

eCTD Implementation Survey Report

By the Czech Presidency of the EU - 2009

(Covering the period from January 2008 to December 2008)

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 HMA meeting in Reykjavik HMA 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. NCA would therefore need to have the infrastructure, the processes and the legal framework in place to handle paperless applications in eCTD format efficiently.

NCA 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) develops and updates the regional European Module 1 of the eCTD in line with the EU CTD guidance and it elaborates EU guidance aiming to help the transition from paper to eCTD.

Acknowledging the fact that veterinary CTD has not been developed at ICH level and the different requirements of the smaller veterinary industry the TIGes has set up a subgroup to develop guidance for electronic application for marketing authorisation of medicinal products for veterinary use. The veterinary sector joined 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 follow up of implementation of eCTD and to update the survey twice a year. The survey report would include comparative results relevant to the human sector between the last and the previous survey with the report being updated every second HMA meeting of each European Presidency of the Council.

The goal of the survey report is to monitor the evolution of readiness of the Network for paperless operation and progress towards the target of 2009.

Methodology

A questionnaire has been elaborated by the TIGes and circulated among all of its members (see Annex 1). Two six month periods are covered by the survey report, corresponding to the two last European Presidencies of the Council.

The questionnaire has been divided into two parts, one on readiness for acceptance of paperless applications of marketing authorisations and the other on statistics of applications for marketing authorisation received in paper, eCTD and other electronic formats during the periods covered by the survey.

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.

Results are presented with graphs showing the consolidated figures provided by all EU regulatory authorities for two periods of six months and with tables showing the results as absolute values and percentages of total applications in any format, and for all procedures covering 12 months and as a percentage of the evolution between both 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 paper copies when applications are received in electronic format is also reported.

Outcome

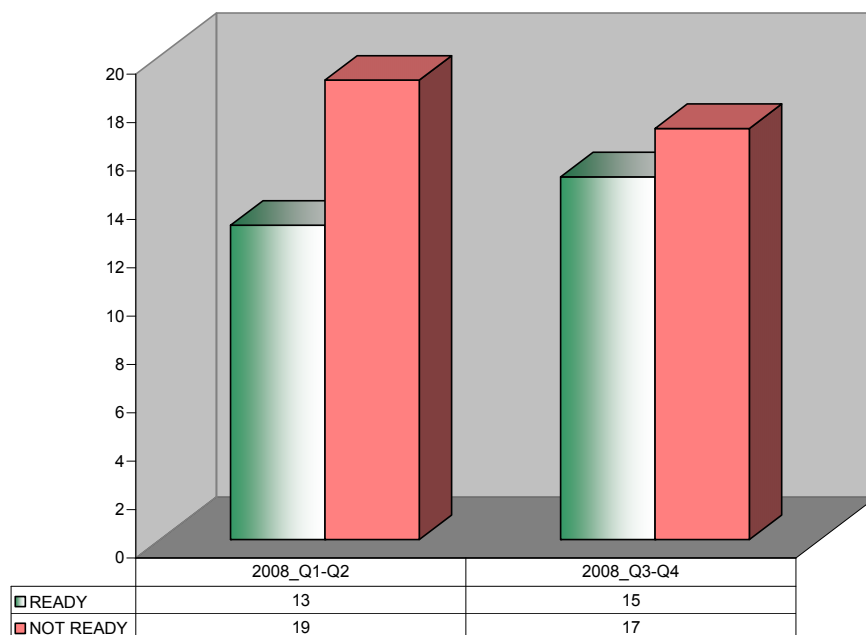
All 32 regulatory authorities (NCA + EMEA) of the European Medicines Regulatory Network competent for medicinal products in the human sector responded to the questionnaire.

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%

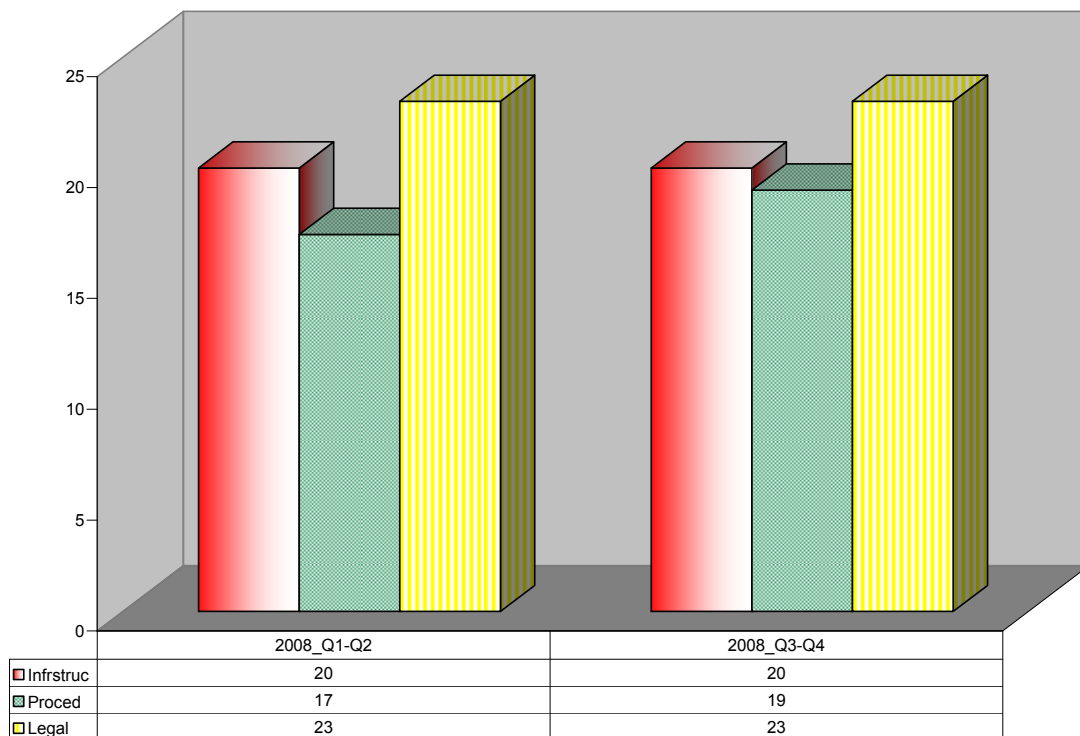


Results:

- **47% of EU Regulatory authorities are ready for management and evaluation of marketing authorisation applications in electronic format only (+ 15%).**

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 %

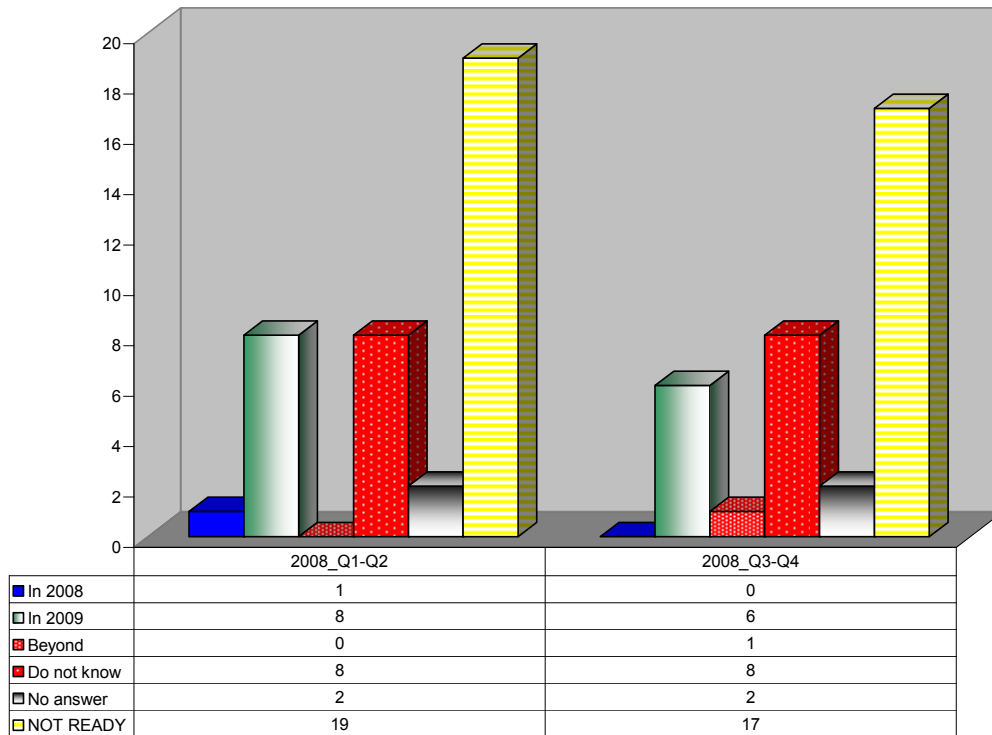


Results:

- **63% of EU regulatory authorities have the infrastructure for paperless management of Marketing Authorisation applications (no change).**
- **59% of EU regulatory authorities have the processes in place for paperless management of Marketing Authorisation applications (+ 12%).**
- **72% of EU regulatory authorities have the legal framework in place for paperless management of Marketing Authorisation applications (no change).**

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: 88%

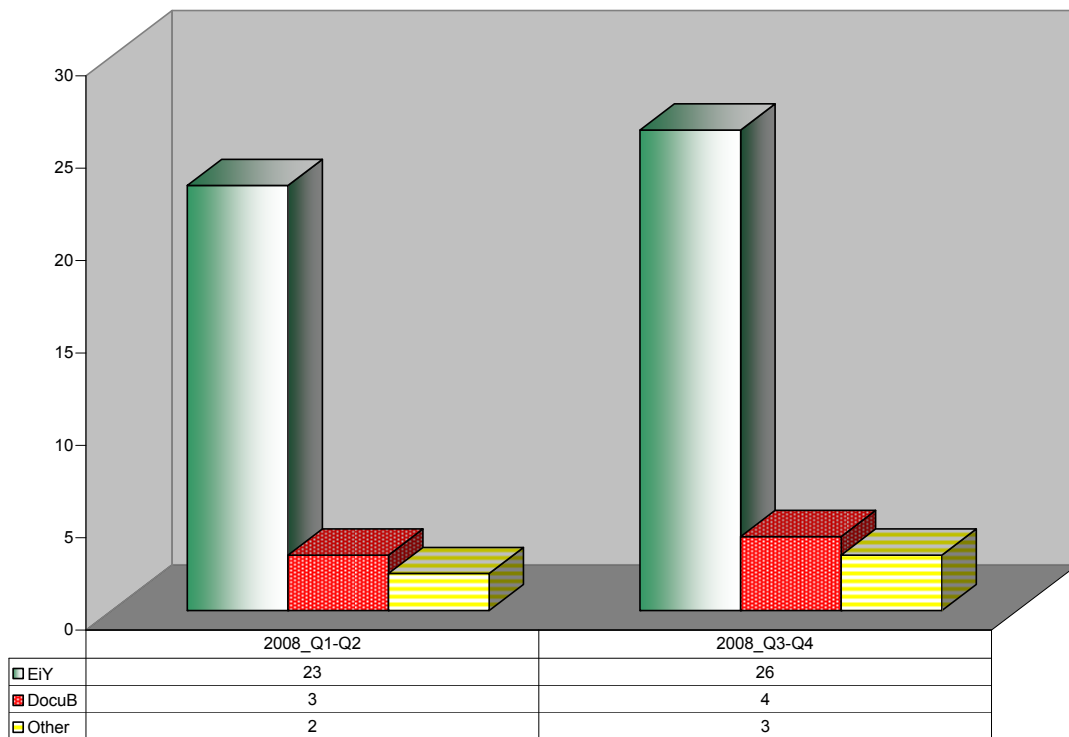
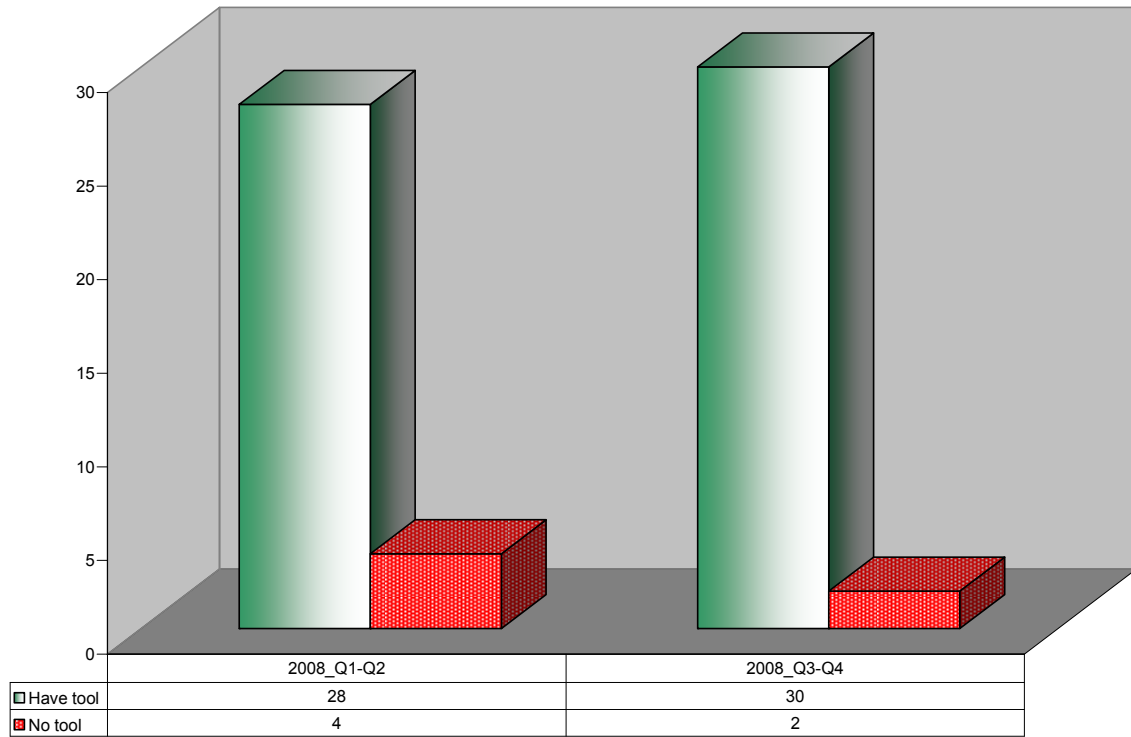


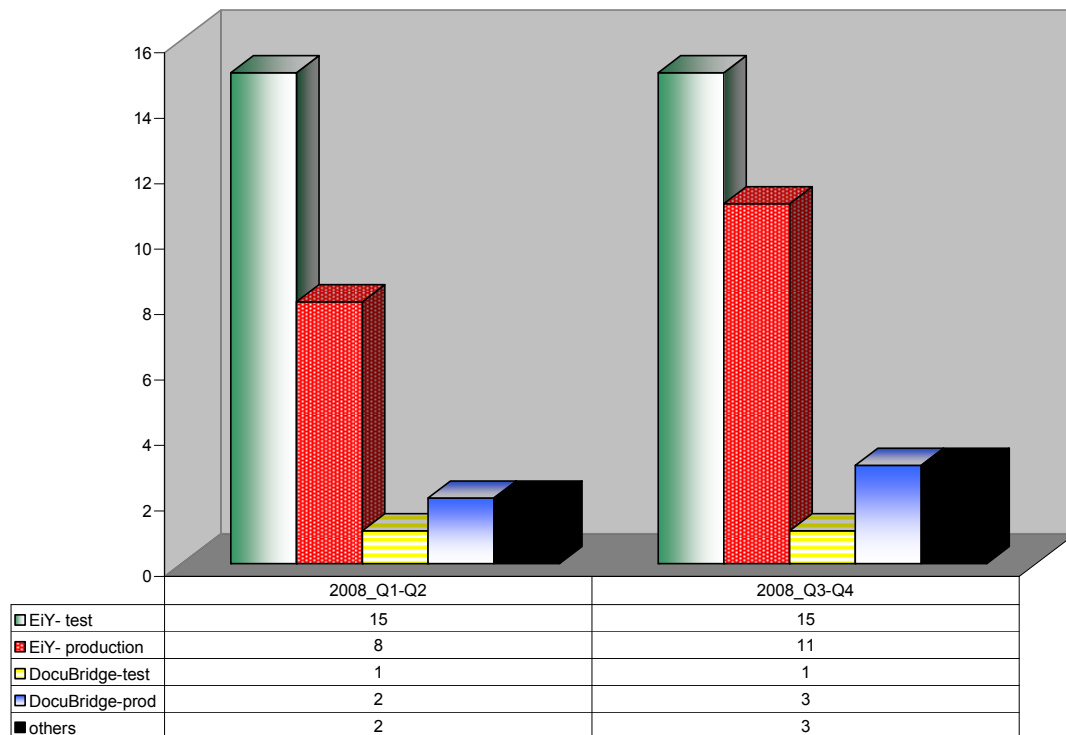
Results:

- **53% 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:**
- **19% more EU regulatory authorities expect to be ready in 2009**
- **25% of EU regulatory authorities still do not know by when they will be ready (no change)**
- **12% No answer**

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

Question response rate: 100%



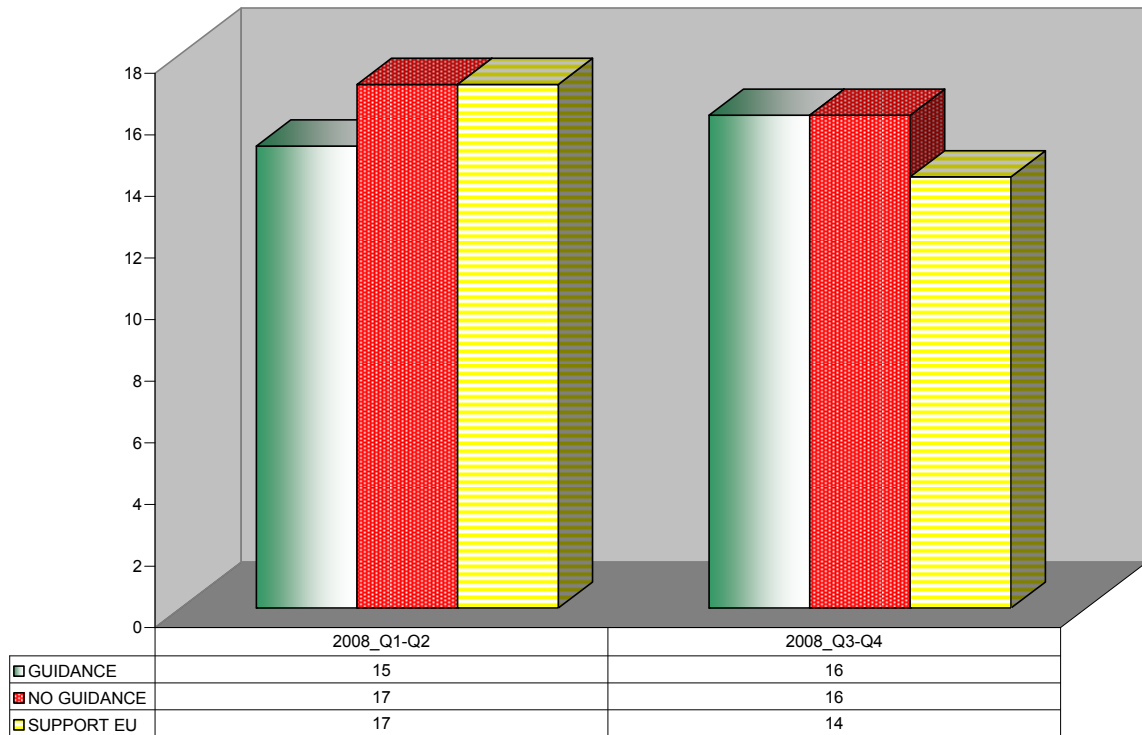


Results:

- **94% of EU authorities have a tool for review of eCTD (+ 7%)**
- **53% of EU regulatory authorities have a tool for review of eCTD in production (+ 42%)**
- **50% of EU regulatory authorities have a tool for review of eCTD under test (no change)**
- **81% of EU regulatory authorities have EiY as tool for review of eCTD**
- **13% of EU regulatory authorities have Docubridge as tool for review of eCTD**
- **6% of EU regulatory authorities have another tool for review of eCTD**

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%

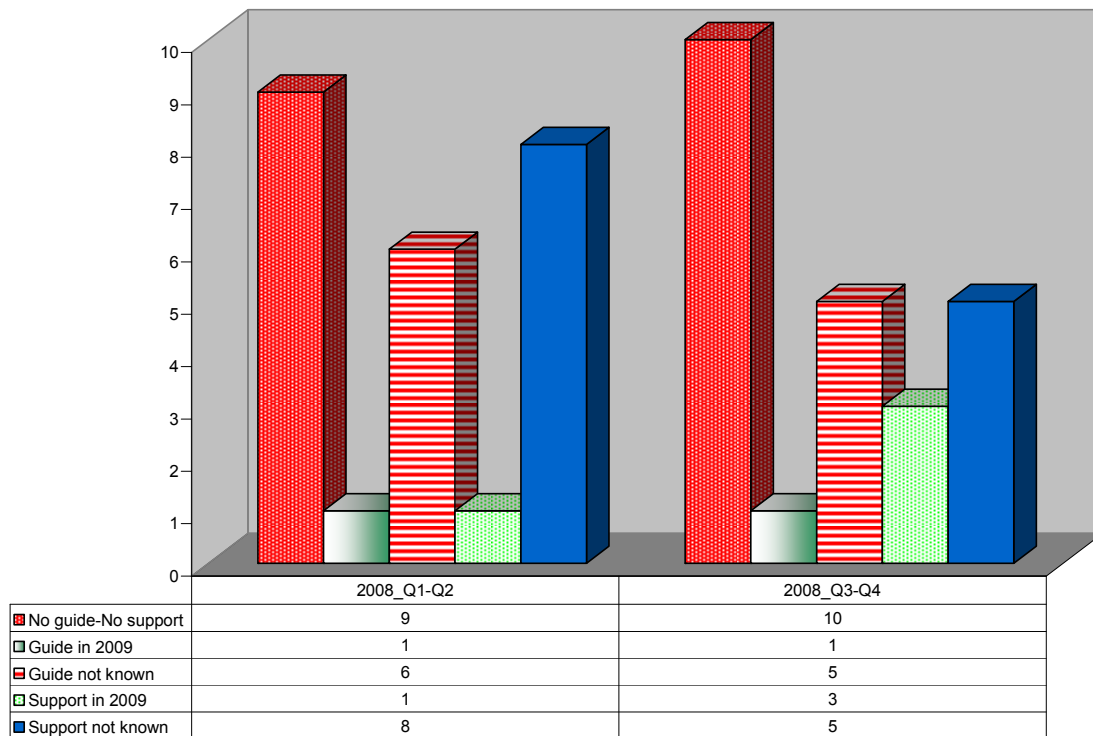


Results:

- **50% of EU regulatory authorities have national guidance (+7%)**
- **44% of EU regulatory supports published EU guidance (-18%)**

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%



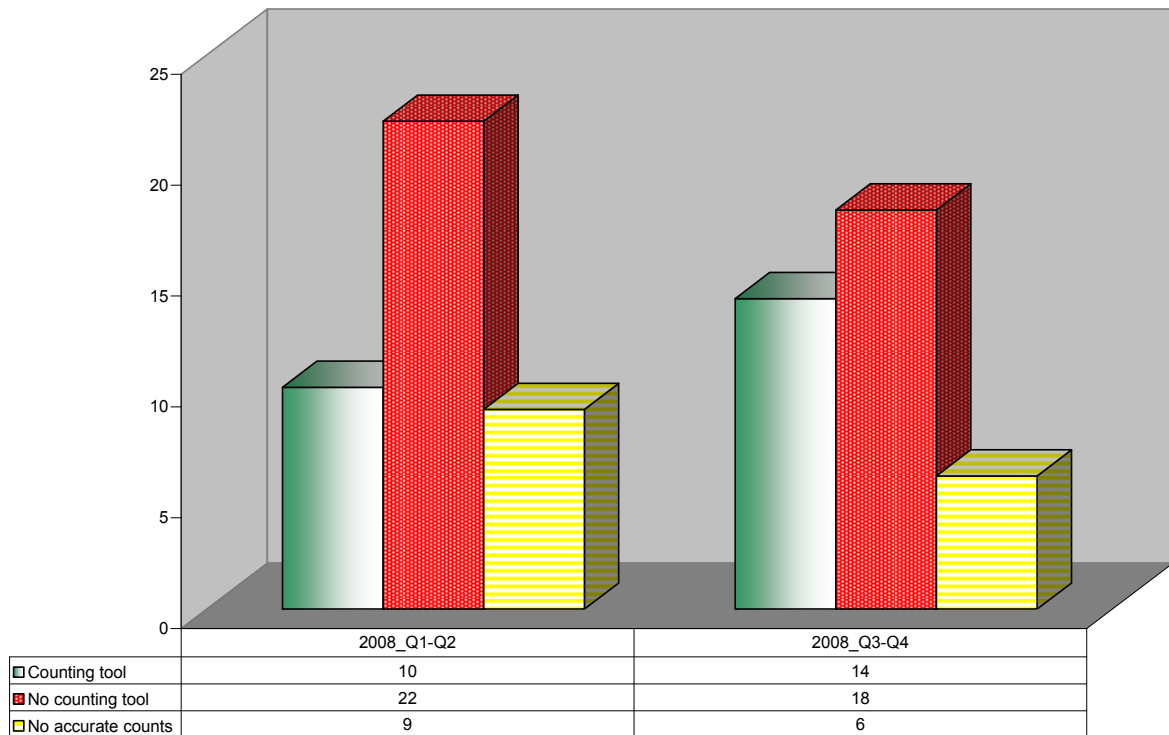
Results:

- **31% 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 (+11%).**
- **3% more EU regulatory authorities expect to have national guidance by the end of 2009 (making a total of 17 or 53% of the Network).**
- **9% more EU regulatory authorities expect to support EU guidance by the end of 2009 (making a total of 17 or 53% of the Network).**
- **15% of all EU regulatory authorities do not know when they will publish national guidance.**
- **15% of all EU regulatory authorities do not know when they will support EU guidance.**

Statistics

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

Question response rate: 100%



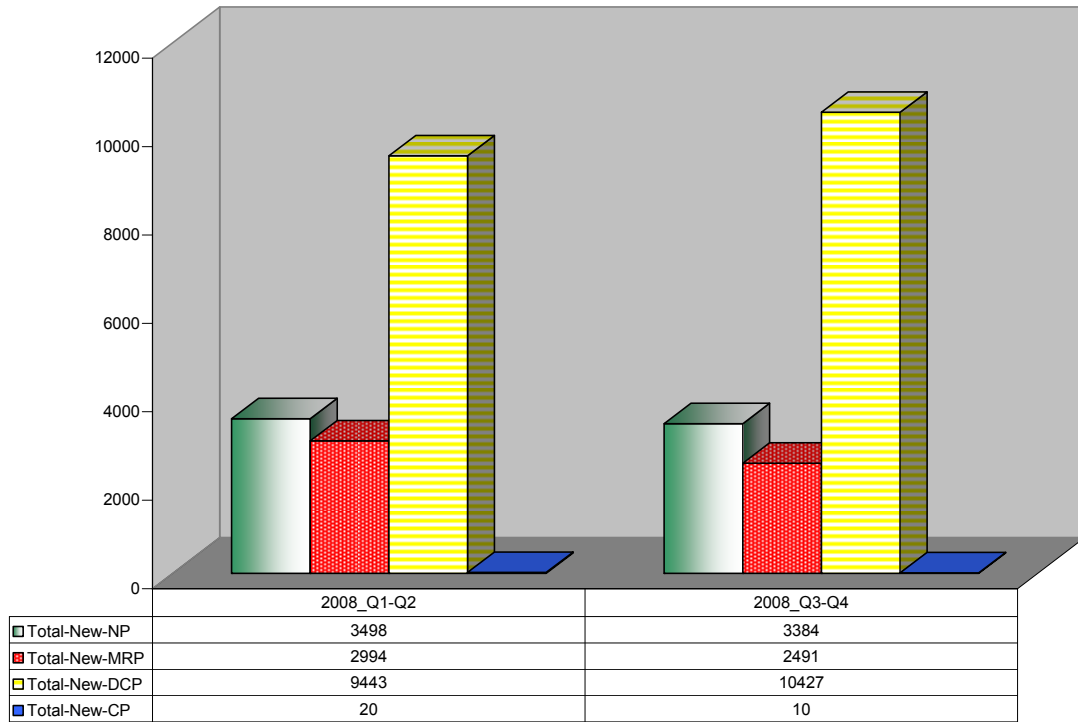
Results:

- 44% of EU regulatory authorities have a tool for regular gathering of numbers of applications received in electronic format (+ 40%).
- 19% of EU regulatory authorities declare being unable to provide accurate figures on applications received in electronic format (- 33%).

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

Q8 - Total number of New applications

Question response rate: 100%

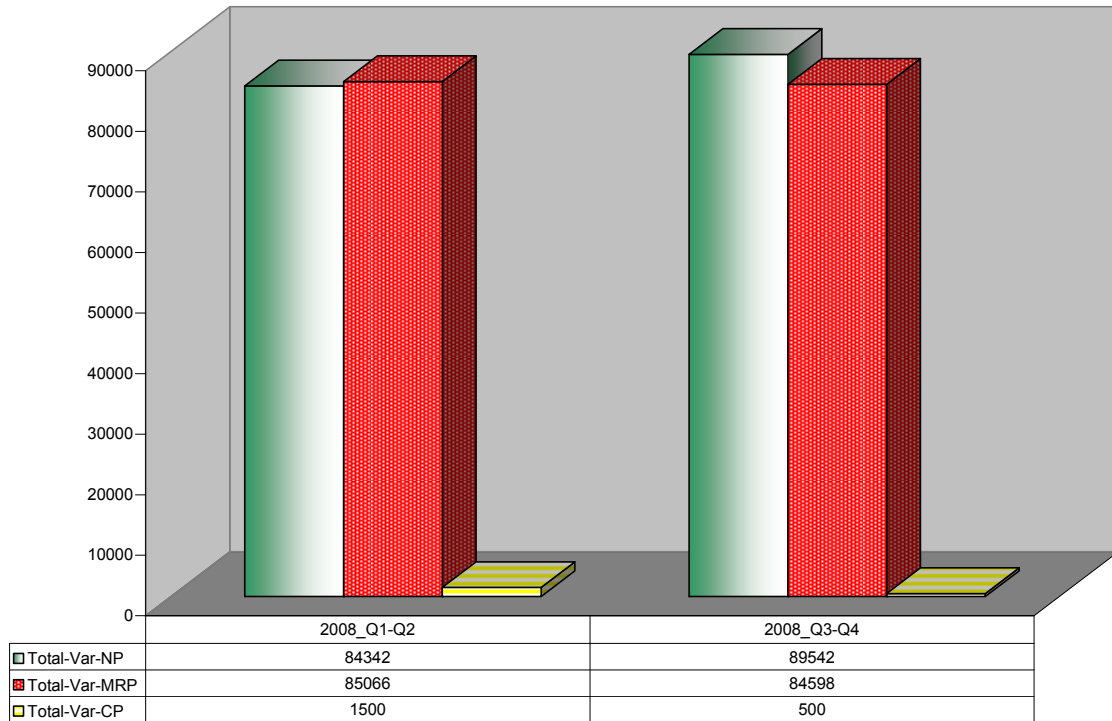


Cumulative results:

	12 months	Δ 6 months
New-NP	6882	-3%
New-MRP	5485	-16%
New-DCP	19870	10%
New-CP	30	-50%
Total-New	32267	2%

Q9 - Total number of Variation applications

Question response rate: 100%

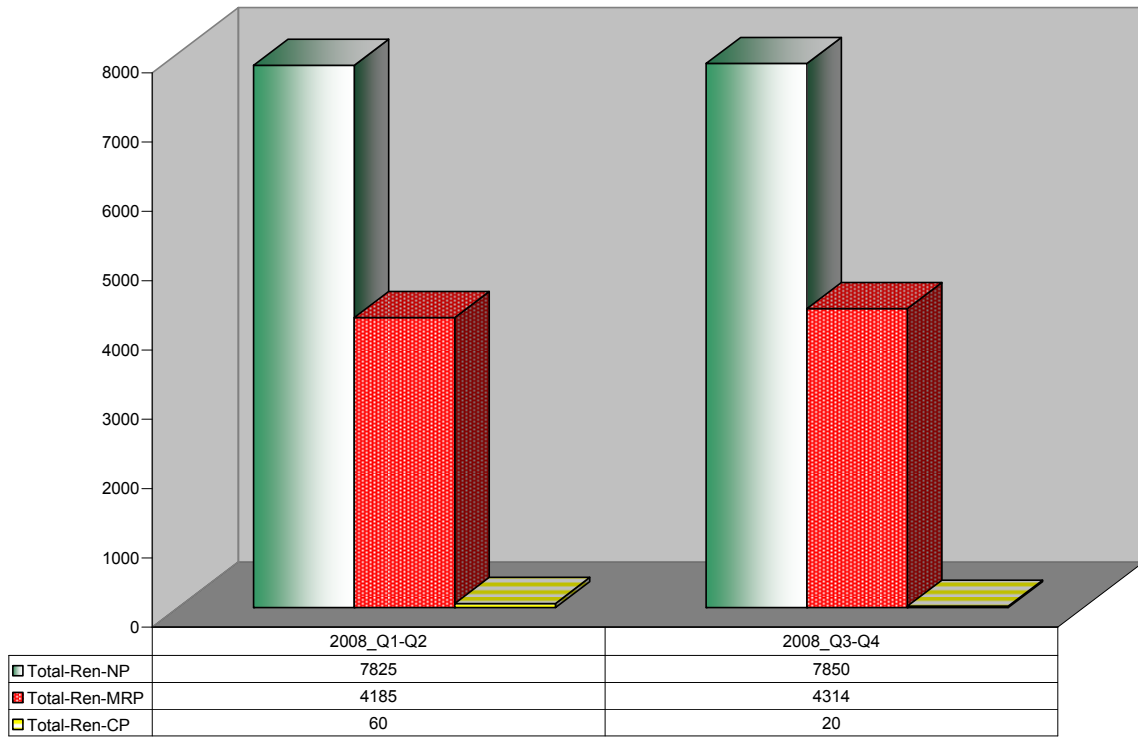


Cumulative results:

	12 months	Δ 6 months
Var-NP	173884	6%
Var-MRP	169664	-1%
Var-CP	2000	-67%
Total-Var	344948	2%

Q10 - Total number of Renewal applications

Question response rate: 100%

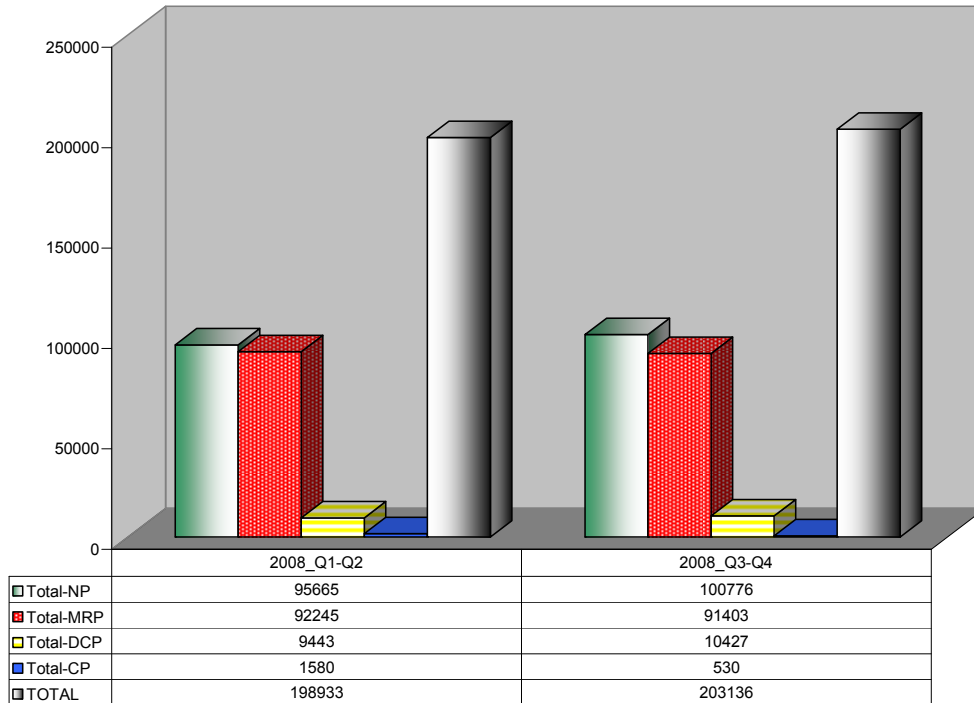


Cumulative results:

	12 months	Δ 6 months
Ren-NP	15675	0.3%
Ren-MRP	8499	3%
Ren-CP	80	-67%
Total-Ren	24254	1%

Q8-Q10 – Total number of applications per procedure

Question response rate: 100%

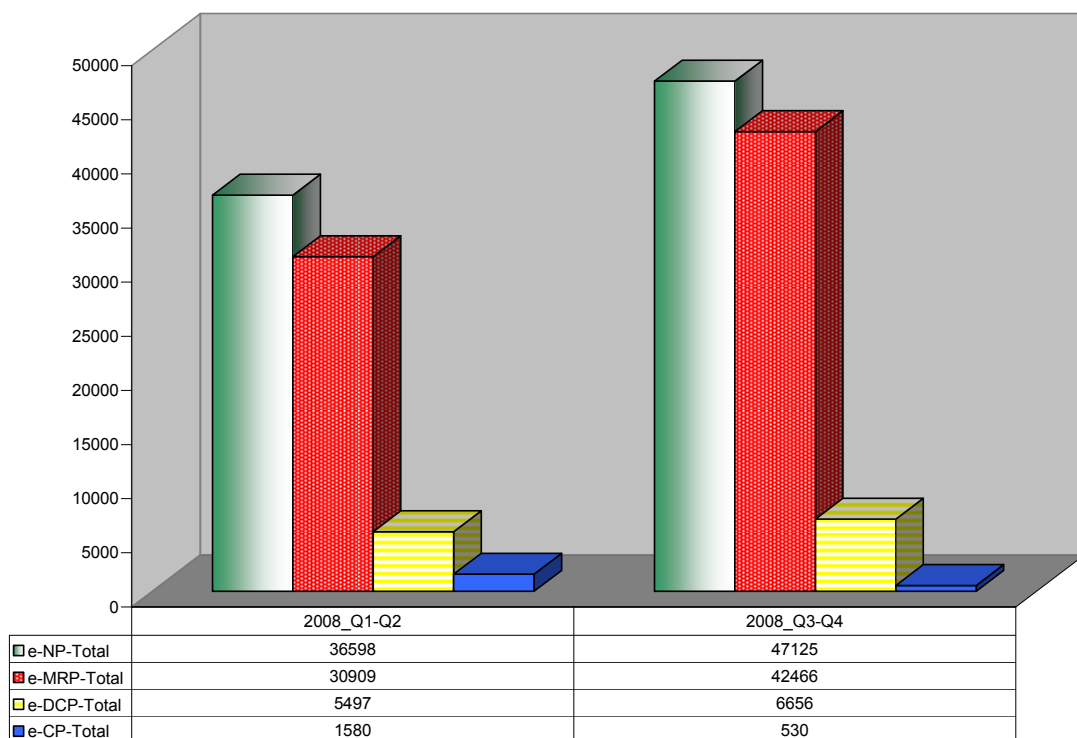
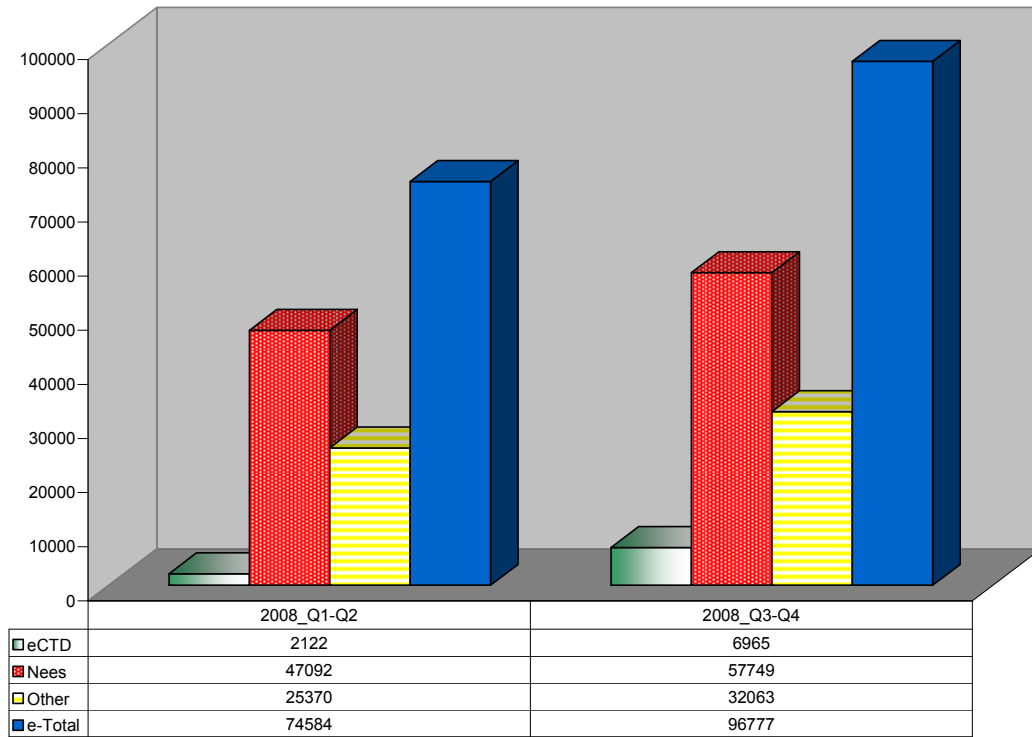


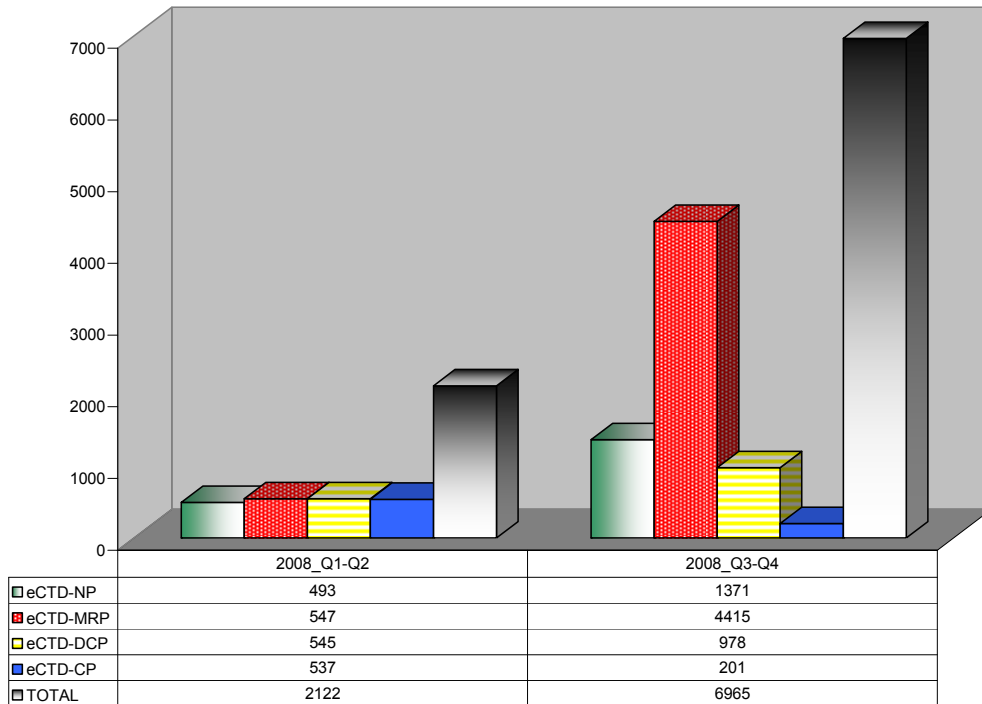
Cumulative results:

	12 months	% of TOTAL	Δ 6 months
Total-NP	196441	49%	5%
Total-MRP	183648	46%	-1%
Total-DCP	19870	5%	10%
Total-CP	2110	<1%	-66%
TOTAL	402069	100%	2%

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

Question response rate: 100%





Cumulative results:

For all electronic-format applications:

	12 months	Δ 6 months	% e-Total
eCTD	9087	228%	5%
Nees	104841	23%	61%
Other	57433	26%	34%
e-Total	171361	30%	100%

	12 months	Δ 6 months	TOTAL *	% of TOTAL
e-NP-Total	83723	29%	196441	43%
e-MRP-Total	73375	37%	183648	40%
e-DCP-Total	12153	21%	19870	61%
e-CP-Total	2110	-66%	2110	100%
e-Total	171361	30%	402069	43%

* Total of applications received in all formats, paper or electronic

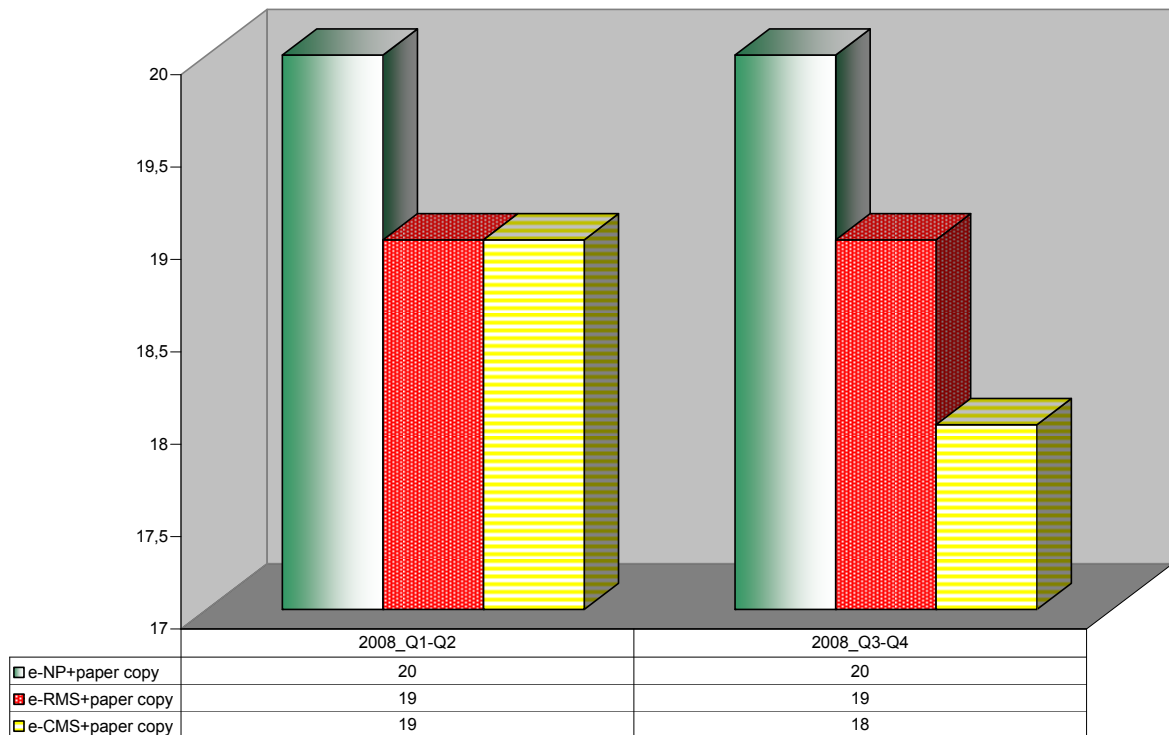
For eCTD applications:

	12 months	Δ 6 months	TOTAL *	% of TOTAL
eCTD-NP	1864	178%	196441	1%
eCTD-MRP	4962	707%	183648	3%
eCTD-DCP	1523	79%	19870	8%
eCTD-CP	738	-63%	2110	35%
eCTD-Total	9087	228%	402069	2%

* Total of applications received in all formats, paper or electronic

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

Question response rate: 100%



Results:

- 63% of EU regulatory authorities require paper when an application through the NP is received in electronic format (no change).
- 59% of RMS EU regulatory authorities require paper when an application through the MRP is received in electronic format (no change).
- 56% of CMS EU regulatory authorities require paper when an application through the NP is received in electronic format (-3%).

Conclusions

The questionnaire has had a 100% response rate.

Summary of results on readiness

The number of EU regulatory authorities that are ready for management and evaluation of marketing authorisation applications in electronic format increased 15% during the second half of 2008 and by the end of 2008 15 NCAs (47% of the Network) were ready. From the 17 of authorities that are not ready 6 plan to be ready within the target set at the end of 2009. However, there were still 8 NCAs that did not know when they would be ready.

63% (20) of EU regulatory authorities have already the infrastructure in place to handle paperless Marketing Authorisation applications and 59% (19) have the specific processes in place. 72% (23) of the Network is ready from the legal point of view.

94% (30) of the authorities have a tool for review of eCTD and this figure increased in the second half of 2008 by 7%. However, almost half of the EU regulatory authorities are still testing the tools and did not use them in production.

50% (16) of the authorities published guidance for management and evaluation of electronic marketing authorisation applications and 44% support published EU guidance. 4 more EU authorities plan to publish national guidance and/or support existing EU guidance by the end of 2009.

Finally, more than half of the EU authorities still require paper with or without the electronic applications.

Summary of results on statistics

A significant increase in the availability of accurate figures was achieved in the present survey as compared with the previous survey, in particular with regard to total applications. However, further improvement is still needed in the gathering of figures on electronic applications.

An important increase of electronic applications overall could be seen during the second half of 2008 (+30%) with 43% of all applications being electronic (with or without paper) in 2008. Progression of eCTD submission was very significant (6965 in the second half of 2008 against 2122 in the first half) reaching 5% of all electronic applications in 2008. The main increase could be seen in MRP with more than half of all eCTD submissions, but also an important increase could be seen in National procedures.

Finally, eCTD reached 2% of the more than 400.000 submissions that were made in the EU in 2008 showing that there is still a long way to go and meaning that more than 40% of electronic applications are made in other formats (Nees and other).

EU Guidance has been published and validation criteria allowing better identification of the submissions and harmonisation in Europe are being developed.

Final remarks

Progress towards the target in terms of readiness could still be seen during 2008. However, a few agencies have difficulties to plan for eCTD implementation.

HMA acknowledged this as an issue for meeting the target of end of 2009 and renewed its commitment at its May 2009 meeting.

It should be noted the very important relative increase in eCTD submissions which encourages the Network to continue its effort.

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.*

ANNEX 2

GUIDANCE

Country	Web Link
BE	https://portal.health.fgov.be/pls/portal/docs/PAGE/INTERNET_PG/HOMEPAGE_MENU/GENEESMIDDELEN1_MENU/HUMAANGEBRUIK1_MENU/REGISTRATIE17_MENU/TOLERANCEZERO9_HIDE/TOLERANCEZERO9_DOCS/ESUBMISSION%20GUIDELINES-2-7_0.PDF
BG	http://bda.bg/ru/ukazania/Guidance_for_eCTD%20BG.pdf
CZ	http://www.sukl.cz/reg-84-version-1
DE-BFARM	http://www.bfarm.de/cln_029/nn_1199130/EN/drugs/2_Authorisation/procedures/amgSub/amgsub-node-en.html_nnn=true , http://www.bfarm.de/cln_029/nn_1198876/SharedDocs/Publikationen/DE/Arzneimittel/2_zulassung/zulVerfahren/amg-ev/Leifaden_20NeeS.templateId=raw.property=publicationFile.pdf/Leifaden%20NeeS.pdf
DE PEI	http://www.pei.de/cln_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 http://www.dkma.dk/db/filarkiv/6985/Human%20guideline%20ved%20e-sumissions.pdf
EE	http://esubmission.emea.europa.eu/doc/eGuidance_Document%201.4.pdf
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	www.eof.gr
NL	http://www.cbg-meb.nl/NR/rdonlyres/C56DC125-3460-4038-930C-AD9B8F5FAEC3/0/eGuidance_Document14.pdf
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/files/humana/Dopis%20za%20na%20splet_eCTD.pdf
UK MHRA	http://www.mhra.gov.uk/mhra/SpecialMail5 , http://esubmission.emea.europa.eu/doc/eGuidance_Document_1.4.pdf
EMEA	http://www.emea.europa.eu/htms/human/genguidance/genreg.htm

ANNEX 3

CONTACT POINTS

Country	Title	Last Name	First Name	Organisation Name	Email
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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
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Latvia	Ms	Harčenko	Svetlana	Zāļu valsts aģentūra	svetlana.harckenko@zva.gov.lv
Liechtenstein	Mag. Pharm	Batliner	Brigitte	Liechtensteinische Landesverwaltung	Brigitte.Batliner@ag.llv.li

Country	Title	Last Name	First Name	Organisation Name	Email
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-Medicini	kevin.mizzi@gov.mt
Netherlands	Mr	van den Hoorn	Ricco	College ter Beoordeling van Geneesmiddelen	r.vd.hoorn@cbg-meb.nl
Norway	Mr	Oksne	Jostein	Statens Legemiddelverk	jostein.oksne@legemiddelverket.no
Poland	Mr	Szczepaniak	Adam	Urząd Rejestracji Produktów Leczniczych, Wyrobów Medycznych i Produktów Biobójczych	adam.szczepaniak@urpl.gov.pl
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	Mr	Florea	Adrian Stefan		adrian.florea@anm.ro
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EMA	Mrs	Holmes	Claire	European Medicines Agency	claire.holmes@emea.europa.eu