CHEMISTRYMANUFACTURINGCONTROL

REGULATORYAFFAIRS

Online Strategy Meeting Jun 2nd 2020

Drug-Device Combination Treatments & Diagnostics

Workshop 2:50 - 3:50 PM

Angela N. Johnson, MSE, PMP, RAC

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Angela N. Johnson, MSE, PMP, RAC

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sigilon therapeutics™ | TEXAS TECH UNIVERSITY

- 15+ years strategic leadership of clinical trials projects in cell and gene therapy, medical devices, and combination products
- Prior Sr Manager of Clinical Operations for GE Healthcare, and Director of Strategic Development of Quintiles/IQVIA
- ASGCT Government Relations Board Member
- ARM EU and US Regulatory Committee Member
- Author of 2017 Medical Devices, and 2019 Gene & Cell Therapy chapters in Best-selling RAPS regulatory strategy textbooks

Agencies Wrote the Regulations.
We Wrote the Book.

Fundamentals of US Regulatory Affairs, 10th Edition

RAPS REGULATORY AFFAIRS PROFESSIONALS SOCIETY

AMERICAN SOCIETY of GENE & CELL THERAPY

Alliance for Regenerative Medicine

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Agenda

Today's discussions are an opportunity for participants to get together in an informal setting to examine issues as they relate to there careers. There is no formal agenda, but there are specific topics. We will plan to spend ~15-20 min on each.

1. **About You** – Tell us about your experience in combination products & diagnostics
2. **Classification, Types of Combos & Diagnostics, & Development Issues**
   a. **FDA Issues** for combination products
   b. **EU MDR & Global** issues for combination products
3. **Co-development and Platform Development Issues:** Diagnostic platforms, co-development in oncology & advanced therapies, and other issues

… remaining time for open discussion

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About You

~ 2:50 - 3:05 PM (15 min)

"When people tell me they've learned from experience, I tell them the trick is to learn from other people's experience"

- Warren Buffett

We will spend ~15 min learning about you and your combo & diagnostic experiences.

Can you share:

1. **Your name, role, and company**
2. **How do you work with combination products and/or diagnostics in your role?**
3. **What was the biggest challenge you encountered with combination products and/or diagnostics in the last year? Ever?**
4. **What policy, industry, or other changes could improve those challenges?**
5. **What is most exciting about combination products and/or diagnostics?** (*e.g. could be a news article, an event a product, or a new technology*)

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Conversation Starters

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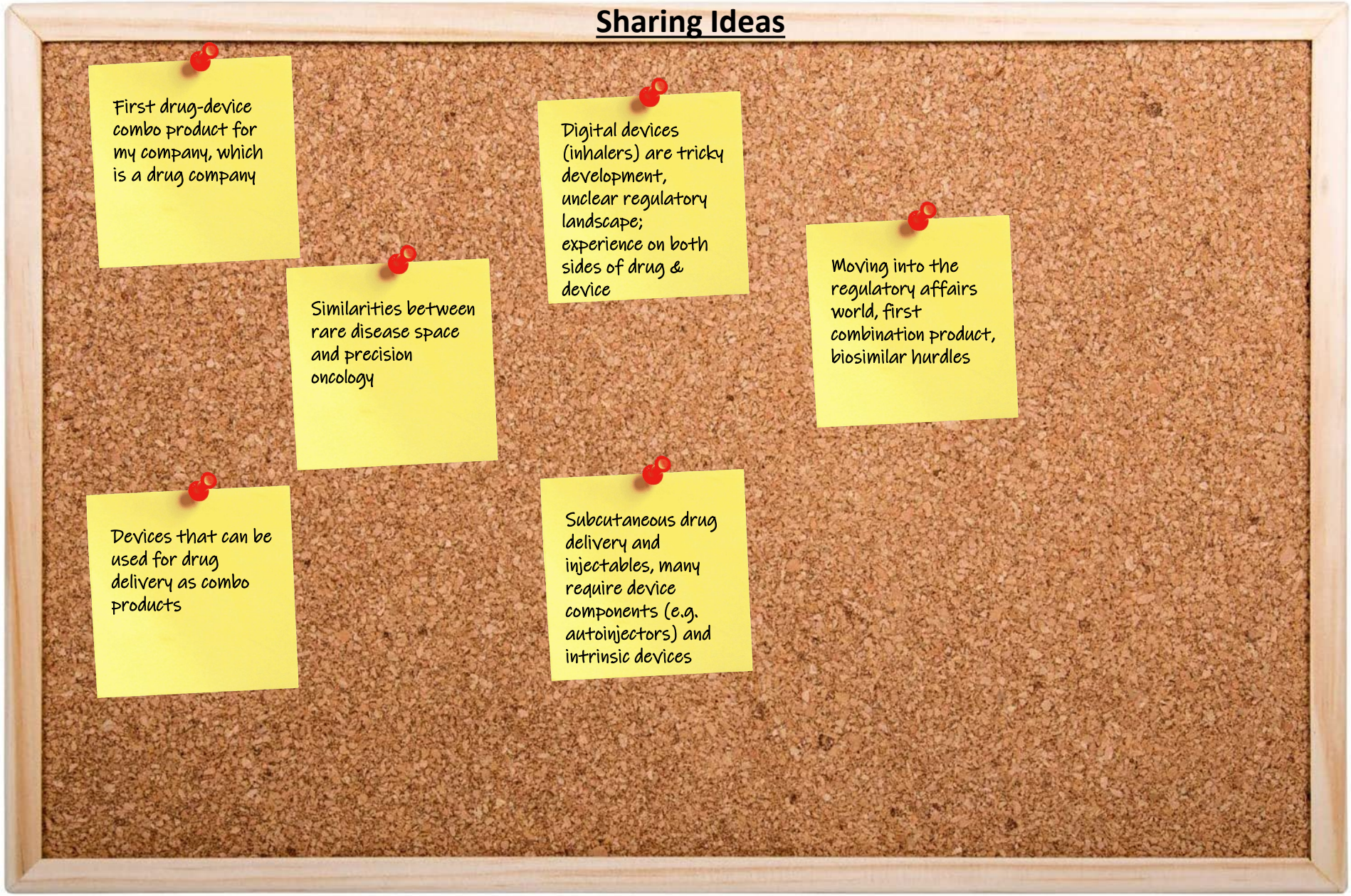
Themes from our about us conversations



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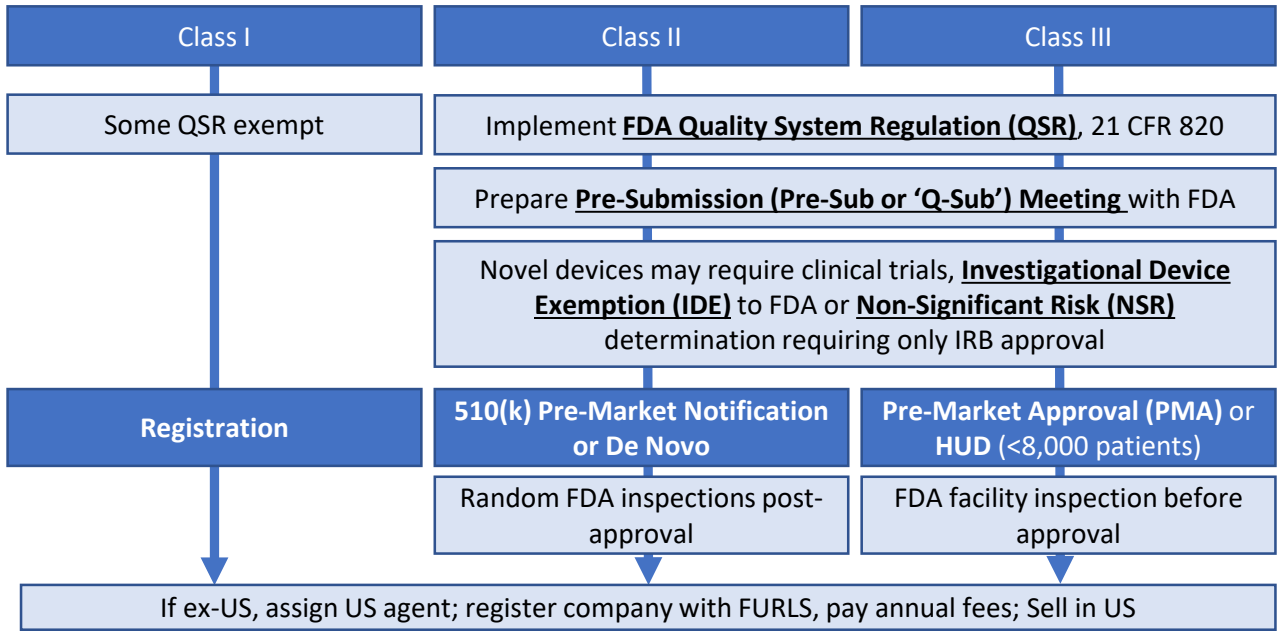
Combo Classification & Development Issues (US)

~ 3:05 - 3:25 PM (15 min)

"FDA expects to receive large numbers of combination products for review as technological advances continue to merge product types and blur the historical lines of separation between FDA's medical product centers"

- *About Combination Products*, FDA

Overview of FDA Medical Device & Diagnostic Pathways



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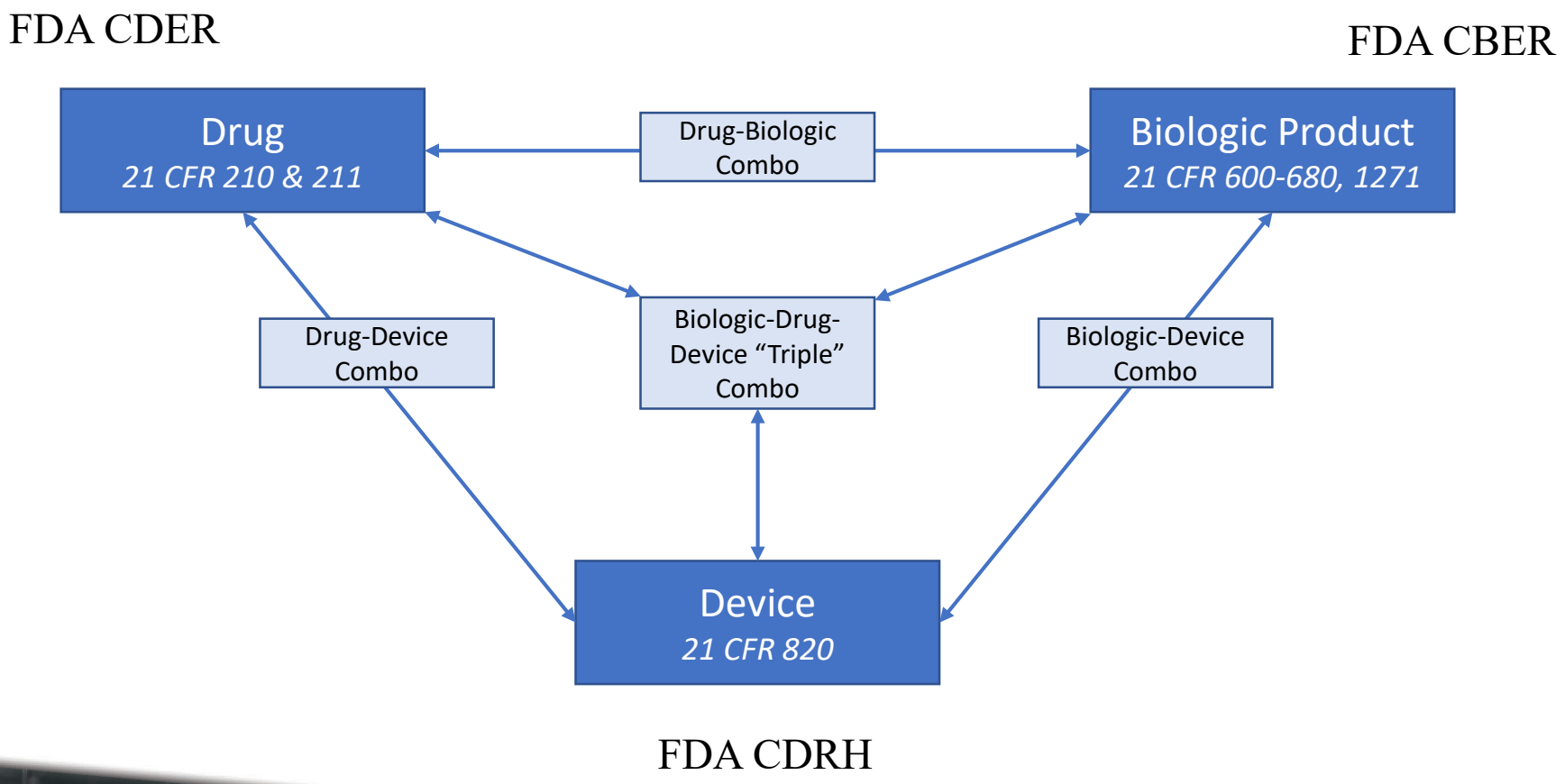

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US FDA Resources and Considerations for Combo Products

- Combination product is defined as any combination of drug, biologic and device per 2 CFR 3.2(e), may be "single entity" (chemically combined), "co-packaged", or "cross-labelled" for use with another product
- FDA Office of Combination Products (OCP)

  "OCP welcomes comments from interested stakeholders on any policy issues that you believe should be addressed or clarified in guidance, regulations or otherwise. OCP also encourages medical product developers to contact us if they are uncertain about the classification or assignment of their products and with questions regarding premarket or postmarket considerations for combination products." – FDA
- Guidance: How to Write a Request for Designation (RFD) (FDA 2011)

- Designation discussions at Pre-IND and other meetings

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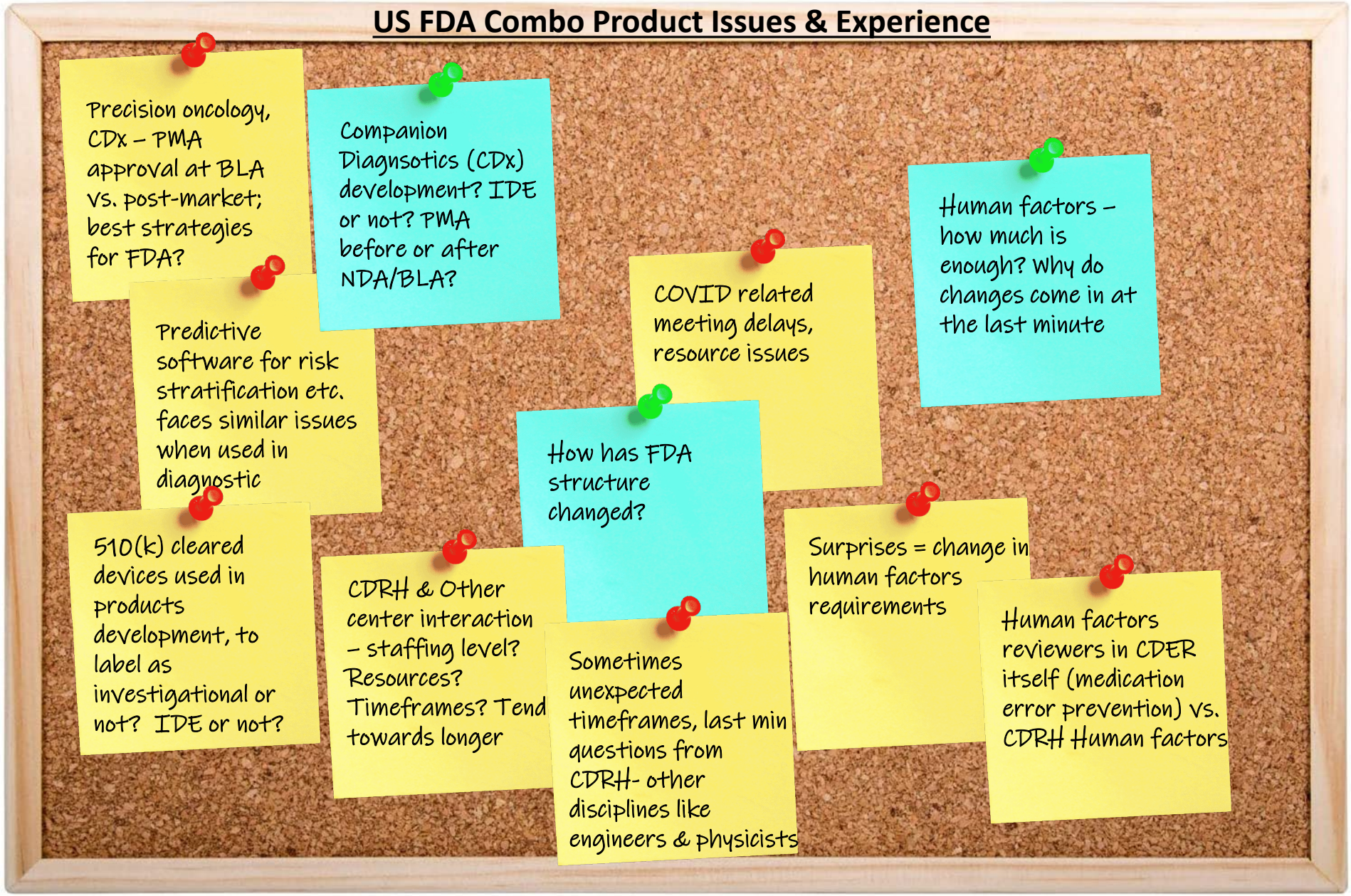
Conversation Starters

1. **Insights from FDA meeting experiences?**
2. **Issues with the RFD Process?**
3. **CMC issues with combo products?**
4. **Other experiences related to US FDA combo products…**

Example: This is an idea we discussed

Example: This is a question raised by the group



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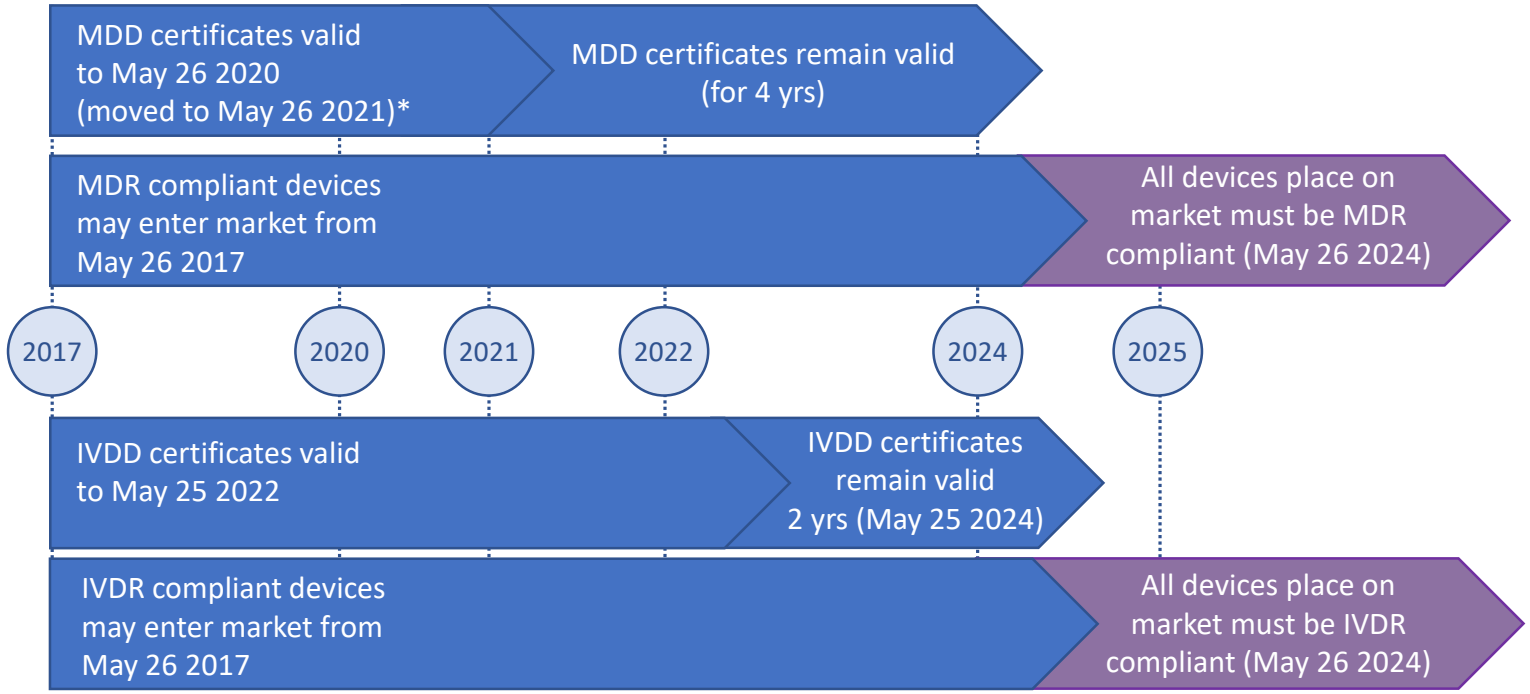
- About Combination Products, FDA

EU MDR & IVDR Timelines



* On April 3rd, 2020 the European Commission proposed a one-year **delay** of the Medical Devices Regulation (**MDR**) to the European Parliament and Council. Originally the Date of Application (DoA) was set on **May 26th**, 2020, but would move to **May 26th**, 2021 according to the EC proposal.

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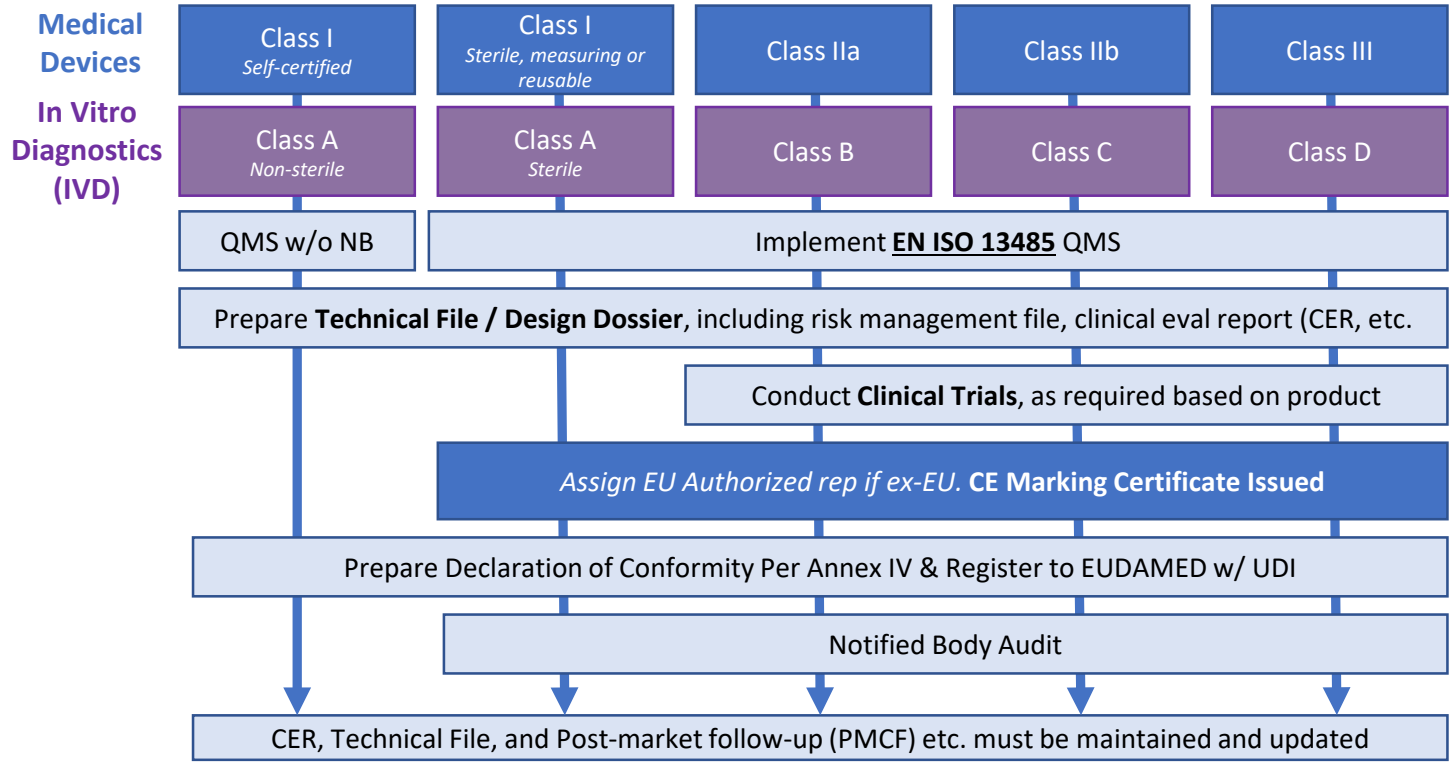
- About Combination Products, FDA

Overview of EU Medical Device & In Vitro Diagnostic Pathways (MDR)*



**EU IVD Directive originally established IVD Classes "general", "Self-testing", "List B" and "List A" IVDR replaced these with Class A, B, C & D*

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Combo Classification & Development Issues (EU)

~ 3:25 - 3:40 PM (15 min)

"The demarcation between medicinal products and devices is becoming ever more important and, with the convergence of emerging novel technologies in Europe"

- *Businesswire London*

EU Resources and Considerations for Combo Products

1. The EU historically did not have a category of product for combinations. The new Medical Device Regulation (MDR) supersedes the previous Medical Devices Directive (MDD), separating Drug-Device Combinations (DDCs) into two categories:
   - Article 1(8) Devices incorporating as an **integral part a substance** that, if used separately, would be considered a medicinal product *and* the action of the substance is principal.
   - Article 1(9) Devices intended **to administer a medicinal product** where they form a **single integral product** intended exclusively for use in the given combination which is not reusable.
2. "Borderline Products" remain an issue in EU
3. Per Regulation (EU) 2017/745 on medical devices Article 117, future MAAs should include a CE certificate or declaration of conformity for the device or, in certain cases, an opinion from a notified body (NB) on the conformity for device components.
4. Guideline: Quality requirements for drug-device combinations (EMA Draft 2019)
5. Discussions of Combination Products at Scientific Advice Meetings and with Notified Bodies

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Conversation Starters

1. **Insights from EU SA meeting experiences?**
2. **Issues with the combination product classification?**
3. **CMC issues with combo products?**
4. **Other global experiences related to combo products…**

Example: This is an idea we discussed

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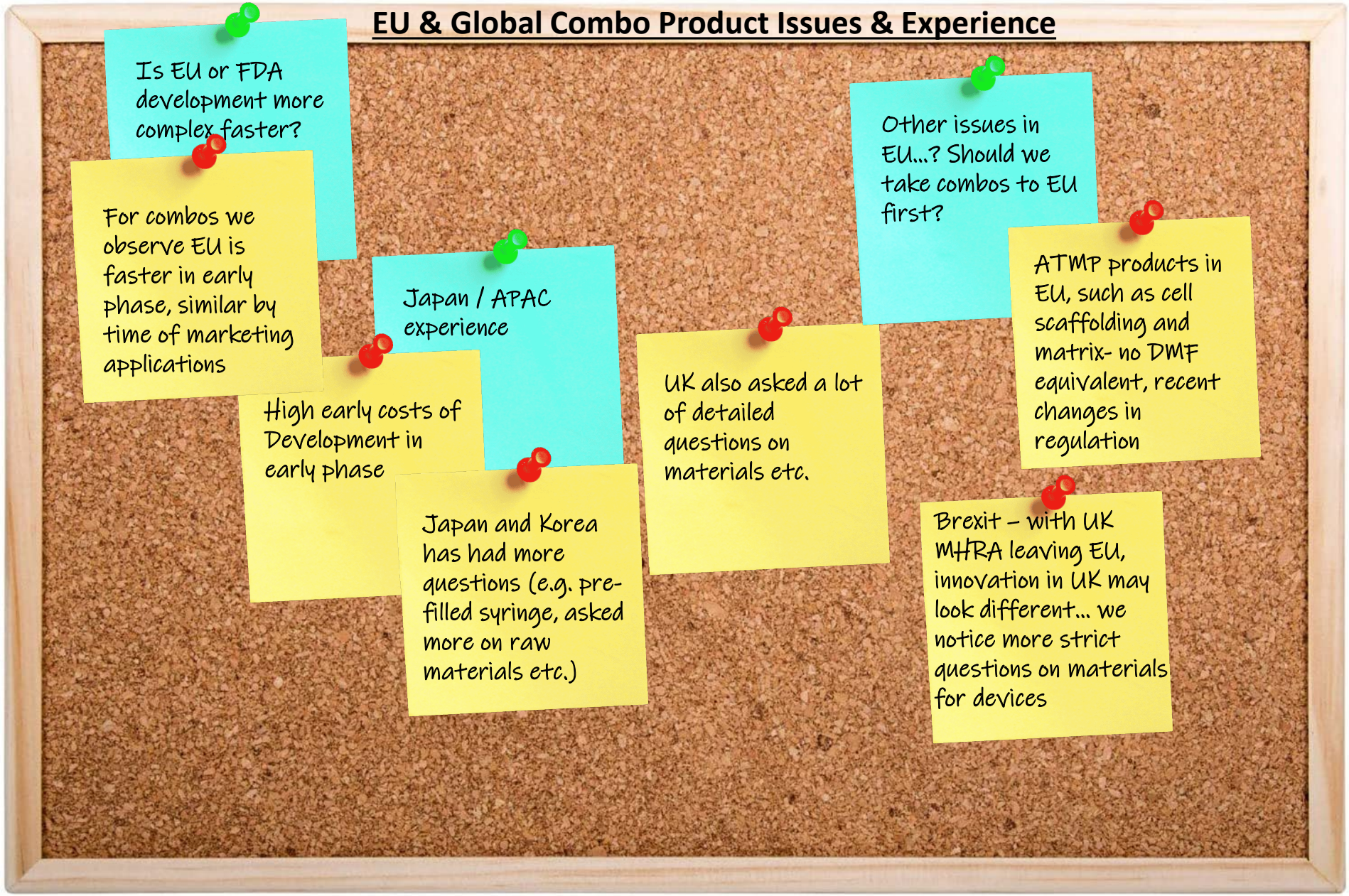

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Codevelopment & Issues in Emerging Tech

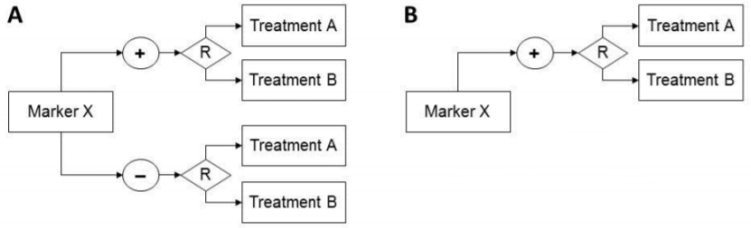
~ 3:40 - 3:55 PM (10 min)

"Co-development partnering allow the parties to securitize value and reduce risk, but keep a part of the potential upside should the product reach the market"

- *ResearchandMarkets.com*

FDA

- Guidance: Codevelopment of Two or More New Investigational Drugs for Use in Combination (FDA June 2013)
- Guidance: Investigational In Vitro Diagnostics in Oncology Trials: Streamlined Submission Process for Study Risk Determination Guidance for Industry (FDA Oct 2019)
- Draft Guidance: Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product (FDA July 2016), enabling concurrent trials of a therapeutic & IVD



EMA

- Guideline: Co-development of pharmacogenomic biomarkers and assays in the context of drug development (EMA 2010)
- Concept paper on predictive biomarker-based assay development in the context of drug development and lifecycle (EMA 2017)
- Impact of new MDR and IVDR regulations

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Other issues in codevelopment

- Codevelopment often occurs as a result of partnership between device and drug companies, leveraging each's unique expertise. This model differs from traditional business licensing and partnership strategy, and can reduce risk
- An increasing number of new oncology therapeutics and advanced therapies (e.g. gene therapy) require highly specific companion IVDs, requiring US PMA and Class III device registration in EU
- Clinical trials can run in parallel, with samples are data "feeding" into another trial, typically a therapeutic trial feeding a diagnostic.
- Digital therapeutics (DTx) and software as a medical device (SaMD, e.g. clincial decision-support software) may be developed alongside traditional therapeutics
- FDA allows hybrid "streamlined" cGMP-QSR for drug-device combos
- The future in EU may mean CE mark "duplicate" requirements apply to MAA products with device components

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Codevelopment and Tech Issues in Device & IVD

Conversation Starters

1. **Experiences with codevelopment?**
2. **Codevelopment challenges**
3. **Advanced therapy & companion diagnostics issues?**
4. **Other topics in combos and co-development**

Example: This is an idea we discussed

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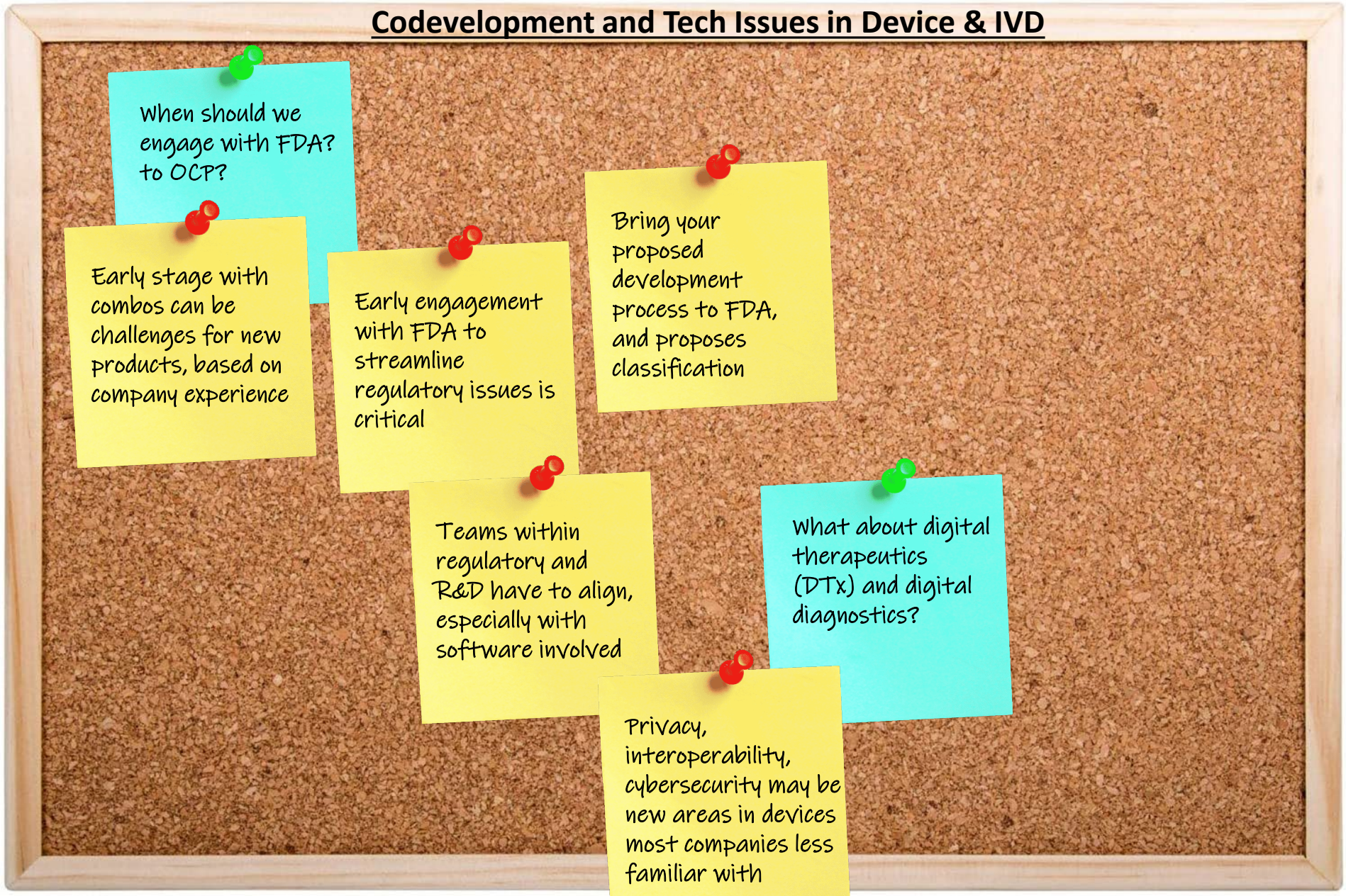

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Discussion and Q&A

Thank you
for attending and sharing your expertise

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