Early Access Session

EUROPABIO EMA INFO DAY

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The European Association for Bioindustries

AGENDA

- Introduction
- Case study
- What worked well
- Our challenges
- Proposals

ABOUT ALEXION

- *A fully-integrated biopharmaceutical company serving patients with devastating and rare diseases around the world*

- *Exclusive focus on life-transforming therapies for patients with devastating, life-threatening disorders*

INTRODUCTION – 3 PRODUCTS

		APPROVAL	
SOLIRIS (eculizumab)	Monoclonal Antibody Complement inhibitor	2007	Accelerated assessment
STRENSIQ (asfotase alfa)	Enzyme replacement therapy	2015	Exceptional circumstances
KANUMA (sebelipase alfa)	Enzyme replacement therapy	2015	Accelerated assessment

	STRENSIQ	KANUMA
ODD in EU	03 December 2008	17 December 2010
BreakthroughtTherapy Designation (US)	May 2013	May 2013
Protocol assistance	4 (2009, 2011)	19 July 2012
Approved PIP	March 2013	April 2013
MAA Submission	01 June 2014	24 November 2014
Start of Procedure (Do)	23 July 2014	24 December 2014
Eligibility for accelerated assessment	01 July 2014	20 November 2014
D120	21 November 2014 *Reverted to regular assessment*	23 April 2015
Answers to D120	22 January 2015	22 May 2015
LoOI N°1	27 March 2015	NA
LoOI N°2	21 May 2015	
CHMP opinion	25 June 2015 (at D210)	25 June 2015 (at D150)
EC decision	28 August 2015	28 August 2015

OVERVIEW OF REGISTRATION PACKAGES

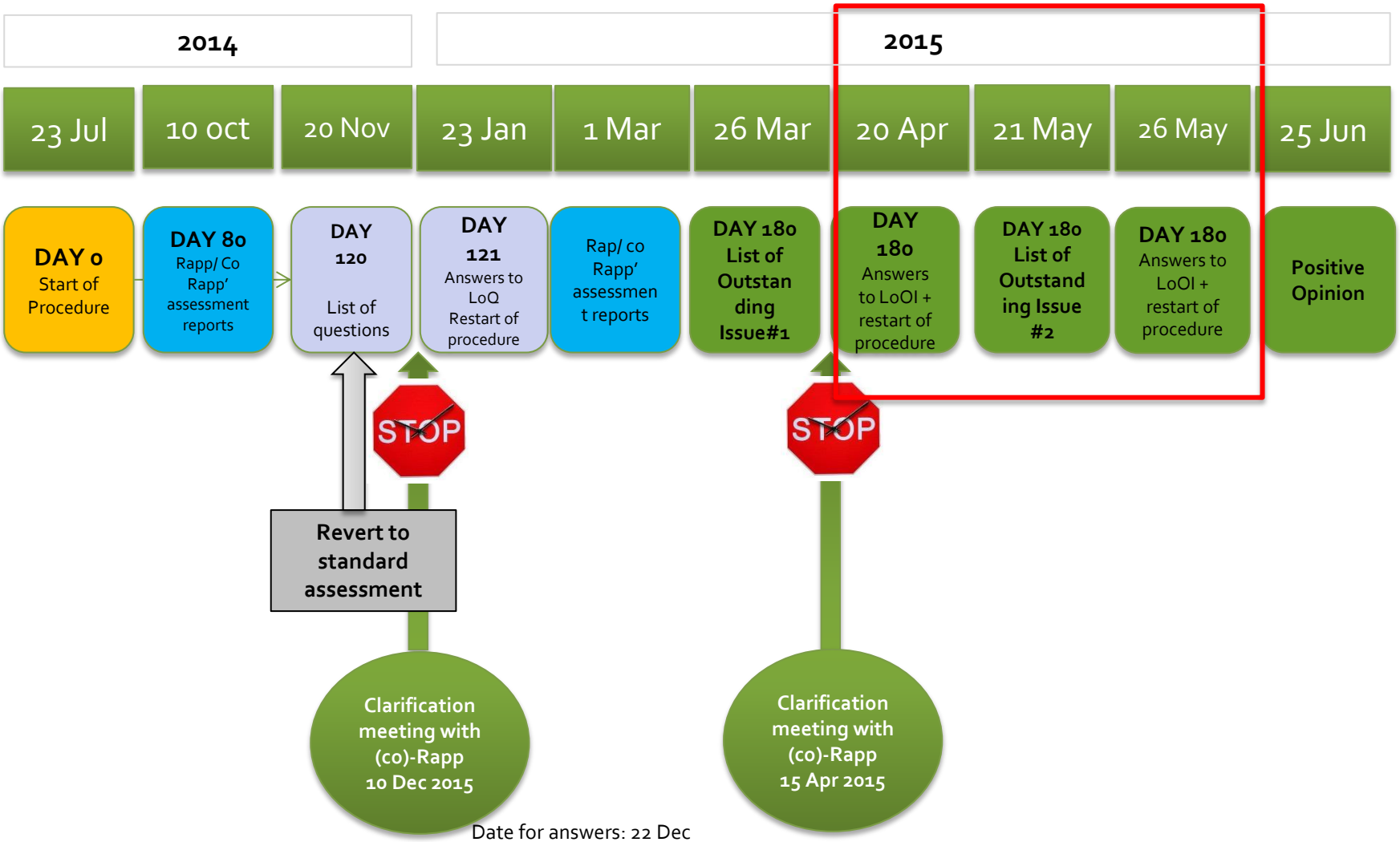
STRENSIQ (asfotase alfa)

- 3 pivotal studies, non controlled
- 1 natural history study (use of historical control)
- 1 supportive trial

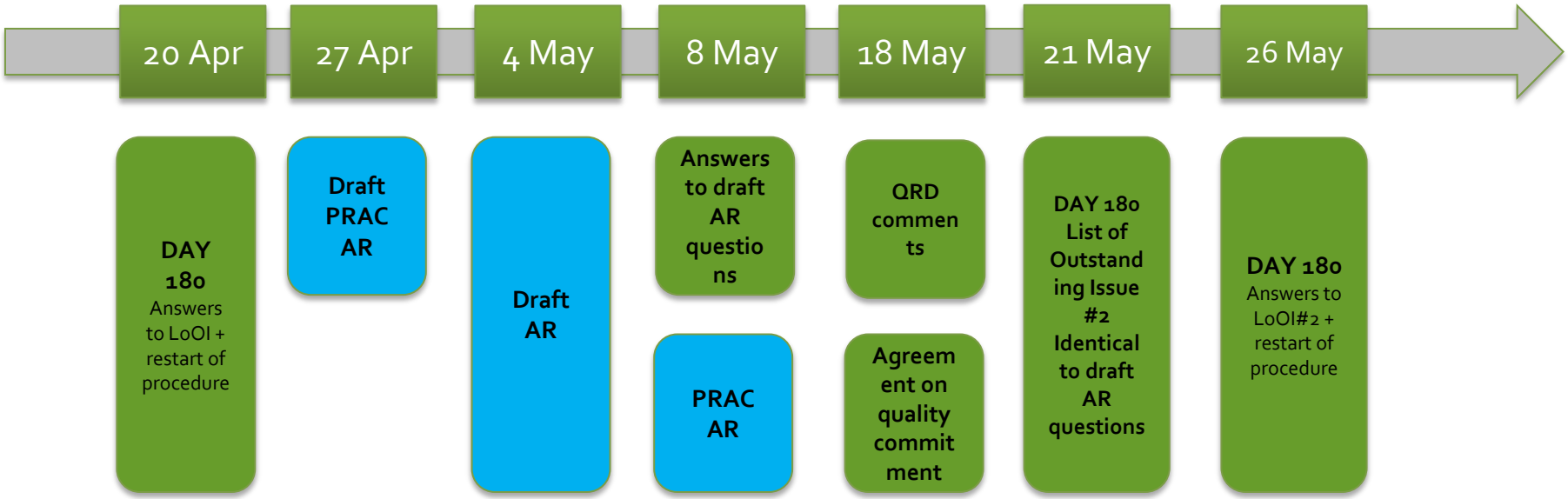
KANUMA (sebelipase alfa)

- 2 pivotal studies (1 controlled and 1 non controlled)
- 2 natural history studies (Use of historical control)
- 1 supportive trials

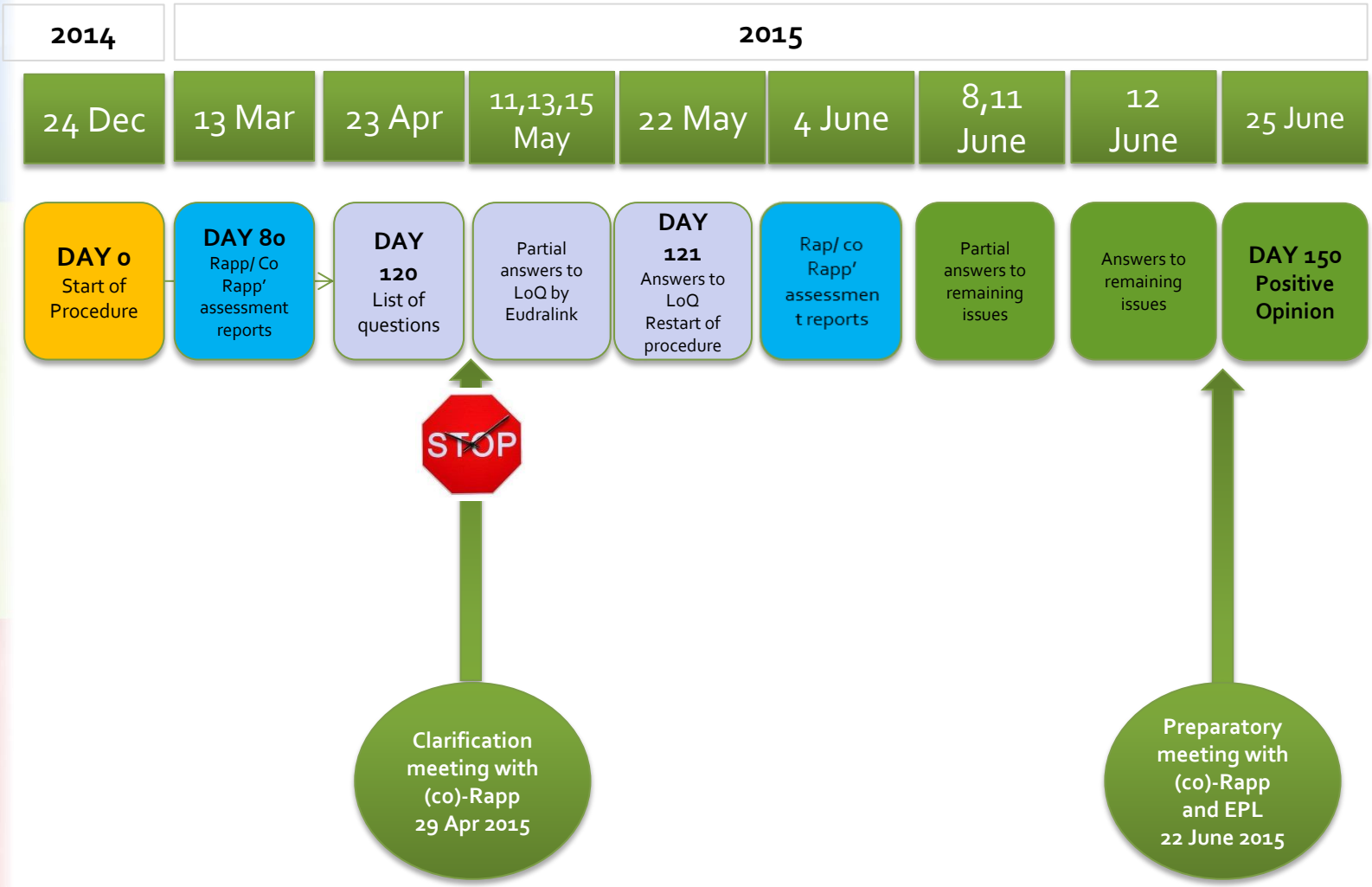
STRENSIQ – OVERVIEW OF ASSESSMENT PROCEDURE 2014 - 2015



STRENSIQ – ASSESSMENT PROCEDURE – DAY 150 - 180



KANUMA – ACCELERATED ASSESSMENT PROCEDURE



CLARIFICATION MEETINGS

STRENSIQ

- Post day 120
- 20 days after RSI (2 days before answer deadline)

- Post day 180 (LoOI N°1)
- 20 days after RSI (5 days before answer deadline)

KANUMA

Post D120:

6 days after RSI

ADDITIONAL MEETINGS

STRENSIQ

- Limited

KANUMA

D120-D150: regular e-mail and phone contact (initiated by EMA and sponsor)

22 June:

- F2F Meeting with (co)rapps and EPL team
- prior to plenary CHMP meeting
- after the plenary CHMP meeting

22-24 June: e-mail and phone contact multiple times per day (initiated by EMA)

WHAT WORKED WELL

- **Well –defined roles and responsibilities within the EPT**
- **Engaged and responsive Procedure Managers**
- **For Kanuma CP: Highly flexible, cooperative team dynamic**

- **Review under accelerated assessment**
  - Kanuma : all « hands on deck » attitude
    - **Driver: Earlier close out of the procedure**
    - Cooperative environment during the entire review procedure and in particular during CHMP week (D150)

OUR CHALLENGES

Strensiq - Approval under exceptional circumstances

- Persistant challenge of the approval route (CMA vs EC)
- Timely scheduling of clarification meetings
- Reaching agreement on date for submission of D120 responses –(public holidays)
- Absence of reviewer interactions –outside of formal meetings
- No opportunity to solve « minor » issues between draft report and CHMP meetings
- Not always «one voice» from EPT , e.g. in case of temporary replacement

TAKE AWAY MESSAGE FROM THE APRIL 2015 INDUSTRY STAKEHOLDERS PLATFORM ON THE OPERATION OF THE CENTRALISED PROCEDURE

- **Industry Experience:**

  « Some PMs apply a pragmatic, flexible approach whereas others are very rigid in their interpretation and /or approach … »

- **Industry Proposals**
  - Request for more transparency on examples of flexibility
  - Earlier close out of the procedure, where possible

STRENSIQ and KANUMA: Two MAA procedures with two different experiences

PROPOSAL FOR IMPROVEMENT OF THE CURRENT STATE – EXCEPTIONAL CIRCUMSTANCES MA

The approval under exceptional circumstances is based on the premises that the applicant is **unable to provide comprehensive data** on the efficacy and safety under normal conditions of use (Directive 2001/83/EC, as amended, Annex I, Part II).

Often applied for life saving medicines such as OMPs in areas without alternative

According to article 14(8) of Regulation (EC) 726/2004 the exceptional circumstances marketing authorisation is granted provided "**specific procedures**" are introduced.

As such, it would be beneficial to discuss:

- Shortening the review process when the data package is limited
  - Such as exchange of Q&A without stopping the clock
- Streamlined dialogue prior and during the review procedure (i.e. possibility to schedule upfront phone calls with EPL/Rapporteurs; regular TCs with EPL at key milestones of the MAA…)

PROPOSAL FOR IMPROVEMENT OF THE CURRENT STATE – ACCELERATED ASSESSMENT

The 210 days assessment period is reduced to 150 days thanks to shorter clock stop and in case of no LoOIs. However, in practice, there appears to be no measurable 'acceleration' of the review period.

- At any time during the MAA evaluation, if the CHMP considers that it is no longer appropriate to conduct an accelerated assessment the CHMP may decide to continue the assessment under standard CP timelines.
- Or, by the applicant in case of need for longer clock stop or other justifiable reason

In summary:

There seems to be no obvious acceleration of the review from the initial steps of the procedure: e.g. validation; more condensed initial assessment.

Additionally, the lack of a mechanism or process for exchange of questions without clock stop ('on the go') and streamlined dialogue with EMA does little to facilitate an "accelerated" assessment.

PROPOSAL – A BLUE SKY VIEW

- **For Accelerated Assessment Procedures**
  1. Clarification meetings included in the procedure timelines prepared at Do
  2. Opportunity for additional interactions (e.g. after availability of draft assessment reports)
  3. More condensed initial assessment; written responses without clock stop (as per draft guideline)
  4. Opportunity for additional dialogue during the review procedure is welcome

FOR THE OPPORTUNITY TO SHARE OUR RECENT EXPERIENCE