EMA /US FDA Workshop on

support to quality development in early access approaches

Regulatory tools to support early access
- Industry perspective-

***Yoko Momonoi, M.S.* (Celgene/EFPIA)**

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Bio Biotechnology Innovation Organization

ebe european biopharmaceutical enterprises

efpia European Federation of Pharmaceutical Industries and Associations

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Outline

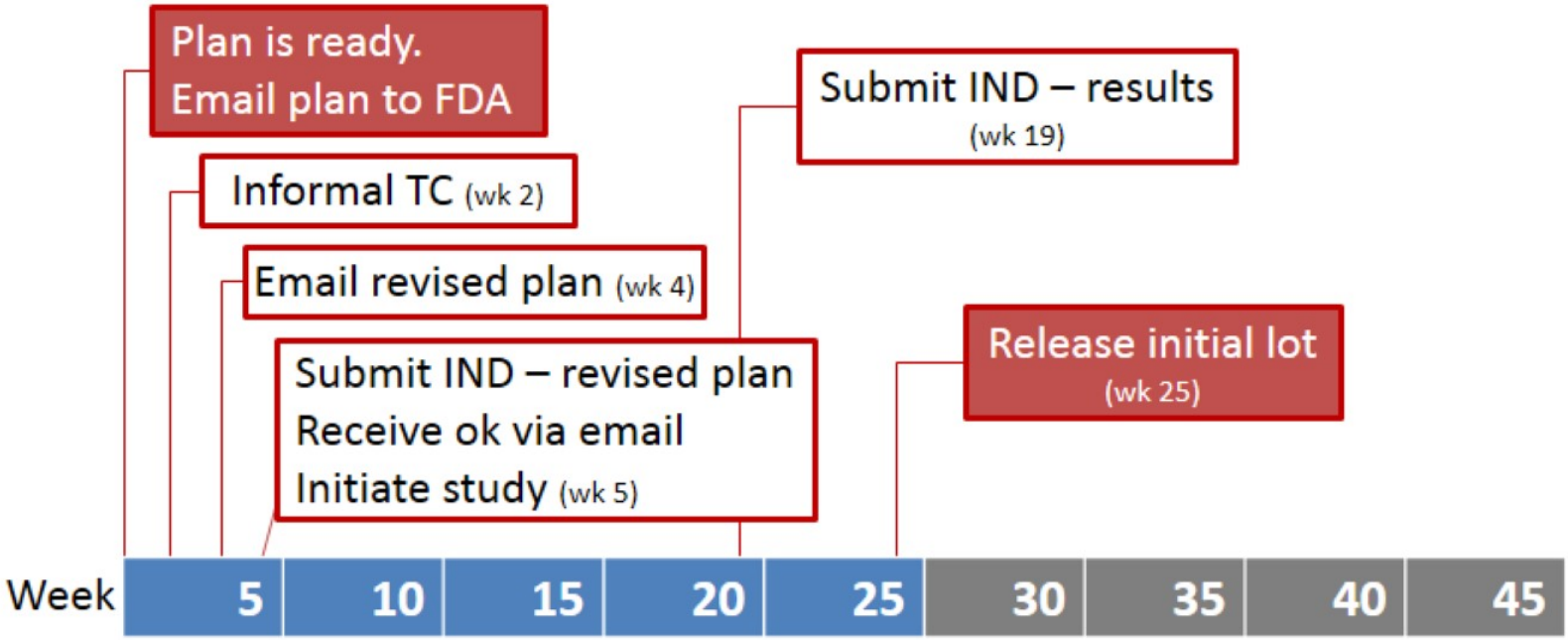
1. Use of Agency Meetings During Development

2. Management of Post-Approval Changes

Use of Agency Meetings During Development
Case study: Site addition for an ATMP

- Change: Manufacturing site addition for an autologous CAR T
  - Vector or drug product for the pivotal trial manufactured at site A
  - Commercial vector or drug product to be manufactured at site B
- Context
  - Rapid development often requires manufacturing to start in site A
  - Understanding of the manufacturing process is evolving
- Considerations
  - Demonstration of analytical comparability is key
  - Clinical manufacturing experience at site B prior to commercial manufacturing is desirable
- 3 scenarios
  - Frequent Agency interactions
  - Separate Agency meetings
  - Parallel Scientific Advice

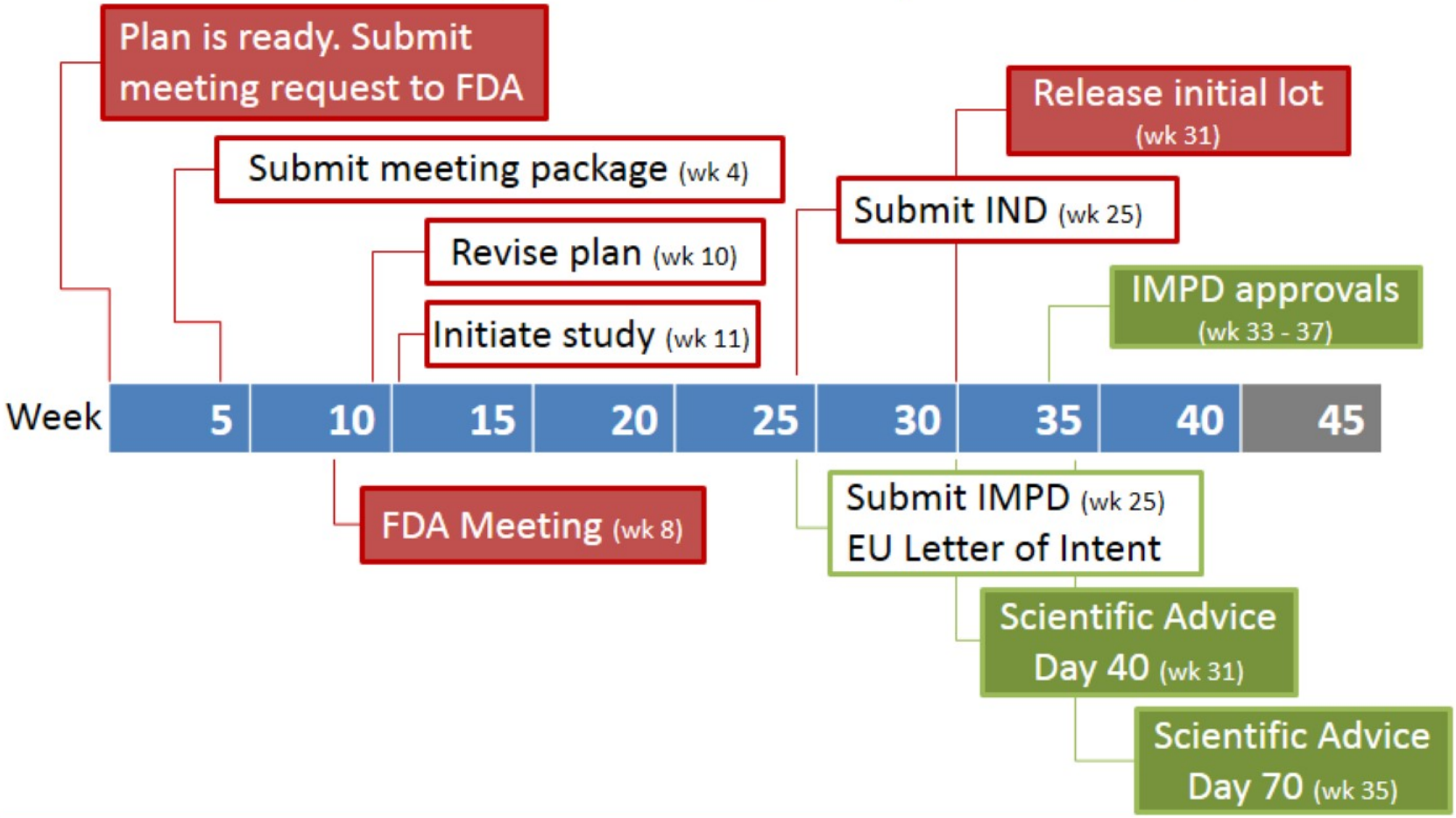
Use of Agency Meetings During Development - with frequent interactions with Agency -



Time from initial plan to release of initial lot: 25 weeks
Less risk due to confirmation of revised plan prior to execution
Input from one Agency only

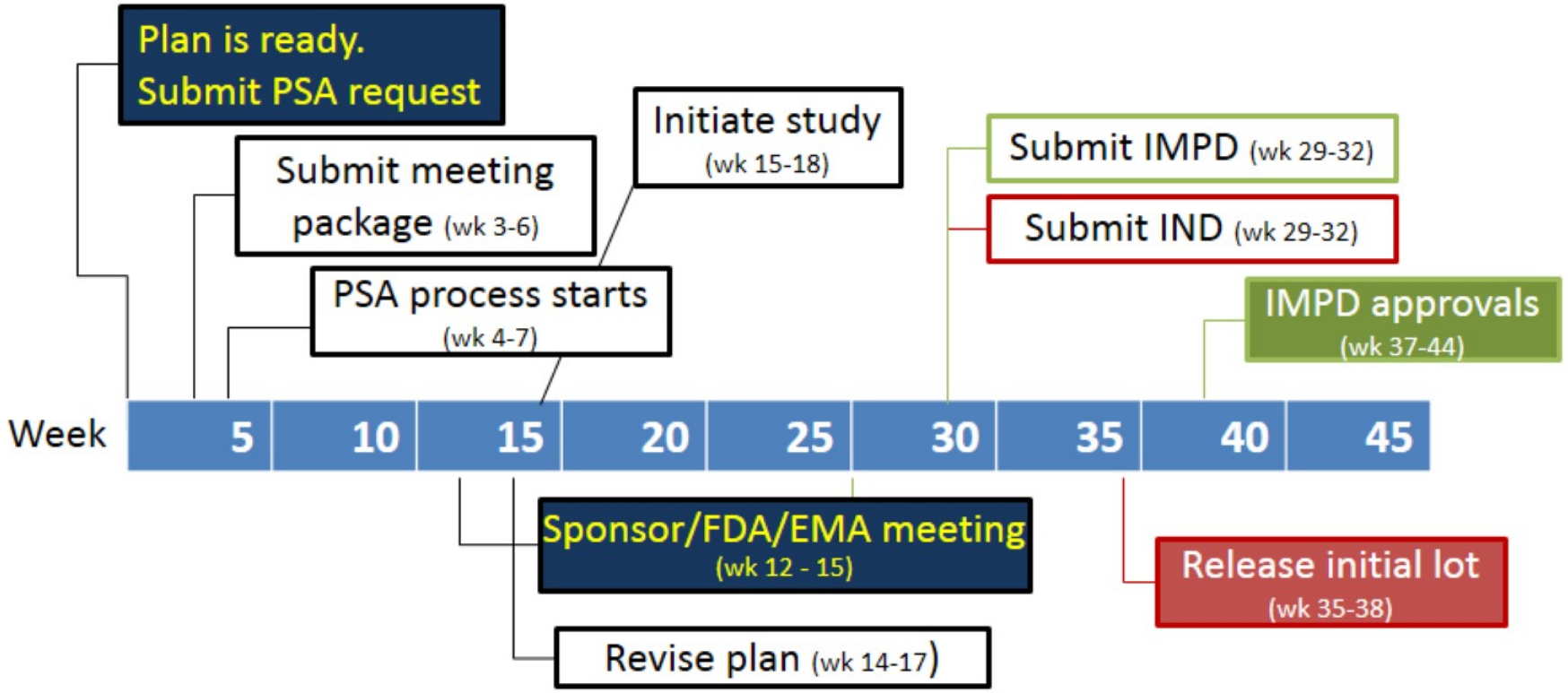
* Scenario is also applicable for EU member states, Japan, Canada

Use of Agency Meetings During Development
- with separate Agency meetings -



Time from initial plan to release of initial lot: 31 weeks
Possibility of different recommendations from different Agencies

Use of Agency Meetings During Development - with Parallel Scientific Advice (PSA) -



Time from initial plan to release of initial lot: 35 weeks
Potential benefit of one agreed plan, Feedback at the same time
Use of PSA in 2017: 3 PSA / 630 SA requests

Use of Agency Meetings During Development Case study: Site addition for an ATMP

- Opportunities
  - Frequency of interactions may differ by topic, product, and reviewer
  - Leverage IMPD reviews by individual national authorities and their knowledge of the product review history
  - Leverage Scientific Advice for IMPD reviews
- Potential solutions
  - High need to discuss anticipated CMC changes through an interactive discussion such as the PRIME Kickoff meeting versus the Scientific Advice
  - More interaction with the Rappoteur for advice outside of formal Scientific Advice
  - Assignment of a Lead Quality Assessor

Management of Post-Approval Changes

- Challenges with Post-Approval Change Management Protocols
  - Difficulties in using PACMPs for anticipated future changes
  - Difficulties in modifying or implementing approved PACMPs as a result of evolving process understanding
  - Lack of harmonisation of PACMP agreement between major Agencies
  - Reduced classification for variation of ATMPs?
    - No ATMP examples currently included in the draft ICH Q12
- Frequent dialogue needed
  - Dialogue with the applicant and a party with deep knowledge of the product and review history
    - Direct and meaningful dialogue with the rapporteur/co-rapporteur
    - Dialogue with the EMA variation team jointly with the rappoteur/co-rapporteur

Summary and Recommendations

- PRIME/BTD products are often complex
  - Complex manufacturing processes, often without prior knowledge
  - Limited and/or evolving process understanding
  - Often follows a rapid development timeline to meet patient needs and keep pace with clinical plan evolution
  - Often requires manufacturing changes that have to be implemented quickly to ensure expedited product development and continued supply
- Expansion and more flexibility of existing tools are desirable
  - A more informal and expedited mechanism to discuss the continuing quality development and evolution of the product throughout development and into the post-approval phase
  - Explore possible harmonization between Agencies e.g. acceptance of a PACMP

Acknowledgements

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Backups

Annual activity report 2017

Evaluation activities for human medicines

Pre-authorisation activities

Workload indicators

Procedure	2014 result	2015 result	2016 result	2017 forecast	2017 result
Scientific advice/protocol assistance pre-submission meetings	137	89	117	120	118
Scientific advice and protocol assistance requests, of which:	551	510	582	632	630
Parallel scientific advice with international regulators	2	3	6	5	3
Joint scientific advice with HTA bodies	11	30	23	30	29
Post-authorisation scientific advice	122	89	148	130	144
Scientific advice for PRIME products	n/a[1]	n/a [1]	4	22	28
Protocol assistance requests	113	137	126	144	159
Novel technologies qualification advice/opinions	22	20	14	20	19
PRIME eligibility requests	n/a[1]	n/a[1]	84	90	81
Scientific advice finalised	432	386	439	484	490
Protocol assistance finalised	101	139	122	144	156
Orphan medicines applications, of which:	329	258	329	277	260
Parallel orphan applications with international regulators	109	86	96	70	55
Submitted applications on the amendment of an existing orphan designation	0[2]	1	4	4	2
Oral explanations for orphan designation	-[3]	-[3]	87	90	80

https://www.ema.europa.eu/documents/report/annual-activity-report-2017_en.pdf