

eCTD Implementation Survey Report

By the Spanish Presidency of the EU - 2010

(Covering the period from July 2009 to December 2009)

Introduction

ICH-eCTD is an internationally driven standard designed to reduce cost in the administration, assessment and archiving of applications for marketing authorisation of medicinal products for human use, reducing the use of paper and streamlining the assessment process.

At the February 2005 meeting of the Heads of Agencies (HMA) in Reykjavik, heads committed to a target of end of 2009 for the implementation of eCTD, meaning that the European Medicines Regulatory Network would be ready to accept “paperless”¹ applications for marketing authorisation in eCTD format by that date. National Competent Authorities (NCAs) would therefore need to have the infrastructure, the processes and the legal framework in place to handle paperless applications in eCTD format efficiently.

NCAs have been progressively adapting their infrastructure, processes and legislation to be able to receive and handle paperless applications for marketing authorisation.

The Telematics Implementation Group for Electronic Submission (TIGes) has been developing and updating guidance for implementation of eCTD in the European Union in line with the International Conference for harmonisation (ICH) standard and European CTD guidance produced by the European Commission.

Acknowledging the fact that ICH has not developed CTD for the veterinary sector and therefore there is no Marketing Application dossier that is applicable in all ICH regions, the TIGes has set up a subgroup to develop guidance for electronic submission of applications for marketing authorisation of medicinal products for veterinary use in line with European guidance.

Heads of agencies of the veterinary sector joined heads of the human sector in its commitment to be ready to accept paperless marketing authorisation applications by the end of 2009.

At the November 2007 HMA meeting in Madeira HMA asked the TIGes to conduct a regular survey of implementation of eCTD and to produce a report twice a year. The goal of the survey is to monitor the evolution of readiness of the Network with a view to following progress towards paperless operation. The survey report would include comparative results relevant to submissions in the human sector and would be updated every second HMA meeting of each European Presidency of the Council.

This is the fifth version of the Survey Report and covers progress of the Network in terms of paperless operation until the end of 2009, the target date committed by HMA at Reykjavik.

¹ Paperless applications mean without paper except for documents where a signature is required. Since there is no digital signature standard in the EU yet signed documents may still be required in paper.

Methodology

A questionnaire has been elaborated by the TIGes and circulated among all of its members (see Annex 1).

The questionnaire has been divided into two parts, one on readiness for acceptance of paperless applications of marketing authorisations and another on numbers of applications for marketing authorisation received in all formats (paper, eCTD and other electronic formats) during the period covered by the survey. The Survey Report covers findings over a six month period under the latest European Presidency of the Council. It is the member of the TIGes from the Member State that holds the current Presidency that collates all the responses to the questionnaire into an "Outcome Spreadsheet" that becomes the source to produce the Survey Report.

Results are presented with graphs showing the consolidated figures provided by all EU regulatory authorities covering either two periods of six months (the latest and the previous semester of each year) with bar graphs or four periods of six months with curves showing a longer term trend. Tables show numbers of submissions as absolute values and percentages of total applications in any format, and for all procedures. They show cumulate results over 12 months and the evolution between the two latest covered six month periods.

Since not all NCA have the infrastructure in place to record the format of applications (paper or electronic) and the criteria to validate different types of electronic format are still not commonly implemented it was requested to indicate in the questionnaire whether figures are the result of exact counting or of rough estimations. The overall estimation rate is reported in the survey, as well as the response rate for each question.

Finally, the requirement of additional paper copies when applications are received in electronic format is also reported.

Outcome

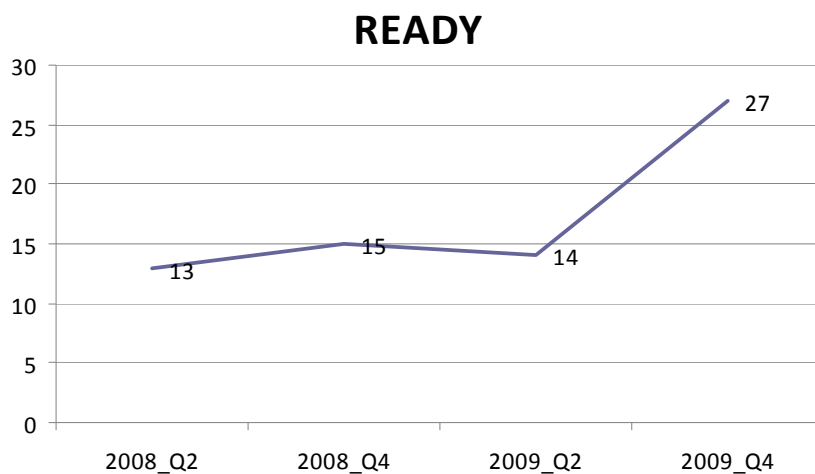
All 32 regulatory authorities (NCA + EMA) of the European Medicines Regulatory Network competent for medicinal products in the human sector responded to the questionnaire.

Questionnaire response rate: 100%

Readiness

Q1.A - % of authorities ready for management and evaluation of marketing authorisation applications in electronic format only.

Question response rate: 100%

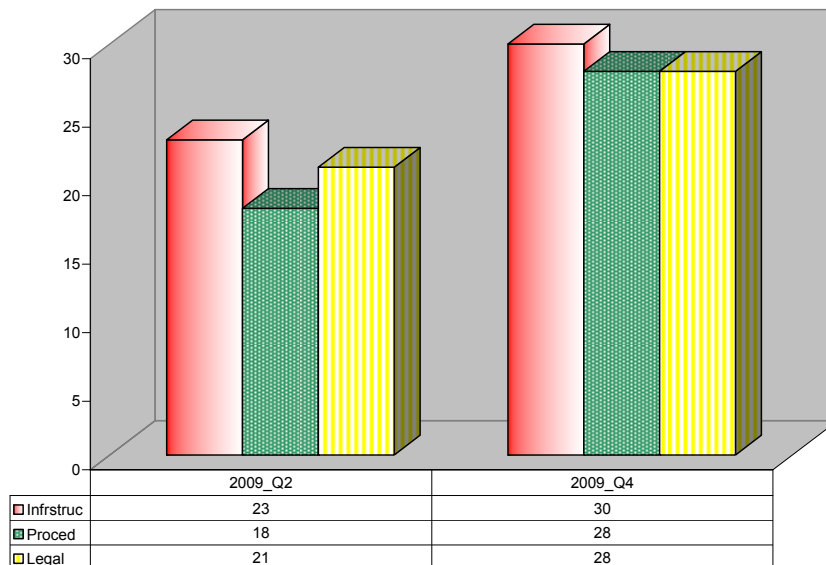


Results:

- **84% of EU Regulatory authorities are ready for management and evaluation of marketing authorisation applications in electronic format only (+ 93%).**

Q1.B - % of authorities that have fulfilled the aspects identified as key for eCTD implementation: Infrastructure, Processes and Legal framework for paperless management of Marketing Authorisation applications.

Question response rate: 100 %

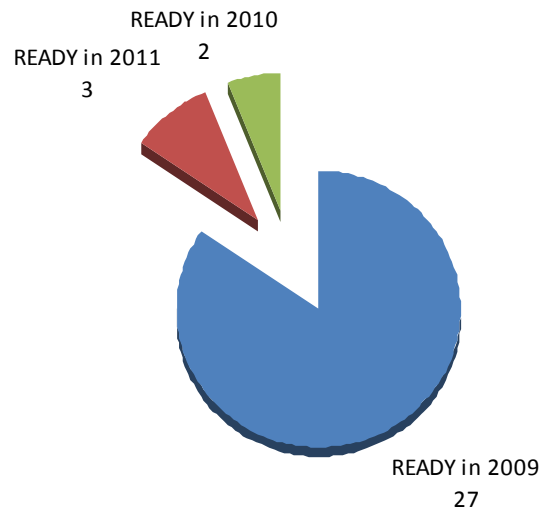


Results:

- **94% of EU regulatory authorities have the infrastructure for paperless management of Marketing Authorisation applications (+ 30%).**
- **88% of EU regulatory authorities have the processes in place for paperless management of Marketing Authorisation applications (+ 56%).**
- **88% of EU regulatory authorities have the legal framework in place for paperless management of Marketing Authorisation applications (+ 33%).**

Q2 – When do EU regulatory authorities that are not ready expect to be ready for management and evaluation of marketing authorisation applications in electronic format only?

Question response rate: 100%

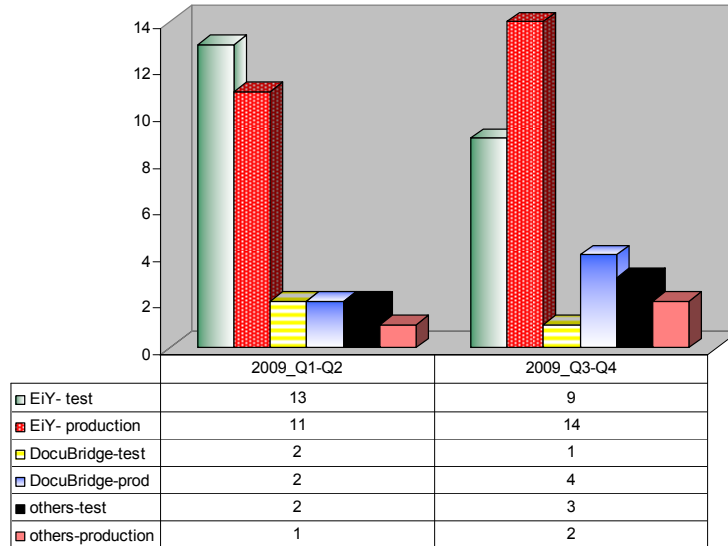


Results:

- **15% (5) of EU regulatory authorities are not yet ready for management and evaluation of marketing authorisation applications in electronic format only. They responded to the question Q2 as follows:**
- **6% (2) EU regulatory authorities expect to be ready in 2010**
- **9% (3) EU regulatory authorities expect to be ready in 2011**

Q3 – % of authorities that are testing a tool for review of eCTD or that have a tool in production (the tool is identified).

Question response rate: 100%

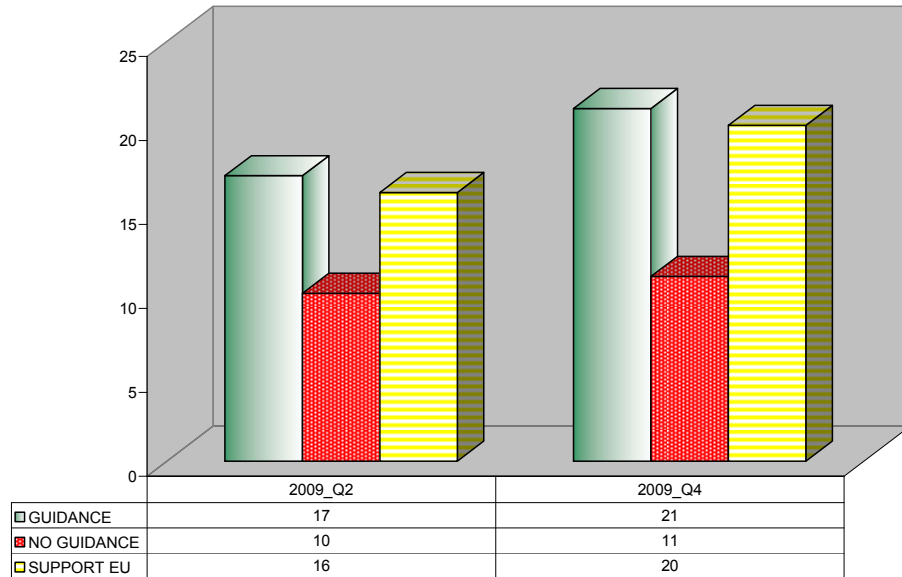


Results:

- **91% (29) of EU authorities have a tool for review of eCTD installed (+ 3%)**
- **63% (20) of EU authorities have a tool for review of eCTD in production (+ 19%)**
- **28% (9) of EU regulatory authorities are testing a tool for review of eCTD (-16%)**
- **72% (23) of EU regulatory authorities have EiY installed (- 1)**
- **16% (5) of EU regulatory authorities have Docubridge installed (+1)**
- **16% (5) of EU regulatory authorities have bespoke tools installed (+2)**

Q4 – % of EU regulatory authorities that have national guidance and/or that support published EU guidance on submission of marketing authorisation applications in electronic format.

Question response rate: 100%

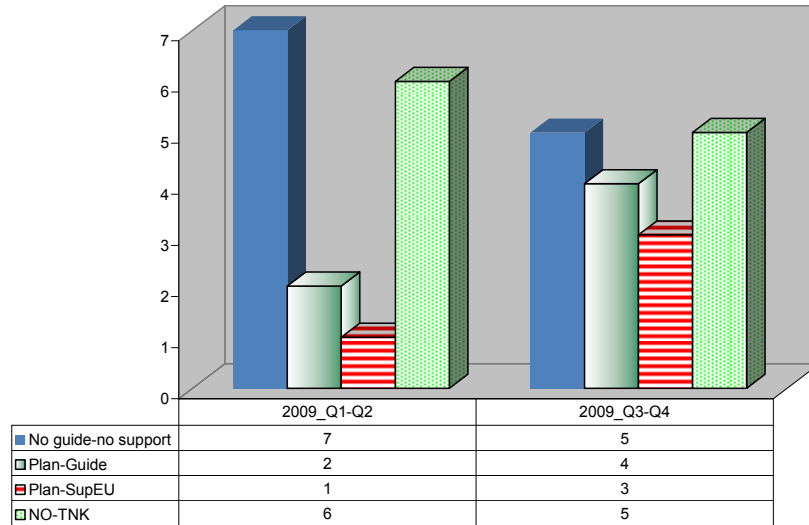


Results:

- **66% of EU regulatory authorities have national guidance (+24%)**
- **63% of EU regulatory supports published EU guidance (+25%)**

Q5 – When do EU regulatory authorities that have no national guidance and do not support EU guidance on submission of Marketing Authorisation applications in electronic format expect to have/support guidance?

Question response rate: 100%



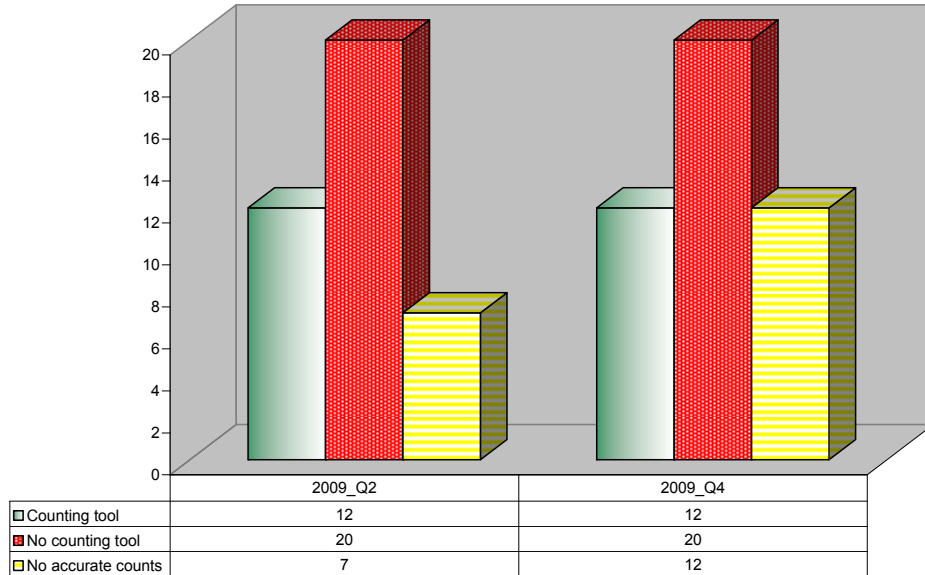
Results:

- 16% (5) of EU regulatory authorities do not have national guidance and do not support EU guidance on submission of Marketing Authorisation applications in electronic format yet (- 6%).
- 13% (4) EU regulatory authorities expect to have national guidance in 2010
- 9% (3) EU regulatory authorities expect to support EU guidance in 2010
- 16% (5) of all EU regulatory authorities do not know when they will publish national guidance or support EU guidance (TNK: Timeline Not Known).

Statistics

Q6- Availability of tools for regular gathering of numbers of applications received in electronic format

Question response rate: 100%



Results:

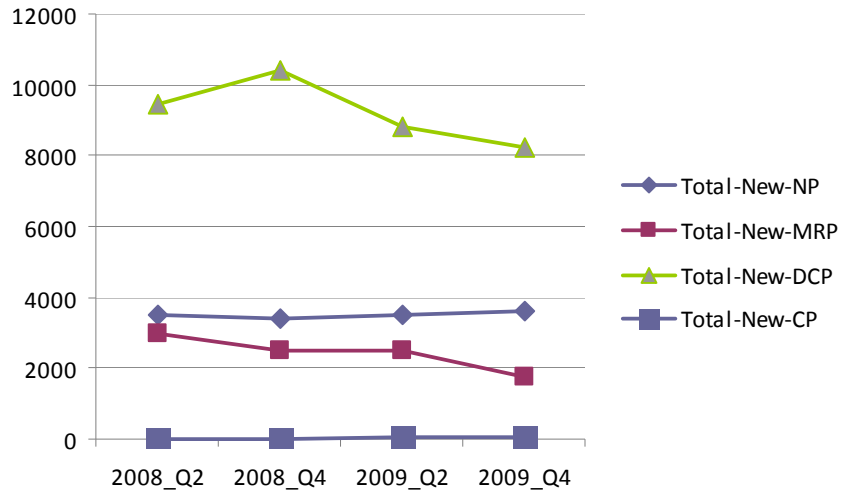
- 38% of EU regulatory authorities have a tool for regular gathering of numbers of applications received in electronic format (no change).
- 63% of EU regulatory authorities declare being unable to provide accurate figures on applications received in electronic format (no change).

Reliability	Total applications				Electronic applications			
	NP	MRP	DCP	CP	NP	MRP	DCP	CP
% estimates Q1-Q2	18	8	3	100	58	54	52	100
% estimates Q3-Q4	9	0	0	100	41	38	38	100

In spite of an improvement on the reliability of the figures provided by Member States, overall 50% of figures are the result of rough estimates of the number of submissions. No error margins can be calculated and results should not be considered as accurate. The Survey Report only shows main trends of the implementation of electronic submission in the European Union.

Q8 – Total number of New Applications

Question response rate: 100%

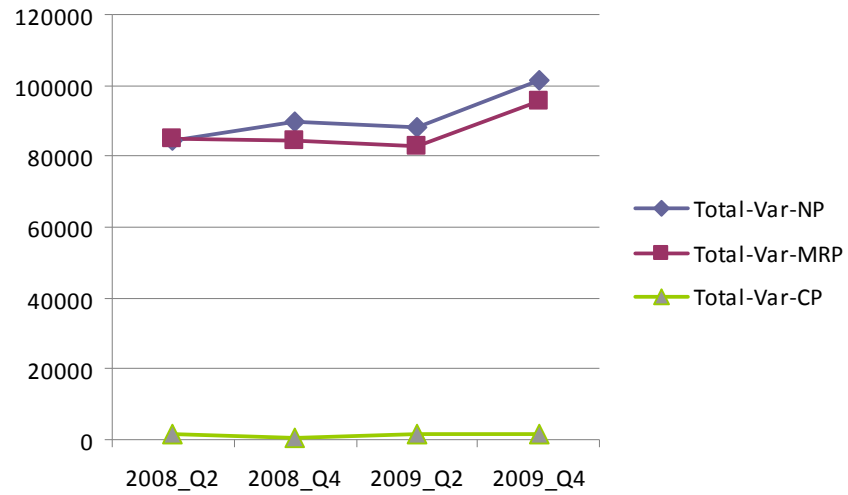


Cumulative results

	12 months	Δ 6 months
New-NP	7110	3%
New-MRP	4270	-29%
New-DCP	17044	-7%
New-CP	60	0%
Total-New	28484	-8%

Q9 – Total number of Variation applications

Question response rate: 100%

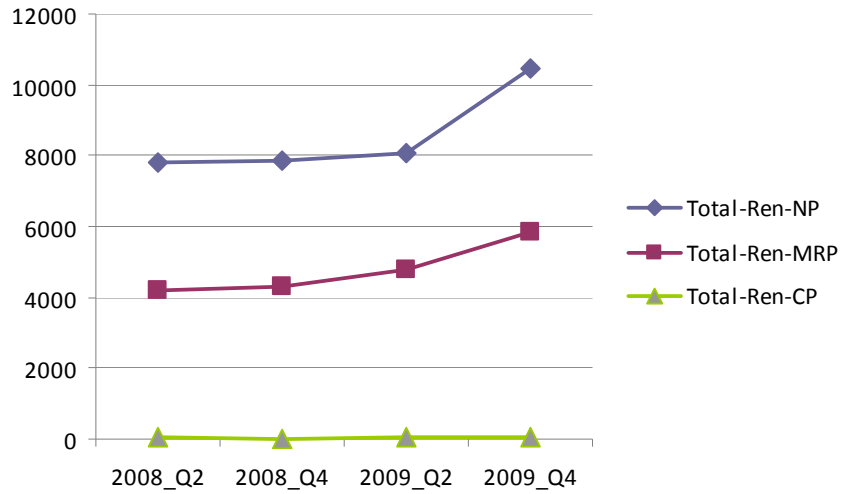


Cumulative results

	12 months	Δ 6 months
Var-NP	189414	15%
Var-MRP	178077	15%
Var-CP	3000	0%
Total-Var	370491	15%

Q10 – Total number of Renewal applications

Question response rate: 100%

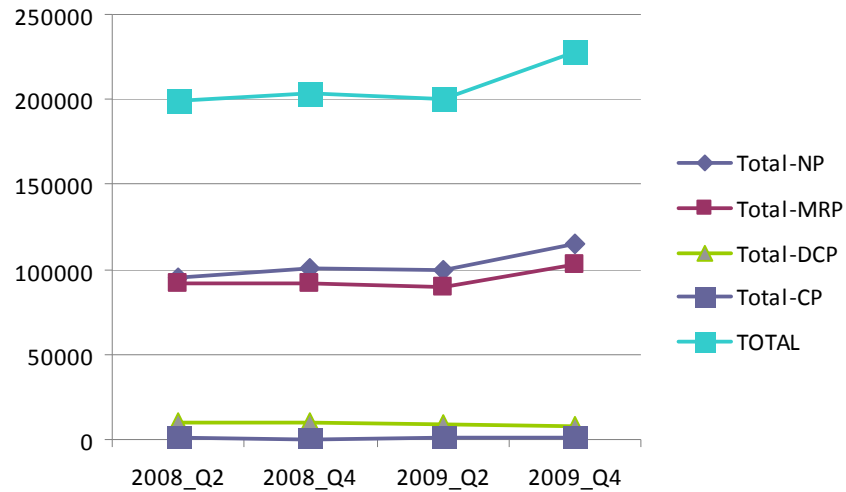


Cumulative results

	12 months	Δ 6 months
Ren-NP	18495	30%
Ren-MRP	10621	22%
Ren-CP	120	0%
Total-Ren	29236	27%

Q10 – Total number of applications per procedure

Question response rate: 100%



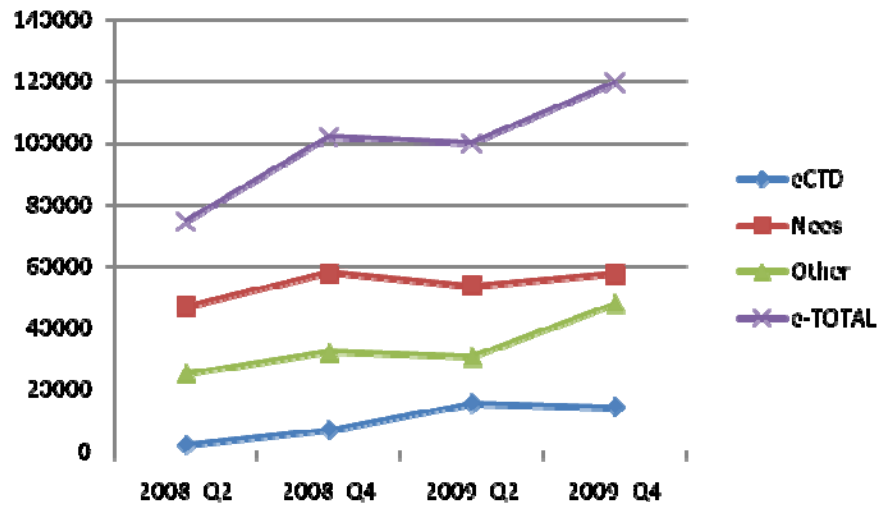
Cumulative results

	12 months	% of TOTAL	Δ 6 months
Total-NP	215019	50%	16%
Total-MRP	192968	45%	15%
Total-DCP	17044	4%	-7%
Total-CP	3180	1%	0%
TOTAL	428211	100%	14%

Q11-Q13 – % of total applications received in electronic format and distribution across formats and procedures.

Question response rate: 100%

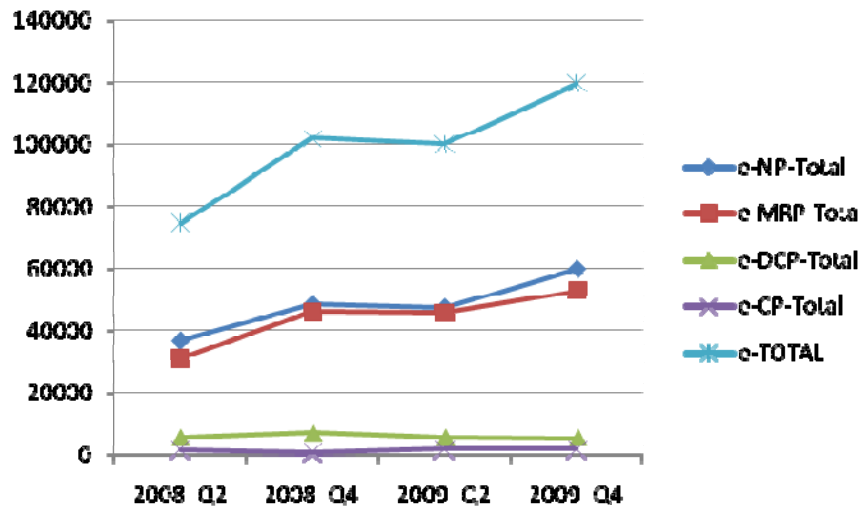
Distribution across formats



Cumulative results

	12 months	Δ 6 months	% e-Total
eCTD	29954	-7%	14%
Nees	111298	7%	50%
Other	78285	56%	36%
e-Total	219537	20%	100%

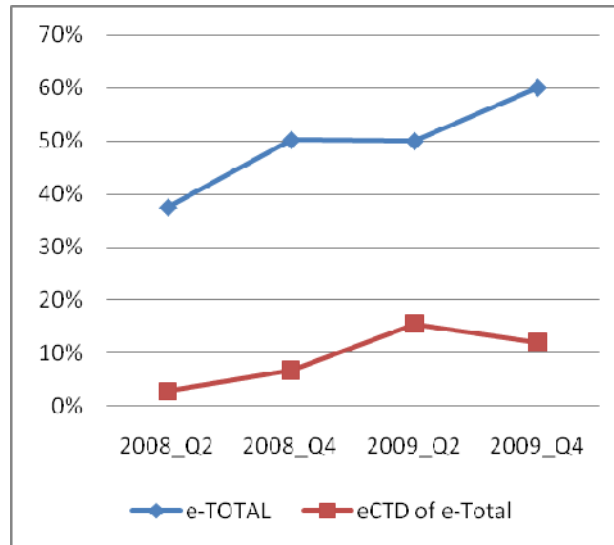
Distribution across procedures



Cumulative results

	12 months	Δ 6 months	% of TOTAL
e-NP-Total	107075	26%	50%
e-MRP-Total	98284	16%	51%
e-DCP-Total	10998	-1%	65%
e-CP-Total	3180	0%	100%
e-Total	219537	6%	51%

Evolution of e-Submission and of eCTD

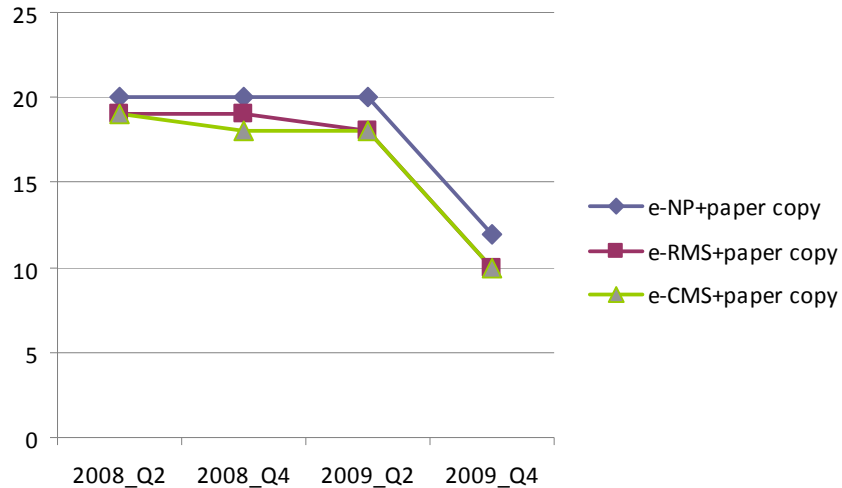


Cumulative results

	12 months	Δ 6 months	% of TOTAL
eCTD-NP	8501	-39%	4%
eCTD-MRP	16264	7%	8%
eCTD-DCP	3555	23%	21%
eCTD-CP	1634	0%	51%
eCTD-Total	29954	-7%	7%

Q14 – Paper copies required for applications through NP or MRP received in electronic format.

Question response rate: 100%

**Results:**

- **38% (12) of EU regulatory authorities still require paper when an application through the NP is received in electronic format (- 40%)**
- **31% (10) of RMS EU regulatory authorities still require paper when an application through the MRP is received in electronic format (- 44%)**
- **31% (10) of CMS EU regulatory authorities still require paper when an application through the NP is received in electronic format (- 44%)**

Conclusions

The number of EU regulatory authorities that were ready for paperless management and evaluation of marketing authorisation applications in electronic format at the end of 2009 almost doubled during the second half of 2009 reaching 84% of the Network. 5 authorities missed the target and were not ready at the end of the year. Of these 5 EU authorities, 2 planned to be ready in 2010 and 3 in 2011.

Around 90% of the EU authorities have key aspects of implementation such as infrastructure, processes and the legal framework in place for paperless operation and 2 thirds have national guidance on electronic submission or support EU guidance. However, there is still a way to go in terms of appropriate review tools for the review of electronic dossiers.

Still 10 of EU authorities are testing tools and only 18 have a tool in full production. In spite of a significant reduction of paper requirements during the period covered by the survey still 10 to 12 EU authorities require paper to be submitted together with the electronic submission.

These results show that the progress made by the Network since HMA committed to go paperless has been very significant, but that there is still some way to go to reach the original goal.

Total applications for marketing authorisation increased during the covered period, in particular variations and renewals and in the national and mutual recognition procedures.

Submissions in electronic format increased overall, but the increase seems to be mainly due to submission of non-standard formats (tagged as "other"), most likely in the national procedure. eCTD submissions decreased slightly compared with the previous period and is mainly used in the centralised and the decentralised procedures. However, its part in total submissions for marketing authorisation in the European Union remains low (7%). 86% of electronic submissions were received in NeeS or other formats.

At the October 2009 HMA meeting HMA requested the TIGes to organise an e-readiness workshop in the margins of an HMA meeting early in 2010 to address the issues and increase networking among Member States to overcome the difficulties. Implementation is already at a stage where it is necessary to increase significantly the rate of marketing authorisation applications in electronic format, and in particular in eCTD format. HMA would look into ways to promote electronic submission by industry.

The main areas where progress seems to be needed are the implementation of reliable review tools by EU authorities involving training of assessors with a view to broadening implementation in Member States and the harmonisation of validation criteria. Both areas are linked together since the available review tools include validation engines, but interpretation of criteria differ between tools and is not consistent between each other. Stand alone validation tools also exist, but criteria need to be refined.

HMA acknowledged that the increase of national on-line portals that would eventually replace the electronic submission on physical media may represent an issue and a source of duplication of work. Therefore HMA is conducting a feasibility study on the development of a Common European Submission Platform that may in the future streamline the processing of electronic submission in the European Union.

It is acknowledged that the Survey Report is not released timely enough to constitute reliable guidance for applicants and Member States and other ways to communicate progress to stakeholders should be found. HMA agreed to update information on e-readiness on its website at shorter intervals and link it with national requirements published by the CMD(h).

HMA would endeavour to complete the paperless implementation across the Network in 2010 and focus not only on improving the capacity of EU authorities to process and review electronic submissions, but also on increasing the numbers of electronic marketing authorisations applications in electronic format.

Annex 1 EU eCTD Implementation Questionnaire (Rev 20090130)

Who is/are the contact(s) in your agency for eSubmission/eCTD?

(N.B If the contact point is not the TIGes member, it is the responsibility of the TIGes member to identify and provide details of the appropriate colleague(s))

Name:

Position:

Email:

TIGes member? Yes

No

Readiness

Q1: Is your agency ready for management and evaluation of Marketing Authorisation *applications* in electronic format only²?

(a) Yes

(b) No

If the answer to Q1 is No, please indicate which aspects of implementation are already solved:

(a) Infrastructure

(b) Processes

(c) Legal framework

(d) Other (Specify.....)

Q2: If the answer to Q1 is No, when does your agency plan to be ready for management and review of the Marketing Authorisation *applications* in electronic format only?

(a) Month/Year:

(b) Timeline not known

Comments:

Q3: Does your agency have a tool(s) for review of eCTD?

(a) Yes

(b) No

(c) If yes, please indicate which tool(s):

• Eurs is Yours (EiY) Test Production

• DocuBridge Test Production

• Other, specify :

• Test Production

Comments:

Q4: Does your agency have any published national guidance and/or support EU published guidance for applicants on submission of Marketing Authorisation *applications* in electronic format?

(a) Yes National guidance EU guidance

(b) No

(c) If yes, please indicate link(s) to guidance:

• National

• EU

Comments:

² “Electronic format only” means without paper except for documents where a signature is required. Since there is no digital signature standard in the EU signed documents may still be required in paper.

Q5: If the answer to Q4 is just No, when does your agency plan to publish national guidance/support EU guidance for applicants on submission of electronic Marketing Authorisation *applications* in electronic format?

- (a) Publish national guidance Month/Year: Timeline not known
 (b) Support EU guidance Month/Year: Timeline not known
 Comments:

Q6: Does the IT infrastructure in your agency allow for regularly gathering of details/statistics on numbers of *applications* received in electronic format (eCTD and Nees)?

- (a) Yes
 (b) No
 Comments:

Q7: If the answer to Q6 is No, would the lack of such functionality prevent you to gather the details/statistics on numbers of *applications* received in electronic format twice a year (e.g. manually)?

- (a) Yes
 (b) No
 Comments:

Statistics

Six months statistics on processed marketing authorisation applications are requested. Please indicate the period considered for which information is available from [MM/YYYY] to [MM/YYYY] (ex: 06/2007 to 12/2007). If the period for which figures are available is shorter or longer the figures will be recalculated on a six month basis for comparison and reporting purposes.

Figures will be reported in the eCTD Roadmap as consolidated global percentages.

Reporting period:

From Month/Year:

to Month/Year:

NOTE: When answering the questions below please indicate whether the figures given are the result of accurate counting (C), ex: 1243 (C), or the result of rough estimation (E), ex: 1500 (E)

Q8: Please indicate the **total** number of **NEW applications*** received in this period:

- 8.1.** Purely national:
8.2. MRP (RMS + CMS):
8.3. DCP (RMS + CMS):

Comments:

* *In all formats, paper or electronic for which a first MA would be granted.*

Q9: Please indicate the **total** number of **VARIATIONS applications*** received in this period:

9.1. Purely national:

9.2. MRP (RMS + CMS):

Comments:

** In all formats, paper or electronic for which a MA would be granted.*

Q10: Please indicate the total number of **RENEWAL applications*** received in this period:

10.1. Purely national:

10.2. MRP (RMS + CMS):

Comments:

Q11: Please indicate the total number of **NEW applications*** received in electronic format :

11.1. Purely national: N° eCTD: N°NeeS: N°Other:

11.2. MRP (RMS + CMS): N° eCTD: N°NeeS: N°Other:

11.3. DCP (RMS + CMS): N° eCTD: N°NeeS: N°Other:

Comments:

Q12: Please indicate the total number of **VARIATIONS applications** received in electronic format:

12.1. Purely national N° eCTD: N°NeeS: N°Other:

12.2. MRP (RMS + CMS): N° eCTD: N°NeeS: N°Other:

Comments:

Q13: Please indicate the total number of **RENEWAL applications*** received in electronic format:

13.1. Purely national: N° eCTD: N°NeeS: N°Other:

13.2. MRP (RMS + CMS): N° eCTD: N°NeeS: N°Other:

Comments:

Q14: Please indicate whether or not **paper copies** of all or some parts of the dossier (signed documents excluded) are still required for *applications* received in electronic format for:

14.1 Purely national:

(c) Yes

(d) No

14.2 MRP/DCP (RMS):

(e) Yes

(f) No

14.3 MRP/DCP (CMS):

(g) Yes

(h) No

Comments:

Annex 2 Published guidance

Country	Web Link
BE	http://www.fagg-afmps.be/en/human_use/medicines/Medicines/MA_procedures/esubmission/index.jsp
BG	http://www.bda.bg/images/stories/documents/ru/ukazania/Guidance_for_eCTD%20BG.pdf
CZ	http://www.sukl.cz/reg-84-version-1
CY	http://www.moh.gov.cy/phs
DE-BFARM	http://www.bfarm.de/clin_103/sid_6AC7F6F3CDF4F537E04745704F981B47/EN/drugs/2_Authorisation/procedures/eSubmission/eSubmission-node.html
DE-PEI	http://www.pei.de/clin_047/nn_162566/EN/infos-en/pu-en/09-submission-dossier-en/sub-node-en.html?__nnn=true
DK	http://www.dkma.dk/1024/visUKLSArtikel.asp?artikelID=11487
EE	http://esubmission.emea.europa.eu/doc/eGuidance_Document_1.4.pdf
FI	http://www.laakelaitos.fi/esubmission
FR	http://www.afssaps.fr/var/afssaps_site/storage/original/application/07aad0b4b47b5d1570eb7df63d7b9f51.pdf http://esubmission.emea.europa.eu/doc/eGuidance_Document_1.4.pdf
GR	http://www.eof.gr
NL	http://www.cbg-meb.nl/NR/rdonlyres/C56DC125-3460-4038-930C-AD9B8F5FAEC3/0/eGuidance_Document14.pdf
PL	http://urpl.gov.pl/ectd/wytyczne-dla-podmiotow-odpowiedzialnych-w-sprawie-skladania-dokumentacji-w-formie-elektronicznej-sledzenie-zmian http://en.urpl.gov.pl/ectd
PT	http://www.infarmed.pt/portal/page/portal/INFARMED/MAIS_NOVIDADES/DETALHE_NOVIDADE?itemid=43876 http://www.infarmed.pt/portal/page/portal/INFARMED/MAIS_NOVIDADES/DETALHE_NOVIDADE?itemid=43886 http://www.infarmed.pt/portal/page/portal/INFARMED/MAIS_NOVIDADES/DETALHE_NOVIDADE?itemid=43926
SE	http://www.lakemedelsverket.se/english/product/Medicinal-products/Electronic-submissions-to-the-MPA
SI	http://www.jazmp.si/index.php?id=191 http://www.jazmp.si/index.php?id=56
UK MHRA	http://esubmission.emea.europa.eu/doc/eGuidance_Document_1.4.pdf
EMA	http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000102.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058002c599

Annex 3

Electronic Submission contact points

Country	Title	Last Name	First Name	Organisation Name	Email
Austria	Mr.	Binder	Harald	AGES PharmMed	harald.binder@ages.at
Belgium	Mr.	Vankeerberghen	Pieter	Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten - Agence Fédérale des Médicaments et des Produits de Santé	pieter.vankeerberghen@fagg-afmps.be
Bulgaria	Mr.	Antonov	Lyudmil	Изпълнителна агенция по лекарствата	lyudmil.antonov@bda.bg
Cyprus	Mr.	Antoniou	George	Ministry of Health	gantoniou@phs.moh.gov.cy
Czech Republic	Ms	Šínová	Ivana	Státní ústav pro kontrolu léčiv	ivana.sinova@sukl.cz
Denmark	Dr	Helboe	Per	Lægemiddelstyrelsen	ph@dkma.dk
Estonia	Mrs	Viispart	Aet	Ravimiamet	Aet.Viispart@ravimiamet.ee
Finland	Mr	Hartikka	Jaakko	Finnish Medicines Agency	Jaakko.Hartikka@nam.fi
France	Mrs	Auriche-Benichou	Caroline	Agence Française de Sécurité Sanitaire des Produits de Santé	caroline.auriche@afssaps.sante.fr
Germany	Dr	Menges	Klaus	Bundesinstitut für Arzneimittel und Medizinprodukte	k.menges@bfarm.de
Germany	Dr	Kern	Andreas	Paul-Ehrlich-Institut	keran@pei.de
Greece	Dr	Michaleas	Sotirios	ΕΘΝΙΚΟΣ ΟΡΓΑΝΙΣΜΟΣ ΦΑΡΜΑΚΩΝ	smichaleas@eof.gr
Hungary	Mr	Haraszi	Csaba	Országos Gyógyszerészeti Intézet	haraszi.csaba@ogyi.hu
Iceland	Mr	Benediktsson	Benedikt	Lyfjastofnun	benedikt.benediktsson@imca.is
Ireland	Mr	Horan	Kevin	Bord Leigheasra na hÉireann	kevin.horan@imb.ie
Italy	Mr	Tranchina	Salvatore	Agenzia Italiana del Farmaco	s.tranchina@aifa.gov.it
Latvia	Ms	Harčenko	Svetlana	Zāļu valsts aģentūra	svetlana.harcenko@zva.gov.lv
Liechtenstein	Mag. Pharm	Batliner	Brigitte	Liechtensteinische Landesverwaltung	Brigitte.Batliner@ag.llv.li
Lithuania	Mr	Sizovas	Eduardas	Valstybinė vaistų kontrolės tarnyba prie Lietuvos Respublikos sveikatos apsaugos ministerijos	EduardasSizovas@vvkt.lt
Luxembourg	Mr	Genoux-Hames	Jacqueline	Ministère de la Santé	jacqueline.genoux-hames@ms.etat.lu
Malta	Mr	Mizzi	Kevin	Awtorità dwar il-Mediċini	kevin.mizzi@gov.mt
Netherlands	Mr	van den Hoorn	Ricco	College ter Beoordeling van Geneesmiddelen	r.vd.hoorn@cbg-meb.nl
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