EU Paediatric Regulation

One Year PDCO

Bonn, DGRA

June 2008

Daniel Brasseur

PDCO at the EMEA


TOGETHER®
SINCE 2007
e Treaty of Rome: 50.europa.eu
TOGETHER®
SINCE 1957
Celebrating the 50th anniversary of the Treaty of Rome: 50.europa.eu

Paediatric regulation

REGULATION (EC) No 1901/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 12 December 2006

on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission

(4) This Regulation aims to facilitate the development and accessibility of medicinal products for use in the paediatric population, to ensure that medicinal products used to treat the paediatric population are subject to ethical research of high quality and are appropriately authorised for use in the paediatric population, and to improve the information available on the use of medicinal products in

Plan

- Committee
- PIP submissions
- PDCO assessment
- Perspectives

PDCO

COMPOSITION:

5 CHMP members
+
1 member per Member State not yet represented
+
6 members from families & HCP associations

Each member has an alternate

PDCO

COMPOSITION:

5 CHMP members

1 member
not y

6 memb
& HC

Each member has an alternate

Link with CHMP reps!
1 Missing … Alternates
No Family, HCP rep yet!

Plan

- Committee
- **PIP submissions, Procedure**
- PDCO assessment
- Perspectives

PIP

Version January 2007

COMMISSION GUIDELINE ON THE FORMAT AND CONTENT OF LICATIONS FOR AGREEMENT OR MODIFICATION OF A PAEDIATRIC INVESTIGATION PLAN AND REQUESTS FOR WAIVERS OR DEFERRALS AND CONCERNING THE OPERATION OF THE COMPLIANCE CHECK AND ON CRITERIA FOR ASSESSING SIGNIFICANT STUDIES

Comments should be e-mailed as word documents using the template to Peter Arlett at the European Commission (peter.arlett@ec.europa.eu)

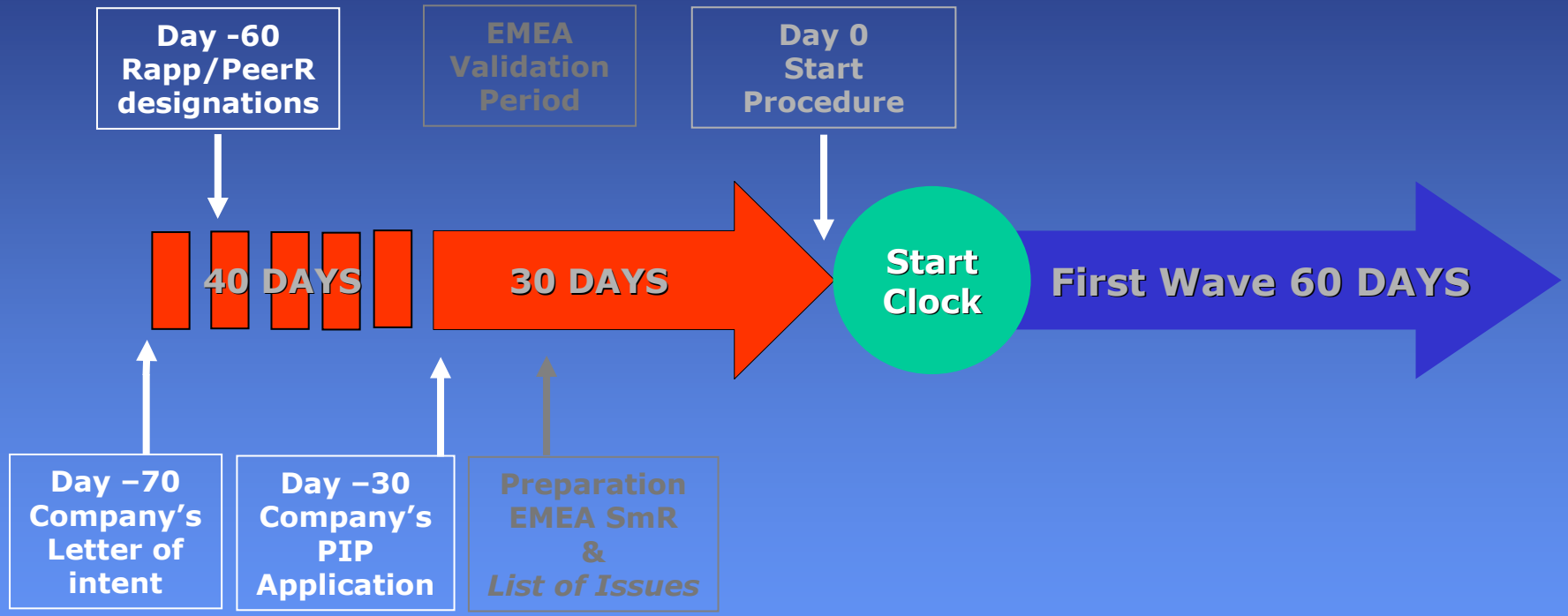
Not published yet

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

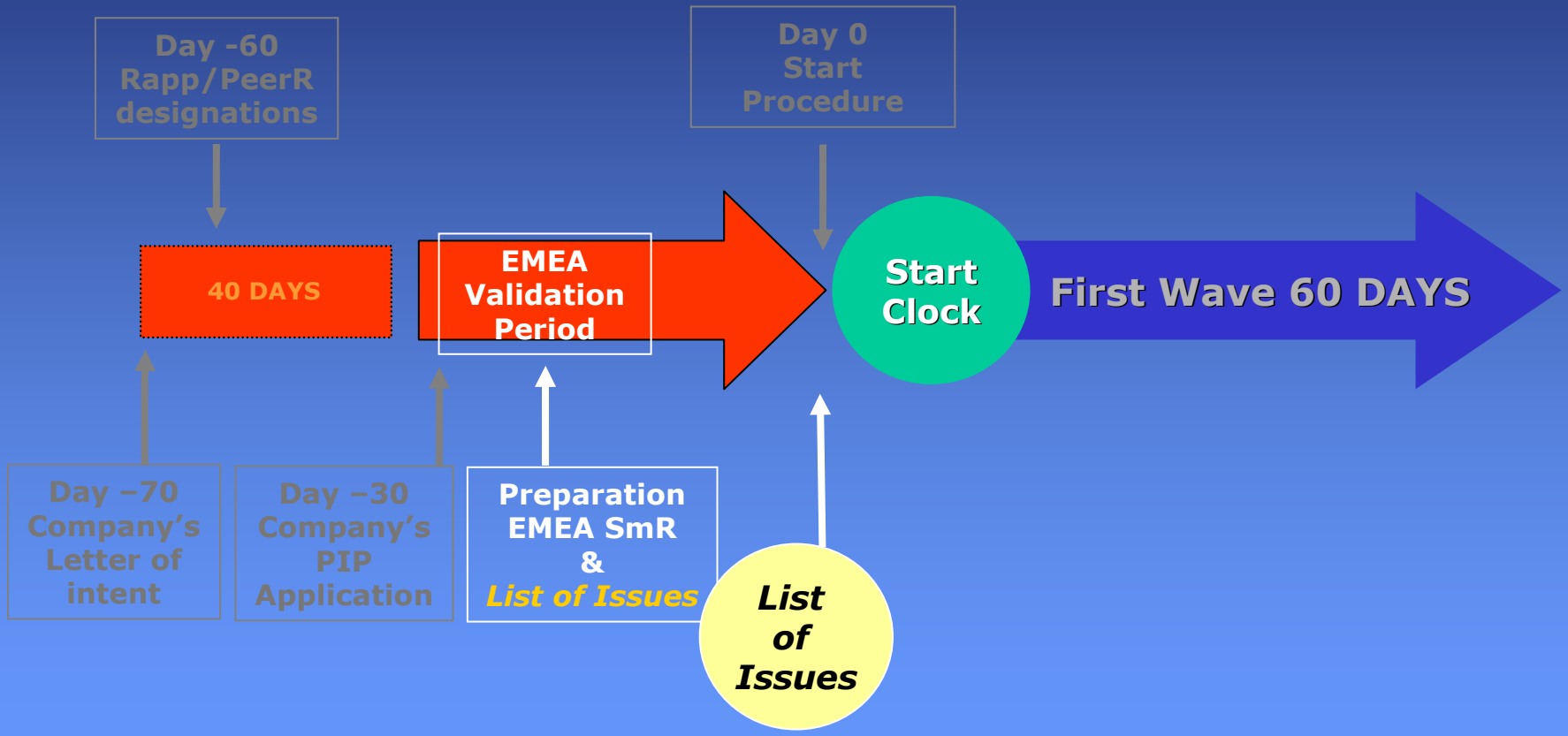
London 1 October 2007
Doc Ref: EMEA/252191/2007-rev 5

Practical aspects on how to submit an application for paediatric investigation plan and requests for waiver and deferral

PIP Procedure 'Intention' Phase



PIP Validation & Summary Report



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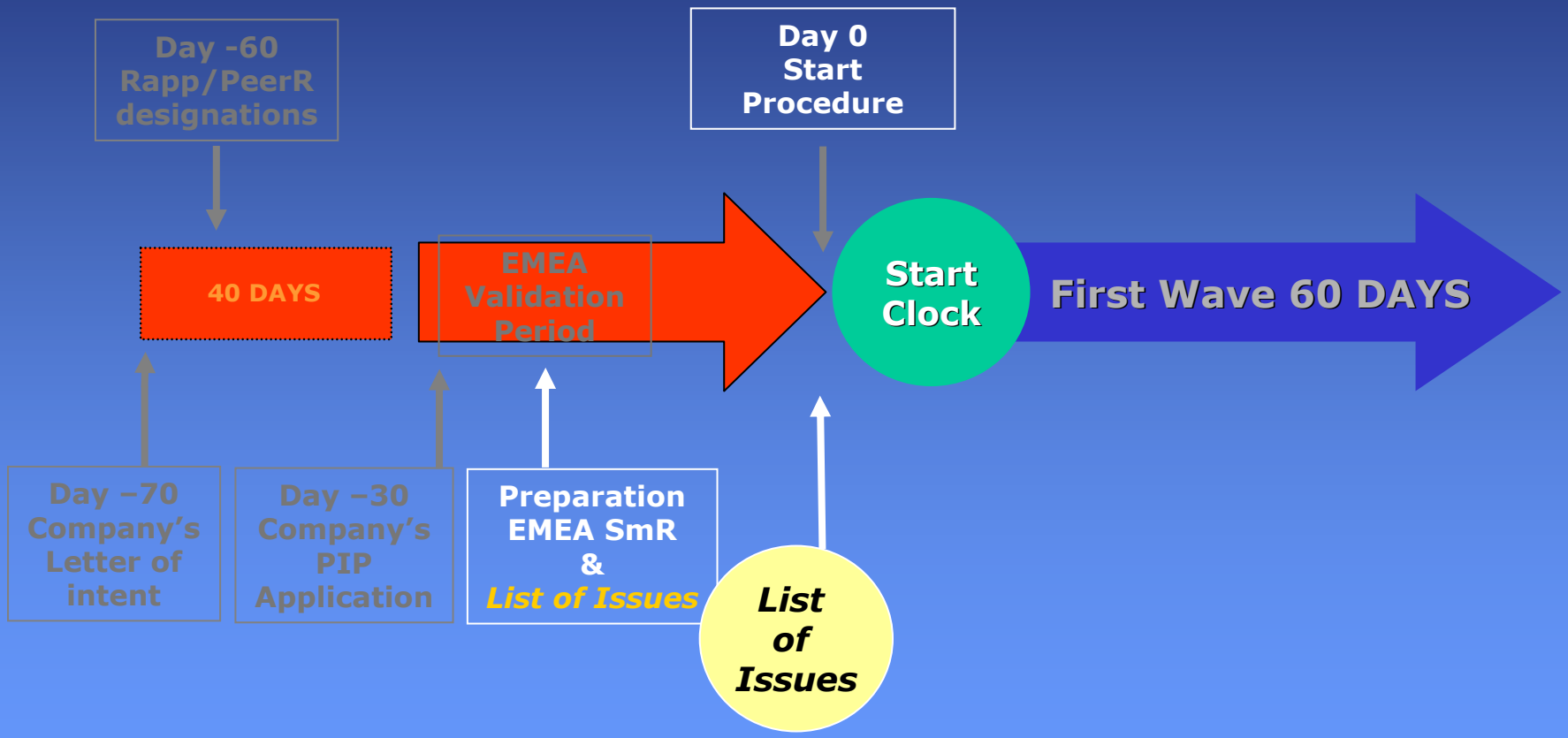
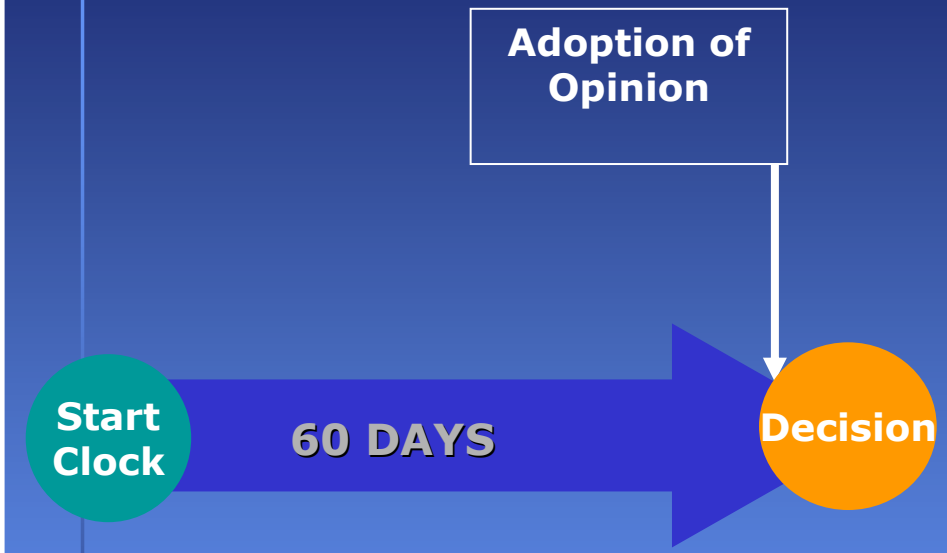


Plan

- Committee
- PIP submissions
- PDCO assessment
  - Timing
- Perspectives

Overview PIP Evaluation



Overview PIP Evaluation

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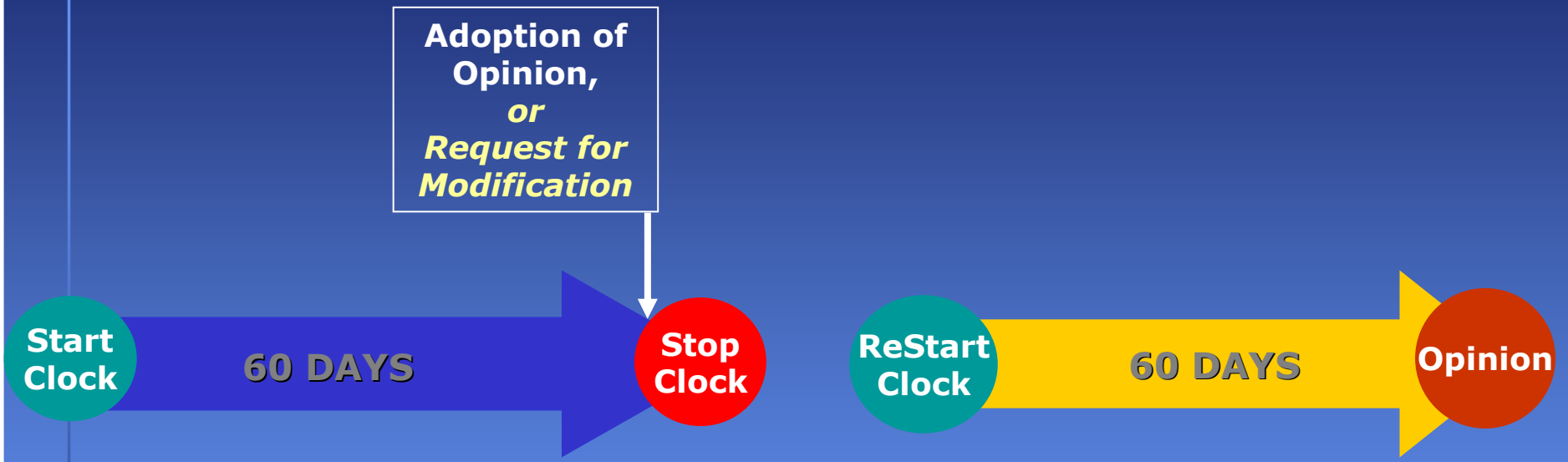


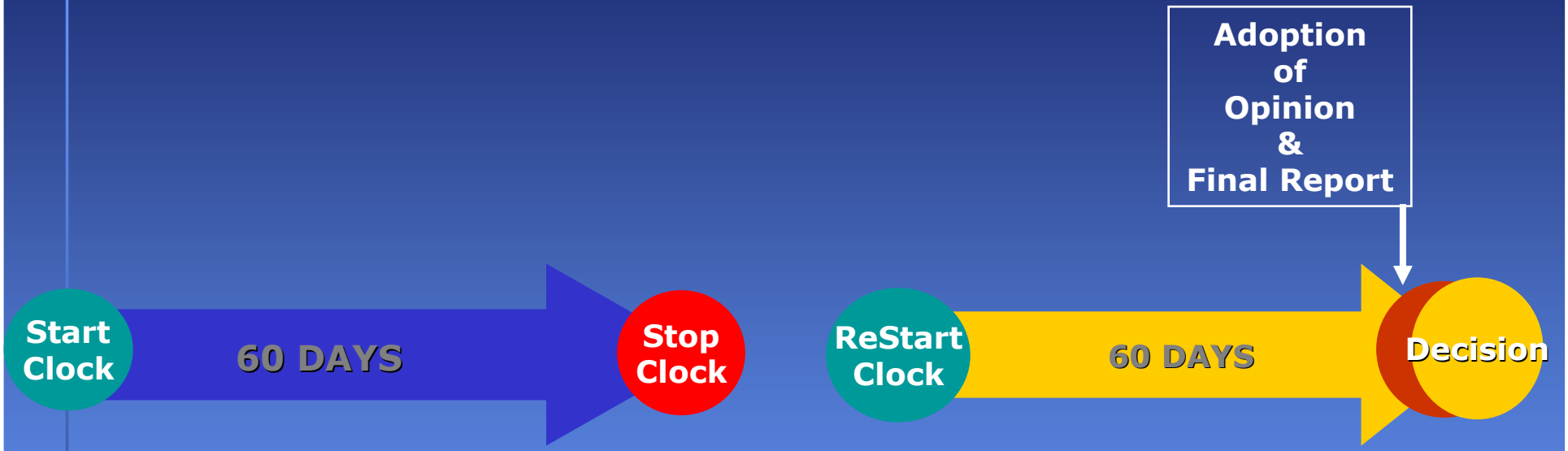
Understand Plan
Detect Problems
Identify Experts
Propose Modifications

Overview PIP Evaluation

Overview PIP Evaluation

Evaluate Changes
Find Agreement
Finalize Plan
Publish Decision

Overview PIP Evaluation



Plan

- Committee
- PIP submissions
- PDCO assessment Outcome
- Perspectives

- **Alzheimer's Disease**
Based on the ground
age of onset of spora
Disease occurs earlie

- **Vascular dementia /**
Based on the ground
Vascular dementia is
conditions and the av

- **Organic amnesic sy**
alcohol and other ps
Based on the ground

- **Amyotrophic lateral**
Based on the ground
reported in the 3rd dec

- **Parkinson's Disease**
Based on the ground
Parkinson's disease i
the age of 40 years.

- **Age-related macular**
Based on the ground
population. The avera

- **Menopausal and oth**
Based on the ground

- **Complications assoc**
Based on the ground
- **Chronic Obstructive**
Based on the ground
of 40 with the cha
Obstructive Lung Dis
Chronic Obstructive
Granting a waiver
development for med
diseases associated w
primary cilia dyskine
to graft-versus-host disease, etc.

- Treatment of adenocarcinoma of the pancreas
- Treatment of gastric carcinoids
- Treatment of adenocarcinoma of the colon and
- Treatment of bladder carcinoma
- Treatment of liver and intrahepatic bile duct carcinoma (excluding hepatoblastoma)
- Treatment of kidney and renal pelvis carcinoma (excluding nephroblastoma, nephroblastomatosis, clear cell sarcoma, mesoblastic nephroma, renal medullary carcinoma and rhabdoid tumour of the kidney)
- Treatment of melanoma
- Treatment of gastric adenocarcinoma
- Treatment of chronic lymphocytic leukaemia
- Treatment of cervix and corpus uteri carcinoma
- Treatment of follicular lymphoma
- Treatment of primary osteoarthrosis (excluding secondary osteoarthrosis)
- Treatment of coronary atherosclerosis
- Treatment of peripheral atherosclerosis
- Treatment of Huntington Chorea
- Treatment of benign prostatic hyperplasia
- Treatment of erectile dysfunction
- Treatment of primary gout (excluding Lesch-Nyhan syndrome and other secondary forms of gout)

Waiver List

Adopted Nov. 23 2007
Updated April. 21 2008

ot normally occur in the
age of 45 and the average
ed in children aged 10-14
(SEER Cancer Statistic

he paediatric population.
s occur already in the 3rd
on low number of cases
ancer Statistics Review

the paediatric population.

1997/2001).

rs)
the paediatric population.
ence reported in children
r 100,000 (SEER Cancer

the paediatric population.
. Rare cases are reported

iediatric population. The
osed above the age of 50.
f cases (< 25) reported in
7/2001).

ric population. Hairy cell

- **Multiple myeloma**
Based on the ground that the condition does not normally occur in the paediatric population. Multiple myeloma median age of diagnosis is 71 years (Cancer, principles and practise of oncology 7th edition) and only 1% of cases occur before the age of 40. No incidence rates are

Oncology

- Pancreatic cancer
- Hepatocellular carcinoma
- Gastric carcinoids
- Colon and rectum cancer
- Bladder cancer
- Liver and intrahepatic bile duct cancer
- Kidney and renal pelvis cancer
- Melanoma of the skin
- Stomach cancer
- Trachea and bronchus cancer
- Chronic lymphatic and chronic myeolotic leukaemias
- Cervic uteri cancer
- Follicular lymphoma

Plan

- Committee
- **PIP assessment,**
  Scientific grounds
- PDCO assessment
- Perspectives

Main Questions...

Has the candidate medicinal product:

1. **any interest for children?**
2. **in which condition(s)?**
3. **in what age range(s)?**
4. **under which form(ulations)?**

Efficacy

Examples

- HTA in children SBP, DBP, MBP???
- Statines: require VWThickness? Blood Flow?
  In the absence of..morbidity, mortality?
  Claim in indication?
- Cancer: PFS? QoL?
- Paediatric Diabetes study design?

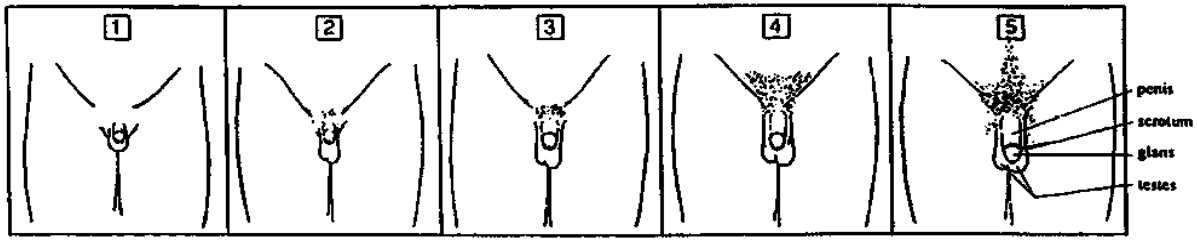
  -add-on therapy on top to metformin/compared to metformin?

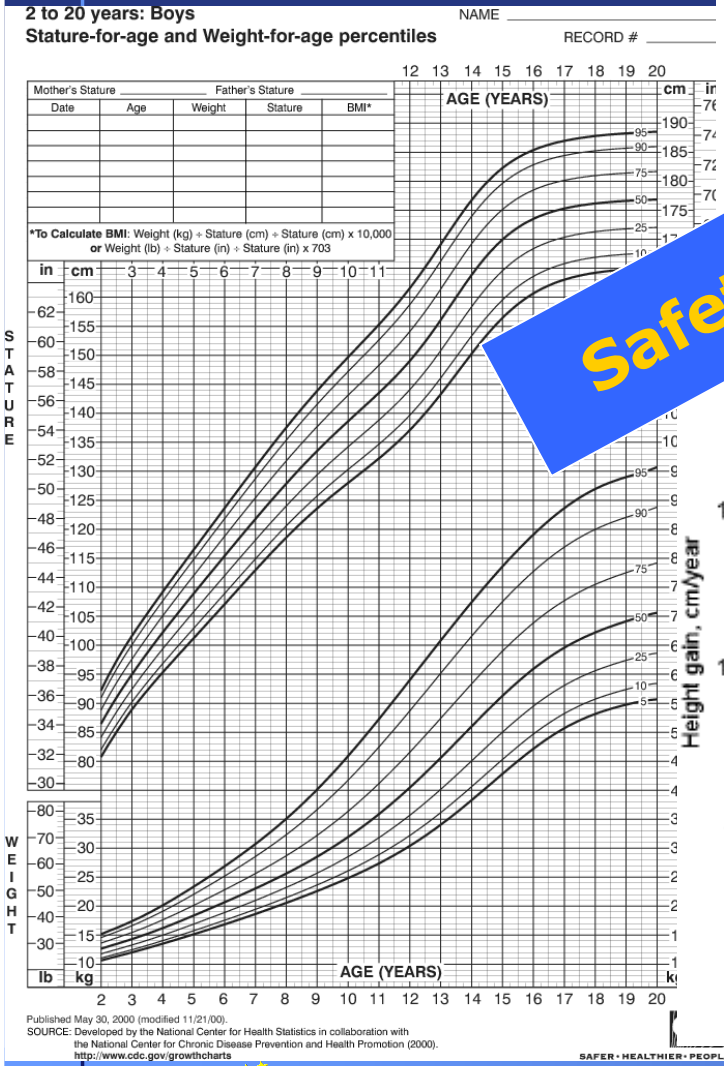
  -non-inferiority design (sample size)

  or

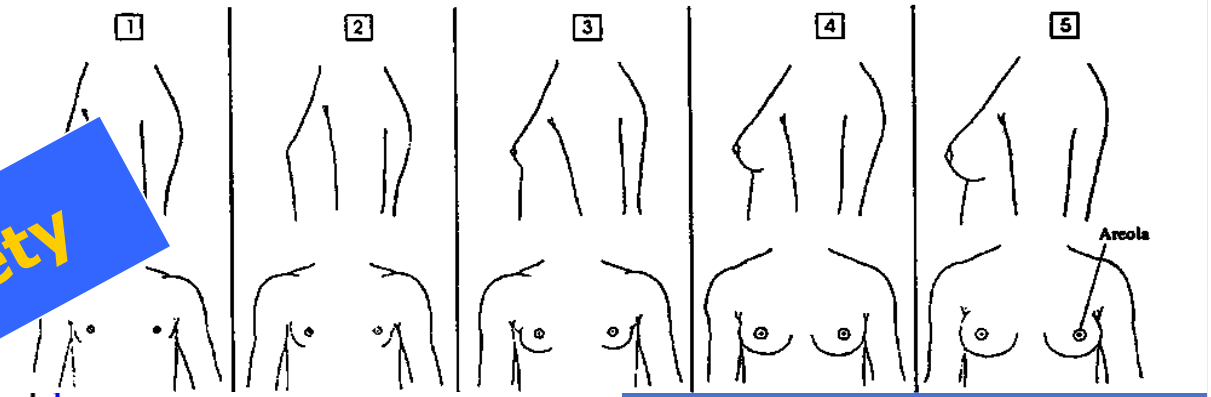
  superiority design against placebo/diet with metformin as internal control?

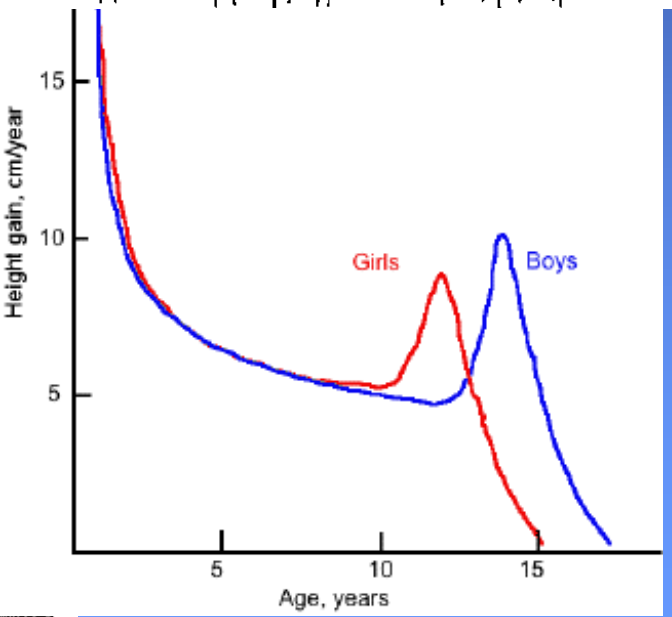
Growth





Safety





Maturation

Achievements
Ongoing submissions

	2007 (August to December)	**2008** (January-May)	**Cumulative Total**
Total number of validated PIP / waiver applications	**85**	**113**[1]	**198**[2]
Applications submitted for a product not yet authorised *(Article 7*[v1]*)*[3]	39	85	124 *(63%)*
Applications submitted for a product already authorised still under patent in view of a submission of a variation/extension for a new indication, pharmaceutical form or route of administration *(Article 8)*	45	23	68 *(34%)*
Applications submitted for an off-patent product developed specifically for children with an age-appropriate formulation *(Article 30)*	1	5	6 *(3%)*
PIPs and full waiver indications covered by these applications	**202**	**159**	**361**

Achievements
Opinions

Number of Paediatric Committee (PDCO) opinions	2007	2008	Total
Positive on full waiver	10	9	19
Positive on PIPs including potential deferral	2	25	27
Negative Opinions adopted	0	1	1

PIP applications

EMEA received after 9 months of activities
(by submission deadline 14.04.2008)

Number of indications covered
in the requests for PIPs or waivers: 361

including full waivers
for the paediatric development
for the whole indication 45

but considering for partial, as an average 4 age classes :

- **waiver *or***
- **deferral *or***
- **'kick-off'**

- **prematures/neonates**
- **-infants**
- **toddlers/school-age children**
- **teenagers or adolescents**

PIP Distribution

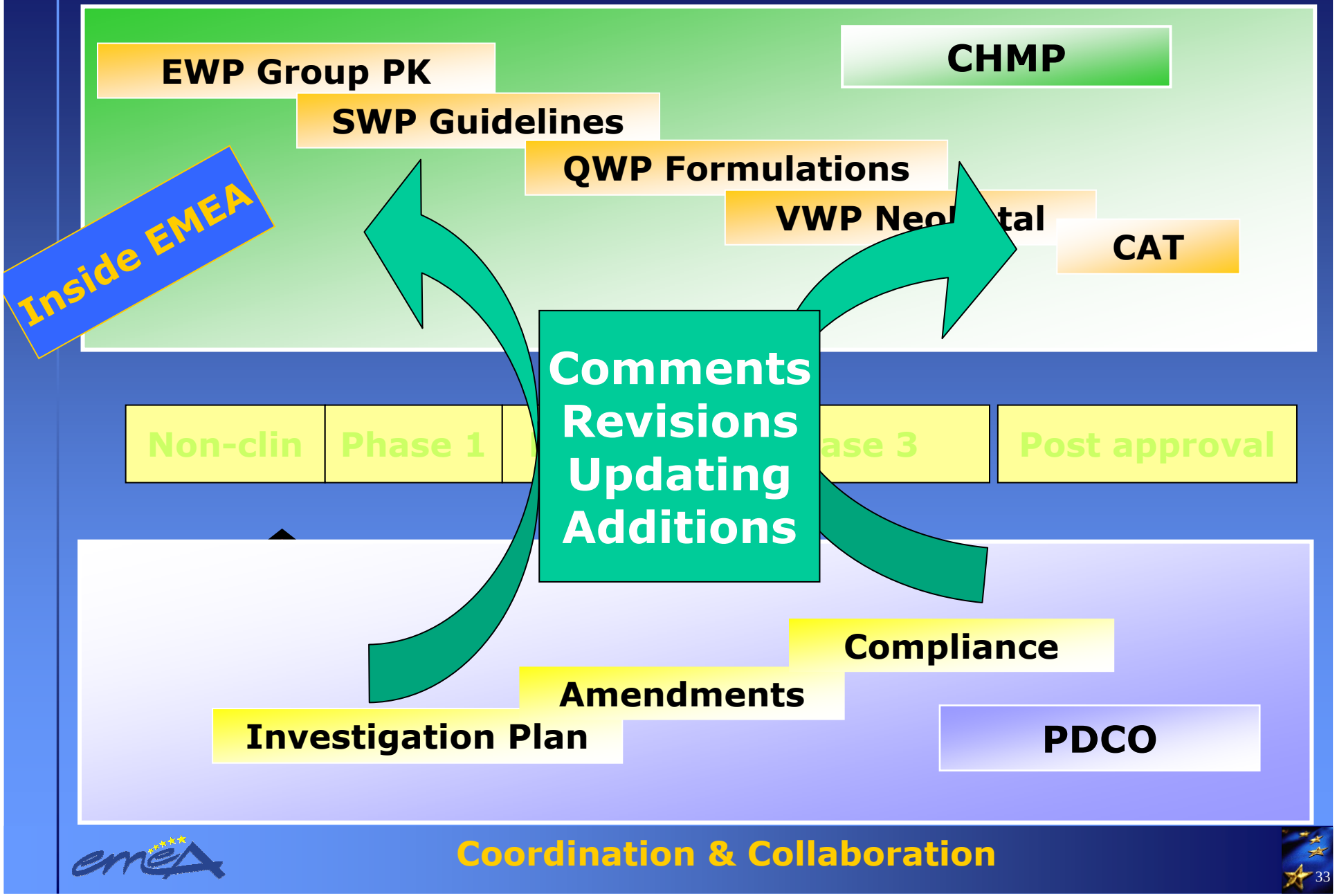
Article 7			
New medicinal products	**(not yet authorised)**	**124**	**63%**
Article 8			
Medicinal product under patent		**68**	**34%**
Article 30			
Off-patent medicines developed specifically for paediatric use with an appropriate formulation		**6**	**3%**

Areas covered by PIPs /waivers	%
• Neurology	12
• Gastroenterology-Hepatology	10
• Pneumology – Allergology	8
• Infectious Diseases	11
• Cardiovascular Diseases	14
• Endocrinology-Gynaecology	18
• Immunology–Rheumatology	4
• Oncology	11
• Vaccines	3

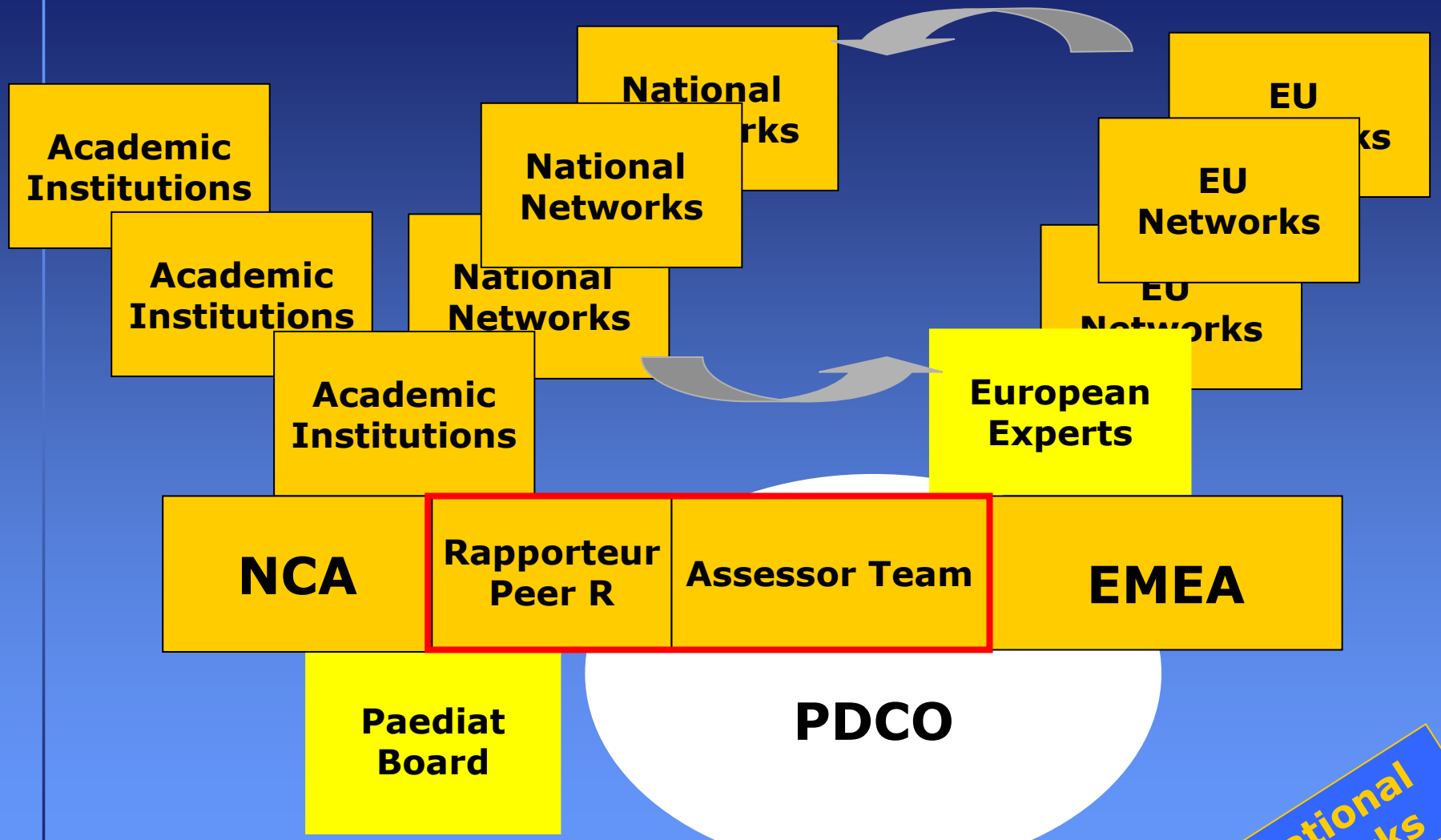
Plan

- Committee
- PIP submissions
- PDCO assessment
- Perspectives
  Interactions

PDCO interactions CHMP WPs



PDCO Activities A team approach

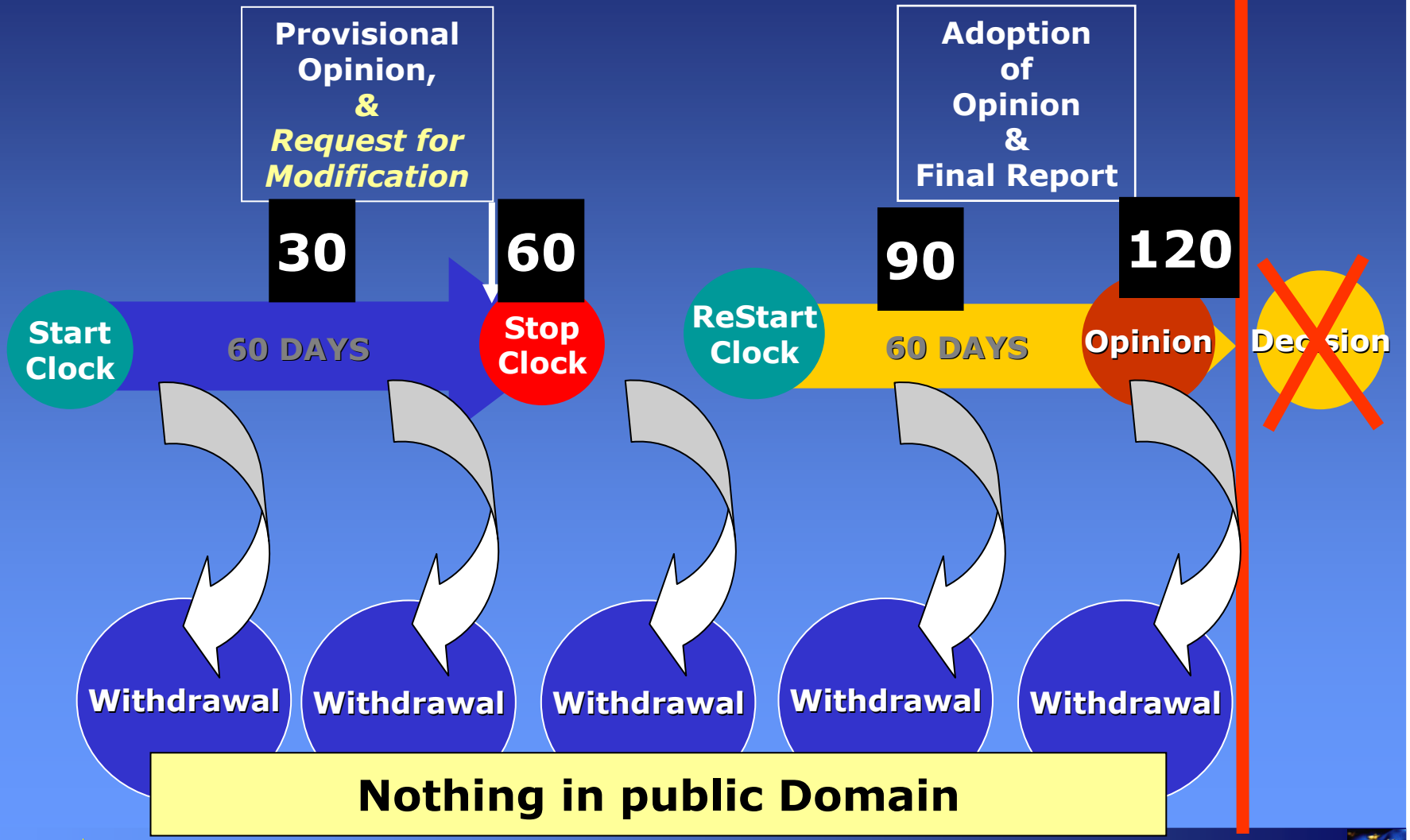


Coordination & Collaboration

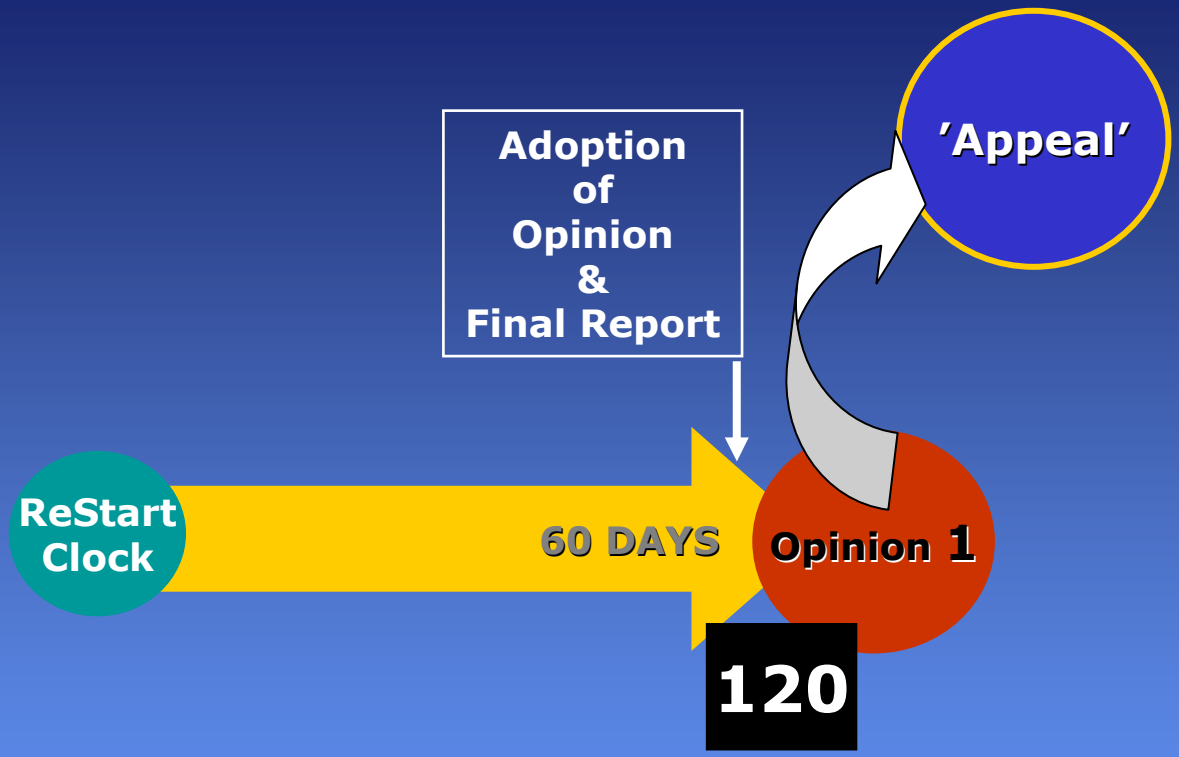
Plan

- Committee
- PIP submissions
- PDCO assessment
- **Perspectives**
  Communication policy

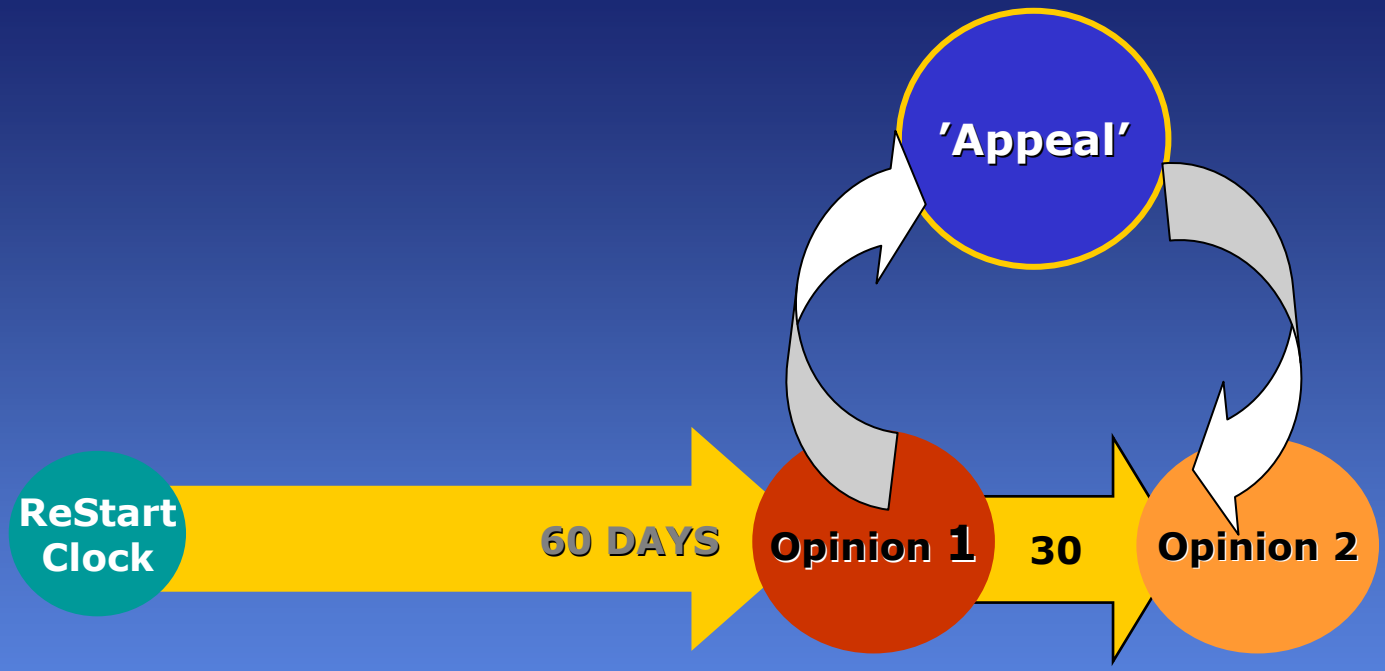
OVERVIEW PIP PROCEDURE



Re-examination



Re-examination



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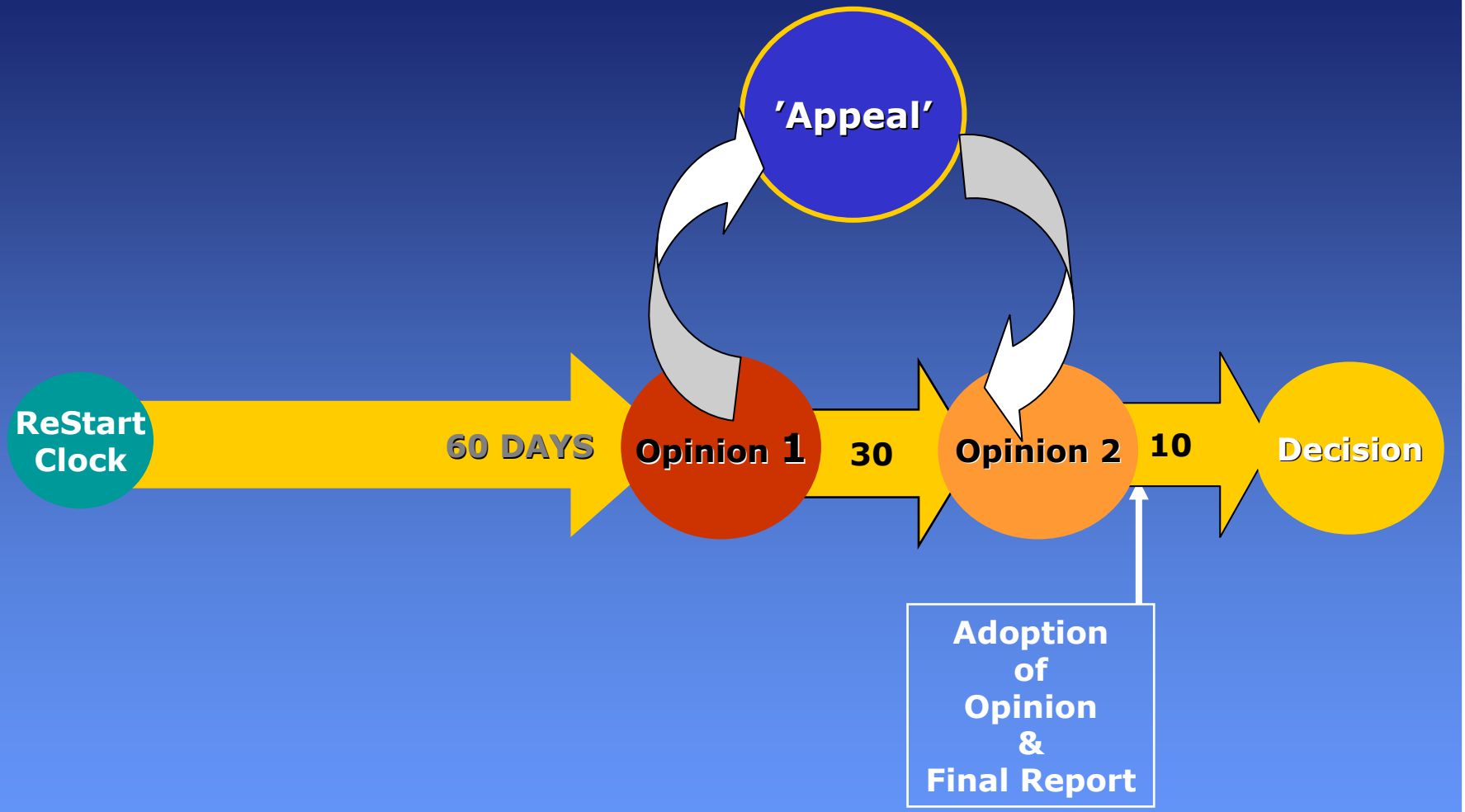

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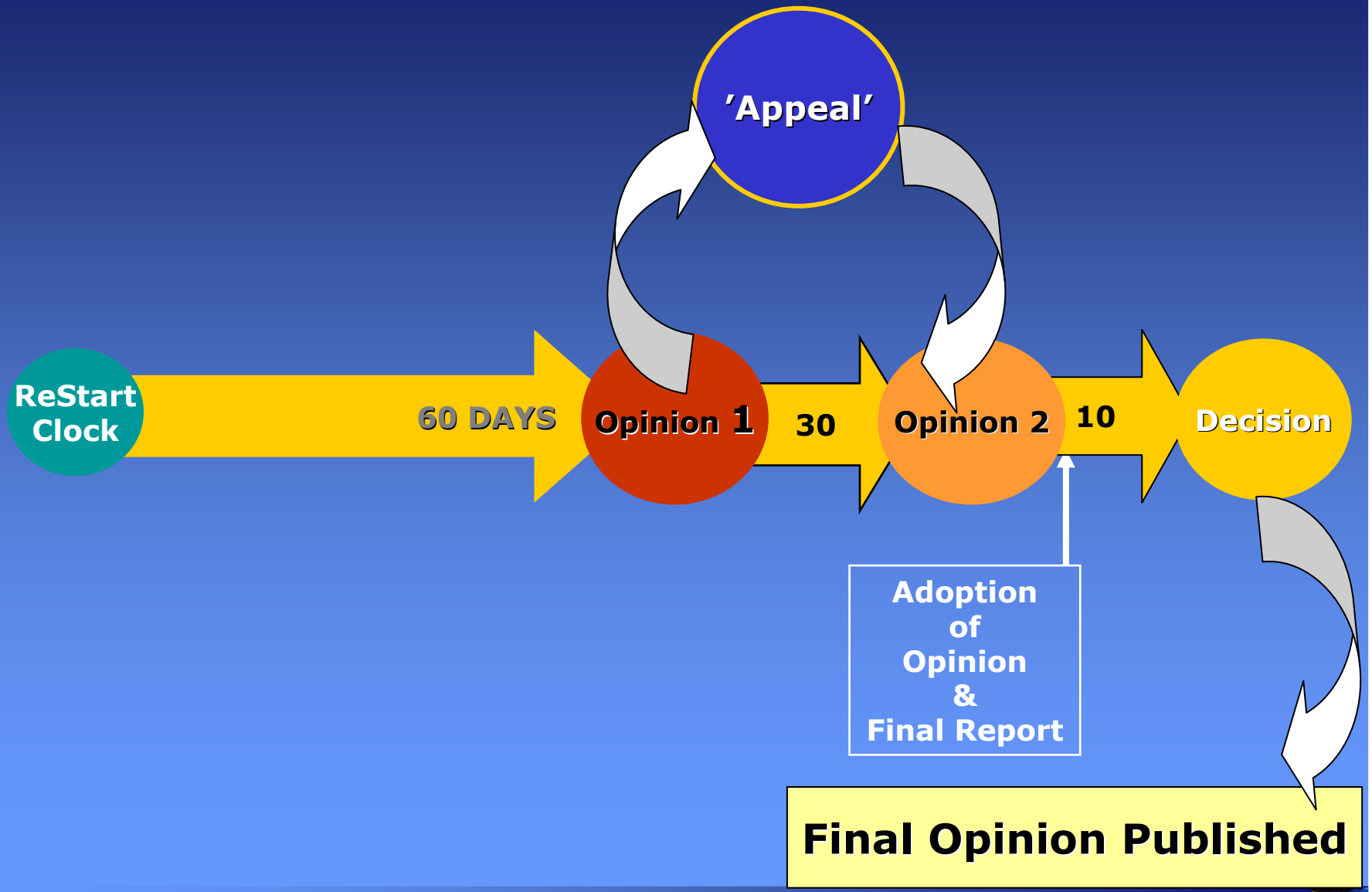

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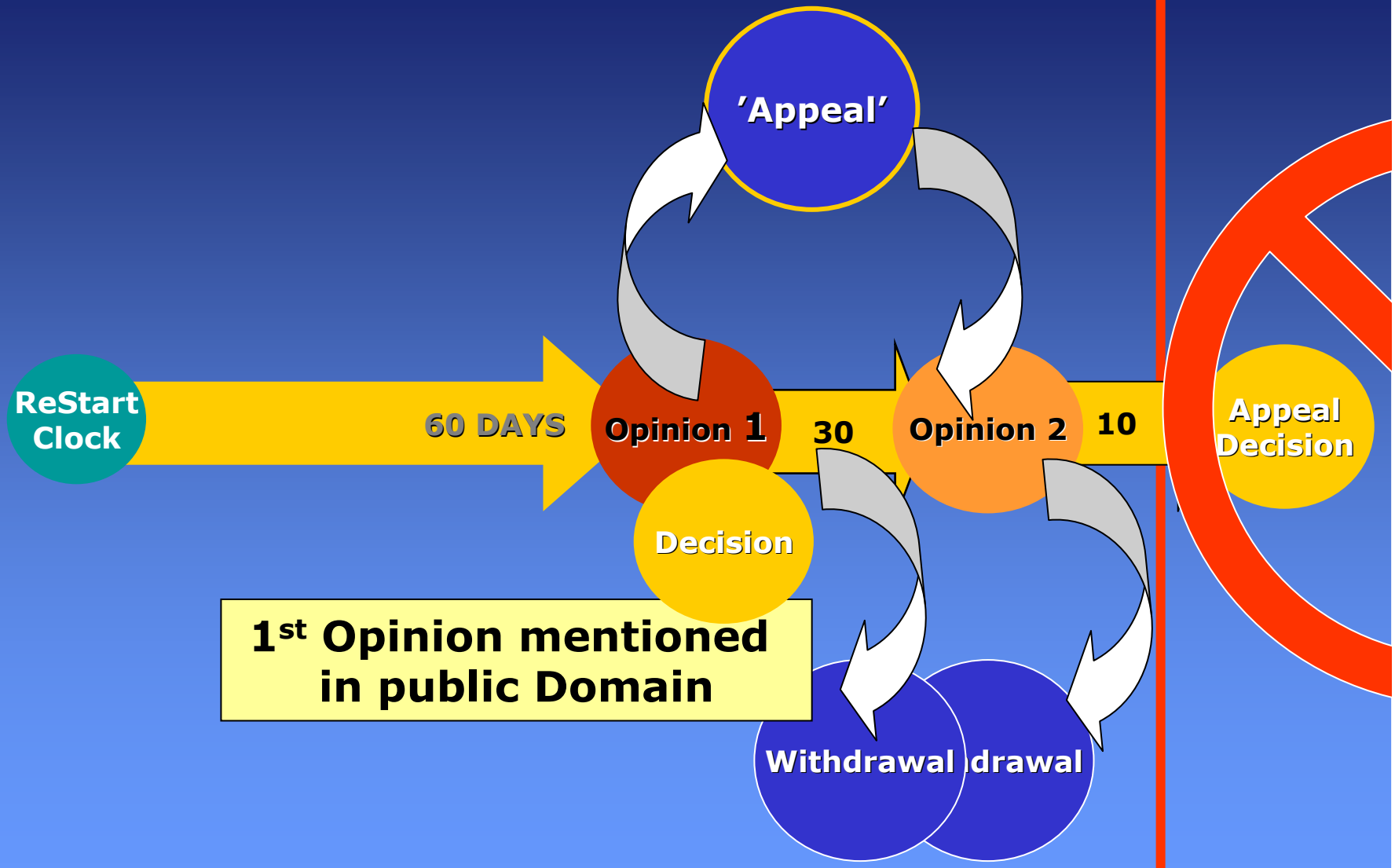

Conclusion

- **Workload as expected, even more…**
- **Timely Deliverables at the cost of…**
- **Fantastic Team Work at the EMEA!**

- **Continuous Motivation to act for ‘free’**
- **Renewed Expertise to assess Novel Fields**
- **Need to simplify, clarify & dialogue**

Conclusion

- Fantastic Team Work
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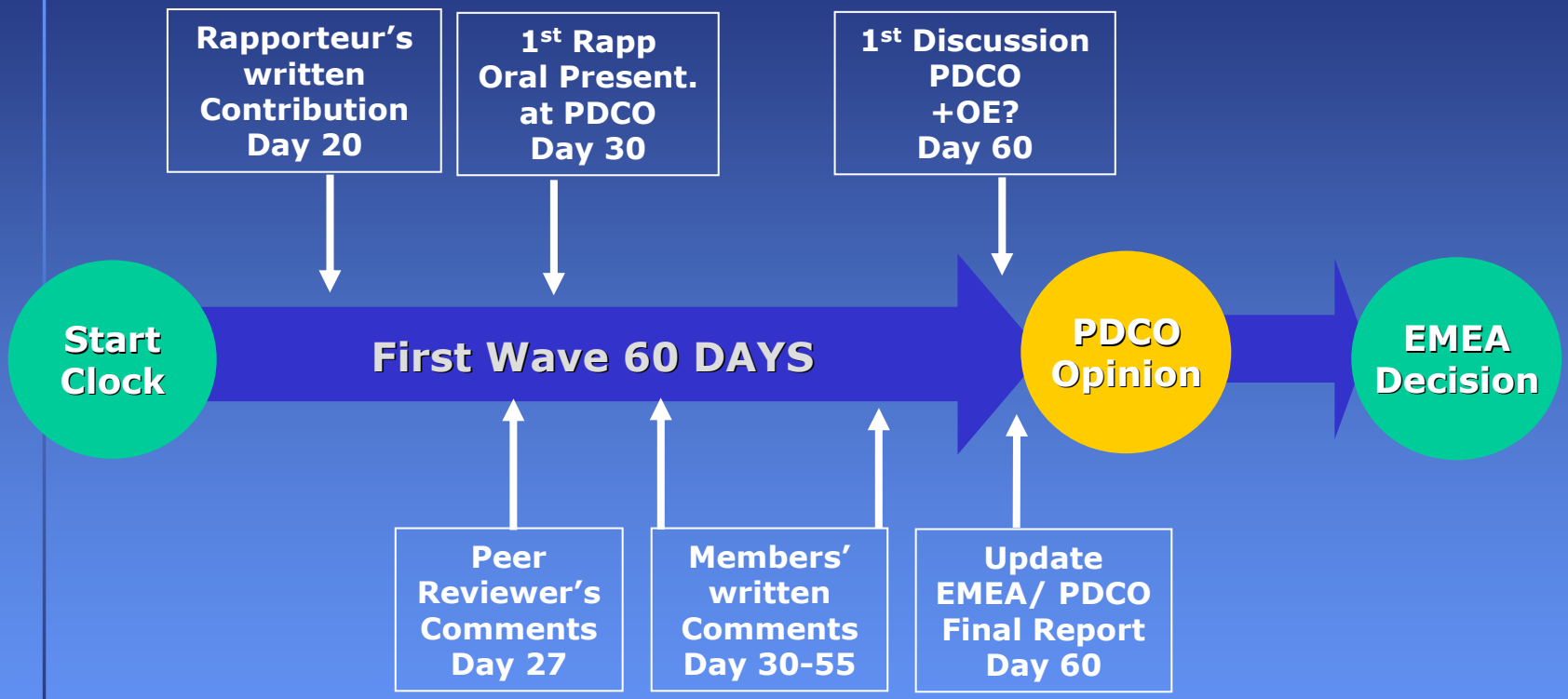
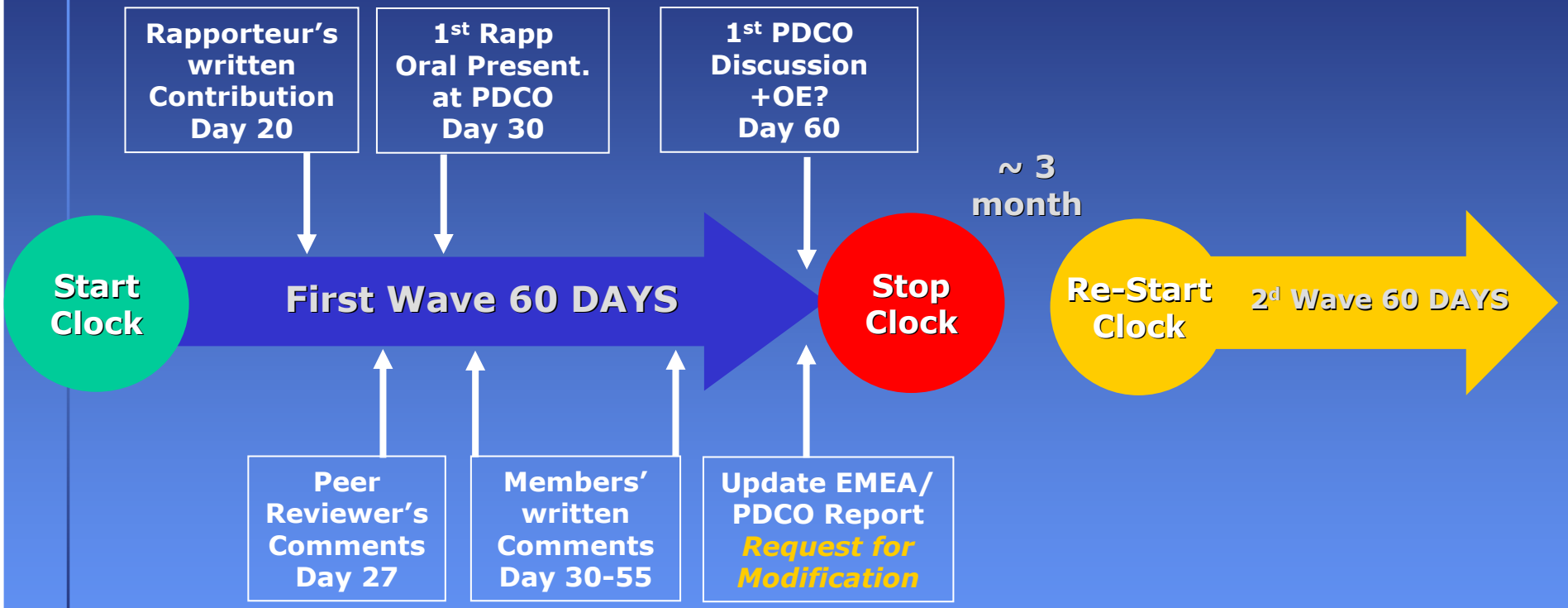
PDCO Activities A team approach

Overview PIP Evaluation



OE= oral explanation

Steps of PIP Evaluation



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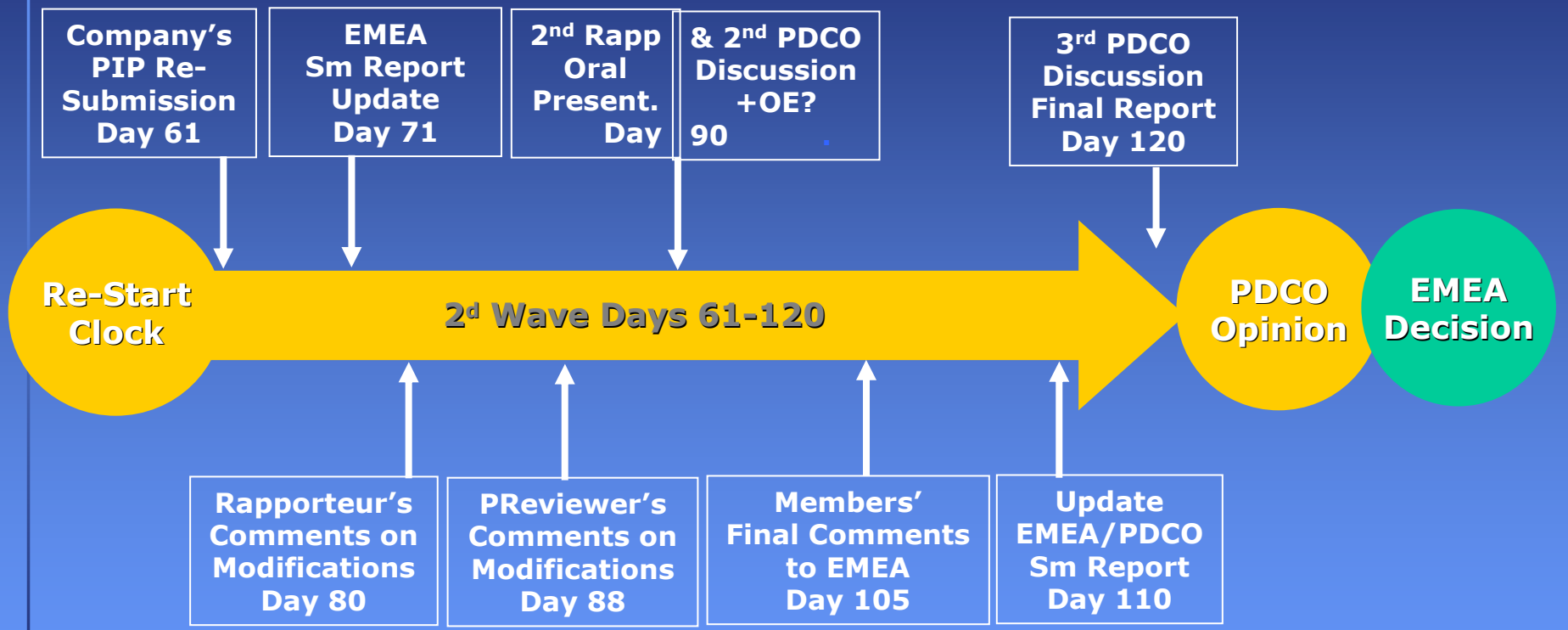

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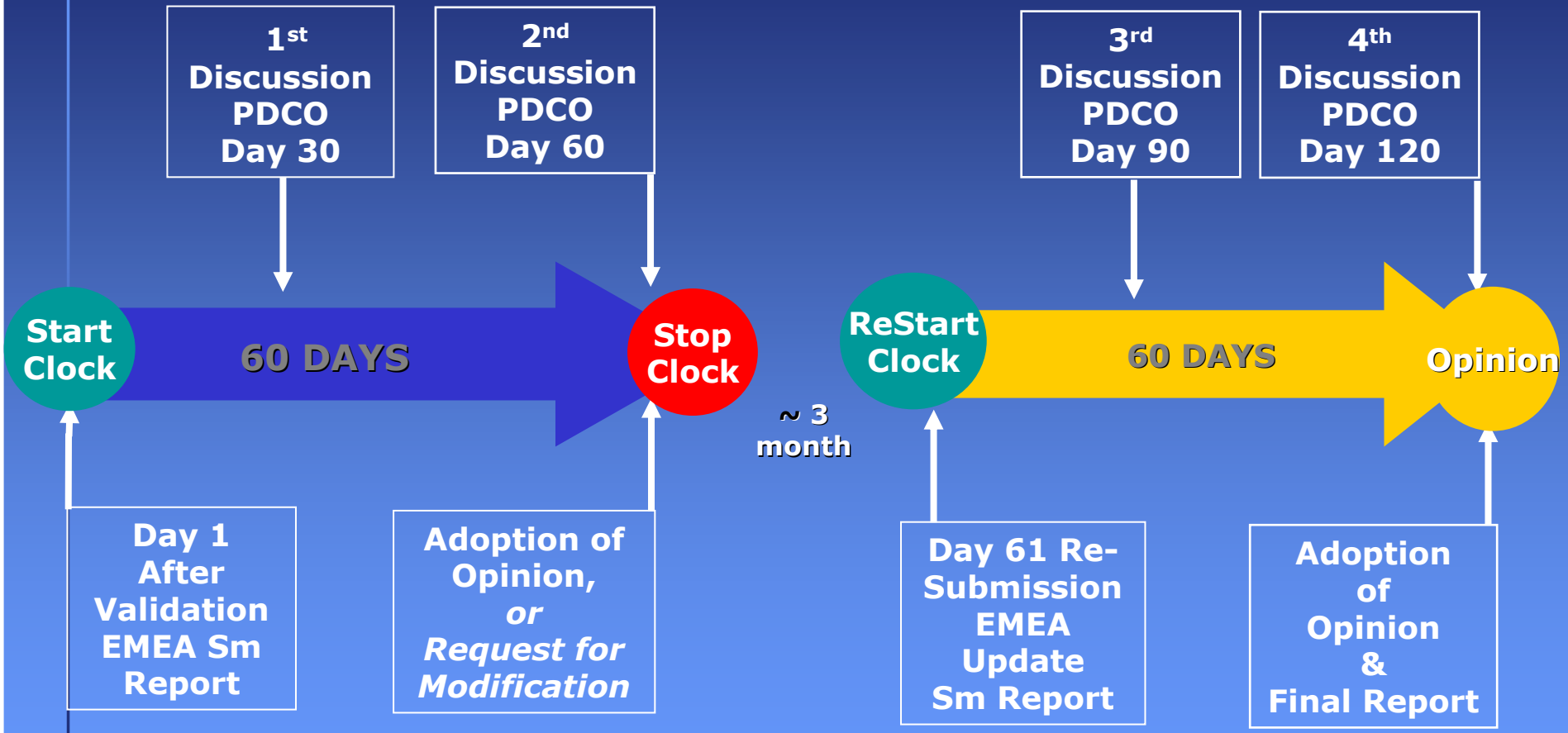

OE= oral explanation

EMEA/PDCO SUMMARY REPORT

on an application for

a

Paediatric Investigation Plan

including a
request for a deferral

and a
request for a waiver

for

PIP Procedure	Date	Procedure Day Number
Report version 0 from EMEA	01/08/2007	1
Report version 1 from Rapporteur	20/08/2007	20
Report version 2 from Peer-reviewer	28/08/2007	28
Report version 3 with comments from PDCO	13/09/2007	44
Report version 4 from EMEA	25/10/2007	61
Report version 5 from Rapporteur and Peer-reviewer	23/11/2007	90
Report version 6 with comments from PDCO	20/12/2007	120

The PDCO Rapporteur for the application were appointed at the PDCO Meeting
PDCO Rapporteur: Prof. Paolo Rossi
Peer Reviewer: Prof. Johannes Taminiau
EMEA Paediatric Co-ordinator: Dr. Annic Weyersberg