



COMBINATION PRODUCT COALITION

Proposed Policies to Enhance the FDA Regulatory Process for Combination Products

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Purpose

- To get promising combinations to market
- To clarify and streamline the regulatory paradigm for combination products through enhancements to the existing process
 - We recognize the OCP has made a number of advances, such as the PMOA proposed rule
- While protecting the public health



Must be Appropriate for All Types of Combination Products

- Integral combination products: Inseparable unit (E.g. drug-eluting stents)
- Kits: Packaged together (E.g. anti-bacterial scrub with catheter)
- Virtual combination products: Products must be used together to achieve intended use, indication or effect, but not packaged as a unit (E.g. Herceptin and Herceptin Test)



Key Priorities for Enhancement

1. Labeling
2. Modification of approved combination products
3. Adverse incident reporting
4. Quality systems
5. Clarification of intra-agency roles



Labeling enhancements

- Require cross-labeling only when:
 - A package insert or instructions for use refer to another product *by brand*; or
 - A product cannot be used safely or effectively without identifying a branded product with which it must be used
- Enable efficient labeling reviews (reviews in parallel, rather than duplicate)
- Develop guidance describing the format and content required for combination product labels and physician and patient labeling



Modification of approved combinations

- For virtual combinations and kits containing a CDRH-cleared device, FDA guidance, *Deciding When to Submit a 510(k) for a Change to an Existing Device* should control for the device
- For device components approved by CDER, guidance using a risk-based model should be prepared
- FDA should follow least-burdensome approach, when possible



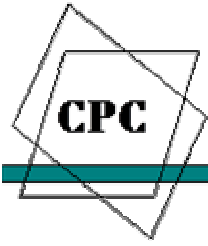
Reporting of Adverse Events

- Short-term: Develop guidance that applies existing rules for drugs, devices and biologics as appropriate, based on the risk and type of combination product involved
- Long-term: Establish a single system of reporting (statutory change)



Quality Systems

- Develop a risk-based guidance that sets forth general principles and clarifies which regulatory scheme applies
 - Need to recognize that one size will not fit all
 - Separateness of components
- Perhaps in subsequent guidance, use case-studies to identify specific QSR and GMP requirements for combination products
 - Include guidance on inspections
- Cross-train inspectors
- Implement system allowing regulatory opinions on manufacturers' QS and GMP processes



Clarification of Roles

- OCP has authorization to take the lead on combination product issues
- OCP should take a strong, visible role in the process
- Clarify roles of centers through guidance to ensure closer consultation at appropriate times



Conclusion

- Combination products face unique challenges for FDA and manufacturers alike.
- The best solutions will be those developed in collaboration with manufacturers and other stakeholders.