Marketing Subpart H (or E) Products

Presented by:

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PhillyCooke Consulting helps companies communicate about FDA-regulated products using 21st century tools, while remaining compliant with regulations written in the 1960s.

PhillyCooke Consulting services focus on

1. Regulatory Review of Promotional Material
2. Ad Agency Submission Preparation
3. Policy Development
4. Review & Approval Process Improvement
5. Medical Editing & Proofreading
6. Training

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Use of examples does not constitute endorsement of the practices shown.

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Topics

1. Subpart H (or E) Drug Development
2. Phases of Promotion
3. FDA Enforcement
4. FDA Feedback
5. Recent Controversy

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Subpart H (or E)
Drug Development

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AIDS Epidemic's Impact

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What is Subpart H (or E)?

These programs “are intended to facilitate and expedite development and review of new drugs to address **unmet medical need** in the treatment of a **serious or life-threatening condition**”

– Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics, FDA 2014, page 1 (emphasis added)

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Why H & E?

21 CFR part 314 subpart H

Accelerated Approval of New **Drugs** for Serious or Life-Threatening Illnesses

21 CFR part 601 subpart E

Accelerated Approval of **Biological Products** for Serious or Life-Threatening Illnesses

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Subpart H (or E) Approvals

FDA may grant marketing approval for a new drug or biological product “upon a determination that the product has an effect on a **surrogate endpoint** that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit”

– Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics, FDA 2014, page 1 (emphasis added)

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Multiple Products

"[I]t is preferable to have more than one treatment approved under the accelerated approval provisions because of the possibility that clinical benefit may not be verified in post approval confirmatory trials. FDA will therefore consider products as addressing an unmet medical need if the only approved treatments were granted accelerated approval based on a surrogate endpoint…"

– Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics, FDA 2014, page 6

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Subpart H (or E) Approval Timeline

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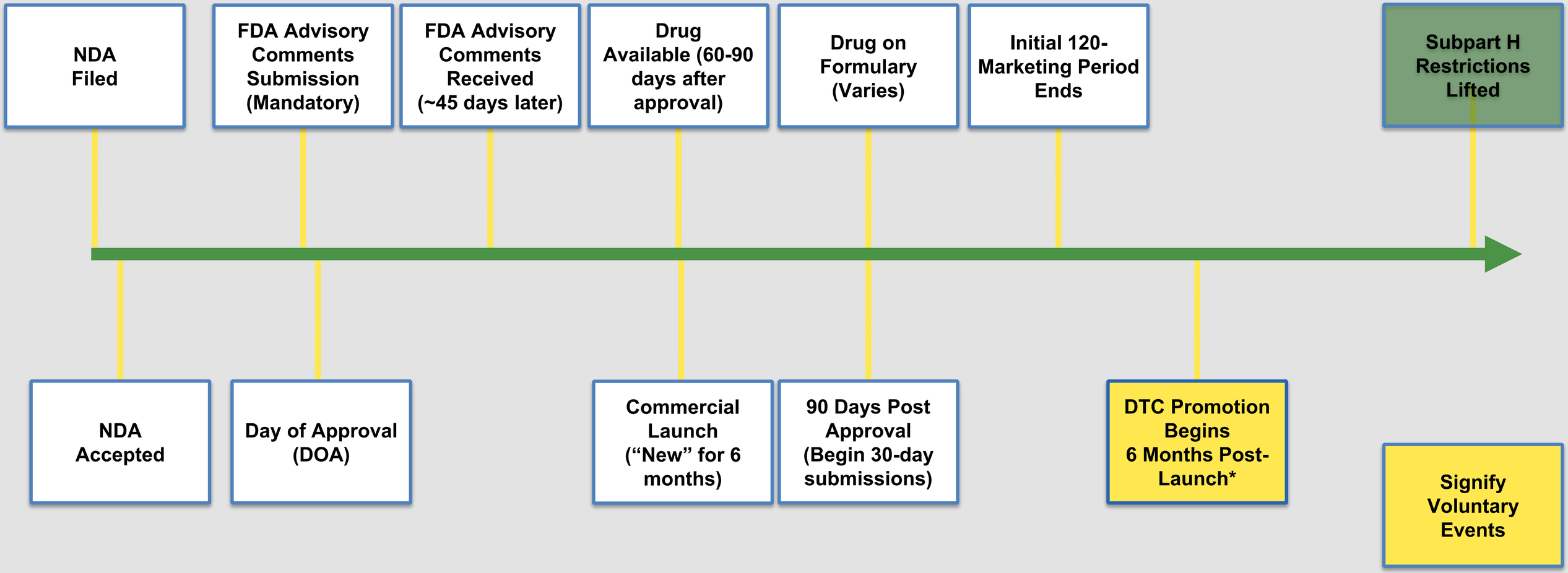

* This 6-month moratorium on DTC is a PhRMA commitment, not an FDA requirement

Phases of Promotion

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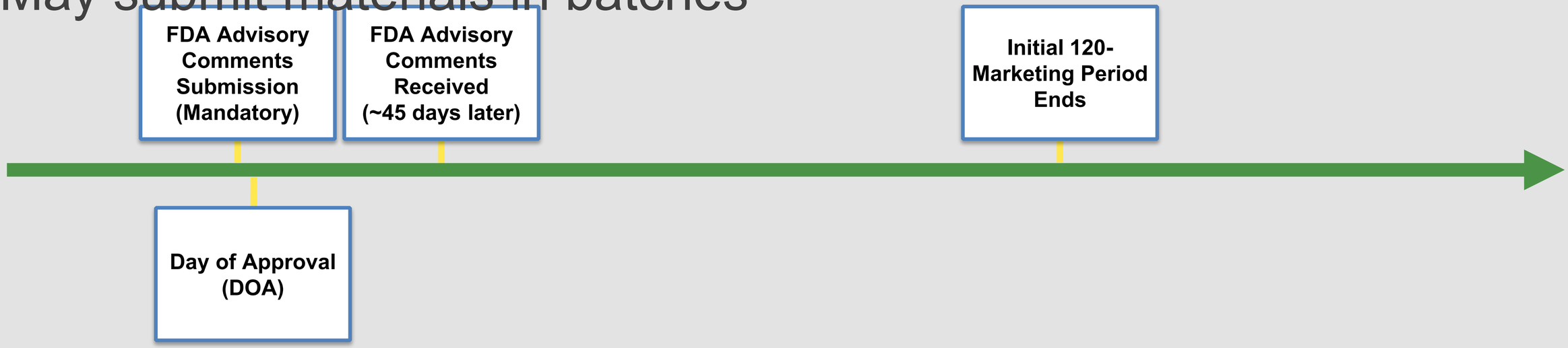
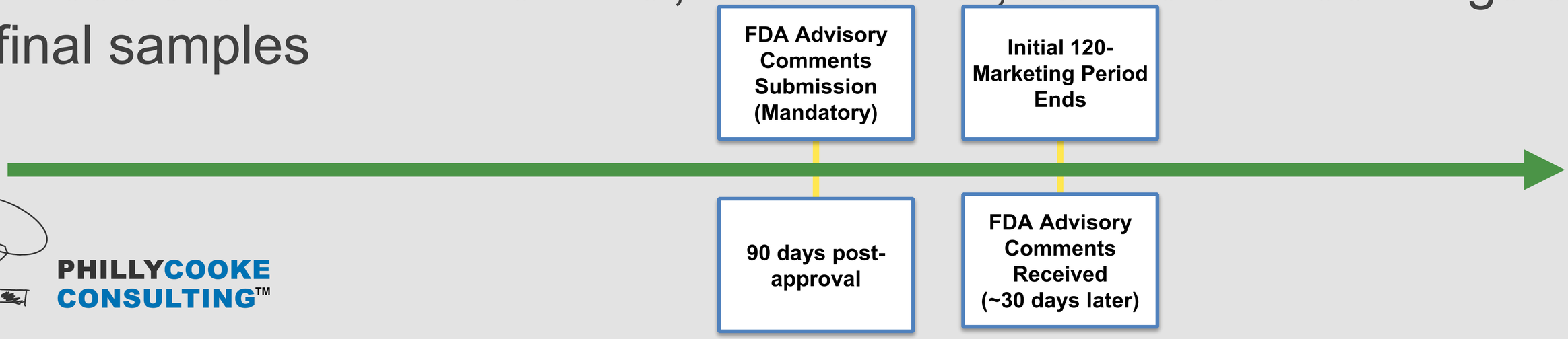
Initial 120-day Period

- ALL MATERIALS for use in the first 120 days after approval must be submitted to the FDA prior to approval
- Agencies must coordinate
- Working from a draft label
- Don’t know exactly when the approval will come, so think six to nine months out, not three months, when planning
- May submit materials in batches



Rolling 30-day Submissions

- ALL MATERIALS must be submitted to the FDA 30 days prior to use FOR REVIEW
  - FDA can extend the 30-day review
  - Initially, there will be feedback
  - Eventually, the feedback will taper off
  - Sent in batches (not daily), coordinated among agencies
- These are IN ADDITION TO, not in lieu of, standard 2253 filings of final samples



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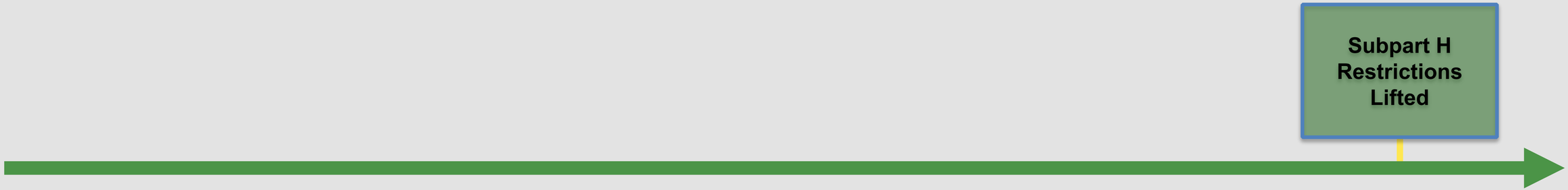
Completion of Confirmatory Trials

- Subpart H (or E) approval is temporary for EACH INDICATION
- Clinical trials will continue
- Confirmatory trials will either demonstrate safety and efficacy or fail to do so
- Either standard approval will be granted or subpart H approval will be revoked for EACH INDICATION



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FDA Enforcement

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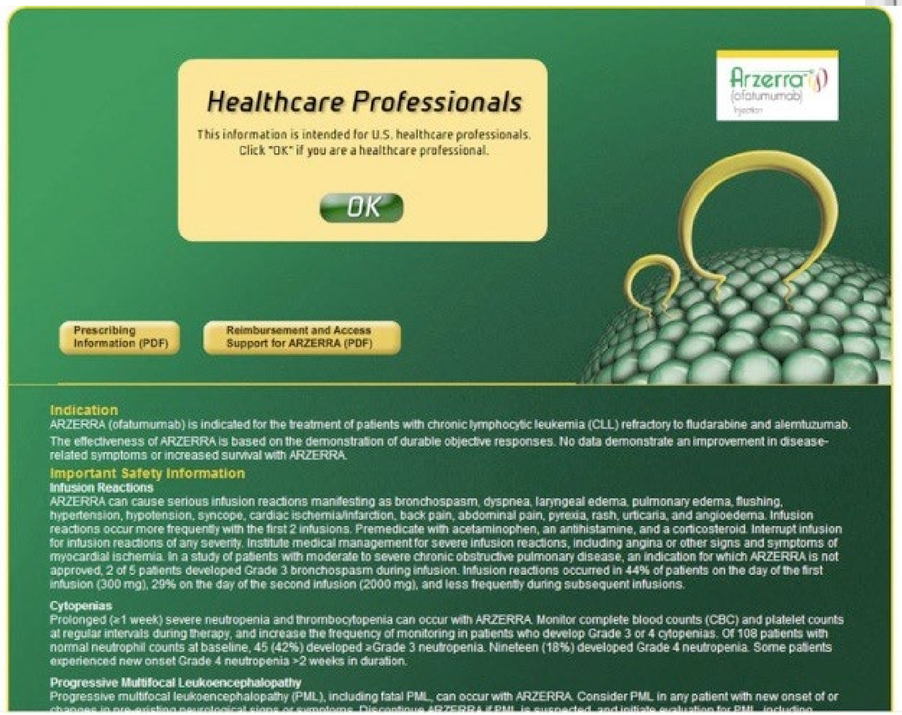
Arzerra Print Ad



http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/W

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Arzerra Print Ad

Lessons

- Mere omission of the product name is insufficient to avoid being a product promotion
- Product description can constitute a product promotion
- For subpart H products, EVERYTHING used in the first 120 days has to be submitted prior to approval

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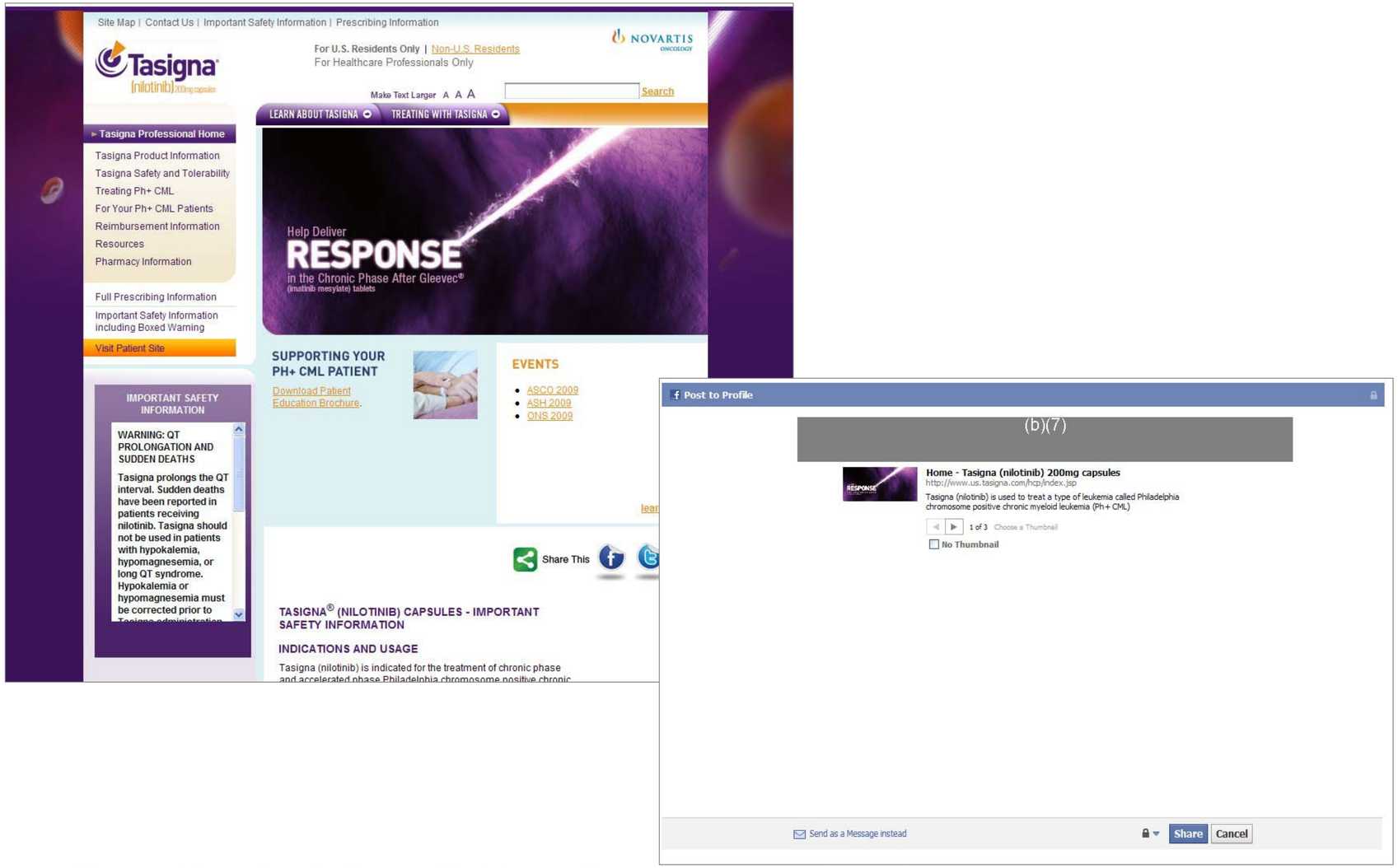
Enforcement for Sharing



http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM208798.pdf

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Tasigna Sharing

Lessons

- Social media is OK if done correctly
- FDA advisory comments can be ignored, but doing so increases the risk of enforcement
- FDA remembers everything
  - "DDMAC has previously provided written advisory comments to Novartis about the misleading implications of the phrase 'next generation' when referring to Tasigna.[5]"
    "[5] See DDMAC advisory letters dated August 14, 2008 and January 25, 2010."

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FDA Feedback

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FDA Advisory Comments

- FDA **NEVER** clears or approves promotional materials
- FDA **CAN** require advisory comment submissions
  - Subpart H & E products
  - As part of a settlement of violative practices

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Planning for Success

- Submissions will be compiled by the client
- Draft labels change frequently
- FDA sees only a single package
- Each agency will be responsible only for a part of the submission
- Multiple agency coordination and communication is essential
- FDA won’t have any background to understand the submission materials
- Annotations must suffice and stand alone
- Timelines must account for delays

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eCTD & Subpart H Submission

- ALL Subpart H submissions will use eCTD
- Must set up eCTD publishing in advance of the pre-approval submission
- Must coordinate with FDA's eCTD team for the submission

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Addressing FDA Feedback

- FDA feedback is not directive
  - Won't say, "Change this sentence to read, 'blah, blah, blah.'"
  - Will say, "This sentence has three problems."
  - Must convert FDA feedback into directive feedback
- Significant gap from initial MLR review to post-FDA feedback MLR review
  - Must capture initial MLR feedback with that in mind
  - Must re-annotate post-FDA feedback with that in mind (two sets of changes at a minimum)
- FDA feedback will cascade to other projects not yet seen by MLR or FDA

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Standard Review vs. Subpart E

Standard Review

1. Concept Review
2. Med-Legal Review
3. Check Changes
4. Executive Committee Review
5. Final Samples

Subpart E Review

1. Concept Review
2. Med-Legal Review
3. Check Changes
4. Executive Committee Review
5. FDA Advisory Comments
6. Med-Legal Review
7. Check Changes
8. Final Samples

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Recent Controversy

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Follow-up Study Failures

- Several brands have failed to complete required follow-up studies in a timely fashion (or to achieve confirmatory results!)
- FDA is under increasing pressure to revoke Accelerated Approvals for these brands
- Congress is looking at changing Accelerate Approvals to address these failures
- April 2021 FDA Committee voted to revoke two approvals

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Aduhelm Approval

- Surrogate endpoint chosen was controversial
- Advisory Committee voted against approval
  - Surrogate endpoint value
  - Benefit-risk assessment
- FDA approved the drug
- FDA requested OIG investigation into inappropriate contacts between the sponsor and the FDA
- CMS greatly restricted patient access

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Questions?

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Dale Cooke is the president of PhillyCooke Consulting, which helps companies communicate about FDA-regulated products using 21st century tools, while remaining compliant with regulations written in the 1960s. Dale has worked with more than 50 pharmaceutical and medical device clients and more than 30 advertising agencies around the world. His insights have been featured in Politico, The Pink Sheet, Stat News, Law360, and other publications. Dale is an active member of the Regulatory Affairs Professionals Society (RAPS), Drug Information Association (DIA), Food and Drug Law Institute (FDLI), the Alliance for a Stronger FDA, and the Digital Health Coalition. Dale teaches in the Temple University School of Pharmacy RAQA program.

Dale is the author of *Effective Review and Approval of Digital Promotional Tactics*, which is now in its second edition in FDLI's Topics in Food and Drug Law series. He is regularly invited to speak at industry conferences on topics including FDA enforcement trends, best practices for review processes, global review practices, and life sciences use of social media.

Dale earned his B.A. in Philosophy from Southern Methodist University, an M.A. in Philosophy from the University of Arizona, studied Epidemiology and Biostatistics at Drexel University's School of Public Health, received a graduate certificate in Healthcare Compliance from Seton Hall University's School of Law, and his J.D. at Drexel University's Kline School of Law.

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