allow the use of semi-structured information for the PI of human medicines. From this perspective, the new format is quite similar to the existing SPL initiative in the USA.

In addition, the new document format meets the HL7 FHIR standard that ensures the reliable sharing and re-use of healthcare data between different IT systems. By using the

FHIR standard, the ePI common standard is fully compatible with other RI projects in the EU, such as SPOR master data. This is a real game-changer for PI creation and maintenance. The new semi-structured format of the PI uses structured content from controlled databases such as SPOR. For this reason, it is important that pharmaceutical companies also upgrade their existing IT infrastructure in RA and related departments. Labelling Management Systems need to be fully aligned with the new FHIR standard and must also allow the creation and maintenance of semi-structured PI documents.

As stated in the set of specifications above, any new Labelling DMS needs to provide the functionality for appropriate management of the new ePI format. If it does not, any new contract for DMS implementation should stipulate that an adequate update of the DMS will be provided as soon as the EU ePI project enters the implementation phase. This is critical for all future Labelling Management programs, as the electronic format will be implemented in a stepwise approach and will be mandatory from a certain date.

7.2.6 DARWIN EU/real-world data

There is still a long way to go before RWE may be used as a standard for assessing medicinal products despite the clear approach in the EU to make better use of real-world healthcare data. The DARWIN project focuses on linking the various independent databases that currently exist in Europe. Collection of collect real-world data on a daily basis and linking the different databases provide a better processing of these valuable data on the use of medicines.

This project will eventually have an impact on PI: The incorporation of real-world data into PI texts as they become available. By including safety-relevant changes in the PI as soon as they are available through RWE, the actuality of the PI documents would increase significantly and ultimately improve patient safety. This would give a whole new meaning to the legal requirement in Art. 23 (3) of Directive 2001/83/EC to keep the PI up to date with current scientific knowledge.

Even if this sounds like a dream of the future, this form of PI management will eventually come to the MAHs, as the better use of real-world data is a declared goal in the EU.

8. Summary

The DM, sometimes referred to as ECM, is a concept that is widely used by companies in order to control and manage the steadily increasing number of paper and electronic documents. This is also the case for the pharmaceutical industry. However, many companies operate an overarching 'one-size-fits-all' DMS for all departments that does not fit all individual department's needs. Other enterprises only use a DMS in certain departments or for certain tasks, e.g. for accounting or for procurement.

This thesis points to the importance of a state-of-the-art Labelling Management system for PI handling within RA departments. The technical specifications, functionalities and non-technical requirements that are needed for state-of-the-art Labelling DMS are elaborated through an in-depth market analysis of the DM/ECM applications on the market. The market analysis provides a scientifically based list of 'must' and 'want' specifications for a suitable DMS for the management of PI documents. However, the evaluation of the market analysis has also shown that selecting the right software solution also depends highly on the pharmaceutical company's special needs and the needs of future users in that company.

In addition, an analysis of RI projects in the EU concludes that for each new IT software solution to be implemented in RA departments, there are specific requirements for interoperability and harmonization of data sets and systems. The ePI project and the ISO IDMP implementation via the SPOR master data system are important RI projects that must be considered with any new Labelling management software, as they place special requirements on PI management tools.

All in all, the results clearly show that a software solution with a specialized set of functionalities, technical specifications and vendor services is needed to meet the requirements of a state-of-the-art Labelling management software. When selecting an 'off-the-shelf' DMS/ECM solution for PI document handling, adjustment programming is required to fulfil all the requirements for a proper PI management.

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Annex I: Search terms used for the literature search in library catalogues and on the internet

- Content Enterprise System
- Content Management
- Digital Office
- DMS
- Document Management System (DMS)
- Document Related Technologies (DRT)
- Dokumentenmanagementsystem (DMS)
- Dokumentationsmanagement
- Dokumentenmanagement
- Dokumentenverwaltungssystem
- Document Management System (DMS)
- elektronisches Dokumentenmanagement
- elektronisches Dokumentenmanagementsystem (EDMS)
- EDMS
- Enterprise Content Management (ECM)
- ECM
- Dokumenten-Management
- Document Management
- ECM+DMS
- ECM DMS Lösungen
- ECM/DMS
- BARC-Guide
- Maaß & Peiter Verlag
- Trovarit
- Wirtschaftlichkeit im Bürobereich

Annex II: Range of offered DMS functionalities and technical specifications/characteristics

DMS functionality/ technical specification	Description
Range of services for DM	
Core DMS functionalities	
Storage/retrieval	Allows safely storing documents in the DMS and then empowers the user to locate and assess that document when needed, mostly with the help of sophisticated folder structures or search functionalities. The secured and controlled storing and retrieval of documents is the most basic principle of a DMS
Search function	Enables searching for documents and therefore ensures document retrieval
Document export/import	Empowers users to transfer or move documents from one system or platform to another, e.g. from the DMS to the users personal computer or shared network drive and vice versa
Check-in/check-out	Allows controlling access to, and editing of, documents. The purpose of check-in/check-out is to prevent multiple users from making changes to the same document simultaneously, which ensures version conflicts and prevents data losses. When a user checks out a documents, they are given exclusive rights to access and edit the document. From the of check-out, the document is locked, and other users are unable to propose changes
Versioning/version management/version history	Enables tracking changes and revisions to documents over time by creating new versions of a stored document based on predefined rules

DMS functionality/ technical specification	Description
Metadata management	Associates descriptive information with documents, such as author, date created and keywords
User management and access control	Empowers administrators to control and manage user access to the system and documents, by defining user roles, assigning permissions, and controlling document access. This helps to maintain document security, confidentiality, and enforce document management policies and procedures
Electronic/flexible file formation	Enables linking related documents with each other, mostly based on metadata. This means that all documents related to a specific topic can be combined into one digital file and ensure that all relevant documents are displayed to DMS users
Define filing structure	Refers to the way in which documents are organized and stored. A well-designed filing structure can help ensure that documents can be easily located and retrieved, and it can also make it easier to manage large numbers of documents over time. Usually, folders are used to contain files and other subfolders, thereby helps to find, access and share documents
Archiving/records management	Allows secure and efficient storage, management and retrieval of electronic records and documents. Necessary module for long-term storage of documents subject to retention. Supports compliance with legal, regulatory, and organizational record management requirements, including retention schedules, access controls, and audit trails.
Advanced DMS functionalities	
Drag and drop	User interface feature that allows to interact with a computer application by grabbing an object with a pointing device (such as a mouse) and dragging it to a different location. The object is typically dropped by releasing the mouse button. This simplifies the import of new documents into the DMS

DMS functionality/ technical specification	Description
Dynamic files/folders	Specific type of file/folder structure that can automatically change and adapt based on certain conditions or criteria. Files and folders are automatically assigned to different locations or categories based on their metadata
Comprehensive filing structure	A system of folders and subfolders that is designed to organize and categorize documents in a logical and meaningful way. Facilitates users to find and access the documents they need based on an organized, hierarchical folder system, without the use of search tools
User management and access control	Enables to control and manage user access to the system and documents, by defining different user roles, assigning user access permissions, and controlling document access. Ensures that only authorized personnel have access to the documents in the system
Audit trail	Tracks and reports on document-related activities, such as who has accessed or edited a document and when. Full audit trail is necessary for GxP system (c.f. Section 4.5.4)
Explorer integration	Refers to the integration of the DMS with the file explorer or the operating system's file manager. This integration enables users to access, manage, and view their documents stored in the DMS directly from their file explorer or operating system's file manager.
Open office integration	Ability of a DMS to interface with the OpenOffice suite of productivity tools, such as Writer (word processing), Calc (spreadsheets), and Impress (presentations). This integration allows users to create, edit, and store documents within the DMS, while utilizing the features and capabilities of the OpenOffice tools

DMS functionality/ technical specification	Description
Microsoft office integration	Refers to the integration of Microsoft Office software (such as Word, Excel, and PowerPoint) into a DMS. This allows users to access and work with Microsoft Office documents within the DMS, without having to switch between different applications
Document editing	Allows users to make changes to documents stored in the DMS by using a built-in document editor or connecting to a third-party document editor
Format converter	Enables converting documents from one file format to another, such as converting ordinary file formats (e.g. docx) into a long-term stable format, e.g. PDF/A
Document compressor	Reduces the size of a document file without affecting its quality. Facilitates document storage and transfer.
Data/document encryption	Enables converting plain text into a code to secure data or documents from unauthorized access. This helps to ensure the privacy and confidentiality of sensitive information stored in the DMS. A DMS may also be used to securely manage encryption keys
Digital signature	Allows users to sign electronic documents, track who has signed them, and verify the validity of signatures. This helps to ensure the security and authenticity of electronic documents Import for managing GxP-related documents that need verifiable signatures for release processes (cf. Section 4.5.4)

DMS functionality/ technical specification	Description
Automated file formation/digital filing	Enables automatic creation and organization of folders in a structured manner based on predefined rules and criteria. Uses the type, content, or other attributes of a document to automatically categorize the document and place it in virtual folders. Helps store documents that are related to each other (e.g. by matching attributes) together in a single folder.This saves time and improves efficiency by reducing manual data entry and reducing the likelihood of misfiling.
Automated document classification	Allows automatic categorizing documents based on certain characteristics such as content, keywords, or metadata. It utilizes machine learning algorithms to analyse the contents of the documents and assign them to the appropriate category or folder based on pre-defined criteria.
Automated metadata assignment	Empowers a DMS to automatically assign metadata to documents as they are created or captured, and keep them up to date throughout their lifecycle in DMS.
Integration of electronic personnel file	Refers to the integration of a DMS with a company's human resource management system. Allows for the management and storage of employee-related documents such as resumes, contracts, and performance evaluations within the DMS
Integration of electronic customer file	Enables a DMS to manage customer information used across the enterprise. Ensures that customer information is easily accessible and consistent across systems and departments, providing a comprehensive view of the customer's interactions with the company.
Range of offered DMS modules (components that go beyond classic DM but are often integrated into DMS applications)	

DMS functionality/ technical specification	Description
Workflow component/BPM tool	Allows administrators to define and manage the processes and steps involved in document management, and to automate many of the manual tasks that are associated with document processing. This helps streamline document management, reduce errors, and improve efficiency. Stand-alone applications are also called BPM tools
Form/template management	Allows users to create, save, and manage standardized forms or templates used for various purposes, such as contracts, invoices, and reports. Templates define the structure, content, and format of a document and enforce the use of consistent information. These forms or templates can be completed and processed electronically, improving the efficiency and accuracy of document-based processes.
Email management	Component of a DMS that is specifically designed to manage and organised emails within the system. It captures e-mail messages and attachments, extracts relevant information such as sender, recipient, date, subject, and content, and organizes the messages within the DMS in a way that makes it easy to find, manage, and track the information over time (email archiving). Ensures that the emails and the information they transmit are stored at a centralized access point. Email management modules may also facilitate the dispatch of mass emails
Contract management	Enables users to create, store, and manage contracts and other legal documents electronically using a DMS. It is a DMS module that is specialized on managing contracts. This leverages DMS features such as versioning, collaboration tools, and access control to ensure that contracts are managed securely and efficiently.

DMS functionality/ technical specification	Description
Knowledge management	Facilitates the systematic process of creating, organizing, maintaining and using knowledge assets within an organization. It is a DMS module specialized in the management of knowledge, i.e. information, within an organization. The module aims to improve the efficiency, effectiveness and flexibility of an organization by making the best use of collective knowledge and know-how.
WCM	Enables you to organize, manage, and publish web content to a website or portal. Facilitates the creation, publishing, and management of web content for non-technical users. WCM is often integrated or connected to a DMS to ensure effective management of digital content throughout its lifecycle – from creation to archiving.
Invoice management/invoicing	Allows creating, sending, tracking and managing invoices for the purpose of payment capture. It is a module specialized in managing invoices. DMS are usually connected or integrated with an invoice management system to provide secure and reliable archiving of invoices and payment confirmations during their legal retention period
Collaboration management	Enables real-time collaboration, communication, and coordination among team members and other stakeholders through the use of a wide range of collaboration tools. These typically include tools for tracking changes, assigning tasks, and commenting. The various collaboration tools are outlined below.
Range of services for collaboration/sharing/groupware	

DMS functionality/ technical specification	Description
Co-authoring	Permits multiple users to work on the same document simultaneously. This feature is especially useful in a DMS where collaboration and teamwork are essential, as it allows users to work together in real-time, regardless of their physical location. This helps reduce the time and effort required for coordination, and allows users to focus on the content of the document rather than on the logistics of collaboration. Ultimately enhances efficiency and productivity
Task management	Enables users to assign tasks and track progress, helping ensure that projects are completed on time and within budget; important collaboration tool to be used in teams or project groups
Wiki	Allows creating, editing and sharing information and content collaboratively. Wikis are designed to be user-friendly and easy to use, allowing to implement changes with just a few clicks. Wikis represent separate modules in DMS. They are ideal for collaboration and group work, as multiple users can work together on a single document, spreadsheet or set of information
Blogs/forum	Enables sharing news, updates, training videos, tutorials, questions and answers and other information about the DMS and its features. Users can share their experience and knowledge about the system. This enables collaboration and increases efficiency
Commenting and annotations	Allows adding comments and annotations to documents, facilitating communication and collaboration among users
Dashboards	Provides data and information on key metrics and performance indicators via an interactive visual display. The dashboard is a tool that provides users with a real-time view of how their documents is being used, shared and managed

DMS functionality/ technical specification	Description
Integration with other collaboration tools	Interfaces with existing collaboration tools used in the company facilitates the use of these applications within the DMS without media disruption. For example, Instant messaging, blogs, email management tool can be interconnected to enable smooth using of the managed documents with these systems and vice versa
Range of services for search module	
Full-text search	Allows searching for words or phrases within the full text of a set of documents, enabling searching for words or phrases within a large amount of unstructured or semi-structured content stored in documents
Intelligent search function	Uses advanced techniques such as natural language processing, machine learning and semantic analysis to deliver more relevant results. This search function tries to understand the meaning behind the query and provides results based on context intent and user history. Enables a more personalized and intuitive search experience for the user
Advanced search function	Provides users with more sophisticated and specialized search capabilities beyond basic keyword search. It uses advanced techniques (such as proximity search, wildcard search and field-based search, among other search operators) to help users receive better search results. Can also incorporate aspects of intelligent search functions
Comprehensive search function	Combines multiple search mechanisms such as full-text search or metadata search to deliver a broader and more complete set of results

DMS functionality/ technical specification	Description
Federated search	Allows users to search across multiple data sources, such as databases, websites, document repositories and applications. Aggregates the results from multiple sources into a single result
Faceted search	Empowers navigating and filtering search results based on specific categories or attributes; a way of organizing search results into multiple categories, or facets, that can be used to refine search results
Metadata search	Enables searching for data based on metadata or additional information that is stored along with the documents. Empowers users to sophistically find specific documents in a large and complex collection of data based on specific attributes and properties. Very helpful search tool for DMSs that manage many documents
Storage of search queries	Stores performed search queries and corresponding search results
Range of services for capture/input management	
Document capture via scanner interfaces/scan module	Allows users to scan paper documents and convert them into digital format for storage and retrieval in the DMS. The purpose of a scan module is to provide a simple and efficient way for users to digitize their paper-based documents, making it easier to manage and access them in an electronic format. Usually includes features such as automatic document recognition, image correction, and compression, making it possible to produce high-quality digital documents that are easy to search and retrieve
Stack processing	Enables scanning and further processing in succession from a batch or stack of documents. Helps to automate document capture

DMS functionality/ technical specification	Description
Capture/text recognition	Enables recognizing scanned images or documents and their conversion into editable text. Improves search for and indexing of document content. Basic functionality to convert images into machine-readable text to enable the use of other document-related technologies such as full-text search.
Manual form recognition	Refers to the process of manually identifying the fields and structure of a form document, such as invoices, contracts, or application forms. Allows users to automatically extract data from the form and store it in the DMS. Simplifies the process of data extraction from scanned documents and enhances the efficacy of the DMS by automating the data entry process
Scanner systems	Hardware devices used to convert paper documents into a digital format for use in a DMS. Used to digitalize paper documents in order to manage them electronically. Essential hardware tool to automate document capture of large numbers of paper documents. High-performance scanners can process and digitize a large number of paper documents, such as invoices or customer letters
Learning form recognition	Ability of a DMS to improve accuracy in automatically recognizing and categorizing information contained in documents through machine learning algorithms during document capture
Range of services for deliver/output management	
Document viewer/display modules	Allows users to view and preview documents stored in a DMS in full or reduced size. Provides a convenient and user-friendly way to access and view documents within the DMS, without the need to check-out or download the document to use additional applications

DMS functionality/ technical specification	Description
Printing/mass printing	Empowers to print one or multiple documents from a DMS. Can be a useful function for various purposes, such as creating hard copies of important documents, distributing copies to stakeholders, or presenting documents in a meeting. Streamlines the document management and can offer various advanced printing tools that enables mass printing (e.g. for marketing purposes)
Thumbnails	Allows users to quickly preview the contents of a file or document via a small image of the original. Can be especially useful in DMS when dealing with large volumes of documents, as it is a handy tool to find the desired document. A thumbnail is a special type of document viewer.
Important technical DMS specifications and characteristics (other than functionalities)	
Compatibility with existing IT infrastructure	The ability of a DMS to work seamlessly with existing hardware, software and networks within an organization. This means that the new DMS should be able to integrate with and utilize existing resources such as servers, storage devices, and software programs without causing disruption or requiring major changes to the existing IT environment. This is important to streamline the use of a new DMS and maximize the benefits of the DMS implementation while minimizing additional risks and costs.
Integration with existing software solutions	This is a general specification that refers to the features of a DMS that enable integration with other IT applications currently used in the enterprise. Where possible, systems should be integrated to minimize switching between different applications and thus improve efficiency
Data integrity	Refers to the accuracy and consistency of the data stored in a system and the measures taken to ensure that the documents and their data remain undamaged and intact. It is an important aspect of the DMS as it helps to maintain the reliability and trustworthiness of the stored documents, their content and metadata

DMS functionality/ technical specification	Description
Data security/data protection	Refers to measures taken to protect sensitive or critical information stored in a DMS from unauthorized access, modification, or destruction. Critical to ensuring the confidentiality, integrity, and availability of stored documents and to maintaining the confidence of users who rely on the DMS to manage and secure critical documents.
Mobile access	Empowers users to access a DMS from a mobile device such as a smartphone or tablet. With this feature, users can access, edit, and share documents from anywhere as long as they have an Internet connection. Improves work efficiency by allowing users to work on documents on the go or remotely. Requires many other technical requirements, such as the use of a web client and cloud technology rather than a pure on-premise DMS solution.
User personalization	Allows users to customize their experience with a DMS to their specific needs and preferences, such as setting up their own interface, choosing which columns to display, or selecting specific folders to display first. This can improve the overall user experience and increase productivity. Important tool for improving user acceptance and employee willingness to actively use the DMS.
System performance/system reliability	Refers to the ability of the DMS to efficiently manage and securely store a large number of electronic documents, ensure fast and consistent access to and retrieval of documents, while protecting sensitive data. It also includes the ability to operate smoothly on a continuous basis, despite many users accessing the system simultaneously.
Scalability/extensibility	Ability of a DMS to handle a growing number of documents and the ability to easily expand the system to handle growing user access. This refers to both the increase in document volume over time and the ability to scale the DMS to allow more users to actively use the system or to introduce new features or functionality to the system, including the integration of additional software modules.

DMS functionality/ technical specification	Description
Developability	The DMS should be programmed in such a way that it can be further developed over time by the company or the service provider. This means that additional modules and interfaces can be integrated into the DMS. Changes and customization programming to existing modules should be possible in order to fully adapt the functionalities and handling of the DMS to the needs of the users.

Sources: (43,44,42,63,65,71,74,77,78,79) (80,81,82,83) (84,85,86,87,88,89,90,91,92)

Annex III: Range of offered non-technical DMS specifications and vendor services

Non-technical specification/ vendor services	Description
User adoption (user-friendly interface and intuitive navigation)	Refers to the process of getting employees to use the DMS effectively and consistently, as well as the usability of the DMS. In general, user acceptance should be high, meaning that the new DMS is practical, easy to use, and is therefore gladly used by the targeted users.
Software implementation and configuration	Vendor service that refers to installation and configuration of the DMS software on the company's IT infrastructure, setting up necessary interfaces with other software programs, creating user accounts, establishing security protocols, etc. In doing so, the vendor helps set up the DMS, configure settings and options to enable smooth 'go-life' and operation of the DMS. This helps the internal IT staff to set up the DMS and fully implement the new program with the help of the vendor professional service team.
Capacity for development and updateability	Describes the ability of a DMS to be updated and developed frequently throughout the life of the DMS after the initial "go-live" of the DMS. Such services are important to ensure that the new DMS does not become obsolete after a short time and can thus be used reliably over a reasonable period of time.

Non-technical specification/ vendor services	Description
Adjustment programming/customization	Depicts the process of customizing a DMS to meet the specific needs and requirements of an organization. This enables a customized DMS that has a greater impact on improving the effectiveness and efficiency of document-related processes. This vendor service should be considered for any DMS solution that manages specialized documents that are not commonly the subject of DMS solutions (e.g. PI documents for medicinal products). This is because many DMSs are designed more to meet the needs of departments that frequently work with DMSs, such as accounting or procurement. This also includes setting up and customizing workflows, defining the folder structure and filing system, configuring the system's security settings, and much more
Alignment with business processes	Defines the need to align the software settings and workflow templates with the document-related business processes currently used in the company. However, this also applies the other way around, i.e. the business processes must be re-evaluated in order to identify possible efficiency gains. The goal is to maximize the benefits of using a DMS with regard to the management of document-related processes.
User training	Vendor service that provides effective training to help users understand the features and capabilities of the DMS and how to use the system to effectively manage their documents. User training can be delivered in various formats, including in-person sessions, webinars, online tutorials, or self-paced training materials. Crucial component for successful implementation and operation of a DMS.
User support	Includes all vendor services to helping users understand and effectively use the various features and functions of the DMS.
Hotline	Dedicated telephone line (contact point) used for providing immediate assistance or support to customers or users

Non-technical specification/ vendor services	Description
Helpdesk	Specific user support to provide assistance to users who need help with the DMS. First point of contact to which users can turn to solve technical or operational problems that may arise when using the DMS
DMS forum/blog	Specific user support feature to assist users with technical and operational issues. Typically staffed by a team of trained support technicians who are available to help users troubleshoot problems, resolve technical issues, and provide guidance on how to effectively use the DMS
SaaS/application service providing	Refers to the delivery model where the DMS is hosted in the cloud and made available to users over the internet via web browsers, using the service providers hardware infrastructure for operation. It allows users to access their DMS from anywhere, on any device, and eliminates the need for them to manage their own IT infrastructure. This is the opposite to an on-premise DMS, where the application is fully run on the company's IT infrastructure.
Application hosting	Refers to vendor services of hosting the DMS software on remote servers rather than on local servers or personal computers (on-premise) within the organization. Provides organizations with a scalable and flexible solution for managing their DMS. Hosted DMSs are typically managed by the vendor, who is also responsible for maintaining and updating the software, as well as providing technical support and security. Reduces the burden on internal IT resources and is more cost-effective than an on-premise solution.
Technical support	Vendor service to assist and guide users and administrators of a DMS regarding any technical issues or problems they may encounter while using the software. Includes a range of services such as troubleshooting, bug-fixes, resolving technical issues, configuration, and answering technical questions. Technical support aims hat helping users to resolve technical issues quickly, reducing downtime and ensuring that the DMS is functioning effectively at all times

Non-technical specification/ vendor services	Description
Business process outsourcing	Refers to services to contract out specific document-related processes such as document scanning, data entry, document indexing, and document storage, out to a third-party service provider. These processes can be complex and time-consuming, and by outsourcing them can free up internal resources and focus on their core business activities
Validation of (hardware) and software modules	Service for evaluating and verifying that the hardware and software components of the system meet the defined requirements and specifications and function as intended. Important to reduce the risk of problems and defects and to ensure that the system is configured correctly. 'Must' requirement if GxP-relevant data or documents are stored in the DMS (c.f. Section 4.5.4)
Dimensioning of hardware and software	Vendor service to determine the necessary hardware and software dimensions needed to operate the new DMS effectively. This involves considering the number of users, the amount of data and documents stored and processed, and the required system performance. It is important to dimension the hardware and software components correctly in order to ensure that the DMS will perform as expected and to minimize the risk of performance issues and downtime
Implementation of hardware	Service provided by the vendor to set up and install the physical IT components required to operate a DMS on the IT infrastructure of the future DMS user. Only required if the entire DMS or some modules are installed on the company's IT infrastructure (e.g. for on-premise solutions, company-hosted private clouds)

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Non-technical specification/ vendor services	Description
On-site service/release support	Refers to services provided by the vendor at the company's premises. On-site service and release support at the time of system implementation can contribute to a smooth rollout of the new DMS. It allows user training, customization programming, and other services to be performed right on the premises, which ultimately leads to better support from the vendor and easier implementation of the new DMS. For example, customization programming and user training are performed at the company's site
Migration service	Describes a provider's service for transferring data from one system or platform to another system. This service is usually needed when a company transitions to a new DMS. It includes the process of moving existing documents, metadata, and other data from an old DMS to a new one. Minimizes the amount of time and effort required to transition to a new DMS
Recovery service	Service that allows restoring lost or corrupted data in the event of a disaster or system failure. This can include the recovery of individual files or entire systems, and may involve restoring data from backup copies, retrieving data from remote data centres, or using other recovery mechanisms. A good DMS should include robust recovery services to ensure that important data is not lost in the event of a disaster or system failure. Appropriate features are automated backup and recovery, real-time data replication and a comprehensive data recovery plan that outlines how data will be restored in the event of an unexpected DMS failure

Non-technical specification/ vendor services	Description
Cost effectiveness	Refers to the balance between the implementation and use of a DMS and the associated costs. A DMS is considered cost-effective if the benefits it provides, such as increased efficiency, improved collaboration, and better document management, outweigh the costs of implementation, maintenance, and ongoing use. To maximize cost-effectiveness, organizations should carefully evaluate their needs and requirements when choosing a DMS, and select a system that provides the features and functionalities they require at a cost that is within their budget
Global implementation	Service to implement the software solution in all business units and in all affiliates worldwide
Prompt implementation	Ability of a software vendor to rapidly implement the software solution in the new enterprise, including all required vendor services, e.g. user training, migration services, customization programming, etc.

Sources: (14,45,42,52,58,59,62,63) (65,69,79,93,80,81,82) (87,86,91,94,92)

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Annex IV: Range of offered workflow features

Workflow feature	Description
Workflow definition	Allows individual workflow planning, creation of workflow templates for reoccurring processes and workflow execution
Rules and conditions management	Defines what conditions and settings have to be met for defined workflows and overall workflow management
Release procedures and functions	Enables workflows for approvals/releases and their programming (‘approval workflows’)
Workflow notifications	Notifies concerned users about workflow tasks and workflow progresses
Resubmission	Allows re-run of workflow if it has been rejected by users
Substitution scheme	Empowers co-workers to run workflows if targeted user is absent
Linking workflow-relevant documents	Links related documents that are important to concerned workflows
Ad-hoc workflows	Allows creation and execution of unplanned workflows for rare or unforeseen business processes
Copying/duplication	Facilitates the re-use of prepared or executed workflows for similar business processes
Workflow monitoring	Enables certain users or user groups to monitor ongoing workflows
Priority control	Displays to users the workflows that should be executed with priority / prioritized so as not to delay time-critical business processes
Graphic modelling/display of workflows	Facilitates intuitive handling of workflows

Workflow feature	Description
Library of workflows and workflow modules	Provides off-the-shelf standard workflows for the users
Support for workflow execution in another application (Lotus Notes, Outlook, etc.)	Allows controlling and executing workflows through other software applications by providing application interoperability with other business software solutions
Cross-company workflow	Enables third-party users to participate in specific workflows that aim to support cross-company business processes

Sources: (14,43,42,63,67,79,93) (80,81,82,92)

Annex V: Document types and formats supported by DMS/ECM solutions

- Office documents (e.g. OpenXML: docx, xlsx, pptx; ODF)
- PDF documents (e.g. PDF, PDF/A)
- Paper documents (e.g. PDF, PDF/A, after imaging)
- Emails
- Structured document formats (e.g. XML)
- Pictures and images (e.g. JPEG, JPEG2000, PNG, GIF, JBIG)
- Audio/video files (e.g. MPEG, MP3, MP4)
- Internet/websites (e.g. HTML)
- Miscellaneous (TXT, ODT, TIFF)

Sources: (13,42,78)

Annex VI: Clients and mobile clients supported by DMS/ECM applications

Clients

- Windows
- Web application/web client
- Thin web clients
- Linux
- MAC OS
- Other

Mobile clients

- iPhone
- iPad
- Windows mobile based devices
- Windows phone based devices
- Android-based devices (Google)

Sources: (42,79,93,80,81,82,92)

Annex VII: Offered cloud delivery models

- Public cloud
- Virtual private cloud – outsourced
- Private cloud – outsourced
- Private cloud – managed
- Hybrid cloud – outsourced
- Hybrid cloud – managed

Sources: (42,79,93,92)

Eidesstattliche Erklärung

Hiermit erkläre ich, Justin-Christopher Bell, an Eides statt, die Arbeit selbstständig verfasst und keine anderen als die angegebenen Hilfsmittel verwendet zu haben.

Ort, Datum	Unterschrift