

# Obsolete



EUROPEAN MEDICINES AGENCY  
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## EMA eSubmission Gateway: Questions and answers relating to practical and technical aspects of the implementation

This question and answer document aims to address the commonly-asked questions and provide guidance regarding technical and practical aspects of the European Medicines Agency's eSubmission Gateway for electronic submissions as part of the Centralised Procedure.

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7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom

**Telephone** +44 (0)20 7418 8400 **Facsimile** +44 (0)20  
**E-mail** [info@ema.europa.eu](mailto:info@ema.europa.eu) **Website** [www.ema.europa.eu](http://www.ema.europa.eu)

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## Objectives of eSubmissions via the Gateway

### ***Q1. What is the eSubmission Gateway? – Updated***

The EMA eSubmission Gateway enables applicants to submit via a secure Internet connection all eCTD format Centralised Procedure applications related to the authorisation and maintenance of medicinal products, e.g. new marketing authorisations, variations, renewals, PSURs, active substance master files (ASMF), Plasma Master Files (PMF) and PSUR single assessment procedures. It is based on the ESTR1 (Electronic Standards for the Transfer of Regulatory Information) gateway standard, which defines a secure data exchange service for regulatory information.

In addition to Centralised Procedure eCTD submissions it will be possible to submit the following procedure types from 1<sup>st</sup> of April 2014 via the eSubmission Gateway:

- All Referral procedures
- All types of Veterinary submissions
- All types of Paediatric submissions

### ***Q2. What is the objective of electronic Submissions via the EMA eSubmission Gateway? - Updated***

The Gateway offers Applicants an easier and quicker way of submitting eCTD and other electronic submissions securely over the Internet. The service is already offered by the European Medicines Agency for Eudravigilance and has now been available for the Centralised Procedure since 9<sup>th</sup> of January 2012 covering all eCTD submissions related to the authorisation and maintenance of medicinal products, including new marketing authorisations, variations, renewals, PSURs, active substance master files (ASMF) and Plasma Master Files (PMF). The scope is extended to cover Referral procedures, Veterinary submissions and Paediatric submissions from 1<sup>st</sup> of April 2014.

The use of the Gateway has significantly improved the Agency's efficiency in handling the submissions received and in making them available quickly within the European Review System (EURS).

### ***Q3. Which types of applications can I submit via the EMA eSubmission Gateway? - Updated***

From 1<sup>st</sup> of March 2014 eSubmissions Gateway service is mandatory for all Centralised Procedure eCTD format applications for Human Products, e.g. new marketing authorisations, variations, renewals, PSURs, active substance master files (ASMF) and Plasma Master Files (PMF). It has already been mandatory since September 2013 to use the eSubmission Gateway (or the Web Client) for the submission of the PSUR single assessment submissions for Nationally Authorised Products (NAPs). The EMA will further extend the use of these tools to all other submission types which currently are outside the scope of the eSubmissions Gateway.

### ***Q4. Is there another solution if our organisation has no access to the eSubmission Gateway Installation?***

The Agency also has the eSubmission Gateway Web Client, which is more suitable for low transmission volumes and which could be used by small and medium-sized pharmaceutical companies.

If you would like register to use the Web Client, please visit the registration [web page](#). If you would like to find out more about the Web Client please view the specific Web Client [Q&A document](#).

## Archival file formats and maximum size

### ***Q5. What archival file formats are available for submission via the Gateway?***

The submission package (including “working documents” if applicable) should be archived as a zip file (Encryption and Password should be disabled on the zip file). As soon as the submission package is received by the Gateway, it is encrypted. Other archival file formats are not allowed. The compressed application file must comply with the ZIP open format.

### ***Q6. Does the applicant have to zip the files or does the software do it automatically before the submission is sent?***

The applicant has to zip the files prior to sending them. The system does not accept packages that are not zipped.

### ***Q7. Does the EMA recommend any zip software to compress the submission sequence folder?***

Any software that can create a valid zip archive can be used. Some examples are winzip, 7z, winrar, the windows archive utility etc.

### ***Q8. Is there a maximum size for a submission made via the Gateway? – Updated***

We have tested the eSubmission Gateway up to 25GB (unzipped). If you have a submission bigger than 25GB, please [contact us](mailto:eCTD@ema.europa.eu) (eCTD@ema.europa.eu), so that appropriate measures can be put in place to successfully receive your submission. Additionally, it is recommended that any submissions that are bigger than 5GB are sent outside “peak hours” when the traffic is lower.

## File naming conventions

(For further details and common examples please refer to [Annex 1.](#))

### **Q9. What is the file naming format for submitting electronic Submissions via the eSubmission Gateway? – Updated**

The filename is used as a means of identifying specific information, allowing the Agency to automate processing of the submission once received.

The filename is broken down into different parts as described in the table below:

Data	Remarks	Case sensitive	Example
<b>SenderRoutingId</b>	Routing ID for Sender as registered by the Gateway, to route MDN receipt & Acknowledgement messages back to the sender.	Upper	ESUBPXYZ
<b>ReceiverRoutingId</b>	Routing ID for EMA's eSubmission Gateway Community, it's required for routing a transmission to its intended destination e.g. eSubmission Test and Production environments use "ESUBVAL" & "ESUBPROD" respectively.	Upper	ESUBPROD
<b>EMA Product No for Centrally Authorised Human Products</b>	e.g. EMEA/H/C/000000 (This must be a 6 digit number)	Upper	EMEAHC000999 or H011111 (Initial application)
<b>Product Name</b>	maximum 30 characters	Upper / Lower	Wonderpill
<b>Submission Type</b>	See list of eCTD Submission types (for CAPs) below	Lower	initial-maa
<b>Sequence Number</b>	0000-9999	N/A (should be numeric)	0020
<b>.zip</b>	.zip	Lower	.zip

#### **Filename Example:**

#### **In the case of Initial MAA:**

ESUBPXYZ\_ESUBPROD\_H011111\_Wonderpill\_initial-maa\_0000.zip

ESUBPXYZ\_ESUBPROD\_HC001111\_Wonderpill\_supplemental-info\_0001.zip

**Applicants are advised that the use of the EMA product number is mandatory. The number can be found in the EMA Eligibility confirmation letter**

#### **List of Submission Types:**

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Mandatory from 1<sup>st</sup> September 2013:

<http://esubmission.ema.europa.eu/eumodule1/index.htm>

EU Module 1 Specifications 2.0 (Appendix 1: The EU Module 1 XML Submission) – see Table 4 “List of Submission Types” e.g. initial-maa, var-type1a, rmp etc. (page 20, 21)

[http://esubmission.ema.europa.eu/eumodule1/docs/EU%20M1%201.4.1/EU%20M1%20v141\\_Spec%20\\_Nov2011\\_FINAL.pdf](http://esubmission.ema.europa.eu/eumodule1/docs/EU%20M1%201.4.1/EU%20M1%20v141_Spec%20_Nov2011_FINAL.pdf)

## Notes:

- Please use an underscore between each data item within the filename. The filename should not contain an underscore other than as a separator for the different components of the filename as shown below
- Do not use an underscore anywhere else other than between each data item of the filename.
- Do not use special characters or spaces in the individual data items of the filename. Acceptable characters are: a to z (upper or lower case), 0 to 9 and “-” (hyphen).
- The maximum number of characters of the filename should be 180.
- The “List of Submission Types” (see above) should be selected from the list [\(link\)](#) provided.

## ***Q9b. What is the file naming format for submitting PSUR single assessment CAP and NAP Submissions via the eSubmission Gateway? – Updated***

The filename is used as a means of identifying specific information, allowing the Agency to automate processing of the submission once received.

The filename is broken down into different parts as described in the table below:

Data	Remarks	Case sensitive	Example
<b>SenderRoutingId</b>	Routing ID for Sender as registered by the Gateway for identification MDN & acknowledgement messages.	Upper	ESUBPXYZ
<b>ReceiverRoutingId</b>	Gateway routing ID to differentiate this eSubmission from other application transmissions.	Upper	ESUBPROD
<b>EMA Product No (CAPs only)</b>	e.g. EMEA/H/C/000000 (This must be a 6 digit number)	Upper	EMEAHC000999 or H011111 (Initial application)
<b>Product Name (CAPs only)</b>	maximum 30 characters	Upper / Lower	Wonderpill
<b>Procedure number</b>	The 8 digit procedure number of the PSUR single assessment procedure for substances contained in both	N/A should be numeric	00000000

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	CAPs and NAPs included in the published EURD list (without the Data Lock Point)		
<b>Substance (for CAPs only)/ Nationally Authorised Product name</b>	Substance name as mentioned in the EURD list*/ For NAPs, replace the substance name by the Nationally Authorised Product name	Upper / Lower	Wondersubstance/ Nationalpill
<b>MAH</b>	MAH submitting the PSUR*	Upper / Lower	MAHname
<b>YYYYMM</b>	Month and year of the DLP	N/A should be numeric	201306
<b>Submission Type</b>	For PSUR Single Assessment always use psusa**	Lower	psusa
<b>Sequence Number</b>	0000-9999	N/A (should be numeric)	0020
<b>.zip</b>	.zip	Lower	.zip

## Filename Example:

### In the case of CAP included in the EU PSUR Single Assessment:

ESUBPXYZ\_ESUBPROD\_HCxxxxxx\_Wonderpill\_00000000\_Substance\_MAH\_YYYYMM\_psusa\_00xx.zip

### In the case of NAP included in the EU PSUR Single Assessment:

ESUBPXYZ\_ESUBPROD\_00000000\_NAPproductname\_MAH\_YYYYMM\_psusa\_00xx.zip

**Applicants are advised that the use of the EMA product number for Centrally Authorised products is mandatory. The number can be found in the EMA Eligibility confirmation letter**

\* For substance and MAH name, please use a 'short' name, maximum of 30 characters. Use only letters no special characters can be used in the file name. Underscore can be used to separate filenaming parts e.g. substance\_MAH; do not leave spaces or use special characters. For example for INFLUENZA VACCINE (SPLIT VIRION, INACTIVATED) / INFLUENZA VACCINE (SPLIT VIRION, INACTIVATED, PREPARED IN CELL CULTURES) use 'InfluenzaVaccine' or Pharmaceuticals Company International Limited use 'PharmaceuticalsCompany'.

\*\*Submission type 'psusa' is only to be used in the filename when submitting the PSUR single assessment submissions to EMA via the Gateway/Web Client. For eCTD submission type 'psur' should be used.

## Notes:

- Please use an underscore between each data item within the filename. The filename should not contain an underscore other than as a separator for the different components of the filename as shown below
- Do not use an underscore anywhere else other than between each data item of the filename.

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- Do not use special characters or spaces in the individual data items of the filename. Acceptable characters are: a to z (upper or lower case), 0 to 9 and "-" (hyphen).
- The maximum number of characters of the filename should be 180.
- The "Type" (see above) should be 'psusa'.

***Q10. What is the difference between Hxxxxxx and HCxxxxxx EMA product number that has to be used in the filenaming convention?***

The Hxxxxxx number is found in the Eligibility confirmation letter. This EMA product number consists of the letter H, followed by seven numerical digits. The HC number is only given after the application has been received by the EMA. This EMA product number contains letters HC (or occasionally "W" or "D" or "K") followed by **six** numerical digits. For the submission of the Initial sequence (0000) of a new MAA, the applicant should use HXXXXXX (six numerical digits, removing the first zero) and for any subsequent submissions, use HCXXXXXX.

**Example:**

In the Eligibility confirmation letter H0001234

In your filename this will become H001234

In subsequent submissions HC001234

***Q11. I registered before releases 2 and 3, do I need to change my routing ID?***

Gateway users registered before 2013 should use their existing routing ID.

***Q12. What is the file naming format for submitting Worksharing and Type IA (IG) Grouping applications? How should I submit Worksharing applications?***

For Worksharing and Type IA Grouping applications, applicants are required to obtain a "EMEA/H/C/WSxxxx" or "EMEA/H/C/IGxxxx" number (via email to [PA-BUS@ema.europa.eu](mailto:PA-BUS@ema.europa.eu)) in advance of submitting their Work-sharing or IA Grouping.

Applicants are required to ensure that each product for the same Worksharing is sent in separate zips. The Worksharing number should be always correctly referred to. Additionally, it is imperative that all products within Worksharing /IA Grouping (IG) are sent on the same day to ensure timely start of the procedure.

If one product in the Worksharing/IA Grouping (IG) fails during the transmission, only this part of the Worksharing /IA Grouping (IG) has to be re-sent. Content validation will only start when ALL parts of the Worksharing / IA Grouping (IG) have reached the Agency. The submission date of the Worksharing / IA Grouping (IG) will be the date of the last submitted product.

**Filename Example:**

**Worksharing:** ESUBPXYZ\_ESUBPROD\_HCxxx123\_Wonderpill\_WSxxxx\_00xx.zip

**Type IA Groupings (IGs) Example:** ESUBPXYZ\_ESUBPROD\_HCxxx123\_Wonderpill\_IGxxxx\_00xx.zip

Please go to [Annex 1](#) for further explanatory notes.

For EU PSUR Single Assessment, see Q9b.

**Q13. I received a 'failure' acknowledgment message; do I need to change my filename and the sequence number? Would using same filename create duplication?**

If your 'failure' acknowledgement is the result of using incorrect file name, please ensure that filenaming convention is followed and amend it accordingly.

However, if you receive 'failure' acknowledgement due to eCTD technical validation, the same filename and sequence number should be used. There will not be duplication as the initial package has not been uploaded in to the review system.

For example if the initial submission (sequence 0000) failed, the corrected submission should also be sequence 0000.

**Q14. How will the submission type in the file name affect validation? Will it lead to negative technical validation if incorrect submission type is used? - Updated**

It is recommended that the current specification of EU Module 1 is used when selecting a submission type. (Appendix 1: The EU Module 1 XML Submission) – see "List of Submission Types". e.g. initial-maa, var-type1a, etc submission types are used, however it will not result in negative technical validation.

Submission type 'psusa' must be used for EU PSUR Single Assessment procedure submissions.

Please refer to the link for relevant updates to EU Module 1:

[http://esubmission.ema.europa.eu/eumodule1/docs/EU%20M1%201.4.1/EU%20M1%20v141\\_Spec%200\\_Nov2011\\_FINAL.pdf](http://esubmission.ema.europa.eu/eumodule1/docs/EU%20M1%201.4.1/EU%20M1%20v141_Spec%200_Nov2011_FINAL.pdf)

For further details on the filenaming conventions, please see Annex 1.

**Q15. Is there a filename convention for working documents folder?**

The EMA recommends using 'xxxx-workingdocuments' where the number (xxxx) equals the sequence number.

**Q16. Does the EMA have any plans to revisit the filename convention to make it easier for the applicants?**

It is very important to get the filename correct. The EMA has carefully reviewed the mandatory elements and minimum requirements for the filename to allow the automated validation and the upload to the review system.

If you have any problems with the filenaming convention, please contact [eCTD@ema.europa.eu](mailto:eCTD@ema.europa.eu).

## Connection and registration process

### ***Q17. What is the connection and registration process required for submitting eSubmissions via the European Medicines Agency Gateway?***

First-time users must first register online via the registration [web page](#).

Once registered, test files must be sent for initial testing of connectivity in the External Compliance/Test environment before being enabled in the production environment.

To note: Applicants already registered for EMA's Eudravigilance (EV) Gateway community will have to re-register to use eSubmission gateway channel.

Once testing against the External Compliance/ Test environment is successful, the EMA will enable the applicant's Production profile and eCTD sequences and other submissions may be transmitted in the Production environment.

More guidance can be found under: <http://esubmission.ema.europa.eu/esubmission.html>

### ***Q18. My company has multiple names (i.e. Pharma Company and Pharma Company Europe) – do I need to register both as separate companies?***

There is no need to register them as separate companies; the same gateway identifier can be used for all companies from the same group.

### ***Q19. We are a consultancy/service provider representing multiple Marketing Authorisation Holders (MAHs). Does each MAH need to register to use the eSubmission Gateway?***

It is not necessary for each MAH to register. We only require one registration for the consultancy only; there is no need to register for each client.

### ***Q20. Can we have multiple users after the registration is complete?***

Once the registration is complete and testing has been verified you do not need to register multiple users.

### ***Q21. How do I update the list of registered products?***

There is no need to update the list of registered products. This is only requested so that during the registration the EMA registration team can confirm that the applicant has a product in the centralised procedure.

If you register before you have submitted your first initial submission for the centralised procedure, please indicate this in the field.

### ***Q22. How long does it take to register?***

The registration process can take up to 10 working days to be completed. It is crucial that the relevant technical information is provided to the EMA in order to complete the process.

## Technical questions

### **Q23. Which Gateway solution is used by the EMA?**

At the EMA we are using a product called Axway Synchrony Gateway Interchange (version 5.xx).

### **Q24. Which protocols should I use when transmitting eSubmissions via the European Medicines Agency Gateway?**

For information on Protocol types, please refer to the eSubmission website

(<http://esubmission.ema.europa.eu/esubmission.html>).

### **Q25. What is the Message Delivery Notification (MDN)?**

An automated Gateway MDN (Message Delivery Notification) message is sent to the applicant acknowledging receipt of the transmission. The MDN is equal to the signature upon delivery by the courier and only confirms that the package has been received by the EMA. It does not confirm that a technically valid (eCTD) submission has been received.

Users sending eCTD Centralised Procedure submissions will also receive an acknowledgement confirming the receipt and pass/fail of the technical compliance check as per the current eCTD validation criteria for all submissions. For failed submissions the error description can be found in the 'failure' acknowledgement (xml) and the submission has to be sent again.

**Please note: If the MDN message is not received the Applicant should stop transmitting and immediately contact the EMA Gateway support. The eSubmission should not be sent repeatedly and automated repeated transmission must be avoided.**

### **Q26. How long should we wait before attempting resubmission if the MDN has not been received?**

The waiting time depends on the size of the submission and the system load at the time the submission was sent. It might take from 5 minutes to 4 hours depending of the size of the submission. If you have not received the MDN after 4 hours, please contact EMA's gateway support at [gatewaysupport@ema.europa.eu](mailto:gatewaysupport@ema.europa.eu).

### **Q27. Which receipt should the applicant/MAH archive, the MDN or the acknowledgement as the official timestamp?**

The MDN is equal to the signature upon delivery by the courier and only confirms that the package has been received by the EMA. It does not confirm that a valid submission has been received. It is however, the timestamp in the MDN that is the time that confirms the delivery of the package to the agency. In the view of meeting the submission deadline the EMA must receive a technically valid package by midnight (23.59 hours) UK time on the day of the submission deadline. It is the responsibility of the applicant to ensure that a valid submission is provided to the agency.

**Q28. Where can I obtain certificates to enable mutual authentication to the EMA Gateway? Does EMA recommend an RSA based algorithm application or a service to generate a public key?**

The EMA provides its public key in a certificate to the companies, and the company provides its public key to the EMA. The company can purchase a certificate from recognised certificate providers, such as VeriSign, Thawte, Globalsign, etc. Most gateways provide the ability to generate a certificate which can also be used. The EMA's certificate is generated by the Axway Gateway. Your private key should never be made available to anyone.

**Q29. What is the recommended asymmetric key length (RSA algorithm)?**

2048 bits is the best choice for encryption key length.

**Q30. What is the difference between AS2 and AS3 Gateway?**

**AS2** (Applicability Statement 2) is a specification about how to transport data securely and reliably over the Internet over http.

**AS3** (Applicability Statement 3), is a standard by which vendor applications communicate over the Internet using File Transfer Protocol (FTP).

**Q31. If an MDN has been received does it mean that the EMA can open the submission successfully?**

No, applicants sending Centralised Procedure eCTD submissions must wait until they receive an acknowledgement confirming the receipt and pass/fail of the technical compliance check as per the current eCTD validation criteria for all submissions. For failed submissions the error description can be found in the 'failure' acknowledgement (xml) and the submission has to be sent again.

You should assume that the application has **not** been received by the EMA if you haven't received the acknowledgement. Please allow 5 minutes to 24 hours to receive the acknowledgement. If you have not received this, please contact EMA's gateway support at [gatewaysupport@ema.europa.eu](mailto:gatewaysupport@ema.europa.eu). In case of the Acknowledgements failure due to eCTD validation, please contact [ectd@ema.europa.eu](mailto:ectd@ema.europa.eu).

It is strongly recommended to send a test submission in the test environment to confirm the receipt of the MDN and the Acknowledgement.

It should be noted that acknowledgements are sent for eCTD submissions only where eCTD validation engine confirms the technical compliance of the submission.

Other types of submissions, such as paediatrics, Veterinary submissions and other non-eCTD submissions are not subjected to eCTD validation criteria and you'll receive MDN receipt, followed by an Acknowledgement (without eCTD Validation results), The applicants should wait for the usual validation letter if this is normally received before proceeding with sending submissions to (Co)Rapporteur and other member states.

**Q32. Do we need to inform the agency before sending a test submission?**

There is no need to contact the EMA before sending test submission in the test environment. All applicants that have registered to use the Gateway are also automatically registered to the External Compliance/Test environment.

The EMA strongly recommends new users to make full use of the test environment available before sending first submissions in the production environment.

**Q33. Where do I obtain the EMA certificate from?**

**External Compliance Testing Environment:**

An encryption certificate is needed to complete the online registration. Please download the EMA root certificate from the Public Website of the European Medicines Agency:

(<http://esubmission.ema.europa.eu/esubmission.html>).

**Production Environment:**

An encryption certificate is needed to complete the completed forms. Please download the EMA root certificate from the Public Website of the European Medicines Agency

(<http://esubmission.ema.europa.eu/esubmission.html>).

**Q34. What happens if the EMA eSubmission Gateway is not responding? Is there a plan how to deal with downtime of the eSubmission Gateway service?**

The EMA eSubmission Gateway has been implemented as a high availability system. The eSubmission Gateway service is included in the Agency's business continuity plan which foresees the recovery of the service in case of a disaster in less than 24 hours.

Downtime caused by planned maintenance periods will be announced 2 weeks before the planned maintenance for the production environment and 1 week before for the external compliance test environment.

If you have to urgently send a submission and the eSubmission Gateway is not working, please contact [eSubmission@ema.europa.eu](mailto:eSubmission@ema.europa.eu) and provide your telephone number for a call back during office hours.

**Q35. How will applicants know if there is a technical issue with their submission?**

Users will receive an acknowledgement confirming the receipt and pass/fail of the technical compliance check as per the current eCTD validation criteria for all submissions. For failed submissions the error description can be found in the 'failure' acknowledgement (xml) and the submission has to be sent again.

**Q36. Do the 'SUCCESS' or 'FAILURE' acknowledgments follow the P/F or Best Practice classifications in the Validation Criteria, i.e. wouldn't BP criteria errors result to a 'FAILURE'?**

Only the 'Pass/Fail' criteria is used to establish whether a submission is 'SUCCESS' or 'FAILURE'.

Please note that you may also receive 'Failure' acknowledgement if the incorrect filename is used.

**Q37. Is the DTD/Schema for the acknowledgement file available?**

The xml definition schema (xsd) is available and it will be published online on the eSubmission website.

**Q38. Why didn't I get an acknowledgement for the submission I sent via the Gateway?**

If you did not receive an acknowledgement or receipt it could be due to the following reasons:

- Check that the routing ID is correct and does not contain any additional spaces or typos
- Please check with IT support (Security) to ensure that the firewall access has been allowed to the following:

**pgateway.ema.europa.eu:4081**

**IP address 195.144.18.218**

A violation of above security rule will prevent the delivery of ACKs from EMA's gateway system.

You should assume that the application has not been received by the EMA if you haven't received the acknowledgement. Please allow 5 minutes to 4 hours to receive the acknowledgement. If you have not received this, please contact EMA's gateway support at [gatewaysupport@ema.europa.eu](mailto:gatewaysupport@ema.europa.eu).

**Q39. Is there any specific technical configuration required to receive the acknowledgment?**

It is recommended to send a test submission in test environment to confirm the receipt of the acknowledgement prior to sending your first submission in production.

**Q40. Our gateway has not been set up to receive acknowledgements. What happens with the acknowledgements you will be sending but not received by us? Do you follow the current workflow?**

Applicants are encouraged to configure their systems so that acknowledgements are received. It is recommended to send a test submission to confirm the receipt of the acknowledgement and configure the Production environment accordingly.

**Q41. How will companies know that submissions sent via the Gateway have been successful?**

Users will receive an acknowledgement confirming the receipt and pass/fail of the technical compliance check as per the current, harmonised eCTD validation criteria for all submissions. For failed submissions the error description can be found in the 'failure' acknowledgement (xml) and the submission has to be sent again.

**Q42. How long do we have to wait to receive an acknowledgement?**

The waiting time depends on the size of the submission and the system load at the time the submission was sent. Dependent on the submission size & transmission queue it can take anytime between 5 minutes to 24 hours maximum. If you have not received the acknowledgement in this time you should assume that the application has **not** been received by the EMA.

**Q43. Do we get MDNs (message delivery notification) and acknowledgements for all submissions sent via the Gateway?**

Yes, all submissions sent via the Gateway will receive a MDN and a separate acknowledgement message confirming the technical validity of each submission. It is only when a positive acknowledgement is received that you can be certain that your submission has been successfully received and uploaded in to the EMA's review system.

**Q44. What is the difference between an acknowledgement and a MDN (message delivery notification)?**

The purpose of the MDN is to confirm that your submission has been delivered to the EMA (a bit like the signature provided to a courier delivering a package). Acknowledgements are also provided for all submissions to confirm that they are technically compliant and have been imported in to the EMA's review system. For failed submissions the error description can be found in the 'failure' acknowledgement (xml) and the submission has to be sent again.

You should assume that the application has **not** been received by the EMA if you haven't received the acknowledgement. Please allow 5 minutes to 24 hours to receive the acknowledgement. If you have not received this, please contact EMA's gateway support at [gatewaysupport@ema.europa.eu](mailto:gatewaysupport@ema.europa.eu).

**Q45. Do I need to wait for the acknowledgement of the sequence to be received before sending the next sequence?**

It is best to await acknowledgements rather than sending multiple sequences all at once. This is especially relevant if one submission relates to another sequence. For example if sequence 0030 is related to sequence 0028, we must receive 0028 first.

**Q46. Does the gateway system accept 'Non-Sequential' order of submissions? i.e. can applicants submit Sequence 0014 after Sequence 0015?**

With exception of Sequence 0000, EMA gateway is able to handle submissions out of numerical order i.e Submission 0014 can be sent after 0015. Please note that Sequence 0000 cannot be sent after submission 0001, 0002 etc.

**Q47. What should we do if a negative acknowledgement is received?**

You should carefully review the error report attached in the acknowledgement, make necessary changes and resubmit the package. Please only contact the EMA on [ectd@ema.europa.eu](mailto:ectd@ema.europa.eu) if you are unable to resolve the issue. Should you need to contact the EMA please include as much description of the error as possible and/or the eCTD validation report for comparison.

'Failure' acknowledgements that are related to incorrect filenaming convention have to be amended according to the description in the [Annex 1](#).

**Q48. In which format the error information will be included in the acknowledgement, text format (words) or in XML code (<text>)?**

The error report is in XML and the DTD schema is available from the [eSubmission website](#).

**Q49. Does the EMA identify the number of files and folders received, similar to what the FDA sends in their second acknowledgement receipt?**

No, the EMA's Gateway does not yet have this feature.

**Q50. Will the acknowledgement have a specific filenaming convention? Or will we just need to identify via partnership routing naming?**

The product number and the sequence number are always included in the acknowledgement.

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***Q51. What if I realise there was a content error in the submission after receiving a successful acknowledgement and we wish to retract the submission and resubmit with correct content?***

Good care should always be taken prior to sending a submission, however, in the unlikely case that erroneous information was included in the submission package, please contact the EMA within hours, to request deletion from the review system. Retraction or deletion of a submission is dependent on the processing stage of that particular sequence.

***Q52. Which validation tool does EMA use? Which tool should we use to ensure the validation criteria is exactly the same?***

The EMA is using EURS validator. The TIGes validation rules should have been implemented in harmonised manner in all tools so applicants are free to choose which validation tool they prefer to use for their submissions.

## Cover letter and registration form

***Q53. Can I only submit applications for products I have registered on the eSubmission Gateway application form?***

No, you can submit all eCTD applications for all your products via the eSubmission Gateway once the registration process has been completed.

***Q54. When registering a consultancy, what products should we include in the registration form?***

When registering a consultancy it is not mandatory to include product name in the registration form, it is sufficient to state that you are a consultancy in the product name field. There is however no problem with providing a name of a product of one of your clients if you wish to do so.

***Q55. Do I need to include a hard copy Cover Letter / Registration form with submission sequences sent via the Gateway?***

There is no need for applicants to send an additional signed cover letter / Registration form in paper format as the transmitted dossier should already contain a signed and scanned electronic cover letter and relevant data (e.g. date and time). Date and time are stored on the Gateway server and the eCTD submission is loaded into EURS, where all the information can be retrieved at a later stage as required.

Please use the EMA published [cover letter template](#) for the submission in the context of the Centralised Procedure. The cover letter template should be inserted in Module 1 of the eCTD submission.

## General questions

### **Q56. What is the cost of the eSubmission Gateway for industry partners?**

The cost depends on the complexity of the configuration but usually starts at €10-15.000. Included in this cost is the software licence for the Gateway and a number of days of consultancy for the installation/configuration of the Gateway. There may be additional costs purchasing and setting up the necessary hardware/servers. A list of suppliers is available upon request.

### **Q57. What is the difference between the ESTRi Gateway and Web Client?**

#### *Features of the Web Client*

The Web Client is a free solution that offers an alternative option in order to give equal submission options to all applicants regardless of their IT budget. The Web Client uses Hypertext Transfer Protocol Secure (HTTPS) to ensure that submissions are sent securely. Users will be required to use a strong username and password authentication when setting up their Web Client profile.

The Web Client requires manual uploading of submissions and is therefore more suitable for lower transmission volumes

#### *Features of the eSubmission Gateway*

The EMA eSubmission Gateway enables applicants to submit all eCTD format applications via a secure Internet connection. It is based on the ESTRi (Electronic Standards for the Transfer of Regulatory Information) gateway standard, which defines a secure data exchange service for regulatory information. There is a cost involved to set up the Gateway service.

The Gateway allows multiple submissions to be sent concurrently with an optimum transmission speed. Applicants with larger submission volumes or automated workflows might wish to benefit from the automated features provided by the connection to the eSubmission Gateway.

A summary of the main features is shown below:

Feature	Web Client	eSubmission Gateway
Removes the need for submitting CDs / DVDs to the EMA	✓	✓
Allows the technical possibility (after relevant registration) to connect to other EMA Gateway communities		✓
Allows eCTD submissions	✓	✓
Encrypts submissions upon receipt by EMA Gateway	✓	✓
Free solution	✓	
Suitable for consultancies / affiliate companies as well as Marketing Authorisation Holders	✓	✓
Provides automated message delivery notification (MDN) / receipt	✓	✓
Provides confirmation of the submission's technical compliance	✓	✓

Compliant with ESTR I (Electronic Standards for the Transfer of Regulatory Information)		✓
Uses HTTPS (Hypertext Transfer Protocol Secure)	✓	
Accessible remotely via a website	✓	
Automated upload of submissions via custom development		✓
Suitable for transmitting multiple submissions		✓
Suitable for larger submission volumes		✓
Allows transmissions up to 25GB	✓	✓

**Q58. What is the criteria used to define small and medium sized companies?**

The Agency applies the definition of micro, small and medium-sized enterprises provided in Commission Recommendation 2003/361/EC. Therefore companies must in principle:

- be established in the EEA, and
- employ less than 250 employees, and
- have an annual turnover of not more than €50 million or an annual balance sheet total of not more than €43 million. Further details can be found here.

**Q59. Can I send additional Media (CD, DVD) along with my Gateway submissions? - Updated**

It is mandatory to use the Gateway or the Web Client for Centralised Procedure eCTD submissions from 1 March 2014. After this date we will no longer accept submissions on CD or DVD.

Submissions on physical media (CD/DVD) for referrals, veterinary submissions and paediatrics will continue to be accepted as an alternative method for the time being. However, it is essential that applicants only use one submission method and do not submit duplicate submissions on physical media or Eudralink as this might lead to a negative technical validation and cause a delay in processing the application.

**Q60. How do I ensure that I do not miss a submission deadline?**

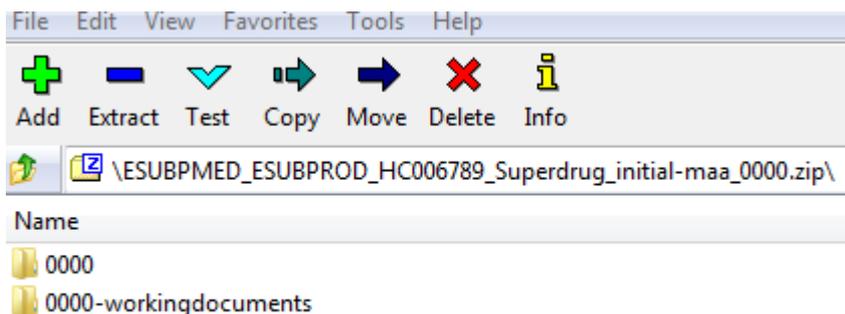
The EMA eSubmission Gateway sends an automatic MDN to the applicant as soon as the gateway has received the entire electronic submission file in eCTD format. The MDN is equal to the signature upon delivery by the courier and only confirms that the package has been received by the EMA. It does not confirm that a valid submission has been received. It is however, the timestamp in the MDN that is the time that confirms the delivery of the package to the agency. In the view of meeting the submission deadline the EMA must receive a technically valid package by midnight (23.59 hours) UK time on the day of the submission deadline. It is the responsibility of the applicant to ensure that a valid submission is provided to the agency.

Therefore it is recommended that the applicant sends the electronic submission file well in advance of the actual deadline. This is particularly relevant for submissions that are larger than 5GB.

## **Q61. How should I provide working documents?**

When working documents are submitted together with the eCTD sequence, the EMA recommends naming the folder 'xxxx-workingdocuments' where the number (xxxx) equals the number of the eCTD sequence being submitted.

You must ensure that the sequence number folder is a root folder in the zip file within the same Gateway transmission as shown below. This is required to help ensure that your submission passes the technical validation.



## **Q62. Is it still required to send eCTD sequences on hard media (CD/DVD) to the Rapporteur, Co-Rapporteur and all CHMP members for eCTD submissions in the Centralised Procedure when at the same time eSubmission Gateway is used for submission to the Agency? Or do all CHMP members have access to the Gateway? - Updated**

Yes, you must continue to send the submissions to the Rapporteur and Co-Rapporteur in accordance with the submission requirements of each National Competent Authority.

The EMA has developed a solution called Common Repository which enables the member states to access submissions sent to EMA in eCTD format within the scope of Centralised Procedure. The introduction of the Common Repository will enable National Competent Authorities (NCAs) to search, browse and download centralised procedure eCTD submissions for human products. An enhanced support period during which the Member States are enabled to receive submissions via the Common Repository is currently underway. The usual distribution channels should be used until the EMA will make announcements when each NCA has confirmed that they no longer need separate submissions on CD/DVD or via CESP.

Until this confirmation has been announced by the EMA, the applicants should continue to submit to rest of the network/NCAs as per the dossier requirements for CAPs. There are number of NCAs who now accept Centralised Procedure submissions via the [CESP](#) channel. Please see the details on '[Dossier requirements for CAPs](#)' document on [EMA website](#).

All applicants are reminded that once an eCTD is submitted through the eSubmission Gateway/Web Client it cannot be retracted for any reasons as it is automatically made visible and accessible for Member States via the Common Repository.

## **Q63. Do we have to use the Gateway for all submissions or is it possible to submit some via the Gateway and some via the CD/DVD media process? - Updated**

It is mandatory to use the Gateway and the Web Client from 1<sup>st</sup> of March 2014 for all Centralised Procedure eCTD submissions. It is also possible to use both, the Gateway and the Web Client, but you

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must not use both for the same submission as this will lead to negative validation and can cause delays in the handling of your application.

***Q64. We are already set up as we have used the Gateway before – do we still need to register?***

Registration is required as e-Submissions has its own community of users, and is not a part of EVTEST or any other existing community. The eSubmission Gateway has its own transport URL and certificate.

***Q66. Is it mandatory to fill in the eCTD envelope for each submission sent via the eSubmission Gateway?***

Yes, the current [eCTD guidance](#) applies to all Centralised Procedure submissions regardless of the submission channel used (Gateway, Web Client).

It should be noted however that submission in NeeS format is allowed for Nationally Authorised Products included in the EU PSUR Single Assessment Procedure (PSUSA) and for ASMF submissions that have not previously been submitted in eCTD format.

## Glossary

<i>Term</i>	<i>Definition</i>
Applicant	A pharmaceutical company or its agent that is submitting information in support of an <b>application</b>
ESTRI Gateway	Electronic Standards for the Transfer of Regulatory Information
Procedure	The centralised registration procedure for the authorisation and maintenance of medicinal products in the European Union. There are 4 types of procedures that operate within the EU – The eSubmissions via the Gateway is only dealing with the Centralised Procedure
Submission	A single set of information and/or documents supplied by the applicant as a part of, or the complete, Application. In the context of eCTD, this is equivalent to ' <b>sequence</b> '
External Compliance Test Environment	External Compliance Test Environment is used to test the compliance of a new applicant from pharmaceutical industry with the EMA's eSubmission Gateway system
Production environment	Production environment is used for live production
Web-based client	A Web-based client/server network is a computer communication system, in which client computers send requests to the server computer for data from its database, and the server returns the results to the clients via Internet/WWW

## Contact us

To register:

<https://esubregistration.ema.europa.eu/registration/>

For technical queries and failures with regards to gateway set-up or Acknowledgements deliveries in the Test or Production environment:

[gatewaysupport@ema.europa.eu](mailto:gatewaysupport@ema.europa.eu)

If you have eCTD validation related issues or non-technical questions that are not adequately addressed by this document, please forward your query or comment to [eCTD@ema.europa.eu](mailto:eCTD@ema.europa.eu)