An Investigation into
Pharmaceutical manufacturing Performance and its relationship to FDA oversight and enforcement actions

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Presentation Agenda

- Introduction to UC Berkeley CSM Research Program
  - Research program purpose and general approach.
  - Manufacturing metric scores.
  - Summary of best practices.
  - Preliminary conclusions.

- Pharmaceutical Manufacturing Research Project
  - Description and approach.
  - Principal investigator capabilities.
  - Research project funding, staffing and timeline.
UC Berkeley CSM Research Program

Why?
- Perceived competitiveness gap among producers.

Charter
- Measure manufacturing performance.
- Identify underlying determinants of performance.
- Benchmark wafer fabrication across industry.
- Carry out focus studies of important practices.

Funding
- Originally by Alfred P. Sloan Foundation; additional funding by Sloan, International SEMATECH, and semiconductor industry.
Value from CSM Research Program

- Developed a new industry standard set of benchmarks for measuring manufacturing performance.
- Provided confidential “scorecard” to manufacturing fabs on how they performed against anonymous others.
- Identified managerial, organizational, and technical practices underlying good (and poor) performance.
- Identified advances in techniques for defect analysis, scheduling, process development, factory organization, etc..

Industry view: Substantial positive financial impact to program participants.
Research Dissemination

- Benchmarking reports (most recent: March 2002).
- Focus study reports (more than 50 reports to date).
- Industry and conference presentations.
- Extension classes for industry managers.
- Academic research papers.
Benchmarking Participants

- 36 semiconductor manufacturing facilities studied:
  - Hyundai and Samsung (2) in Korea.
  - TSMC (2) and UMC (2) in Taiwan.
  - NEC, Oki, LSI Logic, Toshiba, Tohoku and Winbond in Japan.
  - AMD, Cypress (2), DEC, Delco, Harris, IBM, Intel, LSI Logic, Lucent, Micron, Motorola, NSC, Sony, Sony/AMD and TI (2) in USA.
  - DEC, ITT, Lucent, NSC (2) and ST Microelectronics in Europe.
- Over the 1989-2001 period and several technology classes.
Data Collection

- Mail-Out Questionnaire (MOQ).
  - 3-4 years of fab history.
    - Equipment and facilities.
    - Headcount and human resources data.
    - Production volumes, yields, cycle times, etc..

- Data entered into relational database.

- Technical metric scores computed.
  - Yield, cycle time, equipment productivity, etc..
Figure 2.16. CMOS Logic Fab Defect Density

0.7 - 0.9 micron CMOS process flows
Memory Device Defect Density (after repair)
0.33 - 0.4 micron CMOS process flows
Cycle Time Per Layer

Cycle time per layer (CTPL)

- M1
- M2
- M3
- M4
- M5
- M6
- M7

Time

Georgetown University
Washington University in St. Louis
Direct Labor Productivity

Mask layers per direct labor per day

Time

94 95 96 97 98 99 00 0
Site Visits

- Two – three day visit with a structured inquiry protocol.
  - Team of 6-8 faculty and graduate students (plus interpreter when required).
  - Tour fab for evidence of self-measurement, communication, problem-solving activity.
  - Interview cross-section of organization.
    » Managers, engineers, technicians, operators.
  - Conduct information sessions.
    » On approaches to problem areas (yield, equipment efficiency, cycle time, on-time delivery, new process introductions, etc.).
    » On problem solving resources (CIM and information systems, process control, work teams, human resources development, etc.).
Determining Best Practices

- Searched for managerial, technical or organizational practices that were correlated with metric scores.
- Typically, a good practice positively influences several metric scores.
  - Participants tended to score well or score poorly across several metrics.
- Even so, almost every participant had at least one practice that the other participants would benefit by adopting.
Summary of major findings of CSM study

- Wide variations in performance and focus.
- Key operational practices:
  - mistake-proof manufacturing,
  - “information” handling automation,
  - data collection and yield analysis integration,
  - TPM and equipment efficiency measurement,
  - equipment modification scheduling,
  - automated planning and scheduling.
- Key organizational practices:
  - team-based problem-solving approaches,
  - new process development and transfer management,
  - division of labor reductions.
Summary of major findings of CSM study

- Biggest single factor explaining performance is the focus or “religion” of organization:
  - TQM and process control.
  - Statistical analysis of yield vs. in-line data.
  - Cycle time reduction and on-time delivery.
  - TPM and equipment throughput.

- Weak performers in a given category do not have the relevant focus.
Conclusions from CSM study

- Independent of technological differences, performance differences among firms studied were substantial.
- Various metrics have different levels of importance in different product segments.
  - Fast ramp of new production processes to high-yield, high-volume manufacturing is very important.
  - Rates of improvement in yields and throughput are very important.
Conclusions from CSM study

- Fast improvement requires rapid problem identification, characterization, and solution by a large, diverse team.

- Common Themes of Successful Approaches:
  - Leadership and development of personnel.
  - Organizational participation, communication, accountability, responsibility for improvement.
  - Information strategy and analytical techniques to support improvement; not blind automation.

- Manufacturers could and did substantially improve performance by adopting “learnings” from CSM study.
Pharmaceutical Manufacturing Research Project (PMRP)

Why?
- Increasing capital intensity, product complexity, regulatory actions, product stock-outs.

Charter
- Measure manufacturing performance and regulatory outcomes.
- Benchmark pharmaceutical production across industry.
- Identify underlying determinants of performance: regulatory, operational, managerial, and organizational.
- Transfer “learning” to industry.
- Advise FDA on structure of cGMPs to facilitate performance improvement.

Funding
- Seed funding from Georgetown and Washington University.
- Seeking additional funding from foundations.
Proposed Value from PMRP

- Develop industry-standard set of benchmarks for measuring manufacturing performance.
- Provided confidential “scorecard” to plants on how they performed against anonymous others.
- Identified managerial, organizational, and technical practices underlying good (and poor) performance.
- Identify regulatory effects on manufacturing performance.
- Provide positive financial impact to program participants and provide insight to FDA on ways to structure cGMPs for the 21st Century.
PMRP Anticipated Research Dissemination

- Benchmarking reports.
- Industry, FDA, and conference presentations.
- Extension classes for industry managers.
- Academic research papers.
PMRP Data Collection

- Confidentiality agreement with FDA.
- Separate confidentiality agreements with manufacturers.
- Work with manufacturers to determine appropriate benchmarks.

- Product is the unit of analysis.
- Secure web-based questionnaire.
- Follow-up visits for random sample of participants.
- FDA actions and outcomes.
PMRP Data Analysis

- Assess manufacturing and regulatory performance as a function of managerial, technical organizational, and regulatory practices.
- Account for product, technology, and locational factors in statistical analysis.
- Identify best practices that can combine to improve manufacturing and regulatory performance.
PMRP Principal Investigators

- Jeffrey Macher, Georgetown University
  - B.S.E., Computer Engineering, University of Michigan.
  - M.B.A., Amos Tuck School of Business, Dartmouth College.
  - Ph.D., Walter A. Haas School of Business, UC Berkeley.
- Jackson Nickerson, Washington University in St. Louis
  - B.S.M.E., Worcester Polytechnic Institute.
  - M.B.A., M.S.M.E., Ph.D. UC Berkeley.
- Our combined research focuses on the intersection of organization and technology choice, business strategy, and performance.
Next Steps

- Currently in pilot phase.
  - Received cooperation of Dr. Janet Woodcock and CDER.
  - Interviewing FDA personnel.
  - Seeking level of interest and cooperation from industry.
  - Meeting with various manufacturing entities.
  - Develop internet-based survey and plant visit protocol.

- Data collection phase will begin later this year.