EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Conditional marketing authorisation

Report on ten years of experience at the EMA

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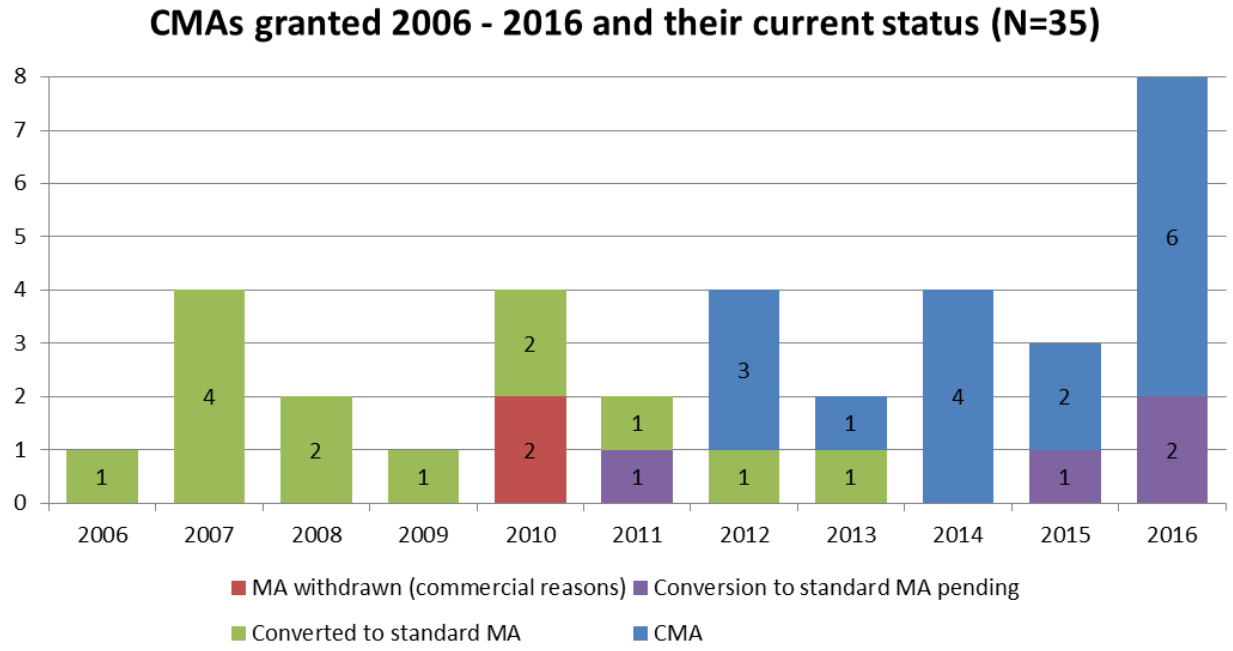
Background

- Conditional marketing authorisation (CMA) **introduced in 2006**
- Previous **STAMP** discussions
- CHMP **Guideline** updated in 2015/2016
- In response to public consultation comments it was suggested to publish a **report** on 10 years of experience with CMA
- Continuous **high interest** in the topic (internally and externally)
- Link with **other activities** on early access

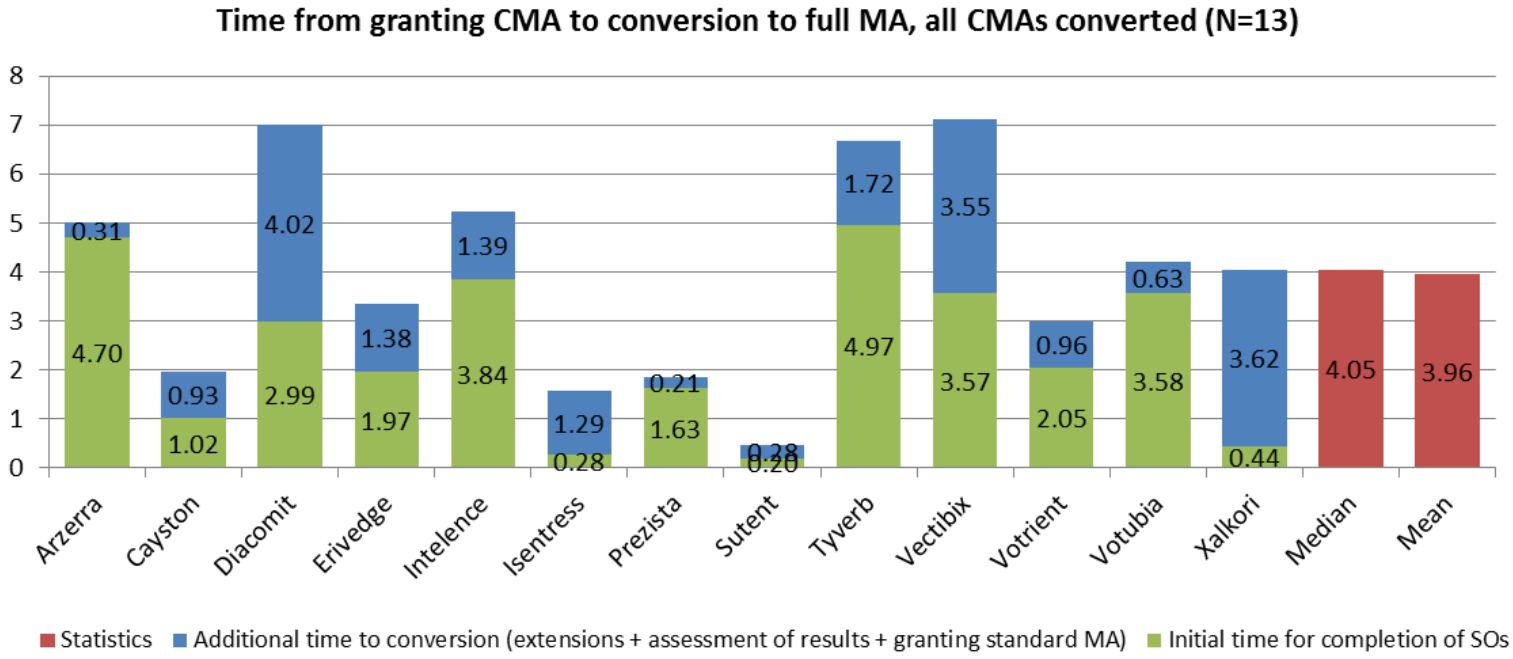
Conditional Marketing Authorisations



Apart from 2016, there is no clear trend in number of CMAs, which remain an 'exceptional' authorisation route

Data updated with DLP 31 Dec 2016

Conversion to standard MA

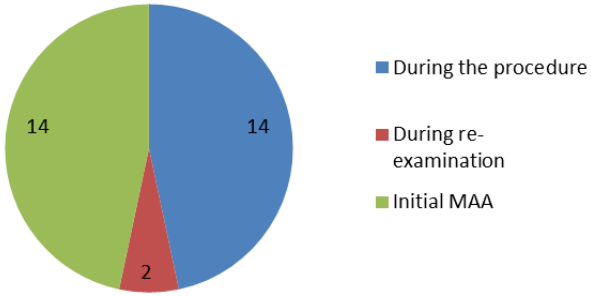


On average **within 4 years** a conditional MA is converted into a standard MA

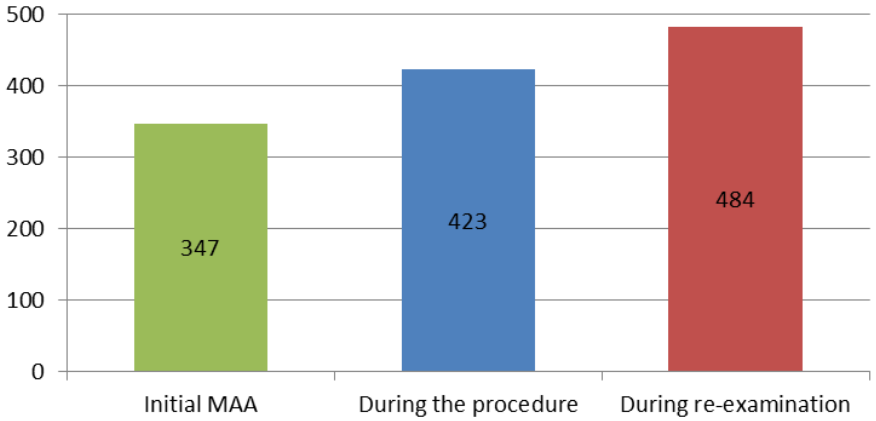
Data updated with DLP 31 Dec 2016

Granting CMAs

Stage of procedure, when CMA was first considered, all CMAs (N=30)

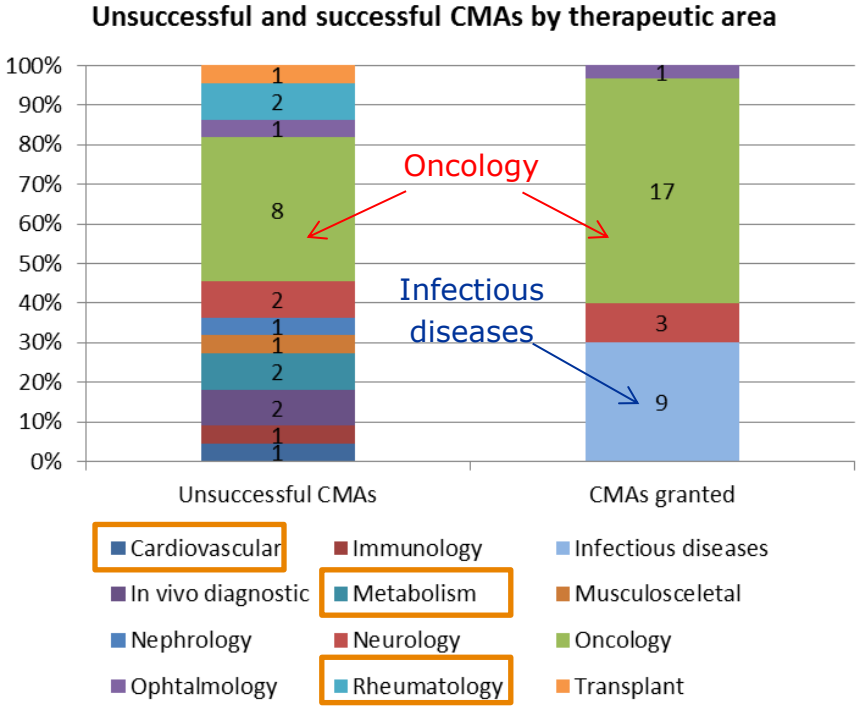


Mean duration of assessment (including clock-stops) by stage of first consideration of CMA (N=30)



Reluctance in pro-active use of CMAs by industry – room for improvement in prospective planning.
CHMP has used the tool actively.
Only three CMAs granted following an accelerated assessment.

Comparison of successful and unsuccessful CMAs



Only few therapeutic areas have managed to use conditional MAs

Data at the time of authorisation

50% Products have (some) results from a **phase III** study in MAA

59% Of main/pivotal studies were **randomised** (34% single arm)

57% Of main/pivotal studies were **open label**

53% Of main/pivotal studies used pre-defined **response rate** as primary endpoint

"Typical" CMA as **pivotal evidence** has 2 phase II or III studies, most often open label, randomised and measuring a pre-defined response rate

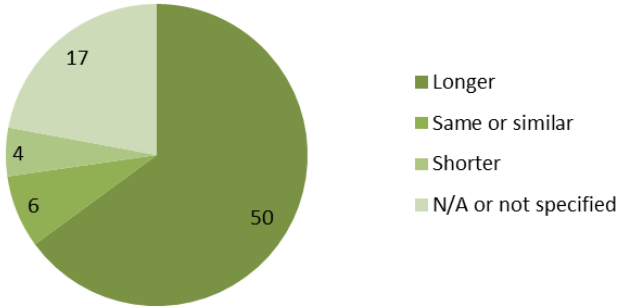
Specific obligations (SOs) imposed

72%	Of SOs were submission of **clinical study results** (excl. interim results)
62%	Of imposed studies were **ongoing** at the time of opinion
52%	Of SO studies were **randomised** (36% single arm)
72%	Of SO studies were **open label**
31%	Of SO studies had **same primary endpoint** as main studies in MAA

"Typical" CMA **SOs** required to conduct two phase II, III or IV efficacy and safety studies, which were open label, randomised or single arm, and measuring an endpoint often different from pivotal studies in CMA application

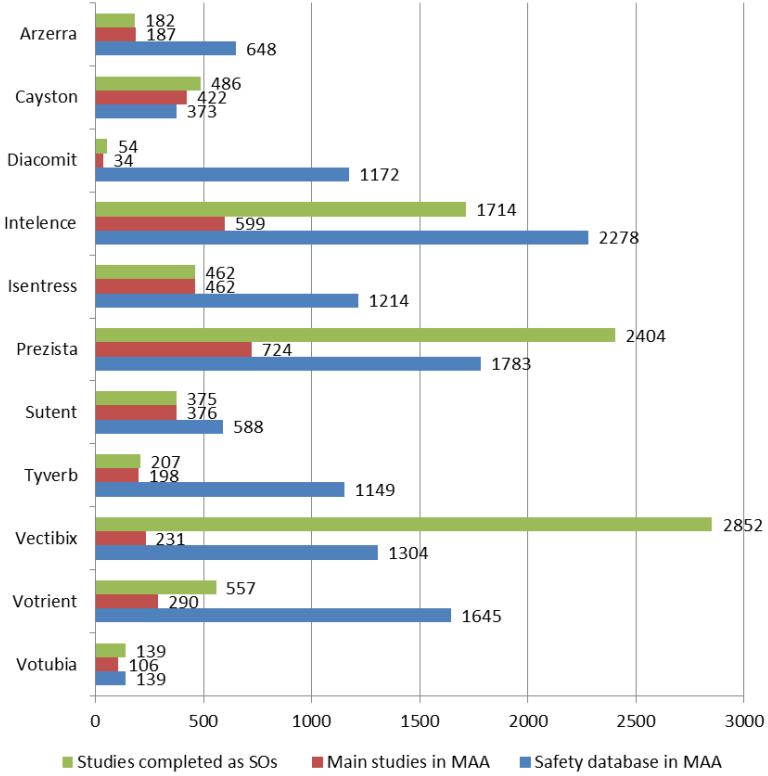
SO data vs. initial data

Duration of median patient follow-up in SO studies vs. the follow-up duration in MAA data (N=77)



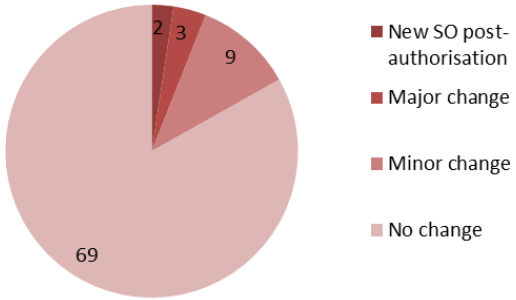
Post-authorisation data required for comprehensive evidence was typically with longer duration / follow-up and in a similar or larger sample size.

Number of subjects receiving CMA product in main studies and safety database at the time of MA and in studies completed as SOs, all CMAs converted (N=11)

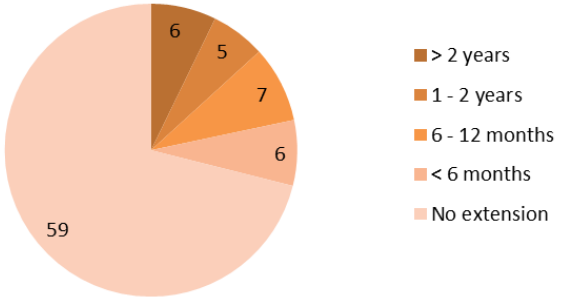


Changes to specific obligations

Changes to scope of specific obligations, all SOs completed or pending, N=83



Extensions of due dates for specific obligations, all SOs completed or pending (N=83)

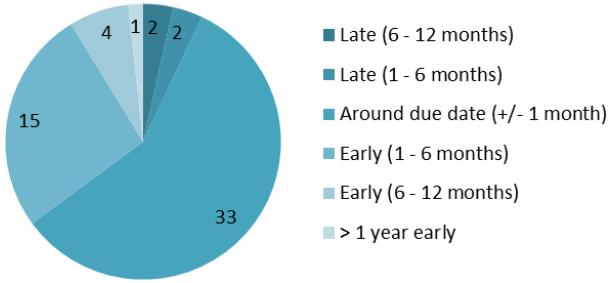


Most specific obligations did not have any change to their scope and due dates. Only very few had major changes to the scope or extensions beyond one year.

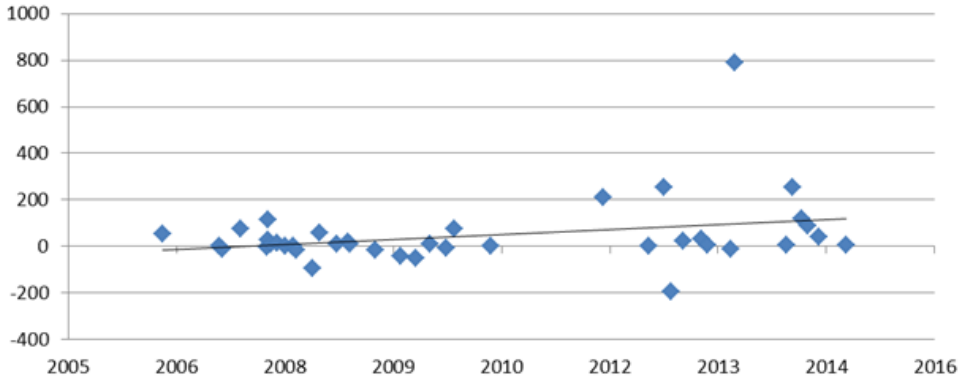
Although often the changes in scope and timelines of specific obligations were related to difficulties in recruitment and study initiation or conduct, in some cases it was linked to better-than-expected outcomes (e.g. lower than expected incidence of metastases or longer overall survival).

Observing the due dates

Submission of SO results in relation to due date (N=57)



Accuracy of submission (number of days in advance of due date (delay = negative), arranged by the submission date)



The due dates for submission of data from specific obligations were generally observed and often (33%) data were submitted more than a month early

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- Report published on the EMA website
- Results presented to EMA scientific committees
- **STAMP discussion**
- Information shared with other stakeholders

Thank you for your attention

Further information

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