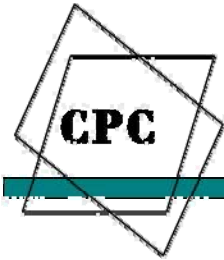


COMBINATION PRODUCTS COALITION

CPC Open Door Forum:

Combination Products Guidance Survey and 2008 Policy Agenda

January 22, 2008



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**The CPC would like to thank
RAPS for their invaluable
assistance with this survey, and for
the generous use of their survey
software.**



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Agenda

1. Brief background on the CPC
2. Today's purpose – validation step
3. Survey purpose, scope and methodology
4. Survey results
 - a. Demographics
 - b. Satisfaction with existing guidance
 - c. Need for FDA guidance – what and why
5. Impact on 2008 policy agenda



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CPC: Mission

- Develop and advocate for public policies on behalf of combination product industry
- Forum for building bridges among drug, device, and biological product industries
- Work collaboratively with FDA on combination product issues



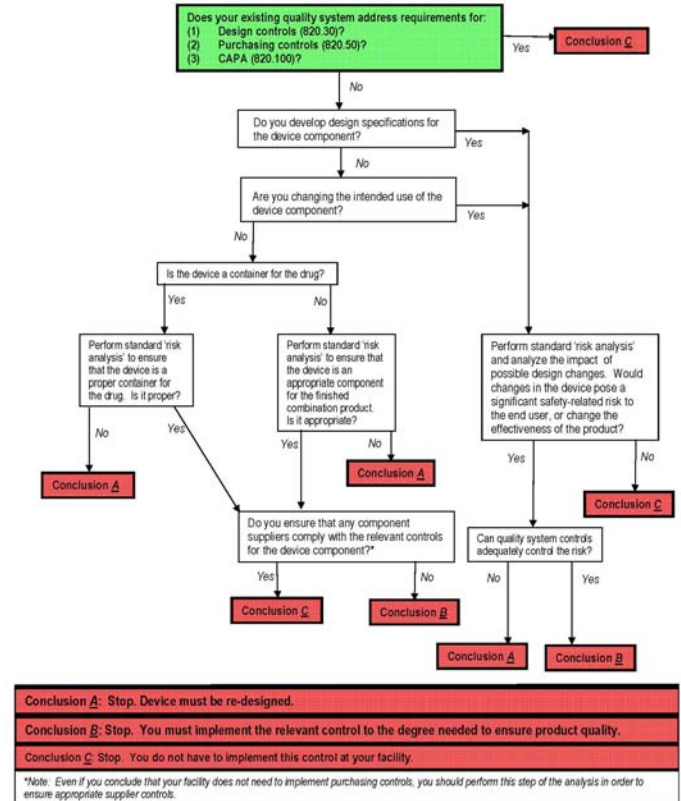
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Activities

- Developing and advocating for consensus policy positions
- Examples:
 - Submitted dozens of written comments, policy documents, proposed guidance documents, and other materials to FDA
 - GMP draft guidance and algorithms
 - Adverse Event Concept Paper
 - Cross-labeling algorithm
 - Planning joint conference with RAPS on GMPs to be held when proposed rule is released
 - Partnered with RAPS to host January 2005 Summit attended by approx. 150 people that resulted in a consensus white paper submitted to FDA

Appendix A: Facility Operating Under Parts 210/211
Adding a Device Component to a Single Entity Combination Product





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Validation

- Opened this webcast to combination products industry
- Validation of survey data and their impact on 2008 policy agenda





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Survey Purpose

- Goals
 - Evaluate current industry concerns and priorities
 - Inform our 2008 policy agenda
 - Communicate these to FDA
- Why now?
 - In 2007, the OCP underwent several leadership and personnel changes; new permanent director effective Jan. 7, 2008
 - Also wanted to take a step back and reflect on our activities

The screenshot shows the FDA Office of Combination Products website. At the top, there is the FDA logo and the text "U.S. Food and Drug Administration" and "U.S. Department of Health and Human Services". Below this is a navigation bar with links for "FDA Home Page", "Search FDA Site", "FDA A-Z Index", and "Contact FDA". The main heading is "Office of Combination Products". The page is divided into several sections: "Overview of the Office of Combination Products" with links for "Definition of a Combination Product" and "Frequently Asked Questions"; "Product Jurisdiction/Assignment of Combination Products:" with a highlighted box for "Final Rule: Definition of the Primary Mode of Action of a Combination Product - Federal Register [PDF 4.91MB] (August 25, 2005)"; "Requests for Comments" with links for "Review of Agreements, Guidances, and Practices in Compliance with the Medical Device User Fee and Modernization Act of 2002 [PDF 72KB] (September 2006)" and "Request for Comments:" with sub-links for "Adverse Event Reporting" and "Number of Marketing Applications for Combination Products (September 2005)"; "Guidance Documents and Procedures" with links for "Guidance for Industry and FDA Staff: Devices Used to Process Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P's) (July 2007)", "Minimal Manipulation of Structural Tissue [PDF 49KB] (September 2006)", "Guidance for Industry and FDA Staff: Early Development Considerations for Innovative Combination Products [PDF 130KB] (September 2006)", and "Plans for Proposed Rulemaking on Good Manufacturing Practice and"; "What's New" with a link for "Recent Examples of Combination Product Approvals"; and "Contact Us" with contact information for Thinkh Nguyen MS., Director of the Office of Combination Products, including address, phone, and email.



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Survey Scope

- Focused questions on:
 - Demographics
 - Satisfaction with existing guidance (FDA and non-FDA)
 - Topics on which more or better FDA guidance is needed
 - What type is needed
 - Why guidance is needed
- Allowed free-form comments



Survey Methodology

- Disseminated widely to the combination products industry
 - Our individual contacts and through trade groups and publications
 - Many thanks to the organizations that helped get the word out:
 - California Healthcare Institute
 - IMDMC
 - *MD&DI*
 - MDMA
 - *MX*
 - NEMA
 - PharmaMedDevice
 - RAPS
- Respondents completed survey via an Internet link that allowed them to remain anonymous (providing identifying information was optional)
- Asked companies to complete only one survey, but to collaborate with their colleagues





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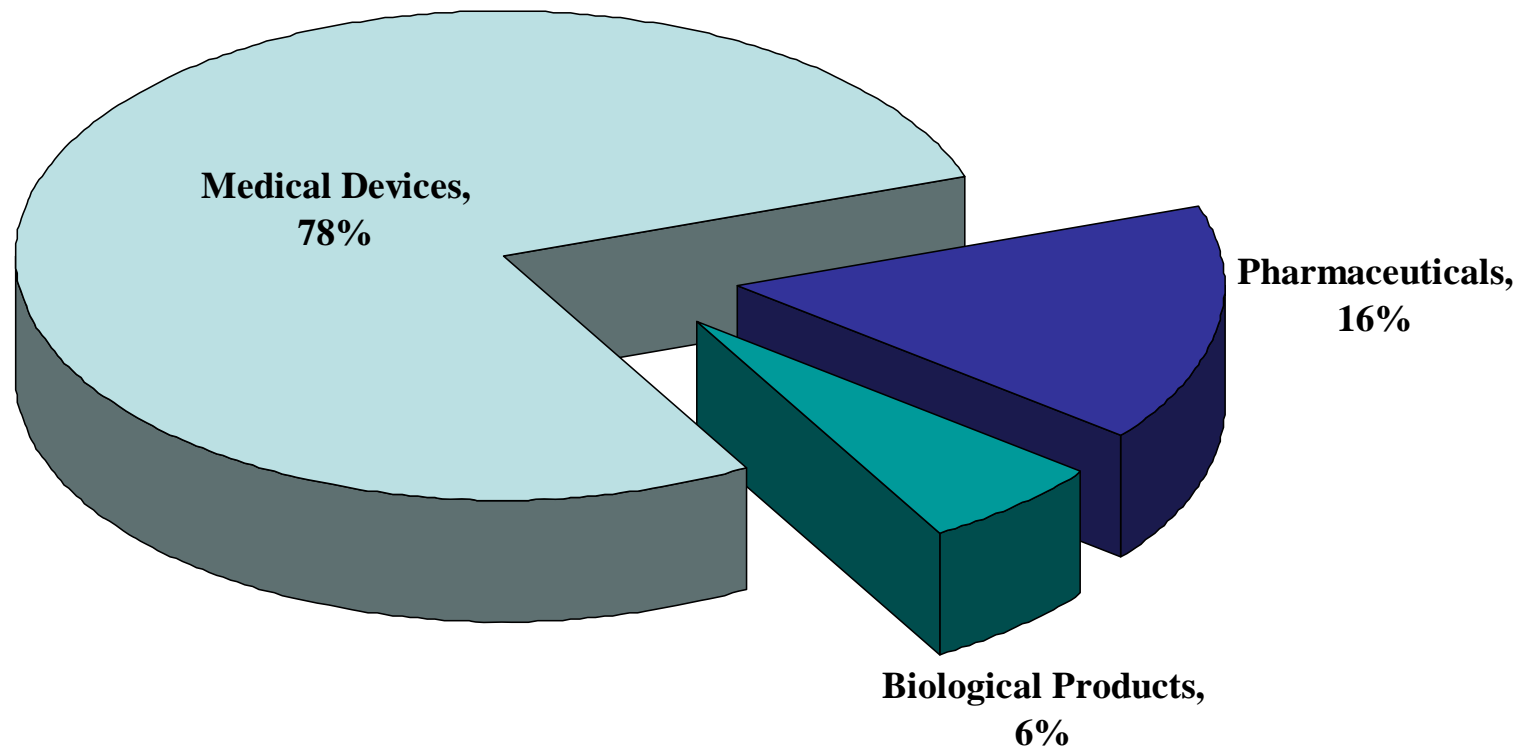
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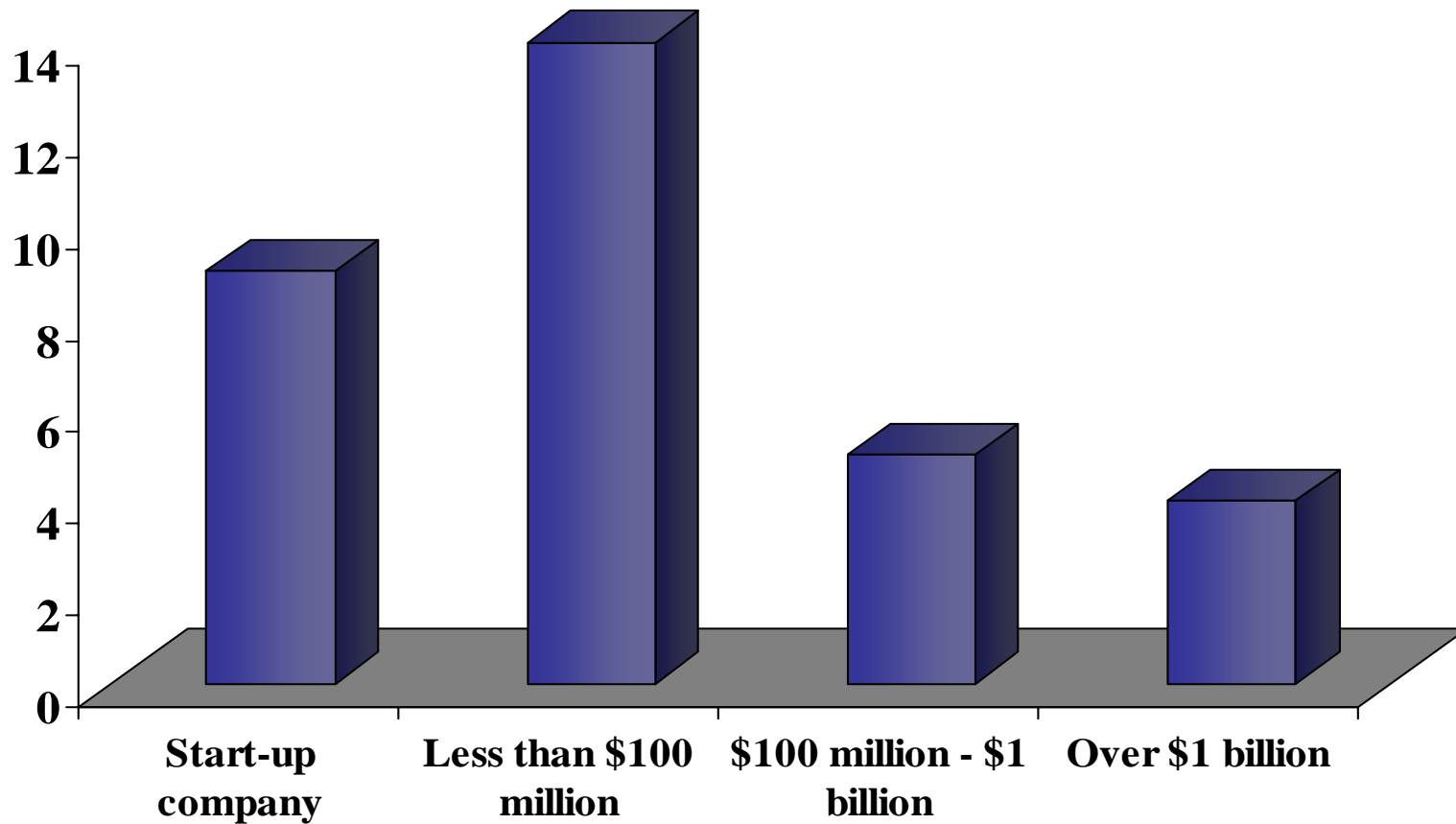
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Primary Product Focus





Annual U.S. Sales of Combination Products

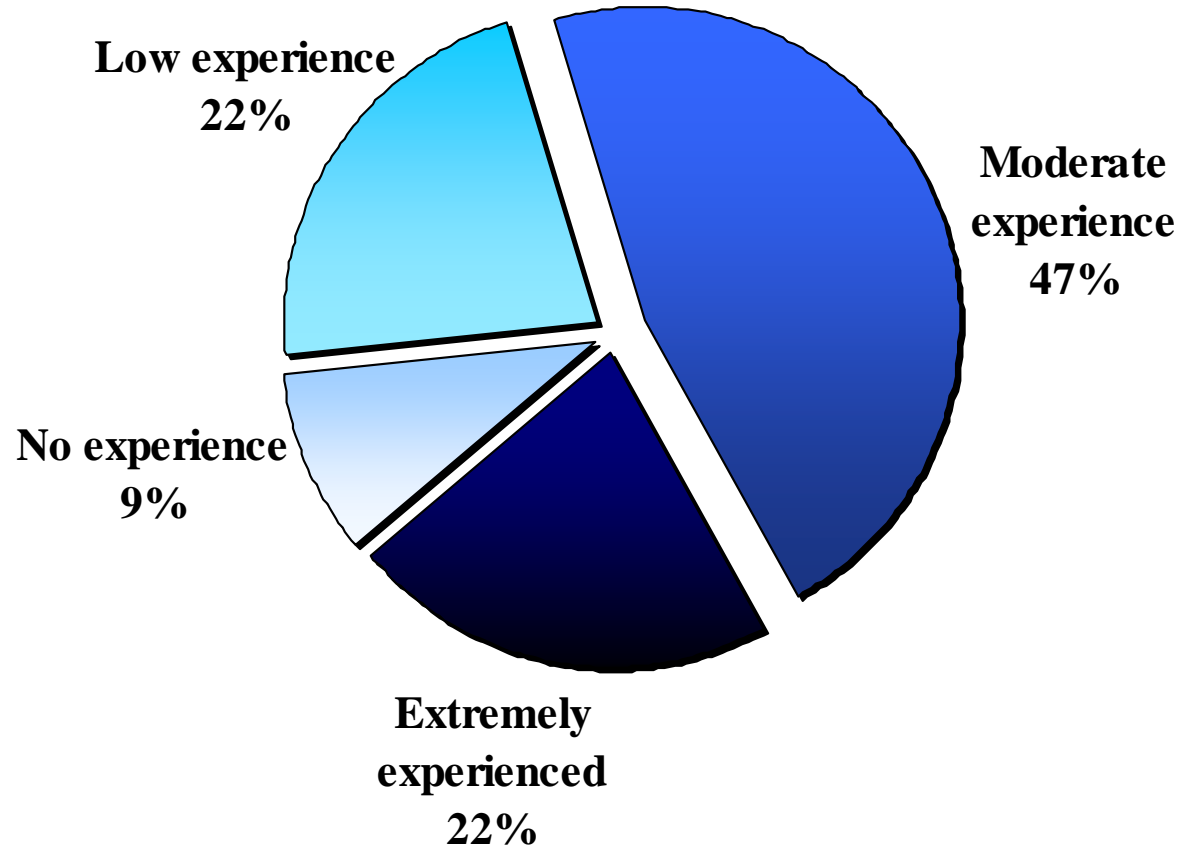




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Level of experience with developing and commercializing combination products

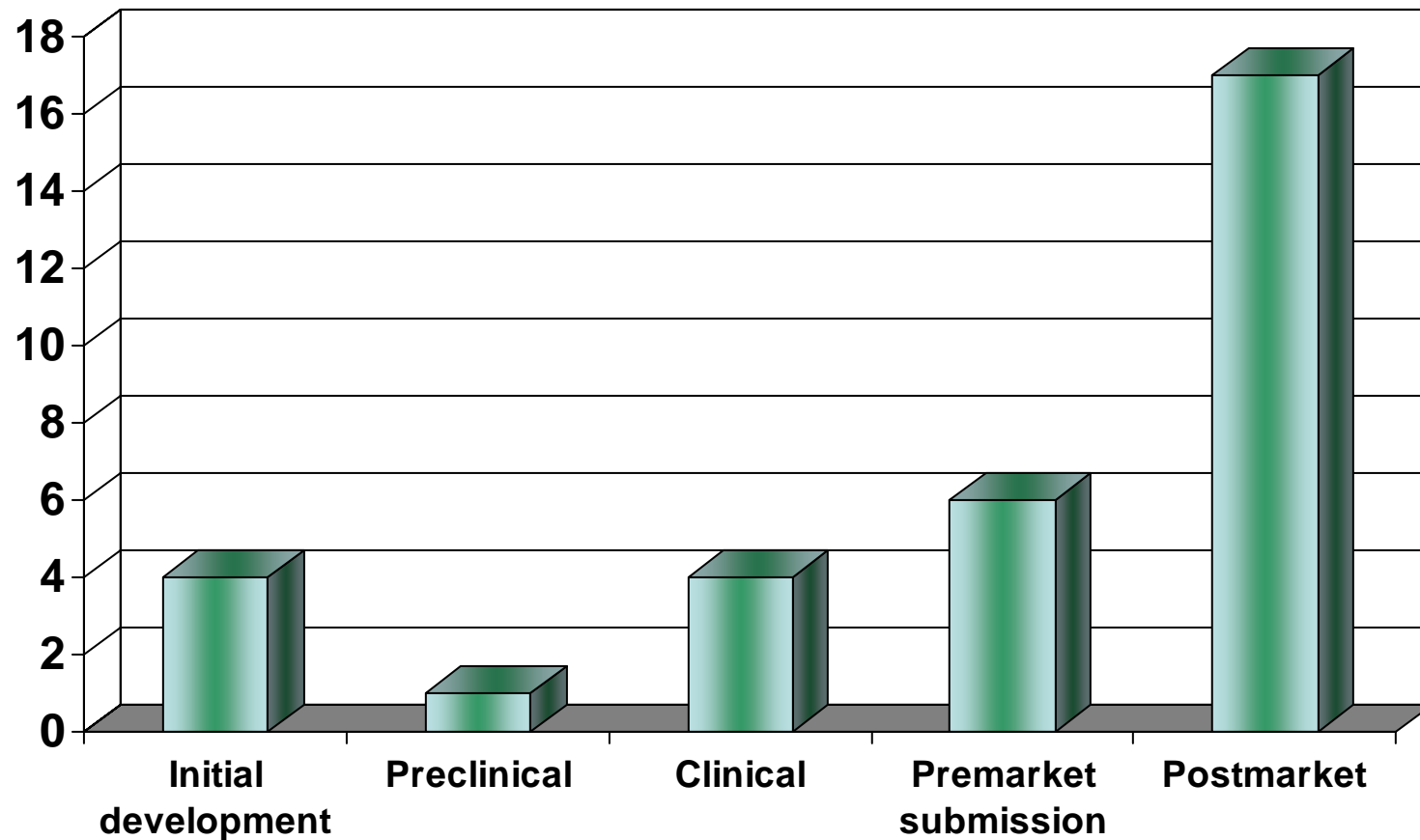




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Stage of development of combination product that is furthest along

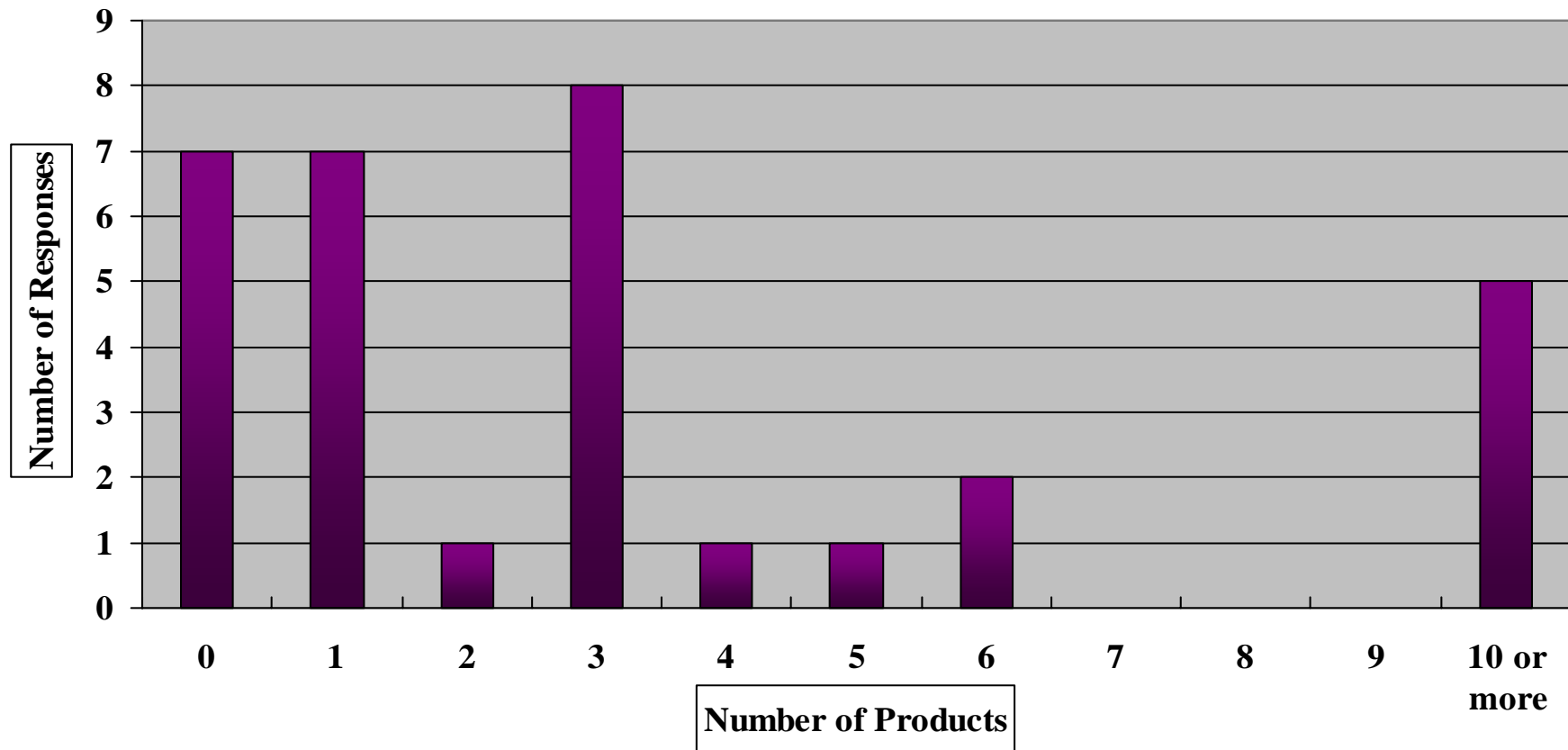




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Number of products developed and brought to market

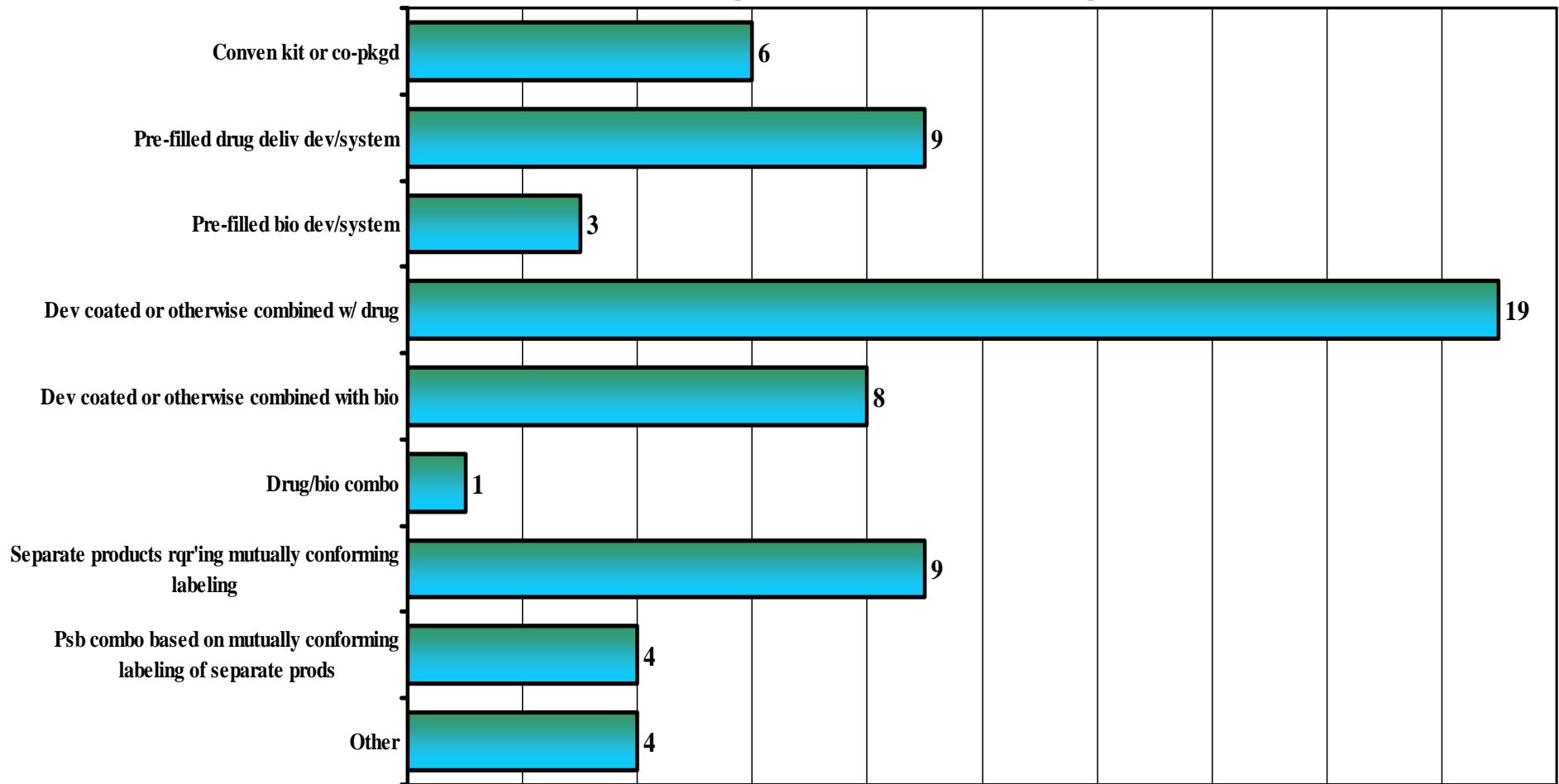




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Types of combination products currently developing or marketing





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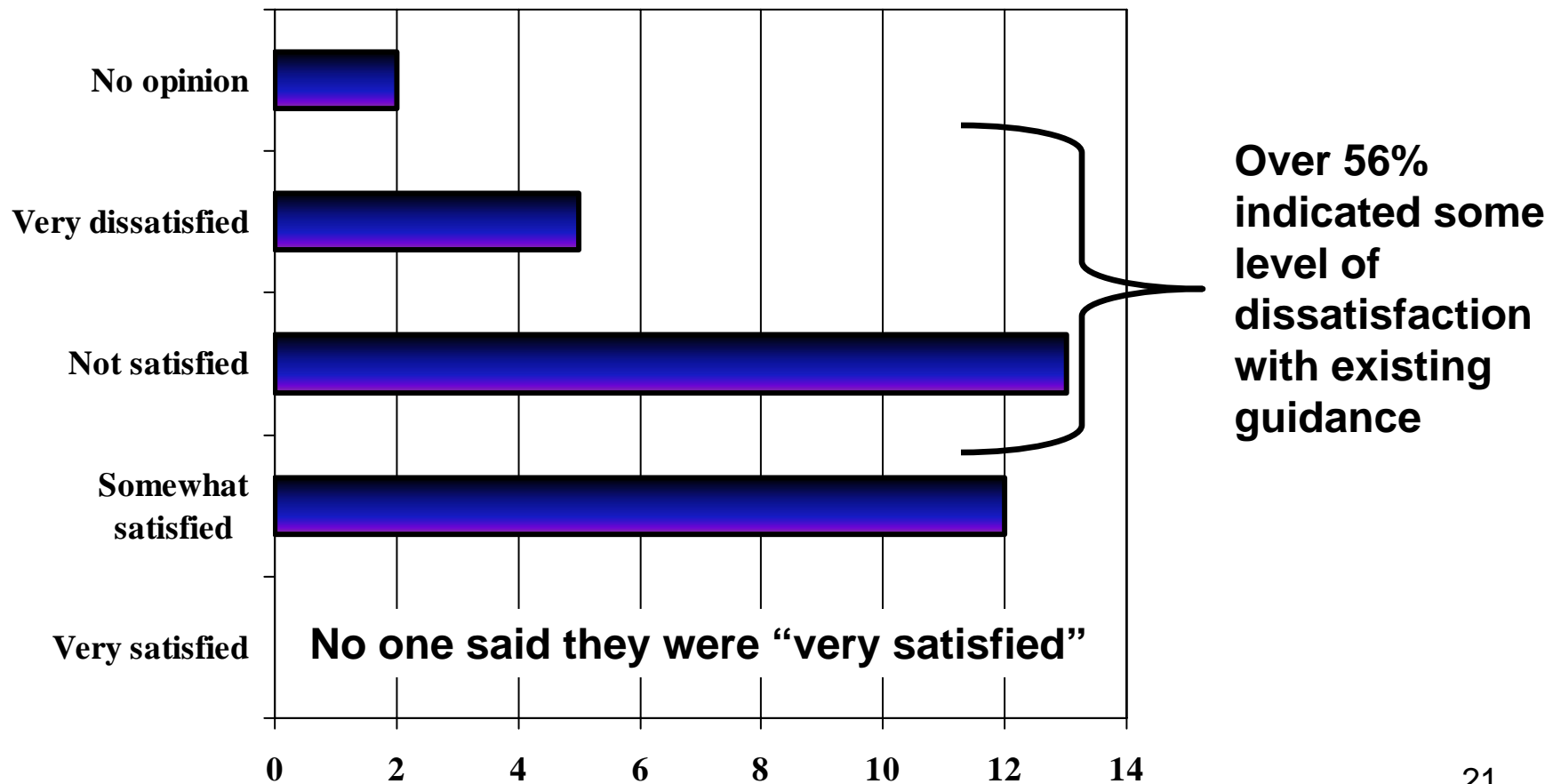
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Level of satisfaction with existing guidance (FDA and non-FDA)





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Selected Comments on Satisfaction*

Part of the problem with existing guidance documents is that they are at the 40,000 foot level, and there needs to be more detailed regulatory guidance at the 10,000 foot level.

FDA should specify in detail [applicable] pharmaceutical requirements, especially for efficacy, quality, and safety.

The commercial application of a device (which is meant to be modified and continually improved) and a drug/biologic (which is meant to stay the same) is leading to horrific change control on the device side

*Comments edited for clarity



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Observations on Satisfaction

- Generally, the companies indicating that they were “Not satisfied” or “Very dissatisfied” didn’t vary much by experience level or by company size
 - However, all 3 respondents who described themselves as having “No experience” were either “Not satisfied” or “Very dissatisfied”
- Only 1 of 6 respondents who were in the “premarket submission” level of development indicated any level of satisfaction
- Only 1 of 5 pharmaceutical companies indicated any level of satisfaction



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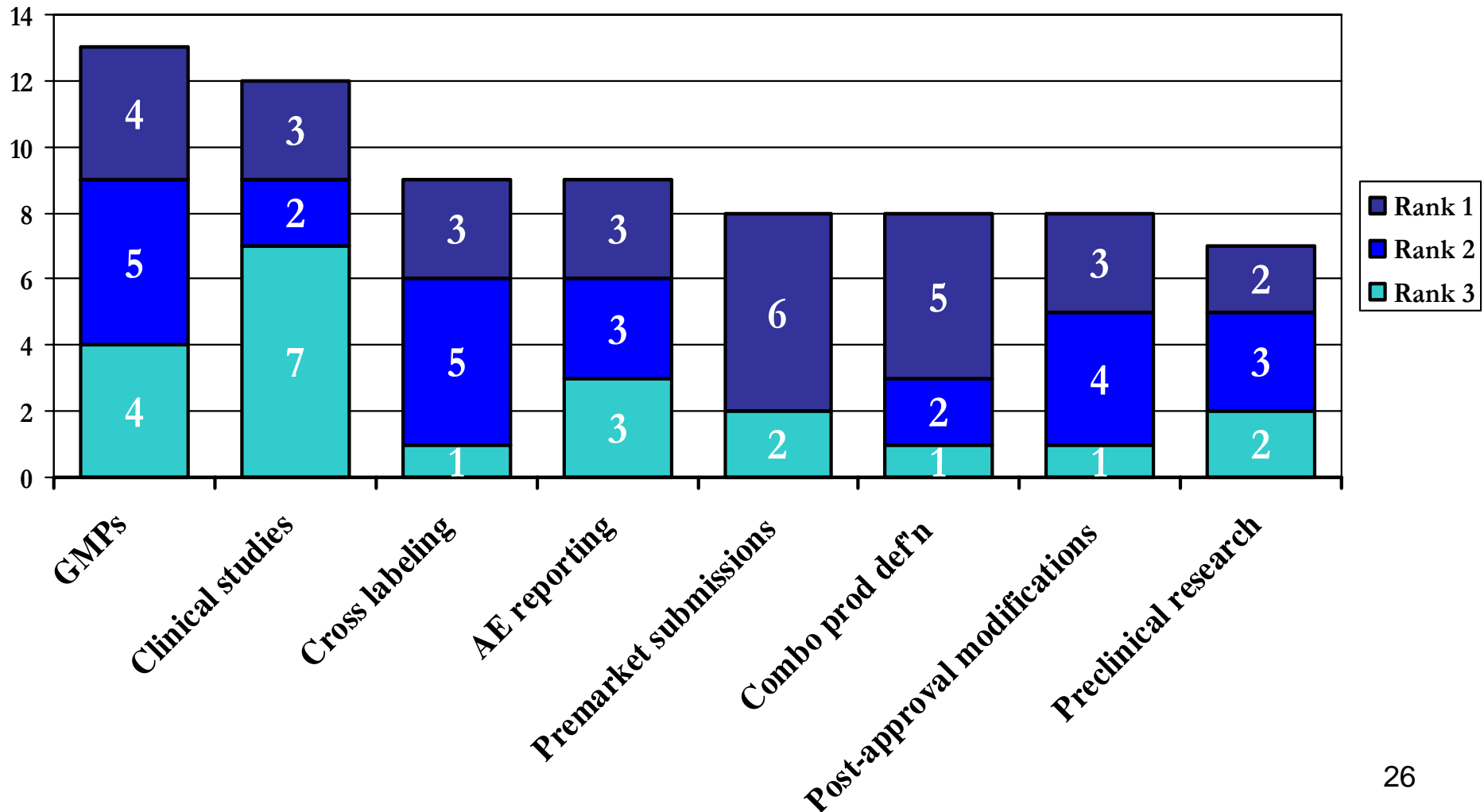
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Overall Weighted Rankings

-
- (1) Clinical Studies
 - (2) GMPs
 - (3) Premarket approval submissions
 - (4) Cross-labeled combination products
 - (5) Adverse event reporting
 - (6) Combo prod def'n & Post-approval modifications (tie)
 - (7) Pre-approval inspections
 - (8) Preclinical Research
 - (9) Labeling
 - (10) PMOA
 - (11) Advertising/promotion & RFD/prod jurisdiction (tie)
 - (12) User Fees
 - (13) Recall requirements
 - (14) Post-approval inspections
 - (15) Resolving disputes



Top-Rated Guidance Topics (Not Weighted)





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Observations on Topics

- GMPs
 - The only companies ranking this as #1 were self-described moderately experienced companies with less than \$100 million in revenue
 - Similarly, nearly 80% of companies that ranked GMPs as 1 or 2 were “moderately experienced”
- Research
 - 20% of all respondents put research (whether as preclinical or clinical) as one of their top 3 priorities, although start-ups and companies with revenue over \$1 billion were somewhat less concerned
 - Of those putting research in the top 3, only 2 were not device companies (and of these 2, it ranked 3rd)



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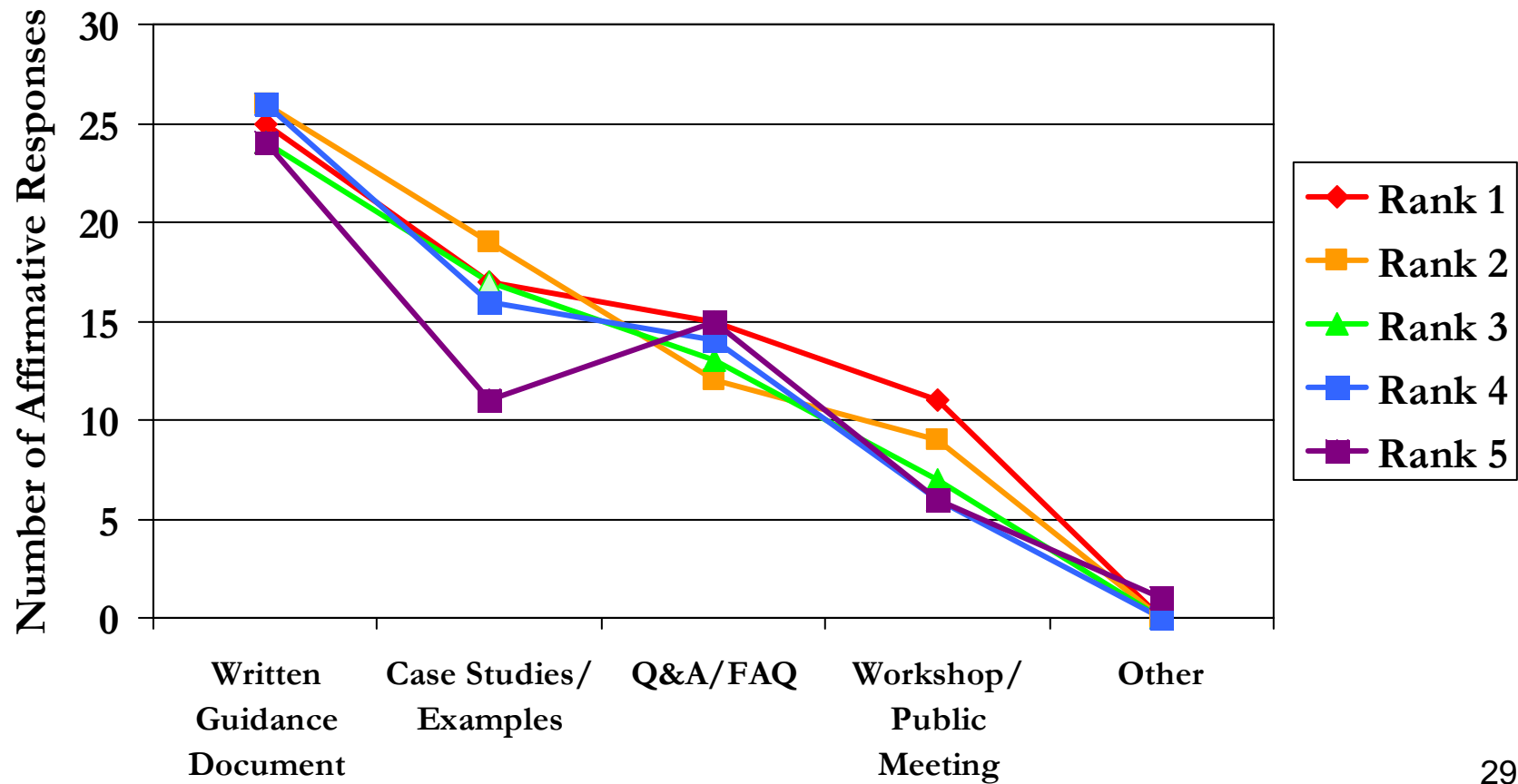
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Observations on Topics

- Adverse event reporting
 - Not ranked highly by companies with low or no experience
 - Not surprisingly, 8 out of 9 companies ranking AE reporting as a top 3 priority was in “postmarket” stage of development
- Also not surprisingly, nearly all companies ranking post-approval modification issues as a high priority were in the “postmarket” stage
- No drug or biological company ranked “combination product definition” in their top 3 priorities, but this seems to be a concern among all types of device companies
- Concerns about cross-labeling and premarket approval submissions remained fairly consistent across company size, development stage, and experience

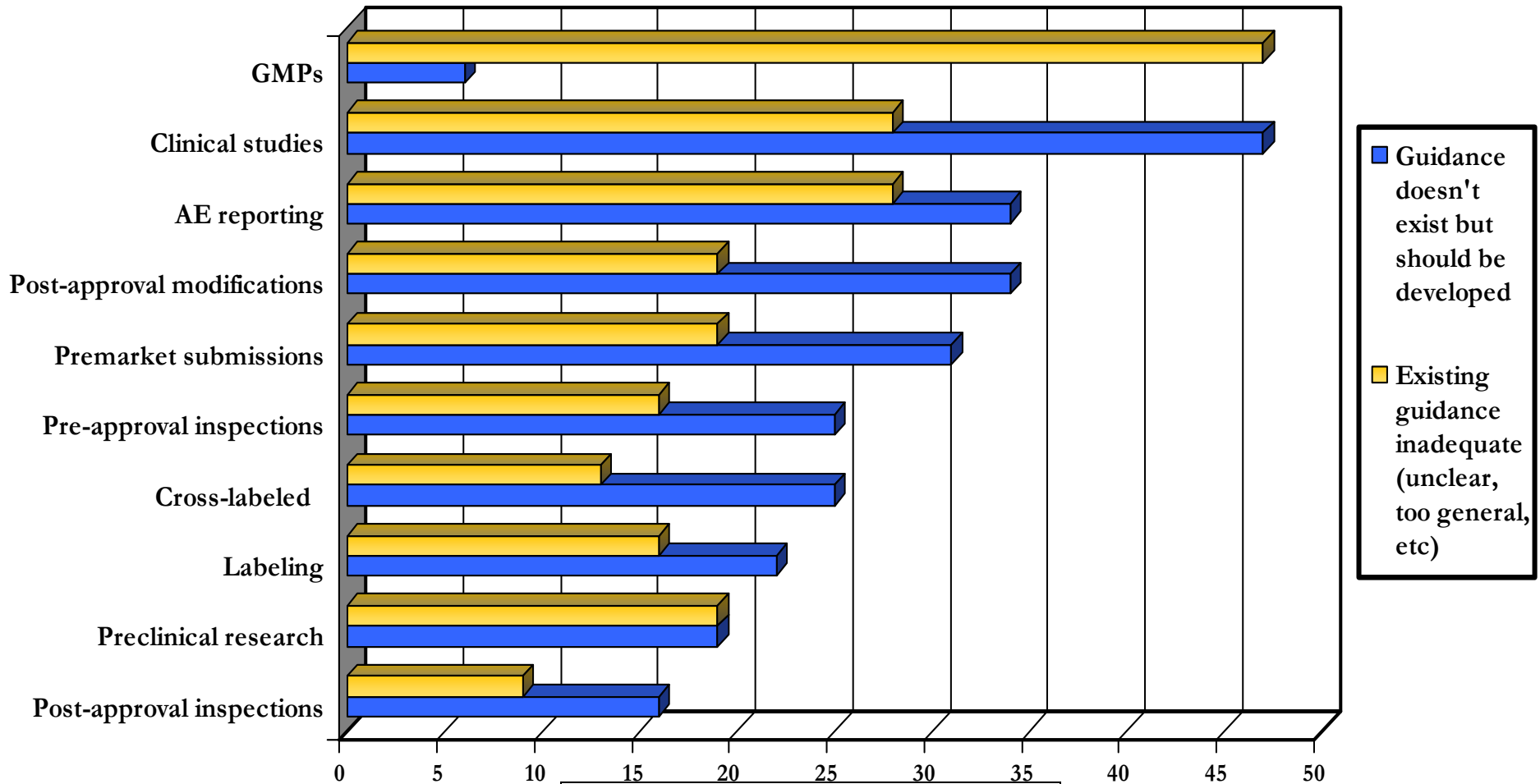


Type of Guidance Needed





Why Guidance is Needed



Percent of Affirmative Responses



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Survey says ...

- Highest priority topics:
 - GMPs (which could be resolved soon)
 - Research
 - Several topics at perhaps a lower priority (AE reporting, cross-labeling, post-approval modifications, the definition of a combination product, premarket submissions)



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Survey says ...

- Consensus that guidance is needed on several topics, particularly written guidance documents and, to a lesser extent, case studies/examples and FAQs
- We'll be conducting further analysis in the coming weeks as we plan for an FDA meeting



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Next Steps

1. Continued detailed analysis of survey data
2. Request FDA Meeting
3. Article in *MX* magazine
4. Open up the survey again?
 - Additional participation by pharmaceutical and biological companies



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FDA Meeting

- Request meeting with Thinh Nguyen, the new OCP director, as well as other key OCP staff
- Intended topics for discussion are:
 - Survey results
 - Potential impact on FDA policy-making agency
 - How the CPC can help
- Include a representative from: California Healthcare Institute, IMDMC, MDMA, NEMA, and RAPS



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