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Attempting to Bench Mark U.S. Pharmaceutical Manufacturing

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ABSTRACT

We summarize the findings of a recent bench marking study carried out in the pharmaceutical industry to assess and compare the manufacturing productivity of U.S., Japanese, and European manufacturers.

INTRODUCTION

In general, bench marking is understood as the process in which companies target key improvement areas within their firms, identify and study best practices by others in the same areas, and implement new processes and systems to enhance their own productivity and quality.

Though no formal industry-wide bench marking effort has been undertaken in the area of pharmaceutical manufacturing, several industry organizations and analysts report on the status of the pharmaceutical industry on a regular basis. The industry as a whole is reviewed annually by the Bureau of the Census, within the U.S. Department of Commerce. There is also a Census of Manufacturers performed every 10 years that reports on the strength of the industry in terms of company membership and certain financial indicators. The U.S. Department of Commerce also publishes an annual industrial outlook report that provides a broad year-by-year account of the industry. There are also private analyst and consulting companies that release annual reports on pharmaceuticals. Further, several trade associations exist within the pharmaceutical industry, among which the PMA is by far the most visible. As part of its high profile, the PMA publishes annual statistics regarding its member firms in two forms: the *Statistical Fact Book* (6) and the short, summary-like *Annual Survey Report* (7). It should, however, be emphasized that manufacturing performance itself, though closely related to the pharmaceutical industry's bottom line, is not an activity measured often. Typically, the industry is measured in financial terms.

In this paper, we summarize the results of a bench marking study done for the U.S. pharmaceutical manufacturing industry by the Laboratory for Research in Pharmaceutical Manufacturing within the Department of Industrial Engineering at Rutgers University (8). A

bench marking methodology requires that industry leaders be identified as bench marking partners, and their practices, processes, and systems be compared to those of the company (in our case, country) of interest. The choice of countries to be included in this comparison as bench marking partners for U.S. pharmaceutical manufacturing is based on a simple rule. The countries included are the leaders in world pharmaceutical manufacturing (in terms of dollar value of production), namely, the United States, Japan, Germany, France, Italy, and the United Kingdom. This interpretation of the term *leading countries* according to the value of pharmaceutical production could be misleading if data for a single year were taken into account. However, examining the pharmaceutical production over the past few years, these same few countries appear as leaders, with minimal changes in rankings from year to year (2,3,10). The European countries (EFPIA members) are treated as a group, in light of the European market unification. The United States and Japan, on the other hand, will be examined independently.

During the preparatory phase of this project, a number of sources for the pharmaceutical industry around the world were identified. In addition to the literature available through publishing organizations, and science and medicine libraries, there are pharmaceutical manufacturers' associations that collect and publish data on the pharmaceutical industry in their respective countries. Among the participating associations are the European Federation of Pharmaceutical Industries' Associations (Brussels, Belgium), the International Federation of Pharmaceutical Manufacturers' Associations (Zurich, Switzerland), the Syndicat National de l'Industrie Pharmaceutique (Paris, France), the Bundesverband der Pharmazeutischen Industrie, e.V. (Frankfurt, Germany), the Japan Pharmaceutical Manufacturers' Association (Tokyo, Japan), the Association of the British Pharmaceutical Industry (London, England), the Pharmaceutical Manufacturers' Association (Washington, DC), and the National Association of Pharmaceutical Manufacturers (New York).

MANUFACTURING MEASURES

The set of manufacturing measures that provides the core of the bench mark for our comparisons consists of the *percentage share of the world pharmaceutical production captured by a country,* expressed as

$$\text{Share of world pharm'l prod'n} = \frac{\text{An. pharm'l production in a country (cst \$)} \times 100}{\text{World an. pharm'l production (cst \$)}} \quad (1)$$

or the *value of production per employee in constant dollars for each country,* in the form

$$\text{Value of prod'n per employee} = \frac{\text{Total an. pharm. production in a country (cst \$)}}{\text{Number of pharm. industry employees in that country}} \quad (2)$$

These two indicators provide production-related information, in the sense that they reveal the leaders and the followers in the pharmaceutical manufacturing competitive arena. As far as other company strategic choices are concerned, one can also examine the following ratio:

$$\text{Mnfg allocation ratio} = \frac{\text{Prod'n of U.S. co's in the U.S. (cst \$)}}{\text{Prod'n of U.S. co's outside the U.S. (cst \$)}} \quad (3)$$

This ratio (examined for countries other than the United States, as well) reveals the relative importance that companies place in producing domestically and overseas. Charting the trend of this ratio on an annual basis helps track shifts in the manufacturing activity that may weaken the pharmaceutical manufacturing strength of a country.

Ratios expressing the *value of production (in constant dollars) per employee-hour*

$$\text{Value of prod'n per employee-hour (VPPEH)} = \frac{\text{Value of an. prod'n (cst \$)}}{\text{No. of employee-hrs. to produce an. output}} \quad (3)$$

or the *number of units of production per employee-hour*

$$\text{No. of units per employee-hour (NUPEH)} = \frac{\text{An. prod'n in units}}{\text{No. of employee-hrs. to produce an. output}} \quad (4)$$

are helpful in obtaining productivity-related information about companies. The concept of an *employee-hour* is more useful than that of *number of production employees,* because it keeps accounting practices from interfering with the correct measurement of these ratios. In companies, for example, where the same employees often work overtime, those ratios would be artificially high if the latter concept were used. Ratio (4) is expressed in such a way that can be used for assessing the productivity at a company, as well as on a country level. Ratio (3), on the other hand, though it does give some productivity-related information, is not strictly considered a productivity measure, because the quantity on the numerator is expressed in dollars. This ratio can be modified in order to be made even more descriptive for use at the company level. If, instead of the value of

production (in constant dollars), the cost of annual production is used, excluding the cost of raw materials used to produce that output, a better idea would be formed of how efficiently a company utilizes its manufacturing-related resources (labor, energy, equipment, etc.). This ratio is a measure of efficiency.

Quality is another area of focus for specific manufacturing measures. The *average number of rejections* (due to poor content uniformity, product appearance, and packaging) as a percentage of the total output for the product, defined as

$$\% \text{ rejections} = \frac{\text{Avg. number of rejected units per batch} \times 100}{\text{Total no. of units produced in batch}} \quad (5)$$

allows for direct comparison of levels of product quality. On the other hand, a closer look into the inspection practices followed by different companies can be obtained by measuring the *amount of visual quality inspection* performed by humans, sensors, and both humans and sensors, as a percentage of total visual inspection. This measure reveals the level of automation and redundancy built into the quality inspection process of a company.

Process reliability (4,5) is another area of emphasis for specific manufacturing measures. The *percentage of production line downtimes* (1) is defined as the percentage of time the production line is down due to equipment breakdown, delays in changeovers between products, scheduling conflicts, human or mechanical errors, or other accidents. This measure is expressed as

$$\% \text{ of prod' n line downtimes} = \frac{\text{Time the line is not operating (hrs) in a given period}}{\text{Time the line should be operating (hrs) in that period}} \quad (6)$$

Inventory is the fourth area for which specific manufacturing measures may be used. The *inventory turnover ratio* is defined as

$$\text{Inventory turnover ratio} = \frac{\text{Annual sales (\$)}}{\text{Avg. annual inventory investment (\$)}} \quad (7a)$$

This ratio is usually tied with other materials handling (functional) productivity measures (9,11). Inventory turnover can also be measured in terms of units sold and units stocked, as given by the ratio

$$\text{Inventory turnover ratio} = \frac{\text{Avg. number of units in inventory per year}}{\text{Number of units sold per year}} \quad (7b)$$

The fifth area of consideration, with respect to specific manufacturing measures, is that of the various operation times. *Average dock-to-stock time* is defined as the period of time that the raw materials spend moving from the receiving dock to storage.

Average stock-to-final-product inventory time can be defined as the time that raw materials spend moving from the raw material storage through the production line to the finished goods inventory. The period starts when the first material needed for the batch is removed from stock and ends when the final product is received at the finished storage area.

Average production lead time is the average time required from the placement of the order for the production of a batch to the time the actual production of the batch is completed.

Finally, *average flow time* is the time a unit of a batch spends in production, from the time it enters the production line to the time it exits it.

DATA GATHERING

In order to gather this information, we have designed an original questionnaire to survey pharmaceutical manufacturing companies in terms of their approach and performance in operations. The questionnaire is designed with a *single product/single facility focus,* in order to minimize aggregate reporting and confusion on the part of the respondents. The questions regarding product information reflect a single product chosen by the respondent himself or herself, whereas the questions referring to facility characteristics concern the facility in which the chosen product is being produced.

The first step in Part II of the questionnaire is to differentiate between to-order and to-stock production systems **(inventory measures)**. Even though pharmaceutical manufacturing is mainly organized as a to-stock activity, the questionnaire had to include this basic question in order to track any possible developments toward new inventory and manufacturing organizations in the industry. In this way, it is also ensured that the inventory policy of the responding facility is understood in terms of its most basic element. The two measures that follow are based on the inventory turnover ratio, in terms of dollar value and units of final product. Questions on ongoing inventory reduction programs are also included in this section. The relative importance placed by the responding manufacturer on reduction of raw material and final product inventories is explored independently for each category. A provision has been made in the available answers for justification of inventory

levels due to regulatory concerns, in case some manufacturers face such restrictions. Finally, the average inventory levels in terms of dollar value and number of units of final product are examined.

The third part of the questionnaire focuses on **product quality and process reliability** issues. As an initial indicator of the facility's commitment and emphasis on quality, a question on candidacy for quality awards opens the section. The question is very specific, in order to provide insight into the actual company attitude, and strategy if one exists, toward quality and yet avoid wish answers of the type, "Of course, we intend to apply for a quality award sometime in the future." The second issue the section covers is that of percentage of visual quality inspection performed by sensors or humans or both, in order to reveal the level of automation and redundancy built into the visual quality inspection system. The questions that follow allow for a comparison of product quality and process reliability levels, covering defect rates in manufacture and final product, and production line downtimes, according to the measures discussed above. A question on product recalls provides an additional measure of product conformance and quality. Finally, the questions on validation and GMP reviews touch upon the actual quality-related practices each company follows.

The areas of **process flexibility** and **system utilization** can be somewhat elusive in terms of measurement. At the recommendation of the executives' reviews, however, process flexibility is being assessed indirectly, through a series of questions that provide insight into how flexible the facility and its production lines are. These questions cover the number of different products and SKUs produced at the facility, the average number of workers manning each line, the average changeover times required between production runs, the number of new product introductions, and product suspensions from manufacture over the past three years. Special attention is given to the average percentage of line changes required when a new product is introduced, as an indicator of the facility's flexibility. Further questions on inventory and production times (quarantine, dock-to-stock, stock-to-final-product, lead times, and cycle times) conclude the section. The manufacturing times are clearly defined in each question, in order to avoid confusion and irrelevant replies. They are being measured separately, rather than together, under the umbrella term of *cycle time,* which is used under various definitions in industrial settings, in order to capture a rich picture of the industry's current status and to point out meaningful potential differences among the international participants of this study.

SURVEY RESULTS

More than eighteen hundred questionnaires were mailed, and an overall response rate of 8.3% (Table 1) was obtained. It was within the range of common response rates experienced in surveys performed through mail (usually 5–10%).

Overall, most of the usable responses (38) came from the American manufacturers, located in the United States and territories, including Puerto Rico. Seventeen usable responses came from Japanese pharmaceutical companies and 15 came from companies in Europe. The European companies that responded to the survey were primarily located in France, Great Britain, and a smaller number of responses came from Germany. Responses came from a wide cross section of the pharmaceutical manufacturing spectrum. A breakdown of the response sample according to the location of origin and the product type appears in Table 2. Approximately 54.3% of the total number of responses came from manufacturers located in the United States and its territories, including Puerto Rico. The remaining responses came from Japanese and European pharmaceutical producers. Approximately 13% of the responses were related to semisolid products and 17% to liquid products. The largest single

Table 1

Survey Mailing and Responses Along with the Overall and Usable Response Rates

	Questionnaires Mailed	Responses Received	% of Usable Total	% of Responses	Total
United States	1002	101	10.08	38	3.79
Japan	500	35	7.00	17	3.40
Europe	366	19	5.19	15	4.10
Total	1868	148	8.30	70	3.75

Table 2

Sample Composition in Terms of Product Type and Location of Origin (actual number of responses in parentheses; percentages may not add up to 100 due to rounding)

	% United States	% Japan	% Europe	Totals
Solid	28.95 (11)	41.18 (7)	46.67 (7)	35.71 (25)
Semisolid	13.16 (5)	11.76 (2)	13.33 (2)	12.86 (9)
Liquid	18.42 (7)	17.65 (3)	13.33 (2)	17.14 (12)
Parenteral	31.58 (12)	23.53 (4)	26.67 (4)	28.57 (20)
Other	7.89 (3)	5.88 (1)	0 (0)	5.71 (4)
All types	54.29 (38)	24.86 (17)	21.43 (15)	100 (70)

group of responses (35.7%) came from manufacturers of solid-type pharmaceuticals, and the second largest was related to parenterals (28.6%). The smallest group (5.71%) was related to the collective "other" types of products. The relative majority of Japanese and European responses was related to solid product forms (41.2% and 46.7%, respectively), possibly reflecting the fact that solid-dosage forms are considered to be well understood from a manufacturing perspective, and are also the single most popular dosage form worldwide. On the other hand, the relative majority of U.S. responses (31.6%) concerned parenteral products. Parenterals is an area that has experienced tremendous growth in recent years with the advent of biotechnology and one that poses major technical challenges in its manufacture. The U.S. pharmaceutical industry is considered to be particularly active in the development and production of these products. These facts may be among the factors contributing to the increased interest that U.S. manufacturers exhibited in the bench marking of parenteral operations.

It should also be pointed out that the distribution of the U.S. portion of the response sample roughly mirrors the market size of each regulatory category of pharmaceuticals, as brand name ethical products represent approximately 70% of the annual pharmaceutical sales in the United States (73.7% of the sample), with OTC and generic products a distant second and third, respectively. Similarly, responses for OTC and generic products from Europe and Japan were scarce, reflecting the fact that these products are not particularly prevalent in their markets, due to regulation and market practices. In terms of annual sales levels, our sample mostly comprised medium- and large-size manufacturers with sales between $10–$100 million and over $100 million, respectively.

The above multiattribute nature of our response sample reveals that the sample as a whole is well balanced with respect to the attributes of interest. Despite the fact that the resulting sets are not particularly large, when the responses are grouped together according to the above attributes, these sets exhibit many of the salient characteristics of the industry. In this sense, our response sample reflects a significant amount of the known population characteristics, as recorded in industry analyses. For example, the response sample accurately mirrors the business activity according to regulation (ethical, OTC, generic) in each location of our study. Hence, the multiattribute analysis performed on the gathered information provides a better understanding of the characteristics of our sample and indicates that it is a good structural representation of the pharmaceutical manufacturing industry. Based on this initial analysis, we further explore the information collected through the survey, according to dosage form, in order to assess the comparative status of operations in the United States, Europe, and Japan.

STATISTICAL OVERVIEW AND ANALYSIS OF THE RESULTS

The statistical analysis of the response sample is performed in terms of the four product types (solid, semisolid, liquid, parenteral, other). This choice is based on the need to compare operations of similar nature and general requirements. It would be less meaningful to perform a comparative analysis of the sample as a whole, as (1) different product types are measured in different units (e.g., liquids in units of volume, semisolids in units of mass), thus rendering many of the survey measures inappropriate for comparison purposes, and (2) manufacturing operations for different product types present very different characteristics, that, in turn, result in significant differences in manufacturing practice. It should be noted that the choice to analyze the data set with respect to product type results in five groups of responses, each of which is smaller than the

Table 3

Sample Sizes Used for Statistical Analysis, According to Product Type

	United States	Japan	Europe	Total
Solid	11	7	7	25
Semisolid	5	2	2	9
Liquid	7	3	2	12
Parenteral	12	4	4	20
Total	35	16	15	66

original group of 70 responses. Despite the statistical and validity limitations that smaller samples present in general, it was considered of primary importance to preserve the construct validity of the analysis, through classification according to product type. In order to perform the statistical analysis, all survey responses were classified according to product type and coded with the aid of a statistical software package (Statgraphics). The analysis that follows is based on the sample sizes appearing in Table 3.

Though these samples are relatively small in size, the performed analysis aims at identifying possible trends that may characterize the data, rather than at making conclusive statements about the industry as a whole. To identify possible data tendencies two types of statistical analysis are performed. The first type of analysis looks at the statistical differences among companies from the United States, Japan, and Europe. This analysis is performed on a measure-by-measure basis, in the same order in which the measures appear in the questionnaire. Information on the median, mean, standard deviation, minimum, and maximum values recorded for each country is tabulated in a concise form, for every quantitative measure.

The second type of analysis focuses on the possible correlations that can be drawn between measures. The objective of this approach is to identify areas that are likely to be interdependent. Certainly, strong correlations do not imply causal relationships between factors, but they do point to directions for further research, especially in the sense that they reflect statistical dependence between factors. Worthwhile correlation results are presented alongside with results from the first type of analysis.

Statistical analysis of solid product manufacturers is based on a sample of 25 international producers, consisting of 11 U.S., 7 Japanese, and 7 European manufacturers. For the quantitative measures of the questionnaire the statistical findings are in Table 4.

From Table 4, it appears that the Japanese respondents to the survey have been producing the solid products they reported on for a longer time (36.4 years) than either of their counterparts. By comparison, U.S. manufacturers reported an average of 14.4 years.

Tables 5 and 6 capture the performance of international manufacturers in terms of two productivity-related measures. It should be noted that the unit of measurement in this case is a single tablet or capsule, since all of the respondents included in this sample reported on either of these two dosage forms. U.S. manufacturers appear to trail in terms of unit productivity per employee-hour, with an average of 41,819 units per employee-hour, slightly less than the European average and approximately 46% of the Japanese average response. Relative to the U.S. and European responses, the Japanese responses were also clustered much closer together, and exhibited a significantly smaller standard deviation. Interestingly, the value of production per employee-hour measure demonstrates the same pattern with respect to the respondents' means, thus somewhat strengthening the finding that U.S. manufacturers trail their counterparts in terms of productivity as measured above.

Tables 7 and 8 summarize the two quantitative measures related to inventory turnover and annual inventory levels in terms of dollar value. As observed from Table 7, the U.S. manufacturers exhibited the slowest inventory turnover (8.7) among the three international counterparts. The Japanese manufacturers appear to lead the way in terms of this measure, selling an average of 21.5 times the amount of production they keep in inventory, over a one-year period. European manufacturers are a close second, with a turnover ratio of roughly 19.4, but

Table 4

Time Since Product Was First Produced at Facility (years)

Location	Average	Median	Standard	Minimum	Maximum
United States	14.4000	12.5000	5.60159	8.00000	26.0000
Japan	**36.4286**	38.0000	9.14435	21.0000	50.0000
Europe	18.1667	20.0000	7.25029	7.00000	25.0000

Table 5

Productivity 1 $\left(\frac{\textit{number of units produced per year}}{\textit{no. of employee-hours to produce these units}}\right)$

Location	Average	Median	Standard	Minimum	Maximum
United States	41819.3	37790.0	30209.4	30209.4	88050.0
Japan	77564.2	83600.0	12734.9	12734.9	89363.0
Europe	42819.0	53983.0	27316.4	27316.4	71000.0

Table 6

Productivity 2 $\left(\frac{\textit{number of units produced per year}}{\textit{no. of employee-hours to produce these units}}\right)$

Location	Average	Median	Standard	Minimum	Maximum
United States	7040.56	1500.00	9138.13	900.000	26708.0
Japan	**10831.4**	12050.0	8474.06	175.000	24400.0
Europe	8293.86	6370.00	3404.04	5850.00	13670.0

Table 7

Sales to Inventory (annual sales/annual inventory investment)

Location	Average	Median	Standard	Minimum	Maximum
United States	8.72667	7.98000	6.59312	2.20000	25.0000
Japan	**21.5000**	20.8000	6.89667	14.0000	30.0000
Europe	19.3786	23.1500	10.3237	3.00000	30.0000

Table 8

Inventory per Year (US $)

Location	Average	Median	Standard	Minimum	Maximum
United States	6.709E7	5.550E7	4.147E7	2.230E7	1.500E8
Japan	5.315E7	3.630E7	3.240E7	3.000E7	1.113E8
Europe	**2.102E7**	1.750E7	1.939E7	545455	6.081E7

with a considerably higher standard deviation than the Japanese. A box-and-whisker plot of the observations gives reason to believe that the population means for inventory turnover in the U.S. and its counterparts may, in fact, be statistically different, based on a statistical rule of thumb, presented in Hogg and Ledolter (12).

However, it is the European manufacturers who post the lowest average annual inventory levels in terms of dollar value, according to Table 8. U.S. manufacturers are on the other extreme of the spectrum, posting the highest annual inventory levels of all manufacturers, over three times as high as the Europeans. It is important to note that the U.S. sample consists of approximately half medium-size companies and half large-size companies in terms of sales, whereas all Japanese manufacturers and most of the Europeans are larger-size manufacturers (over $100 million). A possible explanation to this observation may come from a common philoso-

phy employed by many U.S. manufacturers, primarily of ethical products, who consider it imperative to be able to satisfy demand for their product at any given point in time. They consider this imperative because (1) their products may help in saving a life and thus should always be in stock to provide for emergencies, and (2) ethical products are often associated with high-profit margins, making lost sales a prohibitively expensive option for manufacturers. From this perspective, U.S. manufacturers feel somewhat justified in sustaining such relatively high inventory levels.

Tables 9, 10, and 11 summarize the questionnaire's quantitative measures related to product quality and process reliability. In terms of both finished product and in-process during manufacture rejection rates, U.S. manufacturers reported higher rates than either the Japanese or the European respondents. In terms of these manufacturing measures the Japanese producers appeared to lead the way, posting average rates three times smaller than their U.S. counterparts. European respondents also averaged rejection rates below 1%. Interestingly, there were manufacturers from both Japan and Europe that reported 0% rejection rates in their responses, whereas the single lowest rate reported by a U.S. manufacturer was 0.5%. The observation from Table 1, that Japanese manufacturers reported on products they have been producing for an average of over 35 years, may be related to the lower rejection rates they reported. Based on this plot, there is reason to believe that the population means for percent rejections in the U.S. and Japan are, in fact, statistically different. Further analysis, in terms of the correlation of the two rejection measures, reveals that they appear to be strongly correlated (correlation coefficient $R = 0.797$, significance level at 100%), indicating that statistically those manufacturers who presented lower rejection rates in terms of batches during manufacturing also fared better in terms of finished product rejections.

Table 11 summarizes the responses in terms of percent downtimes of production lines. Again the Japanese manufacturers reported the lowest average (8.5% of the time) among all survey participants. The U.S. manufacturers recorded the second best performance with an average downtime rate of 17.8%, still over two times the Japanese sample mean.

Table 9

Average Percent Rejections of Finished Product

Location	Average	Median	Standard	Minimum	Maximum
United States	2.10000	2.00000	1.29013	0.50000	4.50000
Japan	**0.6857**	1.00000	0.48452	0.00000	1.00000
Europe	0.75000	1.00000	0.72169	0.00000	2.00000

Table 10

Percent of Batch Rejections During Manufacture

Location	Average	Median	Standard	Minimum	Maximum
United States	2.08889	2.00000	1.36789	0.50000	4.50000
Japan	**0.6857**	1.00000	0.48452	0.00000	1.20000
Europe	0.83333	1.00000	0.75277	0.00000	2.00000

Table 11

Percent Downtimes

Location	Average	Median	Standard	Minimum	Maximum
United States	17.7778	15.0000	10.6393	5.00000	40.0000
Japan	**8.5000**	7.50000	6.21825	0.00000	20.0000
Europe	22.4286	12.0000	26.1334	5.00000	80.0000

Table 12

Number of Products Produced at the Facility

Location	Average	Median	Standard	Minimum	Maximum
United States	26.2000	22.5000	26.1865	2.00000	92.0000
Japan	**97.714**	20.0000	200.272	3.00000	550.000
Europe	37.5714	34.0000	34.6788	10.0000	110.000

Process flexibility and utilization metrics for solids manufacturers are summarized in Tables 12 through 28. It was found that U.S. manufacturers produced on the average fewer products in their surveyed facilities than either the Europeans or the Japanese. This observation alone could imply that U.S. facilities are better focused than others, specializing in the production of a few products that are well understood and controlled from a production perspective. However, it could also be argued that the Japanese facilities are larger in size or better organized to handle more products within the same plant. U.S. manufacturers were also found to produce more SKUs on the average in their facilities (Table 13) than the Japanese, but fewer than the European manufacturers. A higher number of SKUs is generally associated with the requirement for more changeovers between SKU production runs and a better responsiveness to market needs.

Additionally, U.S. manufacturers were found to produce on the average the highest number of different products on a single production line compared to their international counterparts. Again, this may be an indication of line flexibility at the possible cost of higher changeover frequencies. Japanese manufacturers, on the contrary, were found to run the smallest number of products or SKUs (Tables 14 and 15) on a given produc-

Table 13

Number of SKUs Produced at the Facility

Location	Average	Median	Standard	Minimum	Maximum
United States	103.400	74.0000	136.300	7.00000	468.000
Japan	85.0000	75.0000	62.7694	10.0000	200.000
Europe	**128.00**	86.0000	86.2806	40.0000	260.000

Table 14

Maximum Number of Products Produced per Line

Location	Average	Median	Standard	Minimum	Maximum
United States	**9.5000**	8.50000	6.86780	2.00000	25.0000
Japan	7.00000	6.00000	5.79655	1.00000	18.0000
Europe	7.28571	6.00000	3.54562	4.00000	15.0000

Table 15

Maximum Number of SKUs Produced per Line

Location	Average	Median	Standard	Minimum	Maximum
United States	32.6667	20.0000	30.8180	6.00000	100.000
Japan	27.6667	29.0000	18.5652	4.00000	54.0000
Europe	**35.571**	30.0000	29.1768	12.0000	100.000

Table 16

Changeover Times (hours)

Location	Average	Median	Standard	Minimum	Maximum
United States	4.75000	4.00000	1.95256	2.50000	8.00000
Japan	**2.0833**	2.25000	1.39344	0.50000	4.00000
Europe	2.39286	2.50000	0.99851	0.75000	4.00000

tion line. It may be that Japanese manufacturers consider focus to be more important on the production line level than on the facility level.

In terms of changeover times between SKUs of the same product (Table 16), the sample mean for U.S. companies was found to be more than twice those of the European and Japanese manufacturers. Changeover times, as described above, ran as high as 8 hours for U.S. producers but only up to 4 hours for either of their international counterparts.

U.S. manufacturers of solid products reported an average of 9 workers per production line, similar to the 9.5 average reported by Japanese producers, but higher than the 5.9 average reported by European pharmaceutical makers. Lower numbers of workers per line could indicate leaner operations or more automated processes (Table 17).

U.S. manufacturers reported the lowest number of dedicated lines at their surveyed facilities (Table 18). Dedicated production lines are designed and utilized exclusively for the production of a single product. This finding, together with the observation that U.S. manufacturers run the highest average number of products on a single production line, may support the conjecture that line utilization is a major consideration for production management in the United States, whereas other considerations take priority in Europe or Japan. This observation also supports the notion that Japanese manufacturers may be more concerned with the production line focus, rather than plant focus, as a dedicated line is a line completely focused to the production of one product.

Tables 19 and 20 are to be considered simultaneously, because together they reflect the average net burden on facilities in terms of products added to the facility over the past three years. Net burden is the difference between the number of products introduced and the number of products discontinued over the past three years. It can be observed that the average net burden on U.S. facilities from our survey was significantly higher than that for the Japanese or the European respondents. This observation could also provide a basis for justification for the higher average percentage of changes required in U.S. production lines associated with the introduction of new products (Table 21). U.S. manufacturers report an average of 27% of changes re-

Table 17

Number of Workers per Line

Location	Average	Median	Standard	Minimum	Maximum
United States	9.10000	9.50000	2.28279	6.00000	12.0000
Japan	9.50000	10.0000	2.66458	5.00000	12.0000
Europe	**5.8571**	6.00000	2.79455	2.00000	10.0000

Table 18

Number of Dedicated Lines at the Facility

Location	Average	Median	Standard	Minimum	Maximum
United States	3.20000	2.00000	3.42540	0.00000	12.0000
Japan	6.66667	6.50000	3.50238	3.00000	12.0000
Europe	**9.5714**	9.00000	5.38074	4.00000	20.0000

Table 19

Number of New Products (past 3 years)

Location	Average	Median	Standard	Minimum	Maximum
United States	**6.4000**	5.50000	7.70570	0.00000	25.0000
Japan	3.85714	3.00000	3.02372	1.00000	10.0000
Europe	5.57143	5.00000	5.09435	1.00000	15.0000

Table 20

Number of Discontinued Products (past 3 years)

Location	Average	Median	Standard	Minimum	Maximum
United States	2.60000	1.50000	3.43835	0.00000	10.0000
Japan	1.00000	0.00000	1.82574	0.00000	5.00000
Europe	**4.4285**	3.00000	4.07665	0.00000	9.00000

Table 21

Percent Changes Required per Line for New Product Introduction

Location	Average	Median	Standard	Minimum	Maximum
United States	27.1429	20.0000	17.0434	5.00000	55.0000
Japan	**12.083**	11.2500	5.10310	5.00000	20.0000
Europe	12.5000	12.5000	5.24404	5.00000	20.0000

quired for their production lines when new products are introduced, compared to approximately 12% for the Japanese and European pharmaceutical makers.

Manufacturing times are additional metrics of the performance of production systems. In terms of all manufacturing times surveyed (Tables 22–26), the U.S. respondents reported averages higher than their counterparts. It appears to take U.S. producers an average of 15 months to make the manufacturing arrangements and produce the first good unit of finished product, from the time the facility is notified of its commissioning to the production of this new product. It should be noted that this is purely a manufacturing-related time, as time required for approval is not included in its definition. It is typical in the pharmaceutical industry to adjust the production line for the new product in advance of the approval date, so that sales of the new product can commence as soon as the approval is obtained (lost sales are undesirable in the industry). Some would argue, however, that manufacturers still have to coordinate their manufacturing activity with the approval process, and consequently, U.S. producers are justified to post a longer new product introduction time, because they are faced with longer approval times. True as this may be, longer new product introduction times may be more costly both in the short and the long term (resources committed to project over a longer period, and longer introduction times may hamper market responsiveness of

Table 22

Time to New Products (months)

Location	Average	Median	Standard	Minimum	Maximum
United States	15.6667	12.0000	7.00000	6.00000	24.0000
Japan	11.1429	12.0000	4.74091	6.00000	18.0000
Europe	**9.5000**	8.00000	4.27200	6.00000	18.0000

Table 23

Quarantine (hours)

Location	Average	Median	Standard	Minimum	Maximum
United States	368.727	336.000	217.931	96.0000	720.000
Japan	**96.000**	96.0000	55.4256	24.0000	168.000
Europe	185.143	120.000	143.140	48.0000	336.000

Table 24

Stock-to-Finished-Product Inventory Time (days)

Location	Average	Median	Standard	Minimum	Maximum
United States	46.6364	40.0000	49.7358	4.00000	180.000
Japan	**8.7142**	7.00000	5.55921	5.00000	20.0000
Europe	11.5714	7.00000	9.62388	3.00000	24.0000

Table 25

Lead Time (days)

Location	Average	Median	Standard	Minimum	Maximum
United States	63.0909	75.0000	29.9682	20.0000	90.0000
Japan	36.2857	45.0000	22.4775	7.00000	60.0000
Europe	**21.1429**	30.0000	13.1963	2.00000	35.0000

Table 26

Flow Time (days)

Location	Average	Median	Standard	Minimum	Maximum
United States	32.8636	30.0000	34.6079	0.50000	120.000
Japan	**1.5714**	1.00000	1.13389	1.00000	4.00000
Europe	9.00000	3.00000	9.03696	1.00000	21.0000

the company). Observed European performance indicates that new product introduction times closer to averages around 9.5 months may be feasible for other manufacturers, as well.

In terms of quarantine times (Table 23), Japan leads the way, with a sample mean as short as 96 hours. Interestingly, 96 hours was the minimum response coming from a U.S. manufacturer, who collectively posted a mean of over 368 hours. The amount of time raw materials remain in quarantine obviously reflects an opportunity cost for the company, as quarantine is not a value-added activity. Similarly, U.S. manufacturers post higher averages for stock-to-inventory times (Table 24), which also involve the nonvalue-added activities of transferring material from stock to the production line, and from the production line to the finished product inventory storage. The U.S. average stock-to-finished-product inventory time is more than five times that recorded by the Japanese manufacturers of our sample, and four times higher than that of the Europeans. Based on this plot, there is reason to believe that the population mean for this measure is statistically higher in the United States than in either Europe or Japan. Stock-to-inventory time exhibits a strong positive correlation with changeover times, as presented above (correlation coefficient $R = 0.753$, significance level 100%). A relation

between the two measures indeed appears plausible, given that higher changeover times would require materials to spend a longer time in the system.

Lead times faced by U.S. manufacturers appear to be two to three times those faced by their Japanese and European competitors, respectively. It is important to note that some international manufacturers posted lead times as low as two days—a time so short that would suggest their systems are extremely well understood and tightly run. It could additionally suggest that these companies have very close ties with their raw materials suppliers. Lead times were found to be negatively correlated with the number of dedicated lines in a facility ($R = -0.526$, significance level 99.88%), possibly because fewer dedicated lines would imply more than one product per production line. This in turn could mean more product and SKU changeovers before a given order could be processed (and changeovers are costly in terms of time) and more than one production schedule to be coordinated before the order could be filled.

Flow times, reflecting the amount of time the product spends in actual production, are also much higher on the average for U.S. manufacturers than for their competitors. Interestingly, the minimum flow time reported in our sample came from a manufacturer in the United States, and merely amounted to half a day. Longer flow times are associated with longer stock-to-inventory times ($R = 0.953$, significance level 100%) and longer quarantine times, as well ($R = 0.661$, significance level 99.97%).

The average reported profit margins for solids manufacturers in our sample were approximately 6.7% in the United States, 6.2% in Japan, and 13.5% in Europe. It should be noted, however, that the statistics appearing below are based on a sample size of 21 respondents (8 U.S., 7 Japan, 6 Europe), as some manufacturers chose not to report the levels of their profit margins (Table 27).

Finally, it was observed that employees of U.S. pharmaceutical manufacturers stayed with the facility for an average of approximately 10 years, compared to 14 years for employees of European manufacturers and 24 years for Japanese producers (Table 28). This hints to a longer-term employer-employee relationship being shaped at Japanese production facilities, and possibly to a higher loyalty of Japanese employees to their employers. Advantages and disadvantages associated with employee loyalty are well documented in organizational literature.

As far as qualitative metrics are concerned, the following patterns in terms of manufacturing practices were observed. Fifty percent of the U.S. manufacturers reported that they were actively pursuing an inventory reduction program, compared to 57.1% of the Japanese manufacturers and 100% of the Europeans. Of those who pursued such programs, the ones from the United States appeared concerned equally with finished product and raw materials inventories, whereas the ones from Japan appeared primarily concerned with raw materials inventories. European manufacturers appeared to place

Table 27

Profit Margin (percent)

Location	Average	Median	Standard	Minimum	Maximum
United States	6.73125	3.70000	6.54702	2.50000	20.9000
Japan	6.17143	7.00000	3.13354	2.50000	11.7000
Europe	**13.5333**	13.6500	3.56071	9.60000	19.3000

Table 28

Time Employees Stay with the Facility (years)

Location	Average	Median	Standard	Minimum	Maximum
United States	10.6667	10.0000	1.93649	8.00000	15.0000
Japan	**24.285**	25.0000	8.86405	10.0000	35.0000
Europe	14.0000	15.0000	4.18330	10.0000	20.0000

primary importance on the reduction of finished products, and secondary, but still significant, importance on raw materials inventories. In the United States, 50% of the time the inventory reduction program initiator was at the corporate level of the company (16.7% at the plant and 33.3% at the department level). In Japan, such programs were initiated 40% of the time at the corporate level (20% at the plant and 40% at the department). By comparison, in Europe, corporate initiative accounted for only 20% of the inventory reduction programs in place (with 40% attributed to plant initiative and 40% to department initiative).

In terms of quality and process reliability related metrics, only one manufacturer responded from a facility that had applied or would be a candidate for a quality award, and this manufacturer was from the United States. Forty percent of U.S. respondents have a formal internal recognition process for product quality, compared to 83.3% of the Japanese and 80% of the Europeans. Formal recognition programs were found to be negatively correlated with the percentage of batch rejections during manufacture (R = -0.568, significance level 99.28%), but surprisingly not correlated with the percentage of finished product rejections recorded by manufacturers from our sample. Eighty percent of the U.S. manufacturers had less than one product recall in the last three years, compared to 85.7% of the respondents from Japan and 85.7% of those from Europe. Only half of the U.S. manufacturers responded that they have a GMP review committee, compared to all of the producers from Japan and Europe. In approximately half of the U.S. and Japanese facilities, and in one-quarter of the European facilities that employ such committees, review of GMP practices takes place four or more times a year. It was found that higher GMP review frequency is negatively correlated with the percentage of finished product rejections (R = -0.538, significance level 98.26%).

In terms of other practices, Japanese and European manufacturers appear to follow organizational approaches that empower individuals at their facilities, to the extent that in all of their responses they indicated that the first employee who notices a problem with the production line is responsible for stopping the line. By comparison, 50% of the U.S. manufacturers gave the above response, and another 50% responded that production line shutdown is the responsibility of the line foreman. Employee empowerment was found to be strongly correlated with lower rejection rates, both in terms of batches during manufacture (R = -0.666, significance level 99.96%) and finished products (R = -0.7017, significance level 99.99%). Employee empowerment was also found to be correlated with higher levels of employee training (R = 0.614, significance level 99.86%), indicating that it may be more sensible to empower better-trained workers. Forty percent of U.S. companies train their production line employees on the job, 20% use a formal training program, and another 40% provide training both on the line and formally. Japanese manufacturers appear to favor the combination of on-the-job and formal training (71.4% of responses) as do Europeans, although to a lesser extent (57.1% of their responses). Employee teams appear to be most popular in Japan, where 85.7% of the surveyed manufacturers reported that their employees are formed in self-managed teams, compared to 30% in the United States and 14.3% in Europe. Respondents whose employees are formed in such teams agree unanimously that teams have proved to be of value to their operations.

Fifty percent of U.S. manufacturers have used some form of competitive bench marking at least once in the past, compared to 100% of the Japanese and 85.7% of the European producers. Over 50% of the all the respondents agree that bench marking is somewhat or very useful, but approximately 40% of the Americans and Europeans and 28% of the Japanese consider the methodology impractical. Manufacturing cost-reduction programs appear to also be popular among respondents. Of the U.S. manufacturers, 90% report they have some type of a cost-reduction program (30% formal, 60% informal), of the Japanese manufacturers 100% (50% formal, 50% informal), and of the Europeans 100% (85.7% formal, 14.3% informal). Formal cost-reduction programs were found to be correlated with lower stock-to-inventory times in solids (R = -0.643, significance level 99.91%), lower finished product rejection rates (R = -0.632, significance level 99.88%) and, to a slightly lesser extent, lower batch rejection rates (R = -0.586, significance level 99.67%). According to the sample's responses, these programs result in a range of savings from 0.4% to 1.0% of sales for U.S. producers, 1.5% for Japanese, and 0.5% to 1.5% for Europeans.

All of the solid product manufacturers that responded to the survey use MRP systems in their operations. Forty percent of U.S. manufacturers employ JIT philosophy in certain aspects of their operations (most com-

monly in packaging), compared to 28.6% of the Japanese and 42.9% of the Europeans. Total quality management (TQM) was reportedly implemented by 40% of the U.S. manufacturers, 42.9% of the Japanese, and 57.1% of the European producers of solid pharmaceutical product types.

CONCLUSIONS

Based on the findings discussed earlier, there is indication that the U.S. pharmaceutical industry is outperformed by at least one of its international counterparts according to most of the measures included in this study. Specifically, there is some evidence suggesting that U.S. pharmaceutical productivity is below that of its Japanese counterparts, both in terms of units produced per employee-hour and in terms of sales realized per employee-hour. There is also indication that the U.S. pharmaceutical manufacturing industry trails both its European and Japanese counterparts in terms of inventory turnover, and maintains approximately twice as high average annual inventory levels than the European industry. As far as product quality and system reliability are concerned, U.S. manufacturers appear to have rejection rates in batches during manufacture, as well as finished product, that are almost twice as high as those of either of their international competitors. On the other hand, there is some indication that the U.S. industry's production line downtime average may be comparable to that of non-U.S. industries. In terms of system flexibility and utilization, it appears to take U.S. manufacturers approximately 30–40% longer than their international counterparts to introduce new products. New product introduction also requires more changes in the existing production systems of U.S. manufacturers compared to their international counterparts. On the other hand, it appears that the maximum number of products run on a single production line is not significantly different among the three locations. U.S. manufacturers appear to trail their international counterparts in terms of manufacturing times, as follows: In achieving short manufacturing lead times the Europeans are ahead (by over 25%) of the U.S. and Japanese manufacturers. In average stock-to-finished product inventory times, as well as in average flow times, the U.S. trails both Japan and Europe. It also appears that the U.S. manufacturers have on the average (two to three times) longer quarantine times than the Japanese.

In terms of manufacturing practices, U.S. manufacturers appear to be pursuing inventory reduction programs almost as frequently as their Japanese counterparts, but significantly less frequently than the Europeans. U.S. manufacturers appear to have fewer formal programs in place, in the areas of quality recognition, or manufacturing cost reduction. By comparison with their international counterparts, half as many U.S. manufacturers empower their production employees to the extent of shutting down the production line. MRP technology appears to be used equally often in the United States as abroad, as is TQM philosophy, and JIT principles that appear to find applications mostly in packaging lines.

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