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Yale-Mayo Clinic Centers of Excellence in Regulatory Science and Innovation (CERSI) B12 Pediatric Device Survey

Online SURVEY COMPONENT 1

We are conducting a study of pediatric medical device development with funding and support from the U.S. Food and Drug Administration (or FDA). You have been identified as having valuable expertise in this field and we are seeking your assistance with this inquiry. The study has two components: one completed on-line, the second with an option to complete either on-line or over the phone (or video call). This on-line component of the survey should require no more than 60 minutes to complete.

Your responses are confidential; if content from any individual responses are reported in publications emerging from this project, they will be attributed to an anonymous study ID number, rather than an identified respondent. Participation in this study is completely voluntary. You are free to decline to participate, to end participation at any time for any reason, or to refuse to answer any individual question without penalty.

Our research team is affiliated with the Yale University-Mayo Clinic Center of Excellence in Regulatory Science & Innovation (CERSI). Our findings may help to inform policy and practice at the FDA; however the agency will not be privy to the primary data collected through this study, will not have access to the identity of any respondents, nor will be directly involved in the analysis of the data collected.

Background

1. Please enter your study ID number included in the email inviting you to participate in this study: _____ [***Have auto-filled if possible***]

2. Which sectors have you worked in? Select all that apply.

   - Clinical Care
   - Medical Device Manufacturer
   - Trade Organization/Industry Representative
   - Regulatory Affairs
   - Payer
   - Investor
   - Other _____ [please fill in]

3. For what type(s) of conditions and indications do you have experience in the development or promotion of **pediatric** medical devices? Select all that apply.

   ☐ Cardiovascular
   ☐ Orthopedic
   ☐ Diabetes Mellitus
   ☐ Neurology
   ☐ Other: _____ [please fill in]

4. For how many devices that you have been involved with **over the past ten years** has there been some consideration of submitting for FDA review **for pediatric uses**?

   ☐ None
   ☐ One
   ☐ Two
   ☐ Three
   ☐ Four
   ☐ Five or more

5. How many devices that you have been involved with **over the past ten years** have actually been submitted for FDA review **of pediatric uses**?

   ☐ None
   ☐ One
   ☐ Two
   ☐ Three
   ☐ Four
   ☐ Five or more

Barriers

We would first like your perceptions of factors that create the largest impediments to developing new products for pediatric use and submitting those products for FDA review. Please consider how these factors influence the medical device industry as a whole, not simply your own company.

6. From your perspective, how frequently are the following barriers encountered to developing products **for the pediatric population**? (
[Response Scale:1=Never 2=Rarely 3=Sometimes 4=Often 5=Always]

Economic Incentives and Market Conditions

- Low priority within existing medical device companies
- Lack of funding from external investors
- Small pediatric market generates inadequate revenue
- Reimbursement challenges related to insurance coverage (coding and coverage)
- Challenges associated with the sales and marketing of pediatric devices
- Costs of marketing pediatric devices

Engineering

- Engineering challenges associated with creating devices for children (e.g., creating devices for bodies that grow, lack of appropriate animal models, determining appropriate bench testing)

Clinical Trials

- Difficulty conducting pediatric clinical trials

Regulation

- Burdensome requirements during FDA regulatory review process
- Challenges associated with obtaining clearance/approval for multiple device sizes
- Lack of international regulatory harmonization

Liability/Reputation Issues

- Increased product liability profile associated with pediatric devices and trials
- Potential negative publicity if a child is harmed by an approved device

7. Which of the following is the *most consequential* barrier to developing products **for the pediatric population**? Select one.

o Low priority within existing medical device companies
o Lack of funding from external investors
o Small pediatric market generates inadequate revenue
o Reimbursement challenges related to insurance coverage (coding and coverage)
o Challenges associated with the sales and marketing of pediatric devices
o Costs of marketing pediatric devices
o Engineering challenges associated with creating devices for children
o Difficulty conducting pediatric clinical trials
o Burdensome requirements during FDA regulatory review process
o Challenges associated with obtaining clearance/approval for multiple device sizes
o Lack of international regulatory harmonization
o Increased product liability profile associated with pediatric devices and trials
o Potential negative publicity if a child is harmed by an approved device

8. Relative to each other, how consequential are each of the following ***broad categories*** of factors in preventing companies from **submitting devices for pediatric review**? Please allocate 10 points among the categories, with a higher number of points for the more consequential barriers.

- Economic Incentives (Market Conditions) ___
- Engineering Devices ___
- Logistics of Clinical Trials ___
- Regulation ___
- Liability and Reputation Issues ___
- Company culture or historical focus ___

TOTAL ____ [*auto sum column; if not = 10 provide error message*].

Incentives

We would now like your perceptions of the incentives or policies that could most effectively motivate the development of medical devices for pediatric use or expand labeling to pediatric populations for devices that have already been developed for the adult population.

9. How much impact would you expect each of the following incentives or policies to have?
(From 1-5, where 1 is no impact and 5 is very large impact.)

Development Incentives

- Tax credit incentives totaling 25% of development costs **of the pediatric application** for FDA-approved device use (i.e., pediatric R&D tax credits)
- Tax credit incentives totaling 50% of development costs of the pediatric application (i.e., more generous pediatric R&D tax credits)
- Tax credit incentives totaling 10% of development costs **of the adult application** (i.e., indirect R&D tax credits)
- Tax credit incentives totaling 20% of development costs of the adult application (i.e., more generous indirect R&D tax credits)

Regulatory Review

Fees and Timing

- Elimination of device user fee for devices developed for both adult and pediatric use
- Elimination of user fee for supplements to expand adult indications to pediatric populations

Review Time

- Defined/mandated timelines for device review / approval process
- Expedited regulatory review for all pediatric submissions
- Expedited review for a follow- up adult indication if a company first develops a pediatric device and obtains clearance/approval for pediatric indication

Review Process and Logistics

- Greater acceptance of pre-clinical modeling
- "Reverse" extrapolation (i.e., extrapolate data from pediatric submissions to adult submissions)
- Use of small confirmatory pediatric trials with supportive data from registries, adult data extrapolation or real-world evidence
- Greater emphasis on post-market data collection or monitoring in lieu of pre-market data
- All reviewers for pediatric applications selected to have expertise in the pediatric population specific expertise

Progressive Review

- Progressive review for all devices
- Progressive review limited to pediatric devices
- Progressive review limited to pediatric devices used in particular settings

Coverage

- Mandated coverage by Medicaid at the national level for all devices receiving FDA review and approval for pediatric use.
- Mandated private insurance coverage for all devices receiving FDA review and approval for pediatric use.
- Breakthrough designation following review process for Medicaid coverage, which would result in a **coverage bonus of 15%** of otherwise reimbursable costs
- Breakthrough designation following review process for Medicaid coverage, which would result in a **coverage bonus of 25%** of otherwise reimbursable costs

Evidence Generation

- Single contract access to a national network of pediatric academic medical centers
- Single IRB review established for such a national network of pediatric academic medical centers

Comparisons to Pharmaceutical Development

10. Some past policies have incorporated combinations of incentives to motivate drug development for particular populations. We would like you to consider four such policies, first considering their suitability for application to pediatric devices, then their likely impact if adapted.

    A. Each of the following policies/practices have been adopted for pharmaceuticals. How **applicable** would these be for pediatric device development? (From 1-5, where 1 is not at all applicable and 5 is very applicable.)

    - **Orphan Drug Act**: tax credits for 50% of development costs, 7-year market exclusivity, and waived user fees.
    - **Best Pharmaceuticals for Children Act (BPCA)**: 6-month market exclusivity to a drug/biologic that conducts testing in children in response to a written request from the FDA.
    - **Pediatric Research Equity Act (PREA)**: mandated pediatric studies for drugs in which the condition exists in children.
    - **Priority Review Voucher**: transferrable vouchers for expedited review of some other drug after approval of a pediatric drug. These vouchers can be resold and used for any product, including those deployed exclusively in adult populations.

    B. How **large of an impact** would these policies likely have on pediatric device development? (From 1-5, where 1 is no impact and 5 is very large impact.)

- **Orphan Drug Act**: tax credits for 50% of development costs, 7-year market exclusivity, and waived user fees.
- **Best Pharmaceuticals for Children Act (BPCA)**: 6-month market exclusivity to a drug/biologic that conducts testing in children in response to a written request from the FDA.
- **Pediatric Research Equity Act (PREA)**: mandated pediatric studies for drugs in which the condition exists in children.
- **Priority Review Voucher**: transferrable vouchers for expedited review of some other drug after approval of a pediatric drug. These vouchers can be resold and used for any product, including those deployed exclusively in adult populations.

Mandates and Regulatory Requirements

11. A final category of policies involve a variety of regulatory requirements for device manufacturers. These requirements could be coupled with incentives to enhance the feasibility of implementation. We would like your assessment of both their general acceptability within the industry, as well as your prediction of the likely impact that they would have on pediatric device development.

    A. How acceptable to the device industry would the following be?
    Response Scale [1=very unacceptable, 2=somewhat unacceptable, 3=Neutral
    4=somewhat acceptable, 5=very acceptable]

Regulatory Mandates Alone

- Require submission of devices for pediatric review if the conditions appear in children above some threshold prevalence
- Mandate that all off-label uses of medical devices in children by reported to a national registry

Regulatory Mandates Combined with Incentives

- Mandatory submission for pediatric review combined with a tax credit for 25% of development costs
- Mandatory submission for pediatric review combined with a tax credit of 50% of development costs
- Mandatory submission for pediatric review combined with a requirement that Medicaid cover all FDA approved pediatric devices
- Mandatory submission for pediatric review combined with a requirement that Medicaid **and private insurance** cover all FDA approved pediatric devices

B. How much of an impact would this have on pediatric device development?
Response Scale: [1= significantly decrease, 2=somewhat decrease, 3=unclear impact
4= somewhat increase, and 5 =is significantly increase]

Regulatory Mandates Alone

- Require submission of devices for pediatric review if the conditions appear in children above some threshold prevalence
- Mandate that all off-label uses of medical devices in children by reported to a national registry

Regulatory Mandates Combined with Incentives

- Mandatory submission for pediatric review combined with a tax credit for 25% of development costs
- Mandatory submission for pediatric review combined with a tax credit of 50% of development costs
- Mandatory submission for pediatric review combined with a requirement that Medicaid cover all FDA approved pediatric devices
- Mandatory submission for pediatric review combined with a requirement that Medicaid **and private insurance** cover all FDA approved pediatric devices

12. What else would you like us to know about the current state of pediatric device development or potential changes that could be made to current practices? (open-ended box)

Thank you for taking time to respond to our survey!