SINGLE DOSSIER: WILL NATIONAL EARLY STAGE TRIALS SUFFER OR BENEFIT? A CRO VIEW :

CASE STUDY : A MULTINATIONAL PHASE I/IIA PROOF OF CONCEPT STUDY

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NEW EU REGULATION 536/2014

- Streamlined application procedure via EU portal
- A single set of documents
- Harmonised procedure for the assessment
  - Part I is jointly assessed by all Member States concerned
  - Part II is assessed by each Member State concerned separately
- Strictly defined deadlines
- Simplified reporting procedures
- Increased transparency as regards clinical trials and their outcomes

PHASE I / IIA STUDIES

- ‘Drive’ to have first assessment of efficacy as early as possible
  - Proof of Concept (POC)
- Phase I / IIa study
  - Healthy Volunteer part
  - Patient part
- Patient population sometimes difficult to find in Western Europe
  - HV part in Western Europe
  - Patient part in Eastern Europe

CASE STUDY
HOW WE MADE IT HAPPEN

INTRODUCTION

- US biotech company
  - Phase I / IIa study with Hepatitis C compound
    - First in Human part in healthy volunteers
    - Patient arm for early proof of concept
  - Potential issue with non-clinical data
- IND received clinical hold by FDA, due to concern on non-clinical data
- Sponsor looking a rapid solution

CASE STUDY
HOW WE MADE IT HAPPEN

AS PERFORMED 1/2

- Assessment of non-clinical issue by internal experts
  - Available non-clinical data deemed acceptable
  - Scientific Advice required
- European scenario proposed
  - Belgium
    - Healthy volunteer part / Patient part
  - Romenia
    - Patient part
  - Poland
    - Patient part
- HV part in Belgium due to short RA timelines
  - HV part almost finished when Romenia / Poland are ready to start patient recruitment
  - Staggered start-up

CASE STUDY
HOW WE MADE IT HAPPEN

AS PERFORMED 2/2

- Type I Scientific Advice in Belgium
  - 30 day written response
- In Parallel preparation of CTA applications
  - Immediate submission if positive scientific advice
- CTA submission approved
  - Belgium: 15 days
  - Romenia: 69 days
  - Poland: 94 days
- HV part almost completed completed when patient recruitment started

CASE STUDY
HOW WE MADE IT HAPPEN

AS IT WILL BE UNDER REGULATION 536/2014

- Scientific Advice
  - 30 day written response
- Constraint
  - Single dossier will lead to single submission
  - No option anymore for staggered start-up
- Two options
  - Submit all countries at once
  - Submit Belgium first for HV part
    - After approval Belgium submit other countries

OPTION 1 – SUBMISSION WITH ALL COUNTRIES

- Single submission
  - Validation:
    - 10 days
  - Assessment (Part I and II)
    - 45 days + 31 days = 76 days

TOTAL: 86 DAYS

- *Single submission approval between 60-106 days, average taken*

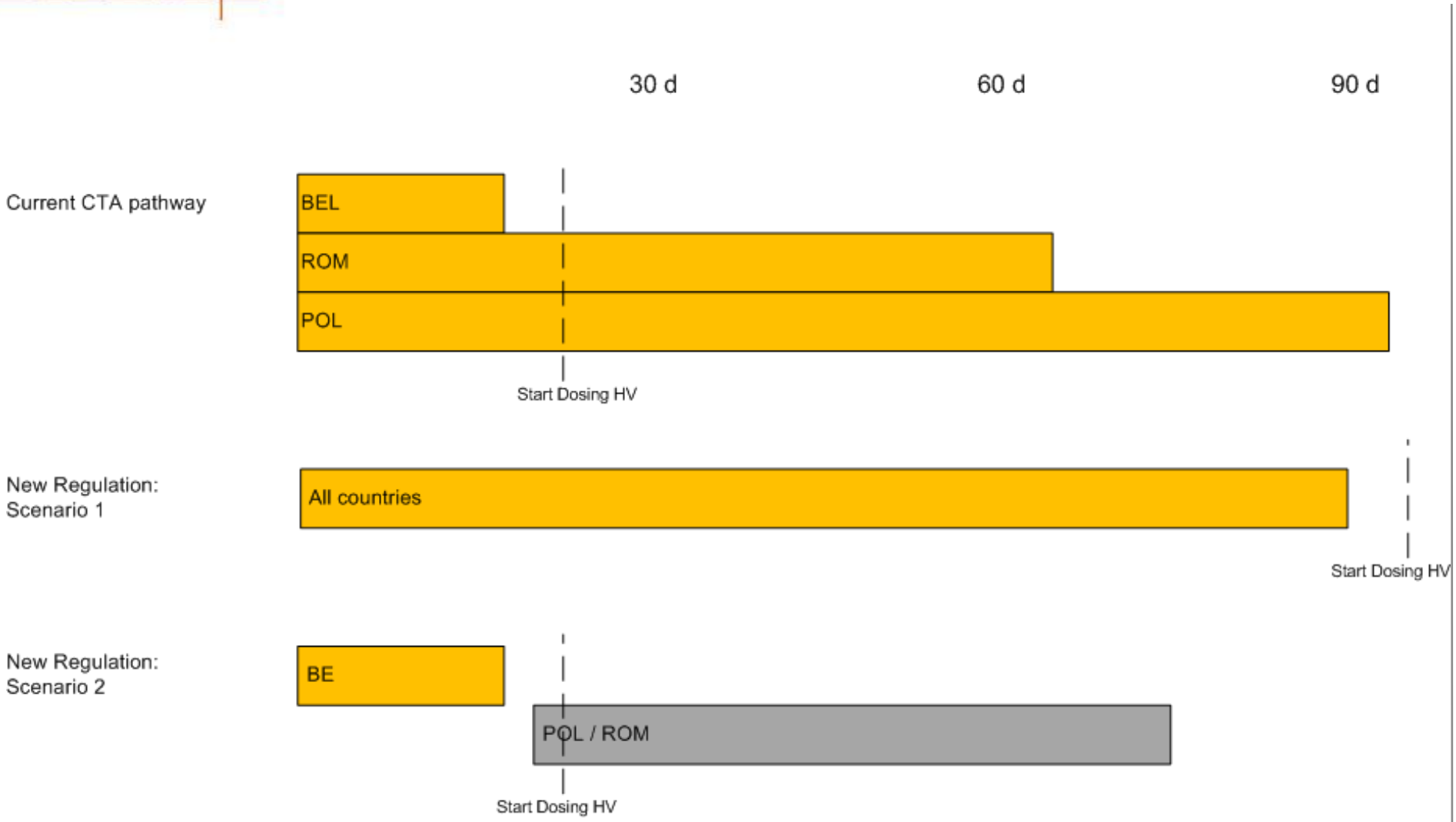
OPTION 2 – STAGGERED SUBMISSION

- Submit application with Belgium only
  - Validation:
    - 10 days
  - Assessment (Part I and II):
    - 45 days + 31 days = 76 days
- Assumption: Belgium
  - Validation: 3 days
  - Assessment: 15 days
- Add Romania and Poland after approval
  - 52 days

TOTAL: 70 DAYS

- *Additional country: 52 – 83 days, 83 days taken*

OVERVIEW


30 d
60 d
90 d
Current CTA pathway
BEL
ROM
POL
Start Dosing HV
New Regulation:
Scenario 1
All countries
Start Dosing HV
New Regulation:
Scenario 2
BE
POL / ROM
Start Dosing HV

CONCLUSION

- Phase I / IIa proof of concept studies
  - Special case, combining early phase and late phase elements
  - Flexibity and smooth start-up required

- New Regulation offers less flexibiltiy
- Workaround possible
- Goodwill of regulators

- Early phase attractiveness more than timelines alone

THANK YOU FOR YOUR ATTENTION

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QUESTIONS?