EMA CAT WORKSHOP

IMPROVE CERTAINTY OF REGULATORY OUTCOME: AN INCENTIVE IDENTIFIED BY STAKEHOLDERS TO FOSTER TRANSLATION OF RESEARCH INTO COMMERCIAL PRODUCTS

"AN SME PERSPECTIVE"

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In this presentation

- Disclaimers
- Introduction
- Setting the Scene
- Outcome of the 3rd IP Group
- Food for Thoughts

Disclaimers

This presentation reflects the views of the speaker from the perspective of a biotechnology SME and as EuropaBio ATMP Topic Leader.

It may not accurately represent the views of all EuropaBio members.

This presentation does not intend to address the contents of the packages discussed in the "Optimising Resources"

Introduction

Interested Parities (IP) welcome any improvement of:

- The Certainty of the Regulatory Path(s) &
- The Predictability of the Outcome(s)

Which would facilitate the translation of Research into Commercial Products.

Increasing Predictability and Clearing the Path of the Regulatory Outcome to:

- Help attract investors (private/public) – as essential element to create/maintain a start-up and support the development of an SME.
- Increase of the Company's assets when Development Path is followed within Reasonable Timeframe.
- Increase "green lights" on Company's dashboard.

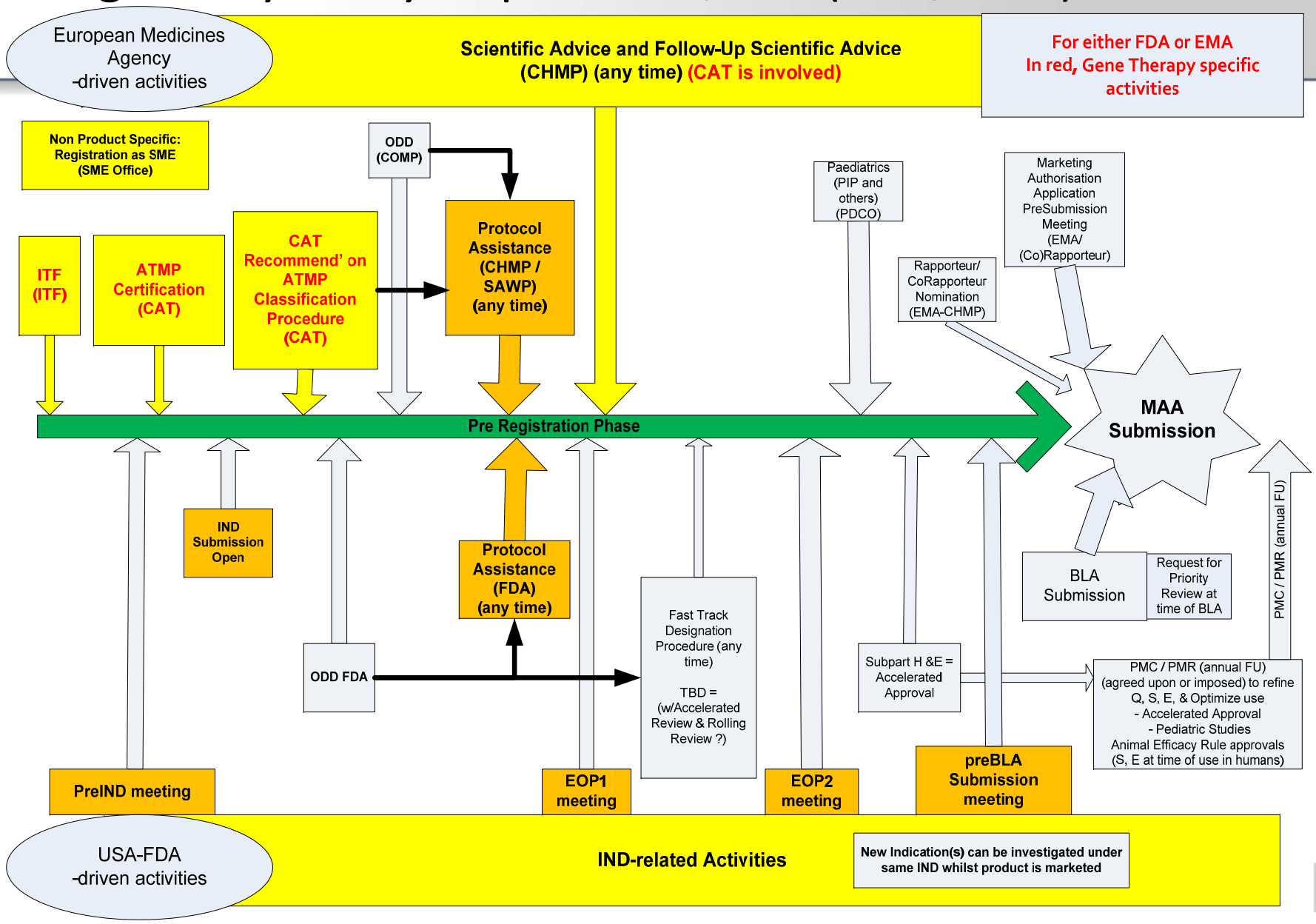
Setting the scene

- Regulatory Players
- Regulatory Lifecycle pre-MAA/BLA (EMA – FDA)
- Regulatory Lifecycle post-MAA (EMA)
- Process Overview for Clinical Trial Authorisation (CTA) (EU/USA)

Regulatory Players
(GTMP as an example)

	EU	US
Definition	Advanced Therapy Medicinal Product (ATMP) / GTMP GMO: Deliberate release (DR) / Contained use (CU)	Gene Therapy (GT)
Regulator Overall	EMA / Committee for Advanced Therapies (CAT)	FDA / Center for Biologics Evaluation and Research (CBER)
Regulator Protocol Dependent	National Competent Authority(ies) in charge of: GCP (CTA); ATMP/GT; GMO.	FDA / CBER NIH / Recombinant DNA Advisory Committee (RAC)
Registration MAA / BLA	Centralised Procedure (if needed GMO built-in assessment)	FDA / CBER

Regulatory Lifecycle pre-MAA/BLA (FDA/EMA)



Regulatory Lifecycle post-MAA (EMA)

Overall

- Annual Re-assessment,
- Specific Obligations (SO)
- Follow-up Measures (FUM)
- Paediatric Information
- PSUR
- Variations (T1/T2)
- 5-year Renewal

ATMP Particulars

Regulatory Lifecycle post-MAA (EMA)
ATMP particulars

Risk Management Plans (at time of MAA) and Follow Up (FU)

http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2009/11/WC500007629.pdf

Post-marketing safety & efficacy FU (e.g.; Reg. on ATMP 1394/2007 Art 14.) *

Long Term FU for patients having received GTMPs

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/11/WC500013424.pdf

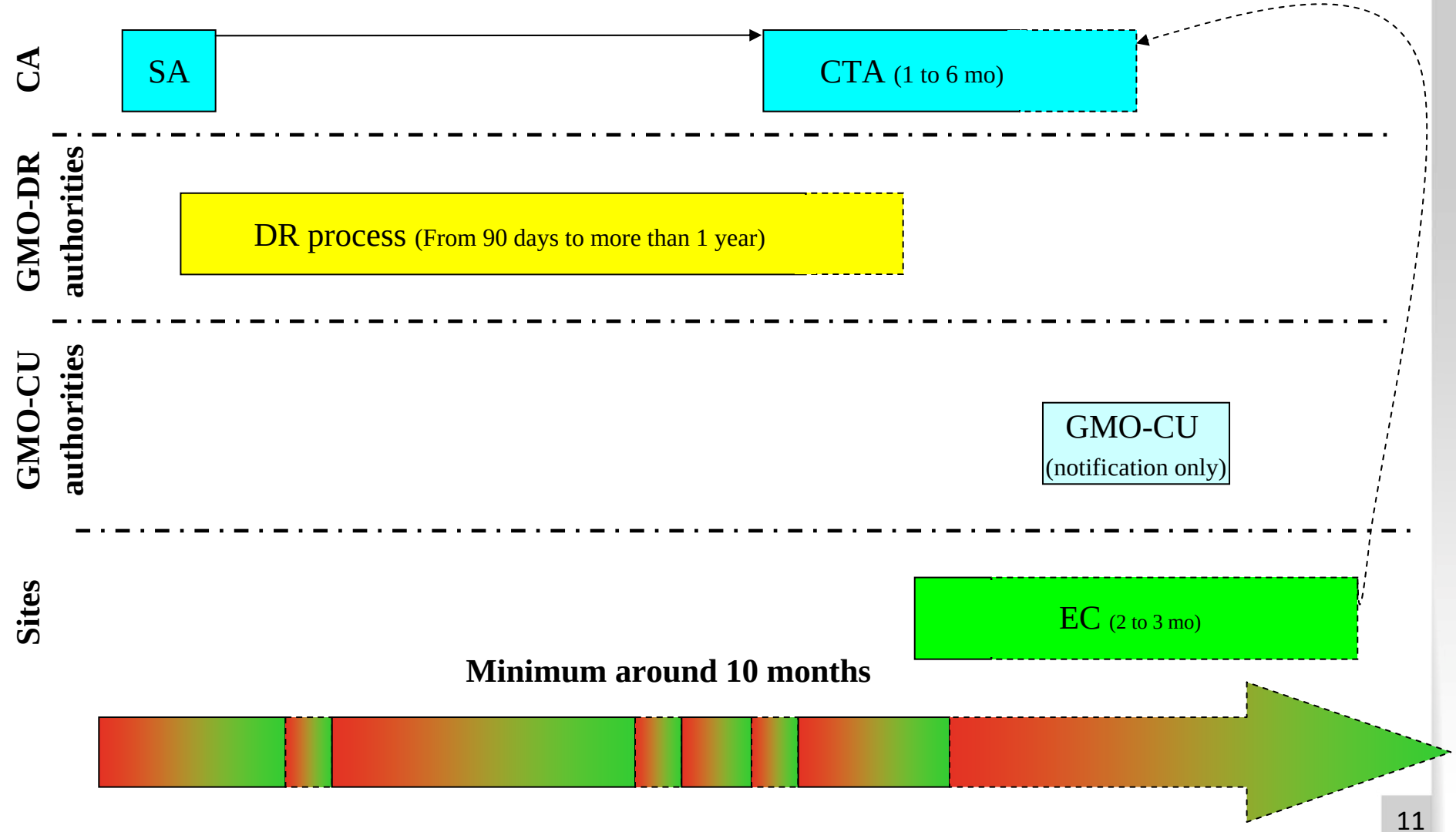
* PV related updates:
Reg. 1394/2007 http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500006326.pdf
Reg. 1235/2010 http://ec.europa.eu/health/files/eudralex/vol-1/reg_2010_1235/reg_2010_1235_en.pdf
Dir. 2010/84/EU http://ec.europa.eu/health/files/eudralex/vol-1/dir_2010_84/dir_2010_84_en.pdf

Process Overview for Clinical Trial Application (CTA) Authorisation - Europe

Europe

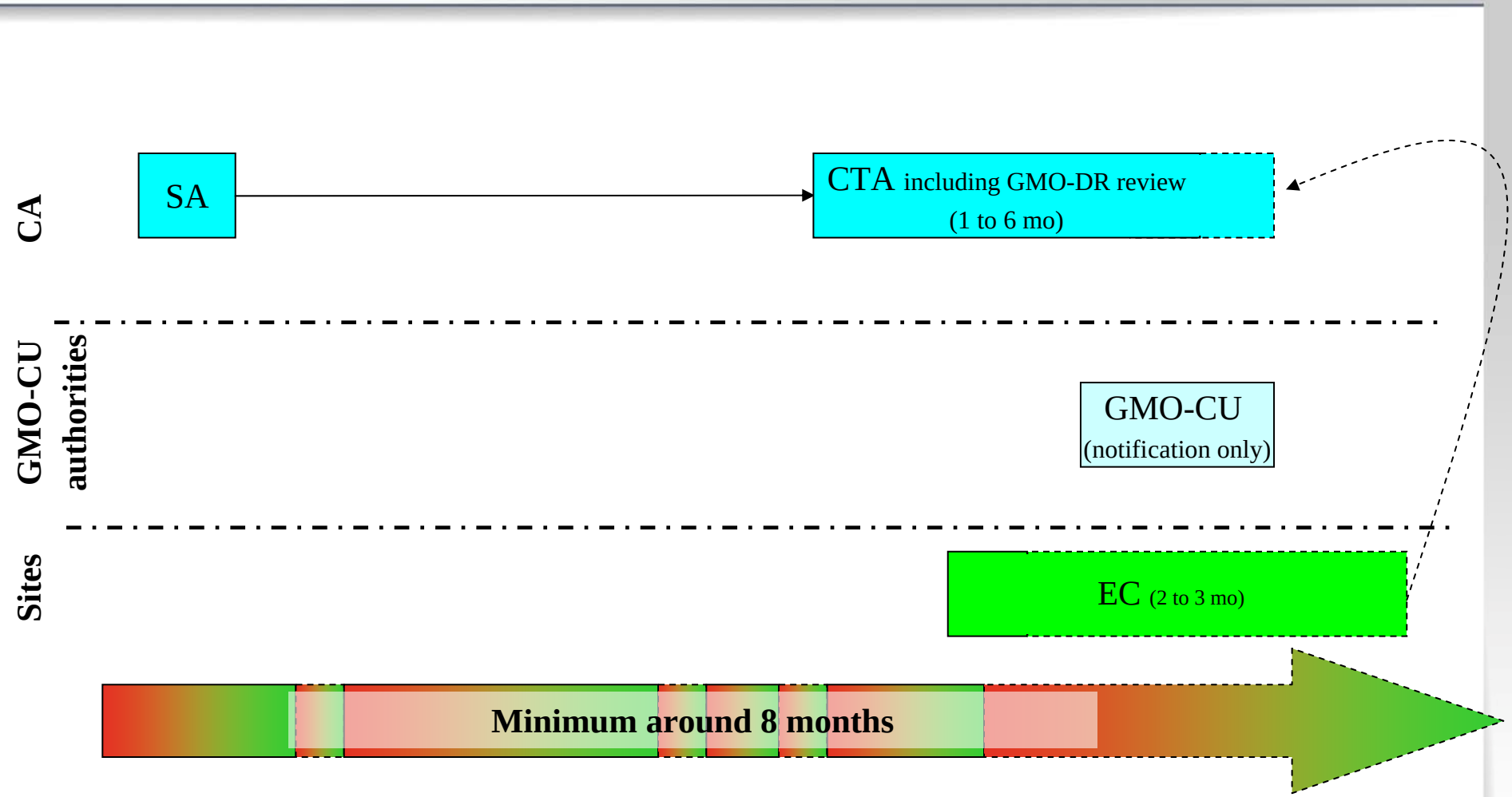
CTA Europe Review/Approval Process

Case 1: GMO DR procedure separate from CTA (BE/NL…)



CTA Europe Review/Approval Process

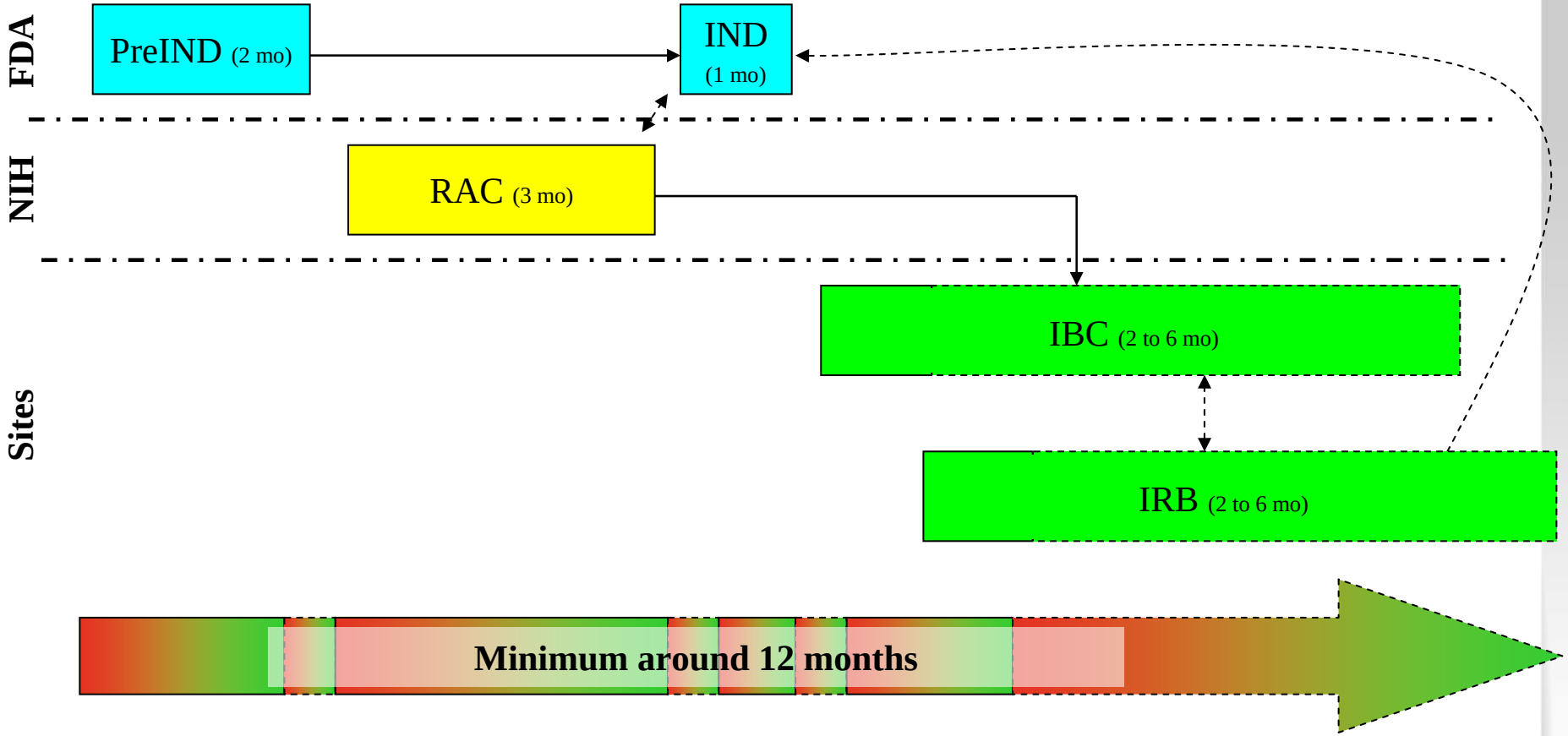
Case 2: GMO DR procedure included within the CTA (SE/FR…)



Process Overview for Clinical Trial Application (CTA) Authorisation – North America - USA

USA

USA Review/Approval Process



Outcome of the 3rd IP Group
(which hold true to SMEs as well)

- 3rd IP group Stakeholders have identified the following facilitation elements
  - Clarification of GMP requirements in different CT phases across EU-MS;
  - Possible adoption of RBA guideline for ATMPs (w/ clear guidance to National-Regional Regulatory/Ethics stakeholders and to Sponsors/Developers);
  - Training and improved dissemination of information for academia including providing support to navigate the regulatory maze;
  - Increasing communication about available incentives and resources for ATMPs developers (see specific slide on Regulatory Lifecycle to MAA).

- Other proposals
  - Discussing product development plans with the CAT to increase the predictability of the regulatory outcome,
  - Simplifying submission processes by allowing stakeholders to use the same file for different regulatory steps (i.e. for SA, for PIP, etc.) and
  - Adapting scientific guidelines to early stage CT requirements

Food for Thoughts
(Between EU-National Stakeholders)

Currently there “seems” to be a “China Wall” between

- The “concepts” discussed at EMA-CAT level for Development Plans and
- The “concepts”/“practice” assessed/approved at National EU-MS level (by a diverse panel of experts) for CT conduct

Need a “central point” (such as CAT) acknowledged for its competence to address ATMP issues (i.e.; such as RAC) via “Recommendations”

Food for Thoughts
(Between EU-National Stakeholders)

Knowledge Sharing & Facilitation

(Serves the Risk Based Approach (RBA))

Need for a 2-way feedback:

- **Top to Down:** CAT to National Specific Stakeholders (NCA, EC, Specific bodies dealing w/ ATMP) with trainings and follow-ups,
- **Down to Top:** Practical experience fed in the "concepts" w/ appropriate interactions & follow-ups.

At time of ITF, SA, ATMP Classification, CAT experts may prospectively explore multi-centric/national CT

- Such as legal input to address "local legal frameworks" (LLF) of CTs designs throughout EU and how to alleviate the barriers w/ RBA (serves the MAA & post-MAA steps) (sometimes these LLF were established as "safety cushions")

Food for Thoughts
(Between EU-National Stakeholders)

Knowledge Sharing & Facilitation
(Serves the Risk Based Approach (RBA))

EMA-based databases contain information on “a” product in development:

- EU Clinical Trials Register (EU CTR) (w/ EudraCT);
- EudraVigilance = tracks Annual Safety Reports & Development Safety Update Reports (DSUR) (later used for Post Registration activities)

CAT (or similar body) should be empowered to navigate this wealth of Information to create Knowledge;

Non-NCA ATMP bodies should have

- Access to this knowlegde and
- Contribute to its development

=> Mapping of this diverse EU landscape is necessary.

Food for Thoughts
(Between Regulators and Interested Parties)

Reducing uncertainty stimulates innovation
by lowering barriers to development

Many national bodies involved in the review/approval of ATMPs, w/ great disparities between EU-MS

=> Need of centralised information on which bodies should be involved in a given EU-MS

(see Dutch Commission on Genetic Modification (COGEM) – International Medical Tourism From The Netherlands for Gene Therapy

http://www.cogem.net/index.cfm/en/publications/publicatie/international-medical-tourism-from-the-netherlands-for-gene-therapy)

Set of information should be made public

- Publishing data from the CT (without hampering IP) would increase knowledge especially in the ATMP area (Is EU CTR sufficient?)
- Have expert panel discussion made public to increase the transparency and the contribution from public, a similar practice is in place at FDA (Advisory Committees) & RAC

(see RAC meeting minutes/presentations of the Public Discussions at http://oba.od.nih.gov/rdna_rac/rac_meetings.html)

- Give greater guidance on suitable approaches to orphan development
- Increase awareness of available tools for Academia & SME

Conclusion

3-way engagement
"To dance, you need 2 partners & the musicians"

Best means of reducing regulatory uncertainty

- Direct engagement between all ATMP Regulatory/Ethics stakeholders & Academia/SME during development plan interactions must be seamless and maintain a continuous dialogue w/ the ATMP National Stakeholders issuing CT authorisation;
- Give non-binding acceptance of design (*ceterus paribus*)
- Advice from the same group/specific experts that will assess results to avoid a perception of abstraction in the SA replies
- To reach out to the Patients (real audience) Expectations, Unmet Medical Need is best served by Risk Based Approach strategy. Example in the applications would be welcome