The 510(k) Survey
Results and Lessons

Tuesday, 24 May 2011 • 8:30 a.m. EDT
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A Comprehensive Analysis of the FDA 510(k) Process
Industry Practice and the Implications for Reform

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National Press Club, Washington, D.C.
May 24, 2011
- Revised July 19, 2011 -
• The Medical Device Industry and Device Development
• Introduction to the Research Study
  • Objectives and Methodology
  • Respondent Characteristics
• Key Findings
  • Predictability and Interaction with FDA
  • Different Impact on Large and Small Companies
  • International Comparison
• Observations: Opportunities for Improvement
• Concluding Remarks
The Medical Device Industry and Medical Device Development
Medical Device Companies by Size

<table>
<thead>
<tr>
<th>Number of Companies</th>
<th>Small companies</th>
<th>Medium companies</th>
<th>Large companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>3,377</td>
<td>1,002</td>
<td>373</td>
</tr>
<tr>
<td>20-99</td>
<td></td>
<td></td>
<td>324</td>
</tr>
<tr>
<td>100-499</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>500+</td>
<td></td>
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</tbody>
</table>

% of Total US Medical Device Employment

- Small companies: 28%
- Medium companies: 18%
- Large companies: 54%

Device Development Is an Iterative Process

- Medical device development is a highly iterative process.
- Need to improve product continuously through frequent, positive iterations, while avoiding unnecessary iterations.
- Efficient planning and execution requires predictable process.
Medical Device Development Functions

- Cross-Functional Management
- Marketing
- Research & Development
- Legal
- Regulatory
- Reimbursement
- Manufacturing & Operations
- Quality
- Clinical
- Sales
Impacts of Regulation on Device Development

Gate 1

1. Project Definition Acceptance/ Concept Charter
2. Initial Design Acceptance/ Development Agreement
3. Final Design Acceptance/ Ramp Up Readiness
4. Product Launch Acceptance/ Launch Readiness

Phases
- Initial Evaluation of possible development of commercial product
- Definition of design input based on customer needs and technical requirements
- Development of product design and of manufacturing process; verification and validation
- Final validation of manufacturing process; preparation of product introduction

Market Analysis
- Competitive Assessment
- Financial Review
- Legal/ IP Analysis and Filings

Early Risk Assessment
- Initial Concept Selection
- Customer Input / VOC
- Early Concept - Preliminary Design
- Detailed & Modified Design
- Market Diff Project Timeline
- Project Core Team Selection
- General Project Plan & Timeline

Product Development/ Verification & Validation
- Initial Design Risk Analysis (dFMEA)
- Initial Reimbursement Strategy
- Initiate DFM (Tooling, Fixturing)
- Design Verification and Validation
- Design Risk Analysis (dFMEA)

Market Introduction of product; continuous improvement
- Final Patent Review with R&D
- Remaining Process IQ/OQ/PQ/PPQ
- EQA & Review of Filings
- Initial Process FMEA (pFMEA)
- Design Outputs = Design Inputs

Almost half of all activities and decisions in the development process are affected by regulatory requirements.
Introduction to the Research Study
Study Objective and Methodology

• Elicit from those engaged in medical device development, what seems to work well and how the 510(k) regulatory process could be further strengthened.

• Collect comprehensive data set to provide the basis for constructive input to strengthening the process:
  – Timelines
  – Interactions with the agency
  – Issues and challenges in current implementation
  – Comparison among international regulatory programs
Approach and Study Methodology

**Topic Identification**
Interviews with 80+ medical device experts (industry and FDA)

**Survey design**
Two rounds of expert review and prioritization

**Data gathering**
Online survey Dec. 22–Feb. 22

**Analysis and Results**
Analysis and results presentation

8/2010

5/2011
• Target respondents:
  – Individuals closely involved with the 510(k) process
  – Broad outreach through professional societies, industry groups, and trade media

• Survey Structure:
  – General part and device-specific part
  – 86 questions total

• Responses:
  – N=356 respondents total
  – Number of respondents varied per question, as not all questions were answered by every respondent
  – N per question stated for each question in graphs and appendix
Respondents’ 510(k)-Related Experience

N = 354

<table>
<thead>
<tr>
<th>510(k)-Related Experience (Yrs.)</th>
<th>Respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 20</td>
<td>26%</td>
</tr>
<tr>
<td>15-19</td>
<td>14%</td>
</tr>
<tr>
<td>10-14</td>
<td>21%</td>
</tr>
<tr>
<td>5-9</td>
<td>21%</td>
</tr>
<tr>
<td>2-4</td>
<td>10%</td>
</tr>
<tr>
<td>&lt; 2</td>
<td>7%</td>
</tr>
</tbody>
</table>

N = 354
## Representativeness: Breakdown by Device Type

<table>
<thead>
<tr>
<th>Type of Device</th>
<th>Actual % of FDA Applications</th>
<th>Survey Respondents %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical, Orthopedic, and Restorative Devices</td>
<td>28%</td>
<td>37%</td>
</tr>
<tr>
<td>Cardiovascular Devices</td>
<td>13%</td>
<td>23%</td>
</tr>
<tr>
<td>Anesthesiology, General Hospital, Infection Control, and Dental Devices</td>
<td>23%</td>
<td>13%</td>
</tr>
<tr>
<td>Reproductive, Abdominal, and Radiological Devices</td>
<td>17%</td>
<td>7%</td>
</tr>
<tr>
<td>Ophthalmic, Neurological, and ENT Devices</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Chemistry and Toxicology Devices</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Immunology and Hematology Devices</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Microbiology Devices</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Other</td>
<td>3%</td>
<td>9%</td>
</tr>
</tbody>
</table>

Actual % FDA applications: Based on all applications to FDA in 2008-2010 (See FDA database at [www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm)).

Survey Respondents %: Based on respondent’s statement about device field with most extensive 510(k) experience.
FDA’s Internal Assessment compared to Survey Responses

Figure 4.9. 510(k) Decisions Issued: FY 2004-2009


* Includes the following responses: De-Novo, Converted to PMA, Other
FDA’s Internal Assessment compared to Survey Responses

Figure 4.5. Average Time to 510(k) Decision by Type of 510(k): FY 2008 Receipt Cohort

- MDUFA Meeting Report, 2011 (as amended/corrected by FDA 7/2011)

¹ SE and NSE only.
Avg. duration for SE: 204 days (N=179); NSE: 279 days (N=18); Withdrawn: 330 days (N=13), with long tail.
Figure 4.8. Number of 510(k) Review Cycles: FY 2002-2008


N= 211; SE: 2.1 cycles (N=191); NSE: 2.8 cycles (N=20)
Withdrawals (not included in computation): 2.9 cycles (N=14)
Key Findings
Predictability and Interaction with FDA
How important are regulatory requirements to your business decision to a major investment in a new product?
For the technologies you have worked on, how important is predictability of the regulatory process in deciding first country for market launch?

- Critically important: 68%
- Important: 20%
- Not of major importance: 12%

N=351
Respondents Perceiving Substantive Changes in FDA Review Process

From your experience in the last 3 years, have you perceived any substantive changes in the FDA review process and/or clearance decision of a 510(k) submission?

- Yes: 85%
- No: 15%

N = 349
In the last 3 years, in what specific areas have you perceived changes in the FDA's requirements?

- Clinical: endpoints, duration, sample size, post-hoc statistical analyses (58%)
- Preclinical work (57%)
- Regulation: appropriateness of 510(k) (53%)
- "Least burdensome" (49%)
- Animal studies (34%)
- Labeling (2%)
- Other (13%)

Note: More than one choice possible per respondent.

N= 337
Clarity of Preparation Requirements for a 510(k) Submission

Based on your understanding, what is the current level of clarity of the requirements for preparation and submission of a 510(k)?

- Very clear/certain: 24%
- Somewhat unclear/uncertain: 57%
- Very unclear/uncertain: 19%

N = 354
Have Guidance Documents been Critical to your Company in Preparing Successful Submissions?

**Yes**: 81%

**No**: 12%

**Other**: 7%

*N = 347*
Availability of Guidance Document has an Impact on the Ultimate Decision

- **Device Specific: Guidance Document Existing for Technology**
  - Total: \( N = 222 \)
  - Total NSE + Withdrawn: 11%
  - SE: 89%

- **Device Specific: Guidance Document NOT Existing for Technology**
  - Total: \( N = 222 \)
  - Total NSE + Withdrawn: 19%
  - SE: 81%

\( N = 93 \) for both categories.
If an appropriate guidance existed and was used by your company during submission of a 510(k), did you perceive any difference between the guidance document and the way the FDA reviewed your submission?

N=300
Reason for Perceived Difference between Guidance Document and FDA Review

- FDA asked for information beyond that required by the guidance: 87%
- FDA indicated that unnecessary information had been provided by the sponsor: 5%
- FDA indicated that all necessary information had been provided by the sponsor, but the way the information was presented was deemed inadequate: 6%

N= 216
Perceived Difference between Pre-Submission Meeting Discussion and FDA Review

Proportion of Time FDA Followed Through on Matters Discussed/Directed

- Did Follow Through: 61%
- Unspecified: 4%
- Did not Follow Through in 11-25% of cases: 2%
- Did not Follow Through in 26-50% of cases: 15%
- Did not Follow Through in 51-75% of cases: 6%
- Did not Follow Through in 76-99% of cases: 3%
- Never Followed Through: 9%
Interaction: Questions/Requests for Information

- Perceived as "scientifically justified": 38%
- Perceived as not adding to safety and effectiveness: 43%
- Perceived as not adding to safety: 4%
- Other: 13%
- Perceived as not adding to effectiveness: 2%
Percent of Requests for Information Obtained During Days 75-90 of FDA’s 90-day Review Period

- Received during days 75-90: 75%
- Other times during review process: 25%

N= 293
Interaction: Respondent’s Perspective

- **Initial submission could have been improved**
  - Yes: 39%
  - No: 61%
  \[N=260\]

- **Percent of reviewer questions that should have been anticipated (in retrospect)**
  - Should have: 26%
  \[N=216\]

- **Percent of the last 10 requests that were already answered in original submission**
  - Already answered: 41%
  \[N=275\]

- **Percent of questions not fully clear**
  - Not fully clear: 27%
  \[N=282\]
Key Findings
Different Impact on Large and Small Companies
### Key Differences between Large and Small Companies

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Small Companies</th>
<th>Large Companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>New product (vs. line extension) [%]</td>
<td>72%</td>
<td>35%</td>
</tr>
<tr>
<td>SE Decision [%]</td>
<td>61%</td>
<td>88%</td>
</tr>
<tr>
<td>NSE Decision [%]</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Interaction with FDA during development process</td>
<td>earlier</td>
<td>later</td>
</tr>
<tr>
<td>Pre-submission meeting with FDA sought</td>
<td>39%</td>
<td>17%</td>
</tr>
<tr>
<td>Duration of pre-IDE process [months]</td>
<td>10.8</td>
<td>7.4</td>
</tr>
<tr>
<td>Change in lead reviewer [%]</td>
<td>19%</td>
<td>10%</td>
</tr>
<tr>
<td>Total avg. review time [days]</td>
<td>330</td>
<td>177</td>
</tr>
</tbody>
</table>
**Key Differences between Large and Small companies**

<table>
<thead>
<tr>
<th>Respondents perceive:</th>
<th>Small Companies</th>
<th>Large Companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major difference with FDA’s risk assessment [%]</td>
<td>48%</td>
<td>23%</td>
</tr>
<tr>
<td>% of FDA requests already answered in original submission</td>
<td>53%</td>
<td>33%</td>
</tr>
<tr>
<td>% of FDA requests “scientifically justified”</td>
<td>30%</td>
<td>42%</td>
</tr>
<tr>
<td>FDA requests having major effect on time [%]</td>
<td>45%</td>
<td>36%</td>
</tr>
<tr>
<td>FDA requests having major or medium effect on financial resources [%]</td>
<td>76%</td>
<td>64%</td>
</tr>
</tbody>
</table>
Key Findings
International Comparison
Comparison of International Review Time from Submission to Clearance/Registration

Graph shows ultimately cleared/registered devices only.

Length of review process in months (based on data points for “1-2”, “3-5”, “6-9”, “10-19”, “20-29”, “30+ months” for the various regulatory systems. N per country: see above.
Within the last 3 years, if your company chose to first bring to market a specific device OUS, what was the major reason?

- **Unpredictable 510(k) requirements**: 49%
- **Cost of clinical trials**: 22%
- **Quicker process**: 9%
- **Easier process**: 5%
- **Other**: 15%
<table>
<thead>
<tr>
<th></th>
<th>EU</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Considered “most predictable regulatory system” [%]</td>
<td>64%</td>
<td>8%</td>
</tr>
<tr>
<td>First regulator/”body” approached to discuss and plan submission [%]</td>
<td>80%</td>
<td>4%</td>
</tr>
<tr>
<td>Review time (submission to decision) for products not requiring clinical data [months]</td>
<td>2.7</td>
<td>5.9</td>
</tr>
<tr>
<td>Review time (submission to decision) for products requiring clinical data [months]</td>
<td>4.8</td>
<td>13.2</td>
</tr>
</tbody>
</table>
Moving Forward to Foster Innovation and Timely Patient Access to Safe & Effective Technologies
Opportunities

Enhance predictability

• Increase number of guidance documents
• Timely update of guidance documents
• Clear and timely communication of new FDA expectations before publication in guidance

Increase process consistency

• Increase training (particularly implementation of current regulations)
• Reduce perceived differences in agency follow-through (by enhanced communication)
• Reduce reviewer turnover
Ensure efficient review process

- Preparation of clear and complete submissions
- Eliminate repeat requests of information already provided
- Timely access to meetings
- Increased use of interactive review concept

Close gap with international systems

- Continued harmonization efforts (GHTF)
- Sharing best practices (particularly on process side), while acknowledging differences in regulatory requirements
Opportunities

Increase attention to specific needs of small companies (while maintaining a level playing field)
• Improve opportunities for interaction
• Provide training support in areas where small companies tend to face particular challenges

Monitor effect of process changes
• Evaluate impact of any process changes through appropriate performance metrics
• Work with industry to monitor process performance over time
Assuming that the FDA will make changes to the 510(k) clearance process, what primary metrics should be used to evaluate the overall performance of the revised 510(k) process?

Respondent-Suggested Metrics to Evaluate Future Changes in the 510(k) Process

- Predictability: 78%
- Appropriate alignment of device risk and review intensity: 77%
- Review time: 68%
- Number of device-related recalls: 30%
- Other: 12%

Note: More than one choice possible per respondent.
Concluding Remarks
Investigators:
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A Comprehensive Analysis of the FDA 510(k) Process
Industry Practice and Implications for Reform

A Research Study

Investigators:

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Professor, Northwestern University

Jon B. Pietzsch, Ph.D.
President & CEO, Wing Tech Inc.
Consulting Associate Professor, Stanford University

Grant recipient: Northwestern University

Read the study press release. Read recent news coverage.

Watch study webcast and inHealth 510(k) Webcasts

Read about January 10 panel event

Funding Source:

Study website @ www.510k.net
• 510(k) Basics
• FDA, Government and Medical Devices
  CDRH, ODE and OIVD documents, Medical Device User Fee and Modernization Act (MDUFMA) and US House of Representatives: Committee on Energy and Commerce
• FDA Guidance Documents relating to 510(k) regulatory process
• Workshops & Conferences - Webinars, TownHall and Public mtgs
• Literature  -  published articles pertaining to 510(k) process
• FDA Training and Continuing Education Courses
• Institute of Medicine of the National Academies (IOM)
  Links to agendas, webcast, presentations and reports from Meetings 1, 2 and 3 relating to 510(k)
• International Regulations
Respondents’ Panel

Susan Alpert, MD, PhD  
Former Senior Vice President and Chief Regulatory Officer  
Medtronic Inc.

Peter Barton Hutt  
Senior Counsel  
Covington & Burling LLP

Philip J. Phillips  
President  
Phillips Consulting Group LLC

Jeffrey E. Shuren, MD, JD  
Director  
FDA Center for Devices and Radiological Health
Thanks for Attending

Review the archived version of this webcast by visiting

www.inhealth.org/510ksurvey

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ORIGINAL RESEARCH WEBCAST

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