European Medicines Regulatory Network
eSubmission Roadmap

V2.0

Final adopted version

This version is an updated, final version 2.0 adopted by EUTMB and endorsed by the HMA in February 2017

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1. Executive Summary

The electronic Submission (eSubmission) Roadmap aims at establishing secure, consistent and efficient electronic submission processes for medicinal products for human and veterinary use across the European Medicines Regulatory Network (ERMN or "the Network"). It aims at defining the way the regulatory information[1] on medicinal products is submitted by applicants electronically and received, validated, processed and distributed by regulatory authorities within the Network. It promotes open international standards and interoperable systems to support the exchange of data and documents.

Implementations listed in the eSubmission Roadmap utilise new technical opportunities to enable and facilitate new ways of collaborative business processes and the re-use of data throughout the medicinal product lifecycle.

All measures will lead to improved efficiency, less administrative burden and increased transparency through sustainable, fully end to end, electronic processing of information. It will also lead to an elimination of paper and physical electronic media.

The common agreed vision for the objectives on eSubmission outlined in this document underpins the decisions taken by the Network to implement the Roadmap.
The relevant components and milestones of the eSubmission Roadmap as well as the schedule are agreed by the Network, based on business requirements and taking into account feedback from pharmaceutical industry associations[2].
The objectives of the Roadmap should be achieved as a result of coordinated development and implementation activities as defined in this document.
Implementation of the eSubmission Roadmap has to be supported by clear and appropriate communication with stakeholders at International, European and National level.

2. Purpose

The eSubmission Roadmap is a high level strategic plan for business and technology change, typically operating across multiple disciplines over several years. It is a tool to align the plans of target groups and help National Competent Authorities (NCAs), EMA and pharmaceutical industry to prepare themselves to forthcoming changes. It clarifies objectives and activities to reach them. It sets a common timeline for development. It helps supporting strategic decisions and resource provisions. It is thus an important communication tool which helps to find a common understanding and commitment. It is therefore addressed to decision makers at executive management level.

The eSubmission Roadmap is the strategic driver and reference that guides the alignment of priorities, resources and commitment put behind implementation for the achievement of the eSubmission objectives. It is also incorporated into the EU Telematics Strategy.

3. Background

Although electronic submission of applications within the Network has increased, the uptake of a standard electronic format for dossiers[3] and the usage of electronic data have been slow[4].

[1] Regulatory information is understood as the complete set of documentation required by law for an application for marketing authorisation or any activity during the lifecycle of a medicinal product.
[2] EFPIA , Medicines for Europe (previously EGA), AESGP, EuropaBio, IFAH-Europe
[3] Electronic Common Technical Document (eCTD) and electronic Application Form (eAF)

In the human sector, electronic submission of applications is widespread. But non-standard electronic submission formats, including NeeS[5], are still largely used as an alternative format for submission of applications for medicinal products for human use.

In the veterinary sector, a specific electronic submission format, VNeeS,[6] has become the reference in the European Union for electronic submission of applications for medicinal products for veterinary use.

A number of initiatives have been undertaken to enable and improve the added value of eSubmission within the Network. For instance, EMA has required mandatory eCTD for applications of Centrally Authorised Products (CAP) for human use from 2010, the Network developed structured electronic Application Forms (eAFs) and HMA set up a Common European Submission Platform (CESP). These initiatives have been achieved with the support of the pharmaceutical industry.

The increase of regulatory requirements introduced by legislation has put the Network under strain and interoperability of systems has become the key for efficient use of data and resources. There was a need for the Network to establish a clear roadmap that would enable pharmaceutical industry and regulatory authorities to plan for the necessary investments and organisational changes.

In the current budgetary climate it is paramount for the Network to find ways to save human and financial resources to cope with the increasing regulatory workload and the electronic processes resulting from the implementation of the eSubmission Roadmap shall help the Network to work more efficiently.

4. The eSubmission Vision

In support of administrative, regulatory and scientific activities related to medicinal product regulatory applications the main objectives of the eSubmission Roadmap are:

1. Consistent, efficient, effective and secured electronic handling (creation, submission, reception, validation, processing and distribution) of information for all procedures throughout the life cycle of medicinal products.

2. Fully electronic processing without paper or any physical media.

3. Usage of structured data in submission processes which can be electronically processed and re-used by both authorities and industry.

4. Identical information made available to all authorities and eventually to one single repository.

5. Use and re-use of master data in eSubmissions where applicable.

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[4] The International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) published its first final version of eCTD in October 2003, allowing for the electronic submission of the Common Technical Document (CTD) from applicants to regulatory authorities. The Network implemented the eCTD EU Module 1 in July 2004, enabling electronic submission of eCTD in Europe.
The Heads of Medicines Agencies (HMA) committed in 2005 to be ready to receive, handle and process eCTD by the end of 2009.

[5] Non-eCTD electronic Submission (NeeS)

[6] Veterinary Non-eCTD electronic Submission (VNeeS)

6. Harmonisation of different message formats leading to a minimum set of electronic message types for the exchange of information.

7. One single entry point for submission of applications to all authorities.

8. Harmonised and reduced requirements for provision of metadata used in eSubmissions.

5. SPOR – Relevance for eSubmission Roadmap

SPOR (Substance, Product, Organisation, Referential) will play a major role in the use and re-use of master data in eSubmission systems.

Therefore, relevant requirements in eSubmission processes will be checked against SPOR deliverables/capabilities. This means that all relevant deliverables of the eSubmission roadmap have to be compliant with IDMP and SPOR standards. The usage of controlled terms from Referential Management Service (RMS), organisation identifiers or data from Organisation Management Service (OMS), substance identifiers or data from Substance Management Service (SMS) and product identifiers or data from the Product Management Service (PMS) must be taken into account in eSubmission processes.

This integration with SPOR will provide higher data quality, the possibility of increased process automation and is an important step towards harmonised data exchange worldwide.

6. Approach

The eSubmission Roadmap describes the current situation of eSubmission in the European Union and issues that need to be addressed. It identifies changes required and defines actions and deliverables with timelines to show progression from the current situation to the target situation in line with the eSubmission vision. In this updated version, it will also show milestones that have been achieved so far.
The scope of the eSubmission Roadmap covers electronic submission of regulatory information on medicinal products for human and veterinary use in all marketing authorisation and lifecycle procedures.

The EU Telematics Strategy of the Network has a broader scope and supports other regulatory activities involving electronic exchange of different types of regulatory information throughout the life cycle of medicinal products, e.g. Clinical Trials, Pharmacovigilance, Inspections, etc. It would align legislation, business needs and technical possibilities with available resources and provides open interfaces ensuring interoperability between centralised systems and national systems for data and documents with the aim to minimize total cost of ownership.

The vision applies to all procedures: European (Centralised, Mutual Recognition and Decentralised procedures) and National procedures. In the short term, priority was given to mandatory implementation of dossier formats for European procedures, one for human product dossiers (eCTD) and one for veterinary (VNeeS). In this updated roadmap, the Network also provides a plan for mandatory use of these formats in National procedures.

The long term objective of the Network is the implementation of common electronic exchange messages for submission of regulatory information for all medicinal products, in

line with international standards. However, specific approaches for medicinal products for human and veterinary use apply within the period covered by this roadmap. Implementing the HL7 RPS Standard[7] allows the same technology to be used regardless of how the content structure should look like (e.g. human and veterinary MA, clinical trials, cosmetics). Only different controlled vocabularies for Context of Use (equivalent to headings) and different keywords (replacing attributes) will be implemented.

A pre-requisite for successful implementation of the eSubmission Roadmap is that all authorities within the Network adopt the same vision, direction and priorities.
The eSubmission Roadmap is part of the overall EU Telematics Strategy developed and agreed within the Network in the framework of the EU Telematics governance structure. It is a key component for the management of transition as it is incrementally developed throughout the phases that cover organisation, processes, information technology and infrastructure.

6.1. Current Situation

This section provides high-level information on where we are, including identified issues.

Area	Current situation	Issues
Submission format	• Centrally authorised products: eCTD (human) and VNeeS (veterinary) • DCP: eCTD (human) and VNeeS (veterinary) • MRP: eCTD, NeeS (human) and VNeeS (veterinary) • NP: eCTD, VNeeS, NeeS other non-standard electronic formats and paper (human/vet)	• Various guidance, validation criteria and processes. • Inconsistent life-cycle management • Switch from one format to another • Non-electronic formats also exists
Submission media	• Paper • CD/DVD • CD/DVD + paper (wet signed paper still required in some NCA) • Electronic messages (documents attached to email or through portals)	• Different handling and means to give access to assessors. • Different processes and infrastructure for archiving • Preventing full electronic only submission for all applications

[7] Health Level 7 (HL7) is a Standardising Organisation jointly cooperating with ISO and ICH. Based on their methodology and toolbox a standard for messages has been developed supporting information and document exchange for any regulated product submission (RPS). The same methodological basis has been used for Structured Product Labelling (SPL) and the Common Product Model (CPM) both employed for the IDMP standards and the submission of medicinal product data.

Submission transfer mechanism	• By courier (CD/DVD and paper) • eSubmission through national portals using national specific registration modes and submission forms • Eudralink • email • eSubmission Gateway/Web Client (retrieved by NCAs via different repositories)CESP	• Multiple entry points • Various reception processes • Automation requires developing and maintaining several different solutions
Content format	• Mainly unstructured electronic format for content (PDF) • Documents are printed and scanned without OCR • Dynamic eApplication Form does not make full use of controlled vocabularies and requires further structuring. • Different data dictionaries across the Network • Lack of available common masterdata systems	• Low data availability for export into databases • Low usability for copy/paste and searching • Different data quality approach • Low data quality for export into databases • Prevent data exchange between databases (European and National)
Content requirements	• Specific national documents required in some countries. • National regulatory activities in MRP/DCP relevant to only one NCA (translations in national language, MAH transfer, Sunset Clause, etc)	• Prevent full harmonisation of the submission. • Prevent efficient handling of submission lifecycle
Processes across the Network	• Specific technical validation criteria (eCTD, NeeS, VNeeS) • Full validation of identical submissions by multiple NCAs • Differences between technical validation reports • Some NCA do not perform technical validation of electronic submissions • CVMP members for CAP and CMS for MRP/DCP receive electronic submissions before technical	• Maintaining of multiple validation criteria may lead to non-compliance of applications, additional exchanges and inefficiency.

	validation by EMA and RMS, respectively.	

6.2. Objectives

This section defines the high-level objectives in priority areas in line with the eSubmission Vision.

Area	Vision	Objectives
Submission format for dossiers	• For dossiers only one format with standards for human and veterinary submissions being just two variants of the same format	• eCTD (v.3.2) mandatory • VNeeS mandatory • Streamline life cycle management of submissions • Define implementation plan for HL7 RPS[8] based message standard utilisation for both human medicinal products (eCTD v4.0) and veterinary products to replace eCTD v3.2.2 and VNeeS respectively.
Submission format for information of medicinal products	• Enable electronic data exchange in business processes between partners and eliminate manual typing in/out of data • Re-use of master data	• Define a minimum set of data message formats describing medicinal products and procedural data • Align the different message formats (for example ICSR, Data Exchange Standards (DES) or XEVMPD) to minimise the effort of maintaining IT-systems processing exchange messages • Promote the automated data exchange in business processes • Integrate SPOR in all relevant implementations
Submission media	• Fully electronic processing of submissions	• Eliminate all physical media (paper, CD/DVD) and other electronic messaging systems such as EudraLink and local portals for regulatory submissions • Eliminate wet signed paper requirements or replace signature requirements by login access credentials.

[8] See footnote 7

Area	Vision	Objectives
Submission transfer mechanism	• One single entry point for secure electronic submission of applications to all authorities for downloading or for automated transfer to the national systems.	• Eliminate all physical media (paper, CD/DVD) • Implement single electronic submission channel for all submissions One single portal for all applications providing a shared service to create application datasets online or to upload application data and supported, wherever possible, by controlled vocabularies and master data and considering the ISO message standards (IDMP and future RPS) achieved by a stepwise approach
Common repository	• Establishing one repository for all procedure types and regulatory activities	• Applicant and all agencies use the same dossier (i.e. the same submission in the same lifecycle) • Missing submissions can easily be retrieved.
Technology of exchanging information	• One technical standard for exchanging information regardless of the content and the structure of the dossier	• Make use of the opportunities the HL7 RPS Standard[9] offers for exchanging information by using the same software and modifying only the controlled vocabularies and keywords. Make use of the SPOR data and avoid complex transitions due to hard-coded software changes
Content requirements	• Identical regulatory information available to all authorities	• Agreed handling of eSubmission for national specific documents and regulatory activities.
Content format	• Support to handle structured content electronically	• Reduce data inconsistency by implementing full systematic use of controlled terminology from RMS, Organisation data from OMS, Substance data from SMS and re-use of master data from PMS • Implement requirements and tools for structured authoring of content • Automate the extraction of structured information into databases
Processes across the	• Enable electronic end to end	• Provide guidelines to the Network to

[9] See footnote 7

Area	Vision	Objectives
Network	processes • Consistent validation of eSubmissions • Efficient and secure electronic handling of regulatory information	ensure electronic end to end processes can be realised • Common approach to technical validation • Validation of dossier and application datasets by EMA/RMS only Implement common repository for remote access to dossiers for review and download dealing with all procedure types

6.3. Roadmap

This section provides high-level information on how the eSubmission vision will be implemented, including detailed actions and estimated timeframes for completion of these actions subject to availability of resources within the Network and other priorities of the EU Telematics strategy.
The roadmap does not include all activities needed to fulfil the long term vision, but covers relevant activities and timelines for the nearest period. Further details for each area, detailing the requirements that have to be fulfilled in order to use and accomplish the deliverables, will be discussed within the eSubmission CMB and communicated to the full network and the stakeholders in due time.

Area	Objectives	Action	Deliverable	Timeframe
Submission format (Human use)	• Streamline the handling of submissions and life cycle management	• Require single electronic format for applications of medicinal products for human use	• eCTD only for New MAA's in DCP • eCTD only for New MAA's in MRP • eCTD only for <u>all</u> submissions in EU procedures (Note: baseline submissions are not required) • eCTD only for New MAA's submissions in National Procedures (Note: baseline submissions are not required) • eCTD only for all submissions in National Procedures (Note: baseline submissions are not	• **Done** • **Done** • **2018 Q1** • **2018 Q3** **See separate Annex for details** • **2019 Q1** **See separate Annex for details**

Area	Objectives	Action	Deliverable	Timeframe
			required) • Planning and preparing for implementation of eCTD v4.0 • Optional use of eCTD v4.0 in CP (timeline subject to outcome of the planning exercise) • Optional use of eCTD v4.0 in MRP and DCP (timeline subject to outcome of the planning exercise)	• **Ongoing** • **2019 Q3 TBC (human)** • **2020 Q3 TBC (human)**
Submission format (Veterinary use)	• Streamline the handling of submissions and life cycle management	• Require single electronic formats for applications of medicinal products for veterinary use	• VNeeS only for New MAAs in DCP and CP • VNeeS only for <u>all</u> submissions in EU procedures • VNeeS only for <u>New MAA's</u> in National Procedures • VNeeS only for <u>all submissions</u> in National Procedures	• **Done** • **Done** • **2018 Q3** • **2019 Q1**
Submission media and transfer mechanism (Human and Veterinary use)	• Eliminate all physical media and implement single submission form	• Implement Single EMA-NCA eSubmission Portal	• Mandatory use of EU eSubmission portal for all submissions • Stepwise approach to one integrated portal (CESP and eSubmission Gateway) with one single user registration • Mandatory use of the Common Repository for transmission of all CP Submissions to the NCAs (6 months after implementation)	• **TBD** • **2019 Q3** **See also 'Content format' section and separate Annex for details** • **Done (human)** • **2018 Q2 (vet)**

Area	Objectives	Action	Deliverable	Timeframe
			• Implement PSUR Repository in line with the new PhV regulation (human only) • Mandatory use of the PSUR Repository (for Industry and NCAs) (human only)	• **Done** • **Done**
Content requirements (Human and Veterinary use)	• Harmonised handling of content of eSubmission to the Network	• Agreed handling of eSubmission for specific national documents and regulatory activities	• Update eSubmission guidance together with relevant regulatory groups (CMDh, CMDv) • Implementing mandatory eCTD for all EU procedures (human only)	• **Done** • **2018 Q1**
Content format (Human and Veterinary use)	• Enable automated extraction of data into databases	• Complete the technical restructuring of eAF	• Step 1: Replace current AF template in word format published by the Commission with eAF for CP • Step 2: Replace current AF template in word format published by the Commission with eAF for all procedures • Step 3: Integration of Human and Vet new MAA eAFs into CESSP* • Mandatory use of CESSP* for new Human and Vet MAA (6 months after implementation) • Step 4: Integration of variation and renewal application forms into CESSP*	• **Done** • **Done** • **2018 Q1** • **2018 Q3** • **2019 Q3**

Area	Objectives	Action	Deliverable	Timeframe
			• Mandatory use of the integrated application form and submission for all submissions through CESSP*	• **2020 Q1**

* Project name CESSP may change at later once the system is being implemented.

6.4. Critical Success Factors

Factors that would enable timely implementation of the roadmap

Factor	Comments
Common understanding and agreement of National Competent Authorities and EMA to create consistent eSubmission architecture for the Network.	Consolidation of EMA and HMA EU Telematics development plans and programs in the framework of the EU Telematics governance structure.
Coordination between technical and regulatory work in order to find common solutions for eSubmission.	Interfaces between technical groups (e.g. IT DEC, IT Directors, EU TMB) and regulatory groups (e.g. CMDh, CMDv, NtAWG and HMA) should ensure sharing of eSubmission objectives and adapt guidance to support technical and regulatory implementation consistently and benefit from new technical and regulatory opportunities.
Agreement within the Network to deal with specific national documents and regulatory activities in eSubmission.	Alternative ways to link specific national documents and regulatory activities submitted electronically in order to handle the full life cycle management should be found.
Pharmaceutical industry awareness and readiness to implement the milestones within the given time frames.	The Network should broadly communicate on the roadmap at National, European and International level.
Implementation of standard terminology related to medicinal product information, e.g. active substances, pharmaceutical forms, routes of administration, MedID, etc.	International implementation of the maintenance process of ISO-IDMP standards for medicinal products for human use is underway. EUTCT database incorporates standard terminology relevant to the EU. The EUTCT maintenance process needs to be implemented across the Network before eSubmission can fully benefit from it.
Coordinated implementation of international exchange standards.	eCTD v4.0 is based on HL7 (Version 3) Standard: Regulated Product Submission Release 2 Normative and relevant Implementation Packages have been developed at ICH and in Europe for submission of regulatory information on medicinal products for human use. This new version uses a technology that would allow implementation for medicinal products for veterinary use as well. Benefits of this technology change should be realised in the Network by implementing according to

Factor	Comments
	an agreed plan.
Implementation of SPOR	Initiatives in the eSubmission Roadmap rely on implementation of SPOR data and therefore timelines and objectives must be aligned

7. Document History

Version	Date	Review
0.1	November 2012	TIGes, Industry associations feedback, TSG, HMA
0.2	March 2013	TIGes, TSG
0.3	April 2013	TIGes, TSG, HMA
0.4	May 2013	TIGes
0.5	June 2013	TIGes
0.6	June 2013	TIGes, TIGes Vet
0.7	June 2013	Distributed to TIGes members and published for consultation
0.8	May 2014	HMA (for endorsement) Distributed for comments to the chairs of CMDh and CMDv and also to the former TIGes members. Referred to eSubmission CMB for further update
1.0 draft	July 2014	eSubmission CMB (draft for endorsement) Distributed to IT Directors Executive Committee (endorsed 24 July 2014) Distributed for information to the IT Directors, the chairs of CMDh and CMDv and to the former TIGes members and also published at the EMA/TIGes eSubmission webpage Distributed to the EUTMB (adopted 1 October 2014)
1.0 final	November 2014	Final update by eSubmission CMB in section 5.3 (the introduction and delivery of PSUR Repository) in line with EUTMB decision For distribution to HMA, IT Directors, CMDh, CMDv and industry associations and for publication on web sites within the network.
1.1	December 2016	Final draft of an updated version by eSubmission CMB. Distributed to IT Directors Executive Committee for endorsement and then intended for further review by IT Directors, CMDh, CMDv and adoption by HMA and EUTMB.
1.2	January 2017	Updated draft version provided for comments to IT DEC. Sent to IT Directors, CMDh and CMDv for comments.
1.3	February 2017	Final draft version including comments from consultation. For adoption by EUTMB and for endorsement by HMA.

Version	Date	Review
2.0	February 2017	Final adopted version.

8. Change Record

Version	Timeline	Authors
Up to version 0.8	Up to June 2014	Karin Gröndahl, Klaus Menges, Kevin Horan, Miguel Bley, Juha-Pekka Nenonen, Pieter Vankeerberghen, Arian Rahj, Olivier Simoen, Kristiina Puusaari (members/chairs within TIGes)
1.0 draft	July 2014	eSubmission CMB members
1.0 final	November 2014	Changes as proposed by the EUTMB and EMA Management implemented in the document by eSubmission CMB
Version 1.1	December 2016	Karin Gröndahl, Klaus Menges, Kristiina Puusaari, Georg Neuwirther, Joerg Bredemeier, Anne-Christin Lantin (members of eSubmission CMB)
Version 1.2	January 2017	IT DEC, Klaus Menges, Karin Gröndahl, Kristiina Puusaari
Version 1.3	February 2017	Updated version after comments from members of IT Directors, CMDh, CMDv and of Human Harmonisation Group provided during consultation period. Klaus Menges, Karin Gröndahl, Georg Neuwirther, Anne-Christine Lantin, Kristiina Puusaari
Version 2.0	February 2017	Final adopted version prepared for publication Klaus Menges, Karin Gröndahl, Kristiina Puusaari.