Drug Formulary Commission

Bureau of Health Care Safety and Quality
Department of Public Health
September 15, 2016

Commonwealth of Massachusetts
Department of Public Health

Presentation Agenda

- Review of July 14th meeting
  - Non-Opioid Pain Management List
  - Draft Formulary and Guidance
- Interchangeable Abuse Deterrent Drug Products Evaluation
  - Xtampza ER®
- Chemically Equivalent Substitutions
  - Xtampza ER®
- Next Steps

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Promulgation of Regulation and Formulary

- Present to the Drug Formulary Commission.
- Propose the draft to Public Health Council as part of the proposal of a redrafted regulation, 105 CMR 720, *List of Interchangeable Drug Products.*
- Present the draft regulation, including the draft Formulary of Chemically Equivalent Substitutions, for public hearing and comment.
- Review comments and amend regulation as appropriate.
- Present final draft regulation and draft formulary to PHC again for promulgation.
- Review by Secretary of State.
- Regulation becomes effective.
- Issue guidance, including:
  - special substitution considerations as decided by the commission, and
  - the requirements and process of substitution.

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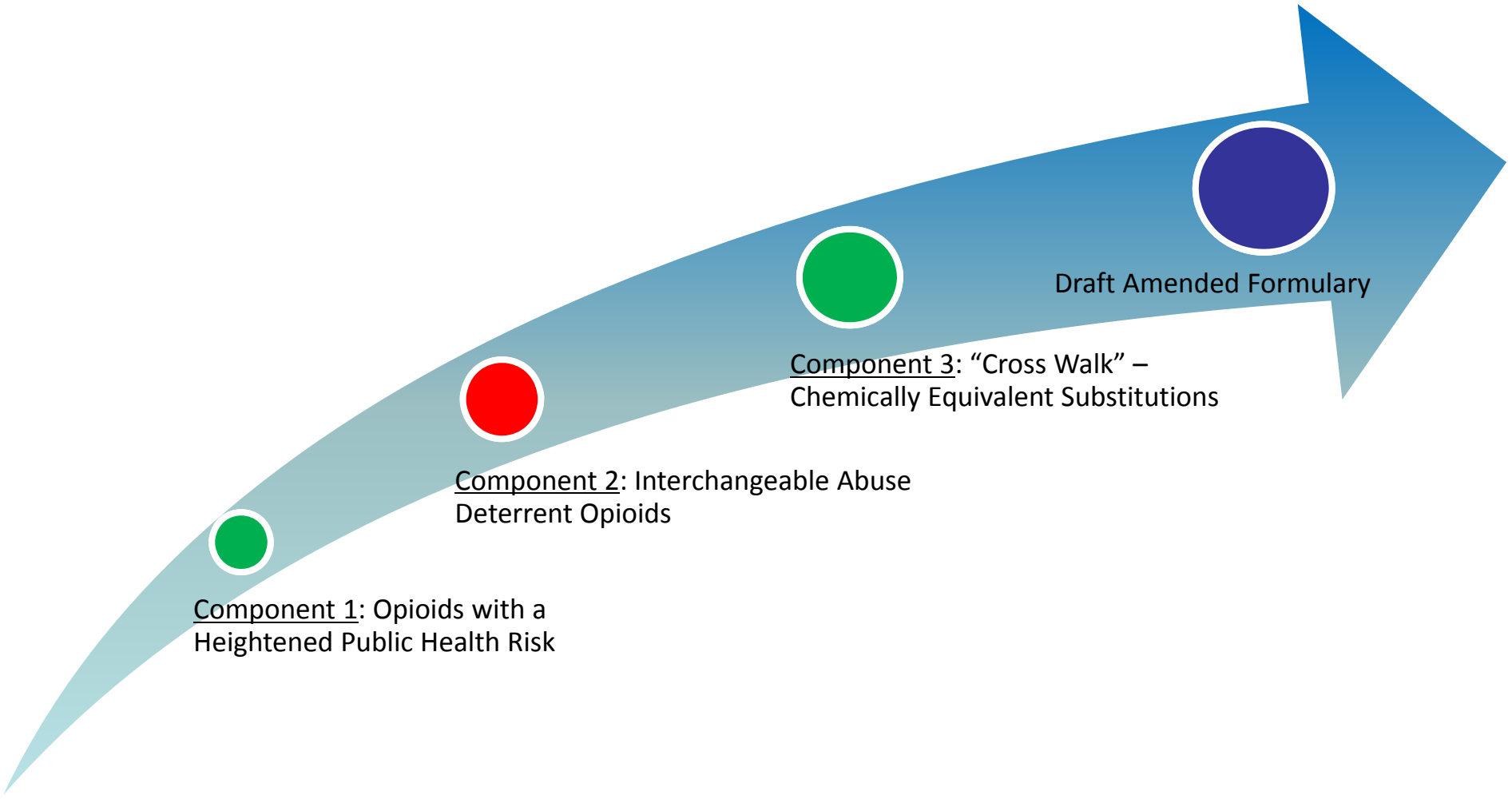
Formulary Review and Evaluation



Xtampza ER® Monograph Review

- Oxycodone extended-release
- ADF Property
  - Physical/chemical barrier
  - Clinical abuse potential studies of the intranasal and oral routes
  - *In vitro* data indicates resistance to injection
- FDA Approval — April 2016 (final)
- FDA ADF labeling approved — April 2016 (final)
- Available Strengths
  - 9 mg, 13.5 mg, 18 mg, 27 mg, 36 mg
  - Equivalent to 10 mg, 15 mg, 20 mg, 30 mg, 40 mg oxycodone HCl, respectively

Potential IAD Drug Product Evaluation
Xtampza ER®

- Xtampza ER® is formulated using DETERx® technology.[2]
- DETERx® combines free active ingredient (oxycodone base) with myristic acid to produce a lipophilic compound. The compound is then suspended in wax microspheres and placed in capsules.[2]
- *In vitro* data indicates the wax microspheres are resistant to particle size reduction and extraction via use of multiple solvents.[2]
- *In vitro* data also indicates injection of the wax microspheres is relatively impossible using needles smaller than 18 gauge.[2]
- An oral clinical abuse potential study indicates both intact and chewed/crushed Xtampza ER® is associated with less drug liking than crushed oxycodone immediate-release.[2]
- An intranasal clinical abuse potential study indicates both intact oral and crushed intranasal Xtampza ER® is associated with less drug liking than crushed intranasal oxycodone immediate-release.[2]
- Pharmacokinetic study data indicates that crushed Xtampza ER® microspheres are bioequivalent to intact Xtampza ER® capsules administered orally.[2]
- Pharmacokinetic study data indicates that the peak plasma concentration (C_{max}) is decreased when Xtampza ER® is crushed and insufflated compared to taken intact orally.[2]

Potential IAD Drug Product Evaluation
Xtampza ER®

- Initial dose (opioid naïve adults): 9 mg every 12 hours with food.[1]
- Initial dose (converting from other opioids): 9 mg every 12 hours with food.[1]
- Initial dose (converting from fentanyl patch): 9 mg every 12 hours with food for each 25 mcg/hr of fentanyl transdermal patch.[1]
- Time to peak plasma concentration (T_{max}) of intact Xtampza ER® capsules is approximately 4.5 hours.[1]
- T_{max} for crushed or chewed Xtampza ER® capsules approximately 4.0 to 4.5 hours.[1]
- Xtampza ER® does not appear to dose dump in alcohol or other commonly ingestible solvents.[1]
- Bioavailability of Xtampza ER® is dependent upon the food consumed and the fat and calorie content of the food consumed. High fat and high calorie meals increase the peak plasma concentration (C_{max}) by 100 to 150% and extent of absorption (AUC) by 50 to 60% compared to fasted administration.[1]

Potential IAD Drug Product Evaluation
Xtampza ER®

- Xtampza ER® is subject to the requirements of the Extended-Release and Long-Acting (ER/LA) Risk Evaluation and Mitigation Strategies (REMS) program.[2]

- The FDA Advisory Committee voted unanimously to approve Xtampza ER® in September of 2015.*

- Final report submissions of formal observational studies intended to determine if the abuse-deterrent properties of Xtampza ER® reduce abuse in the community are due to the FDA in June of 2021.[9]

* http://www.innovativescience.net/fda-adcomm-blog/fda-advisory-committees-unanimously-recommend-approval-of-xtampza-er

Xtampza ER® Summary

• Chemical name	oxycodone extended-release
• Dosage form	Extended-release capsule
• Formulation	DETERx®
• ADP*	Resistant to particle size reduction
	Resistant to dose dumping in solvents
	Resistant to passage through needle sizes under 18G
• ADF studies	Oral and intranasal studies performed

*ADP = Abuse-deterrent properties

Potential IAD Drug Products – Updates

- MorphaBond® (morphine extended-release)
  - FDA approved; however, not commercially available
  - Monograph to be completed when commercially available
- Troxyca ER® (oxycodone extended-release/naltrexone)
  - FDA approved; however, launch planned for 1st Quarter 2017
  - Formulary Dossier to be available for review late 2016
  - Monograph to be completed when commercially available
- Apadaz®(benzhydrocodone/acetaminophen)
  - FDA issued Complete Response Letter, indicating product is not approvable in its current form
- SequestOx® (oxycodone IR/naltrexone)
  - FDA issued Complete Response Letter, indicating product is not approvable in its current form

Potential IAD Drug Products – In Development

- Remoxy® (oxycodone ER)
  - PDUFA date 9/25/16
- Arymo ER® (morphine ER)
  - PDUFA date 10/14/16
  - FDA advisory committee voted with recommendation to approve
- Vantrela ER® (hydrocodone ER)
  - PDUFA date 11/11/15 (past date)
  - FDA advisory committee voted with recommendation to approve

*__PDUFA__ – Prescription Drug User Fee Act (anticipated date of FDA decision)

Medication with ADF Claims or FDA Approved ADF Labeling

List of Medications with Abuse-Deterrent Claims or FDA-Approved Labeling

Product Name	Manufacturer	Ingredient(s)	Dose Form	Method of Abuse Deterrence	DFC Action
Xtampza ER®	Collegium	Oxycodone ER	Capsule	DETERx® Physical/chemical barrier	PENDING
MorphaBond®	Inspirion Delivery Technologies	Morphine ER	Tablet	Physical/chemical barrier	Not yet commercially available.
Troxyca ER®	Pfizer	Oxycodone ER/ Naltrexone	Capsule	Agonist/antagonist	Not yet commercially available. Launch planned for 1st Quarter 2017
Apadaz®	KemPharm	Benzhydrocodone/ Acetaminophen	Tablet	Prodrug	FDA Complete Response Letter indicates product is not approvable in its current form.
SequestOx®	Elite Pharmaceuticals	Oxycodone IR/ Naltrexone	Tablet	Agonist/antagonist	FDA Complete Response Letter indicates product is not approvable in its current form.

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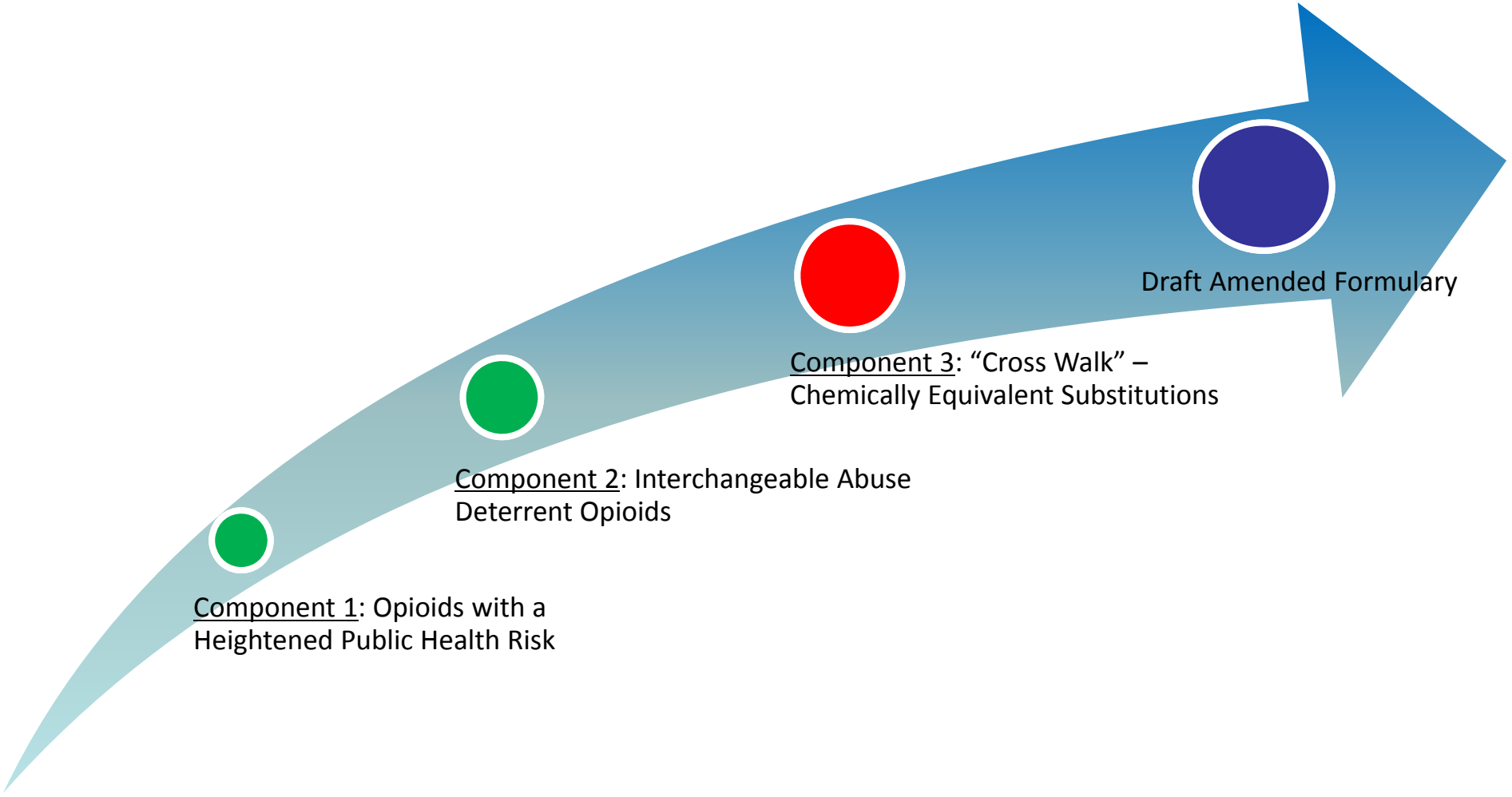
"Cross Walk"



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Meeting Schedule

- ~~October 21, 2016~~
- November 18, 2016
- December 16, 2016
- January 20, 2017
- *February 17, 2017*
- March 17, 2017
- *April 20, 2017*
  - All meetings are from 9:00AM to 12:00PM at 250 Washington Street

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Meeting Summary

- Meeting Recap
- Review of takeaways
- Next steps
- Next Meeting
  - November 18, 2016
    - 9:00AM-12:00PM
    - 250 Washington Street